PONTIFICIA
ACADEMIA
SCIENTIARVM

Acta

20

Scientific Insights into the Evolution of the Universe and of Life

Edited by
Werner Arber
Nicola Cabibbo
Marcelo Sánchez Sorondo

The Proceedings of the Plenary Session
31 October - 4 November 2008

VATICAN CITY
2009

SCIENTIFIC INSIGHTS INTO THE EVOLUTION OF THE UNIVERSE AND OF LIFE

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EX AEDIBVS ACADEMICIS IN CIVITATE VATICANA

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The opinions expressed with absolute freedom during the presentation of the papers of this meeting, although published by the Academy, represent only the points of view of the participants and not those of the Academy.

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PONTIFICIA ACADEMIA SCIENTIARVM
VATICAN CITY

His Holiness Pope Benedict XVI

The Participants of the Plenary Session of 31 October-4 November 2008

Papal Audience of 31 October 2008

The Participants of the Plenary Session of 31 October-4 November 2008

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INTRODUCTION

Research into the origins and evolution of the universe, of matter and of life belongs to the focal topics of the natural sciences. The Pontifical Academy of Sciences has repeatedly paid attention to these questions both in plenary sessions and in specialised meetings. In recent years relevant basic scientific knowledge has been considerably enriched, in particular by the introduction of novel and powerful research strategies. Cosmic investigations can reach ever greater distances, while particle physics and the nanosciences allow scientists to explore structures of ever smaller dimensions. The results of these largely interdisciplinary studies considerably enrich our knowledge about natural reality and they also raise new questions. These concern, for example, a postulated multiverse or dark matter and, more generally, cosmic evolution. In the life sciences more precise structural knowledge on genetic information and on gene products provides insights not only into functional characteristics but also into molecular mechanisms that contribute to the occasional generation of genetic variants – the drivers of biological evolution.

By definition, evolution implies a changing reality. This is what the sciences have postulated as holding both for the inanimate cosmos and for the living world. Ever more powerful research strategies continue to strengthen the validity of these postulates.

The Council of the Pontifical Academy invites the Academicians to present in the forthcoming Plenary Session any scientific contributions that may validate or falsify evolutionary theories and can provide a deeper insight into the evolutionary processes of the living and of the non-living world. This might allow our Academy to update its own knowledge base and to transmit this knowledge to human society to bring its science-based worldview up to date. In addition to traditional wisdom, religious beliefs and educational values, scientific knowledge forms an essential part of the guiding knowledge that we need to make individual and socio-political decisions.

In these scientific debates the Council of the Academy proposes to focus more on the evolutionary process as such than on the postulated origins of things which, however, shall also be discussed. It is our intention to strengthen our knowledge on the dynamics of evolution in its historical dimensions and also to provide prospective views on upcoming developments into the distant future. Contributions on the specific impact that human activities may have on evolutionary processes will also be welcome. The Council also expects to be able to draw from the Plenary Session conclusions that are of relevance to the subject of the creation of something out of nothing and the various forms – also of an evolutionary kind – in which this participation in being, caused by the Being in essence, is realised. Indeed, for Thomas Aquinas, from a philosophical perspective, everything that is by participation is (or is caused) by the Being in essence. Thus not even the evolutionary processes of the universe and of life can be excluded from emanation from the universal principle of being.

Werner Arber & Nicola Cabibbo

PROGRAMME

FRIDAY, 31 OCTOBER 2008

Chair: Prof. Nicola Cabibbo

9:00 *Welcome*
Prof. Nicola Cabibbo, President of the Pontifical Academy of Sciences

9:05 *Commemorations*
Giampietro Puppi (N. Cabibbo); Te-Tzu Chang (P.H. Raven); Kai Siegbahn (M.G.K. Menon); Carlo Enrico di Rovasenda (G. Cottier); Joshua Lederberg (N.M. Le Douarin)

9:25 *Self-Presentation of New Members*
Aaron J. Ciechanover; Stanislas Dehaene; José G. Funes; Takashi Gojobori; Krishnaswamy Kasturirangan; Klaus von Klitzing; Yuan-Tseh Lee; Cesare Pasini; Ignacio Rodríguez-Iturbe; Govind Swarup; Edward Witten

10:30 Coffee Break

11:30 Audience with His Holiness Benedict XVI

12:30 Lunch at the Casina Pio IV

15:00 *The Subject of the Meeting*
Prof. Werner Arber, Coordinator of the Meeting and PAS Academician

15:15 H.Em. Cardinal Christoph Schönborn
The Reflections of Joseph Ratzinger Pope Benedict XVI on Evolution
Discussion

16:15 Coffee Break

SESSION I
Insights Into the Evolution of the Universe
Chair: Prof. William D. Phillips

16:40 Prof. Martin J. Rees
From a Simple Big Bang To Our Complex Cosmos
Discussion

17:20 Prof. Govind Swarup
Scientific Quest into Evolution of Life in the Universe
Discussion

18:00 Prof. Stephen W. Hawking
The Origin of the Universe
Discussion

18:40 General Discussion

19:10 Dinner at the Casina Pio IV

SATURDAY, 1 NOVEMBER 2008

Chair: Prof. M. Govind K. Menon

9:00 Prof. Vera Rubin
What We Know, and What We Don't Know, About the Universe
Discussion

9:40 Prof. José G. Funes
Galaxy Evolution
Discussion

10:20 Prof. Antonino Zichichi
Rigorous Logic in the Theory of Evolution
Discussion

11:00 Coffee Break

SESSION II
Insights Into the Evolution of Life
Chair: Prof. Nicole M. Le Douarin

11:30 Prof. Albert Eschenmoser
The Search for the Chemistry of Life's Origin
Discussion

12:10 Prof. John Abelson
The Birth of Oxygen
Discussion

12:50 Prof. Marshall W. Nirenberg
The Genetic Code and Evolution
Discussion

13:20 Lunch at the Casina Pio IV

Chair: Prof. Wolf J. Singer

15:00 Prof. Giorgio Bernardi
The Role of Chance in Evolution
Discussion

15:40 Prof. Rafael Vicuña
Bacterial Evolution: Random or Selective?
Discussion

16:20 Prof. Werner Arber
From Microbial Genetics to Molecular Darwinism and Beyond
Discussion

17:00 Coffee Break

SESSION III
Insights Into Human Evolution

17:30 Prof. Luigi L. Cavalli-Sforza
Why it is Useful to Know the Modern Theory of Evolution
Discussion

18:10 Prof. Christian de Duve
The Future of Life
Discussion

18:50 Departure from the Casina Pio IV to the Embassy of Brazil (Palazzo Pamphilj, piazza Navona) for the Opera in honour of the Pontifical Academy of Sciences

19:00 Avant-première of the opera 'Carlos Chagas' by Silvio Barbato

20:30 Dinner Buffet at the Embassy

21:30 Departure from the Embassy to the Hotels (Domus Sanctae Marthae and Columbus)

SUNDAY, 2 NOVEMBER 2008

8:30 Departure from Domus Sanctae Marthae to visit the Papal Villa at Castel Gandolfo

10:00 Visit to the Papal Villa

11:00 Presentation of the Pius XI Medal

13:00 Lunch at the Papal Villa

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17:30 Holy Mass at the Casina Pio IV

18:30 Dinner at the Casina Pio IV

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Chair: Prof. Werner Arber

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9:40 Prof. Wolf J. Singer
Genetic and Epigenetic Shaping of Cognition – Prerequisites of Cultural Evolution
Discussion

10:20 Prof. Francis S. Collins
The Language of God
Discussion

11:00 Coffee Break

11:30 Prof. Yves Coppens
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12:10 Prof. Fiorenzo Facchini
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15:00 Prof. Stanislas Dehaene
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16:10 Fr. Prof. Jean-Michel Maldamé
Evolution and Creation: How to Terminate with a False Opposition Between Chance and Creation an Epistemological Note
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16:50 Prof. Ulrich Lüke
The Human Being – God's Plan or Just Sheer Chance?
Discussion

17:30 Coffee Break

18:00 Prof. Gereon Wolters
The Catholic Church and Evolutionary Theory: A Conflict Model
Discussion

18:40 H.Em. Cardinal Georges Cottier
La doctrine philosophique et théologique de la Création chez Thomas D'Aquin
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Chair: Prof. Jürgen Mittelstrass

10:30 Fr. Prof. Stanley L. Jaki
Evolution as Science and Ideology
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11:00 Prof. Ingo Potrykus
Plant Breeding as an Example of 'Engineered' Evolution
Discussion

11:30 Prof. Antonio M. Battro
Digital Intelligence: The Evolution of a New Human Capacity
Discussion

12:00 Prof. Pierre J. Léna
The Teaching of Evolution
Discussion

12:30 Prof. Maxine F. Singer
The Latest Challenge to Evolution: Intelligent Design
Discussion

13:00 Final General Discussion

13:30 Lunch at the Casina Pio IV

15:30 Closed Session for Academicians

18:30 Dinner at the Casina Pio IV

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ADDRESS OF THE PRESIDENT TO THE HOLY FATHER

Holy Father,

We are very grateful to you for this audience on the opening day of the Plenary Session of the Pontifical Academy of Sciences which has as its subject 'Scientific Insights into the Evolution of the Universe and of Life'. It is a great honour for us today to introduce to you the eight new members of the Academy.

The Academy has decided to devote this Plenary Session to the study of evolution, a concept that has enhanced our understanding not only of life but also of the past history of the universe.

The investigations of the particles that are the ultimate building blocks of all kinds of matter, and improved observational techniques, have in recent years enormously extended our understanding of the universe. Cosmologists are now starting to peer beyond the limits posed by the Big Bang. The results of these largely interdisciplinary scientific studies considerably enrich our knowledge about natural reality and they also raise new questions. These concern, for example, a postulated 'multiverse', or the nature of dark matter, or the dark energy that causes the recently discovered acceleration in the expansion of the universe. We look forward to the forthcoming results of the Large Hadron Collider in the Geneva Laboratories of CERN which may clarify some of these new issues.

In the life sciences more precise knowledge of the information contained in genetic material, and the recent advances in analysing and comparing the genomes of different species, have enhanced our understanding of the processes that underlie the evolution of life. In this case, as well, many questions remain open, and these, together with those mentioned above, will be discussed during our meeting.

In this scientific debate the Academy proposes to focus more on the evolutionary process as such than on the transcendent origins of beings, or the creation of the world, which will, however, also be indirectly discussed.

We are conscious that the subject of this meeting is one that you have often addressed in your teaching, and Cardinal Schönborn kindly agreed to present to the Academy your reflections on this important subject. We await your words with great interest and they will certainly illuminate our discussions.

Aware of the many duties that your high office places upon you, we may think here of the recent Synod of Bishops, we are especially grateful to you for granting this audience to us today.

Nicola Cabibbo

ADDRESS OF HIS HOLINESS BENEDICT XVI TO THE MEMBERS OF THE PONTIFICAL ACADEMY OF SCIENCES

Friday, 31 October 2008

Distinguished Ladies and Gentlemen,

I am happy to greet you, the members of the Pontifical Academy of Sciences, on the occasion of your Plenary Assembly, and I thank Professor Nicola Cabibbo for the words he has kindly addressed to me on your behalf.

In choosing the topic *Scientific Insight into the Evolution of the Universe and of Life*, you seek to focus on an area of enquiry which elicits much interest. In fact, many of our contemporaries today wish to reflect upon the ultimate origin of beings, their cause and their end, and the meaning of human history and the universe.

In this context, questions concerning the relationship between science's reading of the world and the reading offered by Christian Revelation naturally arise. My predecessors Pope Pius XII and Pope John Paul II noted that there is no opposition between faith's understanding of creation and the evidence of the empirical sciences. Philosophy in its early stages had proposed images to explain the origin of the cosmos on the basis of one or more elements of the material world. This genesis was not seen as a creation, but rather a mutation or transformation; it involved a somewhat horizontal interpretation of the origin of the world. A decisive advance in understanding the origin of the cosmos was the consideration of being *qua* being and the concern of metaphysics with the most basic question of the first or transcendent origin of participated being. In order to develop and evolve, the world must first *be*, and thus have come from nothing into being. It must be created, in other words, by the first Being who is such by essence.

To state that the foundation of the cosmos and its developments is the provident wisdom of the Creator is not to say that creation has only to do with the beginning of the history of the world and of life. It implies, rather, that the Creator founds these developments and supports them, underpins them and sustains them continuously. Thomas Aquinas taught that the notion of creation must transcend the horizontal origin of the unfolding of events, which is history, and consequently all our purely naturalistic ways of thinking and speaking about the evolution of the world. Thomas observed that creation is neither a movement nor a mutation. It is instead the foundational and continuing relationship that links the creature to the Creator, for he is the cause of every being and all becoming (cf. *Summa Theologiae*, I, q. 45, a. 3).

To 'evolve' literally means 'to unroll a scroll', that is, to read a book. The imagery of nature as a book has its roots in Christianity and has been held dear by many scientists. Galileo saw nature as a book whose author is God in the same way that Scripture has God as its author. It is a book whose history, whose evolution, whose 'writing' and meaning, we 'read' according to the different approaches of the sciences, while all the time presupposing the foundational presence of the author who has wished to reveal himself therein. This image also helps us to understand that the world, far from originating out of chaos, resembles an ordered book; it is a cosmos. Notwithstanding elements of the irrational, chaotic and the destructive in the long processes of change in the cosmos, matter as such is 'legible'. It has an inbuilt 'mathematics'. The human mind therefore can engage not only in a 'cosmography' studying measurable phenomena but also in a 'cosmology' discerning the visible inner logic of the cosmos. We may not at first be able to see the harmony both of the whole and of the relations of the individual parts, or their relationship to the whole. Yet, there always remains a broad range of intelligible events, and the process is rational in that it reveals an order of evident correspondences and undeniable finalities: in the inorganic world, between microstructure and macrostructure; in the organic and animal world, between structure and function; and in the spiritual world, between knowledge of the truth and the aspiration to freedom. Experimental and philosophical inquiry gradually discovers these orders; it perceives them working to maintain themselves in being, defending themselves against imbalances, and overcoming obstacles. And thanks to the natural sciences we have greatly increased our understanding of the uniqueness of humanity's place in the cosmos.

The distinction between a simple living being and a spiritual being that is *capax Dei,* points to the existence of the intellective soul of a free transcendent subject. Thus the Magisterium of the Church has constantly affirmed that 'every spiritual soul is created immediately by God – it is not 'produced' by the parents – and also that it is immortal' (*Catechism of the Catholic Church,* 366). This points to the distinctiveness of anthropology, and invites exploration of it by modern thought.

Distinguished Academicians, I wish to conclude by recalling the words addressed to you by my predecessor Pope John Paul II in November 2003: 'scientific truth, which is itself a participation in divine Truth, can help philosophy and theology to understand ever more fully the human person and God's Revelation about man, a Revelation that is completed and perfected in Jesus Christ. For this important mutual enrichment in the search for the truth and the benefit of mankind, I am, with the whole Church, profoundly grateful'.

Upon you and your families, and all those associated with the work of the Pontifical Academy of Sciences, I cordially invoke God's blessings of wisdom and peace.

COMMEMORATIONS OF DECEASED ACADEMICIANS

GIAMPIETRO PUPPI († 25.XII.06)

Giampietro Puppi was one of the great masters of Italian Physics after the second world war, that had led to the dispersal of the great schools in Rome, Florence and Padua. In Padua he had been a student of Bruno Rossi and Giancarlo Wick. He became Professor of Theoretical Physics in Naples in 1950 and from 1951 in Bologna where he remained, except for short periods in Padua and in Venice, until his retirement in 1989.

Puppi will be remembered in the history of physics for his fundamental contribution to the theory of weak interactions. Puppi was the first to recognise that the beta radioactivity theorised by Fermi in 1934, the nuclear capture of muons, and the decay of muons were effects of a single interaction that acts equally in the three processes – the Puppi triangle. Puppi can thus be considered as the founder of weak interaction theory, and his work is a major contribution to the modern unified theories of particle interactions.

Giampietro Puppi had a leading role in the lauching of modern Italian physics. Turning his interest from theoretical to experimental physics he obtained significant results such as the first proof of parity violation in the decay of strange particles. He had major roles in the birth of Italian radioastronomy, nuclear energy research and space research. He also played a major role in the launching of environmental and earth studies where he realised important collaborations with Italian industry.

The list of the many important positions he covered in many European and Italian institutions, that range from the CERN laboratories to the European and Italian space agencies, to the Italian CNR and in many Italian industries, some of which he founded, and of the many honors he received, is too long to recall here. I would however like to remember his unflagging dedication to our Academy where he served for many years as a member of the council, until the very last years of his life, when failing health forced him to retire. His wisdom and generosity will not be forgotten.

Nicola Cabibbo

Te-Tzu Chang († 24.III.06)

Over the span of his highly productive life, Te-Tzu Chang made major contributions to the alleviation of hunger through the development of improved varieties of rice, the most important food crop in the world. His contributions led to the development of a substantially elevated food supply and thus to the improved well-being of hundreds of millions of people throughout the world. With almost half of the world's people depending on rice as their major source of food, the great importance of Dr. Chang's efforts is easy to understand.

For 30 years, Dr. Chang was principal geneticist and head of the International Rice Germplasm Center at the International Rice Research Institute (IRRI) in the Philippines. His research and the research of the unit he headed on evolution and variation in rice led to advances in the productivity of a number of strains and their resistance to disease. His development of a new variety of dwarf rice, introduced in 1962, let to the possibility of producing an extensive series of semi-dwarf, sturdy rice varieties that greatly improved rice productivity in southern China and in tropical areas throughout the world. He played a major role in the development of the institutions and programs that we count on today to protect the overall diversity of cultivated rice and its wild relatives, with his institute alone arranging for the collection of some 44,000 samples in Asia and Africa, now conserved in IRRI for the benefit of the entire world – an incredible asset for improving the characteristics of cultivated rice varieties for the future. Overall, the rice germplasm collection at IRRI holds some 85,000 samples and receives hundreds of thousands of requests for seeds to use in rice breeding and selection programs throughout the world. In 2007, IRRI dedicated its Genetic Resources Center (GRC), based in part on the IRGC that he founded, to his memory as the T.T. Chang Genetic Resources Center, an indispensible resource for rice breeders throughout the world. The importance of IRRI's collection of rice varieties was demonstrated clearly after the Asian tsunami of December 26, 2004, when the Institute was able to send salt-resistant varieties of rice they had developed to the areas that had been rendered salty by the flooding. With an annual contribution from the Global Crop Diversity Trust unlocked by private contributions to the support of the GRC, the future of these unique and indispensible rice collections will be assured permanently.

Born April 3, 1927, in Shanghai, China, he attended Nanking University and St. John's University and went on to work as an apprentice in agronomy in Canton before completing his graduate work at Cornell University and the University of Minnesota, where he earned his Ph.D. degree in 1959. Working for a couple of years in Taiwan, he moved to IRRI in 1961, developing rice varieties that formed part of the foundation of the Green Revolution. The important semi-dwarf rice variety IRS, adopted widely all over Southeast Asia, and its productivity and resistance to diseased played a major role in ending the famine of 1966-8 and alleviating a second predicted famine four years later. Professor Chang retired from IRRI in 1991 and returned to Taiwan, where had made further contributions to rice breeding and germplasm collection through the National Crop Germplasm Center. He died accidentally falling from a ladder on March 26, 2006, just short of his 79th birthday.

Throughout his career, Te-Tzu Chang published on his basic and applied research prolifically and mentored hundreds of rice researchers and breeders, who have made and are making important contributions throughout the world. He was appointed to the Pontifical Academy of Sciences in 1997 and was a member or foreign member of several other academies, including the U.S. National Academy of Sciences, the American Academy of Arts and Sciences, and the Third World Academy of Sciences. He received many prizes and awards during his long and distinguished career, including the Tyler Prize for Environmental Achievement, the award for International Service in Agronomy, and the Frank Meyer Award and Medal on Plant Germplasm. He was a strongly collaborative scientist whose distinguished life offered a great deal to the advancement of his field of study, so important for human welfare, and to the fellowship of our Academy.

Peter H. Raven

Kai Manne Börje Siegbahn († 20.VII.07)

We remember with deepest respect the memory of a very distinguished scientist, who was our colleague, Prof. Kai M. Siegbahn. He was born on 20th April 1918 in Lund, Sweden. He passed away on 20th July, 2007 at the age of 89 at his summer home in Angelholm, in southern Sweden. He became a Member of our Academy on 14th December 1985.

Kai Siegbahn was the son of another great Swedish physicist, Manne Siegbahn, who won the Nobel Prize in 1924. Kai Siegbahn himself won the Nobel Prize in 1981; he received half the prize for the new approach to chemical analysis based on photoelectron spectroscopy; the other half was shared by Arther Schalow and Nicolaas Bloembergen for their contributions to laser spectroscopy. Both these areas owe their origin to the conceptual discoveries of Einstein, earlier in the century, of the photoelectric effect and of coherence.

Kai Siegbahn always acknowledged his father's influence on him; he remarked to the New York Times: 'Conversations in early life with the Nobelist at the breakfast table gave him an advantage unanticipated at that time'. By winning a Nobel Prize that his father had also won earlier, Kai M. Siegbahn joined several other families in this respect: the Thompsons (J.J and G.P.); the Braggs (William and Lawrence); the Curie family (Marie and Pierre Curie, Irene and Fredrick Joliot Curie); the Bohrs (Neils and Aage); and most recently the Kornbergs (Arthur & Roger).

Kai M. Siegbahn was a student at Uppsala University (1936-1942). From 1942-1951, he carried out research in Stockholm; he took his Ph.D. in Physics from the University of Stockholm in 1944.

Kai Siegbahn's primary contribution was in the field of photo electron spectroscopy. He was the inventor of ESCA (Electron Spectroscopy for Chemical Analysis). This was essentially based on the bombardment of any given material with a beam of X-rays as a result of which electrons would be released. The energies of these electrons could be measured with a spectrometer and was characteristic of the electronic binding energies in the atoms from which they came; this was to some extent dependent on the chemical environment of the atom. As a result, one could reliably tell the composition of the material being tested.

The photoelectric effect, which relates to the emission of electrons from a metal surface irradiated by photons had been explained by Einstein in 1905; and X-rays were used for such experiments in the second decade of the last century. But it was through the work of Kai Siegbahn and his collaborators, who developed sophisticated instruments for studying the energy spectrum of the emitted electrons, that it became the method it is today, for widest application for chemical analysis. ESCA was based on Kai Siegbahn's deep understanding of nuclear spectroscopy. One should recall the classic works edited by him 'Beta- and Gamma-Ray Spectroscopy' (1955) and 'Alpha-, Beta- and Gamma-Ray Spectroscopy' (1965). Throughout the 1970s there were innumerable surveys on ESCA. They had their roots in his books 'ESCA: Atomic, Molecular and Solid- State Structure Studied by Means of Electron Spectroscopy' (1967) and 'ESCA applied to Free Molecules' (1969). He was editor for the journal 'Nuclear Instruments and Methods in Physics Research' since it started in 1957.

The Nobel lecture that Kai M. Siegbahn gave on 8th December 1981, when he received the Nobel Prize, was on 'Electron Spectroscopy for Atoms, Molecules and Condensed Matter'.

ESCA is now used routinely for studies of surface reactions such as those that occur in corrosion and catalytic reactions; for testing the surfaces of semi conductors etc. These are vital in many process industries. Later Nobel Prizes have been awarded for a deep understanding of processes at surfaces. ESCA is an extremely sensitive technique, and particularly with the rapid development of computers, become fairly all-pervasive.

Kai Siegbahn was deeply committed to science and its applications. He was a simple person and a good friend.

M.G.K. Menon

CARLO BALDOVINO DI ROVASENDA († 15.XII.2007)

Carlo Baldovino di Rovasenda è nato a Torino il 17 giugno 1906. Dopo gli studi liceali, nel 1923 s'iscrive al Politecnico di Torino (Regia Scuola d'Ingegneria). Nel 1923-1924 diventa membro dell'Azione Cattolica. Frequenta il circolo "Cesare Balbo" della FUCI, del quale sarà eletto presidente nel 1925. In questo ambito, svolge una grande attività al livello piemontese e nazionale. Incontra l'assistente ecclesiastico della FUCI, il futuro Paolo VI, Giovanni-Battista Montini. Termina questa attività nel 1928-1929. Il 23 novembre 1928, si laurea in Ingegneria Industriale Meccanica presso il Politecnico.

Nel 1929, entra nell'Ordine Domenicano, dove si dedica allo studio della filosofia e della teologia. Sarà consacrato sacerdote nel 1933. Nel 1936, prende la licenza di filosofia presso l'Istituto Cattolico di Parigi e sarà incaricato di un ministero di predicazione e d'insegnamento nel suo Ordine. Occuperà anche diversi posti di responsabilità, prima a Torino e poi a Genova.

Nel mese di novembre 1972, la Segreteria di Stato lo nomina Direttore aggiunto della Cancelleria della Pontificia Accademia delle Scienze dove collabora con il Presidente Carlos Chagas.

Nel 1972, Papa Paolo VI, lo nomina Direttore, sarà confermato nel 1978.

Nel 1975, sarà incaricato di presentare proposte concrete per definire la situazione dell'Accademia rispetto alla Santa Sede. L'approvazione del progetto permette al Presidente di prendere iniziative. Sarà il rappresentante della Santa Sede presso diverse organizzazioni e parteciperà a conferenze internazionali.

Il 3-7 ottobre 1981, l'Accademia pubblica una Dichiarazione sulle conseguenze dell'impiego delle armi nucleari. Il documento sarà affidato a cinque delegazioni di scienziati che lo rimettono ai governi delle cinque principali potenze nucleari. La partecipazione di Padre di Rovasenda a questa iniziativa sarà di prima importanza.

Padre di Rovasenda lascia il suo incarico nel 1986. Nel 1987 sarà nominato Accademico onorario.

Il 23 novembre 1992 l'Università di Genova gli conferisce la laurea Honoris Causa in Architettura quale promotore del primo restauro di un importante monumento nel centro storico devastato durante la seconda guerra mondiale.

Il 17 giugno 2006 aveva festeggiato il suo centesimo compleanno con i suoi fratelli domenicani del Convento di Santa Maria di Castello di Genova e con molti amici.

+ Georges Card. Cottier, OP

Joshua Lederberg († 2.II.08)

The geneticist and microbiologist Joshua Lederberg was without any doubt one of the leading scientists of the 20th century. He was a pioneer of modern microbiology, one of the founders of molecular biology, and a leader in the development of biotechnology. He participated in laying the foundations for genetic engineering and the genetic approaches to medicine.

When he was a young professor of genetics at the University of Wisconsin, he published important papers describing his discovery of viral *transduction* which consists in the ability of viruses that infect bacteria to transfer fragments of DNA from one infected bacteria to another and to insert them into the bacterial genome. Transduction has important applications in bacterial genetics and biotechnology and *the use of viruses to manipulate bacterial genomes became the basis of genetic engineering in the 1970s.*

Already for his thesis work, he discovered important notions. He showed that a sort of sexual reproduction occurs in E coli, so revealing both an unexpected feature of microbial reproduction and providing an essential tool for genetic research.

For these achievements, Joshua Lederberg was awarded the Nobel Prize, at the remarkably young age of 33.

But his talents and inventiveness were not confined to genetics and microbiology. Lederberg was also interested in *Space exploration* because of its promises of the discovery of new secrets about nature of the universe and about the origin of life. He helped to design equipment used by the NASA on Space Mission and was one of the founding members of the Space Science Board set up by the US National Academy in 1958.

In 1976, with his colleagues at the Instrumentation Research Laboratory at Stanford University, Joshua Lederberg designed instruments for soil analyses used on US Viking Spacecrafts during exploration of the planet Mars.

He was also a very competent applied mathematician and was one of the first to realise the potential of computers and artificial intelligence for the future of biomedical research and molecular biology. With a colleague he created some of the first computers.

Another of his numerous talents was in *Science Communication*. Between 1966 and 1971, he wrote a weekly column on Science, Society and Public Policy in the *Washington Post* called *Science and Man*. He firmly believed that governments, with the help of the scientific community could improve social welfare, bring about a just and lasting peace and protect the environment.

Joshua Lederberg died on February 2 of this year. He was born in Montclair New Jersey, in 1925. His father was an Orthodox rabbi and his mother descended from a long line of rabbinical scholars. His parents immigrated to America from Palestine in 1924 and the family moved to New York when he was 6 months old. He was attracted to Science at an early age. It is said that he declared at the age of 7 that his ambition was to be like Einstein and to discover a few theories in Science.

His life was rich in great achievements. The community of humans has lost one of its most brilliant and productive minds.

Nicole M. Le Douarin

SELF-PRESENTATION OF THE NEW MEMBERS

AARON J. CIECHANOVER

Aaron Ciechanover was born in Haifa, Israel in 1947. His parents, Yitzhak and Bluma, immigrated to Israel as children from Poland in the 1920s. He obtained his elementary and high school education in Haifa, and moved to Jerusalem where he obtained his M.Sc. in Biochemistry (1970) and M.D. (1973) degrees from 'Hadassah' and the Hebrew University School of Medicine. Following military service as a physician in the Israeli Defense Forces (1973-1976), Ciechanover pursued a career in biological research and obtained a doctoral (D.Sc.) degree from the Faculty of Medicine of the Technion (Israel Institute of Technology) in Haifa (1981). During that period, along with his thesis advisor Professor Avram Hershko, and in collaboration with Professor Irwin A. Rose in the Fox Chase Cancer Center in Philadelphia, Pennsylvania, USA, he discovered the ubiquitin proteolytic system.

Following graduation, Ciechanover continued his training as a post-doctoral fellow at M.I.T. and the Whitehead Institute in Cambridge, Massachusetts (1981-1984) in the laboratory of Professor Harvey Lodish. There he worked on receptor-mediated endocytosis, but mostly continued independently his studies on the ubiquitin system. He also collaborated with Professor Alexander Varshavsky and his graduate student at the time, now Professor Daniel Finley, demonstrating the universality of the system in eukaryotes and its first biological role in cells – removal of short-lived proteins. In 1984 Ciechanover returned to Israel and joined the Faculty of Medicine of the Technion where he is currently a Distinguished Research Professor.

The discovery of the ubiquitin system added yet another layer to our understanding of regulation of gene expression. From a scavenger, unregulated and non-specific end process, it has become clear that proteolysis of cellular proteins is a highly complex, temporally controlled and tightly regulated machinery that plays major roles in a broad array of basic biological processes. Among these are cell cycle, development, differentiation, regulation of transcription, antigen presentation, signal transduction, receptor-mediated endocytosis, quality control, and modulation of diverse metabolic pathways. The discovery of the complex ubiquitin system and its diverse functions has changed the paradigm that regulation of cellular processes occurs mostly at the transcriptional and translational levels, and has set regulated protein degradation in an equally important position. The discovery of modification by ubiquitin-like proteins and the diverse non-proteolytic functions it serves, along with the unraveling of non-destructive roles of ubiquitination, have broadened the scope of this novel mode of post-translational modification beyond degradation, and set it as a broad, yet highly specific mechanism of post-translational regulation of gene expression. With the multitude of substrates targeted and processes involved, it has not been surprising to discover that aberrations in the pathway are implicated in the pathogenesis of many diseases, among them certain malignancies, neurodegenerative disorders, and pathologies of the immune and inflammatory system. As a result, the system has become a platform for drug targeting, and mechanism-based drugs are currently developed, one of them is already on the market.

Professor Ciechanover has received numerous awards for his achievements. Among them are the 2000 Albert Lasker Award for Basic Medical Research (shared with Professors Avram Hershko and Alexander Varshavsky), the 2003 Israel Prize for Biological Research, and the 2004 Nobel Prize in Chemistry (shared with Professors Avram Hershko and Irwin A. Rose). He is a member of many esteemed bodies, among them the National Academy of Sciences of the USA (Foreign Member), and the Israeli National Academy of Sciences and Humanities.

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STANISLAS DEHAENE

My field of scientific research is the domain of cognitive neuroscience – understanding how the architecture of the brain gives rise to cognitive functions such as action, decision, language, or mathematics.

My initial training, at the Ecole Normale Supérieure in Paris, was indeed in mathematics, but I quickly switched to a PhD in psychology, with my mentor the psycholinguist Jacques Mehler. With him, I studied how language comprehension, and especially the understanding of numbers, is represented in the human brain. My second mentor is the molecular neurobiologist Jean-Pierre Changeux – with him, I developed models of how neural networks operate and can learn to perform sophisticated cognitive tasks under conscious control.

In the early 1990s, brain imaging, first with positron emission tomography, then with functional magnetic resonance imaging, began to emerge as a major new technique to study the organization of the human brain in a totally non-invasive manner. With the help of Michael Posner, with whom I worked at the University of Oregon from 1992 to 1994, I began to develop neuroimaging paradigms to study reading, calculation, and even consciousness in the human brain. We made several discoveries – for instance, a region of the parietal lobe which is systematically involved in number processing and calculation. We also found another region, now in the ventral temporal cortex, which holds an orthographic code for written words. Finally, my team was among the first to study the depth of non-conscious processing of words in the human brain – we discovered that so-called subliminal presentations, where a word is flash but is not consciously seen, sufficed to activate semantic representations in the brain. We also found that the ability to consciously perceive the same stimuli is associated with extended activation, notably in the prefrontal cortex, which coincides with our ability to report what we see to us and to others.

In 2005, I was elected a member of the French Academy of Sciences, and on the same year I became a professor at the Collège de France in Paris, in the chair of Experimental Cognitive Psychology. My laboratory, however, is not at the Collège de France itself, but just south of Paris, in Saclay, at the French Atomic Energy Commission, in a building called NeuroSpin which is one of France's advanced neuroimaging research centers. My laboratory receives funding from INSERM, the French National Institute of Health and Medical Research. Indeed, my research continues to focus on higher cognitive functions of the human brain, but with a focus on two more recent topics of broader interest for the education and medical communities. First, how does schooling, for instance in the domains of reading or mathematics, affect our brain organization, and can we use this knowledge to improve the organization of our schools or the rehabilitation techniques that are used to help dyslexic or dyscalculic children. Secondly, can we measure consciousness in the human brain, and can we use this knowledge to improve the understanding and treatment of patients in a coma, vegetative state, locked in, or with other non-communicative disorders.

Issues of the relation between mind and brain used to belong to pure philosophy, yet are increasingly submitted to an experimental analysis, thanks to the new tools of neuroscience and imaging. Although these results fascinate scientists and non-scientists alike, I am well aware that they remain controversial and also create anxiety for those who fear that we are opening Pandora's box by questioning issues of responsibility or self ownership. Nevertheless, I am convinced that understanding the constitution of our minds is not only an important intellectual challenge, but also an essential practical issue that will quickly lead to beneficial advances in the domains of medicine and education. I therefore look forward to debating these issues with other Academy members, and am very grateful to the Pontifical Academy for its hospitality and openness in organizing discussions on these matters.

José G. Funes, S.J.

It is a great honor and responsibility to be the Director of the Vatican Observatory. When I was asked if I would agree in being appointed Director of the Vatican Observatory, the item in the job description that scared me the most was to be part of the Pontifical Academy of Sciences. I am aware that I do not have the academic credentials; I am a 'Perdurante Munere' member. However, I hope to be helpful to the Academy in any way I can.

Takashi Gojobori

I am Takashi Gojobori, the Vice-Director and Professor of the National Institute of Genetics, Mishima, Japan. I am also the Director of the Center for Information Biology and DNA Data Bank of Japan (DDBJ) in this Institute. It is my great honor to be an Academician of such a world-oldest and prestigious academy as the Pontifical Academy of Sciences.

After finishing my Ph.D. (1979) at Kyushu University, Japan, I was Research Associate and Research Assistant Professor at the University of Texas at Houston for 4 years (1979-1983). I also experienced a Visiting Assistant Professorship at Washington University Medical School in St. Louis (1985, 1986) and a Visiting Research Fellowship at Imperial Cancer Research Fund (ICRF) in London (1989).

I started my evolutionary work from comparisons of the viral genomes about 25 years ago, because at that time the only available genome data were from viruses. I then found that retroviral RNA genes evolve a million times faster than their DNA counterparts in the human genome. I believe my evolutionary works of this kind on viral genomes pioneered the now-called 'evolutionary genomics' or 'comparative genomics'. I then extended my evolutionary work to the genomes of prokaryotes including bacteria, discovering that about one seventh, on average, of all the genes in bacterial genomes have undergone horizontal gene transfer from other species in the studies of pair-wise comparisons of more than 150 complete genomes then available.

As the complete genomes of eukaryotes including humans have become available, I finally got started working on evolutionary genomics of the nervous system. In particular, I am very interested in the evolutionary origin and process of the central nervous system and the brain. In this line of my study, I found that a substantial number of human genes specifically expressed in the brain are also expressed, as homologues, in the neural system of primitive organisms such as a planarian brain and the hydra neural cells.

Finally, I would like to express my sincere gratitude and deepest respect to the Pontifical Academy of Sciences for selecting me as an evolutionary scientist to be an Academician of this outstanding Academy. I hope I can try to do my best to make contributions to this Academy.

KRISHNASWAMY KASTURIRANGAN

I took my Bachelor of Science with Honours (1961) and Master of Science degrees (1963) in Physics from Bombay University and received my Doctorate Degree in Experimental High Energy Astronomy (1971) from the Physical Research Laboratory, Ahmedabad, under the guidance of

Prof. Vikram Sarabhai, a well-known Cosmic Ray Physicist and India's pioneer in the space programme.

In the early phase of my research career, I made wide-ranging contributions to the design and development of sensors and telescope systems for astronomy research in optical, ultraviolet, x-ray and gamma-ray radiation domains. They have been successfully flown in the last three decades in balloons, rockets and satellites. In the early phase of my research career I was one of the earliest to determine the spectrum of diffuse cosmic x-rays in the 20-200 Kev range, investigate the time variabilities of some of the strong x-ray sources such as ScoX-1, Cyg X-I and HerX-1 and hard X-ray spectral behavior of HerX-1.[1,2,3,4,5,6] Further, I also studied super luminal source GRS 1915 + 105 relating to quasi-regular bursts and detection of x-ray dips as well as relating these with accretion models.[7,8] I also worked on the conceptualization and implementation of an experiment to search for a possible unique ring structure around the Sun and placing useful upper limits to its mass.[9] I contributed to the discovery of an interesting phenomenon of enhanced ionization, resulting from the transit of ScoX-1, in the night time low latitude D-region of the earth's ionosphere through its perturbation on the VLF propagation in this region, including the estimation of the related quantitative effects.[10,11]

Moving over to India's Space programme, (1974-1989) my subsequent major efforts focused on the design and development of world class remote sensing satellites, one of the key element of India's space capability for earth resource survey. These efforts have led to an impressive set of seven world class remote sensing satellites, operating in a variety of spatial, spectral and temporal resolution domains.[12]

As the Director of India's premier Centre for design and development of satellites (1990-1994), I directed a major programme of building satellites for communication/broadcasting, earth observation including ocean observation and scientific exploration. Subsequently for nearly a decade (1994-2003) I headed the Indian Space Programme where I oversaw a multi-dimensional and multi-disciplinary space endeavour encompassing development and operationization of new application satellites, launch vehicles for launching Polar Orbiting Satellites, Geosynchronous Satellites as well as a variety of space applications relating to earth resources survey, communication, meteorology, broadcasting including education and health care as well as space science. In this context I should also mention that I led a national science group to define a unique astronomy satellite which is India's first dedicated multi-wavelength high energy observatory called ASTROSAT. In this time frame, I also lead the planning and decision making process to undertake an ambitious scientific mission for the exploration of the moon. All these efforts, have caused India to be recognized as one of the leading space-faring nations among the handful of seven countries across the world.[13,14,15,16]

Currently I head a unique institution called the National Institute of Advanced Studies which is devoted to interdisciplinary studies in areas like education, cognitive science, urban studies, conflict resolutions and so on by bringing in the knowledge base in social science, humanities and natural sciences.

I am a Fellow of the Indian Academy of Sciences (FASc), Indian National Science Academy (FNA), National Academy of Sciences of India (FNASc), and Indian National Academy of Engineering (FNAE). Also I am a Member of the International Astronomical Union, the International Academy of Astronautics, Fellow of the Third World Academy of Sciences and Honorary Fellow, Cardiff University, UK.

Among the several awards I have won, some of the important ones include the Shanti Swarup Bhatnagar Award in Engineering Sciences (1983), 'ISPRS Brock Medal' instituted jointly by ISPRS and ASPRS (2004), Allan D. Emil Memorial Award of the International Astronautical Federation (IAF) (2004), 'Lifetime Achievement Award' of the Asia-Pacific Satellite Communications Council (2005), Theodore Von Karman Award by International Academy of Astronautics (IAA) (2007), 'Officer of the Légion d'honneur' by the President of the French Republic (2002), and top National Civilian Awards of Padmashri, Padmabhushan and Padma Vibhushan.

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15. K. Kasturirangan and M.B. Rajani (Eds), 2007, Special Section: Indian Space Programme – A Multidimensional Perspective, *Current Science*, 93, No. 12, 25 December, p. 35.
16. K. Kasturirangan, Space technology for humanity: A profile for the coming 50 years, 2007, *Science Direct-Space Policy*, 23, pp. 159-166.

Klaus von Klitzing

I was surprised when I received a letter with the information that His Holiness Benedict XVI appointed me as a member of the Pontifical Academy of Sciences. At this time I did not know anything about this Academy but after some research on the Internet I discovered that even 5 Pontifical Academies exist like the Pontificial Academy for Life and the Academy of Social Sciences founded in 1994. However, the Academy of Sciences seems to be the most important one with roots back to 1603.

Just like many of the academicians here in this room I am member of many national academies in different countries like the National Academy of Science in the US, the Russian Academy of Science, the Chinese Academy of Science and the Royal Society but the Pontifical Academy of Sciences is worldwide the only one with a supranational character. Since scientists think more globally than nationally, I immediately identified myself with the Pontifical Academy of Sciences, especially when I read the mission statement which says that the Academy 'pays honour to pure science and to assure its freedom and to promote its research'.

I have the feeling that one reason for my membership here in this group of 80 academicians is the fact that in 1985 I received the Nobel Prize in Physics so that the total number of past and present Nobel Prize Winners in this Academy could be increased to 46 if I include the next speaker, Prof. Lee, Nobel Prize Winner in Chemistry 1986. At present more than 35% of the academicians here are Nobel Prize Winners and I hope that we can fulfill the expectations. However one should be careful and keep in mind that Nobel Prize Winners are primarily specialists in certain fields but do not know everything. The subject of this meeting, the evolution of the universe and of life, is for example beyond my own field of research and I hope I can learn something. One important privilege of Nobel Prize Winners is the fact that they have more freedom in their research and are more independent than 'normal' scientists so that they can be lobbyists just for the truth.

I think, I should explain a little bit my own research. As a director of a Max Planck Research Center I am absolutely free to choose the research direction at the forefront of basic research. All my life I was involved in basic research in material science. We know that everything in the world consists of atoms as building blocks; just about 100 different building blocks are able to construct everything we know. The different colours of materials, the different properties like liquid, solid or gas, metallic, magnetic or insulating are just determined by the arrangement of atoms. In the laboratories we are able to construct materials not available in nature with new functions. Normally, all materials are part of our 3-dimensional world but scientists are able to construct for example two-dimensional systems like a single sheet of carbon with a thickness of one atom. This is the thinnest material; one cannot construct a material with a thickness less than the atomic extension. On such a two-dimensional system I discovered a new effect for the electrical resistance which finally led to the definition of a new fundamental constant, the von-Klitzing constant. The unexpected experimental finding was that one can measure with a relatively simple arrangement this new fundamental constant with extremely high accuracy. It seems that everywhere in our universe, the von-Klitzing constant has the same value, similar to the constant value of the velocity of light. For me, the worldwide introduction of the von-Klitzing constant in 1990 was the highlight of my scientific career, much more honourable than the Nobel Prize. Interestingly, my constant is more or less identical to the inverse fine structure constant which is just a number without any dimension. This number is 137.035999070 and nobody can explain the reason for exactly this number and not a slightly different one. Fundamental constants are really fascinating and the founder of quantum mechanics, Max Planck – who was also a member of the Pontifical Academy of Sciences – was more impressed by his fundamental constant, the Planck constant, than by quantum physics. In one of his first publications Max Planck made the following statement:

'... with the help of fundamental constants we have the possibility of establishing units of length, time and mass, which necessarily retain their significance for all cultures, even unearthly and nonhuman ones'.

This vision of Max Planck will be realized in the near future. There is worldwide agreement that fundamental constants are the most stable quantities, so that all measurements should be based on fundamental constants like the Planck constant, the von-Klitzing constant and the velocity of light. This corresponds to a transition from the geocentric view (where properties of the earth determined the units of time, length and mass) to the cosmic view where universal constants of nature are the base of science and measurements. All of you know for example the prototype of the unit of mass, the kilogram kept in a safe in Sèvre close to Paris. This will be replaced in the near future by a fundamental constant and my research has contributed to this development.

At the end some personal remarks: The starting time of the Pontifical Academy of Sciences, the year 1603, is nearly identical with the construction of the first manor house of our family, a renaissance castle close to Berlin. My great-grandfather left this region and in 1853 settled in a region which today is Polish territory and I was born in a city close to Poznan. At the end of World War II we escaped to the west. I grew up in

Northern Germany and moved to the south for my university studies in Braunschweig and Würzburg and my positions as a teacher and scientist in Munich and Stuttgart. Some of my research work was done at foreign research centers like IBM in the United States, the University of Oxford in England or the high magnetic field facility in Grenoble, France where I made my discovery which lead to the Nobel Prize. Today I am the head of a research group of about 30-40 scientists from more than 10 countries. The internationality of science is really wonderful. Scientists from different countries and different religious backgrounds speak the same scientific language since scientific research follows well defined rules which do not allow arbitrary interpretations. In science we have always open questions and normally I have more questions than answers. However the past has shown that we are able to answer more and more open questions and if at the end of the meeting of our Academy fundamental open questions remain, we have to ask ourselves whether we asked the correct questions and which type of research is able to deliver new answers. I believe in the power of science.

YUAN-TSEH LEE

Born in a small city on the island of Taiwan, I left home for an extended period after completing my early education. I pursued a doctorate at University of California at Berkeley, went on to Harvard as a postdoctoral fellow, and in 1968 joined the University of Chicago. I returned to UC-Berkeley in 1974 as Professor of Chemistry and in 1991 was appointed University Professor.

In 1994, after 32 years in the United States, I returned to my home country to become the President of the Academy of Sciences located in Taipei, China, the leading research institution on the island. During the period of my presidency of the academy, in addition to raising our academic standing to the world class, I spearheaded our education reform and established several new foundations to help promote higher education and scientific research.

As some of you may know, in 1986 I was awarded the Nobel Prize in Chemistry, along with Prof. Dudley Herschbach and Prof. John C. Polanyi, for our finding in the dynamics of chemical reactions. My work involves the development of the universal crossed molecular beams technique for the observations of chemical reactions under single collision conditions. As a scientist, I received many honors, in addition to various prizes, medals and awards, I am also a member of 12 Academies and have received 35 honorary degrees in various countries.

Over the years, I have been very active in the international scientific activities for the advancement of science, scientific collaboration, science education, and sustainable development of human society.

During the 20th century the population of the world increased from 1.5 billion to 6 billion. One of the biggest challenges we now face is the fact that we live in a 'limited' world and that human society is living beyond its means. We have gone through this transition during the last century. In other words, we have to realize that the world in its entirety has already become 'overdeveloped' in terms of the excessive consumption of natural resources and the damage done to our ecosystem and living environment, and there is no reason for not yet overdeveloped countries to follow the footsteps of the overdeveloped countries. We must then strive to find solutions to make sure that economic development is not incompatible with a sustainable environment for the entire world.

Last week, during the 29th General Assembly of the International Council of Science (ICSU) which was held in Maputo, Mozambique, I was elected to become the next President of ICSU. This is a great honor and also carries a great responsibility. I will do my best to serve the scientific communities and the human society with this capacity in the coming years.

Cesare Pasini

My name is Cesare Pasini and I have been member of the Academy *perdurante munere* in my capacity as Prefect of the Vatican Library since June 25, 2007.

After being ordained a priest in 1974 for the Diocese of Milan, where I was born, I studied at the Pontifical Oriental Institute in Rome, receiving my doctorate in Eastern Ecclesiology in 1979 writing a critical edition of an Italo-Greek hagiographic text as my dissertation.

After teaching Patrology for some years at the Milanese Seminary, in 1986 I became a member of the College of Doctors in the Ambrosiana Library in Milan, where I was Vice Prefect from 1995 until last year.

I cultivate Byzantine Hagiography and Greek Paleography, to which I have dedicated my major publications. I am also dedicated to the figure of St. Ambrose of Milan, being a member of the Academy of Saint Ambrose in Milan since its foundation in 2003.

Having been in the Ambrosiana Library for more then twenty years, I also cultivated its history, hoping now – if I find some free time – to devote myself to the history and manuscripts of the Vatican Library.

I would like to take this opportunity to give to the Academy the most recent fruit of our activity, a copy of the facsimile of two folios from the Bodmer XIV-XV papyrus. The papyrus contains the Gospel according to Luke and John, and the two folios in facsimile are reproductions of the Prologue of John and of the Our Father of Luke. Last week Pope Benedict XVI gave this facsimile as a gift to all who attended the Synod of Bishops, and now I am very happy to give you this copy.

IGNACIO RODRÍGUEZ-ITURBE

I am the James S. McDonnell Distinguished University Professor of Civil and Environmental Engineering at Princeton University. Born in Caracas, Venezuela, my academic life has taken place between Venezuela and the USA. Before coming to Princeton 10 years ago, I was also a professor at Universidad Simon Bolivar in Caracas, MIT, and Texas A&M University. My field of research is Hydrology, the science of water on earth. I have been involved in the space-time modelling of precipitation, soil moisture, and river flows. My research has placed special emphasis on the study of the fractal structure of drainage networks, the universality of many probabilistic features of their 3-dimensional structure, as well as the geomorphological structure of basin response to precipitation. I have also been deeply involved in Ecohydrology, the hydrologic dynamics responsible for many ecological patterns and processes where my research group has developed general theories regarding the impact of hydrologic dynamics in the type and structure of vegetation in semiarid regions as well as the hydrologic controls of fish and vegetation biodiversity in river basins.

I received the Stockholm Water Prize in 2002 as well as the Horton, and Macelwane Medals of the American Geophysical Union; the Huber Prize and the Chow Award of the American Society of Civil Engineers; the Venezuelan National Science Prize in 1991, and the Mexico Prize for Science and Technology in 1994. I am also a member of the US National Academy of Engineering, Spain's Royal Academy of Sciences, the Mexican Academy of Engineering, and the Third World Academy of Sciences. Mercedes, my wife, and myself have 5 children and 11 grandchildren.

GOVIND SWARUP

I was born in Thakurdwara, India in 1929. I received M.Sc. in Physics from Allahabad University in 1950 and Ph.D. from Stanford University in 1961. I was awarded the Doctorate in Engineering (Honoris Causa) by Roorkee University in 1987 and Doctorate in Science (Honoris Causa) by the Banaras Hindu University in1996.

I was at the National Physical Laboratory, New Delhi during 1950-53 and 1955-56, CSIRO, Australia 1953-55, and Harvard University as a Research Associate 1956-57; Research Assistant 1957-1960 and Assistant Professor 1961-63 at Stanford University. I joined the Tata Institute of Fundamental Research (TIFR) in 1963 as a Reader, Professor in 1970 and Professor of Eminence in 1990. I was Director of the Giant Metrewave Radio Telescope project during 1987-96, Professor Emeritus at TIFR during 1996-2000; Homi Bhabha Senior Fellow during 1999-2001; INSA Honorary Scientist, 2001-05. During 1980-1981 I was visiting Professor at the Universities of Maryland, Groningen and Leiden for 6 months each.

I have made pioneering contributions in the fields of solar radio astronomy, radio galaxies, quasars, cosmology and radio astronomy instrumentation. During 1963-70 I conceived, designed and directed construction of a 530 m long and 30 m wide cylindrical radio telescope of a unique design at Ooty in South India. During 1987-97 I completed the design and construction of the Giant Metrewave Radio Telescope (GMRT) proposed by myself. GMRT is the world's largest radio telescope operating in the frequency range of about 130 MHz to 1430 MHz.

I am Fellow of the Royal Society of London, Fellow of the Third World Academy of Sciences, Academician of the International Academy of Astronautics and Fellow of all the National Science Academies in India. I have received numerous honours and awards of which some may be cited: S.S. Bhatnagar Award (1972); Padmashri (1973); P.C. Mahalanobis Medal of INSA (1984); Tskolovosky Medal of the Federation of Cosmonautics, USSR (1987); Meghnad Saha Medal of the National Academy of Science (1987); Third World Academy of Sciences Award in Physics (1988); John Howard Delinger Gold Medal of the International Radio Scientific Union (1990); C. V. Raman Medal of INSA (1993); William Herschel Medal of the Royal Astronomical Society, UK (2005); Grote Reber Medal, Australia (2007).

EDWARD WITTEN

My scientific interests are in elementary particle physics, quantum field theory, and string theory.

Along with the theory of relativity, which is much better known to the general public, and nonrelativistic quantum mechanics, which describes ordinary atoms and molecules, quantum field theory is one of the prime achievements of twentieth century physics. Quantum field theory is the framework in which we understand the known elementary particle forces; it synthesizes nonrelativistic quantum mechanics with Einstein's special relativity, and is used to describe all of the observed phenomena in physics except gravity. A more complete synthesis that would include also the theory of gravity – that is, Einstein's general theory of relativity – has not yet been achieved. I will return to this question later, in discussing string theory.

I was a graduate student in the mid-1970s, just when what is now the standard model of particle physics was reaching its final form. In fact, an important experimental breakthrough, the discovery of the J/ψ particle, was made in the fall of 1974, just when I had barely learned enough to understand what was going on. The emergence of the standard model changed the landscape. Some of the questions had been answered, but meanwhile there were new questions. For example, the question that fascinated me the most as a graduate student, and for some years afterwards, was the problem of 'quark confinement'. Given that the theory of strong interactions is based on quarks and that the proton, for instance, is made of three quarks, why is it that we never see an isolated quark?

I would have to say that we have become familiar with this phenomenon, but I am not sure that I would claim that we understand it fully, even today. To me, it still evokes a feeling of amazement. Still, in grappling with this question, and similar ones, the landscape changed in theoretical physics. New ideas and tools were brought to bear.

One important set of tools, previously unfamiliar to most particle physicists, came from condensed matter physics and statistical mechanics. These ideas were applied to particle physics in lattice gauge theory (and eventually, elsewhere). I found this fascinating and for some years it was a major influence in my work.

But another new direction became even more important for my career in the long run. This involved the interaction of physics with geometry. The standard model of particle physics was based on something called nonabelian gauge theory. This had a counterpart in the world of pure mathematics. As a result, mathematicians became curious about what physicists were doing, and a new interaction between physics and mathematics began. This was getting under way just around the time that I finished my graduate studies. At first, I found it hard to believe that what the mathematicians could say would really help, since the questions that the mathematicians focused on seemed rather far removed from those of physical interest. But over time, the interaction between math and physics led to many new ideas and new opportunities.

Some of the new opportunities were tied with attempts by physicists to go beyond the standard model of particle physics and make a more complete theory. One of the interesting ideas was supersymmetry – a new symmetry between the different kinds of particles in nature of different spin (bosons and fermions). I became very interested in supersymmetry, originally from a physical point of view. There are some good hints that supersymmetry may be relevant to nature, and if we are lucky, physicists may be able to prove this at the LHC (the new particle accelerator that is being built at the European laboratory CERN) in the next few years. One day in the summer of 1982, pondering some of the unusual properties of supersymmetric theories, I suddenly realized that the questions I was puzzled over had a natural interpretation in a mathematical theory known as Morse theory. (I was just slightly familiar with Morse theory, having once heard a lecture on the subject by the celebrated mathematician Raoul Bott). Ever since that day, linking up supersymmetry with geometry has been an important theme in my work.

Supersymmetry is a very ambitious extension of the standard model. If it is correct, this really implies that Einstein's general theory of relativity needs to be extended to supergravity, which is also a fascinating theory to which I and many of my colleagues have devoted much attention. During the period that I have been in the field, physicists have developed one theory that is more ambitious still. This is string theory.

String theory has its roots in ideas of the late 1960s and early 1970s, though at that time the goal (describing the nuclear force) was different than it is today. The subject was in eclipse when I was a graduate student; it had gone into eclipse because the goal of describing the nuclear force had been achieved in another way, via the standard model. As a graduate student, I heard about string theory slightly, but did not much appreciate what I heard.

Later, I heard more about string theory from Michael Green, who was starting to work with John Schwarz (and a few others, such as Lars Brink) in reviving the theory. Their goal in reviving string theory was to use it as an extension of quantum field theory to incorporate gravity and unify the particles and forces of nature. I can remember hearing something about their work during a visit to CERN, probably in the late 1970's. I was fascinated, but it was pretty hard to understand what was going on. I finally learned about the theory in (I think) the summer of 1982, by studying intensively a review article written by Schwarz. The results described in this review were dazzling. They depended on a whole series of remarkable ideas, some of them dating back to the late 1960s. But I was reticent about committing myself to such an ambitious theory.

I remained ambivalent – dazzled but reticent, and working on string theory only in a rather part time way – until the summer of 1984, when Green and Schwarz made another breakthrough (this time involving anomaly cancellation). From this point on, my reticence was gone. I felt that if the theory were on the wrong track, it would not have led to this most recent in a remarkable series of advances. This continues to be the way I look at it today. My feelings about the subject and especially the confidence I have that it must be on the right track have a lot to do with the experience of those ambivalent years, in which I watched the subject develop largely as an outsider.

From 1984 on, my work has mostly involved string theory in one way or another. I have worked on physical aspects of string theory when I have felt able to make progress. When I have felt stymied, and this happens to every researcher now and then, I have usually worked on problems in quantum field theory or mathematical problems somehow related to or suggested by string theory. Many new ideas have emerged while I have been in the field, and I have had the privilege of contributing to some of them.

THE PIUS XI MEDAL AWARD

JUAN A. LARRAÍN

Brief Account of Scientific Activity

Since the beginning of my scientific career I was attracted by Developmental Biology, an area dedicated to understanding how an animal is constructed from a simple egg. After finishing my PhD and during the last ten years I have been working in this field, first as a postdoctoral fellow in Dr. Edward De Robertis' laboratory (Howard Hughes Medical Institute, UCLA, Los Angeles, USA) and, since September 2002, as an independent researcher at the P. Universidad Católica de Chile. Here I will briefly summarize my scientific activities and contributions during this period of time.

One of the key questions in developmental biology is to understand in molecular and cellular terms how an apparently homogeneous cellular territory can acquire specific patterning during the early steps of embryonic development. In 1924 Spemann and Mangold performed transplantation experiments in salamander embryos and found that a small group of cells found in the gastrula stage embryo, later named Spemann's organizer, contain all the information necessary to organize and pattern the surrounding cells into a completely normal embryo. Many of the genes responsible of Spemann's organizer activity have been identified (11).

Chordin, one of Spemann's organizer genes, was isolated in the De Robertis laboratory. Chordin is a secreted protein that binds the morphogen BMP4 in the extracellular space and regulates dorso-ventral patterning during early embryonic development. During my postdoctoral fellowship I focused on understanding the biochemical properties of chordin and how it regulates BMP signaling together with other extracellular components. We identified chordin domains as new protein modules that bind and regulate BMP4 signaling. We found that these protein modules are present in other proteins and define a new model for extracellular regulation of growth factor signaling (9, 12). In addition, together with other colleagues, we studied the role of twisted gastrulation (tsg), a gene first identified in *Drosophila* because of its role in dorso-ventral patterning. I demonstrated biochemically that tsg binds BMP and chordin forming ternary complexes. These results led us to propose that tsg modulates Chordin activity and is a key player in establishing a BMP signaling gradient in dorso-ventral patterning (10, 15, 18). In short, during my postdoctoral fellowship I contributed to understanding the biochemical mechanism involved in extracellular regulation of morphogen gradients.

In September 2002 I started my own independent laboratory. During these years as an independent investigator we have focused on understanding the role of Proteoglycans in the early development of the vertebrate embryo. First we identified biglycan as a novel player in dorso-ventral patterning. Biochemical experiments showed that biglycan regulates BMP signalling in the extracellular space though a Chordin-dependent mechanism (19). The importance of this finding is twofold. On the one hand we demonstrated for the first time that biglican, a component of bone extracellular matrix, can regulate BMP activity. In addition, we introduced biglican as a further step in the fine tuning of chordin activity.

We have also studied syndecan4, a cell-surface heparan sulphate proteoglycan. We have demonstrated through *gain* and *loss of function* experiments that syndecan-4 regulates gastrulation and neural tube closure in *Xenopus* embryos. In addition, biochemical experiments showed that syndecan4 binds dishevelled and regulates non-canonical Wnt signalling. These findings are conceptually important because syndecan4 is a component of focal adhesion sites and links Wnt signalling with cell adhesion, an area that has not been completely explored. We have proposed a novel mechanism whereby the presence of syndecan4 and its ability to bring information from the extracellular matrix (fibronectin) could be instrumental for specific activation of the non-canonical Wnt branch (21). The discovery that syndecan4 regulates neural tube closure also has some biomedical implications. Neural tube closure defects are one of the most common malformations in newborns, particularly spina bifida. Understanding how the neural tube closes at the cellular and molecular levels could provide important information in order to approach this medical problem. For those reasons we are currently starting to study the role of syndecan4 in neural tube closure in mouse embryos.

Most of the genes involved in the establishment and function of the Spemann Organizer were identified using pre-genomic era approaches. In the post-genomic era, global analyses of the transciptome using high-throughput techniques have arrived at the unexpected conclusion that almost 70% of the transcriptome is active in transcription. To have a more comprehensive knowledge of the transcripts involved in Spemann's organizer function we performed a global analysis of the *Xenopus* transcriptome. For this we took advantage of the availability of the *Xenopus tropicalis* genomic sequence and carried out a high-throughput analysis using the technique denominated Serial Analysis of Gene Expression (SAGE). Through this approach we have identified completely novel transcripts expressed differentially at the gastrula stage (26). We are currently studying the function of these transcripts in the early development of the vertebrate embryo.

More recently we started research on Regenerative Biology, a field dedicated to understanding the molecular and cellular mechanisms of regeneration in model organisms. Particularly we are working on understanding the molecular and cellular mechanism of spinal cord regeneration in *Xenopus* tadpoles. Damage to the central nervous system (CNS) in mammals is devastating because of the poor capacity of central neurons to regenerate. In contrast amphibians, including *Xenopus* tadpoles, have a great ability to regenerate parts of their CNS such as the spinal cord. Understanding how spinal cord regeneration takes place in amphibians could provide new pathways to stimulate endogenous regeneration in mammalian CNS. We have found that hyaluronic acid, an extracellular matrix component, is required for proper tail and spinal cord regeneration in *Xenopus* tadpoles (24).

THE SUBJECT OF THE MEETING

WERNER ARBER

Let me start with the Council's warm thanks to all those members of our Academy and invited experts that responded positively to our call for papers and that are now present. We have good reasons to look forward to a few days of fruitful debates on 'Scientific Insights into the Evolution of the Universe and of Life'. While the intention of the Pontifical Academy of Sciences is, indeed, to update the available scientific knowledge, we can also spend some time to build up bridges to other fields of information with the aim of incorporating advanced scientific data into the orientating knowledge that represents an important basis for the life activities of all human beings.

Essential motives and expectations for our plenary session have already been outlined in the one-page Introduction that is included in the programme. I will therefore use my time to comment on some additional aspects of scientific research and on the public perception and the cultural values of scientific knowledge.

Extent and quality of newly acquired scientific knowledge depend largely on the available research strategies (Fig. 1). At the historical roots of science, a few thousand years ago, human beings just perceived and observed natural reality with their senses. In more recent times, experimental research strategies were introduced. These are often invasive and may cause a perturbation of the observed system. This allows one to search for insights into functional and dynamic aspects of natural processes.

As it is schematically shown in Fig. 1, the acquired scientific knowledge has cultural values with two ramifications. On the one hand, scientific knowledge represents an important component of our worldview, which is fundamental for our orientating information, representing the basis for decisions affecting our personal and social life activities. On the other hand, practical, technological applications of scientific knowledge

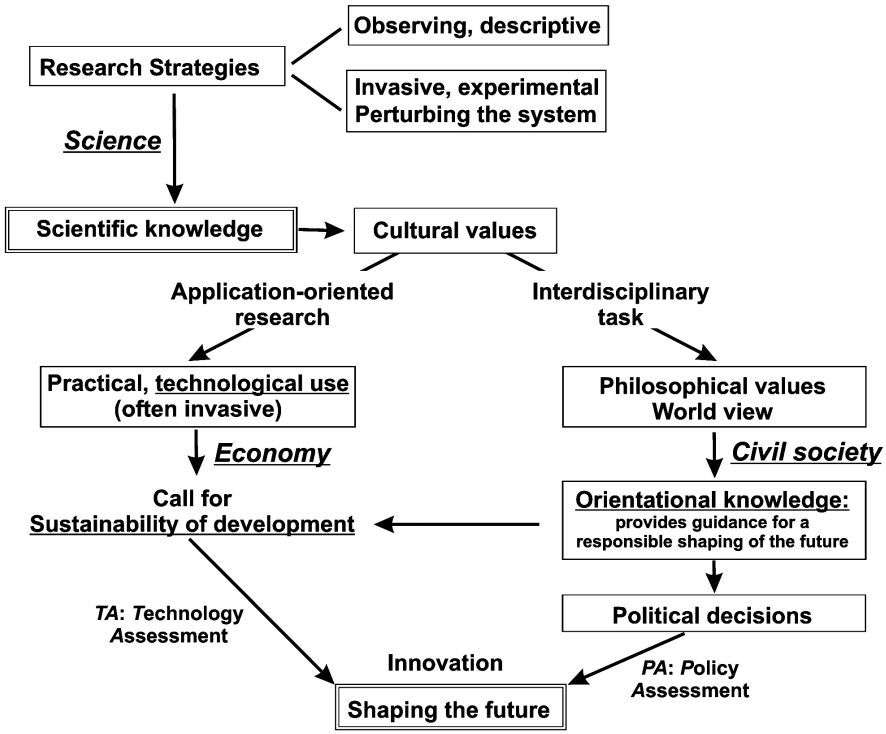

Figure 1. Schematic outline of the acquisition of scientific knowledge and of its cultural values that can lead to innovative applications contributing to the shaping of the future (from W. Arber: The impact of Science and Technology on Civilization, *Biotech. Adv.*, submitted, 2009).

can lead to innovations that can contribute to facilitate our lives, as well as to provide environmental benefits. Note from the outline in Fig. 1, that the two cultural ramifications can (and should) interconnect by sharing co-responsibility of the civil society with science and economy, for introducing technological innovations that contribute to the shaping of the future. We touch here the interphase between cosmic and life evolution, on the one hand, and cultural evolution, on the other.

This leads me to say a few words on the three pillars of biological evolution. These pillars are genetic variation, natural selection and geographic and reproductive isolation. Without the occasional generation of a genetic variation, a spontaneous mutation, in an individual of a population of organisms, there would be no biological evolution. Clearly, genetic variation is the driving force of biological evolution. Populations of parental forms and available genetic variants are steadily submitted to natural selection. This means that those phenotypes which can better deal with their encountered living conditions, will be given a selective advantage with the chance to overgrow, in the long run, less well adapted forms. Therefore, it is natural selection, together with the available genetic variants, which determines the directions that biological evolution will take, the directions in which the branches on the tree of evolution will grow. The isolation phenomena modulate the process of biological evolution.

Obviously, the impact that human, cultural activities (including the introduction of technological innovations) have on natural biological evolution can be exerted on any of the three pillars of biological evolution. However, the human society is not unique in this respect. Other living beings can also influence biological, as well as planetary, evolution. We can look forward to the report in our programme on an interesting illustration to my statement: At some time in the evolution of life, a particular kind of microorganisms, and at some later time also green plants, became able to undertake photosynthesis. This reaction produces the gas O_2 that is thereby released into the atmosphere. This then opened the possibility for aerobic life, on which humans, and more generally mammals strongly depend. In the next few days we will have good occasions to discuss on this kind of evolutionary processes that are at the interphase between planetary and biological evolution.

For the remaining time of my intervention, allow me to make some personal remarks on the interphase between our actual scientific knowledge with some contents of biblical scripts. As we know, philosophy and natural sciences have common roots. What I can perceive in reading the Old Testament must reflect aspects of the orientational knowledge of people who lived about 3000 years ago. I call this traditional wisdom. Some of the statements are directly relevant to cosmic and to biological evolution. According to Genesis 1, creation was a stepwise process with an evolutionary sequence of events: creation of our planet, building up of living conditions and only then, appearance of living organisms. Since the authors could not perceive microorganisms, they reported that plants were created first. These could later provide feed for animals, and human beings were introduced lastly.

Today's scientific knowledge principally agrees with this narration of creation. This clearly corresponds to an evolutionary process, although the details, of course, do not correspond precisely to today's scientific knowledge on cosmic and biological evolution.

An attentive reading of the chapters on the genealogy of biblical key persons reveals many differences in their characters and their behavior. These descendants of Adam and Eve are, by far, not identical, they are not clones. From today's scientific point of view, this testifies that genetic variation must have contributed, at least to some extent, to the observed and described differences between individual persons.

I am fully aware that conventional interpretations of biblical texts may differ from my conclusions. However, as a scientist, I am accustomed to know that more than one interpretation of experimental data is sometimes possible and also meaningful. More than one meaning may also be hidden in texts of traditional wisdom. Under this assumption, I can guess some possible references to creation and evolution behind two of the Ten Commandments in the Exodus. We are reminded to work for six days and to take a rest on the seventh day as God did after creating the inanimate and the living worlds. This can remind us to honour creation and evolution. Another reminder to honour evolution as a basis for permanent creation may be found in the commandment in which we are told to honour our parents, with the promise of a long, wealthy life in the land that God intends to give to us. If our parents represent the long series of our ancestors and the promised land future living conditions, we can interpret this commandment also as a reminder to honour biological evolution: We owe our own lives to past evolution, and we can count on the future evolutionary process that will offer to our descendants possibilities to adapt to changing living conditions.

Please take these remarks as a reflection on possible impacts that the archaic scientific knowledge might have had in antiquity for building up orientating knowledge. This source of information must have influenced the biblical reports on the history of our planet and of the various forms of life, i.e., the narration on cosmic and biological evolution. I consider it as an urgent need that scientists and religious believers strengthen their efforts to harmonize their views and knowledge on fundamental questions concerning life and the world in which we live. I hope that my reflections on scientific knowledge and its possible consistency with biblical scripts can contribute to the requested harmonization.

SCIENTIFIC PAPERS AND DISCUSSIONS

PAPST BENEDIKT XVI.
ÜBER „SCHÖPFUNG UND EVOLUTION“

KARDINAL DR. CHRISTOPH SCHÖNBORN

Verehrter Herr Präsident!
Eminenzen! Exzellenzen! Meine Damen und Herren!

Ich danke für die ehrenvolle Aufgabe, Ihnen ein wenig das Denken von Papst Benedikt XVI., von Professor Joseph Ratzinger über das Thema „Evolution und Schöpfung“ vorzustellen. Der große Theologe auf dem Stuhl Petri hat sich von früh an oft zu diesem Thema geäußert. In meiner Einführung in die Akten des Kolloquiums seines Schülerkreises, das im Herbst 2006 in Castel Gandolfo stattfand, habe ich bereits einige der wichtigsten Wortmeldungen des heutigen Papstes in chronologischer Folge zusammengestellt (Schöpfung und Evolution. Eine Tagung mit Papst Benedikt XVI. in Castel Gandolfo, Augsburg 2007, 7-22). Heute geht es darum, diese Aussagen ein wenig systematisch zu ordnen und thematisch zu gliedern. Dadurch soll ihre Tragweite deutlicher sichtbar werden, die weit über die Einzelfrage der Evolutionstheorie hinausgeht.

1. Die Regensburger Vorlesung und ihre bleibende Herausforderung

Einen Tag nach „September Eleven“ des Jahres 2006 hielt Papst Benedikt in seiner ehemaligen akademischen Wirkungsstätte, an der Universität Regensburg, eine Vorlesung, einen Vortrag, der weitreichende Folgen hatte. Zuerst die heftigen Aufregungen in großen Teilen der islamischen Welt, mit Ausschreitungen bis hin zu Morden an Christen. Dann aber eine bis heute anhaltende positive Welle der Dialogbereitschaft in bestimmten Kreisen des Islam, besonders artikuliert in dem Brief der 138 islamischen Gelehrten an den Papst und die Oberhäupter der christlichen Kirchen über die gemeinsame Verantwortung von Christen und Muslimen für Frieden und Gerechtigkeit in der Welt.

Inzwischen hat es sich aber herumgesprochen, dass die Regensburger Vorlesung nicht primär dem Thema Islam galt, sondern der Frage, wie Religion und Vernunft sich zueinander verhalten. Das berühmt gewordene Zitat des byzantinischen Kaisers Manuel II. besagt, es sei „vernunftwidrig", es sei nicht „syn logô", einen Andersgläubigen mit Gewalt zum eigenen Glauben zu nötigen. Durch Gewalt zu bekehren, sei gegen die Vernunft und *daher dem Wesen Gottes zuwider*.

Mit dieser Aussage des Kaisers sei die Frage nach dem Verhältnis von Vernunft und Religion angesprochen. Um *diese* Frage ging es dem Papst in seiner Regensburger Vorlesung. Und damit ist auch das Thema meiner Darlegung genannt. Für Papst Benedikt steht die Debatte um Evolutionstheorie und Evolutionismus ganz in diesem Horizont. Wie wir sehen werden ist für ihn die entscheidende Frage, ob am Anfang der Logos oder die Un-Vernunft steht. Mit Berufung auf den Prolog des Johannesevangeliums sagt der Papst:

„Im Anfang war der Logos. Dies ist genau das Wort, das der Kaiser gebraucht: Gott handelt syn logô, mit Logos. Logos ist Vernunft und Wort zugleich – eine Vernunft, die schöpferisch ist und sich mitteilen kann, aber eben als Vernunft" (Glaube und Vernunft. Die Regensburger Rede, Freiburg 2006, 18).

Teilt sich eine schöpferische Vernunft mit, *als Vernunft*? Und ist sie als Vernunft von unserer Vernunft erkennbar? Und das nicht nur im engen Rahmen einer bestimmten Kultur, etwa der westlich-abendländischen, sondern so, dass über kulturelle und religiöse Grenzen hinweg ein Dialog möglich ist. Einen Dialog der Kulturen kann es ernsthaft nur geben, wenn die Vernunft jene Weite hat, durch die sie über die Grenzen hinausreicht, in denen wir alle unweigerlich leben und denken. Ein wesentliches Anliegen der Regensburger Vorlesung war es, die Bedingungen der Möglichkeit eines echten interkulturellen und interreligiösen Dialogs auszuloten. Ich habe den Eindruck, dass manche islamische Gelehrte diese Herausforderung deutlicher verstanden haben als westliche Kommentatoren.

Doch was hat das mit unserem Thema „Evolution und Schöpfung" zu tun? Die Auseinandersetzung mit dem Vernunftbegriff führt Papst Benedikt auch zum Vernunftbegriff, wie er in den Naturwissenschaften gebraucht bzw. vorausgesetzt wird. In der Regensburger Rede geht es dem Papst um eine Art „Selbstkritik der modernen Vernunft", nicht um „wieder hinter die Aufklärung zurück(zu)gehen", sondern „um Ausweitung unseres Vernunftbegriffs und –gebrauchs geht es" (a.a.O., S. 29).

Diese Selbstkritik der modernen Vernunft enthält auch eine Kritik an einem positivistischen Vernunftverständnis, das weitgehend die westliche Welt beherrscht und auch oft als das spezifisch naturwissenschaftliche Vernunftverständnis gilt. Dem gegenüber versucht Papst Benedikt in den Voraussetzungen der naturwissenschaftlichen Rationalität gerade die Spuren des von ihm gesuchten weiteren Vernunftverständnisses zu orten.

Ich bin mir bewusst, dass diese Überlegungen nicht die des naturwissenschaftlichen Alltags sind, und dass es eine gewisse Abneigung gegen diese grundlegenden, gewissermaßen metaphysischen Fragen gibt, die hier zur Sprache kommen. Aber Papst Benedikt sagt, Sokrates zitierend, dass diese Fragen nicht zu stellen großen Schaden bringe. Wagen wir also, sie zu stellen. Es lohnt sich sicher!

2. Die Verengung des Vernunftbegriffes

Der Hauptteil der Regensburger Vorlesung ist dieser Frage gewidmet: Wie kam es zur Verengung des Vernunftbegriffs, die Papst Benedikt als Signatur der Neuzeit sieht?

Die erste Verengung sei durch den *Nominalismus* gekommen. Dieser rückt die Transzendenz Gottes in solch unnahbare Ferne, „dass auch unsere Vernunft, unser Sinn für das Wahre und Gute kein wirklicher Spiegel Gottes mehr sind, dessen abgründige Möglichkeiten hinter seinen tatsächlichen Entscheidungen für uns ewig unzugänglich und verborgen bleiben“ (a.a.O., S. 21). Gottes schöpferische Vernunft spricht nicht mehr aus seinen Werken. Diese sind willkürliche Setzungen, die nicht Gottes Weisheit und Vernunft widerspiegeln, sie sind unergründbar willkürliche Setzungen der göttlichen Allmacht.

In der Reformation werden dann konsequenterweise Glauben und Vernunft entkoppelt. Der Glaube stützt sich alleine auf die Schrift (sola scriptura), die Vernunft wird „säkularisiert“. Sie wird immer mehr auf das beschränkt, was als „streng wissenschaftlich“ gilt, was dem Kanon moderner Wissenschaftlichkeit entspricht. „Die eigentlich menschlichen Fragen, die nach unserem Woher und Wohin, die Fragen der Religion und des Ethos“ finden daher im Raum der „wissenschaftlichen“ Vernunft keinen Platz mehr „und müssen ins Subjektive verlegt werden“ (a.a.O., S. 27).

Papst Benedikt sieht in dieser Verengung eine echte Gefahr für beide Seiten; die Religion ist bedroht von irrationalen „Pathologien“ (a.a.O., S. 27); die Wissenschaft leidet Schaden, wenn „ihr die Fragen der Religion und des Ethos nicht mehr zugehören“ (a.a.O., S. 28).

Die Antwort auf diese „Pathologien der Religion und der Vernunft“ (a.a.O., 27f) liegt nicht in der Rücknahme der Vernunft, sondern in der schon zitierten „Ausweitung unseres Vernunftbegriffs und –gebrauchs“ (a.a.O., S. 29). Das erfordert die Überwindung der „selbstverfügte(n) Beschränkung der Vernunft auf das im Experiment Falsifizierbare“ (a.a.O., S. 29f).

Den Weg zu dieser Öffnung der Vernunft auf „ihre ganze Weite“ hin sieht Papst Benedikt als eine Möglichkeit, die die moderne naturwissenschaftliche Vernunft in sich selber trägt (vgl. a.a.O., S. 30). Es geht um die Rückfrage nach den Voraussetzungen naturwissenschaftlichen Arbeitens. Dazu der Papst:

„Sie (i.e. die naturwissenschaftliche Vernunft) muss die rationale Struktur der Materie wie die Korrespondenz zwischen unserem Geist und den in der Natur waltenden rationalen Strukturen ganz einfach als Gegebenheit annehmen, auf der ihr methodischer Weg beruht. Aber die Frage, warum dies so ist, die besteht doch und muss von der Naturwissenschaft weitergegeben werden an andere Ebenen und Weisen des Denkens – an Philosophie und Theologie“ (a.a.O. S. 30f). Besonders die Theologie schöpft aus einer Erkenntnisquelle, „der sich zu verweigern eine unzulässige Verengung unseres Hörens und Antwortens wäre“ (a.a.O., S. 31).

3. Wege ins Weite der Vernunft

Zehn Tage vor der Regensburger Vorlesung traf sich in Castel Gandolfo der „Schülerkreis“ mit seinem Meister und Lehrer zum jährlichen Austausch. Papst Benedikt hatte sich selber das Thema „Schöpfung und Evolution“ gewünscht. Die Debatten, die mein „opinion editorial“ in der New York Times ausgelöst hatte, sah er als providentiell, um das Thema wieder verstärkt öffentlich zu machen (vgl. Schöpfung und Evolution, S. 149). Vier Referate wurden in seiner Anwesenheit gehalten: die Referenten waren Prof. Peter Schuster, Prof. P. Paul Erbrich, Prof. Robert Spaemann und ich selber. Die persönlichen Stellungnahmen von Papst Benedikt sind im Symposiumsband dokumentiert und geben uns einen lebhaften Einblick in sein Denken über unser Thema. Einige wichtige Punkte dieser Stellungnahme muss ich hier referieren.

Da ist zuerst die klare Abgrenzung gegen den sogenannten „Kreationismus“, „der sich der Wissenschaft grundsätzlich verschließt“ (a.a.O., S. 150). Es muss klar sein, dass für die katholische Sicht keine wissenschaftlichen Erkenntnisse ein Hindernis für den Glauben darstellen.

Papst Benedikt erinnert aber auch daran, dass die Evolutionstheorie ihre Lücken hat, die sie nicht überspielen darf, und dass sie sich nicht Fragen verschließen darf, die über ihre methodischen Möglichkeiten hinausgehen. Denn die Evolutionstheorie impliziert Fragen, „die der Philosophie zugeordnet werden müssen und von sich aus über den Innenbereich der Naturwissenschaften hinausführen“ (a.a.O., S. 150).

Ich erlaube mir, Ihnen hier ein längeres Zitat aus dem Diskussionsbeitrag von Papst Benedikt wiederzugeben. Wie wir es so oft mit ihm erlebt haben, sind seine frei gesprochenen Wortmeldungen immer wieder von faszinierender Klarheit, druckreif und sprachlich formvollendet. Ich zitiere:

„Die Naturwissenschaft hat große Dimensionen der Vernunft erschlossen, die bisher nicht geöffnet waren, und uns dadurch neue Erkenntnisse vermittelt. Aber in der Freude über die Größe ihrer Entdeckung tendiert sie dazu, uns Dimensionen der Vernunft wegzunehmen, die wir weiterhin brauchen. Ihre Ergebnisse führen zu Fragen, die über ihren methodischen Kanon hinausreichen, sich darin nicht beantworten lassen. Dennoch sind es Fragen, die die Vernunft stellen muss und die nicht einfach dem religiösen Gefühl überlassen werden dürfen. Man muss sie als vernünftige Fragen sehen und dafür auch vernünftige Weisen des Behandelns finden.

Es sind die großen Urfragen der Philosophie, die auf neue Weise vor uns stehen: die Frage nach dem Woher und Wohin des Menschen und der Welt. Dabei ist mir zweierlei neuerlich bewusst geworden, was auch die drei folgenden Referate verdeutlicht haben: Es gibt zum einen eine Rationalität der Materie selbst. Man kann sie lesen. Sie hat eine Mathematik in sich, sie ist selbst vernünftig, selbst wenn es auf dem langen Weg der Evolution Irrationales, Chaotisches und Zerstörerisches gibt. Aber als solche ist Materie lesbar. Zum anderen scheint mir, dass auch der Prozess als Ganzes eine Rationalität hat. Trotz seiner Irrungen und Wirrungen durch den schmalen Korridor hindurch, in der Auswahl der wenigen positiven Mutationen und in der Ausnutzung der geringen Wahrscheinlichkeit, ist der Prozess als solcher etwas Rationales. Diese doppelte Rationalität, die sich wiederum unserer menschlichen Vernunft korrespondierend erschließt, führt zwangsläufig zu einer Frage, die über die Wissenschaft hinausgeht, aber doch eine Vernunftfrage ist: Woher stammt diese Rationalität? Gibt es eine ursprunggebende Rationalität, die sich in diesen beiden Zonen und Dimensionen von Rationalität spiegelt. Die Naturwissenschaft kann und darf darauf nicht direkt antworten, aber wir müssen die Frage als eine vernünftige anerkennen und es wagen, der schöpferischen Vernunft zu glauben und uns ihr anzuvertrauen“ (Schöpfung und Evolution, S. 151f).

Ich denke, hier hat Papst Benedikt in wenigen Sätzen das Wesentliche zusammengefasst, was es zur Debatte, die uns beschäftigt, zu sagen gibt.

Wieso ist die Materie „lesbar"? Wieso hat der ganze Prozess der Evolution etwas Rationales? Woher stammt diese Rationalität? Diesen Fragen darf die Vernunft nicht ausweichen, will sie sich nicht selber aufgeben, wie ich, Papst Johannes Paul II. zitierend, in meinem New York Times-Artikel sagte. Es wäre aber ein Fehler, zu erwarten, dass die Naturwissenschaften mit ihrer Methode auf diese Fragen selber Antworten geben wollten. Das ist wohl der methodische Fehler der „Intelligent-Design-Schule". Sie stellen die richtige Frage: Woher kommt das evidente *design* in der Natur? *„Finding design in nature"* war der Titel meines umstrittenen „op-eds". Nicht die naturwissenschaftlich arbeitende Forschung findet das *design* in der Natur. Wohl aber der über seine Forschung nachdenkende *Mensch*, der sich frägt, was es bedeutet, dass die Materie ihm „vernünftig" auf seine Fragen antwortet, und der darüber nachsinnt, warum seine Vernunft diese Antworten vernehmen kann.

4. Die Evolutionstheorie als „erste Philosophie"

Im Jahre 1999 hielt Kardinal Ratzinger eine vielbeachtete Vorlesung an der Sorbonne in Paris. Sie gehört zweifellos zu den großen Reden seiner langen Laufbahn. Ihr Thema hat auf den ersten Blick gar nichts mit unserem Thema zu tun. Der Kardinal wagte es, sozusagen im „Tempel der Aufklärung", der Sorbonne, die Frage nach der Wahrheit des Christentums zu stellen: „Das Christentum – die wahre Religion?" (in: Glaube, Wahrheit, Toleranz. Das Christentum und die Weltreligionen, Freiburg 2003, S. 131 – 147).

Als ein Beispiel für die Skepsis gegenüber dem Wahrheitsanspruch des Christentums nennt Kardinal Ratzinger die Evolutionstheorie, die, so scheint es, die Schöpfungslehre als überholt erscheinen läßt (S. 132). Der allgemeine Relativismus scheint für die christliche Glaubenslehre von einer geschaffenen, von Gott gedachten und gewollten Welt nur mehr symbolische Bedeutung übrigzulassen. Das Christentum hat sich nicht damit abgefunden, *ein* symbolischer Ausdruck neben anderen für den – nie erreichbaren – Sinn der Welt zu sein, sozusagen ein Mythos unter anderen, ohne besonderen Wahrheitsanspruch. Das Christentum verstand sich als vernünftig, und Kraft seiner Vernünftigkeit allen Menschen zugänglich.

„Rückschauend können wir sagen, dass die Kraft des Christentums, die es zur Weltreligion werden ließ, in seiner Synthese von Vernunft, Glaube und Leben bestand", so fasst der Kardinal den Rückblick auf die weltweite

Ausbreitung des Christentums zusammen, um dann zur kritischen Frage zu kommen: „Warum überzeugt diese Synthese heute nicht mehr? Warum gelten heute im Gegenteil Aufklärung und Christentum als einander widersprechend, ja, ausschließend?“ (a.a.O., S. 141).

Ich denke, dass die nun folgenden Ausführungen des Kardinals gerade im Blick auf das bevorstehende Darwin-Jubiläum (2009) von großer Bedeutung sind, da sie den großen geistesgeschichtlichen Rahmen abstecken, in dem die heutigen Debatten stattfinden. Kardinal Ratzinger sieht den jüdisch-christlichen Schöpfungsglauben als ein großes Potential der Aufklärung, als Emanzipation vom Mythos. Gott ist nicht die Natur, sondern der Schöpfer der Natur. Da sie geschaffen ist, spricht sie vom Schöpfer, spricht der Schöpfer durch sie. Durch die Schöpfung spricht er den Menschen, sein Geschöpf an, gibt er ihm Wegweisung, zeigt ihm, was er tun soll. In der Neuzeit verblasst der metaphysische Horizont der Welt. Joseph Ratzinger sieht die Evolutionstheorie als einen Teil jener geistesgeschichtlichen Bewegung, die „die durch das christliche Denken vollzogene Trennung von Physik und Metaphysik“ immer mehr zurücknehmen will. „Alles soll wieder ‚Physik‘ werden“.

„Immer mehr hat sich die Evolutionstheorie als der Weg herauskristallisiert, um Metaphysik endlich verschwinden, die ‚Hypothese Gott‘ (Laplace) überflüssig werden zu lassen und eine streng ‚wissenschaftliche‘ Erklärung der Welt zu formulieren“ (a.a.O., S. 143f).

Kardinal Ratzinger hatte bereits 1985, anlässlich des römischen Symposiums über „Evolutionismus und Christentum“ (Weinheim 1986) darauf hingewiesen, dass „Evolution“ heute, „über ihren naturwissenschaftlichen Gehalt hinaus zu einem Denkmodell erhoben worden ist, das mit dem Anspruch auf Erklärung des Ganzen der Wirklichkeit auftritt und so zu einer Art von ‚ersten Philosophie‘ geworden ist“ (a.a.O., S. VII). Alles, auch Erkenntnis, Ethos, Religion, sollen aus dem Generalschema Evolution abgeleitet werden. Im Grunde gehe es um „die Rückführung aller Realität auf Materie“ (a.a.O., S. VIII).

Im Rahmen dieses Totalitätsanspruchs des Erklärungsmodells „Evolution“ „muss der christliche Gottesgedanke als unwissenschaftlich gelten“(Sorbonne-Rede, a.a.O., S. 144).

Im Symposium von 1985 stellte Kardinal Ratzinger unmissverständlich fest: „Auf keinen Fall sollte der Anschein eines neuen Streits zwischen Naturwissenschaft und Glaube entstehen, um den es in der Tat in diesem Gespräch in keiner Weise geht“ (a.a.O., S. VIII). Es macht dem Glauben keine Schwierigkeit, „die naturwissenschaftliche Hypothese Evolution sich gemäß ihren eigenen Methoden ruhig entfalten zu lassen“ (ebd.).

Nicht die exakte wissenschaftliche Arbeit an der Evolutionstheorie ist das Problem, sondern deren „Umfunktionierung" in ein philosophisches Erklärungsmodell mit Totalanspruch. Und der Kardinal fügt hinzu: „Die eigentliche Gesprächsebene ist die des philosophischen Denkens: Wo Naturwissenschaft zur Philosophie wird, ist es die Philosophie, die sich mit ihr auseinandersetzen muss. Nur so stehen die Gesprächsfronten richtig; nur so bleibt deutlich, worum es sich handelt: um einen rationalen philosophischen Disput, der auf die Sachlichkeit rationaler Erkenntnis abzielt, nicht um einen Einspruch von Glaube gegen Vernunft" (a.a.O., S. VIII).

Ähnlich ist die Schlussfolgerung der Rede an der Sorbonne: „Jedenfalls führt an dem Disput über die Reichweite der Evolutionslehre als erster Philosophie und über die Ausschließlichkeit positiver Methode als einziger Weise von Wissenschaft und Rationalität kein Weg vorbei. Dieser Disput muss daher von beiden Seiten sachlich und hörbereit in Angriff genommen werden, was bisher nur in geringem Maß geschehen ist" (a.a.O., S. 144).

Papst Benedikt bringt hier zum Ausdruck, was wohl in der öffentlichen Debatte meist übersehen wird: Die Alternative lautet doch nicht: entweder Kreationismus oder Evolutionismus! Sie heißt auch nicht: Entweder Glaube oder Wissenschaft! Es geht vielmehr um *die philosophische Frage*, was denn Reichweite und Grenzen der streng quantitativen Methode der Naturwissenschaften sei: Zwischen Glauben und Naturwissenschaften bedarf es als vermittelnder Instanz der Philosophie. Die Philosophie ist gefragt, um Grenzen der naturwissenschaftlichen Methoden und ihrer Reichweite zu formulieren, um Grenzüberschreitungen aufzudecken, um Verengungen des Vernunftbegriffs zu öffnen. Eine gute Philosophie der Natur kann helfen, die heute auf beiden Seiten drohenden Fundamentalismen zu vermeiden, den religiösen und den wissenschaftlichen.

5. Im Anfang war das Wort

Aber auch Philosophien haben ihre Grenzen, gerade wenn es um die letzten Fragen geht. Papst Benedikt hat das oft angesprochen. In der Sorbonne-Rede sagt er: „Letzten Endes geht es um eine Alternative, die sich bloß naturwissenschaftlich und im Grunde auch philosophisch nicht mehr auflösen lässt. Es geht um die Frage, ob die Vernunft bzw. das Vernünftige am Anfang aller Dinge und auf ihrem Grunde steht oder nicht. Es geht um die Frage, ob das Wirkliche aufgrund von Zufall und Notwendigkeit (…), also aus dem Vernunftlosen entstanden ist, ob also die Vernunft ein zufälliges Nebenprodukt des Unvernünftigen und im Ozean des Unvernünftigen letztlich auch bedeutungslos ist, oder ob wahr bleibt, was die Grundüberzeugung des christlichen Glaubens und seiner Philosophie bildet: In principio erat Verbum – am Anfang aller Dinge steht die schöpferische Kraft der Vernunft. Der christliche Glaube ist heute wie damals die Option für die Priorität der Vernunft und des Vernünftigen. Diese Letztfrage kann nicht mehr, wie schon gesagt, durch naturwissenschaftliche Argumente entschieden werden, und auch das philosophische Denken stößt hier an seine Grenzen. In diesem Sinn gibt es eine letzte Beweisbarkeit der christlichen Grundoption nicht. Aber kann eigentlich die Vernunft auf die Priorität des Vernünftigen vor dem Unvernünftigen, auf die Uranfänglichkeit des Logos verzichten, ohne sich selber aufzugeben?“ (a.a.O., S. 146).

Damit ist wohl die entscheidende Frage gestellt. Joseph Ratzinger hat sie bei vielen Anlässen immer neu formuliert. Seine Äußerungen zu unserem Thema sind zahlreich, und wir konnten hier nur eine kleine Auswahl bieten. Zu Joseph Ratzinger gehört neben der großen begrifflichen Klarheit immer auch ein sehr lebensnaher, existentieller Zugang zu den Fragen, die er behandelt. Diese enge Verbindung von hoher Intellektualität, tiefer Frömmigkeit und großer Lebensnähe macht wohl auch den anhaltenden Erfolg seiner Vorlesungen, Vorträge und Predigten aus.

So kann es nicht fehlen, dass ich abschließen auf das hinweise, was Joseph Ratzingers‘, Papst Benedikts‘ Äußerungen zum Thema „Evolution und Schöpfung“ im tiefsten bestimmt: der Logos, der im Anfang war und der alles trägt und vernünftig macht, ist untrennbar von der Liebe: „Der Logos erschien nicht nur als mathematische Vernunft auf dem Grund aller Dinge, sondern als schöpferische Liebe bis zu dem Punkt hin, dass er Mit-Leiden mit seinem Geschöpf wird“. Dieser Logos ist Mensch geworden und hat in seiner Auferstehung von den Toten „die größte Mutation“ in der langen Geschichte der Evolution des Lebens vollzogen, wie Papst Benedikt in seiner ersten Osterpredigt sagte (15.4.2006); dieser Logos ist selber Liebe, und wenn dieser Logos am Anfang von allem steht und auch am Ende aller Dinge, dann ist die Liebe der tiefste Grund von allem. Oder, mit den Worten von Papst Benedikt: „Die wahre Vernunft ist die Liebe, und die Liebe ist die wahre Vernunft. In ihrer Einheit sind sie der wahre Grund und das Ziel alles Wirklichen“ (a.a.O., S 147).

POPE BENEDICT XVI
ON 'CREATION AND EVOLUTION'

CHRISTOPH CARD. SCHÖNBORN

Honoured Mr President,
Your Eminences and Excellencies, Ladies and Gentlemen,

I am grateful for having been entrusted with the privilege of giving you a little insight into the thinking of Pope Benedict XVI, of Professor Joseph Ratzinger, on the topic of 'Evolution and Creation'. The great theologian in the Chair of Saint Peter has often and early on commented on this subject. In my foreword to the records of the colloquium of his *Schülerkreis* (circle of former graduates), which took place at Castel Gandolfo in autumn 2006, I already compiled in chronological order some of the most important statements of the present Pope (*Creation and Evolution. A Conference with Pope Benedict XVI in Castel Gandolfo*, San Francisco 2008, pp. 7-23).[1] Today, it is a matter of putting these statements in some systematic order and of structuring them thematically. In doing so, their importance is to be made more clearly visible, since it reaches far beyond the individual question of the theory of evolution.

1. The Regensburg Lecture and its Lasting Challenge

One day after September 11, 2006, Pope Benedict gave a lecture at his former academic place of activity, the University of Regensburg, delivering a speech which had far-reaching ramifications. First, there was that

[1] Original German edition: 'Schöpfung und Evolution. Eine Tagung mit Papst Benedikt XVI. in Castel Gandolfo, Augsburg 2007'.

great uproar in large parts of the Islamic world, with riots culminating in the killings of Christians. This was followed, however, by a positive wave of readiness to engage in dialogue shown by certain circles of Islam, which has lasted up to date, and which was particularly articulated in the letter to the Pope and the heads of the Christian churches signed by 138 Islamic scholars addressing the joint responsibility of Christians and Muslims for peace and justice in the world.

In the meantime, however, it has got around that the Regensburg lecture was not primarily directed at the topic of Islam, but rather at the question of how religion and reason are mutually interrelated. The quote rendered famous by the Byzantine emperor Manuel II indicates that it is 'contrary to reason', that it is not 'syn logô', to spread one's faith through violence. Forced religious conversion is contrary to reason and *therefore contrary to God's nature.*

With this statement by the emperor the question concerning the relationship between reason and religion shall be addressed. It is *this* issue that the Pope wanted to raise in his Regensburg lecture. And this is also the topic of my exposition. Pope Benedict views the debate on the theory of evolution and evolutionism in this very light. As we shall see, for him the decisive question is whether in the beginning there was the logos or un-reason. With reference to the prologue of the Gospel of John the Pope says:

'*In the beginning was the logos*. This is the very word used by the emperor: God acts *syn logo*, with *logos*. *Logos* means both reason and word – a reason which is creative and capable of self-communication, precisely as reason' (The Regensburg Address, paragraph 5).[2]

Does creative reason communicate itself, *as reason?* And is it, by our reason, recognizable as reason? And recognizable not only within the narrow scope of a certain culture, such as the Western occidental one, but in such a way that a dialogue beyond cultural and religious boundaries will become possible? A genuine dialogue of cultures can only be entered into if reason is of such breadth that it surpasses the boundaries which all of us inevitably live and think in. It was one quintessential matter of concern of the Regensburg lecture to explore the conditions for the possibility of

[2] English version quoted from the Regensburg Address: 'Faith, Reason and the University. Memories and Reflections', available at: http://www.vatican.va/holy_father/benedict_xvi/speeches/2006/september/documents/hf_ben-xvi_spe_20060912_university-regensburg_en.html. Original German edition: 'Glaube und Vernunft. Die Regensburger Rede, Freiburg 2006'.

a genuine intercultural and interreligious dialogue. It is my impression that some Islamic scholars have understood this challenge in a more explicit way than Western commentators.

But what does this have to do with our topic of 'Creation and Evolution'? The examination of the concept of reason also leads Pope Benedict to the concept of reason as it is used, respectively presupposed, in the natural sciences. In his Regensburg Address, the Pope postulates a kind of 'critique of modern reason from within', not with the intention of 'putting the clock back to the time before the Enlightenment', but of 'broadening our concept of reason and its application' (loc. cit., par. 15).

This self-criticism of modern reason also contains a criticism of the positivistic concept of reason that widely dominates the Western world and that is often deemed to be the specifically scientific concept of reason, too. By comparison with this, Pope Benedict is trying to locate in the preconditions of scientific rationality the very traces of the broader understanding of reason that he has been looking for.

I am aware that these considerations are not the kind found in everyday scientific life, and that there exists a certain aversion towards these fundamental, quasi-metaphysical questions raised here. Quoting Socrates, however, Pope Benedict says that it would be greatly detrimental not to raise these questions. Let us therefore venture to raise them. It will certainly be worthwhile!

2. Reducing the Concept of Reason

The main part of the Regensburg lecture is dedicated to the following question: What led to the reduction of the concept of reason, which Pope Benedict sees as a particular sign of modern times?

The first reduction is understood to have arrived with *nominalism*. It has moved the transcendence of God so far beyond reach 'that our reason, our sense of the true and good, are no longer an authentic mirror of God, whose deepest possibilities remain eternally unattainable and hidden behind his actual decisions' (loc. cit., par. 7). God's creative reason no longer speaks through his works. The latter are arbitrary positings that do not reflect God's wisdom and reason; they are unfathomable arbitrary positings of divine omnipotence.

During the Reformation, faith and reason are, consequently, uncoupled. Faith relies solely on Scripture (*sola scriptura*), while reason is 'secularized'. The latter is more and more restricted to what is deemed 'strictly scientific' and to that which corresponds to the canon of modern science. 'The specifically human questions about our origin and destiny, the questions raised by religion and ethics, then have no place within the purview of collective reason as defined by "science" […] and must thus be relegated to the realm of the subjective' (loc. cit., par. 13).

Pope Benedict sees in this reduction a real danger for both sides; religion is threatened by irrational 'pathologies' (loc. cit., par. 13); science will suffer damage, if the 'questions of religion and ethics no longer concern it' (loc. cit., par. 13).

The answer to these 'pathologies of religion and reason' (loc. cit., par. 13) does not lie in the reduction of reason, but in the already cited 'broadening [of] our concept of reason and its application' (loc. cit., par. 15). This requires the overcoming of the 'self-imposed limitation of reason to the empirically falsifiable' (loc. cit., par. 15).

The path to this engagement of the 'whole breadth' of reason is regarded by Pope Benedict as a possibility that is intrinsic to modern scientific reason (cf. loc. cit., par. 16). It is a matter of reversion to an understanding of the requirements for scientific study. The Pope says on this:

'Modern scientific reason quite simply has to accept the rational structure of matter and the correspondence between our spirit and the prevailing rational structures of nature as a given, on which its methodology has to be based. Yet the question why this has to be so is a real question, and one which has to be remanded by the natural sciences to other modes and planes of thought – to philosophy and theology' (loc. cit., par. 16). Theology in particular draws upon a source of knowledge, 'and to ignore it would be an unacceptable restriction of our listening and responding' (loc. cit., par. 16).

3. Ways to Engage the Breadth of Reason

Ten days prior to the Regensburg lecture, the members of the *Schülerkreis* met with their master and teacher at Castel Gandolfo for the annual scholarly exchange. Pope Benedict himself had wished the topic to be 'Creation and Evolution'. He regarded the debates triggered by my 'opinion editorial' in the New York Times as providential for a new and reinforced public review of the topic (cf. *Creation and Evolution*, p. 161). Four presentations were given in his presence, the speakers being Prof. Peter Schuster, Prof. P. Paul Erbrich, Prof. Robert Spaemann and myself.

Pope Benedict's personal comments are documented in the symposium volume, giving us a vivid insight into his thoughts on our topic. I shall here have to refer to some key issues in these comments.

First, there is the clear dissociation of the so-called 'creationism that is closed off from science as a matter of principle' (loc. cit., p. 161). It must be clear that to the Catholic point of view no scientific findings will present an obstacle to faith.

Yet, Pope Benedict also reminds us that the theory of evolution has its gaps which it must not make light of, and that it must not close its eyes to questions going beyond its methodical possibilities. For the theory of evolution implies questions 'that must be assigned to philosophy and that in and of themselves lead beyond the internal scope of the natural sciences' (loc. cit., p. 162).

I am taking the liberty to render to you, at this point, an extended quote of Pope Benedict's contribution to the discussion. As we have so often witnessed with him, his freely spoken statements are, time and again, of fascinating clarity, well-worded and linguistically perfect in form. I quote:

> [...] science has opened up major dimensions of reason that previously had not been accessible and have thereby provided us with new knowledge. But in its joy over the greatness of its discoveries, it tends to confiscate dimensions of our reason that we still need. Its findings lead to questions that reach beyond its methodological principles and cannot be answered within science itself. Nevertheless these are questions that reason must ask itself and that must not simply be left to religious feeling. We must look at them as reasonable questions and also find reasonable ways of dealing with them.
>
> These are the great perennial questions of philosophy, which confront us in a new way: the question of where man and the world come from and where they are going. Apropos of this, I recently became aware of two things that the three following lectures also made clear: There is, in the first place, a rationality of matter itself. One can read it. It has mathematical properties; matter itself is rational, even though there is much that is irrational, chaotic, and destructive on the long path of evolution. But matter per se is legible. Secondly, it seems to me that the process, too, as a whole, has a rationality about it. Despite its false starts and meanderings through the narrow corridor, the process as such is something rational in its selection of the few positive mutations and in its exploitation of the minute probabilities. This twofold rationality,

> which in turn proves to correspond to our human reason, unavoidably leads to a question that goes beyond science yet is a reasonable question: Where does this rationality originate? Is there an originating rationality that is reflected in these two zones and dimensions of rationality? Science cannot and must not answer this question directly, but we should acknowledge that the question is a reasonable one and dare to believe in the creative Reason and to entrust ourselves to It (loc. cit., p. 163f).

I believe that Pope Benedict has here, in few sentences, captured the essence of what there is to say on the debate that we are engaged in.

Why is matter 'legible'? Why does the whole process of evolution have something rational? Where does this rationality originate? Reason must not avoid these questions if it does not want to abdicate itself, as I said in my New York Times article by quoting Pope John Paul II. It would be a mistake, however, to expect the natural sciences to be eager, by way of their method, to provide their own answers to these questions. This, perhaps, is the methodical mistake of the 'school of intelligent design'. They are asking the right question: Where does this evident *design* in nature originate? '*Finding design in nature*', that was the title of my disputed 'op-ed'. It is not scientifically operating research that finds *design* in nature. On the contrary, however, it will be found by *man* reflecting on his research, who wonders about the meaning of matter giving him 'reasonable' answers to his questions, and who ponders the question why his reason is capable of perceiving these answers.

4. Theory of Evolution as a 'First Philosophy'

In the year 1999, Cardinal Ratzinger gave a much-noticed lecture at the Sorbonne in Paris. It undeniably belongs to the great speeches of his long career. Its subject, at a first glance, has nothing to do at all with our topic. At the Sorbonne, in the 'temple of enlightenment', so to speak, the Cardinal dared pose the question about the truth of Christianity: 'Christianity – The True Religion?' (in: *Truth and Tolerance. Christian Belief and World Religions*. San Francisco 2004, pp. 162-183).[3]

[3] Original German edition: 'Glaube, Wahrheit, Toleranz. Das Christentum und die Weltreligionen, Freiburg 2003, pp. 131-147'.

Cardinal Ratzinger names the theory of evolution as one example of the scepticism towards the truth claim of Christianity, since it makes – as it seems – the theory of creation appear obsolete (cf. loc. cit., p. 163). General relativism seems to leave nothing but symbolic meaning for the Christian theology of a created world according to God's design and intent. Christianity has not resigned itself to being *one* symbolic expression among others for the – never attainable – significance of the world, a myth among others, as it were, without any particular claim to truth. Christianity has understood itself as reasonable, and due to its reasonableness accessible to all people.

'Looking back, we may say that the power of Christianity, which made it into a world religion, consisted in its synthesis of reason, faith, and life'; this is how the Cardinal summarizes the retrospective view of the worldwide expansion of Christianity, in order to then raise the critical question: 'Why is this synthesis no longer convincing today? Why, on the contrary, are enlightenment and Christianity regarded today as contradicting each other or even as mutually exclusive?' (loc. cit., p. 175).

I believe that the following deliberations by the Cardinal are of great importance especially in view of the approaching Darwin anniversary (2009), since they define the great scope of intellectual history that hosts the debates of today. Cardinal Ratzinger regards the Judaeo-Christian belief in creation as a great potential for enlightenment, as an emancipation from myth. God is not nature, but the Creator of nature. As it has been created, it speaks of the Creator and the Creator speaks through it. Through creation He speaks to man, His creature, shows him the way and shows him what to do. In modern times the metaphysical horizon of the world is fading. Joseph Ratzinger sees the theory of evolution as part of that movement of intellectual history which wishes to steadily cancel 'the separation of physics from metaphysics achieved by Christian thinking'. 'Everything is to become "physics" again. The theory of evolution has increasingly emerged as the way to make metaphysics disappear, to make "the hypothesis of God" (Laplace) superfluous, and to formulate a strictly "scientific" explanation of the world' (loc. cit., p. 178).

As early as 1985, Cardinal Ratzinger had, on the occasion of the Roman symposium on 'Evolutionism and Christianity' (Weinheim 1986), pointed out that 'evolution' has today 'been exalted above and beyond its scientific content and made into an intellectual model that claims to explain the whole of reality and thus has become a sort of "first philosophy"' (quoted in: *Creation and Evolution*, p. 9). Everything, even knowledge, ethics, religion, is to be derived from the general scheme of evolution. It is ultimately about 'the derivation of all reality from matter' (loc. cit., p. 10).

In the context of this totalitarian claim of the explanatory model of 'evolution', 'the Christian idea of God is necessarily regarded as unscientific' (Sorbonne Address in: *Truth and Tolerance*, p. 178).

In the symposium of 1985, Cardinal Ratzinger unmistakably stated: 'In no case should the appearance of a new dispute between natural science and faith be created, because in fact that is not at all what this dialogue is about' (quoted in: *Creation and Evolution*, p. 10). It does not pose a problem to faith to allow 'the scientific hypothesis of evolution to develop in peace according to its own methods' (*ibid*.).

It is not the exact scientific work on the theory of evolution that is the problem, but its 'remodelling' into a philosophical explanatory model with a claim of totality. And the Cardinal adds: 'The real level of discourse is that of philosophical thought: when natural science becomes a philosophy, it is up to philosophy to grapple with it. Only in that way is the contentious issue framed correctly; only then does it remain clear what we are dealing with: a rational, philosophical debate that aims at the objectivity of rational knowledge, and not a protest of faith against reason' (quoted in: *Creation and Evolution*, p. 10f.).

His speech at the Sorbonne ends with a similar conclusion: 'There is at any rate no getting around the dispute about the extent of the claims of the doctrine of evolution as a fundamental philosophy and about the exclusive validity of the positive method as the sole indicator of systematic knowledge and of rationality. This dispute has therefore to be approached objectively and with a willingness to listen, by both sides – something that has hitherto been undertaken only to a limited extent' (loc. cit., p. 179).

Pope Benedict here voices what seems to be mostly overlooked in the public debate: The alternative does not read: Either creationism or evolutionism! Nor does it read: Either faith or science! It is rather about *the philosophical question* as to the scope and the limits of the strictly quantitative method of the natural sciences: Philosophy is required as an entity mediating between faith and the natural sciences. Philosophy is sought in order to formulate the limits of the scientific methods and their scope, in order to reveal boundary crossings, in order to open up any narrowed concepts of reason. A good philosophy of nature can help avoid the fundamentalisms imminent on both sides today, i.e. the religious as well as the scientific ones.

5. In the Beginning was the Word

Yet, philosophies, too, have their limits, particularly if it is a matter of posing the ultimate questions. Pope Benedict has often addressed this issue. In his Sorbonne speech he says: 'In the end this concerns a choice that can no longer be made on purely scientific grounds or basically on philosophical grounds. The question is whether reason, or rationality, stands at the beginning of all things and is grounded in the basis of all things or not. The question is whether reality originated on the basis of chance and necessity [...], and, thus, from what is irrational; that is, whether reason, being a chance by-product of irrationality and floating in an ocean of irrationality, is ultimately just as meaningless; or whether the principle that represents the fundamental convictions of Christian faith and of its philosophy remains true: "In principio erat Verbum" – at the beginning of all things stands the creative power of reason. Now as then, Christian faith represents the choice in favor of the priority of reason and of rationality. This ultimate question, as we have already said, can no longer be decided by arguments from natural science, and even philosophical thought reaches its limits here. In that sense, there is no ultimate demonstration that the basic choice involved in Christianity is correct. Yet, can reason really renounce its claim to the priority of what is rational over the irrational, the claim that the Logos is at the ultimate origin of things, without abolishing itself?' (loc. cit., p. 180f.).

It seems that, with these words, the decisive question has been posed. Joseph Ratzinger restated it over and over on many occasions. His remarks on our topic are numerous, and we have merely been able to provide a small selection here. Inherent to Joseph Ratzinger, besides his immense conceptual clarity, is always a very true-to-life and existential approach to the questions he addresses. It is perhaps this close interrelation of high intellectuality, deep piety and close bond with real life that account for the sustained success of his lectures, speeches and sermons.

Thus, I shall not conclude without referring to the very thing that most profoundly determines Joseph Ratzinger's, Pope Benedict's statements on the topic of 'Creation and Evolution': This logos, which was in the beginning and which bears everything and makes everything reasonable, is inseparable from love: 'The Logos was seen to be, not merely a mathematical reason at the basis of all things, but a creative love taken to the point of becoming sympathy, suffering with the creature' (loc. cit., p. 182). This logos was made man and, in its resurrection from the dead, underwent ‘the greatest mutation’ in the long history of the evolution of life, as Pope Benedict said in his first Easter Vigil (15 April 2006); this logos itself is love, and if this logos is at the beginning of everything as well as at the end of all things, then love is the most profound reason of everything. Or, using the words of Pope Benedict: ‘[…] the true reason is love, and love is the true reason. They are in their unity the true basis and the goal of all reality’ (loc. cit., p. 183).

DISCUSSION ON CARDINAL SCHÖNBORN'S PAPER

PROF. COLLINS: Thank you for a very thoughtful presentation. When you refer to the realisation that evolution has gaps in its understanding, that, obviously, is a trigger for some people to worry about God being placed in those gaps in a way that narrows God's providence instead of giving God the authorship of all Creation. So I would be curious to understand a little bit more in that reference to gaps in evolution: exactly what sorts of gaps are being referred to.

CARD. SCHÖNBORN: This quotation was part of the Castel Gandolfo debate, where Professor Schuster, the President of the Austrian Academy of Science, spoke himself about the points where the evolution theory still has question marks, and Pope Benedict referred to that in his reply, but it is evident that for him these questions are not the place where he locates the Creator. The Creator is not in the shrinking gaps, he would be shrinking in his place, in his Creation. What Pope Benedict clearly states is that the question of rationability, readability of matter, the question of why is it possible that we can penetrate reality with our research, why nature does give answers, and very precise answers, why there is a correspondence between our intelligence and reality, this is the point where he asks: where does this rationability come from? Can it be the product of irrationality? Can it be the product of a mere random process without any rationality? And, therefore, he affirms, in this second point on rationability, that the overall process of evolution has its own rationality. Despite all the meanders evolution has taken and all the terrible things that have happened in the process of evolution, nevertheless the whole process makes sense. This double rationability of matter and of the whole process is, for him, the place where he asks for the God Creator, and not in the gaps.

PROF. MITTELSTRASS: Obviously, in the centre of, or, one could even say, the framework of Pope Benedict's concept, is the concept of reason. In German, it is *Vernunft*. Now, *Vernunft* is a very difficult term. In German, at least in the Kantian tradition, *Vernunft* is a normative concept, in contrast to *Verstand*, which is a descriptive or explanatory concept. Sometimes, both meanings are part of a more general concept, also called *Vernunft*. In English, the distinction would be between 'reason' and 'understanding', or 'reason' as a general concept, including 'reason' in its narrow (normative) sense and 'understanding'. In its narrow (normative) sense, *Vernunft* (reason) is the subject of philosophy and theology. I understand Pope Benedict as using *Vernunft* (reason) as the general concept emphasising at the same time its normative meaning.

CARD. SCHÖNBORN: I would say that the same difficulty arises in Greek, with Logos: 'En arke en o logos' (Ἐν ἀρχῇ ἦν ὁ λόγος) means 'In the beginning was the word', no, 'was the reason'. Goethe has another interpretation in Faust: 'In the beginning was *Sinn*, meaning'. But in Hebrew it is even stronger: *dabar* means 'word' and 'acting'. We have in English *reason* and *intelligence*, and we have also these two aspects. I think what the Pope insists on is that rationality, the analytic use of reason in the natural sciences is a legitimate and necessary use, but we should not limit reason, intelligence to this limited use. There are other dimensions of intelligence, of reason, however you use the words, that are true understanding, true intelligence, without being scientific, without being quantitative, measurable. The intelligence of the heart, as Pascal said, 'The heart has its reasons', the intelligence of the heart. There is an ethical intelligence which is not accountable with the scientific methodology and, nevertheless, it is true reason. That is mainly the argument: Do not limit the concept of reason, of intelligence, only to that, and his critique of evolutionism, not the theory of evolution, but it is the enlargement of the model of evolution to practically all fields of knowledge, of intelligence. The understanding of the origin of intelligence, in the evolutionary intelligence theory, sociobiology, evolutionary ethics, all these fields are limiting to a model of evolution that is taken from a scientific theory which is probably overexpanded beyond its true limits. I think this is the core critique the Pope has to evolutionism, as, let us say, perhaps ideology.

PROF. ARBER: Just a comment rather than a particular question. Of course, we scientists are aware that one of Charles Darwin's ideas was that some phenotypic advances rendered the life of some living beings easier, that means that they could overgrow the population of their parental forms. This was actually the idea of the natural selection, which is the important part of his theory. One hundred and fifty years ago no one had any idea of how that worked, so the theory had no rational basis, but it was a good idea. Later on, of course, genetics was introduced, again on the basis of differences in phenotypes. The introduced concept of genes was yet absolutely abstract, without knowledge of a material basis for a gene. Almost a century later, the original Darwinism and classical genetics finally became fused into Neo-Darwinism around 1940. It is only in the middle of the 1940s that, from microbiological investigations, it became clear that the basis for the genes are nucleic acids rather than a protein, as it was usually believed. From this knowledge, molecular genetics was then developed, and we are now in a process of fusing molecular genetics with evolutionary biology. Today we have an experimentally validated knowledge of the molecular basis of altered phenotypes: This is a changed nucleotide sequence. So we have to carefully define what we understand under 'theory of evolution'. Are you referring to the original Darwinism, to Neo-Darwinism or to the actual molecular Darwinism? We have also to note that a theory is, by definition, never a final proof of something that we study. Even today, there are a number of open questions, but I am convinced that, despite all this progress, scientific approaches will never prove whether God is behind evolution or not. I fully agree with you that science and spirituality are two different worlds. We should make that quite clear to the general public.

PROF. PHILLIPS: My question, I think, in a sense synthesises the questions and comments that a number of people have made, but I want to ask it to establish more clarity about your presentation. You mentioned several times your controversial article in *The New York Times*, and given the context of that article it is difficult for me to separate my understanding of what you believe from what you believe that Pope Benedict believes. So, I would like you to answer both with respect to your own belief and what you believe the Holy Father believes: It appears to me, from what you have said and from the clarifications given in your answers to the preceding questions, that you would say, given the understanding that no scientific theory is ever complete, that the theory of biological evolution gives a correct description of the way in which biological organisms have come to be the way they are. But, on the other hand, you believe that extension of the concepts of biological evolution to other areas, such as social or moral evolution, might very well be completely inappropriate and that an unthinking extension of what has been learned in biological evolution to other areas is not something we should take for granted. That is one point. Another point is that evolution as a point of view, or science in general as a point of view, is not the whole story when it comes to human understanding. Science has its place, but it is not a complete story of what human beings consider quite rightly to be important in their lives. You talked about 'evolutionism', but one could just as easily say 'scientism' as a point of view, meaning the view that science gives a complete description of everything that is important. You would say, I think, that such a viewpoint is not correct. So what I am wondering is: have I given, in this short discourse, an accurate description of your belief and what you believe Pope Benedict believes?

CARD. SCHÖNBORN: Certainly, I do not pretend to present him exactly. I personally would be sceptical if a scientific theory affirmed that it is really the exact description of what happened. Especially when it is an historical theory as evolution theory is. We did not witness the appearance and disappearance of the dinosaurs. So that is my first question. The second point is the application of the evolution model to other fields like social biology, evolutionary ethics, evolutionary intelligent theory. All these applications are legitimate under one condition: that they do not pretend to be an exhaustive explanation, to say that ethical behaviour or intelligence is only and exclusively the product of an evolutionary process. I would say that evolution theory can shed light on the phenomenon of intelligence, of its genesis, maybe, that is legitimate, but not to make it an exhaustive explanation. I fully agree that the basic question is the choice between true science and scientism, and scientism is certainly an overexpansion of what, within the limits of science, is legitimate and exact and precise. Scientism is the pretension to explain more than science can explain. So I think, in this sense, what Dawkins actually does is not science, it is his own belief, but he does not do good to science with what he does.

PROF. PHILLIPS: So, to return to the question you put to me, as to whether I can say that the modern theory of evolution gets everything right, I tried to preface my remarks by saying, 'with the understanding that no scientific theory can be said to be completely right'. Do you believe that, given that understanding, evolution has it pretty much right or do you believe there are serious problems with the theory of biological evolution?

CARD. SCHÖNBORN: Well, I am not a scientist, I have only questions to scientists. For instance, Professor Schuster in his talk in Castel Gandolfo admitted that the classical theory of the little steps of evolution is no longer valid. He said that evolution theory today needs to admit jumps, and not step by step. This is a big change in the scientific theory. He said that this is a deficiency of the traditional Darwinian or Neo-Darwinian theory. The famous Austrian Nobel prize-winner, Konrad Lorenz, spoke about 'fulguration', evolutionary steps are fulgurations.

PROF. ARBER: Just one word. For a relatively long time, when it was seen that mutations are on the DNA, one looked at very local changes, nucleotide substitutions and so on. Many of these theories, also Schuster's, are based on only that as an evolutionary strategy. We know today that DNA segments can be rearranged internally and DNA segments can be acquired from other living beings. This can be the source of these sudden changes of phenotypes, although this possibility has, so far, not been generally validated.

PROF. WOLTERS: I would like to ask whether you still hold the position you took at the Castel Gandolfo meeting, saying there that relying on random variation on natural selection was not science but ideology. I am just quoting.

CARD. SCHÖNBORN: The quotation, sorry, is not exact. I said, 'to rely *exclusively* on that'.

PROF. WOLTERS: What else should a biologist rely on?

CARD. SCHÖNBORN: I did not speak about what scientific methodology can explain within its limits but to pretend that this is all that we can say about reality, this would be not science, but ideology, if science pretends to explain matters that are not in the field of science. That was my intention. I admit it was a little bit rough in the expression.

PROF. ZICHICHI: I would like to go back to the meaning of reason and the origin of reason. I think the importance of calling the attention of modern culture on reason as done by Benedict XVI is twofold: one is the meaning of reason, the other is its origin. We are the only form of living matter endowed with this property called reason. Can this be proved? The answer is yes. In fact we are the only form of living matter which has invented permanent collective memory, better known as *written language*, rigorous logic, the most rigorous being *mathematics* and, out of all possible logics, *science*. The existence of Language, Logic and Science is due to the existence of Reason. I have discussed in my lecture why bringing Reason at the centre of modern culture is in synthony with the frontiers of our scientific achievements. The principal scientific questions raised by the Cardinal were taken up in my paper, 'Rigorous Logic in the Theory of Evolution'. I pointed out that the most advanced frontier of scientific knowledge implies that three fundamental transitions (or leaps) must have taken place for the universe to exist as it is, endowed with the properties of life and reason. The question of 'intelligent design' has to be investigated with reference to these three leaps.

The first fundamental leap is the famous Big Bang which describes how from a vacuum the universe, which now consists of 10^{82} protons, neutrons and electrons, began to evolve. This is Big Bang-1: the transition from a vacuum to inert matter. Big Bang-2 deals with the problem of how to describe the transition from inert matter to living matter. Big Bang-3 deals with the transition from living matter without 'reason' to living matter endowed with 'reason'. It is thanks to Big Bang-3 that we are able to discuss Big Bang-2 and Big Bang-1. The fact that out of the innumerable number of different forms of living matter there is only one endowed with the property called 'reason' needs to be explained in detail.

At present only Big Bang-1 is based on the Galilean scientific method, i.e. using experimental reproducible results and mathematical rigour for their description. Big Bang-2 and Big Bang-3 are below the third level of Galilean science.

In my paper I pointed out that the basic message of Galilean science is that a 'fundamental logic' governs all forms of inert and living matter. This 'fundamental logic' is based on the three fundamental forces of nature and three families of elementary particles. The three forces are: the electroweak, the subnuclear-strong and the gravitational. The three families of elementary particles consist of six quarks and six leptons. This fundamental logic started to be discovered four centuries ago by Galileo Galilei. Those who claim that this logic is not there are in conflict with science and its most advanced achievements.

One must recognise that man is not the author of physical or biological laws but he alone discovers them. If a fundamental logic exists the Author of this logic must exist too. Atheistic culture claims that the Author is not there, but no one is able to prove, using the Galilean method, that this is the case.

The reason why it is not enough to be intelligent to understand this fundamental logic was discovered by Galileo Galilei. He pointed out that the Being who created the world is more intelligent than all of us. This is why we need not only to formulate a theoretical hypothesis, using mathematical formalism, but also to carry out experiments if we want to know a correct answer to a given question of a physical or biological nature. To perform a Galilean-type experiment is an act of intellectual humility. In a few words: posing a question only in theoretical terms is not sufficient. For example, the question concerning the existence of the superworld is formulated in a rigorous theoretical way using relativistic quantum string (RQS) theory. Nevertheless, no physicist is able to give a correct answer before experimental results are obtained. Only through the 'experimental results' of four hundred years of Galilean science has man obtained successful 'answers' from the Author of the fundamental logic. Thanks to these 'answers' we now have the RQS theory.

The hypothesis of 'intelligent design' is valid to the extent that it is based on the fact that a fundamental logic exists in the universe, as discovered by the most advanced frontier of science. The existence of this fundamental logic compels us to admit the existence of an Omnipotent Intelligence, superior to the intelligence of man, and on which the world depends: here is how the hypothesis of 'intelligent design' comes in. If I understand his observations, this is the meaning of what Cardinal Schönborn said on 'intelligent design'. And this is correct as far as science and logic are concerned. It is necessary to discern the different epistemological levels of our discussion and the theological and philosophical points of views. We have to extend reason beyond the ideology of naturalistic scientism.

CARD. SCHÖNBORN: I agree with what Professor Zichichi said better than I can express it.

PROF. M. SINGER: I have a question about the use of the word 'gaps'. When you responded to Professor Collins' question, you said that the Pope does not think that the Creator is in the gaps. So, the first point that I want to make is that if that is the case, then you have responded to the word 'gaps' in a very different way *from* what most people in the public consider gaps in evolution's story. I think that the answer might or might not surprise people who are not scientists but who worry about gaps. The second thing is a question, because I think probably I misunderstood what you meant to say when you tried to explain that the Pope would not say that the Creator is in the gaps but that God is in our ability to rationalise what we see in the natural world and to deal with evidence about gaps. If that is what you meant, and perhaps it was not and I misunderstood, then, I am left with the question about where you see God functioning with respect to all the other creatures on the planet, if God is in our ability to rationalise the natural world.

CARD. SCHÖNBORN: I think the difficulty is that in our culture the concept of Creation, of Creator, has become very much shaped by a mechanistic concept. The watchmaker, whether he is blind or not, the watchmaker is more or less the model we have in our minds when we think about the Creator. My impression is, in reading a lot about Darwin and on Darwin and from Darwin, that he had the problem with his religious education that he could imagine only a mechanistic understanding of Creation and he fought against that, rightly, he wanted to overcome a concept of a God that intervenes from time to time to arrange his clock, to repair his clock or to make the passage from one species to the other, and he found this genius, simple theory, of the natural explanation of the origin of species. But what was wrong with him was that he opposed this to the idea of a Creator, because with the concept of Creation, our difficulty is that we have no evidence, no analogy in our experience of God's creating act, because all that we do is changing matter. We work with matter and we change it, we transform it, and so we imagine a God working, transforming. But what is the original, Biblical idea of a God that said and it became, created out of nothing? This is not an exterior work, it is philosophically speaking, giving the being, making it be. As the Bible says: 'He said and it was, and he saw that it was good'. So, I think what we would need is to reform our concept of Creation, which is not an exterior work but a giving that is beyond analogy. It is only in Faith that we can really assume Creation. It is not rational evidence.

PROF. POTRYKUS: Thank you for giving me the possibility to ask a question. First, a brief comment: I am a biologist and I am interested in evolution, and I agree with you that we have a lot of homework to do to fill all the gaps we still have in knowledge about evolution. It is the best possible concept to explain what we know at the moment, but we have to work hard to fill what we do not know. But my question is completely different: where, to the understanding of the Catholic Church, does the soul come into evolution? I remember that one of the most impressive books I read when I was younger was the book by Pierre Teilhard de Chardin, who for me gave an honest attempt to explain how we could imagine that the soul comes into evolution. What is the opinion of the Catholic Church at the moment?

CARD. SCHÖNBORN: I can be short on that, because Pope Benedict today spoke about the immediate creation of the soul as one elementary, essential teaching of the Catholic Church shared also with Judaism. The soul is created by God, if we believe in the existence of the soul. That means that the human being is human from the beginning. There is not a transition, there may be a bodily transition between pre-forms and the appearance of *Homo sapiens sapiens*. Certainly there are many steps, but when it is a human being it is a human being. That, I think, is the core of the teaching, that the soul is created by God. The human person is not a product of nature, it is our body, our genetics, that is a product of nature. But that we are human beings is something different. That is Catholic teaching, and I think it is biblical teaching.

PROF. DEHAENE: Thank you very much, I am enjoying this discussion very much, I think it is very interesting. Your presentation is mostly on the limits of science, and, in particular, you say there are questions that science cannot and should not be asking. I wonder, however, whether this is the correct position from the history of science. If you ask scientists in this room, they will all agree that there are sharp limits to their knowledge. Nevertheless, in the long run, however, science is progressing, and it is historically extremely difficult to decide whether some questions belong to a reserved area that will never be addressable by science. There were times when the rainbow, featuring beautifully in the Bible, was considered outside of science and, of course, it became a cornerstone of Newton's contribution. So I wonder, really, whether we can ever see where science will lead. It is, I think, a very deep nature of science that it creates new ways, new paths into the unknown. I want to ask specifically about the notion of reason, which features very prominently in your presentation. I personally am really not sure whether the origins of reason is a question which is outside of scientific questioning. I will, of course, give some elements about that on Monday but I do not think it is so clear that we are the only species with reason. Of course, it will depend on how you define reason. But if some of our ancestors, who were clearly not human, did not have some form of reason they would not have survived. Reason is an adjustment to the external world, to a large extent, and part of our science is to define steps in the evolution of the reasoning ability. Some of them belong to the human species and some do not belong to the human species. So I wonder how you would react to this type of scientific investigation.

CARD. SCHÖNBORN: First of all, there is certainly no question that science should not be allowed to ask. If I have been understood in that way then I was misunderstood. I am trained with Thomas Aquinas, and in the Middle Ages, which were absolutely not dark compared to the 20th century, at a university in the Middle Ages every question was permitted, there was no exclusion of any question. The question is only whether, with the chosen methodology, you can give the answer to all questions. That I think is the point the Pope made, that, with the limited methodology of natural science, you cannot pretend to give answers to all questions. But, of course, you may ask the question of the origin of intelligence and investigate scientifically as much as you can, but if you give the explanation, 'now I got what intelligence is', and you have a purely materialistic explanation, I would philosophically oppose it and then we would have to make a philosophical debate about whether that is really intelligence or reason.

PROF. ZICHICHI: In my lecture I have given the definition of reason based – as wanted by science – on experimentally observable quantities. Reason is the property which allows living matter to produce Language, Logic and Science.

PROF. DE DUVE: It is a privilege to be the last speaker, especially since what I am going to say is extremely simplistic. I am a little disturbed when I hear people talking about the theory of evolution. This would be like talking about the theory of heliocentrism. Heliocentrism was a theory four hundred years ago, in the times of Galileo and Copernicus. Today it is a fact. Evolution was a theory two hundred years ago, when the hypothesis was proposed simultaneously by Lamarck in France and by Erasmus Darwin, the grandfather of the famous Charles, in England. I think, today, biological evolution is a fact, it is based on overwhelming evidence and so when we talk about theories, evolution is no longer a theory. Mechanisms of evolution are theories. You can discuss the importance of natural selection or genetic drift or other mechanisms. But the fact of biological evolution is, in my opinion, and I think in the opinion of all scientists, undisputable.

CARD. SCHÖNBORN: I admit that I still have questions, and as I just said to Professor Dehaene, all questions are permitted. I would appreciate very much if also questions by simple people like me, who are not scientists, who question also points of the evolution theory, were not banned but were permitted, for instance, the questions of the transition from one species to the other. I have plenty of questions about that, and I am very happy if I receive good and sufficient answers to these questions, and I hope that this is good for science, that questions are still around.

PROF. ZICHICHI: I have a telegraphic statement on Professor de Duve's definitions of 'theory' and 'facts' in the field of 'biological evolution'. To be clear, let us imagine going back by 150 years in the field of physics. We have a series of 'facts' in electricity, magnetism and optics. All these 'facts' have the same origin, as demonstrated by the 'theory' called quantum electrodynamics (QED). It would be a great achievement if all the 'facts' discovered in the field of 'biological evolution' produced a mathematical structure like QED. This 'theory' would be a superb achievement in this field of research and would allow biological evolution to became Galilean science.

Session I

INSIGHTS INTO THE EVOLUTION OF THE UNIVERSE

FROM A SIMPLE BIG BANG TO OUR COMPLEX COSMOS

MARTIN J. REES

This isn't a sermon but I'll start with a text – the famous closing lines of the 'Origin of Species': 'There is a grandeur in this view of life..... Whilst this planet has gone cycling on according to the fixed law of gravity, from so simple a beginning, forms most beautiful and most wonderful have been and are being evolved'.

Darwin's 'simple' beginning – the newly formed Earth – is already very complex, chemically and geologically. Astronomers aim to trace things back far further – to set Darwin's vision in a still broader expanse of space and time. We are starting to understand how, starting from some still mysterious genesis event nearly 14 billion years ago, atoms, stars, planets, and biospheres evolved – and how, on at least one planet around at least one star, Darwinian selection led to the emergence of creatures able to ponder their origins. That's a key theme of this meeting.

Since this is the first scientific presentation at this meeting, I shall offer a brief cosmic context.

One important realisation during the last decade is that many (perhaps most) stars have retinues of planets. So far, we can only detect big ones – like Jupiter and Saturn, the giants of our Solar System. But an astronomical highlight of 2009 will be the launch in March of NASA's Kepler spacecraft, which should be sensitive enough to reveal planets no bigger than our Earth by detecting the slight dimming of a star when a planet transits in front of it. It will be a decade or two before we can actually image Earth-like planets – a firefly next to a searchlight – using giant arrays in space or the next generation of ground-based optical telescopes.

Life's origin on Earth is still a mystery so we cannot lay firm odds on its likelihood elsewhere. But we may learn, in the coming decades, whether biological evolution is unique to the 'pale blue dot' in the cosmos that is our home, or whether Darwin's writ runs in the wider universe. The quest for alien life is perhaps the most fascinating challenge for 21st century science – its outcome will influence our concept of our place in nature as profoundly as Darwinism has over the last 150 years.

As well as stars themselves we see places where stars are still forming – condensing from a dusty, slowly spinning cloud, as our Solar System once did. And we see stars dying, and throwing debris back into interstellar space.

Our galaxy is a kind of ecosystem where gas is processed and recycled through successive generations of stars. This process generates, from pristine hydrogen, the elements of the periodic table. All the carbon, oxygen and iron on Earth, and in our bodies is ash from long-dead stars. We are the 'nuclear waste' from the fusion power that makes stars shine. We can understand why carbon and oxygen are common; why gold and uranium are rare.

Let us now enlarge our horizons further. If we could get two million lightyears away and look back, our home Galaxy – the vast band of stars that we call the Milky Way – would look something like the Andromeda galaxy does to us. A vast disc, viewed obliquely, containing a hundred billion stars orbiting a central hub. Our Sun would be an ordinary star, out towards the edge. Within range of powerful telescopes are many billions of galaxies.

We can now look very far back in time. Deep exposures with the Hubble Space Telescope show that the sky is densely speckled with faint smudges of light. Each smudge is actually an entire galaxy, which appears so small and faint because of its huge distance. The light from these remote galaxies set out as much as 10 billion years ago. They are being viewed when they have only recently formed. Some consist mainly of glowing diffuse gas that hasn't yet condensed into stars.

What happened before galaxies formed? Cosmologists are confident that this whole panorama – as far as our telescopes can see – is the expanding aftermath of a 'big bang' nearly 14 billion years ago. Cosmic history can be traced back to a hot dense state – a state that was almost homogeneous (and the word 'almost' is important). We can be very confident back to a second, and fairly confident back to a microsecond. But the initial tiny fraction of a second is still shrouded in uncertainty, because the physical conditions were then more extreme than can be simulated in our laboratories – even at the LHC in Geneva.

Our present complex cosmos manifests a huge range of temperature and density – from blazingly hot stars, to the dark night sky. People sometimes worry about how this intricate complexity emerged from an amorphous fireball. It might seem to violate a hallowed physical principle – the second law of thermodynamics – which describes an inexorable tendency for patterns and structure to decay or disperse.

The answer to this seeming paradox lies in the force of gravity, which reverses our normal intuitions from thermodynamics. Self gravitating systems – stars, for instance – have negative specific heat. If the nuclear burning in the Sun were to turn off, the Sun would slowly deflate as it lost heat – but its centre would get hotter as well as denser. Gravity drives things further from equilibrium.

And even in the early amorphous stage of cosmic expansion, before stars formed, gravity was enhancing the density contrasts. Any patch that starts off slightly denser than average would decelerate more, because it feels extra gravity; its expansion lags further and further behind, until it eventually stops expanding and separates out.

Astrophysicists have carried out extensive computer simulations of 'virtual universes'. The simulations show incipient structures unfolding and evolving into galaxy-scale concentrations of material, within which gravity enhances the contrasts still further, and gas is compressed into stars. Each galaxy is an arena within which stars, planets and perhaps life can emerge.

Where did the initial fluctuations come from? The answer takes us into speculation about the very earliest stages – when the universe was far less than a microsecond old, and energies and densities were so extreme that experiments offer no direct guide to the relevant physics.

One of my favourite magazine covers showed a red circle, beneath the caption 'the universe when it was a trillionth of a trillionth of a trillionth of a second old – actual size'. According to a popular theory, the entire volume we can see with our telescopes 'inflated' from a hyper-dense blob no bigger than that; the irregularities that form galaxies and larger structures started out as microscopic quantum fluctuations generated at that time; and it was at that time that the content of the universe – the mix of nucleons, dark matter and radiation – was established.

There is an interconnectedness between microworld and cosmos – between the inner space of atoms and the outer space of the universe. There are links between small and large. Our everyday world – of life and mountains – is determined by atoms and chemistry. Stars are powered by fusion of nuclei within those atoms. And Vera Rubin will discuss another link: galaxies are seemingly held together by swarms of subnuclear particles that make up the'dark matter'.

The microworld is the domain of the quantum. On cosmic scales Einstein's theory holds sway. General relativity, and quantum theory are the twin pillars of 20th century physics. But they haven't yet been meshed together into a single unified theory. In most contexts, this does not impede us because their domains of relevance do not overlap. Astronomers can ignore quantum fuzziness when calculating the motions of planets and stars. Conversely, chemists can safely ignore gravitational forces between individual atoms in a molecule because they are nearly 40 powers of ten feebler than electrical forces. But at the very beginning, everything was squeezed so small that quantum fluctuations could shake the entire universe.

To confront the overwhelming mystery of what banged and why it banged we need a unified theory of cosmos and microworld. This is the topic on which Edward Witten is better qualified than anyone else to speak.

Now for another question: How big is the universe? We can only see a finite volume – a finite number of galaxies. That is essentially because there's a horizon – a shell around us, delineating the distance light can have travelled since the big bang. But that shell has no more physical significance than the circle that delineates your horizion if you're in the middle of the ocean. We'd expect far more galaxies beyond the horizon.

There's no perceptible gradient across the volume of space-time within range of our telescopes – that fact alone suggests that the domain astronomers can see could be only a tiny fraction of the aftermath of our big bang. It may go on much further – even for ever. But that is not all. 'Our' big bang may not be the only one. What we have traditionally called 'the universe' could be just one patch of space-time in a vast cosmic archipelago. This hugely expanded cosmic perspective takes Copernican modesty one stage further. To put this on a firm footing, we'll need a unified theory that link the very large and the very small.

There is, however, a third frontier on intermediate scales: very complex entities such as us. We ourselves are midway between atoms and stars: large enough, compared to atoms, to have layer upon layer of intricate structure; but not so large that we're crushed by our planet's gravity. To understand ourselves, we must understand the atoms we're made of, and the stars that made those atoms.

But stars are simple: they're so big and hot that their content is broken down into simple atoms – stars don't match the intricate structure of even an insect, let alone the human brain (I really mean this – I'm not just being polite to the biologists in the audience).

We can identify the key stages in the emergence of complexity:

– The first particles – protons and neutrons
– The first stars and galaxies
– The synthesis of the periodic table in stars
– Formation of planets around later-generation stars

– And then of course, on at least one planet, the formation of a biosphere, that led to the emergence of brains capable of pondering their origins.

What are the key prerequisites for a universe that can offer the arena for this chain of events?

Crucial to the whole emergent process is gravity – which enhances density contrasts, and allows structures to form. It is a very weak force. But, unlike the electrical force, everything has the same 'sign' of gravitational charge: when sufficiently many atoms are packed together, gravity wins. It is unimportant for an asteroid-size lump. But it makes planets round, and any object more massive than Jupiter is squeezed to make a star.

The fact that, for individual protons, it is weaker by 36 powers of 10 than the electrical force, means that there can be many layers of structure between the microworld and the scales that get crushed by gravity.

Also, stars are not only big but live a long time. And any emergent complexity – like the growth of an animal, requires billions of successive chemical reactions, and Darwinian evolution requires millions of generations of animals.

So, though gravity is crucial, ironically, the weaker it is, the better. Were it stronger, stars (gravitationally confined fusion reactors) would be much smaller and wouldn't last long. Creatures like us would be crushed by gravity. The strength of gravity, compared to other forces, is one of the key numbers of physics, not yet explained.

Another requirement for a biosphere is that chemistry should be non-trivial. This requires a balance between the nuclear force (the 'strong' interactions that binds together the protons in a nucleus) and the electric repulsive force that drives them apart. Otherwise there would be no periodic table.

There are other requirements. The universe must contain an excess of matter over antimatter. It must expand at the 'right' rate – not collapse so soon that it offers inadequate time for the emergence of complexity, nor expand so fast that gravity cannot pull together the structures that lead to stars and galaxies. And there must be some fluctuations for gravity to feed on. Otherwise the universe would now be cold ultra-diffuse hydrogen – no stars, no heavy elements, no planets and no people.

To understand these numbers is a challenge to fundamental physics and cosmology. And there is a key question: The numbers are the same over the entire domain we observe. But it remains a possibility that, far beyond our horizon, they take different values. Whether this is so, is a topic of key debate. Perhaps they are genuinely universal. But perhaps in the grandest perspective, what we call the laws of nature are mere parochial bylaws. Four hundred years ago, Kepler thought that the Earth was unique, and its orbit was a circle, related to the other planets by beautiful mathematical ratios. We now realise that there are billions of stars, each with planetary systems. Earth's orbit is special only insofar as it's in the range of radii and eccentricities compatible with life.

Maybe we're due for an analogous conceptual shift, on a far grander scale. Our big bang may not be unique, any more than planetary systems are. Its parameters may be 'environmental accidents', like the details of the Earth's orbit. In this hugely expanded cosmic perspective, what we've traditionally called fundamental constants and laws could be mere parochial bylaws in our cosmic patch. They might derive from some overarching theory governing the ensemble, but not be uniquely fixed by that theory.

The hope for neat explanations in cosmology may be as vain as Kepler's numerological quest. Our universe isn't the neatest and simplest. It has a rather arbitrary seeming mix of ingredients – in the parameter range that allows us to exist.

We don't know if these conjectures are right. But they're speculative science, not metaphysics. What could give us confidence in unobservable domains? The answer seems clear – we will believe in them if they are predicted by a theory that gains credibility because it accounts for things we can observe? We believe in quarks, and in what general relativity says about the inside of black holes, because our inferences are based on theories corroborated in other ways.

A challenge for 21st century physics is to decide whether there have been many 'big bangs' rather than just one – and (if there are many) how much variety they might display.

These still unsettled debates are very important. Nonetheless, for 99 percent of scientists, they are irrelevant. The task of chemists, geophysicists and biologists is to understand the complexity that's the eventual outcome of cosmic processes.

The sciences are sometimes likened to different levels of a tall building – particle physics on the ground floor, then the rest of physics, then chemistry, and so forth: all the way up to psychology – and the economists in the penthouse. There is a corresponding hierarchy of complexity: atoms, molecules, cells, organisms, and so forth. But the analogy with a building is poor. The 'higher level' sciences dealing with complex systems are not imperilled by an insecure base, as a building is. They have their own autonomous concepts and theories.

To understand why flows go turbulent, or why waves break, subatomic details are irrelevant. We treat the fluid as a continuum (and even if we could solve Schrodinger's equation for every atom of a turbulent fluid, it wouldn't offer any insight into turbulence).

An albatross returns predictably to its nest after wandering ten thousand miles in the southern oceans. But this is not the same kind of prediction as astronomers make of celestial orbits. And scientific statements about humans are more different still.

Problems in biology, and in environmental and human sciences, remain unsolved not because scientists don't understand subatomic physics well enough. These problems are difficult because of the complex structures that are involved – far most complex than anything that physicists and astronomers think about. Stars are simple: they're so big and hot that their content is broken down into simple atoms – none match the intricate structure of even an insect.

One final question – is there a special perspective that astronomers can offer to evolutionary science? They can set our home planet in a vast cosmic context: billions of galaxies, each containing billions of planets. Even more, they can offer intimations that physical reality is hugely more extensive – and perhaps far more intricate – than the volume we can observe with our telescopes. Moreover, astronomers can offer an awareness of an immense future.

The stupendous timespans of the evolutionary past are now part of common culture. Our present biosphere is the outcome of more than four billion years of evolution, But most people still somehow think we humans are necessarily the culmination of the evolutionary tree. That hardly seems credible. Our Sun formed 4.5 billion years ago, but it will take 6 billion more before the fuel runs out. It then flares up, engulfing the inner planets and vaporising whatever remains on Earth. And the expanding universe will continue – perhaps for ever – destined to become ever colder, ever emptier.

Any creatures witnessing the Sun's demise 6 billion years hence, here on earth of far beyond, won't be human – they'll be as different from us as we are from the first monocellular organisms. So a question for the biologists is: Could we be barely at the half way stage of evolutionary development? Could posthuman evolution be as prolonged as pre-human?

But let us finally focus back on the here and now. Even in this ultra-compressed timeline – extending billions of years into the future, as well as into the past – this century may be a defining moment. It is the first in our planet's history where one species – ours – has Earth's future in its hands, and could jeopardise not only itself, but life's immense potential.

So this pale blue dot in the cosmos is a special place And we are its stewards at a specially crucial era.

DISCUSSION ON PROF. REES' PAPER

PROF. WITTEN: The quote you ended with suggests an answer to a question Professor Zichichi raised before. Once we had a language and agriculture our subsequent evolvement was incredibly rapid compared to the whole span of evolution of the earth and life on the earth, and because of that it would be an incredible coincidence if two separate species reached the same stage of language and agriculture and all the rest of it simultaneously.

PROF. REES: Yes, that is a reason to be pessimistic about the so-called SETI programme, but also I think it strengthens the point I was making, that the developments in the future are going to be more dramatic, perhaps, than what has happened over the entire four billion years up to now, because not only is there at least as much time in the future, but, for the reasons you are saying, that change is controlled by intelligence, and so post-human evolution could be far more dramatic and far speedier than what has happened up to now.

PROF. WITTEN: Do you feel one can estimate the timescale, if we survived the next few generations, to spread beyond the solar system?

PROF. REES: Well, this is in the domain of science fiction, but, as I tell my students, it is better to read first-rate science fiction than second-rate science! But we do not know whether there is any life out there and nor do we know what the long-term future of our life will be: will it be silicon-based or will it be organic? Incidentally, I welcome the fact that there are searches for intelligent life elsewhere. It may be disappointing if those searches are doomed to fail but of course it would allow us to have a less modest perspective on our place in the cosmos, because it could well be that we are the only place where life has evolved to its present complexity, even if simple life is widespread.

PROF. COLLINS: So you have alluded to this remarkable set of constants that determine the behaviour of matter and energy and the strong and weak nuclear forces and so on, and the fact that their precise values seem not to tolerate any variation without losing the complexity of the universe. What do you think that the chances are again – this is probably asking you a science fiction question – that those constants will turn out to be connected to each other in ways that we currently do not understand by theoretical means, and then maybe there is not as much as a tapestry of opportunity as it currently appears.

PROF. REES: First of all, this is an Ed Witten question rather than one for me. We can, of course, consider counterfactual universes with different constants and see whether they could evolve complexity. I illustrated that some laws might not permit any periodic table, or might have too short a lifetime. Now, there are some theories which do allow multiple Big Bangs but, to answer your question, you need to have a detailed theory, because in order to say how improbable a particular configuration is, you have got to put a measure on the space and you have got to know what the probabilities are. So, if one had a detailed theory, which told us what the relative probability was of different sets of numbers, and whether they were correlated, we could then answer that question. All you can say is that the emergence of any level of complexity requires some non-uniformity. There must be one large number to allow large space and time compared to microscopic structures and so on, but clearly one can envisage counterfactual universes which would not allow the complexity that has led to our existence.

PROF. KASTURIRANGAN: You know there are these possibilities, as the observational capabilities evolve, to look at the other stellar systems with respect to planetary systems that are already moving very fast and then the possibility of the planets holding atmospheres in the right ecosphere of that sun and ultimately, of course, to have the right type of atmosphere, which is carbon, nitrogen, oxygen and so on. If one has to do that kind of research, ultimately, to look at an earth-like habitat elsewhere, what would one look for in terms of life itself? Would it be a carbon-based life or are there alternate conjectures on this? So that we are not taking one sample and trying to deduce too much on that in the context of all that we are talking about.

PROF. REES: I think I would be trespassing on later talks by more expert people if I were to answer that question in detail, but let me just say that the one thing which, I think, most astronomers would now confidently say. There are many many earth-like planets, planets like the young earth, the same sort of mass and at the same distance from a stable star as our earth is, so that water neither freezes nor boils. But of course, there are then two much harder questions for the biologists. One is, how life began, was it such a rare fluke it happened just here, or would simple life get started elsewhere? Even if that question is answered, there is a separate question. How likely is it that simple life, once started, develops into a complex biosphere, even given the same environment? We have no idea about that question either, but I would trespass on the talks of Dr de Duve and Dr Swarup if I went further. (*Discussion continued on page 65*).

SCIENTIFIC QUEST INTO EVOLUTION OF LIFE IN THE UNIVERSE

GOVIND SWARUP

1. Introduction

The Big Bang Model of the Universe is now well established (Hawking 1983; Weinberg 1977; Spergel *et al.* 2007). Electrons, protons, neutrons were formed in the first few minutes, leading to the nearly 75% mass of hydrogen, 25% helium, and some light elements, that later cooled and gave rise to a visible mass of stars and galaxies. Theoretical models also predict heavier particles that are likely to be the constituents of the dark matter in the Universe. Radio astronomers have discovered over 100 molecules in the interstellar surroundings. Thus it seems likely that the initial electrical and chemical affinity of electrons and protons gave rise to increasingly complex forms on the Earth. However, it is yet not clear as to what processes resulted in the growth and appearance of the first cell with its ability for self replication. It is a challenging area of experimental science being pursued by many biologists, geneticists and others.

Our Universe is vast. There are billions of galaxies in our Universe. Each galaxy has billions of stars. Life may be widespread in the Universe. The possibility of searching for life in distant galaxies is a remote possibility. However, the search for life elsewhere in our solar system and also in planets with favourable conditions in our Galaxy is likely to be made by mankind using larger and more sophisticated instruments for decades to come.

In Section 2, possible scenarios for the origin of life on the Earth are discussed. Section 3 briefly summarizes scientific evidence for the evolution of life from extremophiles to mammals to mankind. The search for life elsewhere in our solar system is discussed in Section 4. As described in Section 5, astronomers have discovered 340 planets in nearby stars and this number continues to increase rapidly. Finally, the important question: are we alone? Section 6 describes endeavors by radio astronomers in the Search for Extraterrestrial Intelligence (SETI) that started with the pioneering effort by Frank Drake in 1959 using a relatively modest radio telescope and receiver system. Many SETI observations have been made over the last 50 years using larger radio telescopes. However, the sensitivity of existing radio telescopes is not sufficient to search for very weak signals from distant parts of our Galaxy. I describe in Section 7 new initiatives for SETI that would allow probing towards millions of stars. Optical SETI is briefly described in Section 8. Summary is given in Section 9.

2. Origin of Life on the Earth

Three main scenarios have been proposed for the origin of life on the Earth.

(a). *Did lightning and volcanoes spark life on the Earth?*

Soon after the formation and cooling of the Earth about 4.5 billion years ago, numerous large volcanoes and lightning occurred on the Earth that may have provided sufficient energy for the synthesis of molecules. In a famous experiment carried out in 1953, Stanley Miller, a graduate student of Harold Urey, put ammonia, methane, hydrogen and water in a sealed flask, applied electrical sparks and detected 5 amino acids that are some of the building blocks of proteins (Miller 1955). After Miller's death in May 2007, Dr. Bada, who was one of the graduate students of Miller, got access to a boxful of vials containing dried residues resulting from the various experiments carried out by Miller during 1953 and 1954. In 2007, Adam Johnston joined Dr. Bada's laboratory on an internship. Besides the apparatus known in textbooks, Miller also used one that generated a hot water mist in the spark-flask, simulating a water vapor-rich volcanic eruption. Johnston reanalyzed the original extracts of this experiment using modern techniques. The volcanic apparatus produced 22 amino acids including those that were not identified from the Miller-Urey experiment (Johnston *et al.* 2007). However, many doubts have been raised about this scenario for the origin of life, such as Earth's environment and its constituents 3.5 billion years ago that may not have been conducive to the growth of life.

(b). *Origin of Life in deep sea hydrothermal vents*

In recent years scientists have discovered a rich variety of simple forms of life (extremophiles: see Section III) in deep sea hydrothermal vents containing sulfides and other minerals. It is currently believed that these hydrothermal vents may provide a suitable environment where the building blocks first came together for the evolution of life gradually over millions of years.

(c). *Life forms on earth came from Outer Space*

Radio astronomers have discovered over 100 molecules in the interstellar medium. It may be that cellular life exists elsewhere in our Galaxy and could be carried far and wide by comets, seeding the planets in our solar system (hypothesis of panspermia). It is not clear whether such life forms will survive in comets over a long period against bombardment by cosmic rays containing very energetic protons. Nevertheless, the discovery of amino acids in some of the meteorites has suggested that the building blocks of life on the Earth came from outer space, eliminating the need for finding chemical processes that could produce pre-biotic material on Earth. Another possibility is that the meteorites carried life forms from a planet such as Mars in our solar system. However the organisms travelling on a rock ejected from one body in the solar system to another would be subjected to radiation, vacuum and extreme temperatures. Continuing exploration of planets and some of their satellites may find *none, same or different forms of primitive life therein, and thus discriminate between various models*.

3. Evolution of Life

It is a vast subject and has been discussed in detail by many authors in these proceedings (also in a textbook by Jones 2006). I give here a sketchy summary in order to postulate that there is a reasonable probability that life may exist elsewhere in our Galaxy.

Fossil records provide evidence that there existed RNA/DNA-protein life ~2.5 billion years ago. The origin of life took place much earlier. Its origin is likely to have taken place from the pre-biotic stage to the RNA world, but details are not clear and remain a scientific challenge. Tens of thousands of fossil records show that evolution took place from single-celled prokaryotes to eukaryotes that have long genetic codes. Evolution seems to have taken over millenniums by natural selection, adaptation etc. from cynobacteria, archaens, prokaryotes, to eukaryotes to fish to amphibians to reptiles to mammals, apes to homo sapiens. However, the genesis of the anaerobic first cell, the progenote of the RNA world is an open question.

Extremophiles: Bacteria have the potential to adapt and grow in extreme conditions (www.astrobiology.com/extreme.html; www.bacteriamuseum.org). Extremophiles include anaerobes, thermophiles, psychrophiles, acidophiles, alkalophiles, halophiles, barophiles and xerophiles. A wide variety have been found, e.g. in hot geysers in deep oceans, in hot springs at temperatures up to ~130 degree Celsius (hot springs of Yellowstone National Park and geothermal features all over the world); in soils or floors of the ocean with high salinity (Mediterranean); in ice at -60 degree Celsius (Antarctica), etc. It is quite probable that microbes may grow and thrive in other similarly hostile places in the solar system and elsewhere in planets of distant stars.

4. Looking for Life in Mars

Besides the recent landed missions on Mars, orbiting satellites by ESA and NASA have made photographic and spectroscopic exploration of outer planets and their moons, particularly of Mars, Jupiter and Saturn. In 2004, the scientists analyzing data of the Mars Express of ESA reported that they had detected methane in the atmosphere of Mars. Recently, astronomers have confirmed the presence of methane searching for the chemical 'fingerprints' in the spectrum of Martian atmosphere using an optical telescope in Hawaii. Some regions on Mars displayed higher concentrations than others. 'Is it geology, in which case it is the reaction between water and rock that is producing the methane, or it is biology, in which case the microbes are producing the methane?

NASA's 'Spirit' and 'Opportunity' vehicles that landed on Mars ~5 years ago provided spectacular scenery of many interesting geological features. The broken wheel of the 'Spirit' had a silver lining: it was digging trenches during its journey and some of these showed the presence of 90% silica, indicating evidence of water. NASA's Phoenix landed on Mars in May 2008 and has made extensive explorations. It has confirmed the presence of ice-water and also snow falling from Martian clouds. Soil experiments have provided evidence of past interaction between minerals and liquid water, processes that occur on the Earth. Now with the presence of methane, signs of life are getting even stronger. It would be extremely interesting to explore whether extremophiles, even archea or cynobacteria, extinct or even living, exist on Mars or elsewhere in the solar system.

5. Search for Extrasolar Planets (Exoplanets)

The first exoplanet was found in 1992 orbiting a radio pulsar by accurate timing. In 1995 Michel Mayor of the Geneva Observatory discovered a planet orbiting a nearby star by measuring very tiny shifts in the spectral lines of the star caused by Doppler shift due to the planet orbiting the star. The orbiting planet results in the star rotating about a common centre of gravity of all the masses, and is called the Wobble method. It easily detects gas giants comparable or larger than the massive Jupiter, though some smaller planets are also found. Besides the above method, several other techniques are being used for searching for exoplanets (Pudritz *et al.* 2007).

If the orbital axis of a planet lies nearly perpendicular to the direction of a star, we can observe its transit causing a decrease in the luminosity of the star's light, allowing measurement of its mass. Also the light from the star probes the atmosphere of the planet giving measurements of the nature of its gaseous contents. This is called the WINK method. Transit observations have been made of ~27 exoplanet. Another method used is to search for gravitational microlensing of far away planets towards a star. This method, though time consuming, has allowed detection of a near earth size planet from a far away star.

Nearly 340 exoplanets have been discovered so far, mostly by the Wobble method, including ~27 multi-planet systems**,** (www.obspm.fr/encycl/catalog.html). We are living in exciting times! New discoveries continue to be made every few months. On 20 March 08, methane was found in the atmosphere of an exoplanet; on 17 June 08, a trio of super-earths was found orbiting a nearby star, 42 light years away (4.2 to 9.4 earth masses); on 29 September 08, a planet of mass Mp = 0.53Mj with an orbital period of 3.7 days was discovered.

Over the next decade or two several thousand planets are likely to be discovered by space telescopes, such as Kepler (recently launched), COROT, Cassini, James-Web Telescope and many ground based telescopes, including the proposed Extremely Large Telescopes (ELT) of 30m in size in USA and 42m in Europe. In the future NASA's Terrestrial Planetary Finder and ESA's Darwin will seek Earth-size planets with temperatures ~300K. Highly sensitive spectrometers may discover signs of life by detection of methane and other constituents such as CO_2, ozone, oxygen, water, etc.

6. Search for Extra-Terrestial Intelligence (SETI)

In 1959 Frank Drake made a pioneering attempt using an 85ft radio telescope to search for any narrow band radio signals, presumably transmitted by an extra-terrestrial intelligent civilization. In 1959 he also postulated that the estimated number of civilizations in our Galaxy depends on a number of probabilities: the Drake Equation has 7 terms (Drake and Sobel 1967). In brief the estimate depends upon the assumed number of suitable habitable planets in our Galaxy similar to that of the Earth in the Solar system, fractions with advanced communication skills, their mean lifetime, etc. Estimates vary from one (rare Earth) to ~10000. Further it is not clear whether an advanced civilization will broadcast signals and if so in what form.

In 1959, Cocconi and Morrison suggested that a preferred frequency for SETI could be the natural emission line of the neutral Hydrogen at 1420 MHz, since Hydrogen is the building block of stars and galaxies. A distant civilization may choose some other frequency, or we may attempt to search for leakage radiation from their transmitters. There are technical reasons for searches to be carried out in the frequency range of about 1000 MHz to 10,000 MHz. This window offers a minimum in the value of the sky noise, consisting of the galactic background and atmospheric noise, and thus provides maximum sensitivity for a given radio telescope. It is called the water hole as it covers the frequency range of the line emission of neutral hydrogen, HI, and molecules OH and H_2O.

Over the last few decades radio astronomers have made general searches towards various directions of the sky, and more intensively towards selected nearby stars using available radio telescopes for any signals that may have been sent by an extra-terrestrial civilization. No signal has been detected so far. However, the sensitivity of existing radio telescopes is not sufficient to search far and wide. The results of searches made so far have helped in determining upper limits on the power flux density incident on the Earth from any ETI signal. Some of the most sensitive searches carried out so far are the following:

Southern sky: A decade ago, the SETI institute and Australian scientists carried out a search towards 200 solar type stars using the Parkes Radio telescope of 64m diameter in Australia, giving a detection sensitivity limit of ~10^{-25} W/m².

Northern sky: The University of Berkeley group is using the Arecibo Radio Telescope of ~200m diameter. They have surveyed ~800 solar type stars, reaching a sensitivity of ~10^{-26} W/m². The search is continuing. Data is also being analyzed using thousands of computers across the world (SETI@Home).

No signal has been detected so far from any transmitter that may be located up to a distance of ~100 light years away, radiating towards the earth, say with a power of 10 MW connected to an antenna of 60m diameter (such transmitters exist on the Earth).

7. New Seti Searches

7.1. *There are many technical challenges:*

Radio telescopes with much higher sensitivity are required with a large collecting area, multiple beams, wide bandwidth and a very large digital spectrometer. It can be shown that the signal of a transmitter *can be detected farthest away,* if the bandwidth of the receiver is very narrow, say 0.1 Hz (~CW signal). Alternatively one may search for wide band narrow pulses using a receiver with large bandwidth. Therefore, we require spectrometers with terra-Hz capability that is possible today as Moore's law continues to be valid! It is also important to note that modern technology allows SETI to be carried out simultaneously with normal astronomical observations, and thus we can search millions of potential stars with modest additional investments. I describe below some new initiatives.

7.2. *Allen Radio Telescope (ATA), USA*

ATA consists of a radio telescope array of 350 antennas of 6m diameter. The antennas and associated electronics provide high performance. ATA has been set up at Hat Creek in California by the SETI Institute and the University of California, Berkeley (www.seti.org/ata). Forty antennas that are funded by Paul Allen of Microsoft are operational. ATA provides a large instantaneous bandwidth of ~100 MHz, 200 million spectral channels and several antenna beams of its phased array, for simultaneous searches towards many stars. It covers the frequency range of ~1 GHz to 11 GHz (the water hole described earlier). The goal of the SETI survey with ATA is to investigate hundreds of nearby stars over a wide frequency range from 1 to 11 GHz, with adequate sensitivity to detect a transmitter equivalent of the Arecibo radar ($2x10^{13}$ W EIRP) located in a planet in a far away star. Another SETI survey of about 20 square degrees along the galactic plane in the direction of the galactic center will cover thousands of distant stars over a frequency range of 1420 MHz – 1720 MHz with a long integration time. At the distance of the galactic center, a detected transmitter would be radiating power equivalent to more than 25,000 Arecibo radars.

7.3. *The Giant Metrewave Radio Telescope (GMRT), India*

The Giant Metrewave Radio Telescope (GMRT) built in India has been in operation since 1999 (www.ncra.tifr.res.in). It is located ~80 km north of Pune in India. It consists of 30 nos. of 45m diameter dishes located in an array of ~25km in extent. It can observe over ~80% of the sky. It is currently the world's largest radio telescope operating in 5 frequency bands from ~130 MHz to 1430 MHz. GMRT is currently being upgraded and will provide nearly continuous coverage from ~40 MHz to 1430 MHz. Wide band feeds and low noise amplifiers are being installed. A software correlator with 32 MHz bandwidth has been installed recently and it will also provide multiple beams within a year. A software/hardware correlator with a bandwidth ~256 MHz or 400 MHz, with a large number of spectral channels, is planned to be completed over the next 3 years. In addition to providing cross-products of voltage outputs of all the 30 antennas for each of the spectral channels, as required for imaging, the GMRT correlator system also produces an independent output giving a sum of the voltage signals received by the 30 antennas of 45m diameter, making it equivalent to a 200m diameter dish, 5 times more powerful than any other radio telescope covering the southern sky. Therefore, the upgraded GMRT, providing an independent output of narrow band channels of < 1 Hz over tens of MHz, can be used for a SETI, simultaneously with the normal astronomical observations.

7.4. *Square Kilometer Array (SKA): a very challenging project in radio astronomy*

SKA will be ~100 times more powerful than any existing radio telescope (www.skatelescope.org). SKA is planned to be built, during 2012 to

2020, by 17 countries, including Australia, China, India, South Africa, UK, Netherlands, Italy, Canada, USA, Argentina and Brazil. It will have thousands of antennas to be located in an array of ~3000 km across. Already two independent pathfinders for the SKA are under construction in Australia and in South Africa for demonstrating technologies required for the SKA. SKA will be located in one of these two countries. It will be a very versatile instrument using advanced electronics. It is being designed to answer certain key questions, such as: ultra-strong field limit of relativistic gravity; origin of cosmic magnetism; galaxy evolution; epoch when first stars formed and also ETI. Over the next 20 years, the SKA will search towards millions of stars for any signals sent by an advanced civilization and also any leakage signals from their radars or fixed and mobile transmitters.

8. Optical SETI

It may be that an advanced civilization in our Galaxy may develop powerful lasers for interstellar communication. Considering the above possibility, searches have also been carried out recently using optical telescopes with receivers that are sensitive to pulses of very narrow time duration, of less than a millionth or a billionth of one second. However, atmospheric absorption and intergalactic dust may restrict communication over long distances.

9. Summary

Extensive scientific work has been done over the last 150 years concerning evolution of life on our planet. Valuable insights are being obtained using modern tools in paleontology, biology, bio-chemistry, genetics, neurosciences, etc. The origin of life remains a scientific challenge. Mankind has made great progress over the last ~10000 years, particularly over the last few hundred years. What is our future? We must continue to ensure that our civilization becomes more peaceful? *Is human intelligence also subject to Darwinism?* Do advanced civilizations become altruistic in order to be peaceful and not destructive of their surroundings?

Should we search? If we do not search how can we say that we are alone? Searching for life elsewhere in the solar system may give us new clues. Exciting developments are likely over the next decade from the discoveries of earth-like planets in distant stars, and planned observations of their bio-signatures. SETI with new radio instruments, such as ATA and SKA, upgraded GMRT, and optical SETI will allow us to search towards millions of stars.

Man has wondered for long about the origin and evolution of the Universe. More than 3000 years ago, sages in India wondered (Rig Veda: Chapter 10, stanza 129/1):

There was neither existence nor non-existence then,
Neither the world nor the sky that lies beyond it;
What lay enveloped? and where? and who gave it protection?
Was water there, deep and unfathomable?

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DISCUSSION ON PROF. SWARUP'S PAPER

PROF. LÉNA: Since you take us on speculative grounds I have a question. A technological civilisation such as the one SETI aims to detect, may not be detectable, except for a short period of time, as these 'wise beings' may also develop a way to become invisible to external observers. The time span of 'detectable technology', which is critical for the measurement you think of, may be very short and then the detectability of a wise planet may also be very limited.

PROF. SWARUP: My own personal feeling is that we are really not wise enough. I think we have a selfish gene; there may be chaos in a lot of cultures and a lot of conflicts across but I think we will become wiser in future. I think our humanity on this earth is not going to disappear in hundreds of years, I think we will live thousands of years, this is my personal belief if you look at the past. But this is an open question and it is an extremely important question for the people in this conference: in the future, how to make sure that we protect our environment, so that we will live for a long time. But certainly we must keep on searching: if we do find life elsewhere, it will be extremely interesting, or if in the next 20 to 50 years we do not find it, that will also be very interesting.

PROF. KASTURIRANGAN: Is it that the search strategies that you identify really mean radio and optical? Here too the search space is, in terms of bandwidth, very large, and then to look at a search bandwidth which is very small, so it is almost, as it has been often said about these kinds of strategies, like searching for a needle in a haystack. Now, the question is whether these kinds of strategies demand that we are able to communicate with a system which is also looking at us, and that means two probabilities to happen together and the current sensitivity will even be stretched to the limits in the coming decades, will not go beyond say 20, 30 or maybe 100 light years or whatever it is. So this puts limits on the search strategy. The question that I would like to seek the answer from you is that, some years back, Freeman Dyson suggested that, instead of doing a search strategy like this, why can't we look at the effects of extraterrestrial civilisation in terms of total planetary activity, i.e. why can't look for any anomalies in the infrared radiation which could be indicative of an activity of an extraterrestrial intelligence, so you are trying to look at the impact of a planetary scale activity rather than trying to look at a very special signal coming out either through an optical laser or a radio wavelength. What is the present status of such an idea and would it be better than just trying to look for these kinds of which the probability is pretty low.

PROF. SWARUP: When you look at infrared or optical, dust is a problem, so you can only see a few hundred light-years, not deep. Radio astronomers hope to search the entire galaxy. The question of the needle in a haystack used to be said, but what has convinced me with the rapid growth of digital spectrometers, which are being built, that while you are observing (radiotelescopes work 24 hours 7 days a week), simultaneously in the same direction you would look for what you said, smoke, any signals, any transmissions they may be using. So both strategies have to be done, you have to look for infrared, which I did not touch upon, with required special instrumentation, which has not yet been planned. People are searching for very narrow pulses with optical telescopes but certainly over the years, as more optical telescopes get built, maybe look for infrared kind of leaky signal as you call it. We have to keep on searching, using larger radio telescopes built for understanding cosmology and if we can build instrumentation to search in the same directions to search for a wider variety of signals that modern computers allow.

THE ORIGIN OF THE UNIVERSE

STEPHEN HAWKING

Early accounts of the origin of the world were attempts to answer the questions we all ask: Why are we here? Where did we come from? The answer generally given was that humans were of comparatively recent origin, because it must have been obvious, even at early times, that the human race was improving in knowledge and technology. So it can't have been around that long, or it would have progressed even more. On the other hand, the physical surroundings, like mountains and rivers, change very little in a human lifetime. They were therefore thought to be a constant background, and either to have existed forever as an empty landscape, or to have been created at the same time as the humans.

Not everyone however, was happy with the idea that the universe had a beginning. For example, Aristotle, the most famous of the Greek philosophers, believed the universe had existed forever. Something eternal is more perfect than something created. He suggested the reason we see progress, was that floods, or other natural disasters, had repeatedly set civilization back to the beginning.

If one believed that the universe had a beginning, the obvious question was, what happened before the beginning? What was God doing before He made the world? Was He preparing Hell for people who asked such questions? The problem of whether or not the universe had a beginning was a great concern to the German philosopher Immanuel Kant. He felt there were logical contradictions, or Antimonies, either way. If the universe had a beginning, why did it wait an infinite time before it began? He called that the thesis. On the other hand, if the universe had existed forever, why did it take an infinite time to reach the present stage? He called that the antithesis. Both the thesis, and the antithesis, depended on Kant's assumption, along with almost everyone else, that time was Absolute. That is to say, it went from the infinite past, to the infinite future, independently of any universe that might or might not exist in this background.

This is still the picture in the minds of many scientists today. However, in 1915, Einstein introduced his revolutionary General Theory of Relativity. In this, space and time were no longer absolute, no longer a fixed background to events. Instead, they were dynamical quantities that were shaped by the matter and energy in the universe. They were defined only within the universe, so it made no sense to talk of a time before the universe began. It would be like asking for a point south of the South Pole: it is not defined.

If the universe was essentially unchanging in time, as was generally assumed before the 1920s, there would be no reason that time should not be defined arbitrarily far back. Any so-called beginning of the universe would be artificial, in the sense that one could extend the history back to earlier times. Thus, it might be that the universe was created last year, but with all the memories and physical evidence to look like it was much older. This raises deep philosophical questions about the meaning of existence. I shall deal with these by adopting what is called the positivist approach. In this, the idea is that we interpret the input from our senses in terms of a model we make of the world. One cannot ask whether the model represents reality, only whether it works. A model is a good model, if first it interprets a wide range of observations, in terms of a simple and elegant model. And second, if the model makes definite predictions that can be tested, and possibly falsified, by observation.

In terms of the positivist approach, one can compare two models of the universe. One in which the universe was created last year, and one in which the universe existed much longer. The Model in which the universe existed for longer than a year can explain things like identical twins, that have a common cause more than a year ago.

On the other hand, the model in which the universe was created last year, cannot explain such events. So the first model is better. One cannot ask whether the universe *really* existed before a year ago, or just appeared to. In the positivist approach, they are the same.

In an unchanging universe, there would be no natural starting point. The situation changed radically however, when Edwin Hubble began to make observations with the hundred-inch (2.5m) telescope on Mount Wilson, in the 1920s.

Hubble found that stars are not uniformly distributed throughout space, but are gathered together in vast collections called galaxies.

By measuring the light from galaxies, Hubble could determine their velocities. He was expecting that as many galaxies would be moving towards us, as were moving away. This is what one would have in a universe that was unchanging with time. But to his surprise, Hubble found that nearly all the galaxies were moving away from us. Moreover, the further galaxies were from us, the faster they were moving away. The universe was not unchanging with time, as everyone had thought previously: it was expanding. The distance between distant galaxies was increasing with time.

The expansion of the universe was one of the most important intellectual discoveries of the 20th century, or of any century. It transformed the debate about whether the universe had a beginning: if galaxies are moving apart now, they must have been closer together in the past. If their speed had been constant, they would all have been on top of one another, about 15 billion years ago. Was this the beginning of the universe?

Many scientists were still unhappy with the universe having a beginning, because it seemed to imply that physics broke down. One would have to invoke an outside agency, to determine how the universe began. They therefore advanced theories in which the universe was expanding at the present time, but didn't have a beginning. One was the Steady State theory, proposed by Bondi, Gold, and Hoyle in 1948.

In the Steady State theory, as galaxies moved apart, the idea was that new galaxies would form from matter that was supposed to be continually being created throughout space. The universe would have existed forever, and would have looked the same at all times. This last property had the great virtue, from a positivist point of view, of being a definite prediction that could be tested by observation. The Cambridge radio astronomy group, under Martin Ryle, did a survey of weak radio sources in the early 1960s. These were distributed fairly uniformly across the sky, indicating that most of the sources lay outside our galaxy. The weaker sources would be further away, on average.

The Steady State theory predicted the shape of the graph of the number of sources, against source Strength. But the observations showed more faint sources than predicted, indicating that the density of sources was higher in the past. This was contrary to the basic assumption of the Steady State theory, that everything was constant in time. For this, and other reasons, the Steady State theory was abandoned.

Another attempt to avoid the universe having a beginning was the suggestion that there was a previous contracting phase, but because of rotation and local irregularities, the matter would not all fall to the same point. Instead, different parts of the matter would miss each other, and the universe would expand again, with the density remaining finite. Two Russians, Lifshitz and Khalatnikov, actually claimed to have proved that a general contraction without exact symmetry, would always lead to a bounce, with the density remaining finite. This result was very convenient for Marxist-Leninist dialectical materialism, because it avoided awkward questions about the creation of the universe. It therefore became an article of faith for Soviet scientists.

When Lifshitz and Khalatnikov published their claim, I was a 21-year-old research student, looking for something to complete my PhD thesis. I didn't believe their so-called proof, and set out with Roger Penrose to develop new mathematical techniques to study the question. We showed that the universe couldn't bounce. If Einstein's General Theory of Relativity is correct, there will be a singularity, a point of infinite density and space-time curvature, where time has a beginning.

Observational evidence to confirm the idea that the universe had a very dense beginning came in October 1965, a few months after my first singularity result, with the discovery of a faint background of microwaves throughout space. These microwaves are the same as those in your microwave oven, but very much less powerful. They would heat your pizza only to minus 271.3°C, not much good for defrosting the pizza, let alone cooking it. You can actually observe these microwaves yourself. Set your television to an empty channel. A few percent of the snow you see on the screen will be caused by this background of microwaves. The only reasonable interpretation of the background is that it is radiation left over from an early very hot and dense state. As the universe expanded, the radiation would have cooled until it is just the faint remnant we observe today.

Although the singularity theorems of Penrose and myself predicted that the universe had a beginning, they didn't say how it had begun. The equations of General Relativity would break down at the singularity. Thus, Einstein's theory cannot predict how the universe will begin, but only how it will evolve once it has begun. There are two attitudes one can take to the results of Penrose and myself. One is that the way the universe began is not within the realm of science. The other interpretation of our results, which is favoured by most scientists, is that it indicates that the General Theory of Relativity breaks down in the very strong gravitational fields in the early universe. It has to be replaced by a more complete theory. One would expect this anyway, because General Relativity does not take account of the small-scale structure of matter, which is governed by quantum theory. This does not matter normally, because the scale of the universe is enormous compared to the microscopic scales of quantum theory. But when the universe is the Planck size, a billion trillion trillionth of a centimetre, the two scales are the same, and quantum theory has to be taken into account.

In order to understand the Origin of the universe, we need to combine the General Theory of Relativity with quantum theory. The best way of doing so seems to be to use Feynman's idea of a sum over histories. Richard Feynman was a colourful character, who played the bongo drums in a strip joint in Pasadena, and was a brilliant physicist at the California Institute of Technology. He proposed that a system got from a state A to a state B by every possible path or history.

Each path, or history, has a certain amplitude or intensity, and the probability of the system going from A to B is given by adding up the amplitudes for each path. There will be a history in which the moon is made of blue cheese, but the amplitude is low, which is bad news for mice.

The probability for a state of the universe at the present time is given by adding up the amplitudes for all the histories that end with that state. But how did the histories start? This is the Origin question in another guise. Is the initial state of the universe determined by a law of science?

In fact, this question would arise even if the histories of the universe went back to the infinite past. But it is more immediate if the universe began only 15 billion years ago. The problem of what happens at the beginning of time is a bit like the question of what happened at the edge of the world, when people thought the world was flat. Is the world a flat plate, with the sea pouring over the edge? I have tested this experimentally: I have been round the world, and I have not fallen off.

As we all know, the problem of what happens at the edge of the world was solved when people realized that the world was not a flat plate, but a curved surface. Time, however, seemed to be different: it appeared to be separate from space, and to be like a model railway track. If it had a beginning, there would have to be someone to set the trains going.

Einstein's General Theory of Relativity unified time and space as space-time, but time was still different from space, and was like a corridor which either had a beginning and end, or went on for ever. However, when one combines General Relativity with Quantum Theory, Jim Hartle and I realized that time can behave like another direction in space under extreme conditions. This means one can get rid of the problem of time having a beginning, in a similar way in which we got rid of the edge of the world. Suppose the beginning of the universe was like the south pole of the earth, with degrees of latitude playing the role of time. The universe would start as a point at the South Pole. As one moves north, the circles of constant latitude, representing the size of the universe, would expand. To ask what happened before the beginning of the universe would become a meaningless question, because there is nothing south of the south pole.

Time, as measured in degrees of latitude, would have a beginning at the South Pole, but the South Pole is much like any other point, at least so I have been told. I have been to Antarctica, but not to the South Pole.

The same laws of Nature hold at the South Pole, as in other places. This would remove the age-old objection to the universe having a beginning that it would be a place where the normal laws broke down. The beginning of the universe would be governed by the laws of science.

The picture Jim Hartle and I developed of the spontaneous quantum creation of the universe would be a bit like the formation of bubbles of steam in boiling water.

The idea is that the most probable histories of the universe would be like the surfaces of the bubbles. Many small bubbles would appear, and then disappear again. These would correspond to mini universes that would expand, but would collapse again while still of microscopic size. They are possible alternative universes, but they are not of much interest since they do not last long enough to develop galaxies and stars, let alone intelligent life. A few of the little bubbles, however, will grow to a certain size at which they are safe from recollapse. They will continue to expand at an ever-increasing rate, and will form the bubbles we see. They will correspond to universes that would start off expanding at an ever-increasing rate. This is called inflation, like the way prices go up every year.

The world record for inflation was in Germany after the First World War: prices rose by a factor of ten million in a period of 18 months. But that was nothing compared to inflation in the early universe: the universe expanded by a factor of million trillion trillion in a tiny fraction of a second. Unlike inflation in prices, inflation in the early universe was a very good thing. It produced a very large and uniform universe, just as we observe. However, it would not be completely uniform. In the sum over histories, histories that are very slightly irregular will have almost as high probabilities as the completely uniform and regular history. The theory therefore predicts that the early universe is likely to be slightly non-uniform. These irregularities would produce small variations in the intensity of the microwave background from different directions. The microwave background has been observed by the Map satellite, and was found to have exactly the kind of variations predicted. So we know we are on the right lines.

The irregularities in the early universe will mean that some regions will have slightly higher density than others. The gravitational attraction of the extra density will slow the expansion of the region, and can eventually cause the region to collapse to form galaxies and stars. So look well at the map of the microwave sky: it is the blueprint for all the structure in the universe. We are the product of quantum fluctuations in the very early universe. God really does play dice.

We have made tremendous progress in cosmology in the last hundred years. The General Theory of Relativity and the discovery of the expansion of the universe shattered the old picture of an ever existing, and ever lasting universe. Instead, general relativity predicted that the universe, and time itself, would begin in the big bang. It also predicted that time would come to an end in black holes. The discovery of the cosmic microwave background and observations of black holes support these conclusions. This is a profound change in our picture of the universe and of reality itself.

Although the General Theory of Relativity predicted that the universe must have come from a period of high curvature in the past, it could not predict how the universe would emerge from the big bang. Thus, general relativity on its own cannot answer the central question in cosmology, Why is the universe the way it is? However, if general relativity is combined with quantum theory, it may be possible to predict how the universe would start. It would initially expand at an ever-increasing rate. During this so-called inflationary period, the marriage of the two theories predicted that small fluctuations would develop and lead to the formation of galaxies, stars, and all the other structure in the universe. This is confirmed by observations of small non-uniformities in the cosmic microwave background with exactly the predicted properties. So it seems we are on our way to understanding the origin of the universe, though much more work will be needed.

Despite having had some great successes, not everything is solved. We do not yet have a good theoretical understanding of the observations that the expansion of the universe is accelerating again, after a long period of slowing down. Without such an understanding, we cannot be sure of the future of the universe. Will it continue to expand forever? Is inflation a law of Nature? Or will the universe eventually collapse again? New observational results, and theoretical advances are coming in rapidly. Cosmology is a very exciting and active subject. We are getting close to answering the age-old questions: 'Why are we here?' 'Where did we come from?' I believe these questions can be answered within the realm of science.

Thank you for listening to me.

DISCUSSION ON PROF. HAWKING'S PAPER

PROF. PHILLIPS: What I would like to do now, in keeping with discussions with Professor Hawking, is to ask for two questions to be posed to Professor Hawking and while he is thinking about those questions and composing an answer, then we will return to questions for the earlier speakers and then check to see how the answers from Prof. Hawking are coming along. So, questions for Professor Hawking?... If no one else will ask a question, I will. My question is this: You spent a good deal of time explaining the difficulty of there being a beginning of time and came to this very nice analogy that asking what came before the beginning would be much like asking what is south of the South Pole. So, given that we accept that understanding, what I would like to ask is about the way in which time unfolds after that beginning of time. Today we define time in terms of atomic time. Now, if we go back to the early universe, before there are atoms we might wonder, 'what does time mean?' But we could just say that before there were atoms there were nuclei and we could use some other natural, nuclear timescale. But at some early enough time there was nothing we would identify as being anything like the kind of matter that we know today. How should we understand what time is like at such early times? That is my question. Are there others?

PROF. COLLINS: Thank you. A more philosophical question. In the final comments, Professor Hawking suggests that these observations from theory and experiment might answer the question, 'why are we here?' It seems to me more it might answer the question 'how did we come to be here', and it might fall short of why. I would like to hear more about the 'why' part.

PROF. PHILLIPS: Professor Hawking is thinking about those questions and preparing an answer. Let us return to Martin Rees' talk and ask whether there are any leftover questions from then. Professor Zichichi.

PROF. ZICHICHI: I have a question concerning complexity. Complexity is ill defined. There are seventy definitions of complexity and, therefore, it is important to see what are the experimentally observable quantities which suggest the existence of complexity. Despite the seventy definitions of complexity, the experimentally-observable quantities from which we derive the notion of complexity are the same, they are two. The unexpected events with enormous consequences, that historians call 'Sarajevo-type events' and the Anderson-Feynman-Beethoven (AFB) phenomena. Namely, Beethoven can compose masterpieces of music but ignores quantum electrodynamics. Without quantum electrodynamics we could not have music. So the existence of UEEC (Sarajevo-type events) and AFB phenomena are the experimentally observable quantities for complexity to exist. If you accept this, then the conclusion is that complexity exists at the fundamental level. You do not need to go from atoms to mankind to say that complexity is there; and you do not need billions of atoms to have complexity. At the very elementary level, AFB phenomena and UEEC events exist and therefore complexity exists even at the Planck scale.

PROF. REES: This is really a semantic question. The potential for complexity may exist, but a universe that was completely uniform, diffuse neutral hydrogen but nothing else, is surely a less complex universe than the one we are in. So we can argue the semantics, but I think everyone knows that a living thing is very complex and a universe of neutral uniform hydrogen, and nothing else, is much simpler.

PROF. ZICHICHI: My question is not semantic but fundamental. The origin of the Logic of Nature (four fundamental forces and three families of elementary particles) has its roots in EEC events and AFB phenomena. These are exactly the same roots for complexity to exist when you study large-scale events.

PROF. PHILLIPS: I think I would like to ask a question to Martin Rees, a very naïve question. You talked, in the early part of your lecture, about there being a horizon for seeing events at 14 billion years but saying, just as with the ordinary horizon, there is no reason to believe there are not things beyond it. Well, my naïve question is, if the universe began 14 billion years ago, and if things expanded no faster than the speed of light, how could there be anything beyond 14 billion years? I am imagining the answer probably has something to do with inflation and general relativity and the way one thinks about time, but, understanding the naivety of my question, can you somehow relieve that naivety for me?

Prof. Rees: If the universe accelerates, then there can be domains which disappear from our view and are, in a sense, going faster than light, but I can give, perhaps, a clarification. People sometimes worry about not quite your question but a related one. They worry about how we can be looking back 90% of the way to the Big Bang when we look at distant galaxies. You can answer that question in a simple universe where everything moves uniformly. In special relativity clocks run slow, so, if something is moving away from us at 99% of the speed of light, by its clock it does go maybe 10 light years in one year. In that very simple universe, there is no contradiction in saying that we are seeing something whose light set out 90% of the time back to the Big Bang.

Prof. Phillips: Yes, I do not have any problem with that. It is the existence of things that are at distances beyond – in light years – the age of the universe.

Prof. Rees: Well, that has to be understood in terms of an accelerating universe. Can I just add one more thing? You are familiar with the idea that in a black hole you see something falling in and you only see a finite part of its history, however long you watch. Similarly, if the universe is accelerating, then we see a galaxy, but the galaxy will have an increasing red shift, and we will only see a finite part of its history. So there could be domains of space-time that are beyond our horizon.

Prof. Phillips: I see; so in the same sense that when we watch something fall into a black hole it looks like it disappears but from its point of view it…

Prof. Rees: I wanted to emphasise that the aftermath of our Big Bang could be vastly more extensive than the domain that we can see with our telescopes, and the horizon on the ocean is a good analogy. But then I went one step further and said that the aftermath of our Big Bang may not be everything there is, because there are many ideas, for instance one called 'eternal inflation', where there are many Big Bangs. There could be an immensely complex space-time structure on this hugely larger scale than we can directly observe.

Prof. Rubin: Part of the end of your answer is related to the question I was going to ask, which is rather a personal question to you, whether you ever worry that the things that look or that we say now are very simple, it is just a lack of our understanding, and some of that you discussed in answering Bill's question.

PROF. REES: That raises the question of how confident we can be about statements we make in science. I think Thomas Kuhn did a great disservice by his concept of scientific revolutions. There are only one or two really good revolutions that I can think of in science, the Copernican revolution and the quantum revolution. Einstein did not prove Newton wrong, he transcended Newton and got a deeper understanding into gravity and the theory which extended to a wider range of domains than Newton did. There is a periphery between what we understand well and what we do not understand. That periphery, that frontier, moves out and gets longer as we settle old questions. Then new questions are posed that could not even have been posed beforehand. Stephen's talk reminded us that whether there was a Big Bang or a 'steady state' was controversial until the mid-1960s. We then moved on to questions of what was the early universe like, and is the universe accelerating or decelerating: we have had some surprises there, but I do not think the story of the Big Bang back to one second is going to be changed drastically, any more than our picture of the earth as being basically round is going to be changed. But of course the issues of what is beyond the horizon, what happens in the first tiny fraction of a second, are still completely uncertain, because the physics, although we speculate about it, is not battle-tested experimentally. I would just like to make one point about the so-called multiverse concept which is often derided as something which is not part of science because it can never be tested. It is entirely speculative now, but it could, I think, be put on a firm basis if it was a predicted consequence of a theory which we could test in other ways. For instance, we believe that the sun is getting its energy by nuclear fusion, not because we can actually observe in the centre of the sun but because we can observe nuclear fusion in the lab and we can do calculations etc. So we have a theory of how nuclei react, which we can test in other ways and apply to the sun. Similarly, if we had a theory which gave us a unified picture of quantum and gravity and if it explained many features of the world which we cannot otherwise explain, then that theory would gain credibility. If that theory, for instance, predicted some model like Lindé's 'eternal inflation' then we should take those predictions seriously, just as we take seriously what is implied by our theories about the universe after one second. So it is not necessary for a theory to have all its consequences testable, it just must have some consequences testable. To give another example, Einstein's theory of relativity has been tested in a number of ways and we therefore believe what it says about the inside of black holes, even though we cannot observe there. Similarly, perhaps one day we will know whether or not the multiple Big Bang theory is correct. We do not know now, but it is speculative science, not metaphysics.

PROF. PHILLIPS: So, just to follow up on that point about how one might test things that we cannot directly observe, it would seem that the idea of things beyond the event horizon fall into a rather different category than, say, the multiple Big Bangs or the multiverse, because the things beyond the event horizon you figure, well, they are going to have to be something like that if we had inflation, and inflation has some traces that we might be able to observe. On the other hand, while I would not say that there is no way that we are going to find out about the multiverse, we do not quite know yet how we are going to do that. Would you agree with that characterisation?

PROF. REES: I do not regard inflation as fully battle-tested yet, because we do not know what the detailed physics was when the universe was 10^{-36} seconds old. But the details of inflation depend on that physics, and people like André Lindé have shown that, if you make specific assumptions, then you get this 'eternal inflation'. He makes definite assumptions that lead to that result. If, some years or decades from now, we know what the right physics is to put in, then we will know whether eternal inflation would happen. Of course I am optimistic, we may never settle these. Another question we should not overlook is that there is no particular reason why our brains, human brains, should be matched to these deep questions. It is amazing that our brains that evolved to cope with life in the African savannah have been so successful in coping with the quantum world and the cosmic world, which is so far beyond the everyday scales. But nonetheless there could be some key theories which apply to cosmology or indeed to the biological world which are simply beyond the human brain. Just like my dog cannot understand quantum theory, maybe there are theories which are equally beyond the human intellect. But these deep issues may in the future be understood, because it is really important to bear in mind that the future of evolution could be as prolonged and far more fantastic than what has happened up to now.

PROF. PHILLIPS: Another question.

PROF. FACCHINI: Prof. Hawking said that the science will be able to answer the question 'why are we here?', about the ultimate origins of our existence. I ask what does it mean 'why': origin or significance? Is the significance within the realm of sciences?

PROF. PHILLIPS: Are you folding this question into the question that Francis Collins asked of Professor Hawking? OK, so we will take that under advisement. Do we have any questions for either Professor Rees or Professor Swarup.

PROF. DEHAENE: This is a very naïve question, but since we have experts here: do physicists really refrain from thinking about what was before the Big Bang? I remember hearing a lecture from my colleague Gabriele Veneziano who was speculating about what was happening before the Big Bang. Is this just science fiction or not?

PROF. REES: That is indeed an alternative theory, very different from what Stephen has just been telling us. But one general point is that the further we extrapolate back towards the initial instant, the further we get from everyday concepts. As we extrapolate back near the beginning then it could be that the whole idea of before and after, which implies a direction of time, has to be jettisoned, just in the same way that familiar common sense concepts have to be jettisoned when we get down to the quantum scale.

PROF. PHILLIPS: I suppose that if one is worried about the question of what happens before the Big Bang, that if you believe in multiverses, then at least you can figure there were other Big Bangs that were going on either before or after ours, and maybe that might make you feel better.

PROF. REES: And then, of course, there is the other idea that not all the extra dimensions are all rolled up very tightly. That leads to the idea that there could be another universe, as it were, alongside ours, both embedded in an extra dimension, just as you can imagine a whole lot of ants crawling around on this sheet of paper, which is their two-dimensional universe, and being unaware of another population of ants on a parallel sheet of paper. So likewise there could be another universe just a millimetre away from ours but, if that distance is measured in some fourth spatial dimension and we are imprisoned in our three, we would not be aware of it. Just one pedantic point: some people say quite rightly that we should use the word 'universe' for everything there is, so what are we doing talking about multiple universes? My answer to that would be that, if the idea of multiple Big Bangs were put on a firm basis, then we should adopt some new terminology and invent some new word like *metagalaxy* for what we have traditionally called the astronomical universe. But, for the moment, we should stick to the terminology where astronomers describe the volume they can directly study as 'the universe'. But then, of course, we need some word like *multiverse* for the totality of physical reality, which may be larger than the aftermath of our Big Bang.

PROF. PHILLIPS: Prof. Vicuña, what was your question?

PROF. VICUÑA: In a sense I think it has been answered, but I was wondering. I know that common sense does not work well in cosmology, but if there have been several Big Bangs, would there be measurable space between them? If only one Big Bang took place, the space that we see is all there is, but if there have been more Big Bangs, what is there in between the universes?

PROF. REES: I think this is a context where we have to accept that common sense notions are not good enough!

PROF. PHILLIPS: I would like to pose a question to Professor Swarup. You spoke about the origins of life and the development of simple cells and of different kinds of cells. My biologist friends tell me that, by the time you get cells, you have already got a tremendous amount of the complexity that is involved in life, so what I am wondering is, if I am trying to imagine how life started, at what point of complexity is the rest of the development of life essentially a foregone conclusion? Do I need self-replicating viruses? Do I need a cell before I am confident that the rest of biological evolution is going to unroll or do I need something as big as insects? What is your view on that?

PROF. SWARUP: I think that the most important thing is to be able to produce a unicell, to reproduce it: if we can do it in our laboratory, we have made a tremendous progress in understanding how life evolves. Whether that can be done there are experts here, a lot of people who are doing experiments on this and I would love to hear from them.

PROF. PHILLIPS: So you think of the cell as being the breaking point. Once I have got a cell, for sure I am going to get more complexity.

PROF. SWARUP: Yes, the simplest of cells. While I am on the microphone let me ask a question to Martin Rees. You see, I was giving a talk to students describing universe and multiverses and they asked me the question, generally in science you always make a prediction. If the prediction is not done then it is not correct, you throw the hypothesis out. So my student said he understands the universe is there, it is natural to expect multiverses but if there is no predictability are we talking of some new method of science, are we talking of some new terminology, as he says, of science? How would Martin Rees answer in a simple way to a student in college?

PROF. REES: Just to expand what I said earlier, the 'multiverse' will only be a serious part of science if it is a consequence of a theory we can test in other ways. If we had a sufficiently detailed theory, which predicted a range of possible Big Bangs, we could then put a probability measure on different options. We could then ask the question, are we in a typical member of the subset of such 'universes' in which we could exist? That is a well-posed question that could only be answered if we had a theory that was precise enough to put a probability measure on all the options. Can I give another example? I gave the analogy of a multiverse with planetary orbits. We do not believe, as Kepler did, that the earth's orbit is all that special. We just think it is an orbit of a planet which allows life to evolve. That, therefore, means it has got to be at roughly the distance from its parent star such that water neither freezes all the time nor boils and also that the orbit is not very eccentric. So we are not surprised to be living on a planet that does not have an eccentric orbit, because if it was a very eccentric orbit then it would be harder for life to evolve. But suppose that the earth's orbit was exactly circular to a position of one part in a million, then an anthropic explanation would not be good enough because there is no particular reason why it should be that circular. So if we observe a particular configuration, we can ask, 'is that just what we would expect?', otherwise we would not be here.

PROF. ABELSON: This is not a new question. Francis Crick weighed in on what could be the simplest form of life in the early 1970s and concluded it would have to self-replicate and the only thing he could imagine at that point that could self-replicate was nucleic acid. It is not easy to see how a protein can self-replicate itself. Because we are not going to hear David Baltimore's talk about the RNA world, I would add that we now know that RNA itself can be catalytic. A lot of progress has been made towards engineering an RNA that can catalyse its own replication. The abiogenic synthesis of a self replicating RNA early in the history of the planet, as improbable as it seems, could have been the first step in the origin of life. Once you can self-replicate, then evolution can begin.

PROF. PHILLIPS: So you are willing to push it back a little bit earlier than cells.

PROF. ABELSON: Yes.

PROF. REES: I recall Craig Venter making a statement that the simplest conceivable reproducing organism had about 200 genes in it. I am not quite sure what the status of that is, but I am sure that Francis could explain whether it makes sense.

PROF. COLLINS: That was based on an experiment where you take already a very simple bacteria, *Mycoplasma genitalium*, and start knocking out one by one the genes in that to see which of them are dispensable, and you get down to a certain number that are dispensable and you assume that is the minimal set. That experiment is risky, because probably combinations of genes that are individually tolerable, if you lose more than one of them in the same organism it may no longer be tolerable, so I suspect that is probably an underestimate but again this is starting already with a complicated organism called a cell, with all of its machinery. That does not mean that if you started from the ground up you would end up with something that is self-replicating. I agree with the Crick definition of what you are looking for. Some have argued though that maybe simply a catalytic RNA that is able to replicate itself would not quite do it, because it would not last long, and you need some kind of a membrane around it, some sort of way of constraining its diffusability, and certainly the people who are trying now to synthesise life forms of all sorts of very unusual forms are working very hard on the membrane part as well.

PROF. PHILLIPS: I would like to ask perhaps a rather odd question, in connection with the talk that we heard from Professor Swarup. So, let me preface my question by telling a story. Many years ago there was a lot of excitement about the possibility that researchers had found evidence of life on Mars. You remember this: supposedly there was some spallation from some meteorites and it ended up in Antarctica and it showed a lot of promising stuff and then it turned out to be, well, a little bit premature. But there was a big press conference at the time and people talked about all the evidence for this and a colleague said to me, after that press conference, 'Well, if this is so, won't this really cause a lot of consternation to people of religious belief?' And I thought, well, no, because if it is so that there is life on Mars then it just tells us that we have perhaps a larger view of how wonderful God's Creation is. But I am wondering (I am an amateur when it comes to theology) if any of the professional theologians here, or philosophers, would have something to say about whether there is an impact theologically if we discover that there is life elsewhere than on earth. Would any of the ordained people here care to make a comment on that?

PROF. FUNES: I am not a professional theologian, I am an amateur theologian, I say that I am an astronomer who once studied philosophy and theology, but I became famous in a few days because of an answer I gave to a journalist about the same question. Just to tell you briefly that in this universe, with a hundred billion galaxies, with a hundred billion stars in these galaxies, with planets, it may be possible that there is life as we know it. And just one line, because sometimes journalists need a headline, so for them I said, 'the extraterrestrial is my brother'. In the context of Franciscan theology I would say, this is very simple theology, but I do not see that there would be any problem for theology to consider the possibility of life. I think, I may be wrong, it was more traumatic for theologians when Europeans found Native Americans in America, in the whole of America, I think that was more traumatic for theology than finding extraterrestrials would be now… there are many other issues like original sin, the possibility of redemption, but I do not think that there would be a conflict. It is not related to this but, if I have time, I would like to say a brief comment, a quotation from George Coyne, regarding what Professor Hawking said, God does play dice, he said that and he added, he knows that the dice are loaded.

PROF. PHILLIPS: Does anybody who comes from a tradition outside of the Judeo-Christian tradition have any comment on my question? Does anybody have an opposing view or a different viewpoint from the Vatican astronomer?

PROF. GOJOBORI: I think I have a question which I would like to ask Professor Rees, maybe and Professor Hawking, too. The story of the phenomenon of the universe reminds me of the late Susumu Ohno concept. That means, he thinks of the world, or the universe, like a repetition that expands and sometimes shrinks. If you define repetition as order, then this concept can be applied to the DNA. The repetition might be the origin of the genetic materials and in gene duplication, genome duplication, repetition may be one of the most important properties. In Buddhism there is always reincarnation, since you are asking me, asking the outside of Christianity, so how do you see this kind of property, to be repetitive, that is so important to cosmology? I think that in biology certainly this might be one of the properties. I do not think this is doctoring, but still it might be important, therefore incarnation, repetition, how do you see it in cosmology, this is my question.

PROF. PHILLIPS: I might make the following comment. I have a colleague who is a Buddhist, he would consider himself to be a non-theistic Buddhist, and he is also a cosmologist, and finds the idea of a distinct beginning of the universe to be difficult. So, that is just one anecdote. But, Martin, do you have any comment about that?

PROF. REES: I do not, really. Among my cosmologist colleagues there are people with all kinds of faiths, fundamentalist Christians, Roman Catholics and people like you mention. They probably just keep their lives in different compartments if there are any potential conflicts, that is my impression.

PROF. PHILLIPS: Martin, now I would like to ask you the following question. You suggested that we do not really know whether it would have been possible for the universe to have had a different set of laws or a different set of constants. Now I know these two things are often said together, but it seems to me there is a very big difference between having a different set of constants and having a different set of laws. As far as I understand, we do not really know any reason why the constants should be what they are. On the other hand, I think we know pretty well that there are certain classes of laws for the universe that just would not work. I cannot imagine, for example, how we could have a universe that was based on classical physics. So, what I am wondering is, what can you say about the range of possibilities of different kinds of laws as opposed to different kinds of constants.

PROF. REES: It is just a question of how deep down the bedrock laws are. The conventional view is that there will be some exact formulae that people can write on their T-shirts which will give us the mass of the proton and the mass of the electron etc. But the alternative view, which is taken by a number of people (and Ed Witten is the world expert, he can comment) is that perhaps there are bedrock laws but those laws allow a variety of basic structures of the so-called vacuum which would allow different values for the masses and the strength of the forces. The question is whether what we conventionally call the 'constants of nature' are at the bedrock level or whether they are secondary arbitrary features. I think it would be good if Ed could comment on one of the big debates in string theory: whether there is a unique vacuum state or not.

PROF. WITTEN: Well, I cannot say what the truth is, but I can describe a situation that is often considered, and that is that there are many different regions that are all subject to relativity, quantum mechanics and gravity so in that very general sense they have the same laws but they have different, for example, gauge groups, so in one case there is a nuclear force and there is a weak force like we have it but the details of the particle forces are different. So the trouble with the question is that the notion of what is a law was a little bit hazy. To summarise this again, to try to clarify it for everyone, what is often considered is that there is a very general framework of relativity and quantum mechanics and gravity that they would all have in common, but the rest of what is in the textbooks would be different in each region.

PROF. PHILLIPS: So that is a good distinction, because, on the one hand, you have laws and on the other hand you might have, we might call it *forces*, weak force, strong force, it could be something different but it would still have to follow quantum mechanics.

PROF. WITTEN: Well, for example the electrical force is often called a law, Coulomb's Law.

PROF. PHILLIPS: Yes, sure! So the question of what is a law obviously is a question of semantics. I believe that Bernard d'Espagnat made a distinction like that but I cannot remember exactly what it was. One more question? OK, it has been quite a while so let us see, are we talking about the first question? It was about time. So the question I asked was, if we understand or at least accept the resolution of the difficulty about there being a beginning of time, how should we understand how time rolls out when the usual ways we have for keeping time do not seem to make any sense at the very early stages of the universe?

PROF. HAWKING: My answer to the first question is that I use the positivist approach. A theory is just a model; time is a quantity in that model; atoms are elements in that model which we can use to model but the model contains time independently of atoms.

PROF. PHILLIPS: OK. What is the answer to the second question?

PROF. HAWKING: My answer to why are we here is that, if we have a consistent model that exists as an asymmetrical model we would be a subsystem in that model and our observations and our feelings of self-consciousness would be defined by that model.

WHAT WE KNOW, AND WHAT WE DON'T KNOW, ABOUT THE UNIVERSE

VERA C. RUBIN

We live in a universe that is incredibly beautiful, enormously large, and very complex. It is also evolving. As stars evolve and age, they act as chemical factories, transforming their light elements into heavier ones; as galaxies evolve, they acquire more mass from their surroundings; as cluster of galaxies grow, they gravitationally attract nearby galaxies. Only in the last 100 years have we understood this evolution of the Universe.

'The progress of astronomy during the past 100 years has been rapid and extraordinary'. These were the opening words in *A Popular History of Astronomy during the Nineteenth Century*, a book written one hundred years ago by Agnes Clarke (1). It is an equally valid description of progress in the 20th century, and it will surely describe progress one hundred years from now.

Early civilizations had myths about the sky. When Galileo turned his newly constructed telescope to the sky in 1609, he not only initiated modern observational astronomy, but he also solved a mystery that had occupied civilizations past: he learned that the Milky Way is 'nothing but a congeries of stars arranged in clusters.' His discovery that the planet Jupiter has moons orbiting it helped to displace the Earth from its unique position in the universe. He accurately timed balls sliding down inclined planes to learn how objects fall. Stillman Drake's book (2) describes Galileo's experiments and makes fascinating reading.

Isaac Newton has been called the 'chief architect of the modern world' (3), certainly the modern world of science. He identified and defined gravity as a force; he explained the orbits of the known planets as the combination of their gravitational attraction by the Sun and their forward motion.

He recognized that each planet has its own gravity; the Earth's gravity attracts its moon and Jupiter attracts Jupiter's moons. He understood that the planets would perturb each other; he extended this to universal gravity. He included comets in his gravitational theory, and he understood the tides. Newton studied the eye, vision and colors, and he constructed a reflecting (rather than refracting) telescope, to avoid the colored rings that plagued refracting lenses.

At the start of the 20th Century, scientists knew the astronomy of Galileo, Newton, and more. They knew that we live in a galaxy of stars. They did not know that the Earth was not located at the center of the Galaxy. They did not know if the small, faint galaxies detected with telescopes were located in our Galaxy, or if they were larger objects much farther away. A combination of observations and theories has given us the model of the Universe we know today.

A very simplified sketch of our Universe is shown in Figure 1 (see p. 593). Our sun, carrying the planets (A) with it, is one of more than 100 billion stars in our Galaxy. The planets orbiting our Sun formed from the rotating disk of debris that remained after the Sun formed some 4.6 billion years ago. We, sun and planets, are located about one-half of the way out from the center of our Galaxy (B), a center that harbors a black hole. It takes our Sun and planets about 200 million years to orbit once about the center of our Galaxy, even though we move with a speed of 500,000 miles per hour. Our Solar System has made this circuit only a few dozen times.

In a galaxy, stars are very far apart, relative to their diameters. Thirty million stars would fit between our Sun and Proxima Centauri, the nearest star to our Solar System! In contrast, galaxies are very close to each other relative to their diameters. Our nearest large galaxy is the Andromeda galaxy, only a few galactic diameters away. Andromeda, our Galaxy, plus dozens of smaller galaxies in our celestial neighborhood, comprise the Local Group (C) of galaxies. The Local Group may ultimately merge with the Virgo cluster (D), a collection of several thousand galaxies. But before this happens, our Galaxy and Andromeda will spend several billion years merging with each other, a galactic ballet that has been mathematically choreographed for computer by John Dubinski and John Kameel Farah (4).

When we look in any direction in space, we detect clusters of galaxies that are billions of years old, whose light is currently reaching our telescopes and/or our eyes. These clusters form web-like structures across our Universe (here white) separated by voids (E). Our view of the earliest Universe comes from cosmic microwave background radiation, produced almost 14 billion years ago, about 400,000 years after the Big Bang (our name for the origin of the Universe). The Universe, initially exceedingly hot, has been expanding, cooling, and evolving ever since. The cosmic microwave background radiation presently arriving at our detector has cooled to a cold 2.75 degrees above absolute zero (5).

Tiny temperature fluctuations in the cosmic microwave radiation are shown here (F) as color variations. From these, first sub-atomic particles, then simple elements, hydrogen, helium, some lithium, evolved, and eventually stars. During their lifetimes, stars transform light elements into heavier elements. From these heavier elements come more stars producing more elements, and with time come planets, geology, ultimately biology and life. We understand some parts of the evolution of the universe. Future generations will know more.

Astronomy advanced rapidly in the 20th Century. In 1913, Albert Einstein wrote to George Ellery Hale, Director of the Mount Wilson Observatory, to ask if the deflection of light rays from a distant object, distorted by passing near the Sun, would be bright enough to be detected without an eclipse (6). This deflection is predicted by relativity theory. The answer was 'No'; the bright Sun would mask the faint light from the background object. An easier experiment was successfully conducted with the Sun darkened during the 1919 solar eclipse. Enormous publicity followed the observation that the Sun had distorted background starlight. The publicity made Einstein a celebrity. Earlier, in 1915, Einstein used relativity theory to explain the 'not quite right' timing of the orbit of Mercury, the planet closest to the sun (7). Newton's laws of planetary motion had to be modified for the first time. In Einstein's words 'matter tells space how to bend; space tells matter how to move'. Thus science progresses.

It was not until the 1920s that astronomers learned that our Sun and its planets reside far from the center of our Galaxy, and that the small galaxies viewed with telescopes are large galaxies comparable to our own, but located at enormous distances. These galaxies have surprisingly high velocities with respect to our galaxy; this is the evidence that the universe is expanding.

In 1933, Fritz Zwicky, an astronomer at Mount Wilson Observatory, noted that the 7 galaxies in the Coma Cluster of galaxies with known velocities have velocities that range from 6600 to 8500 km/sec (8). This large range of velocities implies either that the cluster is dispersing, or that matter that we do not see is holding the cluster together. Zwicky named this 'dark matter'. Surprisingly, his discovery was mostly ignored for about 40 years, perhaps in part because some astronomers thought that clusters could be dissolving.

From the 1950s to the 1980s larger telescopes were built, sophisticated detectors could observe a wider region of the electromagnetic spectrum, and rockets and space telescopes returned new images and data. Celestial objects were imaged in various spectral regions, some not visible from Earth: radio, microwave, infrared, ultraviolet, x-ray, and even gamma-ray regions. These images showed astronomers and the public the great beauty in some formerly 'invisible' objects.

Millions of stars in our Galaxy are imaged in Figure 2 (see p. 594). The whiter regions are uncountable numbers of stars along our line-of-sight. These distant stars define the northern Milky Way, the central plane of our Galaxy. The red blobs are Hydrogen clouds. A real treasure is the small bright object at the bottom. This is M31, the Andromeda galaxy, the nearest large galaxy to our Galaxy.

In 1965 I moved from teaching at Georgetown University to DTM, the Department of Terrestrial Magnetism of the Carnegie Institution of Washington. There I joined Dr. Kent Ford, a young scientist who had built an image-tube spectrograph for use at a telescope. This early electro-optical device reduced telescope exposure time by a factor of ten. Kent's interest was in demonstrating what such a device could do. My interest was in studying the motions of stars far out from the centers of their galaxies, a difficult task with conventional photographic plates.

Kent and I started observing the velocities of stars and gas clouds in M31, as they orbit the center of that galaxy. Before going to the telescopes (at Lowell Observatory and Kitt Peak National Observatory), I spent months measuring deep photographic images of M31, in order to measure accurate distances from bright stars to each faint region for which we wanted a velocity. These regions were too faint to be seen in the telescope. With our new equipment we obtained a spectrum of a region in one or two hours; each showed bright lines of various chemical elements. By measuring the exact position of the H alpha (hydrogen) line and comparing it with the laboratory rest position of the line, I could determine the velocity of that region.

When Newton plotted the velocities of the planets orbiting our Sun versus their distances from the Sun, he produced a figure much like Fig. 3, except that here I also include the outer planets not known to Newton. The planet Mercury, whose distance from the Sun is 1/100th that of Pluto, orbits with a velocity that is 10 times (e.g., the square root of 100) as rapid as Pluto's velocity. Kent and I expected the velocities of stars in M31 to exhibit a similar 'inverse square law' falling pattern; galaxies farther from the nucleus would orbit with slower velocities.

We were surprised. In 1970 Kent and I published (9) velocities for about 70 regions (Figure 4, open circles and points with error bars), velocities in

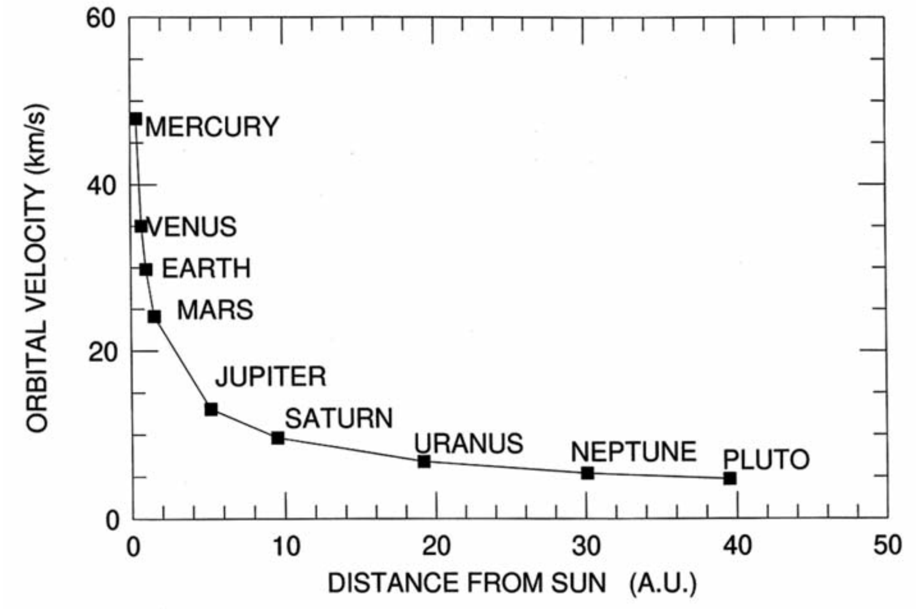

Fig. 3. The orbital velocity plotted versus distance from the Sun, for the planets in our Solar System. The AU (astronomical unit) is a unit of distance; the distance of the Earth from the Sun is one AU. Data for the first five planets come from Newton's *Principia*. When I plotted these data some years ago, Pluto was still a planet.

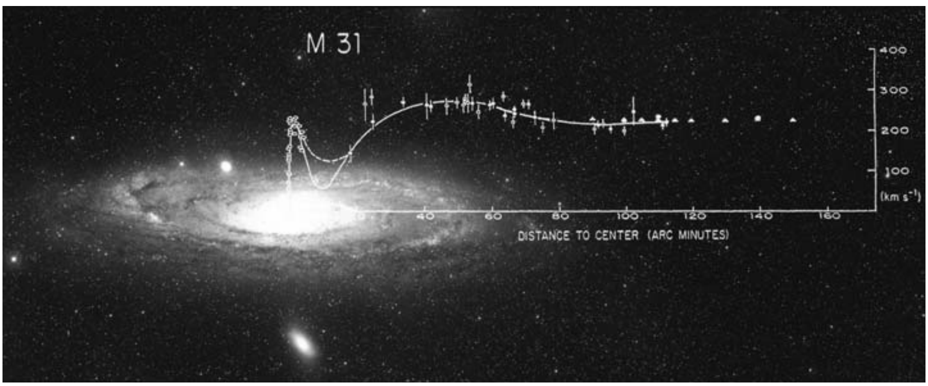

Fig. 4. The orbital velocities of stars and gas clouds in M31, the Andromeda galaxy, superposed on a Digital Sky Survey photo of M31(9)(10). The curve connects the optical data points (1970); the outer triangles are data from radio observations (1975). This flat rotation curve was one of the first to attract astronomers' attention.

the nuclear region and velocities well beyond the apparent optical limits of Andromeda. As plotted here, velocities from one side of the galaxy center are flipped over and plotted along with the other side. The drawn curve connects these optical velocities. In 1975, Roberts and Whitehurst (10) published velocities of more distant regions using a Green Bank Radio Observatory telescope. Optical and radio observations, superposed on the galaxy image, show that beyond the inner regions, stars and gas clouds in M31 orbit with remarkably constant velocities. The expected velocity decrease with distance, as observed in the Solar System, is not seen.

It took a decade, and rotation curves of about 100 more galaxies, for the subject of flat rotation curves to seem real and important. A brilliant review of the available galaxy data by Sandra Faber and Jay Gallagher (11) was important in convincing scientists that we must modify our concepts of the Universe. It is disappointing that after 40 years, and rotation curves for tens of thousands of other galaxies, the composition of the dark matter is still a dark mystery.

We lack important knowledge about our Universe for we lack knowledge of most of its mass. The current generally accepted model is (1).

(1) There is much dark matter (DM) in a galaxy; the amount increases linearly with radius and extends several diameters beyond the galaxy optical image to produce the observed flat rotation curve. It is known that dark matter interacts with matter only gravitationally, so it cannot be baryonic, e.g., composed of conventional atoms and sub-atomic particles. Dark matter constitutes about 95% of the mass in the Universe; conventional matter that we see and know contributes less than 5% of the Universe mass. This model has been adopted by most of the scientific community.

(2) An alternative, less conventional explanation is that there is no dark matter. Instead, Newton's inverse square law must be modified, for it does not apply at distances far from the centers of galaxies. A few dedicated scientists, initially Jacob Bekenstein and Moti Milgrom (12), have modified Newton's gravitational theory so that flat rotation curves result. Their modified Newtonian dynamics (MOND) accounts for the observations. An October 2008 email to me from Bekenstein states: 'Despite widespread doubts by DM aficionados, it has become possible to cast the essence of MOND into relativistic form (TeVeS and now various imitations of it) so that one can begin to confront it with gravitational lenses and cosmology'.

Richard Feynman presents a brilliant discussion of gravity in his little book, *The Character of Physical Law* (13). He notes that it is not exact, that 'Einstein had to modify it' to account for Mercury's orbit, and that 'there is always an edge of mystery always a place where we have some fiddling around to do yet'. This was before we knew of flat rotation curves.

Still other puzzles accrue. About 10 years ago, astronomers started gathering evidence that suggests that the universe is currently expanding faster than it had been expanding in the past. This phenomenon is named dark energy. However, dark energy is unrelated to dark matter, except that the observations were unexpected and the explanation is still unknown. Observations continue, and we will know more in the future.

Einstein knew that light from a background object would be gravitationally distorted by passing behind a massive foreground object. His 1913 query to the Mount Wilson Observatory Director was answered in the positive in 1979, with the discovery of the first gravitationally lensed image (14). In Figure 5 (see p. 595), the Abell 2218 cluster of galaxies at a distance of about 2 billion light-years from Earth has distorted the light from more distant galaxies into arcs and rays of various colors. The background galaxies are 5 to 10 times more distant than the Abell 2218 cluster. Our most distant views of the Universe at present come from *very* distant objects that are gravitationally lensed by distant objects.

Astronomers and physicists attempt to answer the many questions that arise from observations of the Universe. For astronomers, the second half of Century 2000 was remarkable for the instrumentation that it produced, and for the new knowledge that was uncovered. One of the great surprises came with the understanding that chemistry, physics and sciences in general are similar throughout the Universe. Although we understand that important surprises lie ahead, we are not wise enough to imagine what the new discoveries will be. With over 200 billion galaxies in our Universe, many with more than billions of stars, the likelihood of stars and planets with similar evolutionary paths is not small. It is likely that we will learn that other Universes exist and that we will learn to communicate with them. But distances are large, and finances are limited, and communication methods must speed up to be faster than light.

In the year 984 A.D. astronomer Al Sufi produced the first known image of the Andromeda galaxy, the faint fuzz in the sky that the fish is about to swallow (Fig. 6). Al Sufi could never have imagined what we know today about his fuzz, about the Andromeda galaxy and about the Universe. It seems likely that some of our science of 2000 will appear equally quaint to astronomers in the year 3000. But there is something remarkable about being a scientist and learning unimagined things about our Universe. Science truly is *The Endless Frontier* that Vannevar Bush (15) wrote about in 1945.

Fig 6. On this oldest known image of the Andromeda galaxy, Andromeda is about to be swallowed by the fish.

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DISCUSSION ON PROF. RUBIN'S PAPER

PROF. MENON: Thank you very much, Vera, for that beautiful, historical and highly personal account of astronomy through the ages and, more particularly, your own contribution which is truly outstanding and which is, I think, the central question in astroparticle physics today and we are very grateful to you for that lecture. Now the talk is open for questions.

PROF. ARBER: You described so nicely the tremendous speed by which our solar system orbits. My question would be, during that travel, does the solar system pick up or lose matter? It may encounter other matter, dark matter or even other matter: does it take some with it or lose it during that travel?

PROF. RUBIN: The density of dark matter is not enormous. Space, I cannot say it is empty, because we now believe it has dark matter, but the separation of stars in a galaxy and the separation of galaxies one from each other are really enormous distances. I am not sure whether that is an answer to your question. I once, many many years ago, calculated how many suns, how many objects the size of our sun we could place between our sun and the next nearest star and, if my memory is correct, it was more than fifty million. So the density of dark matter is not enormously high. So I think the effect is certainly second-order in terms of the things I was mentioning.

PROF. CABIBBO: Excuse me, Vera, what is the time scale of that video of our galaxy and the Andromeda galaxy merging?

PROF. RUBIN: I have shown just a small cut of a longer video made by John Dubinski and John Farah. The time scale you saw covers about 2 billion years; their total simulation covers about 5 billion years. But for someone in our galaxy, it would be a very slow interaction. There would be plenty of time to prepare for the future. Andromeda is presently approaching our galaxy, but at a very slow pace. To the accuracy we can presently measure, its distance does not change.

PROF. CABIBBO: We feel better!

PROF. RUBIN: Yes, you do not have to worry, that is right! But your children's children's children's children's and so forth, but they will have plenty of time, this is a slow thing, it is not catastrophic in the sense that it would come overnight.

PROF. PHILLIPS: So when we look at this movie it looks really cataclysmic, but if we were in an earth like ours, around a sun like ours, at the time this was happening, other than what we might see in the heavens, would it change our lives very much?

PROF. RUBIN: No, no, unless you were very very unlucky and, I think, even then, you have many many years, you see things in the sky and you understand ultimately what is happening and probably can trace the orbit and I think you would be pretty safe. If it were a central hit, if the centre of our galaxy hit the centre of Andromeda, we would not have to move, according to this simulation, so you can rest well tonight.

PROF. W. SINGER: Did I understand correctly that the existence of dark matter is still a hypothesis and that it would have to be abandoned if we depart from different original assumptions, if Newton's laws were not generally valid then you could get away without the hypothesis of dark matter?

PROF. RUBIN: If we alter Newton's laws only slightly, yes, we can explain exactly what we are seeing. But any change now would have to incorporate everything else that we presently understand about the Universe. This is more difficult. But even at present, there are still properties of the Universe that we do not understand. Of major importance, we have no fundamental understanding of gravity. Until our science advances to understand more of these unknowns, I think it makes sense to consider alternatives. And there are alternative models of the Universe that do not require dark matter.

PROF. W. SINGER: And then we would not have to postulate the existence of dark matter.

PROF. RUBIN: That is right, then dark matter would not exist.

PROF. W. SINGER: Great.

PROF. RUBIN: You have reminded me that the first meeting I ever went to, to discuss dark matter, was at Harvard in, I think, 1980, it might have been 1970 – Martin Rees is smiling because he knows what I am going to say, because I have said it before – at that time they said, 'in ten years we will know what dark matter is' and then, when that did not happen, they said, 'in ten years we will know what it is', and then Martin gave a talk and he said, 'in five years we will know what it is', and I think it was after that talk that I got up and said, 'and now you have added another five?'

PROF. W. SINGER: But is this not crucial for our understanding of the further development of the universe if it exists or if it does not exist, it seems as if we ignore a crucial variable.

PROF. RUBIN: Yes, it is interesting, when Einstein had all of his ideas, relating to changing Newton's laws, he never looked for an alternative, he just changed the law and everyone believed him. I do not know what would have happened if someone had approached these observations that way and said, 'now we have to change Newton's laws': people would have looked at the alternative.

PROF. MENON: Thank you, I think that debate can go on, but on a personal basis, because we will now take the last two questions on this interesting topic.

PROF. REES: A comment on Wolf Singer. I think it is fair to say that there is no credible alternative. At first sight you might think you could just change the inverse square law at large distances, but that does not work because you see this deviation on a range of scales. Also, Vera Rubin showed a picture of a cluster of galaxies, and you get complete consistency in the mass estimates if you assume dark matter and assume relativity and the light bending is what you would expect if the masses are what you infer by Newtonian theory. Taking that evidence into account, plus the agreement between the simulations of galaxy formation and what we observe, leaves no credible alternative to the idea that gravity is the way we think it is, and there is dark matter which is in some sort of collisionless non-interacting particles.

PROF. WITTEN: I completely agree with what Martin just said, but on the previous comment by Vera Rubin, imagine if Einstein had set out to modify Newton's laws to account for the discrepancy with Mercury, he almost certainly would have gone completely wrong, because you could meet that discrepancy by keeping Newton's logic and just adding one more term in the potential, and anyone, I think any physicist who decided on purpose to modify Newton's laws to account for what Mercury was doing would have done something like that. Einstein changed the logic without thinking about Mercury and then it turned out that it gave the right answer for Mercury.

PROF. RUBIN: Thank you.

PROF. KASTURIRANGAN: There is this departure from the inverse square law on which you have ascribed the attraction due to the dark matter. Is there an epochal dependence for those kinds of attractions? Is there a possibility that that kind of departure could be significant in the context of the evolution of the universe and particularly in the early phase?

PROF. RUBIN: If I understand the question, I think I know of no study that investigated modifications or anything other than for the flat rotation curve. Were you asking about other departures? I do not think anyone has looked into that at all in a serious way.

PROF. MENON: Thank you very much, Vera, for both the talk and the discussion.

GALAXY EVOLUTION

JOSÉ G. FUNES, S.J.

1. Introduction

Galaxy evolution is one of the most active research areas in astrophysics. In the preface of his famous book *The Realm of the Nebulae* (1936), Edwin Hubble wrote: 'the book is believed to furnish an authentic picture of a typical case of scientific research in the process of development'. This statement is still true today for galaxy evolution.

It is widely accepted that galaxy evolution occurs within the framework of a Λ Cold Dark Matter cosmology; that is to say that clustering and merging is how galaxies gain in mass, and can also determine the shape and structure of galaxies.

Galaxy formation and evolution is a complex combination of hierarchical clustering, gas dissipation, merging and secular evolution. While gravity drives the bottom-up assembly of cosmic structures, gas cools at the centers of dark matter halos forming a disk that acquires angular momentum through tidal torques from nearby structures. Gas eventually fragments and forms stars. The mass and the angular momentum that settle into the disk are assumed to be fixed fractions of the mass and the angular momentum of the halo respectively. Since the mass and the size of the halos are tightly linked to the density of the Universe at the time the halos were formed, disk galaxies are expected to grow with cosmic time.

For reviews and books on this subject, see Avila-Rees 2006; Kormendy & Kennicutt 2004; Spinrad 2005; Keel 2002.

In this paper I would like to address the following question: What observational evidences do we have for galaxy evolution? Before doing so I will introduce some important concepts regarding galaxy structure and properties.

I will only focus on galaxies in the local universe. We can ask ourselves what is the importance of their study. As it was pointed out by Sandy Faber in the Conference Summary of the first Vatican meeting on formation and evolution of galaxy disks held in 2001, galaxies are the crossroads of astronomy because they look up to cosmology and they look down to the interstellar medium and star formation. They are the true link between the present universe we observe and the properties of the early universe. Galaxies evolve according to the initial and boundary conditions given by cosmology. As Vera Rubin has pointed out nearby galaxies are the best laboratories to test a 'nearby cosmology'. The study of galaxies is crucial when trying to connect our knowledge of the universe as a whole with the formation of stars and planets.

2. Galaxy components and properties

A galaxy is a system of stars, gas, dust and dark matter gravitationally bound together with a mass ranging from 10 million to 1000 billion times that of the sun. The stellar component is distributed in a spheroidal component (the bulge and the halo) and in a flat component (the disk). Some spiral galaxies show a bar and ring structures in the disk component. Gas and dust are the material between stars and it is called interstellar medium. This is the material from which new stars form. We don't know yet the nature of dark matter. We have detected and weighted the dark matter and we also know that it does not emit light. We do know that dark matter is located in the galaxy halos.

These galaxy components (stars, interstellar medium, and dark matter) vary from galaxy to galaxy and define the morphology of a galaxy. Galaxies have a disk component and a spheroidal component. Stars in the disk are bluer and younger than stars of in the spheroidal components.

Edwin Hubble classified galaxies in spirals and ellipticals. He also noticed that there is small fraction of galaxies that can be grouped in a third major type called irregular galaxies.

With the advent of a wealth of data coming from surveys like Sloan Digital Sky Survey, COMBO-17, etc., it has become clear that there is a bimodal distribution of galaxy colors at all redshifts[1] $z<1$ (see Bell *et al.*

[1] The redshift is usually characterized by a dimensionless quantity called z. The largest observed redshift, corresponding to the greatest distance and furthest back in time, is that of the cosmic microwave background radiation; the numerical value of its redshift is about z=1089 and z=0 corresponds to present time. The correspondence between redshift and time depends on the cosmological model adopted.

2007 and references within). It is possible to identify a red sequence of non-star forming galaxies and blue cloud of star-forming galaxies. According to this scheme ellipticals and early type spirals (spirals with a prominent bulge) would be part of the red sequence while late-type spirals (spirals with a small bulge and rich in gas and dust) and irregulars would form the blue cloud.

3. Galactic time scale

Galaxies are tracers of cosmic evolution over the last 13 billion years. Galactic time scale is the combination of two clocks. One time scale is the cosmological one (the Hubble time, i.e. basically the age of the universe) and the other scale is related to stellar evolution. The combination of both gives rise to galaxy evolution.

I would like to recall an observational obvious fact in the study of galaxy evolution. We never see an object to evolve from or to and we only have a 'snapshot' in time.

4. Which properties of galaxies can evolve and be measured?

Is there any way of measuring or detecting galaxy evolution? To answer this question we need to find galaxy properties that can evolve and be measured.

Due to the nuclear stellar evolution we expect to observe evolution in the stellar content which is shown in the change of color and luminosity measurable in galaxies at different redshifts. Intimately connected with the evolution of the stellar content is the evolution of the gas mass fraction. We expect a 'noisy' decline of the gas mass fraction with time, given the evidence for clustering mergers of gas rich systems and ejection to the interstellar medium of material released by supernovae. Since generations of stars continually recycle the same galactic matter through their cores, chemical evolution is an inevitable by-product of continual star formation.

Galaxies also evolve or transform due to the interaction with other galaxies. Galaxies are not exactly 'island universes'; they don't evolve in isolation. Spiral galaxies tend to collect in groups of galaxies, which contain up to several dozen galaxies. Elliptical galaxies are more common in clusters of galaxies. Mergers are an important factor that drives galaxy evolution. Merger rates increase with cosmic lookback time when the universe was smaller and galaxies were closer.

5. Evolution of the stellar content

One way to quantify galaxy evolution is through the calculation of the growth of stellar mass in galaxies.

As Bell *et al*. (2007) have pointed out, recent observations have demonstrated a significant growth in the integrated stellar mass of the red sequence. In their paper, they use the COMBO-17 photometric redshift survey in conjunction with deep Spitzer 24 mm data to explore the relationship between star formation and the growth of stellar mass. They calculate star formation rate (stars formed per unit of time in M_{sun} yr^{-1}) functions in four different redshift slices between z=0 and z=1, also splitting them into contributions from the red sequence and blue cloud for the first time. They find that the growth of stellar mass since z=1 is consistent with the integrated star formation rate.

6. The cosmic star formation history: galaxy evolution in the act

The cosmic star formation history is one of the primary goals of galaxy formation and evolution studies. The modeling of galaxy evolution requires a better understanding of the relationships between large-scale star formation rate and the physical properties of the parent galaxies.

Star forming galaxies in the local universe provide vital clues to the evolutionary properties of galaxies and the physical processes that derive that evolution. In the last 15 years hundreds of nights on the largest telescopes in the world are being used to measure the star formation properties of distant galaxies and the star formation history of the universe. Ironically, until few years ago, we had a more complete inventory of star formation rates for galaxies with redshifts (z>3) than for galaxies in the local universe (z<0.03).

Luckily, ideal samples, which meet these requirements, now exist. The Local Volume Legacy survey (Lee *et al*. 2008) is a project that looks through data already collected by the Spitzer Space Telescope for a sample of 258 galaxies located within 11 megaparsecs (about 36 million light years; on the scale of a visible universe that extends nearly 14 billion light years across, this counts as the 'local' volume of space). This included all known galaxies within the closest 3.5 megaparsecs, and a sampling of spiral and irregular galaxies from the larger and more representative region.

The goal is to produce a census of the local galactic neighborhood, with data in many different colors, including even the faintest galaxies, taking advantage of Spitzer's high resolution and ability to measure wavelengths of light that cannot be seen from the surface of the Earth. These data will then be compared with data on the same objects from a number of other surveys, using both large Earth-based telescopes.

This Local Volume Legacy project will fill in critical gaps in the current Spitzer coverage of the galaxies in the Local Volume, providing spectral energy distribution coverage from the ultraviolet to the far-infrared, and thus supplying the astronomical community with a core archival data set on the galactic neighborhood.

7. Chemical evolution

Another property that we can measure to monitor in galaxies is the abundant of heavy elements (metallicity) in the stellar population and in interstellar medium. Although our understanding of the actual physical process of star formation and its interaction with interstellar medium is acutely limited, models and observations have shown the evolution of metallicity in the galactic structural components (disk, bulge, and halo). For instance the enriched gas from the halo can pollute the bulge stars and the later forming disk during the process of galaxy formation.

As Tremonti *et al.* (2004) have pointed out stellar mass and metallicity are two of the most fundamental physical properties of galaxies. Both are metrics of the galaxy evolution process, the former reflecting the amount of gas locked up into stars, and the latter reflecting the gas reprocessed by stars and any exchange of gas between the galaxy and its environment. Understanding how these quantities evolve with time and in relation to one another is central to understanding the physical processes that govern the efficiency and timing of star formation in galaxies. They have presented the mass-metallicity relation for 53,000 star-forming galaxies in the Sloan Digital Sky Survey at z~0.1. Their results imply that metallicity is not a straightforward metric of galaxy evolution because metals can escape galactic potential wells.

8. Dynamical evolution. Galaxy transformation. Secular Evolution

Changes in the galactic structure are the result of the exchange energy and angular momentum between the different components: disk, bars, and rings and with environment through interactions and mergers.

Transformations in morphology, and not just in stellar content, can be observed and interpreted through computer simulations. Two processes rule galaxy evolution, the hierarchical clustering process and the secular evolution. Hierarchical clustering is a violent and rapid mechanism that dominated the growth of galaxies at early times of the universe. On the other hand, secular evolution is slow but will be dominant in the future universe.

Which signs can we find in galaxies that can lead us to think that there is or there was a merger in act? These are some:

- Images of pairs of galaxies may reveal tails and bridges of stars and gas that are signs of interactions.
- Counter-rotation. In some galaxies that otherwise look pretty 'normal', there is evidence that one of the components is counter-rotating or rotating orthogonally to the other component. For example, in a stellar disk, the inner disk is rotating in the opposite direction of the outer disk, or the spheroidal component regarding the disk component.
- Structural details in elliptical galaxies. For instance, elliptical galaxies with dust lanes have undergone a major event at some point in their evolution. The younger population of stars in these galaxies could have formed at a later stage of the evolution of the galaxy through either a merger event or a secondary in situ star-formation burst by the acquisition of gas from the environment.
- Observations show that collisions trigger bursts of star formation.
- N-body simulations of such collisions confirm that the merger of two spiral galaxies can form an elliptical galaxy.

Series of simulations by Debattista *et al.* (2006) to study the secular evolution of disk galaxies in a ΛCDM universe have shown that during disk assembly, secular evolution must have played a role in shaping the structure of disk galaxies as we see them at z=0. Bars can drive a substantial redistribution of mass and angular momentum in the disk. A possible product of bar-driven evolution is the formation of a bulgelike component.

Which structural properties of present-day disk galaxies are primordial and which are the result of internal evolution? Observations by Lilly *et al.* (1998) suggest that the structural properties of disk galaxies have not changed substantially since then. If the quiescent phase of disk assembly starts early, as current cosmological simulations suggest, secular evolution might have already been operating by z~1.

There is also recent evidence for a rapid secular galaxy evolution. Genzel *et al.* (2008) have provided observational evidence that massive bulges may have formed on a timescale of 1–3 10^9 years through secular evolution from gas-rich, turbulent disks.

They speculate that the thick, old stellar disks seen in the Milky Way and nearby galaxies are the remnants of this phase.

9. Final thoughts

These are not conclusions; it would be conceited on my side to do so with the abundant literature in this field that I have not covered. I have only tried to show in this paper that we have a coherent picture for the evolving process in galaxies with robust observational evidence well integrated and understood in the framework of the ΛCDM scenario.

There are still some unsolved problems for the ΛCDM scenario such as the nature of dark matter, halo density profiles of dark matter, the excess of substructure (satellite galaxies), the early formation of massive red elliptical galaxies, size of and angular momentum of the disks, etc. These important issues are not discussed in this paper.

There is also a need of a better understanding of the star formation physics that can explain the relationship between the star formation properties that we observe at the galactic scale and the properties and physical processes that we observe at a smaller scale.

Our knowledge of galaxy evolution showcases our understanding of cosmology, stellar evolution, and galaxy dynamics. It is an excellent example of how scientific knowledge achieved independently can be put together to shed light on a complex process that involves other physical processes at different scales. Our scientific understanding of galaxy evolution is still evolving…

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DISCUSSION ON PROF. FUNES' PAPER

PROF. MENON: Thank you very much Professor Funes, the topic is now open for discussion.

PROF. RUBIN: Thank you. Your last sentence, the need of a theory of star formation physics, what is holding that back?

PROF. FUNES: For example, when we calculate the star formation rate from different methods, I would say for example H-alpha, UV, broadband colours, infrared, in those determinations there are some model assumptions, like for example the initial mass function, those kinds of things that are in a much smaller scale. There is also a need for a better understanding of the star formation physics that can explain the relationship between the star formation properties and physical processes we observe at a smaller scale.

PROF. PHILLIPS: Early in your talk you said that, in connection with the discussion on morphology, that the merger rate increased with lookback time. So, what I was wondering was, is that just a simple result of the fact that the density of the universe was bigger earlier or is there something more subtle going on?

PROF. FUNES: I say that Martin Rees can answer much better than me, but basically what I understand is that, in the past, the universe was smaller, the volume was smaller, so the chances of mergers were bigger.

PROF. DEHAENE: Given what you know about the evolution of galaxies, what can you say about the position of our solar system and our galaxy? Are they in any sense in a special position or are they in the standard system of evolution, at a standard moment?

PROF. FUNES: Martin Rees and Vera Rubin have shown our location in the universe. I would say that we do not have a privileged position in the universe. The sun is a common star, a main sequence star, nothing special, there are many stars like the sun. We argentinians have a very bad time, especially in Latin America, because we believe that – or people say that we believe – that we are the centre of the universe: we are not, and the earth is not the centre of the universe or in a special location of the galaxy.

PROF. REES: Just a comment. I agree that, at early times, there were more mergers etc. The simulation I showed in my talk does show that the dark matter starts to accumulate in smaller units and then they merge together, and the dark matter is 85% of the gravitating stuff in the universe so it is really the agglomeration of the dark matter that determines how galaxies form. As a footnote to what Vera said, I would like to emphasise that, when people calculate the gravitational clustering of the dark matter, they find from the simulations what the density profile of the dark material is and it indeed does have the property that gives rise to flat rotation curves. So there is a link between the outcome of the simulations of how the dark matter clusters and the rotation curves that Vera showed, so there is a certain consistency in the models which do fit a whole lot of data.

RIGOROUS LOGIC IN THE THEORY OF EVOLUTION

ANTONINO ZICHICHI

Introduction

Three fundamental transitions are needed in order to go from the vacuum to the Universe, as it is now, with living matter endowed with Reason. These transitions called, *Big Bang-1*, *Big Bang-2* and *Big Bang-3*, are discussed in chapter 1. *Big Bang-1* describes the transition from the vacuum to the Universe made only of inert matter. *Big Bang-2* describes the transition from inert matter to living matter.

Among the million forms of different species of living matter which should be the result of the Living-Matter-Evolution-Process, LMEP, there is one species, and only one, whose existence needs another transition. This one, very peculiar indeed, we call *Big Bang-3*. This is the transition from the status of *living matter* to the status of *living matter endowed with Reason*.

At this point it is necessary – and this we do in chapter 2 – to recall that there are three levels of Galilean Science. An event and its subsequent evolution which happens only once, needs the third level Galilean Science in order not to be out of scientific rigour.

It is therefore necessary to see where these three Big Bangs are in the whole of our intellectual activity, where Complexity comes in.

Evolution and Complexity must be studied. This is the content of chapter 3.

In chapter 4 we review evolution in History and Science, the two opposite asymptotic limits of Complexity.

In chapter 5 our ignorance in the knowledge of the evolution of the Universe is presented in terms of known facts.

In chapter 6 the problems in the study of evolution are presented, pointing out the relevance of first level Galilean Science.

In chapter 7 it is shown why the Biological Evolution of the Human Species (BEHS) is below the third level of Galilean Science. To clarify this the best example of the third level, cosmic evolution, is confronted with BEHS.

In chapter 8 the evolution of Science is studied in terms of its origin and of the results so far achieved.

In chapter 9 the basic point is discussed whose logic is that the hardware governing all forms of matter is the same, despite the fact that the elementary forms of matter have zero interaction with the environment.

The proof that only one form of living matter possesses the privilege of being endowed with Reason is discussed in chapter 10.

A brief recapitulation is the content of chapter 11. The conclusion is in chapter 12.

1. Scientific Rigour, the Three Big Bangs and Their Evolution

When we speak about evolution we should not forget the two basic pillars of Galilean Science: experimental reproducibility and mathematical rigour. A theory can be formulated using words, i.e. Language and its Logic. This Logic allows predictions to be made. These predictions have no mathematical rigour since the Logic at work is based on Language. This was the case before Galilei's arrival.

A theory can be expressed using mathematical formalism and its logic. This allows predictions to be made using the power of mathematical formalism. According to Galilei [1] *Scientific Logic* requires that a key experiment must exist in order to put the theory under experimental test. If no experiment can establish if the theory is *right* or *wrong*, the theoretical structure which describes a certain phenomenon or a series of phenomena remains out of what we call Galileian Science.

The theory of evolution should describe how it happens that we are here, something like $(15\text{-}20)\times 10^9$ years after the classical and famous Big Bang. This Big Bang is in fact the first one, *Big Bang-1*, and refers to the transition from the vacuum to the Universe which now has about 10^{82} protons, neutrons and electrons. These particles are an inert form of matter.

The transition from inert matter to living matter is necessary in order to explain how it happens that we are here. This field of scientific research is called 'minimal life' and has two approaches: the *bottom-up* and the *top-down*. Since this is not my field of research activity I will only limit myself to saying a few words on the two approaches. In the *bottom-up* approach the formation of the minimal form of living cell is studied starting from atoms and molecules. In the *top-down* approach the basic 'pieces', the inert parts of matter, are taken from living matter and the problem is to see how many pieces are needed to build the minimal living cell. The transition needed to go from inert matter to living matter is to be called *Big Bang-2*. The evolution here has to deal with millions of forms of vegetable and animal matter.

Out of this enormous number of different forms of living matter there is one, and only one, endowed with a special property, called Reason. We are the only form of living matter having this incredible property, which generates Language, Logic and Science (discussed in chapter 10). Another Big Bang is needed to describe the transition from the innumerable number of examples of living matter to the unique one which is us. We call this transition *Big Bang-3*.

The three theories of evolution start therefore with the three Big Bangs, illustrated in figure 1.

THE THREE BIG BANGS

BB1 ⇒ *from Vacuum to the Universe of Inert Matter*

BB2 ⇒ *from Inert Matter to Living Matter*

BB3 ⇒ *from Living Matter to Living Matter with Reason*

Figure 1.

The evolution after *Big Bang-1* refers to the evolution of inert matter and therefore the evolution of our Universe: cosmic evolution. This theory of cosmic evolution is founded on the three levels of Galilean Science, discussed in chapter 2.

Big Bang-2, which explains the transition from inert to living matter, is followed by the theory of evolution needed to describe how it happens that a very large number of forms of living matter evolved.

Finally *Big Bang-3*, which explains how Reason emerges from living matter, is followed by the third type of evolution.

The three Big Bangs and the three theories of evolution need both the reference to experimental reproducibility at each step of the evolutionary process, and the mathematics capable of describing the different processes. The problem of experimental reproducibility is linked to the three levels of Galilean Science that will be discussed in chapter 2. Here it is necessary to point out that the three evolution processes, following each *Big Bang*, have their roots in the same hardware. In fact the basic constituents and the fundamental laws of Nature, are common to all of them.

In our present Universe we are all made with the same protons, neutrons and electrons. All forms of matter, inert, inert with life but no Reason, and inert with life endowed with Reason, have therefore the same basic hardware, which will be illustrated in chapters 8 and 9. My body is made with protons, neutrons and electrons which are exactly the same as those needed for a stone, a flower or a bird. All these forms of matter exist in the same Space-Time whose properties we go on studying even today, since many problems need to be solved. For example we do not know if the four dimensions of the Space-Time we see with our senses (3 Space + 1 Time) have their roots in a Superspace-Time with 43 dimensions, as will be discussed in chapter 2. What we are sure of is that Space and Time cannot be separated, and therefore evolution is unavoidable at the fundamental level of our existence. When we move in Space we necessarily move also in Time. Everything which exists in Space-Time must evolve. The only quantities in the world which do not evolve are the fundamental constants of nature: the Planck action, the speed of light and the Newton constant. The basic units of Time, Space and Energy needed to describe the world in all its structures can be derived from these three fundamental constants. These units are called Planck's units. For example the Time needed for *Big Bang-1* is given by this unit, as we will see in chapter 2.

The fundamental property called 'evolution' was not discovered in the study of living matter by Darwin [2], but in the study of the foundations of the Logic of Nature, i.e. in first level Galilean Science. The work of Darwin was aiming at the discovery of the origin of the human species [2] and the property of living matter called 'evolution' was intended to prove what the origin was of the human species.

From the scientific rigorous point of view the origin of all living forms of matter is *Big Bang-2* which is a completely open problem. No one knows how to go from inert matter to living matter. Furthermore, when dealing with the unique form of living matter endowed with Reason, i.e. the human species, the origin is in *Big Bang-3*. There is no doubt that these two Big Bangs need to be understood in addition to the evolutions which follow each Big Bang. No one can claim that *Big Bang-2*, *Big Bang-3* and the evolutions following each of these basic transitions have been scientifically solved by Darwin and his successors. In fact the most interesting discoveries in order to understand the Logic of Nature have been obtained when studying evolution using inert forms of matter, where no change is needed.

In the study of matter with life the definition of the property called 'evolution' is coupled with the fact that the piece of matter evolving must change. Evolution in Space-Time at the fundamental level of our existence does not require a 'change' in the piece of matter being studied.

The first person who studied in a quantitative way the evolution of a 'stone' in Space-Time was Galileo Galilei. Using as a clock the pulses of his heart he measured the evolution of a 'stone' going through a piece of wood having different inclinations thus discovering how to measure the acceleration due to the gravitational attraction of the Earth. This discovery brought him to the incredible prediction that a feather and a piece of lead would evolve in Space-Time exactly in the same way if air friction could be cancelled.

This experiment has been implemented on the Moon, by the astronaut David Scott head of Apollo XV, who exclaimed '*Galileo Galilei was right*'. Studying another form of the evolution of inert matter, a stone bound with a string, Galilei discovered the laws of the pendulum. It was not a trivial discovery. All civilizations during ten thousand years were measuring Time using the sundial. This gave an uncertainty of one second every day.

Now we measure Time with an uncertainty of one second every lifetime of the Universe: 20 billion years. And this just four centuries after Galilei and his pendulum. Another big discovery of Galilei was obtained via the study of the evolution of a stone while moving under gravitational attraction. Measuring the trajectory of a stone launched from a point 'A' to another point 'B', Galilei found that the trajectory is a parabola. This result is a consequence of the fact that motion in a field where gravitational attraction is effective must follow the law dictated by Space-Time being inseparable and 'complex', not real.

We have said that everything which exists in the world cannot be in Space isolated from Time, but in Space-Time, absolutely coupled and inseparable. Another unavoidable condition is the fundamental property of Space-Time, which cannot be 'real' but 'complex': i.e. either Space is real and Time is imaginary or Time is real and Space is imaginary. Their inseparable coupling, Space-Time, needs to be 'complex'. The consequence of this 'complex' property is that the invariant quantity in going from 'A' to 'B' must be the minimum geometric distance in Space minus the maximum Time. The result is the parabola going from A to B.

We will see in chapter 6 that the evolution in complex 'Space-Time' of the first elementary particle ever discovered in the history of Science, the electron, has opened new horizons in the Logic of Nature, such as the existence of antimatter. Going from the evolution of a 'stone', with Galileo Galilei, to the evolution of the most elementary piece of inert matter, with Paul Dirac, we have discovered that the condition required by the specialists who study living matter, i.e. changes, is not necessary in order to understand the basic logic which governs all forms of matter, including *Big Bang-1*, *Big Bang-2*, *Big Bang-3* and the subsequent processes of evolution.

Let us imagine that, instead of Galileo Galilei, the first fellow to study evolution had really been Darwin. All research work with living matter, when brought to the extreme fundamental limit would have produced the Maxwell equations, Quantum ElectroDynamics (QED) and, finally, the hardware which we will discuss in chapters 8 and 9. The fact that all forms of matter, inert, living and living with Reason, have the same hardware would have taken much longer to discover. The most direct way was the one implemented by Galileo Galilei, with the study of the evolution of stones, the simplest form of inert matter. It is from these studies that the three levels of Science were discovered.

2. The Three Levels of Galilean Science

Galilei teaches that Science has three levels, synthetically expressed in figure 2. Let me elaborate on these three levels.

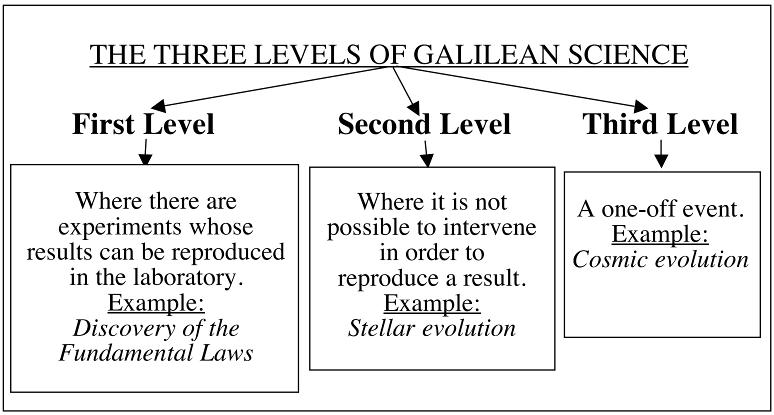


Figure 2.

The first level of Galilean Science is that which entails: (1) logical rigour in the formulation of a problem, (2) the invention of an instrument capable of carrying out the key experiment for giving an answer to the problem, and (3) the reproducibility of the result obtained. The reproducible result is one of the basic foundations of Galilean Science.

The result must be expressed in mathematically rigorous terms. It is this that permits the elaboration of a theory capable of describing not only the reproducible result that is obtained thanks to the invention of the original instrument, but it also points out further experiments to be conducted with new instruments in order to put the new mathematical formulation under the scrutiny of further experimental tests. An example is at the present day frontier of Physics: the Superworld. We think that a description of the phenomena known so far requires a Space-Time with 43 dimensions: 11 bosonic and 32 fermionic. The elaboration of the mathematical structure that describes this reality concludes that new particles must exist; we have dedicated the last decade to the search for these particles without being able to get any reproducible experimental proof. The Superworld theory is an example in which there is mathematical rigour in the formulation of the problem but there is no reproducible experimental proof. Therefore it could be that the Superworld theory is not part of the Logic of Nature. This is what the years to come will tell. The Superworld is an example of first-level Galilean Science to the extent that the experimental tests are susceptible to direct control: in case of doubt it is possible to intervene by repeating the experiments and by inventing new instruments that allow us to overcome doubts that may arise in the course of data analysis for a particular experiment: an experiment that we are able to keep totally under control, here on Earth.

The second level of Galilean Science is that in which it is impossible to keep the experimental test under control. There is mathematical rigour in the formulation of the problem and there is the invention of new instruments for observing the effects searched for, but there is no direct intervention. An example: the theory of stellar evolution. In one part of the sky, we observe the birth of a Star. In another part, the shining of another Star. In yet another part, the death of yet another Star.

Different observations of many Stars being born, of others that are living and still others that are collapsing, allow for the elaboration of a theory of stellar evolution. There is mathematical rigour. Reproducibility is guaranteed by the observation of different examples of Stars as they are being born, during their lifetime and as they are dying. What is missing, however, is the possibility of direct intervention. In cases of doubt we cannot turn off or turn on a Star. We cannot change the characteristics of a particular Star in order to scrutinize, through experimental tests, an idea that could arise from the theory of stellar evolution's mathematical elaboration itself.

This theory is *strongly linked to the first-level* of Galilean Science. Example: in the theory of stellar evolution no astrophysicist could have imagined the existence of neutron Stars. It was first necessary to discover neutrons here on Earth by conducting Galilean-type experiments at the first level of Science. It was the discovery of the neutron that permitted the elaboration of mathematical models that led to the theoretical hypothesis of the existence of neutron Stars.

Quite recently, the observation of certain stellar phenomena has been interpreted as indicating the possible existence of 'quark Stars'. The existence of this new class of particles, the quarks themselves, however, was discovered here on Earth by conducting Galilean-type experiments at the first level of Science. This is the link that exists between the first and the second level.

The third level of Science refers to phenomena that occur only once. At first glance it could seem that the third level contradicts the notion of 'experimental reproducibility'. This is not so. The third level needs the results obtained at the first level, and in no case can it be in contradiction with the results obtained at the first level where 'reproducibility' is granted.

An example of a phenomenon that happens only once is cosmic evolution. The Cosmos has the Physics of the pre-Big Bang as its initial phase. Then comes the Big Bang whose duration is Planck's Time: 54 billionths of billionths of billionths of billionths of billionths of a second ($54 \cdot 10^{-45}$ sec). Then comes Alan Guth's Time: 10^{-34} sec. At the end of the evolutionary inflation period in addition to the gravitational force the Three Fundamental Forces enter into play: strong subnuclear, weak subnuclear and electromagnetic. And so one arrives at the few seconds necessary for having the Cosmos made essentially with the particles familiar to us: protons, neutrons and electrons.

The plasma composed of these particles in the sea of 'photons' lasts a few hundreds of thousands of years (according to the most recent data, the Time interval is 380 thousand years).

At this point the Cosmos, made essentially of protons, electrons and photons, passes into the phase in which the Stars and the Galaxies are born. According to the most recent theories, it could be that 'Black Holes', made with the very primitive form of elementary particles which existed before those of the 'Standard Model' particles, act as nuclei for the formation of the first galactic structures in which Stars are born. The duration of this phase of cosmic evolution is millions of years. After 15–20 billion years we reach the present with ourselves, the Sun, the Earth, the Moon, the oceans, the mountains, the sunrises and sunsets. All this is inert matter.

In addition to inert matter, cosmic evolution, thanks to *Big Bang-2*, produced living matter, both vegetable and animal. Among the countless forms of living matter, thanks to *Big Bang-3*, one and only one has been endowed with Reason. It is in fact thanks to Reason that we have Cathedrals, Michelangelo's Pietà and the incredible details that have resulted from the cosmic evolution of inert matter.

It is thanks to *Big Bang-3* that it has been possible to discover Permanent Collective Memory (PCM), which originates from the most primitive form of Language, which, via evolution, produces first PCM, then rigorous Logic and finally Science, as discussed in chapter 10. The evolution which follows *Big Bang-3* produces the whole of our knowledge which we now discuss.

3. The Whole of Our Knowledge: Evolution and Complexity

Figure 3 is a synthesis of all we think we know about the world in which we live. We see where the three Big Bangs, described in figure 1, are located. The content of figure 3 shows how complex it is to study the evolution in the different fields of our knowledge. In fact evolution exists in many fields of our world such as Science and History. The whole of our knowledge comes from *Big Bang-3*.

In the whole of our knowledge, Science is considered the asymptotic limit of Simplicity, while History is taken to be the asymptotic limit of Complexity. Nature allows for the existence of many other structures whose Complexity seems to lie in between these two extreme limits. Figure 4 shows a sample of systems, which, according to the present way of looking at the world, are considered as being complex.

These systems go from the traffic flux, to the internet network, to earthquakes and seismicity, to social and economic systems, to the behaviour of financial markets, to the study of minimal life, of vegetal life, to the study of cosmological structures, and so on.

Despite the diversity of the fields investigated, the key experimentally observable quantities which allow these systems to share the property called 'Complexity' are the same:

1) The Anderson-Feynman-Beethoven-type phenomena (AFB) i.e. phenomena whose laws and regularities ignore the existence of the Fundamental Laws of Nature from which they originate;

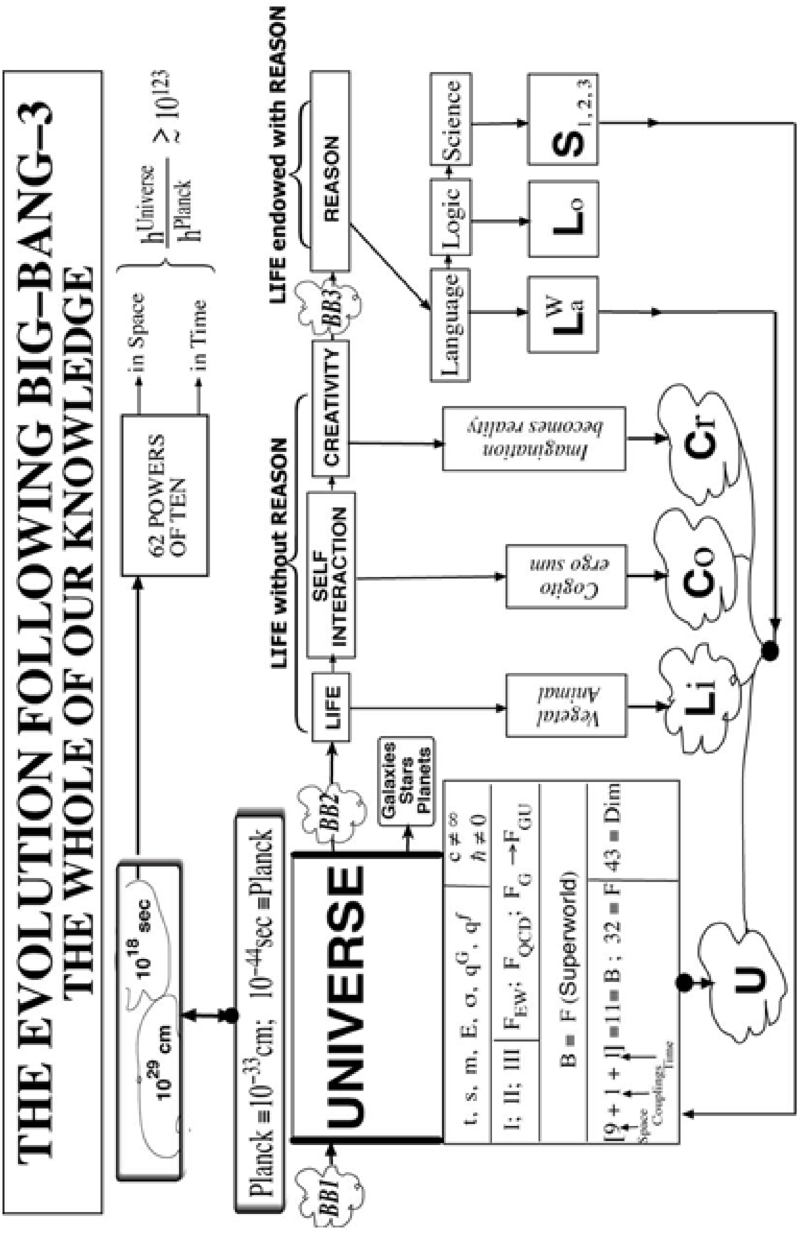

THE EVOLUTION FOLLOWING BIG–BANG–3
THE WHOLE OF OUR KNOWLEDGE
62 POWERS OF TEN
in Space
in Time
Planck
UNIVERSE
Galaxies Stars Planets
LIFE without REASON
LIFE endowed with REASON
LIFE
SELF INTERACTION
CREATIVITY
REASON
BB1
BB2
BB3
Vegetal Animal
Cogito ergo sum
Imagination becomes reality
Language
Logic
Science
B ≡ F (Superworld)
U

Figure 3.

2) The Sarajevo-type effects, i.e. Unexpected Events of quasi irrelevant magnitude which produce Enormous Consequences (UEEC).

These effects exist at all scales, and therefore Complexity exists at all scales, as illustrated in figure 5 where we see History at the extreme end of a high degree of Complexity and Science at the opposite range where the degree of Complexity is at the minimum value.

AFB and UEEC events are discussed in Appendices I, and II plus III, respectively. Let us discuss the two asymptotic limits: History and Science.

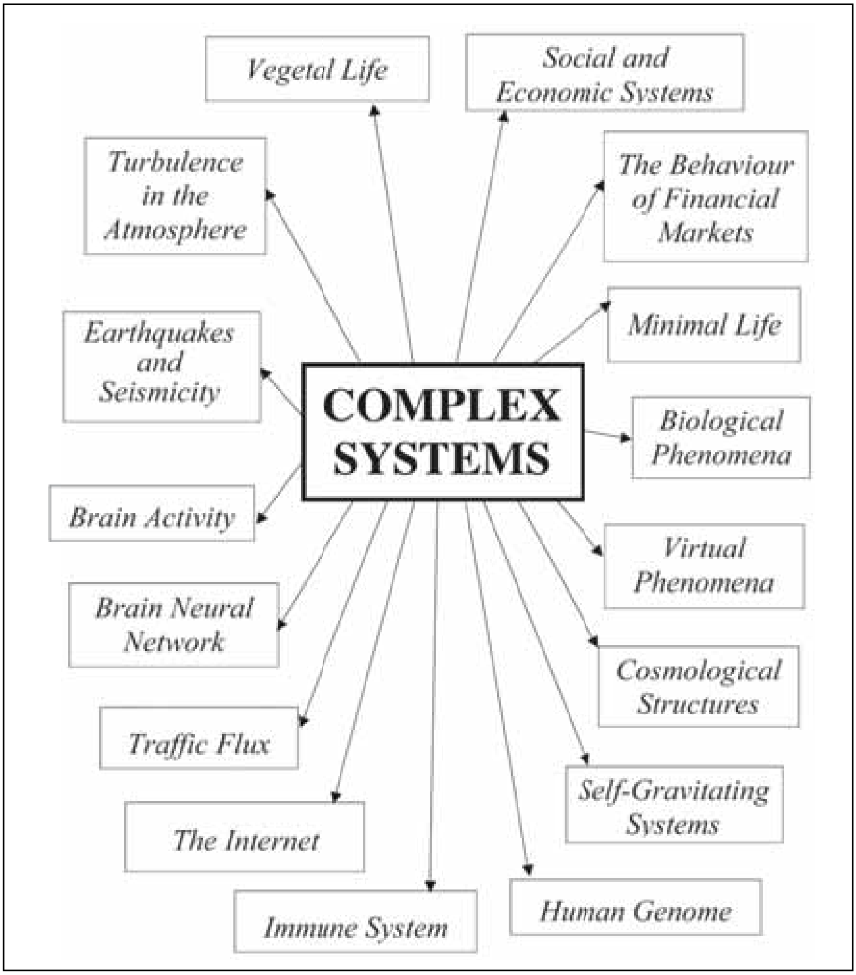


Figure 4.

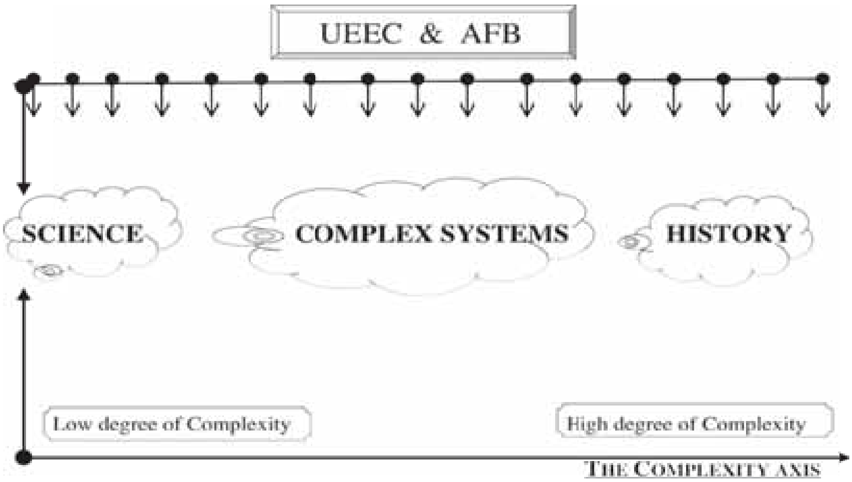


Figure 5.

4. Evolution In The Two Asymptotic Limits Of Complexity: Science And History

Science (the asymptotic limit of Simplicity) and *History* (the asymptotic limit of Complexity), *share a property, common to both*: evolution.

It is interesting to define *Science* and *History* in terms of this property, *probably the only one*, which they share; i.e. evolution.

- Science is the Evolution of our Basic Understanding of the laws governing the world in its Structure ≡EBUS.
- History is the Evolution of the World in its Real Life ≡EWRL.

The world is characterized by two basic features, which are on the opposite side of one another: *Simplicity* and *Complexity*.

It is generally accepted that *Simplicity* is the outcome of *Reductionism*, while *Complexity* is the result of *Holism*.

The most celebrated example of *Simplicity* is *Science* while the most celebrated example of *Complexity* is *History*.

Talking about asymptotic limits, the general trend – as said before – is to consider *History* the asymptotic limit of *Holism* and of *Complexity*; *Science* as the asymptotic limit of *Reductionism* and of *Simplicity*. This is illustrated in figure 6.

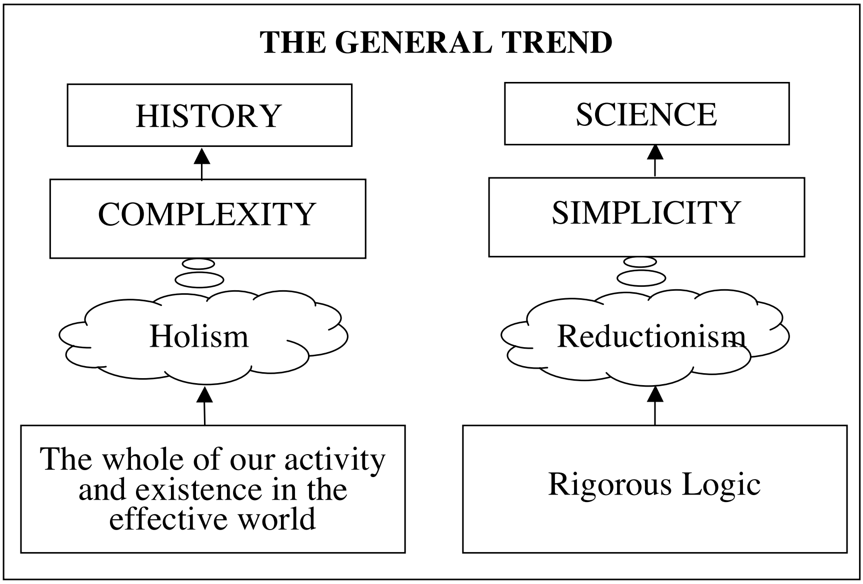


Figure 6.

In Table 1 we compare these two asymptotic limits – History and Science – on the basis of 'What if?'; a condition elaborated by the specialists in what is now known as 'virtual history' [3].

On the basis of 'What if?' these specialists conclude that the world would not be as it is, if one, or few, or any number of 'What ifs?' had not been as History tells us. They define this as the 'virtual world'. This is not the case of Science. The world would have exactly the same laws and regularities, whether Galileo Galilei or somebody else had discovered F = mg (F ≡ force; m ≡ mass; g ≡ acceleration due to gravity), and so on for all the other scientific discoveries.

It is in the consequences of 'What if?' that the two asymptotic limits of Simplicity and Complexity seem to diverge, despite the fact that the sequence of 'What if?' in Science belongs to the 'totally unexpected events' (UEEC) exactly like the others listed in the column of History.

Table 1.

'WHAT IF ?'

	In History = EWRL		In Science = EBUS
I	What if Julius Caesar had been assassinated many years before?	*I*	What if Galileo Galilei had not discovered that $F = mg$?
II	What if Napoleon had not been born?	*II*	What if Newton had not discovered that $F = G \frac{m_1 \cdot m_2}{R_{12}^2}$?
III	What if America had been discovered a few centuries later?	*III*	What if Maxwell had not discovered the unification of electricity, magnetism and optical phenomena, which allowed him to conclude that light is a vibration of the EM field?
IV	What if Louis XVI had been able to win against the 'Storming of the Bastille'?	*IV*	What if Planck had not discovered that $h \neq 0$?
V	What if the 1908 Tunguska Comet had fallen somewhere in Europe instead of Tunguska in Siberia?	*V*	What if Lorentz had not discovered that space and time cannot both be real?
VI	What if the killer of the Austrian Archduke Francisco Ferdinand had been arrested the day before the Sarajevo event?	*VI*	What if Einstein had not discovered the existence of time-like and space-like real worlds? Only in the time-like world, simultaneity does not change, with changing observer.
VII	What if Lenin had been killed during his travelling through Germany?	*VII*	What if Rutherford had not discovered the nucleus?
VIII	What if Hitler had not been appointed Chancellor by the President of the Republic of Weimar Paul von Hindenburg?	*VIII*	What if Hess had not discovered cosmic rays?
IX	What if the first nuclear weapon had been built either by Japan before Pearl Harbour (1941) or by Hitler in 1942 or by Stalin in 1943?	*IX*	What if Dirac had not discovered his equation, which opens new horizons, including the existence of the antiworld?
X	What if Nazi Germany had defeated the Soviet Union?	*X*	What if Fermi had not discovered weak forces?
XI	What if Karol Wojtyla had not been elected Pope, thus becoming John Paul II?	*XI*	What if Fermi and Dirac had not discovered the Fermi–Dirac statistics?
XII	What if the USSR had not collapsed?	*XII*	What if the 'strange particles' had not been discovered in the Blackett Lab?

5. Evolution of the Universe: An Example of Third Level Galilean Science

Cosmic evolution is Galilean Science to the extent that it is formulated in rigorous mathematical terms and linked to the first level. From the pre-Big Bang on, everything is based on what has been discovered at the first level. It is impossible to prove experimentally the reproducibility of cosmic evolution.

No one knows how to make a Big Bang to verify the details that we would like to put under experimental test. We can only conduct experiments to understand what happens as we come close to the Big Bang. Today we have arrived at a tenth of a billionth of a second (10^{-10} sec). At this time we can perform experiments to check our theoretical models. Since Planck's Time lasts $54 \cdot 10^{-45}$ sec, it is wise not to forget the 34 powers of ten, which separate us in terms of Planck's Time from the Big Bang. This is the instant before inflationary expansion bursts forth. These 34 powers of ten are the measure of our ignorance in the rigorous knowledge of that which we call the 'theory of cosmic evolution'.

This theory helps us to understand just how difficult the study of phenomena belonging to the third level of Galilean Science is.

6. Evolution in Terms of Galilean Rigour and Experimental Reproducibility

All the phenomena that happen only once, as it is the case for the Biological Evolution of the Human Species (BEHS), belong, let us repeat once again, to the third level of Galilean Science. Our species being the only form of living matter endowed with Reason, it is important to place the 'theory of Biological Evolution of the Human Species' under the Galilean-type rigour.

There are those who say that this 'theory' represents the frontier of Galilean Science. We would like this to be true. To accomplish this, however, it is necessary to establish a foundation for this theory in terms of mathematical rigour and of experimental reproducibility. Doing this requires an analysis attentive to the phenomenon called 'evolution'. Evolution exists at the level of elementary particles, at the level of aggregates made up of inert matter, and at the level of aggregates of living matter.

The first rigorous study of evolution at the level of elementary particles concerns electrons. The electron is the first example of an 'elementary particle' (discovered by Thomson in 1897).

Dirac, fascinated by the discovery of Lorentz that Space-Time could not be a real quantity but instead a complex one (if Space is real, Time must be imaginary, and vice versa), decided to study with rigour the evolution of the electron in Time and Space. This was how he discovered his equation.

The rigorous study of evolution at the level of elementary particles brought Dirac to discover a reality that no philosopher, no poet, no thinker of any epoch or civilization was able to imagine. This reality begins with antiparticles and brings us to the discovery of antimatter, antistars and antigalaxies to arrive at our world, which seems to be made up only of matter, stars and galaxies, without any antistars or antigalaxies. An experiment to be conducted in the International Space Station (ISS) will tell us if it is really true that in the course of cosmic evolution every trace of antimatter was annihilated with matter in order to build up a Universe, like the one in which we are living, that consists only of matter. If in our laboratories we had discovered that antimatter could not exist, the problem of a Universe made only of matter would not exist. This is not so. The existence of antimatter was established in a rigorously Galilean manner in 1965. Nevertheless, in the Universe there is probably no antimatter.

It is possible to formulate in a mathematically rigorous way the theory of cosmic evolution that cancels out antimatter at a certain point. According to this theory of cosmic evolution, we are here thanks to the fact that, in the process of 'annihilation', a tiny fraction (one part in 10 thousand million (10^{10})) of matter prevailed over antimatter. No one could say if this theory is that which corresponds to the cosmic reality of which we are a minimal part. The only certainty is that this theory will be scrutinized closely via Galilean-type experimental tests in the years to come, thanks to the AMS experiment in the ISS.

Starting from the evolution of an elementary particle we have arrived at the problems of cosmic evolution. This means that we have passed from typical structures of the subnuclear world (10^{-17} cm) to galactic structures up to the borders of the Universe (10^{29}cm); better still, if the inflationary evolution of Alan Guth is true, to even greater cosmic distances.

All we have discussed so far deals with the theory of evolution in the study of inert matter, from the heart of a proton (10^{-17}cm) to the borders of the Cosmos (10^{29}cm): an interval of space which extends over 46 powers of ten. We have done this using the three levels of Galilean Science.

This is the most rigorous knowledge we have, when dealing with the study of the evolution of inert matter.

Table 2 lists problems encountered in the study of the evolution of inert matter.

Table 2. EVOLUTION IN THE STUDY OF INERT MATTER: *PROBLEMS*

EVOLUTION IN THE FUNDAMENTAL STRUCTURE OF INERT MATTER

The Elementary Particles and the Macroscopic Structure of Matter

Evolution in Space-Time of the lightest electrically charged lepton: the **Dirac equation**.

Evolution in the description of the elementary processes involving inert matter: the **Feynman diagrams** and the problem of **Renormalization** (i.e. no divergent results in theoretical calculations).

Evolution in the macroscopic structure of inert matter.

The crystals.

Other forms of conglomerate matter and the understanding of their properties.

The Universe

Evolution in the Universe and in its structure.

The Physics of the **pre-Big Bang**.

The Physics of the **Big Bang**.

The basic structure of matter and of the Fundamental Forces in the evolution of the Universe: from the **Planck Scale** to present day (see figure 7).

The origin of Galaxies and their **distribution** in Space-Time.

The origin of a Star and its evolution (Gravitational, Electroweak and Strong Forces).

The origin of condensed forms of cold matter (Planets, Asteroids, Comets and others cosmic objects).

Table 3 lists problems concerning the transition from vegetal to animal forms of living matter. Finally, Table 4 lists problems referring to the evolution which goes from living matter without Reason to living matter endowed with Reason. The key question here is why is there only one form of living matter with Reason: us.

Table 3. EVOLUTION IN LIVING MATTER: *PROBLEMS*

THE TRANSITION FROM INERT MATTER TO LIVING MATTER
Evolution in the enormous variety of "**vegetal**" forms of Living Matter.
The transition from "vegetal" to "animal" forms of Living Matter.
The evolution in the enormous variety of "animal" forms of Living Matter.

Table 4. EVOLUTION IN LIVING MATTER WITH REASON: *PROBLEMS*

THE TRANSITION FROM THE INNUMERABLE POSSIBILITIES OF LIVING FORMS OF MATTER WITHOUT THE PRIVILEGE OF REASON TO THAT OF LIVING MATTER WITH "REASON"
The evolution of the specific form of Living Matter called **"the human species"**.
The discovery of Collective Memory, i.e. **Written Language**.
The discovery of Logic and of its most rigorous form: **Mathematics**.
The discovery of Science: the **Logic of Nature**.
Reflections on how it happens that we are the **only form of Living Matter** with "Reason".

All these problems need to be fully understood before we reach the level where we need to think about how we happen to be the only form of living matter with 'Reason'.

In fact, the extraordinary characteristic of the world in which we live is that the *Hardware* is the same for all forms of matter: from the most elementary inert piece of matter to the Universe and finally to the most advanced form of matter with Life and Reason (the Human Species). The *Hardware* will be described in chapter 9.

Since the *Hardware* is the same, the following remarks are in order. It could very well have been that the basic *Hardware* was there, but not Life itself. It could also have been that the basic *Hardware* plus Life were there, but no Reason. These problems are illustrated in Table 5. It happens that Reason is present with its three great achievements: Language, Rigorous Logic and Science, as previously mentioned, and as reported in Table 6.

Table 5. *PROBLEMS*

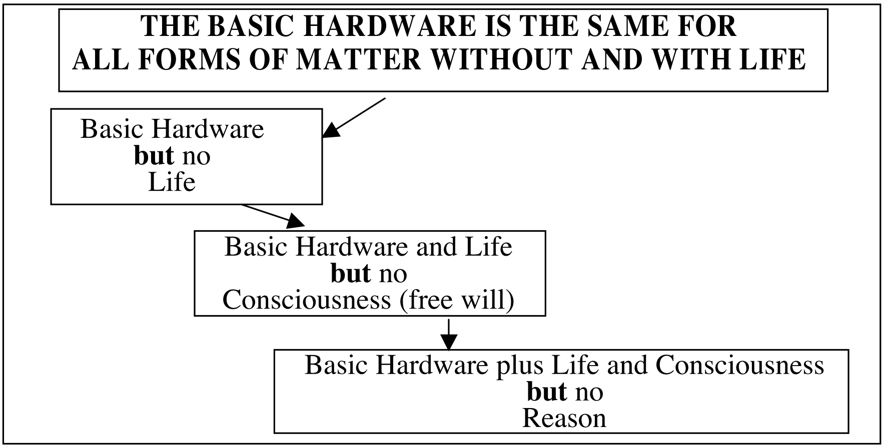
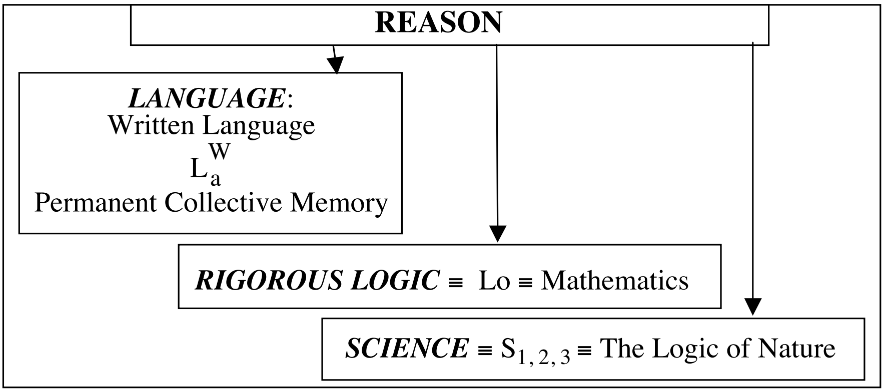


Table 6.



It is thanks to the existence of a rigorous Logic of Nature that the evolution of the Universe can be described as illustrated in figure 7.

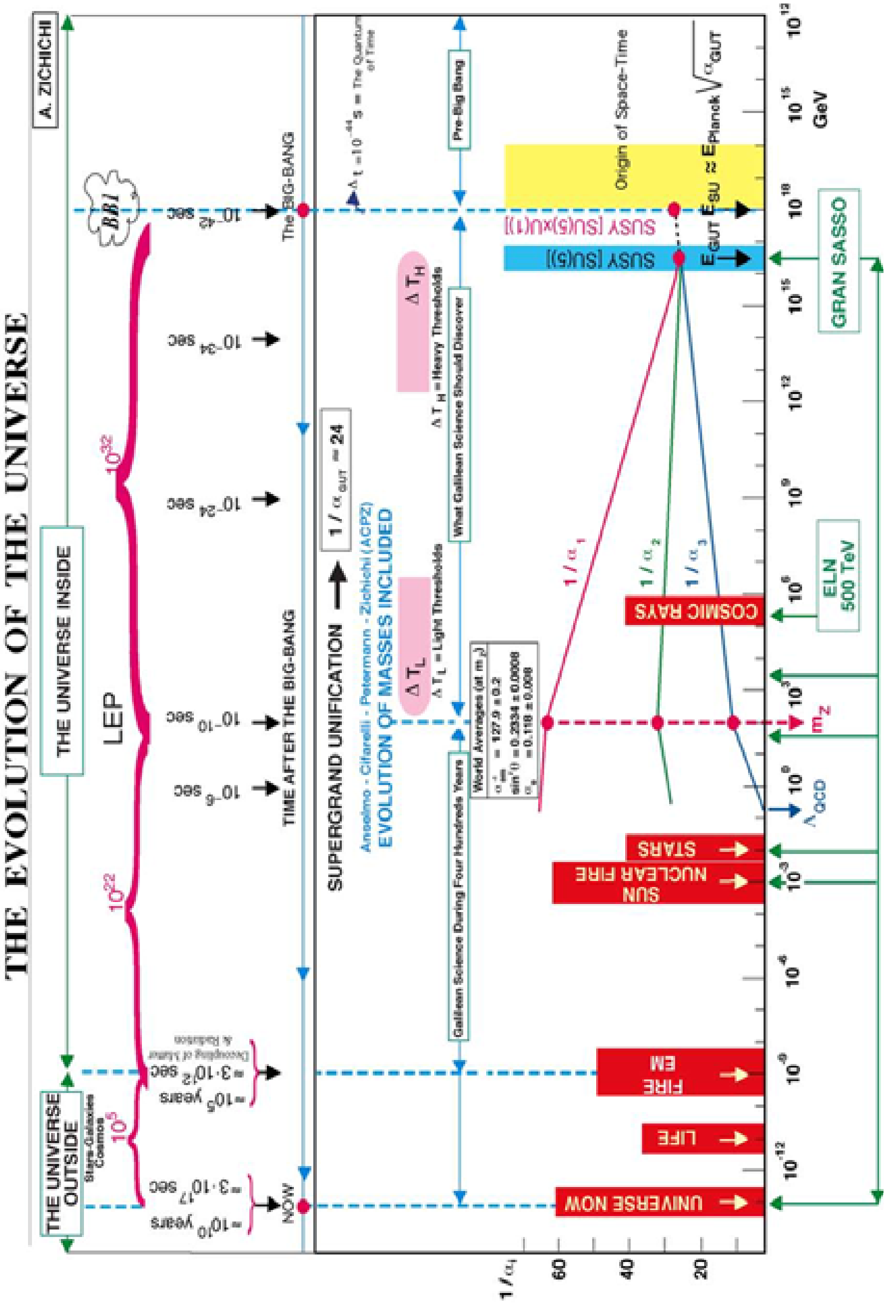

THE EVOLUTION OF THE UNIVERSE
A. ZICHICHI
THE UNIVERSE INSIDE
THE UNIVERSE OUTSIDE
LEP
The BIG-BANG
TIME AFTER THE BIG-BANG
NOW
SUPERGRAND UNIFICATION
EVOLUTION OF MASSES INCLUDED
Pre-Big Bang
What Galilean Science Should Discover
Galilean Science During Four Hundreds Years
Origin of Space-Time
SUSY [SU(5)xU(1)]
SUSY [SU(5)]
COSMIC RAYS
STARS
SUN NUCLEAR FIRE
FIRE EM
LIFE
UNIVERSE NOW
GRAN SASSO
ELN 500 TeV
GeV

Figure 7.

We see that the ‘Universe’ illustrated in figure 7 consists of many important details. The ‘Universe outside’ is the one which comes after the decoupling of protons, electrons and photons; when atoms started their formation, 380 thousands years after *Big Bang-1*. This part of figure 7 is shown in figure 8.

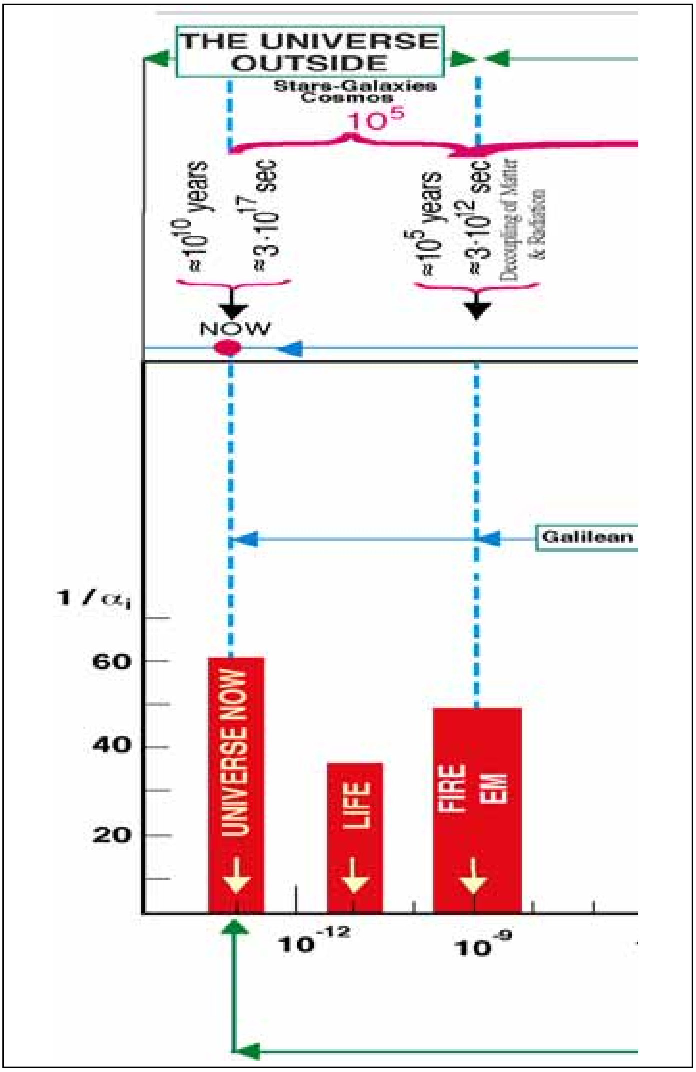


Figure 8.

We could not be here if the Logic of Nature did not allow the formation of Galaxies, Stars and planets. The 'Universe inside' is the one which we study in our Laboratories. The description of the evolution of the Universe, illustrated in figure 7, could never have been conceived without the existence of Science at its first level.

7. The Biological Evolution of the Human Species (BEHS) is Below the Third Level of Galilean Science

Let us start with the facts known about the origin and the evolution of the human species. 1) The Earth has existed for about five billion years; 2) The evidence of living organisms composed of simple cells goes back nearly 3.5 billion years; 3) Multicellular organisms have existed for about seven hundred million years; 4) Vertebrates, for four hundred million years; 5) Mammals, for 200 million years; 6) Primates, for seventy million years.

The group of Hominids starts with the Dryopithecus, about 20 million years ago and splits into two branches. One branch, Pongidae, which produces Chimpanzees, Gorillas and Orangutans. The other branch, Hominidae, produces Homo habilis (stone age), Homo erectus (fire age), and Homo sapiens neanderthalensis, with a brain having a volume larger than our brain.

According to the Biological Theory of Evolution of Human Species (BEHS), Homo sapiens neanderthalensis disappears, but no one knows how. And in an analogous unknown way, Homo sapiens appears, twenty to forty thousands years ago.

This sequence of events is reported in figure 9 which is a very simplified version of the evolution of living matter.

A 'theory' with missing links, extraordinary developments, inexplicable extinctions, sudden disappearances, is far from being Galilean Science. This 'theory' needs the two pillars of Galilean Science: experimental reproducibility and mathematical rigour to describe the observed facts.

According to Darwin, the living matter species, of which we are an example, is the result of small steps in a chaotic series of events where natural selection played a decisive role. Concerning this basic pillar of Darwinistic evolution it has been recently pointed out by Gregory G. Gibson that natural selection is only one, and probably not the most important factor, in the biological evolution of living matter. Recently the Genome sequence of *the*

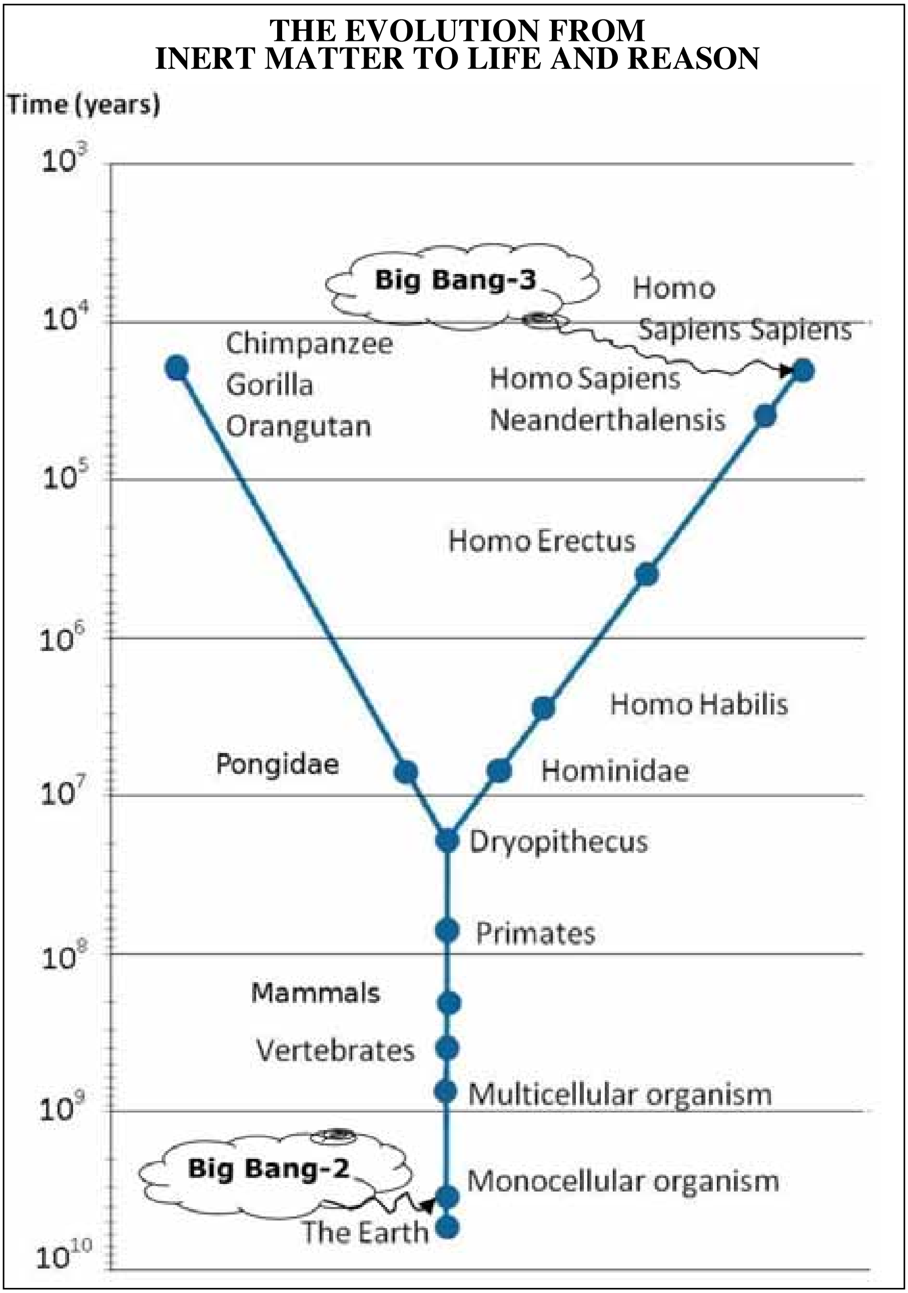

THE EVOLUTION FROM
INERT MATTER TO LIFE AND REASON
Time (years)
10^3
10^4
10^5
10^6
10^7
10^8
10^9
10^10
Big Bang-3
Homo
Sapiens Sapiens
Chimpanzee
Gorilla
Orangutan
Homo Sapiens
Neanderthalensis
Homo Erectus
Homo Habilis
Pongidae
Hominidae
Dryopithecus
Primates
Mammals
Vertebrates
Multicellular organism
Big Bang-2
Monocellular organism
The Earth

Figure 9.

Ornithorhynchus anatinus[1] has been published [4]. This work, according to some specialists, corroborates the theoretical idea that the evolution of living matter cannot proceed via small steps and random changes.

Concerning the mutations with very low probability, an interesting result has been published [5] by Richard Lenski from the University of Michigan. He has observed a mutation in *Escherichia coli*, after 33,127 generations. The author estimates that the probability of such an event is in the order of 10^{-12}. Despite this very low probability event *Big Bang-3* has not taken place. This will be the case for an even lower probability event, since the only species of living matter where *Big Bang-3* can take place is the Human Species.

Many interesting discoveries have been obtained concerning the evolution of different forms of living matter, but a transition from one species to another has never been observed. The mechanism which produces mutations and the relevance of natural selection are still open problems.

The theory of BEHS has to take in due account the extremely interesting results on the structure of our brain obtained using the NMR technology (Nuclear Magnetic Resonance, now called Resonance Imaging).

These results have opened our eyes to the extraordinary complexity of our brain. This complexity has twisted the 'electromagnetic model' of our brain.

The new model[2] has abandoned the 'circuits' and has adopted the 'antenna'; with this choice the number of electromagnetic interactions between given points in the brain reaches the level of hundreds of powers ten, $10^{>100}$, in order to formulate an original idea.

A further point needs to be put in evidence: to extend to the human species the results obtained in the study of evolution of other forms of living matter is incorrect. In fact, even the lowest probability event observed by R. Lenski (mentioned above) to occur at the 10^{-12} level has not produced any *Big Bang-3*. The reason being that we are the only form of living matter endowed with a unique privilege: Reason. This privilege has allowed our species to reach the three great conquests quoted before: Language, Logic and Science (see chapter 10).

[1] A detail concerning the sexual chromosomes. Normal mammals possess a pair of sexual chromosomes, XX for females, XY for males. The living matter species quoted above, *Ornithorhynchus anatinus*, has 10 sexual chromosomes. Five pairs XX for females, 5 X and 5 Y for males, with a total of 52 chromosomes. We need only 46 chromosomes.

[2] Donald Glaser, the inventor of the Bubble Chamber.

It is thanks to Language that Permanent Collective Memory (PCM), better known as Written Language, has been invented. No other form of living matter has left traces of PCM. And no other forms of living matter have been able to discover the most rigorous form of Logic, called Mathematics (for details see chapter 10). Out of all possible forms of rigorous Logic, one has been selected in order to build the world where we are. This special form of Logic is called Science and it is the Logic which governs all forms of inert matter. No other forms of living matter deal with the problems of Science.

It would be a remarkable step forward to establish what experiments should be performed in our laboratories in order to discover the experimental reproducible basis underlying the BEHS theory. At present no one knows the mathematical structure – corroborated by reproducible experimental results – capable of describing the transition from inert matter to the various forms of living matter (*Big Bang-2*). And no one knows how to go from the innumerable forms of living matter to the one and only one, which is capable of producing Language, Logic and Science (*Big Bang-3*).

Waiting for this formidable result to be achieved, it is necessary to call attention to the fact that BEHS is an activity of study and research, deprived of experimentally reproducible results and of mathematical rigour in the description of these results. In fact BEHS has neither first level nor second level Galileian Science and the third level has no formulation in terms of mathematical rigour, as it is the case for the cosmic evolution, illustrated in figure 10, which is a simplified version of figure 7. This is why BEHS is below the third level of Galilean Science.

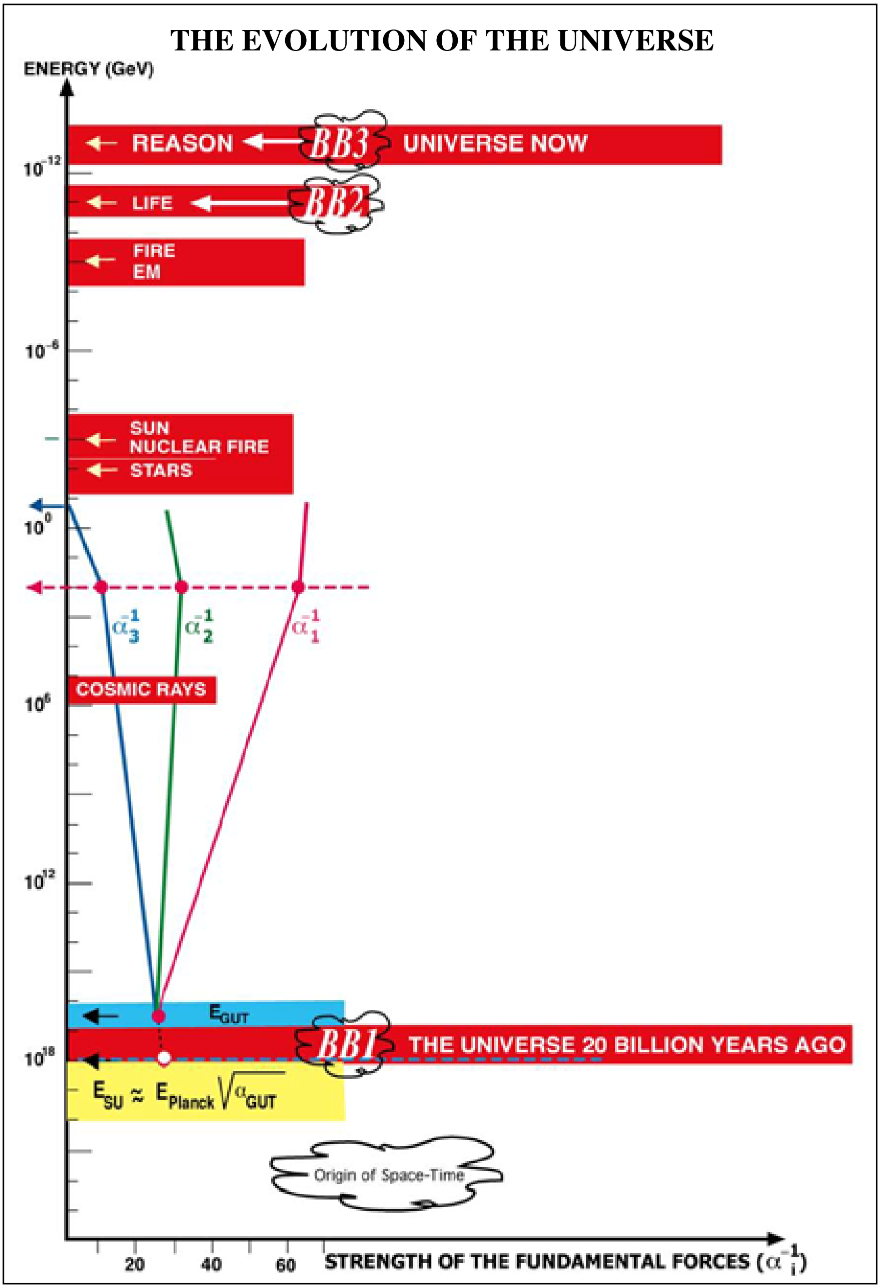

THE EVOLUTION OF THE UNIVERSE
ENERGY (GeV)
REASON
BB3
UNIVERSE NOW
LIFE
BB2
FIRE
EM
SUN
NUCLEAR FIRE
STARS
COSMIC RAYS
E_GUT
BB1
THE UNIVERSE 20 BILLION YEARS AGO
E_SU ≈ E_Planck √α_GUT
Origin of Space-Time
10^-12
10^-6
10^0
10^6
10^12
10^18
20
40
60
STRENGTH OF THE FUNDAMENTAL FORCES (α_i^-1)

Figure 10.

8. The Hardware Which Governs All Matter, Inert and Living, is Dominated by Ueec Events Which Represent the Evolution of Science

In this chapter we briefly recall the sequence of UEEC events from Galilei to 1947, already used to compare History and Science on the basis of 'What if?' (Table 1).

Point XIV refers to the period which lasted about 3/4 of a century; to be more precise it started in the early 1930s with Yukawa whose apparently very simple proposal to explain the reason why protons and neutrons can stay glued in a nucleus, gave rise to an impressive series of discoveries defined 'The Yukawa goldmine' [6].

This brought us to realize that the two particles called proton and neutron (and thought to be elementary) do in fact contain in their intimate structure a world totally different from the one we are familiar with, i.e. the subnuclear world.

It is from this UEEC sequence of events (figure 11) that we have reached the Hardware which governs all matter, inert and living. This Hardware is the synthesis of all scientific knowledge [called the *SM&B* (see chapter 9)].

"UEEC"
TOTALLY UNEXPECTED DISCOVERIES
FROM GALILEI TO FERMI-DIRAC, THE "STRANGE" PARTICLES AND THE YUKAWA GOLDMINE

I	Galileo Galilei: F = mg .
II	Newton: $F = G\dfrac{m_1 \cdot m_2}{R_{12}^2}$
III	Maxwell: the unification of electricity, magnetism and optical phenomena, which allows to conclude that light is a vibration of the EM field.
IV	Becquerell: radioactivity.
V	Planck: $h \neq 0$.
VI	Lorentz: space and time cannot both be real.
VII	Einstein: the existence of time-like and space-like worlds. Only in the time-like world, simultaneity does not change, with changing observer.
VIII	Rutherford: the nucleus.
IX	Hess: cosmic rays.
X	Dirac discovers his equation, which opens new horizons, including the existence of the antiworld.
XI	Fermi: weak forces.
XII	Fermi–Dirac and Bose–Einstein discover two completely different statistical laws.
XIII	The "strange particles" are discovered in the Blackett Lab.
XIV	The Yukawa goldmine.

Figure 11.

9. The Hardware of Evolution: From Basic Quantities to the SM&B

My field of scientific activity is subnuclear physics. It is thanks to this field of Science that it has been possible to identify the Basic Quantities needed to build the world where we live, as shown in figure 12.

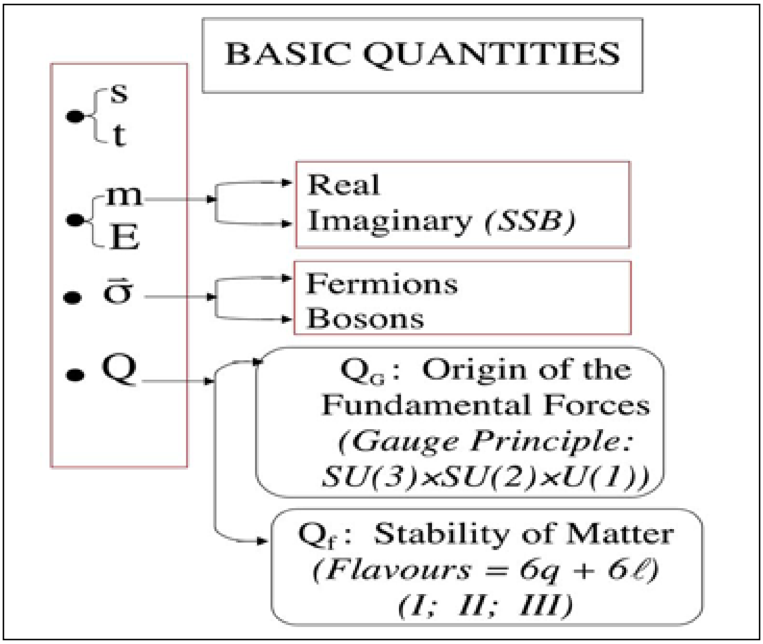


Figure 12.

From these '*Basic Quantities*' the evolution of our knowledge brings us to the most advanced synthesis of scientific knowledge called *SM&B*, i.e. the Standard Model and Beyond. The steps needed in this evolution of our knowledge are reported in Appendices I and II plus III. The *SM&B* is the Logic which governs the basic hardware of the fundamental constituents of all forms of matter.

If the present ideas on the *SM&B* are valid, the result is that we know how, from the origin of Space-Time the Superworld started, then by evolution in Space and Time became our world.

The three lines in figure 13 are taken from figure 7. They represent the strengths, respectively α_1, α_2, α_3, of the three Fundamental Forces of Nature as a function of energy.

The three forces are: the electromagnetic, the weak subnuclear and the strong subnuclear.

These three forces meet at the energy level called E_{GUT}, where GUT stands for Grand Unified Theory, if the number of expanded Space-Time dimensions is (3 Space + 1 Time).

If other dimensions are expanded, it could be that E_{GUT} goes down by many orders of magnitude (for example at the 10^4 GeV level) as indicated in figure 13.

The evolution we have so far discussed refers to inert matter where the interaction with the environment has no effect at all.

When we go from Basic Quantities, Atoms and Molecules to Proteins, Genes, Living Cells (C) and more complex forms of Living Matter (L), the interaction with the environment cannot be neglected, as shown in figure 14.

The most intense interaction with the environment and its evolution is described by History, which is in fact the asymptotic limit of Complexity, as discussed in chapter 4.

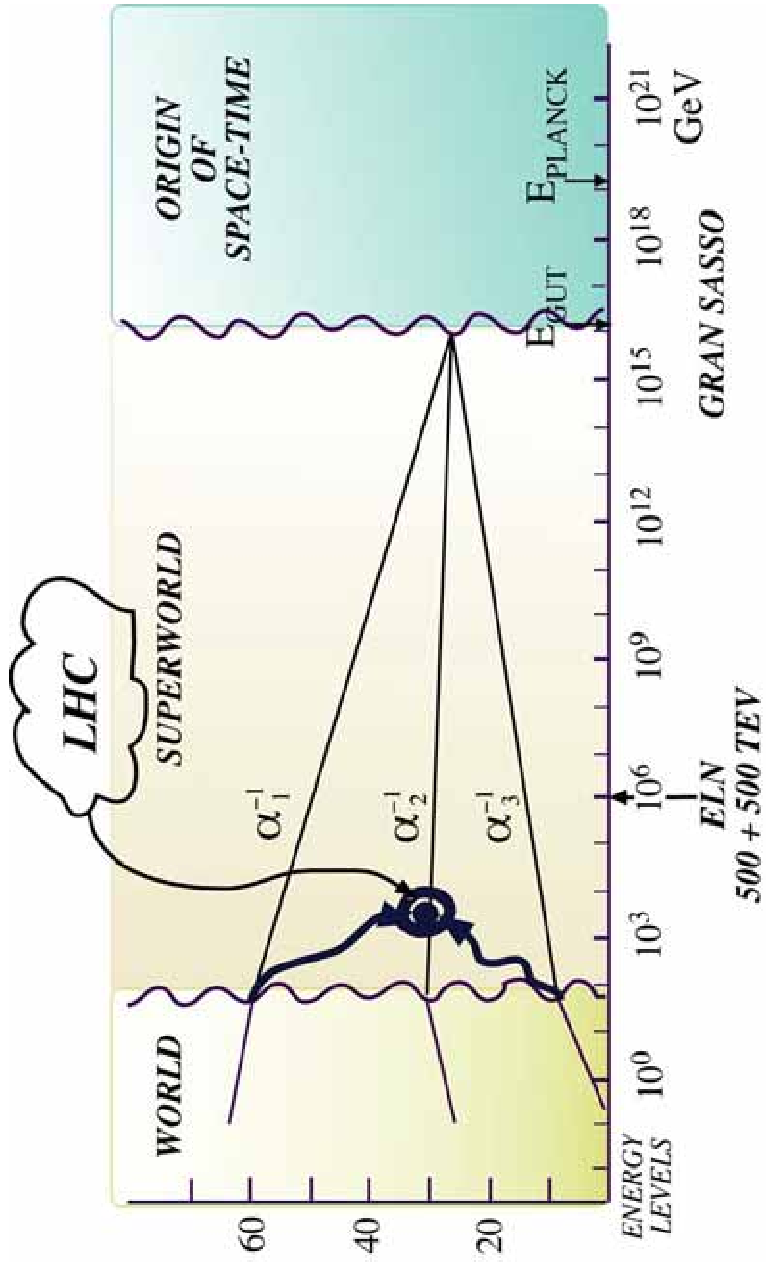

ORIGIN
OF
SPACE-TIME
SUPERWORLD
WORLD
LHC
α_1^{-1}
α_2^{-1}
α_3^{-1}
E_{GUT}
E_{PLANCK}
60
40
20
ENERGY
LEVELS
10^0
10^3
10^6
10^9
10^{12}
10^{15}
10^{18}
10^{21}
GeV
ELN
500 + 500 TEV
GRAN SASSO

Figure 13.

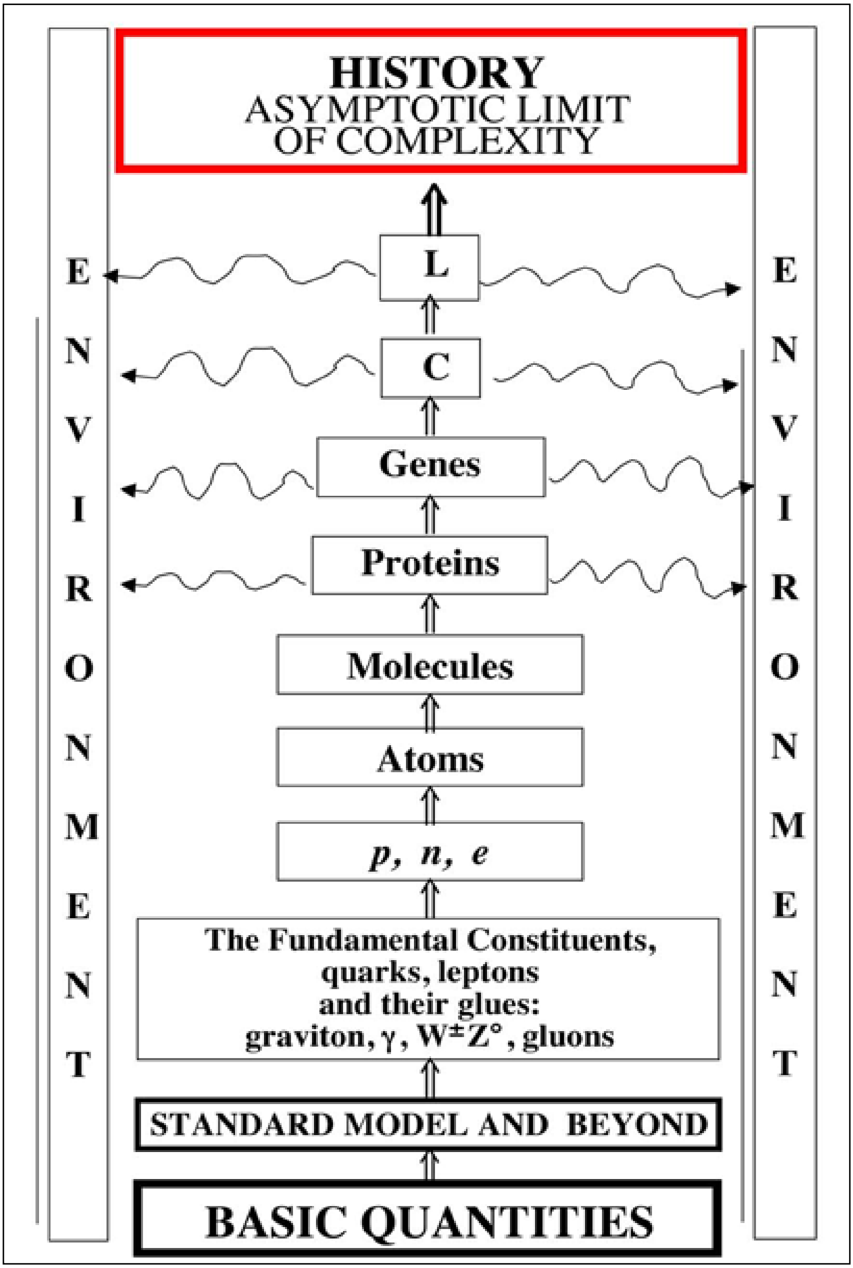

HISTORY
ASYMPTOTIC LIMIT
OF COMPLEXITY
L
C
Genes
Proteins
Molecules
Atoms
p, n, e
The Fundamental Constituents,
quarks, leptons
and their glues:
graviton, γ, W±Z°, gluons
STANDARD MODEL AND BEYOND
BASIC QUANTITIES
E N V I R O N M E N T
E N V I R O N M E N T

Figure 14.

10. Proof That Only One Species of Living Matter is Endowed with Reason: Language, Logic and Science

As stated previously, we are the only form of living matter endowed with Reason, the proof being that no other forms of living matter have been able to discover the three conquests of Reason: Language, Logic and Science. The time-evolution of Language, Logic and Science is reported in figure 15. The lowest level of Language is the one needed in order to understand a 'message' (i.e. a group of words constructed on the basis of appropriate rules).

We can call this level 'Language-understanding'. The next level is at a much higher degree of intellectual ability. It is the one needed in order to elaborate a 'message'. Our species is the only species able to elaborate 'messages'.

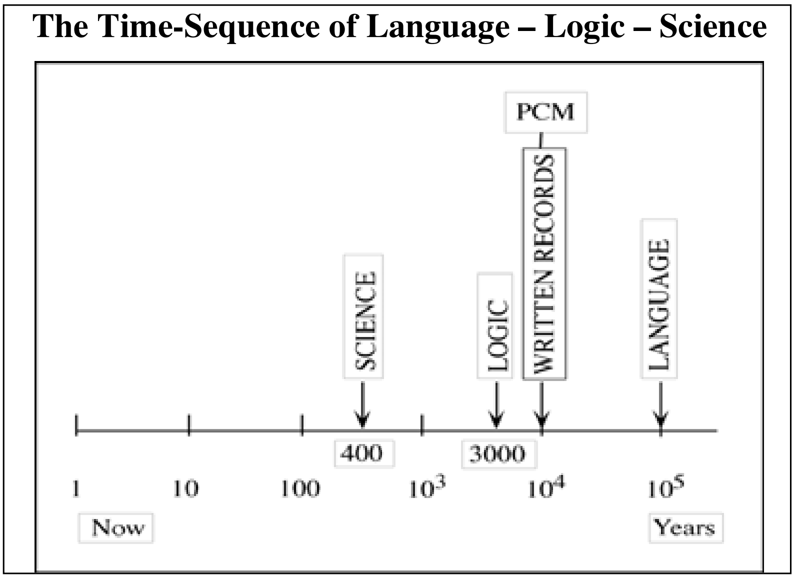


Figure 15.

In figure 16 we report the intellectual achievements due to Language at its highest level.

The most clear way to realize what are the activities defined by the word 'Language' can be obtained by pointing out that all these activities would exist even if neither Rigorous Logic nor Science had been discovered.

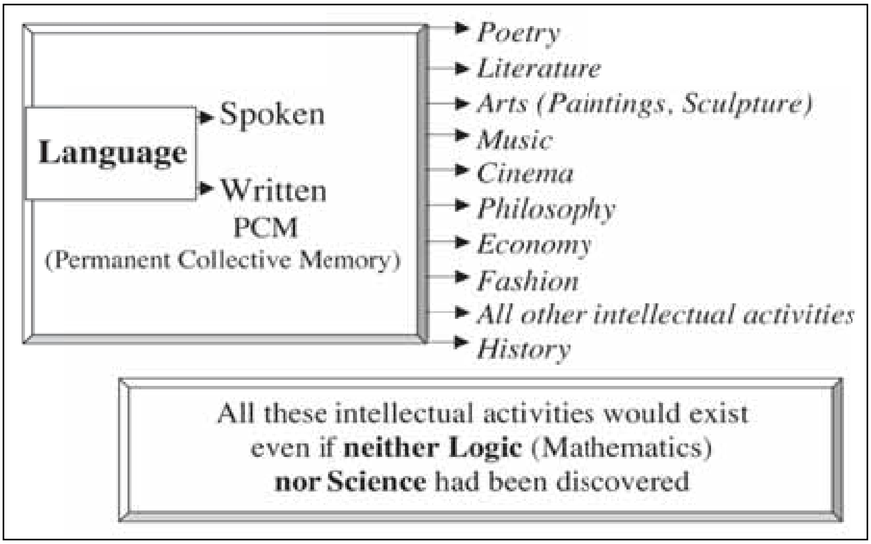


Figure 16.

In figure 17 the main achievements of Rigorous Logic are reported. All these achievements would exist even if Science had never been discovered.

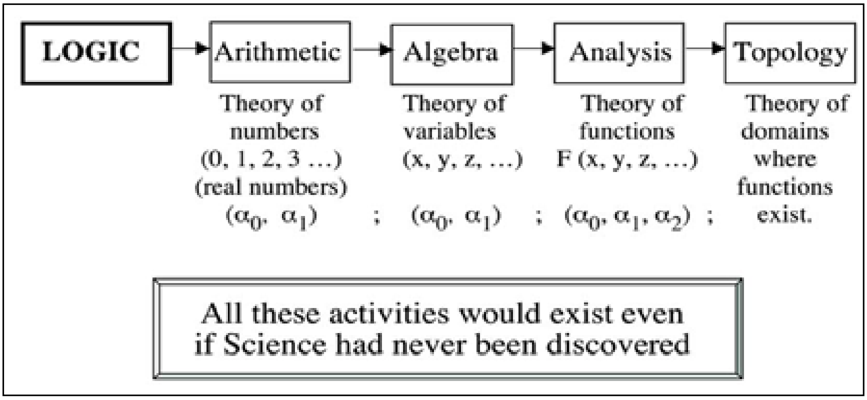


Figure 17.

In the following figures (18, 19, 20) the point to notice is the vital condition which allows the three achievements to exist; i.e. 'to be fascinating' for Language,[3] the 'non-contradiction' for Logic and the 'the real world' for Science.

In figure 18 there is an attempt to express Language in terms of a mathematical formalism. The symbols refer to sum '$\sum$' and product '$\prod$' of the various functions '*f*' describing the large number of constituents of a linguistic structure, as indicated by the symbols R, Cr, Co, Li and U, whose meaning is reported.

$$La \equiv F_{La}(R, Cr, Co, Li, U) \equiv \sum_{j,k,l,m,n} \left[f^{j}_{La}(R) \oplus f^{k}_{La}(Cr) \oplus f^{l}_{La}(Co) \oplus f^{m}_{La}(Li) \oplus f^{n}_{La}(U) \right] \oplus$$

$$\oplus \prod_{j,\, k,\, l,\, m,\, n} \left[f^{j}_{La}(R) \otimes f^{k}_{La}(Cr) \otimes f^{l}_{La}(Co) \otimes f^{m}_{La}(Li) \otimes f^{n}_{La}(U) \right] \Rightarrow$$

$\Rightarrow$ **Be Fascinating**

Reason	$\equiv$ R	$\Rightarrow$ j	=	$1, 2, 3, \ldots\ldots n_j$
Creativity	$\equiv$ Cr	$\Rightarrow$ k	=	$1, 2, 3, \ldots\ldots n_k$
Self Conscience	$\equiv$ Co	$\Rightarrow$ l	=	$1, 2, 3, \ldots\ldots n_l$
Life	$\equiv$ Li	$\Rightarrow$ m	=	$1, 2, 3, \ldots\ldots n_m$
Universe	$\equiv$ U	$\Rightarrow$ n	=	$1, 2, 3, \ldots\ldots n_n$

LANGUAGE

Figure 18.

[3] Jorge Luis Borges says: with Language we can say anything including its opposite. The result is 'nothing'. This 'nothing' must be fascinating. Poetry is the supreme expression of Language. Let me give you an example of a poem whose purpose is to say nothing, but possesses the privilege of being 'fascinating': '*... Pellegrina colomba immaginaria che accendi nel cuore gli ultimi amori, anima della musica e dei fiori, pellegrina colomba immaginaria'. (Imaginary wandering dove lighting final loves in the heart, spirit of music and of flowers, imaginary wandering dove).* Jorge Luis Borges in *Conversazioni*, Tascabili Bompiani 2000, p. 19.

$$\mathbf{Lo} \equiv \mathbf{F_{Lo}}\ (\textbf{Arithmetic};\ \textbf{Algebra};\ \textbf{Analysis};\ \textbf{Topology}) \Rightarrow$$

$\Rightarrow$ **Non-Contradiction**

LOGIC

Figure 19.

$$\mathbf{S_{1,2,3}} \equiv \mathbf{F_{S_{1,2,3}}}\ (\textbf{Inventions};\ \textbf{Discoveries};\ \textbf{Measurements}) \Rightarrow$$

$\Rightarrow$ **The Real World**

SCIENCE

Figure 20.

As pointed out in chapter 2 there are three levels of Galilean Science, S_1, S_2 and S_3. The most spectacular example of third level Science is the evolution of the Universe.

11. Brief Recapitulation

No matter what, everything which exists in Space and Time is subject to the process of evolution. This can be rigorously studied for elementary particles, for example the 'electron', with results which go beyond the power of human imagination, as is the existence of antiparticles, antimatter, antiworld. It is from these studies that the various theories of cosmic evolution have been formulated, including *Big Bang-1*, which describes the transition from the vacuum to the Universe of inert matter. Evolution also affects very complex systems; the asymptotic example of Complexity being History. Here evolution is dominated by UEEC (Unexpected Events with Enormous Consequences, called Sarajevo-type events by historians). The experimentally observable quantities, for Complexity to exist, are UEEC events and AFB phenomena. The most famous example of AFB is Beethoven who was able to compose masterpieces of music while having never studied QED (Quantum ElectroDynamics). But if QED laws were not there, neither music nor mankind could exist. Examples of complex systems have been reviewed together with the three levels of Galilean Science, whose third level is needed to describe events which happen only once. The Biological Evolution of Human Species (BEHS) needs two such events: *Big Bang-2*, to describe the transition from inert matter to living matter, and *Big Bang-3*, to describe the transition from living matter without reason to living matter endowed with reason. A comparison between cosmic evolution and the evolution of the human species shows that BEHS is below the third level of Galilean Science. It is to be pointed out that there is one, and only one, form of living matter endowed with Reason. It is therefore not obvious that results obtained with other forms of living matter can be extended to the human species. A theory of evolution, no matter in what field, cannot ignore the pillars of Galilean Science: experimental reproducibility and mathematical rigour. Where this is not the case, no one can claim that the research work being implemented is Galilean Science.

12. Final Conclusion

The most spectacular example of third level Galilean Science is the evolution of the Universe illustrated in figure 7 of chapter 7. Let us not forget that it is thanks to Galilean Science that the Logic of Nature has been discovered. This corroborates the famous Statement by John Paul II: '*Science* *has its roots in the Immanent but leads man towards the Transcendent*'. In fact if there is a Logic, the Author of this Logic must exist. We have seen that far from having a rigorous, Galilean-type, scientific foundation, the Biological Evolution of the Human Species (BEHS), illustrated in figure 9 of chapter 7, is below the third level of Galilean Science.

We would like to encourage our colleagues engaged in the study of biological evolution to reach the goal of bringing BEHS (the Biological Evolution of the Human Species) to the third level of Galilean Science, as it is the case for the evolution of the Universe, cosmic evolution.

The impressive series of problems discussed, and awaiting a rigorous scientific solution, point to the conclusion that probably help from the transcendental sphere of our existence is needed.

Let me close with the first 'Easter Vigil' (15 April 2006) of Benedict XVI where in the Homily of His Holiness the words 'evolution' and 'mutation' are introduced in a context which refers to the transcendental sphere of our existence:

> Christ's Resurrection is something more, something different. If we may borrow the language of the theory of evolution, it is the greatest 'mutation', absolutely the most crucial leap into a totally new dimension that there has ever been in the long history of life and its development: a leap into a completely new order which does concern us, and concerns the whole of history (...) It is a qualitative leap in the history of 'evolution' and of life in general towards a new future life, towards a new world which, starting from Christ, already continuously permeates this world of ours, transforms it and draws it to itself.

APPENDIX I

AFB Phenomena From Beethoven To The Superworld

Beethoven and the laws of acoustics

Beethoven could compose superb masterpieces of music without any knowledge of the laws governing acoustic phenomena. But these masterpieces could not exist if the laws of acoustics were not there.

The living cell and QED

To study the mechanisms governing a living cell, we do not need to know the laws of electromagnetic phenomena whose advanced formulation is QED. All mechanisms needed for life are, to a great extent, examples of electromagnetic processes. If QED was not there, Life could not exist.

Nuclear physics and QCD

Proton and neutron interactions appear as if a fundamental force of nature is at work: the nuclear force, with its rules and its regularities. These interactions ignore that protons and neutrons are made with quarks and gluons.

Nuclear physics does not appear to care about the existence of Quantum ChromoDynamics (QCD), the fundamental force acting between quarks and gluons at the heart of the subnuclear world.

Nuclear physics ignores QCD but all phenomena occurring in nuclear physics have their roots in the interactions of quarks and gluons.

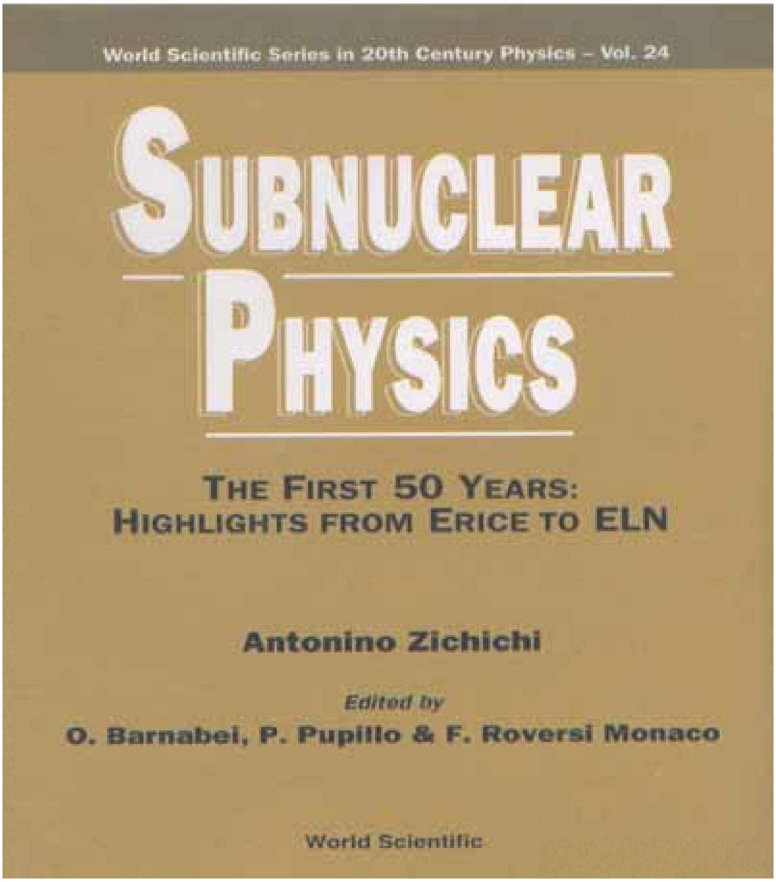
In other words, protons and neutrons behave like Beethoven: they interact and build up nuclear physics without 'knowing' the laws governing QCD.

The most recent example of an Anderson-Feynman-Beethoven-type phenomenon: *apparently the World could not care less about the existence of the Superworld*.

APPENDIX II

UEEC EVENTS, FROM GALILEI UP TO SM&B

In figure 11 there is a sequence of *UEEC* events from Galilei to Fermi-Dirac and the 'strange particles'. This figure has already been reported in chapter 8 and it is here for the convenience of the reader. In figures 21, 22, 23 there is the sequence of *UEEC* from Fermi-Dirac to the construction of the Standard Model. These figures (21, 22, 23) cover the first fifty years of Subnuclear Physics, whose detailed description can be found in my book whose front cover is reproduced here. In figure 24 there is a synthesis of the UEEC events in what we now call the Standard Model and Beyond (*SM&B*).



"UEEC"
TOTALLY UNEXPECTED DISCOVERIES
FROM GALILEI TO FERMI-DIRAC, THE "STRANGE" PARTICLES AND THE YUKAWA GOLDMINE

I	Galileo Galilei: $F = mg$.
II	Newton: $F = G\dfrac{m_1 \cdot m_2}{R_{12}^2}$
III	Maxwell: the unification of electricity, magnetism and optical phenomena, which allows to conclude that light is a vibration of the EM field.
IV	Becquerell: radioactivity.
V	Planck: $h \neq 0$.
VI	Lorentz: space and time cannot both be real.
VII	Einstein: the existence of time-like and space-like worlds. Only in the time-like world, simultaneity does not change, with changing observer.
VIII	Rutherford: the nucleus.
IX	Hess: cosmic rays.
X	Dirac discovers his equation, which opens new horizons, including the existence of the antiworld.
XI	Fermi: weak forces.
XII	Fermi–Dirac and Bose–Einstein discover two completely different statistical laws.
XIII	The "strange particles" are discovered in the Blackett Lab.
XIV	The Yukawa goldmine.

Figure 11 (from page 128).

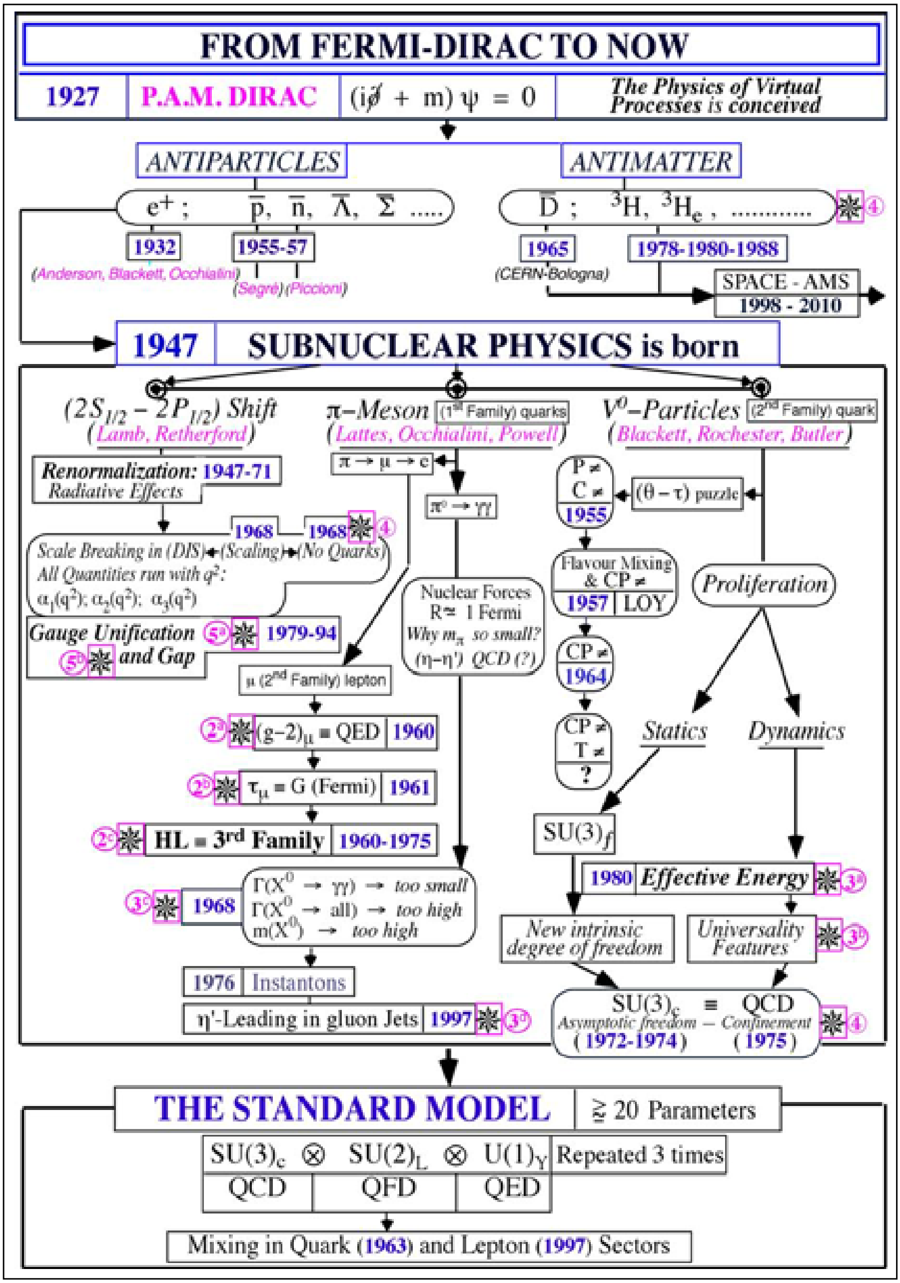

FROM FERMI-DIRAC TO NOW
1927
P.A.M. DIRAC
(i∂̸ + m) ψ = 0
The Physics of Virtual Processes is conceived
ANTIPARTICLES
ANTIMATTER
e+ ; p̄, n̄, Λ̄, Σ̄ .....
D̄ ; ³H̄, ³H̄e , ...
1932
1955-57
(Anderson, Blackett, Occhialini)
(Segrè) (Piccioni)
1965
(CERN-Bologna)
1978-1980-1988
SPACE - AMS
1998 - 2010
1947
SUBNUCLEAR PHYSICS is born
(2S1/2 – 2P1/2) Shift
(Lamb, Retherford)
π–Meson
(1st Family) quarks
(Lattes, Occhialini, Powell)
V0–Particles
(2nd Family) quark
(Blackett, Rochester, Butler)
Renormalization: 1947-71
Radiative Effects
π → μ → e
π0 → γγ
P ≠
C ≠
1955
(θ – τ) puzzle
1968
1968
Scale Breaking in (DIS)←(Scaling)←(No Quarks)
All Quantities run with q²:
α1(q²); α2(q²); α3(q²)
Flavour Mixing & CP ≠
1957
LOY
Proliferation
Nuclear Forces
R ≃ 1 Fermi
Why mπ so small?
(η–η') QCD (?)
Gauge Unification
and Gap
1979-94
CP ≠
1964
μ (2nd Family) lepton
CP ≠
T ≠
?
Statics
Dynamics
(g–2)μ ≡ QED
1960
τμ ≡ G (Fermi)
1961
HL ≡ 3rd Family
1960-1975
SU(3)f
1980
Effective Energy
1968
Γ(X0 → γγ) → too small
Γ(X0 → all) → too high
m(X0) → too high
New intrinsic degree of freedom
Universality Features
1976
Instantons
η'-Leading in gluon Jets
1997
SU(3)c ≡ QCD
Asymptotic freedom – Confinement
(1972-1974)
(1975)
THE STANDARD MODEL
≳ 20 Parameters
SU(3)c ⊗ SU(2)L ⊗ U(1)Y
Repeated 3 times
QCD
QFD
QED
Mixing in Quark (1963) and Lepton (1997) Sectors

Figure 21.

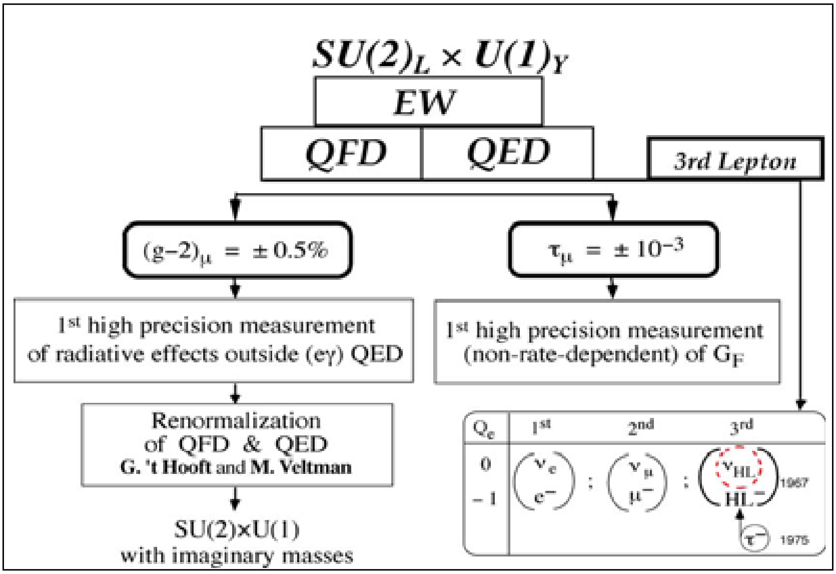


Figure 22. Details from figure 21, concerning $SU(2)_L$ and $U(1)_Y$.

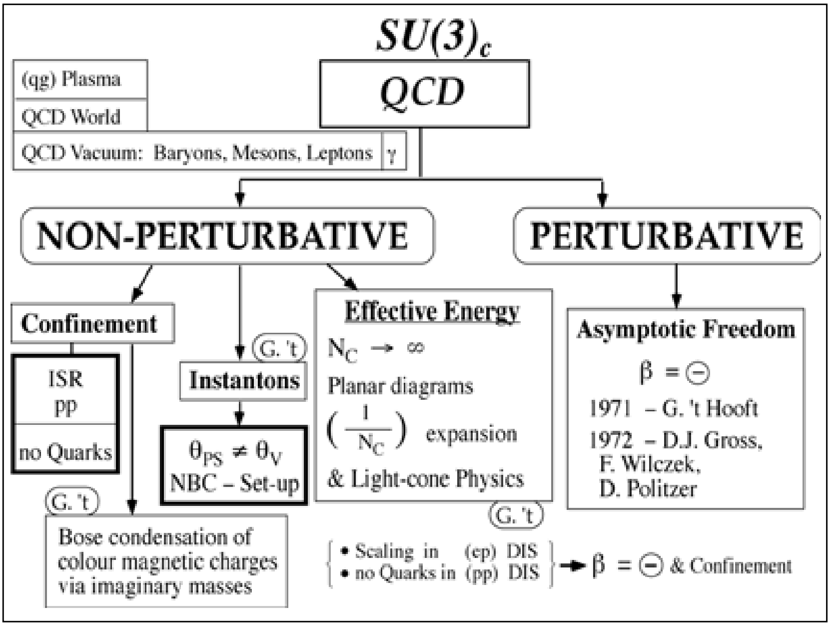


Figure 23. Details from figure 21, concerning $SU(3)_c$.

SM&B

THE STANDARD MODEL AND BEYOND

① RGEs $(\alpha_i\ (i = 1, 2, 3);\ m_j\ (j = q, l, G, H))$: $f(k^2)$.
- GUT $(\alpha_{GUT} = 1/24)$ & GAP $(10^{16} - 10^{18})$ GeV.
- SUSY (to stabilize $m_F/m_P = 10^{-17}$).
- RQST (to quantize Gravity).

② Gauge Principle (hidden and expanded dimensions).
— How a Fundamental Force is generated: SU(3); SU(2); U(1) and Gravity.

③ The Physics of Imaginary Masses: SSB.
— The Imaginary Mass in SU(2)×U(1) produces masses ($m_{W^\pm}$; m_{Z^0}; m_q; m_l), including $m_\gamma = 0$.
— The Imaginary Mass in SU(5)⇒SU(3)×SU(2)×U(1) or in any higher (not containing U(1)) Symmetry Group ⇒ SU(3)×SU(2)×U(1) produces Monopoles.
— The Imaginary Mass in $SU(3)_c$ generates Confinement.

④ Flavour Mixings & CP≠ , T≠ .
— No need for it but it is there.

⑤ Anomalies & Instantons.
— Basic Features of all Non-Abelian Forces.

Note:				
q	≡ quark and squark;		m_F	≡ Fermi mass scale;
l	≡ lepton and slepton;		m_P	≡ Planck mass scale;
G	≡ Gauge boson and Gaugino;		k	≡ quadrimomentum;
H	≡ Higgs and Shiggs;		C	≡ Charge Conjugation;
RGEs	≡ Renormalization Group Equations;		P	≡ Parity;
GUT	≡ Grand Unified Theory;		T	≡ Time Reversal;
SUSY	≡ Supersymmetry;		≠	≡ Breakdown of Symmetry Operators.
RQST	≡ Relativistic Quantum String Theory;			
SSB	≡ Spontaneous Symmetry Breaking.			

The five basic steps in our understanding of nature. ① The renormalization group equations (RGEs) imply that the gauge couplings (α_i) and the masses (m_j) all run with k^2. It is this running which allows GUT, suggests SUSY and produces the need for a non point-like description (RQST) of physics processes, thus opening the way to quantize gravity. ② All forces originate in the same way: the gauge principle. ③ Imaginary masses play a central role in describing nature. ④ The mass-eigenstates are mixed when the Fermi forces come in. ⑤ The Abelian force QED has lost its role of being the guide for all fundamental forces. The non-Abelian gauge forces dominate and have features which are not present in QED.

Figure 24.

Let me devote some attention to the discussion of UEEC events in nuclear physics.

Nuclear Physics and UEEC events

It is considered standard wisdom that nuclear physics is based on perfectly sound theoretical predictions. People forget the impressive series of UEEC events discovered in what I have decided to call the 'Yukawa goldmine' [6].

Let me quote just three of them:

1. The first experimental evidence for a cosmic ray particle believed to be the Yukawa meson was a lepton: the muon.
2. The decay-chain: $\pi \rightarrow \mu \rightarrow e$ was found to break the symmetry laws of Parity and Charge Conjugation.
3. The intrinsic structure of the Yukawa particle was found to be governed by a new fundamental force of Nature, Quantum Chromo Dynamics: QCD.

As you know 2007 was the centenary of the birth of Hideki Yukawa, the father of theoretical nuclear physics. In 1935 the existence of a particle, with mass intermediate (this is the origin of 'mesotron' now 'meson') between the light electron, m_e, and the heavy nucleon (proton or neutron), m_N, was proposed by Yukawa [7].

This intermediate mass value was deduced by Yukawa from the range of the nuclear forces. Contrary to the general wisdom of the time, Yukawa was convinced that the particles known (electrons, protons, neutrons and photons), could not explain how protons and neutrons are bound into the extremely small dimensions of a nucleus.

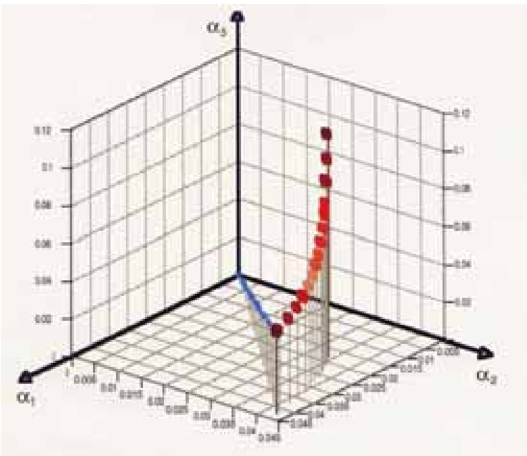
In order to make this 'prediction', Yukawa needed the Heisenberg uncertainty principle: a totally unexpected theoretical discovery. The origin of it was the totally unexpected discovery of the dual nature of the electron (wave and particle) and of the photon (wave and particle). Heisenberg himself tried to explain the binding forces between the proton and the neutron, via the exchange of electrons, in order not to postulate the existence of a new particle. The very light electron, m_e, could not stay in the very small dimension of the nucleus.

The author of the uncertainty principle and father, with Dirac and Pauli, of Quantum Mechanics, did not realise this contradiction. The need for a new 'particle' was the reason. What no one was able to predict is the 'goldmine' hidden in the production, decay and intrinsic structure of this new 'particle'. This 'goldmine' is still being explored nowadays and its present frontier is the Quark-Gluon-Coloured-World (QGCW) [8].

I have recently described [6] the unexpected conceptual developments coming from the study of the production, the decay and the intrinsic structure of the Yukawa particle.

Let me just quote the most relevant UEEC events: chirality−invariance, spontaneous symmetry breaking, symmetry breaking of fundamental invariance laws (P, C, T), anomalies, and 'anomaly-free condition', existence of a third family of fundamental fermions, gauge principle for non-Abelian forces, instantons and existence of a pseudoscalar particle made of the quanta of a new fundamental force of Nature acting between the constituents of the Yukawa particle.

The *SM&B* is the greatest synthesis of all times in the study of the fundamental phenomena governing the Universe in all its structures. The basic achievements of the *SM&B* have been obtained via UEEC events; moreover the *SM&B* could not care less about the existence of Platonic Simplicity. An example is shown in figure 25 where the straight line (small dots) would be the Platonic simple solution towards the Unification of all Fundamental Forces.



The points have a sequence of 100 GeV in energy. The last point where the "ideal" platonic straight line intercepts the theoretical prediction is at the energy of the Grand Unification. This corresponds to $E_{GU} = 10^{16.2}$ GeV. Other detailed information on the theoretical inputs: the number of fermionic families, N_F , is 3; the number of Higgs particles, N_H , is 2. The input values of the gauge couplings at the Z^0-mass is α_3 (M_Z) = 0.118 ± 0.008; the other input is the ratio of weak and electromagnetic couplings also measured at the Z^0-mass value: $\sin^2 \theta_W (M_Z) = 0.2334 \pm 0.0008$.

Figure 25.

Nevertheless the effective unification is expected to be along the sequence of points (the big ones) computed using the Renormalization Group Equations (*RGEs*) [9].

APPENDIX III

EXAMPLES OF UEEC EVENTS IN THE CONSTRUCTION OF THE STANDARD MODEL AND BEYOND: A PERSONAL EXPERIENCE

There are many *UEEC* events in the construction of the Standard Model and Beyond (*SM&B*). In some of them I have been directly involved. They are summarized in figure 26.

Each *UEEC* event (except the last one) is coupled with a *despite*, in order to emphasize the reason why the event is unexpected. The no. 7 event has only the unexpected details.

UEEC EVENTS
IN THE CONSTRUCTION OF THE
SM&B = MY PERSONAL EXPERIENCE

① **The 3rd lepton, HL** (now called τ) with its own neutrino, ν_{HL} (now called ν_τ),
despite *the abundance of neutrinos:* ν_e *and* ν_μ.

② **Antimatter**
despite *S-matrix and C, P, CP, T breakings.*

③ **Nucleon Time-like** EM structure
despite *S-matrix*

④ **No quarks** in violent (pp) collisions
despite *scaling.*

⑤ **Meson mixings**
$\theta_V \neq \theta_{PS} : (51^o) \neq (10^o) \neq 0$ ***despite*** $SU(3)_{uds}$.

⑥ **Effective energy:** the Gribov QCD-light
despite *QCD.*

⑦ **The running** of α_1 α_2 α_3 versus **energy**:
the EGM effect, the GAP between E_{GUT} *and* E_{SU}*, and the absence of the Platonic straight line convergence.*

Figure 26.

Let me explain some of these UEEC events. 1) *Antimatter*: the mass ≠ matter problem; 2) *Meson mixings*; 3) *Effective energy*: the Gribov QCD-light; 4) *The running of* α_1 α_2 α_3 *versus energy*: the gap between the GUT energy and the string unification energy.

APPENDIX III.1

FROM THE ANTIELECTRON TO ANTIMATTER THE MASS ≠ MATTER PROBLEM

Seven decades of totally unexpected discoveries were needed to go from the antielectron to antimatter in order to understand a fundamental property which guarantees our existence: the stability of matter.

The fact that mass and matter had to be two different physical quantities, i.e. the mass ≠ matter problem, started with Einstein's discovery that $E = mc^2$. The symbol 'm' was originally considered to represent 'matter' and thus the famous Einstein equation became the problem of explaining the stability of matter.

The meaning of 'm' had to be different from 'matter'. This is how the distinction between 'matter' and 'mass' came to the forefront of fundamental physics. Einstein proposed to solve the problem mass ≠ matter, saying that matter is coupled with a 'charge', the electromagnetic one. Since this 'charge' is a conserved quantity, matter cannot transform itself into energy. Thus the famous Einstein equation is valid, provided that mass is not coupled with an electric charge, and the stability of matter is granted.

Figure 27 shows the final result of seven decades of experimental and theoretical research work. The solution of the mass ≠ matter problem

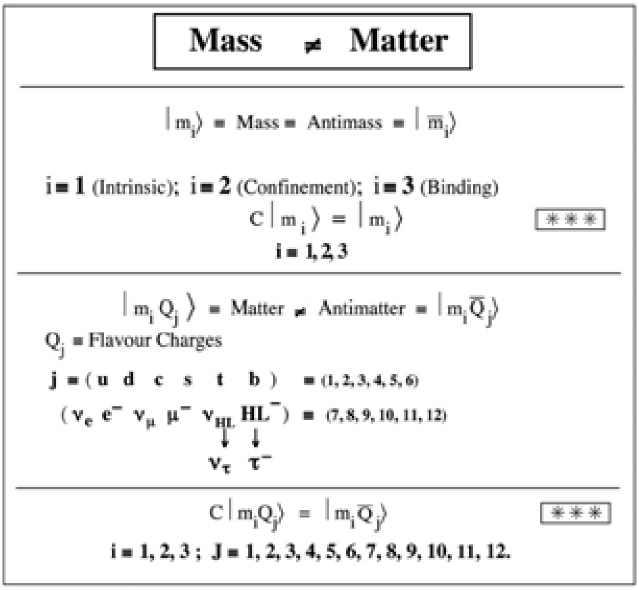


Figure 27.

THE INCREDIBLE SERIES OF UEEC EVENTS
NEEDED TO EXPLAIN THE STABILITY OF MATTER
SEVEN DECADES: FROM THE ANTIELECTRON TO ANTIMATTER
AND THE UNIFICATION OF ALL GAUGE FORCES

- **The validity of C invariance from 1927 to 1957.**

After the discovery by Thomson in 1897 of the first example of an elementary particle, the Electron, it took the genius of Dirac to theoretically discover the Antielectron thirty years after Thomson.

1927 → Dirac equation [10]; the existence of the antielectron is, soon after, theoretically predicted. Only a few years were needed, after Dirac's theoretical discovery, to experimentally confirm (Anderson, Blackett and Occhialini [11]) the existence of the Dirac antielectron.

1930-1957 → **Discovery of the C operator** [(charge conjugation) H. Weyl and P.A.M. Dirac [12]]; discovery of the P Symmetry Operator [E.P. Wigner, G.C. Wick and A.S. Wightman [13, 14]]; discovery of the T operator (time reversal) [E.P. Wigner, J. Schwinger and J.S. Bell [15, 16, 17, 18]]; discovery of the CPT Symmetry Operator from RQFT (1955-57) [19].

1927-1957 → Validity of C invariance: e^+ [11]; $\bar{p}$ [20]; $\bar{n}$ [21]; $K_2^0 \to 3\pi$ [22] but see LOY [23].

- **The new era starts: C ≠ ; P ≠ ; CP ≠** (*).

1956 → Lee & Yang P ≠ ; C ≠ [24].

1957 → Before the experimental discovery of P ≠ & C ≠, Lee, Oehme, Yang (LOY) [23] point out that the existence of the second neutral K-meson, $K_2^0 \to 3\pi$, is proof neither of C invariance nor of CP invariance. Flavour antiflavour mixing does not imply CP invariance.

1957 → C.S. Wu et al. P ≠ ; C ≠ [25]; CP ok [26].

1964 → $K_2^0 \to 2\pi \equiv K_L$: CP ≠ [27].

1947-1967 → QED divergences & Landau poles.

1950-1970 → The crisis of RQFT & the triumph of S-matrix theory (i.e. the negation of RQFT).

1965 → Nuclear antimatter is (experimentally) discovered [28]. See also [29].

1968 → The discovery [30] at SLAC of Scaling (free quarks inside a nucleon at very high q^2) but in violent (pp) collisions no free quarks at the ISR are experimentally found [31]. Theorists consider Scaling as being evidence for RQFT not to be able to describe the Physics of Strong Interactions. The only exception is G. 't Hooft who discovers in 1971 that the β-function has negative sign for non-Abelian theories [32].

1971-1973 → $\beta = -$; 't Hooft; Politzer; Gross & Wilczek. The discovery of **non-Abelian** gauge theories. Asymptotic freedom in the interaction between quarks and gluons [32].

1974 → All gauge couplings $\alpha_1\ \alpha_2\ \alpha_3$ run with q^2 but they do not converge towards a unique point.

1979 → A.P. & A.Z. point out that the new degree of freedom due to SUSY allows the three couplings $\alpha_1\ \alpha_2\ \alpha_3$, **to converge towards a unique point** [33].

1980 → QCD has a 'hidden' side: the multitude of final states for each pair of interacting particles: (e^+e^- ; $p\bar{p}$; πp; Kp; νp; pp; etc.)
The introduction of the Effective Energy allows to discover the Universality properties [34] in the multihadronic final states.

1992 → All gauge couplings converge towards a unique point at the gauge unification energy: $E_{GU} \cong 10^{16}$ GeV with $\alpha_{GU} \cong 1/24$ [35, 36].

1994 → The Gap [9] between E_{GU} & the String Unification Energy: $E_{SU} \cong E_{Planck}$.

1995 → **CPT loses its foundations at the Planck scale (T.D. Lee)** [37].

1995-1999 → **No CPT theorem from M-theory (B. Greene)** [38].

1995-2000 → A.Z. points out the need for new experiments to establish if matter-antimatter symmetry or asymmetry are at work.

(*) The symbol ≠ stands for 'Symmetry Breakdown'.

Figure 28.

proved to be very different from what Einstein had in mind. There are three classes of 'masses': intrinsic, confinement and binding. There are 12 'flavour' charges to distinguish 'matter'

from 'mass'. These 'flavour charges' are the basic quantities which guarantee the stability of matter.

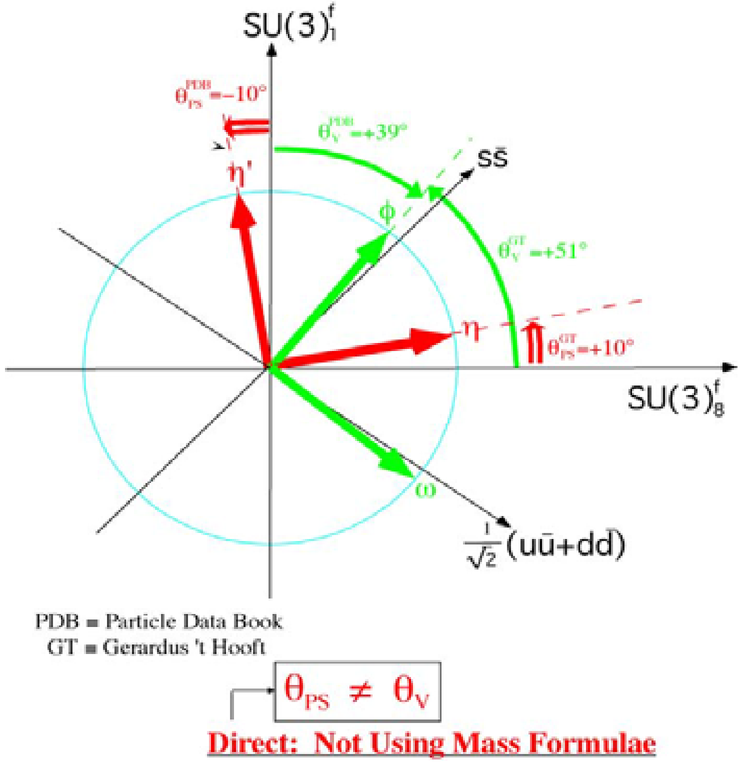
The incredible series of UEEC events needed to discover the origin of the fundamental forces and of the stability of matter is described in figure 28.

During these seven decades it has been discovered that the same word 'charge' corresponds to two basic properties of Nature. This is why the word 'charge' has been coupled with another term, either 'gauge' or 'flavour'. The 'gauge charge', in recent times also called 'colour charge', generates a Fundamental Force of Nature, while the 'flavour charge' is responsible for the stability of matter.

APPENDIX III.2

MESON MIXINGS THE PSEUDOSCALAR AND VECTOR MESONIC MIXINGS

The problem started when experimental physics was dominated by bubble chambers and the 'mixing' was determined using mass-formulae: i.e. a tautology. I designed and built a non-bubble-chamber detector, NBC; it consisted of an original neutron missing mass spectrometer coupled with a powerful electromagnetic detector which allowed to clearly identify all final states of the decaying mesons into (e^+e^-) or $(\gamma\gamma)$ pairs. The mass of the meson (be it pseudoscalar or vector) was measured by the neutron missing mass spectrometer. The two 'mixing angles', the pseudoscalar θ_{PS} and the vector θ_V, were directly measured (without using the masses) to be, not as expected by $SU(3)_{uds}$, i.e. $\theta_{PS}=\theta_V=0$, but, $\theta_{PS}\neq 0$, $\theta_V \neq 0$ and totally different $\theta_{PS}\neq\theta_V$. Many years were needed and Gerard 't Hooft instantons to explain why $\theta_{PS}\simeq 10°$ and $\theta_V\simeq 51°$.



SU(3)$^f_1$
θ^{PDB}_{PS}=−10°
θ^{PDB}_{V}=+39°
ss̄
η'
ϕ
θ^{GT}_{V}=+51°
η
θ^{GT}_{PS}=+10°
SU(3)$^f_8$
ω
$\frac{1}{\sqrt{2}}$(uū+dd̄)
PDB = Particle Data Book
GT = Gerardus 't Hooft
$\theta_{PS} \neq \theta_V$
Direct: Not Using Mass Formulae

Figure 29.

APPENDIX III.3

EFFECTIVE ENERGY THE GRIBOV QCD LIGHT

When the physics of strong interactions finally became the physics of quarks and gluons, QCD had a problem, defined by Gribov as being its 'hidden QCD side': i.e., the large number of different final states produced by different pairs of interacting particles, such as (πp, pp, pp, Kp, e^+e^-, p, μp, ep, etc.). I did not limit myself to suggesting that a totally different approach was needed to put all these final states on the same basis. I found what this basis could be and this is how the 'Effective Energy' became the correct quantity to be measured in each interaction.

The 'Effective Energy' was not predicted by QCD. To perform this study, it was necessary to analyze tens of thousands of (pp) interactions at the ISR. This was done despite all the difficulties to overcome. And this is how what Vladimir Gribov defined the 'QCD light' was discovered (figures 30 and 31). Gribov pointed out what follows. Newton discovered that QED light is the sum of different colours. In QCD we have quarks and gluons interacting and producing Jets made of many pions, as for example in the (pp) reaction

$$pp \rightarrow \pi + X$$

whose spectrum is shown in figure 30. The horizontal axis is for the fractional energy of the pion (also called Feynman x), while the vertical axis is for the number of pions having fractional energy x_F. The spectrum in figure 30 is the sum (∑) of all spectra shown if figure 31 where each one corresponds to a single value of the 'Effective Energy' (defined in terms of $2E_{had}$).

p-$p \rightarrow \pi^+ + X$

Nominal Energy of the (pp) collision = $\sqrt{s}$= 24 GeV

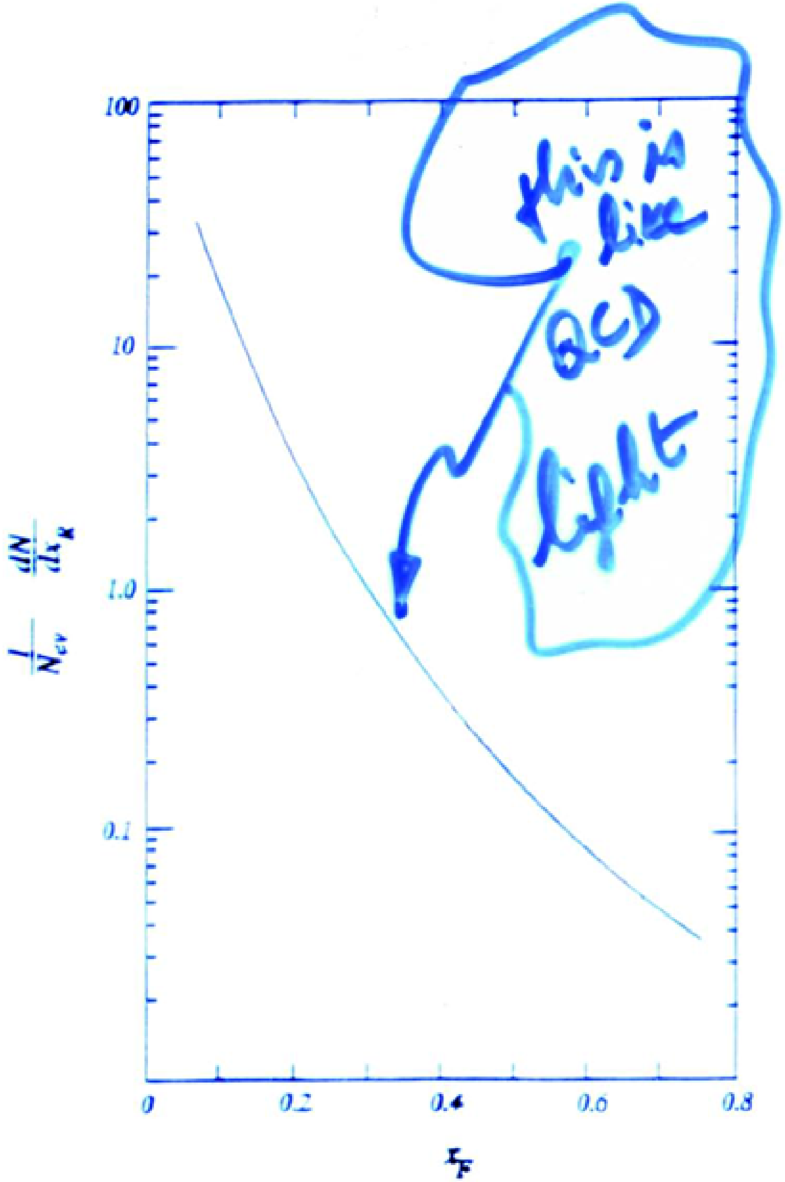
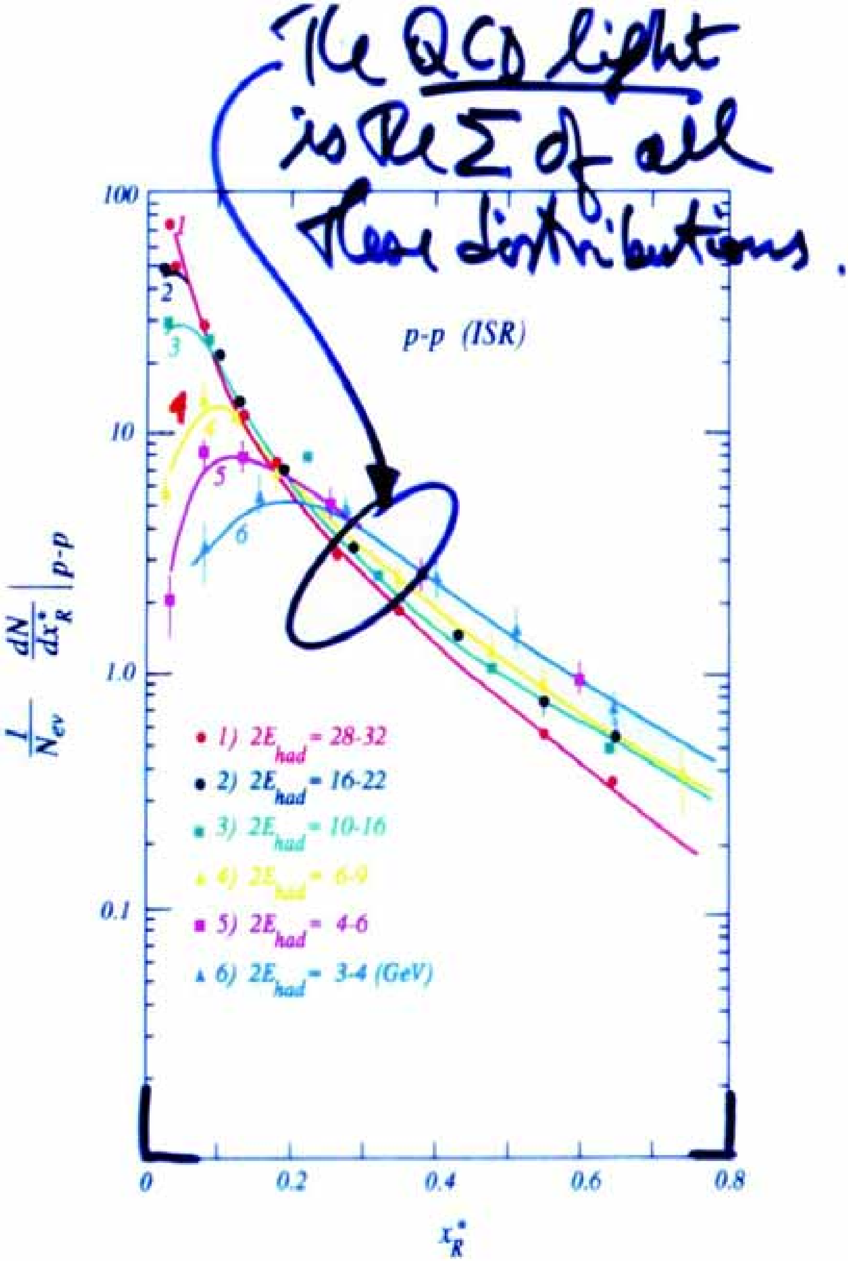


Figure 30.



The QCD light
is the Σ of all
these distributions.
p-p (ISR)
100
10
1.0
0.1
0
0.2
0.4
0.6
0.8
x_R^*
$\frac{1}{N_{ev}} \frac{dN}{dx_R^*}\big|_{p-p}$
1) $2E_{had}$ = 28-32
2) $2E_{had}$ = 16-22
3) $2E_{had}$ = 10-16
4) $2E_{had}$ = 6-9
5) $2E_{had}$ = 4-6
6) $2E_{had}$ = 3-4 (GeV)

Figure 31.

APPENDIX III.4

The Running Of (α_1 α_2 α_3) Versus Energy the Gap Between E_{GUT} And E_{SU}

The exact use of the Renormalization Group Equations, RGEs, for the running of the three gauge couplings (α_1 α_2 α_3) has given many interesting results. One of these is the existence of a gap between the energy E_{GUT} where the three gauge couplings converge and the String Unification Energy E_{SU}.

The value of E_{GUT} is two powers of ten below E_{SU}. This is shown in figure 7 (which is the same as figure 7 of chapter 6).

The details which refer to the Gap between E_{GUT}, E_{SU} and E_{Planck} are shown in figure 32.

The lines are the result of calculations executed with a supercomputer using a system of three weakly coupled differential non-linear equations:

$$\mu \frac{d\alpha_i}{d\mu} = \frac{b_i}{2\pi} \alpha_i^2 + \sum_j \frac{bij}{8\pi^2} \alpha_j \alpha_i^2$$

describing the evolution of all phenomena including the superworld, from the maximum level of energy, E_{GUT}, to our world at the minimum of energy.

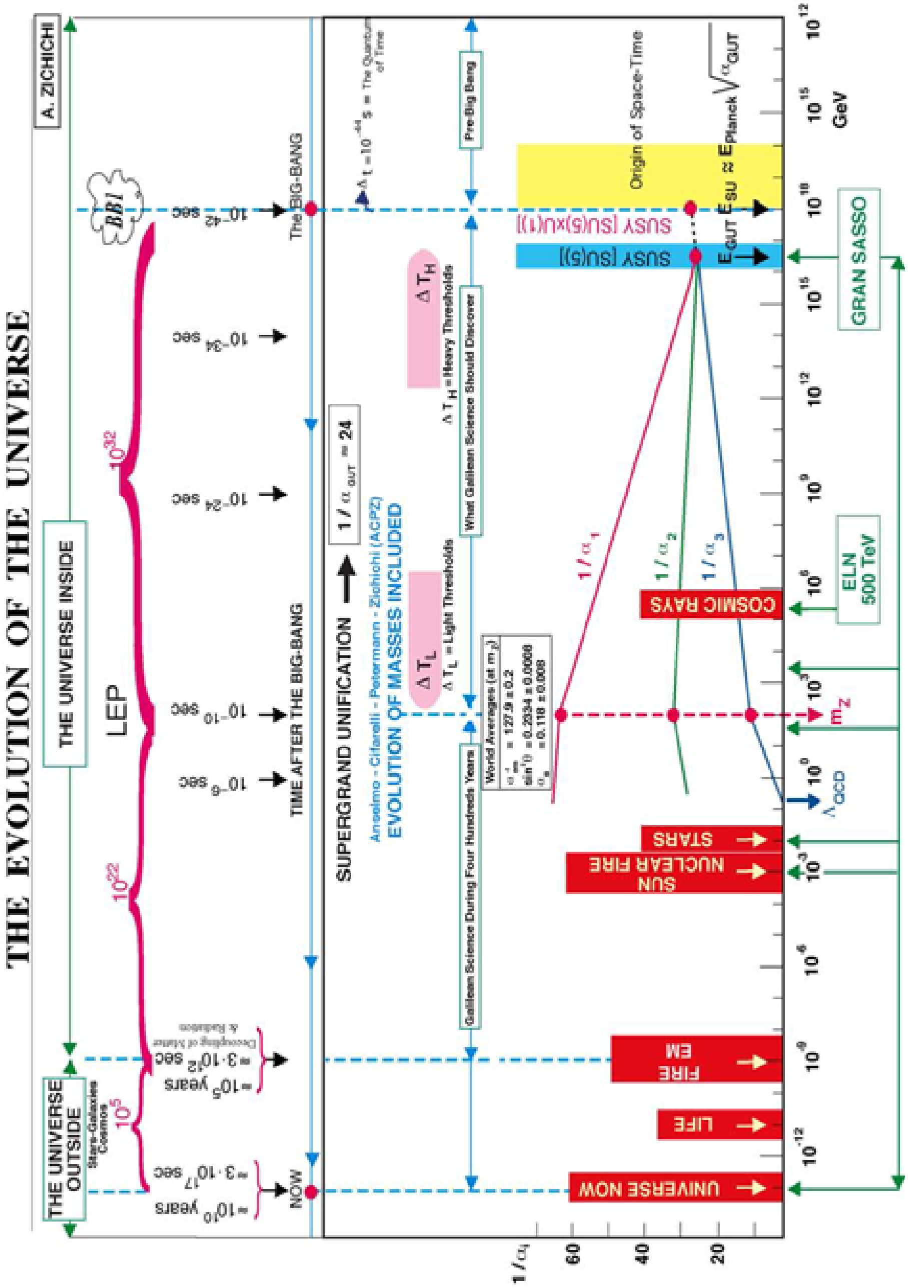


Figure 7 (from p. 120).

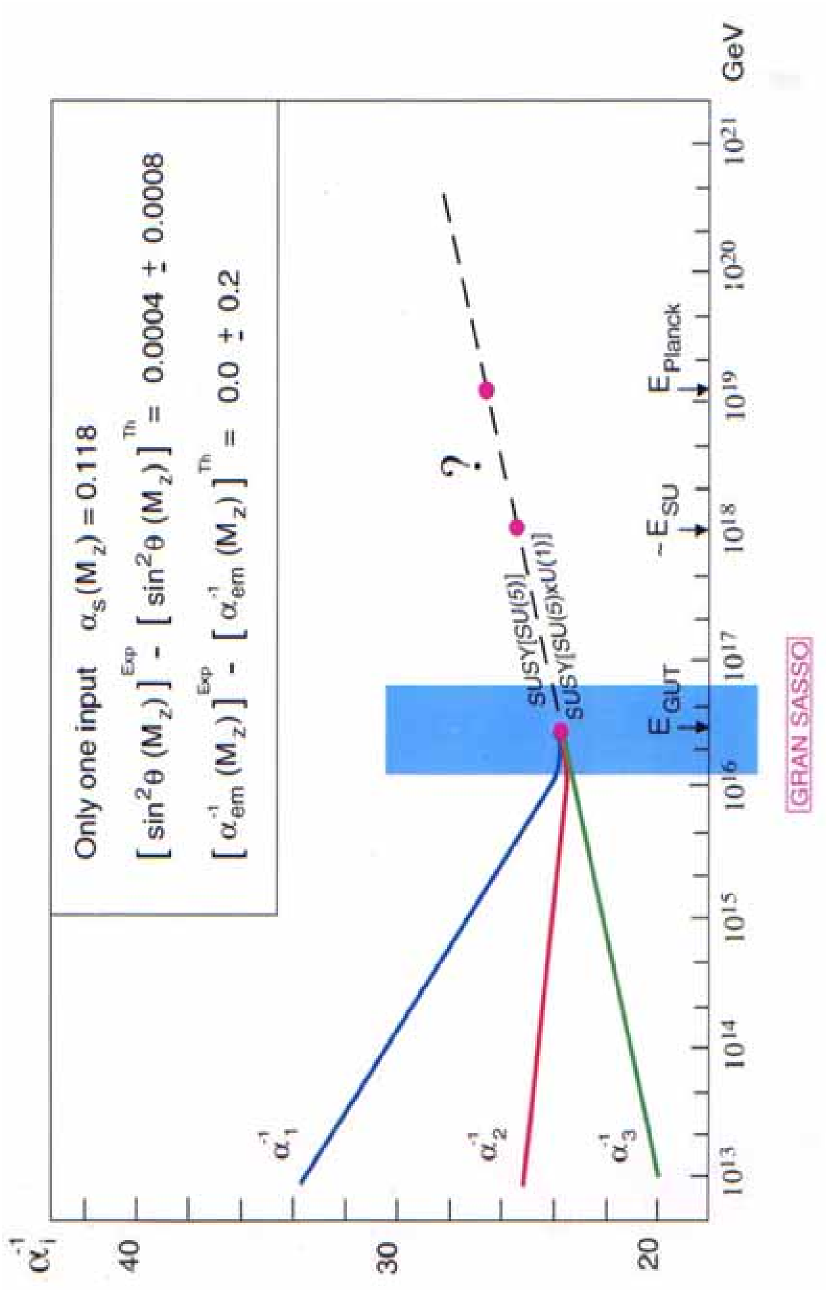

Only one input $\alpha_s(M_Z) = 0.118$
$[\sin^2\theta(M_Z)]^{Exp} - [\sin^2\theta(M_Z)]^{Th} = 0.0004 \pm 0.0008$
$[\alpha_{em}^{-1}(M_Z)]^{Exp} - [\alpha_{em}^{-1}(M_Z)]^{Th} = 0.0 \pm 0.2$
α_i^{-1}
40
30
20
α_1^{-1}
α_2^{-1}
α_3^{-1}
SUSY[SU(5)]
SUSY[SU(5)xU(1)]
?
E_{GUT}
$\sim E_{SU}$
E_{Planck}
10^{13}
10^{14}
10^{15}
10^{16}
10^{17}
10^{18}
10^{19}
10^{20}
10^{21}
GeV
GRAN SASSO

Figure 32.

APPENDIX IV

THE PLATONIC GRAND UNIFICATION

Let us look at figure 25 from Appendix II again, since this is the best example of Platonic Grand Unification. The points have a sequence of 100 GeV in energy. The last point where the 'ideal' platonic straight line intercepts the theoretical prediction is at the energy of the Grand Unification. This corresponds to $E_{GUT}=10^{16.2}$ GeV. Other detailed information on the theoretical inputs: the number of fermionic families, N_F , is 3; the number of Higgs particles, N_H, is 2. The input values of the gauge couplings at the Z^0-mass is α_3 $(M_Z)=0.118\pm0.008$; the other input is the ratio of weak and electromagnetic couplings also measured at the Z^0-mass value: $\sin^2\theta_W$ $(M_Z)=0.2334\pm0.0008$.

The Platonic Grand Unification should be along the straight line, small dots (blue), but Nature seems to follow the big dots (red).

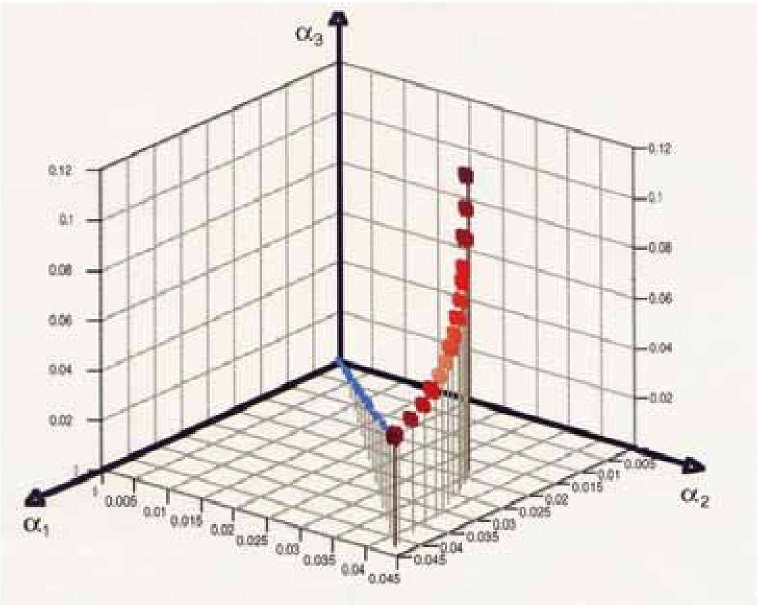


Figure 25 (from p. 146).

APPENDIX V

THE PLATONIC SUPERSYMMETRY

Figure 33.

APPENDIX VI

Seven Definitions of Complexity

People speak of 'Complexity' as a source of new insights in physics, biology, geology, cosmology, social sciences, evolution of the human species and in all intellectual activities which look at the world through the lens of a standard analysis in terms of either Simplicity or Complexity. *But* 'Complexity' is ill-defined, as shown by the existence of at least seven definitions of Complexity.

Definition Number 1

Complexity is a property of systems that are somewhere in between a completely random and a completely regular state, often described by a highly non linear set of equations but sometimes not describable by equations at all.

Definition Number 2

Bad ones:
1) Chaos.
2) The need for lengthy calculations.
3) The need for many distinct variables.
Better ones:
4) Unexpected difficulty when attempting to describe
something in a precisely formulated theory.
5) What is left over after all systematic approaches failed.
But it could also be that: Complexity is an excuse for sloppy
thinking.

Definition Number 3

The Complexity of a theory (problem) is the minimum amount of computer time and storage required to simulate (solve) it to a specified level of precision.

Definition Number 4

If we admit that biological or linguistic evolution, or financial dynamics are complex phenomena, then their typical dynamics are somehow between strong chaos (i.e. positive Lyapunov exponents) and simple orbits (i.e. negative Lyapunov exponents). In other words, Complexity (or at least some form of it) is deeply related to the edge of chaos (i.e. vanishing maximal Lyapunov exponent). Since the edge of chaos appears to be related paradigmatically to an entropy index 'q' different from unity, there must be some deep connection between Complexity and generalized entropies such as 'Sq'.

Definition Number 5

From the mathematical point of view:

- A problem can be polynomial, which means that it is not to hard to predict surprises.
- A problem can be NP or NP-complete, which represent different degrees of difficulty in predicting surprises.
- •• Surprises means: UEEC event (see later).
- •• That degree of difficulty can be associated with the level of Complexity.

Definition Number 6

A system is 'complex' when it is no longer useful to describe it in terms of its fundamental constituents.

Definition Number 7

The simplest definition of Complexity: '*Complexity is the opposite of Simplicity*'. This is why we have studied the platonic Grand Unification (Appendix IV) and its extension to the platonic Superworld (Appendix V), in order to show that Nature does not follow Platonic Simplicity.

APPENDIX VII

The Basic Points on the Correlation Between Predictions and UEEC

It is often stated that scientific predictions are the most advanced frontiers of our exact knowledge.

It is therefore necessary to clearly establish the relation which exists between scientific predictions and progress at the frontier of our knowledge which, as we have emphasized on several occasions, is based on UEEC events.

It is also necessary to clarify the experimental evidence for the existence of predictions and how predictions are correlated with UEEC. *Predictions*.

The experimental evidence for the *existence* of *predictions* is the result of many scientific reproducible experiments.

Quantum ElectroDynamics, QED, is the best example. The anomalous magnetic moments, in symbols (g–2), of the electron (e) and of the muon (μ):

$$(g-2)_{e,\,\mu}$$

are theoretically computed at an extraordinary level of precision (few parts in ten billion parts for the electron) and are experimentally verified to be correct. Could the

$$(g-2)_{e,\,\mu}$$

be theoretically predicted before the discovery of the Maxwell equations and the existence of Quantum ElectroDynamics (QED)? The answer is obviously no.

The sequence which correlates UEEC events and predictions is very clear.

Predictions at the *fundamental level of scientific knowledge* depend on *UEEC events*.

For example: it is the discovery of the laws governing electric, magnetic and optical phenomena (all totally unpredicted) which produced the mathematical structure called QED.

The mathematical structure was not discovered before the innumerable series of UEEC events was found in electricity, magnetism and optics. This series of UEEC events allowed Maxwell to express 200 years of experimental discoveries in a set of 4 equations.

Mathematical formalism comes *after* a totally unexpected discovery: an *UEEC event* which no one was able *to predict*.

In the whole of our knowledge rigorous predictions exist only in Science. These predictions are based on the mathematical description of a single UEEC event or a series of UEEC events. This description can either be the result of new mathematics (for example the Dirac δ-function) or the use of existing mathematical formalism (example: Einstein's use of the Ricci tensor calculus). The UEEC event at the origin of the Dirac equation is the fact that the electron was not a 'scalar' particle but a spin ½ object.

The UEEC events at the origin of Einstein's mathematical formulation of the gravitational forces are the discoveries of Galilei ($F = mg$), of

$$\text{Newton}\ \left(F = G\frac{m_1 \cdot m_2}{R_{12}^2}\right),$$

and of Lorentz that Space and Time could not be both real and that all electromagnetic phenomena obeyed a new invariance law, now called Lorentz-invariance. These are just two examples of the fact that the greatest steps in the *progress of Science* come from totally unpredicted discoveries. It is the mathematical formulation of these discoveries which allows predictions to be made. Once made, these predictions need experimental checks.

Even when we have a mathematical formalism coming from a series of UEEC events, if this formalism opens a new frontier, as it is in the case for the Superworld, experimental proof is needed to verify the validity of the new theoretical frontier.

Today we have a reasonable mathematical formalism to describe the *Superworld*, but in order to know if the Superworld exists we need, as pointed out in previous chapters, the experimentally reproducible proof of its existence. And it could be that, while searching for the Superworld, a totally unexpected discovery (UEEC) is found. This is the reason why we need to perform experiments, as Galileo Galilei realized 400 years ago.

APPENDIX VIII

THE TEN CHALLENGES IN THE EVOLUTION OF OUR UNDERSTANDING THE BASIC HARDWARE OF ALL FORMS OF MATTER

Here is the list

1. Non-perturbative QCD.
2. Anomalies and Instantons.
3. The Physics of NSSB (non-Spontaneous Symmetry Breaking: CP≠,T≠, CPT≠ [4] Matter-Antimatter Symmetry).
4. The Physics of Imaginary Masses: SSB (part of this is the Higgs particle/particles).
5. The Physics of 43 dimensions (part of this is Supersymmetry).
6. Flavour mixing in the quark sector.
7. Flavour mixing in the leptonic sector.
8. The problem of the missing mass in the Universe.
9. The problem of Hierarchy.
10. Physics at the Planck scale and the number of expanded dimensions. Here the most interesting consequence would be that, given the best value for an expanded dimension, it could be that the E_{GUT} scale goes down to the range of the Fermi scale, as illustrated in figure 13 of chapter 9.

[4] The symbol ≠ means that a Symmetry law is non spontaneously broken as it happens with C, P, CP and T). [C (charge conjugation, i.e. interchange of charges with anti-charges); P (parity, i.e. interchange of left and right); T (inversion of the arrow of Time)].The products CP and CPT mean the simultaneous Symmetry laws for all operations CP and CPT, respectively. The existence of Matter-Antimatter Asymmetry would be a proof of CPT ≠ .

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DISCUSSION ON PROF. ZICHICHI'S PAPER

PROF. ARBER: Thank you very much. Big Bang 3: According to your definition: you said that it has occurred only once, is that limited to our planet or to our galaxy or the entire universe?

PROF. ZICHICHI: Very interesting question, thank you. I have not yet published a work that I have been engaged in for the last couple of years. Nevertheless, I will give you the results. When you compute the conditions to have life endowed with reason such as ours, able to transmit signals, therefore quantum electrodynamics has been discovered, the standard model has been discovered, what Edward Witten is studying has been understood, which is not the case now, once you take all this into account, the result is that the probability for the existence of life like our life in the universe is 10^{-54}. Since there are 10^{22} stars, the probability for existence of life in the cosmos is 10^{-32}. This means that Big Bang 3 is limited to our planet. It is a miracle that we are here. On the other hand if you look at SETI, like our friend Swarup, this means that you are looking for another miracle. In fact we have to look for the existence of life capable of communicating with us, so they must be as smart as we are or even smarter than us, sending electromagnetic signals.

PROF. VICUÑA: Dr Zichichi, you mentioned twice that Big Bang 1 is a transition from the vacuum to a universe of inert matter. In this context, does vacuum have a physical meaning or a philosophical meaning?

PROF. ZICHICHI: No, no, it is a physical vacuum, which is the state of minimum level of energy. The laws of vacuum are the laws of nature. There are theories which have vacua which describe the world in 43 dimensions. Out of these 43 dimensions only 3+1 (three space and one time) are expanded, the other dimensions remain collapsed. There are vacua with different laws, different regularities, different couplings, different constants than those of our world. The reason why I like string theory is because we have learned a lot on fundamental concepts, not because string theory is Galilean science.

If I ask my friend Ed Witten what experiment should I do to find out if string theory is right or wrong, there is no experiment to be done. So the answer to your question is that vacuum is not a philosophical concept, it is a physical concept, it is the status of minimum energy. According to string theory there is an infinite number of possible vacua, called 'vacuum landscape' by Leonard Susskind who has been heavily engaged in this field.

PROF. CABIBBO: 10^{500}, according to Susskind.

PROF. ZICHICHI: Yes, 10^{500}, it is now infinite.

PROF. HÄNSCH: Professor Zichichi, couldn't one argue that DNA represents some kind of written language and collective memory, so in this way we are not that unique?

PROF. ZICHICHI: No. DNA is not a written language. Written language is the result of DNA having produced man-like organs. These organs like ours, need a certain number of protons, neutrons and electrons to exist; but they have to produce permanent collective memory. The point you have raised is very interesting. I have discussed it with some of my friends, but the conclusion, which is also my personal conclusion, is that DNA is a necessary but not a sufficient condition to create you and me-like objects. For this to happen we need Big Bang 3.

PROF. GOJOBORI: I would like to address one question about your statement that the study of evolution is below Galilean science according to your definition, because I understand that you stated that this may not be reproducible in terms of experiment. However, I would like to say that, in the case of RNA viruses, which change a million times faster than our organism, therefore, if you take RNA viruses you can observe a million years' time as just one year in humans. So how do you respond?

PROF. ZICHICHI: My answer to your question is the following: 150 years of experimental discoveries in electricity, magnetism and optics have produced, thanks to Maxwell, the four Maxwell equations, which have allowed us to understand an enormous variety of reproducible processes. If you have reproducible processes with very high mutation rates you should be able to find the few fundamental equations from which you deduce BEHS, the biological evolution of the human species. I have nothing against the field of biological evolution; I would like to see the equivalent of quantum electrodynamics coming from these reproducible experiments, otherwise you are still waiting for the new Maxwell to express this enormous variety of discoveries, totally unexpected, into a rigorous mathematical formalism.

PROF. M. SINGER: I think that your response to the last question clarified for me the question I want to ask. You appear to be saying that only the methods of physics can stand as science and you are trying to lay on biology that requirement, whereas, in fact, biology is very different from physics. It is not at all clear that the same kind of standard is relevant and, in part, that is because of the contingency of the evolutionary process and also the contingency of much that goes on in cells, and therefore in organisms. It is important for me to understand what you are requiring, so that I can decide whether I think that your comment is useful in my trying to understand biology. Thank you.

PROF. ZICHICHI: You say that my requirements for science concern only physics and cannot be extended to biology. This is why I cannot say, either you do what we do or you are out of science. What I want to say is that you have to be like we have been in the past, namely using intellectual humility, not to claim that you have understood something, when it is not true that you have really understood what you claim you have understood. Why? Because there are different levels of understanding. Let us imagine that we turn back the clock by 150 years. Then we physicists have a tremendous amount of discoveries in electricity, totally unexpected, in magnetism, totally unexpected, and in optics, again totally unexpected. We would discuss here what we are doing, and then you would say that physics is a complex system, like biology. There are people who claim that there are fields of our knowledge, like the one you mention, i.e. biology and especially the biological evolution of the human species (BEHS) that belong to the so-called science of complexity. I have been interacting with these specialists and found that there are 70 definitions of complexity. Complexity is ill defined. The reason why you cannot reduce all you know to a few equations is because BEHS is not as simple as physics. I invite you to please read my paper and write to me 'on page n. X you made a mistake'. I would be grateful to you. The point is that the basic experimentally observable quantities, which allow anyone to conclude that a given field is complex, are UEEC events, (Sarajevo-type events) and Anderson-Feynman-Beethoven phenomenology. As reported in my lecture these two effects exist in physics; so our field is like your field but we have been using intellectual humility. Instead of stating that we have understood everything we have continued our research and have been probably lucky enough to discover the few fundamental laws which generate the enormous number of reproducible phenomena called physics. So the day when you will find the fundamental laws which allow you to derive the enormous amount of reproducible phenomena in biology from these few equations, we will say that biology is Galilean science. Let me give you an example. Quantum electrodynamics allows to understand the enormous variety of phenomena we are familiar with: this microphone, television, radio, computer, nanotechnology. When you are able to tell us what are the few fundamental equations which produce the enormous amount of reproducible phenomena discovered in your field, we can say that your field is Galilean science. I am not against your field. I would like this field to become Galilean science.

PROF. DEHAENE: Professor Zichichi, thank you very much for reminding us of the exigency which physics requires from both the theory and the data. I think that this is a well-taken point. Certainly, even in psychology, some physicists have made very important contribution to the currently prevailing rigour. Helmoltz and Mach were among the first, actually, to contribute to our field, but of course there are domains that are more advanced than others and I always cite in this context Richard Feynman, one of the heroes of physics, who said that physicists should not have contempt for biologists because physicists took all of the easy problems and the biologists are left with the hard ones (the hard ones, not necessarily the complex ones). But I want to address specifically the notion of reproducibility in the domain of the evolution of human reason. I think there are several solid discoveries which actually make this science fit well within what you call the second level of Galilean science. One, and I think we may hear Professor Coppens about that, is the discovery of fossils, of precursors of humans, some of which are different species. We know now that Neanderthal is a different species, and yet it had reason, at least sufficient enough to bury its dead or enjoy works of art. The second concerns the issue of reproducibility. Every day, on earth, about several million babies are born and these babies develop reasoning abilities. We can measure it and study it, and, of course, this is what we do in psychology. Furthermore, because of unfortunate experiments of nature, some of these babies do not reach the level of reason that you are describing. For instance, some, like Professor Lejeune described, will have trisomy on chromosome 21 and will not develop the brain architectures that allow for reason. These are two sources of reproducible findings in the study of human evolution, and there are many others. I would argue that every discovery of a new human fossil is a test of the theory that Yves Coppens and other people are describing. Such tests, in my opinion, make these studies fully part of the second Galilean level that you described.

PROF. ZICHICHI: The clearest example of second level Galilean science is stellar evolution. The clearest example of third level Galilean science is cosmic evolution. Why are stellar evolution and cosmic evolution Galilean science? Because no fellow can ever propose a theory of stellar evolution or of cosmic evolution which violates the fundamental laws established at the first level. This is why I insist on the first level: there cannot be a second and third level if the first level Galilean science is missing. So even if you satisfy the condition of the second level, the first needs to be there, to give credibility to the other levels, otherwise you are not in the field of Galilean science. Galilei is the greatest fellow ever born on this planet. Let me tell you, once again, why. How do you explain the existence of science? Why didn't other civilisations discover science? Read Galilei as I did, when I was young. These readings either you do when you are very young and you have time, or you never do them. I am not a historian of science, I was fascinated by Galilei when I was very young so I read all Galilei. If you read you find out why science was discovered by Galilei. He said: the fellow who built the world must be smarter than all of us, no one excluded. This is why we have to put questions to him, and how do you put questions to him? In Galilei's time there was no telephone, but even now I cannot phone the fellow who created the world to ask him if the superworld exists. We have problems understanding cosmic evolution. If a detail is not there evolution stops. At present evolution brings us to formulate the mathematical existence of the superworld. If the superworld is not there we have to understand why. In order to know where to go, the only way is to implement experimentally reproducible results and this is what we will do with LHC, the new CERN collider capable of reaching the highest energy levels in this world. The problem described by Professor Lejeune and mentioned by you refers to BEHS (the biological evolution of the human species) and has to be scientifically investigated. Exactly as it happens to be the case in our field when we discover that something does not follow what is expected by our understanding.

PROF. MENON: I am afraid we now have to stop the discussion. The last question will be by the President.

PROF. CABIBBO: It is not a question but a statement. I have a very deep respect for biological science for a very simple reason: many of us would not be here if biological science were not really so effective. First thing. Secondly, your argument is essentially Bellarmino's argument. Bellarmino told Galilei, 'I don't believe in your ideas about Copernicus and the moving earth etc and I will only believe it when you show it to me, when you give me a proof'. This is in a letter to Foscarini that you probably know and I think your argument against biologists is not Galilean but Bellarminian, and I think the argument of Bellarmino and therefore your argument is wrong, because, in fact, he was right in that Galilei had no proof of Copernican motions. In fact he had proof but it was wrong, but he was right in a prophetic way because the real proof arrived later, for example aberration of stellar light was about a hundred years after Galilei died, and Foucault's experiment two hundred years after Galilei died, etc so I think these ideas of logic sometimes do not work and I think Bellarmino's logic was wrong and it was the basis for the famous trial against Galilei.

PROF. ZICHICHI: First answer: for 'biological science' to exist we need to understand the transition from inert matter to living matter: i.e. Big Bang 2. No one knows how to study this transition in terms of Galilean science. To answer your second point it is necessary to explain why my classification of BEHS in terms of Galilean science is not Bellarmino's logic but rigorously Galilean logic. Let me start with your 'prophetic' definition of Galilei's work. Galilei was not 'prophetic' about the two earth motions. Galilei was able to explain why a stone dropped from the leaning tower of Pisa does not go a hundred metres towards the West. This was the strongest argument from all those who did not want the earth to have a motion around its own axis (spin motion). If this motion exists it is the earth which rotates not the stars and all celestial bodies. During thousands of years since the first proposal of the earth's spin motion by the Greeks (Heraclitus, IV BC) no one was able to give an answer to the argument against the earth's spin motion. Galilei, in fact, predicted that the stone would fall displaced by a few centimetres towards the East, due to the fact that the speed at the top of the tower is higher than the speed at the basis of the same tower. This displacement was measured in 1791 by Giovanni Battista Guglielmini, a professor at the Bologna University. This is the first proof of the earth's spin motion. Foucault pendulum came sixty years later, in 1851. Concerning the other motion of the earth around the Sun (proposed by Aristarchus in III BC many centuries before Copernicus) Galilei knew that the decisive proof was to measure the parallax of a star. He tried to measure the parallax but did not succeed. The reason being – according to Galilei – that the stars are much more distant that thought at that time. Galilei was right. James Bradley discovered the aberration of light in 1727 while he was trying to measure stellar parallax. He did not succeed in measuring the parallax. Bradley would not have been able to explain the aberration of light if Römer had not been able to measure, fifty years before, the speed of light, using Galilei's 'celestial clock' (based on the Jupiter satellite Io). The fellow who finally succeeded in measuring the stellar 'parallax' was Bessel in 1837, a hundred and ten years after Bradley, and more than two centuries after Galilei's first attempts to measure it. This is the correct sequence of events after Galilei. Foucault's pendulum was invented in 1851 in order to provide a spectacular proof of the spin motion of the earth, not because there was any doubt about its existence, established by Guglielmini 60 years before. Concerning your statement about Bellarminian logic let me explain why my logic is Galilean. Bellarmino's logic was: give me the direct proof of the earth's motions. Here comes a clear case of second and first level Galilean science. The study of the earth's motion is second level Galilean science. The understanding of this motion needs first level Galilean science. In no case can the understanding of the earth's motion be in contradiction with the results which we are able to get in a series of reproducible experiments implemented in our laboratory where we can change conditions and details in order to find a rigorous mathematical description of the results obtained. Galilei, on the basis of first level science, discovered the principle of inertia, the law of composition of velocities, the equivalence of inertial and gravitational masses, the correct law which establishes that a force is not proportional to a velocity but to the change of velocity (acceleration); he invented the pendulum in order to study friction-free motions; on the basis of these studies he extrapolated the results of first level science to the motion of the liquid earth surface where the reason why 'tides' exist had never been found. He knew that the direct proof of the orbital motion of the earth is the stellar 'parallax' and in fact he tried to measure it. He correctly interpreted the negative result obtained in terms of the distance of the stars, which Galilei correctly thought had to be much more distant from the earth than thought at the time. Galilei wanted to explain the tides using the discovery of the composition of velocities, which is first level Galilean science. He knew that the velocity of the earth's surface due to its spin motion was very high and in fact he discovered, at first level science, the principle of conservation of the linear momentum (called quantity of motion), thus explaining why the trajectory of a stone falling down, if launched from the Pisa tower is not displaced hundreds of metres towards the West. He could not imagine that the velocity of the earth around the Sun is hundreds of times higher than the velocity at the earth's surface due to its spin motion. This is why the composition of velocities discovered by Galilei at first level science could have no effect on the 'tides'. Galilei could not imagine the tides due to the gravitational attraction of the moon and of the Sun. The tides have a period of 12 hours while the composition of the two velocities (due to spin and orbital motion) repeat every 24 hours. There was a flagrant discrepancy. But Galilei thought this could be solved later. He was interested to find other laws at first level science. For example to measure the acceleration by gravity 'g', using the invention of the 'inclined plane', one of the greatest inventions of mankind. Without the value of 'g', Newton could not have discovered that the moon falls down like a stone launched from the Pisa tower. Galilei's attempt to explain the 'tides' with the law of composition of velocities, discovered using first level science, is the first example of extension to second level science of what is found at the first level. This extension has allowed mankind, in the very short period of 400 years, to understand the enormous variety of phenomena observed in the sky and never understood during thousands and thousands of years. Galilei's extension of what he was discovering at the first level to the second level science has allowed mankind to understand the real nature of a star. Something that could never be explained if mankind continued to work using only second level science. The fact that his extrapolation was wrong can be justified by the fact that this is the beginning of the most fascinating conquest of our intellect: the discovery of first level science, and the possible extension of the laws discovered at the first level to the phenomena observed at the second level. During these last four hundred years we have seen the formidable results of this extrapolation. For example neutron stars. No one could have imagined the existence of a neutron star if Chadwich in 1932 had not discovered, using first level science, the existence of the neutron. So much in order to defend Galilei from the attack for his attempt to explain the tides. Let me now go back to Bellarmino's logic. The reason why Galilei is the father of science is not because of the geocentric versus the heliocentric theory. This is second level Galilean science. The reason why Galileo Galilei is the father of science is his other book, '*Discorsi e Dimostrazioni Matematiche intorno à due nuove scienze*' (*Dialogues Concerning the Two New Sciences*): this is where Galilei discovered the first fundamental laws of nature. This is the reason why Galilei was celebrated in China in 1991. China's is the only government of the planet who celebrated the famous discovery of Galilei, F=mg. If you read the Encyclopaedia Britannica this is attributed to Newton. It is not true. And how did it happen that Chinese culture knew this? Because immediately after the publication of Galilei's book in Holland, the Jesuits translated it into Chinese and brought it to China. I am referring to Galilei's book quoted above. In this book there are no errors made by Galileo Galilei. He is the father of the first three fundamental laws of mechanics, which in the Encyclopaedia Britannica are attributed to Newton and which in my book, which has been translated in Chinese, are correctly attributed to Galilei with all quotations. Bradley (1727), Guglielmini (1791), Bessel (1837) is the correct sequence of discoveries needed for proving that Galilei was right in establishing via first level Galilean science the understanding of the spin and of the orbital earth motions. The understanding of BEHS in terms of first level Galilean science is at present missing and therefore my classification of BEHS in terms of Galilean science is not Bellarmino's logic. It is rigorously Galilean logic. A final remark. The sentence following the famous trial against Galilei that you mentioned was not signed by three Cardinals and never signed by the Pope.

PROF. MENON: Galileo is certainly someone we all honour, as you are all aware. As we meet in this Academy of Sciences we are not discussing conflicts between physical sciences and biological sciences and the like, what we are really talking about is the scientific method as applicable across the whole spectrum, which has been marvellous, and Galileo is certainly one of the pioneers in that. Thank you all very much for a very interesting morning.

Session II

INSIGHTS INTO THE EVOLUTION OF LIFE

THE SEARCH FOR THE CHEMISTRY OF LIFE'S ORIGIN

ALBERT ESCHENMOSER

A central *postulate* of contemporary natural science states that life emerged on Earth (or elsewhere) through a transition of chemical matter from *non-living* to *living*. The transition is seen as a *contingent* consequence of the second law of thermodynamics and the chemical properties of matter by one group of scientists, and as an *imperative* of that law and those properties according to the belief of others. Chemical matter is postulated to have been capable of organizing itself out of disorder by channeling exergonic geochemical reactions into reaction networks that had a *dynamic structure* with kinetic (as opposed to thermodynamic) stability and were driven by autocatalytic molecular replication cycles. The postulate implicates that such chemical systems eventually became *self-sustaining* (capable of exploiting environmental sources for reconstituting itself), *adaptive* (capable of reacting to physical or chemical changes in the environment such that survival as a system is maintained) and – by operating in compartments – capable of *evolving*. From this perspective, *life's origin is seen as* a *seamless transition from self-ordering chemical reactions* to *self-sustaining chemical systems that are capable of Darwinian evolution* [1]. Figure 1 delineates – in terms of a 'conceptual cartoon' – such a programmatic view in more detail.

Evidence from paleontology, biology, geology and planetary science posits the appearance of life on Earth into a period of 3 to 4 billion years ago. Whereas the course of biological evolution is documented by a wealth of fossils of extinct organisms and, more recently, by information from comparative analysis of the genomes of biological species, there are no 'fossils' that would reliably document the nature of the molecules that were involved in the chemical processes at the dawn of life. We do not know whether at the beginning there existed a multitude of different life forms from one of which the one we know today has derived, neither do we know whether the type of molecules and chemical processes on which such

A “Conceptual **Cartoon**” of Chemical Self-Organization:

Due to the existence of **kinetic barriers** to transformations of molecules, an assemblage of chemicals can exist in a chemically immobilized state **far from thermodynamic equilibrium**.

Equilibration, as demanded by the 2nd law of thermodynamics, may selectively be accelerated by **catalysts,** such that chemical changes towards equilibrium proceed preferably along the specific reaction channels opened by catalysts.

Along such channels, new substrates and new catalysts may be formed or encountered, new reaction channels may be opened and, in principle, **catalysts may emerge that catalyze their own formation**.

Substrates, catalysts and self-replicating catalysts may constitute cooperative **chemical systems** that have a **dynamic structure** with **kinetic** (as opposed to thermodynamic) **stability**.

When such a system - driven by the free energy of its chemical input and assisted by compartmentalization – will have acquired
(a) the capability of **producing its constituents under the control of replicating catalysts,**
(b) the complexity for being capable to **adapt** teleonomically to external changes, and
(c) the potential to **evolve** along gradients of increasing kinetic stability and chemical autonomy,
it may be said to be “alive”.

Figure 1. A ‘conceptual cartoon’ of chemical matter’s self-organization towards life.

ancestral lives may have been based were or were not akin to the biological molecules and processes we are familiar with today. Such uncertainty notwithstanding, observations made in half a century of prebiotic chemistry (see below) point to a high probability for an origin of life scenario, in which the continuity postulated to have connected the emergence of adaptive behaviour on the chemical level with the beginnings of evolutionary processes on the biological level was paralleled by a constitutional continuity in the type of molecules that were involved in the transition. This continuity is supposed to be embodied in the chemical structures of α-amino acids, sugars, nucleobases, cofactor molecules and, in addition, in basic biochemical reactions that we find operating still today as enzyme-assisted processes in primitive anaerobic microbes.

The experimental search for the chemistry of life’s origin has been proceeding under the label ‘prebiotic chemistry’ for more than half a century now. This field of research has its conceptual roots in the writings of the Russian biochemist *A.I. Oparin* [2] and the British biologist *J.B.S. Haldane* [3] who, around the first quarter of the last century, independently propounded for the first time explicit views on a natural chemical origin of life

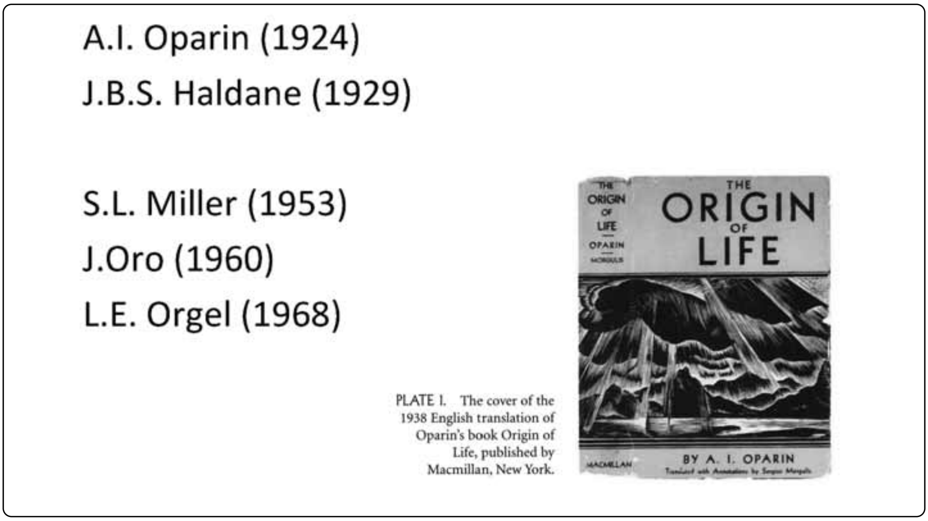


Figure 2. Pioneers of conceptual and experimental prebiotic chemistry in the last century [2][3][4][5].

on Earth (Figure 2). These views were launched into public awareness by the famous experiment of *Stanley L. Miller* [4] in 1953, where it was shown that hammering with excess of energy on gaseous mixtures of hydrogen, methane, ammonia and water induces the formation of – apart from large amounts of undefined organic material – the simplest representatives of the family of proteinogenic α-amino acids (Figure 3). In 1960, the Catalanian biochemist *Juan Oro* [5] discovered the formation of adenine – a molecule prototypical of contemporary biology – from HCN (hydrocyanic acid) in aqueous solution (Figure 4). *Leslie D. Orgel,* the last of the chemical pioneers listed in Figure 2, initiated in 1968 systematic experimental work towards the non-enzymic simulation of biology's arguably most important life process, the autocatalytic replication of nucleic acids [6].

Hydrocyanic acid (HCN), an unambiguously elementary, highly reactive organic molecule, is a central intermediate in Miller-type experiments [4,7] and known to be present on celestial bodies such as Titan and others (Figure 5), as well as to exist in astronomical quantities in interstellar space [8}. Chemically highly significant coincidences were observed between the constitutional spectrum of products formed in Miller-type experiments and the spectrum of organic compounds found in carbonaceous meteorites [9]. A recently published long-time/low-temperature experiment (Figure 6)

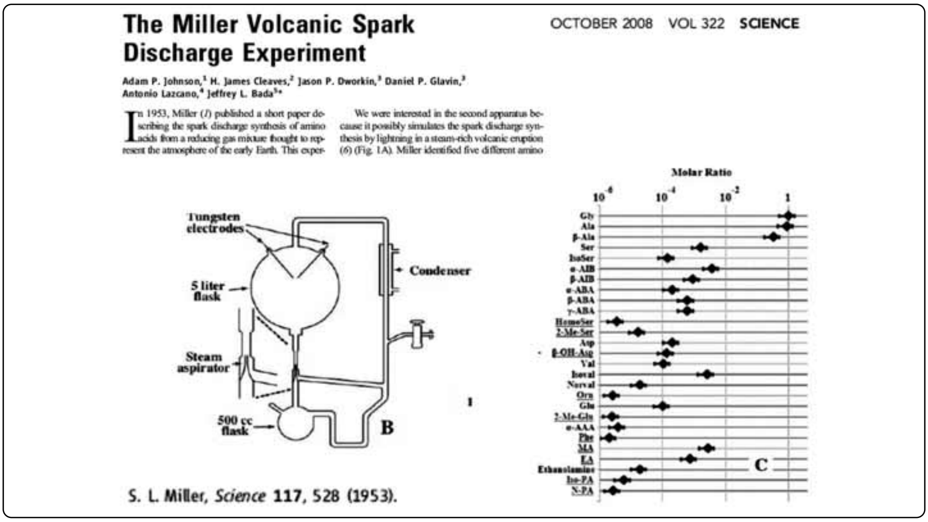


Figure 3. Recent re-analysis by modern analytical methods of the composition of authentic product mixtures obtained by *Stanley Miller* (deceased 2005) in the 1950s [7]. Absolute and relative amounts of biomolecules are still extremely low in such experiments, yet higher than observed before, and many more different molecules have now been identified.

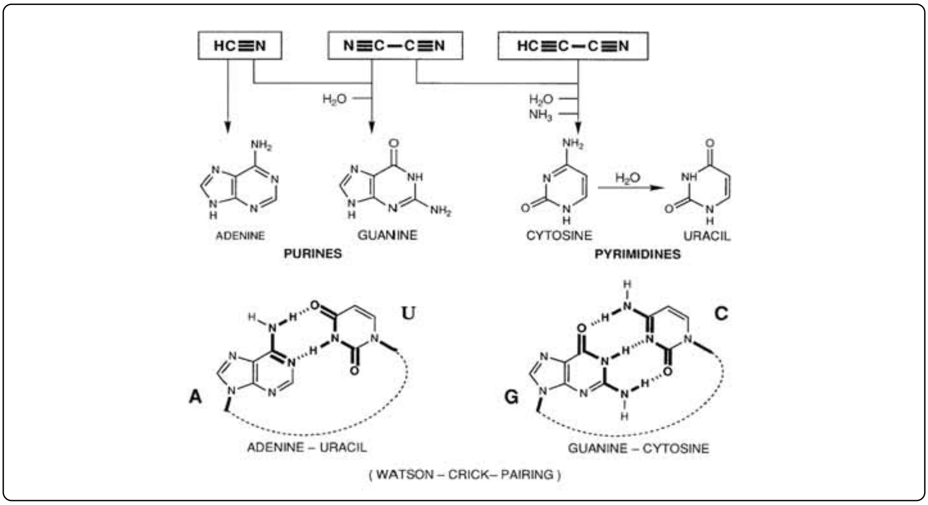


Figure 4. The central biomolecular structure of adenine is composed – formally as well as experimentally – of five molecules of HCN. A close and equally astonishing chemical relationship exists between related elementary carbon/nitrogen compounds and other canonical nucleobases. The lower part of the Figure depicts the two canonical Watson-Crick base-pairs, one of the, if not the, most fundamental biomolecular interactions in whole biology.

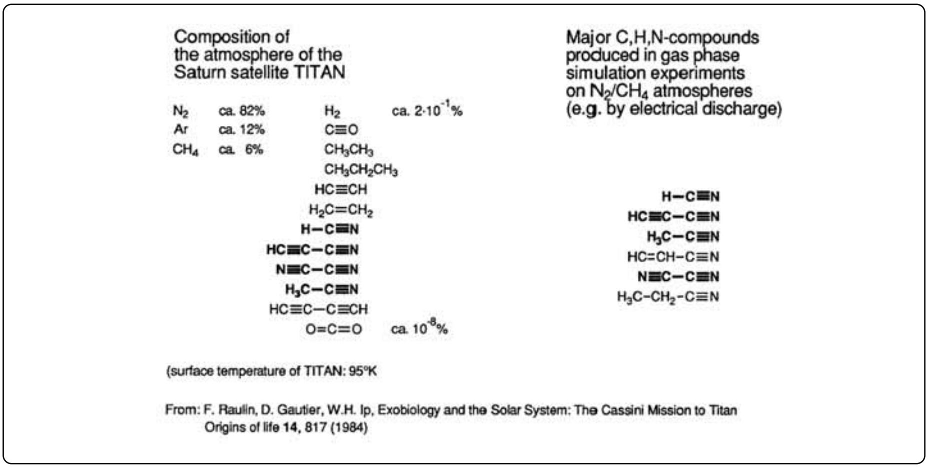
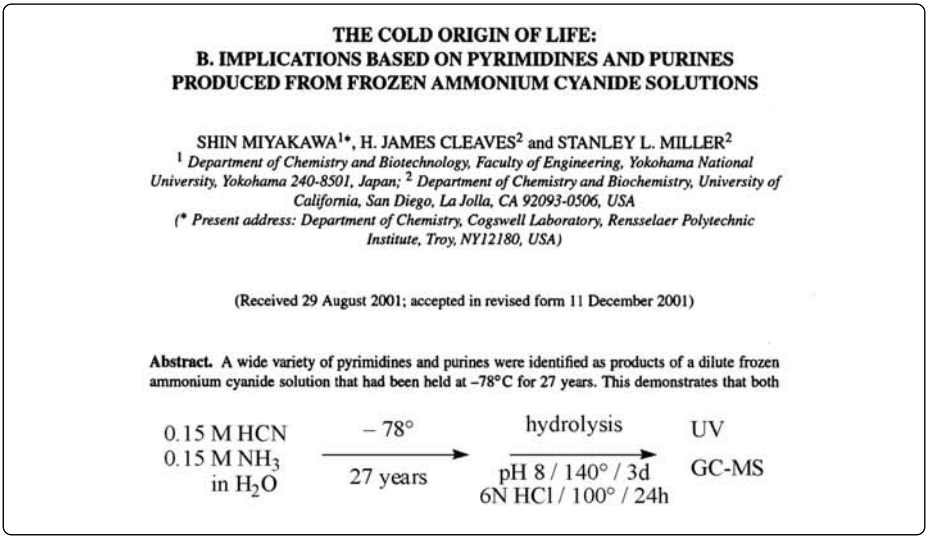


Figure 5. Whenever excessive energy hammers on carbon, nitrogen and hydrogen containing material of any sort, highly reactive carbon/nitrogen/hydrogen compounds such as HCN and higher derivatives of it (nitriles) are formed. Some of them (see formulae in bold, with triple-bonds) are highly reactive and, as HCN itself, chemically closely related to the structure of biomolecules. Note the similarity in the structure type of nitriles of extraterrestrial (natural) and terrestrial (experimental) origin.



THE COLD ORIGIN OF LIFE:
B. IMPLICATIONS BASED ON PYRIMIDINES AND PURINES PRODUCED FROM FROZEN AMMONIUM CYANIDE SOLUTIONS

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Abstract. A wide variety of pyrimidines and purines were identified as products of a dilute frozen ammonium cyanide solution that had been held at –78°C for 27 years. This demonstrates that both

Figure 6. In a recently disclosed remarkable long-time/low-temperature experiment by *Stanley Miller* and (former) collaborators [10], the ammonium salt of HCN in aqueous medium was frozen to solid CO2 temperature, kept for 27 years, and finally its product composition analyzed after hydrolysis with aqueous acid or aqueous base (see Figure 7).

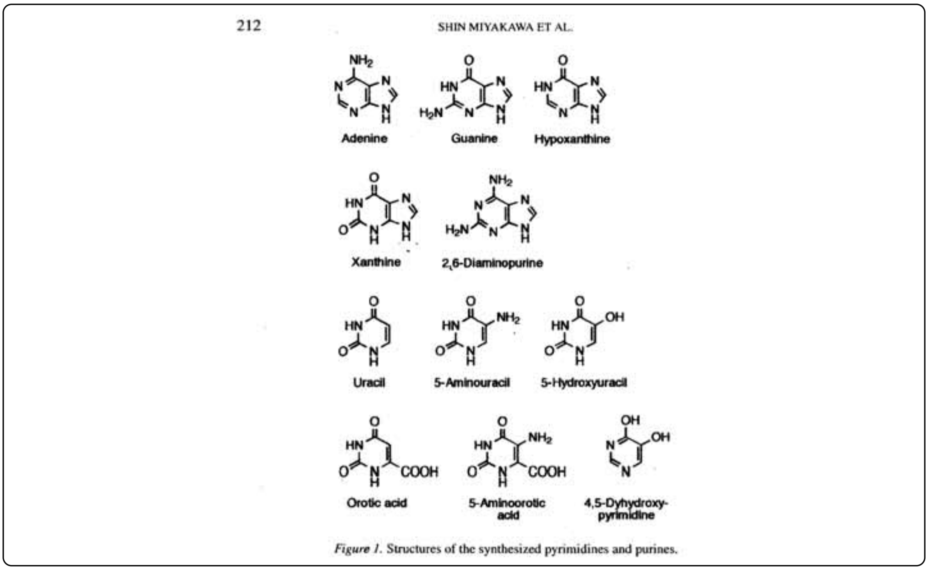


Figure 7. Chemical structures of heterocyclic organic compounds that have been identified (out of a mixture containing a large number of unidentified components) in the experiment described in Figure 6. Among the identified components are two canonical purines (adenine and guanine) and one canonical pyrimidine (uracil), besides two purines (hypoxanthine, xanthine) and one pyrimidine (orotic acid) that are part of the contemporary metabolism.

most impressively demonstrates the remarkably close chemical relationship between HCN and some of the fundamental biomolecules. Prominent in the palette of identified products of that experiment (Figure 7) are canonical purines and pyrimidines, basic constituents of the contemporary nucleic acids [10].

Experimental prebiotic chemistry suffers from the kind of handicap that is inherent in empirical research on historic processes. One is reminded of the fate of the anthropologist's Thor Heyerdahl famous Kon-Tiki experiment in 1947 (Figure 8) [11] by which it had been demonstrated that the original population of the Polynesian Islands could have come from South America. Yet that splendid demonstration of what is technically possible became eventually overridden by criteria anthropological in nature, convincing scientists that Polynesia's original population came from Asia.

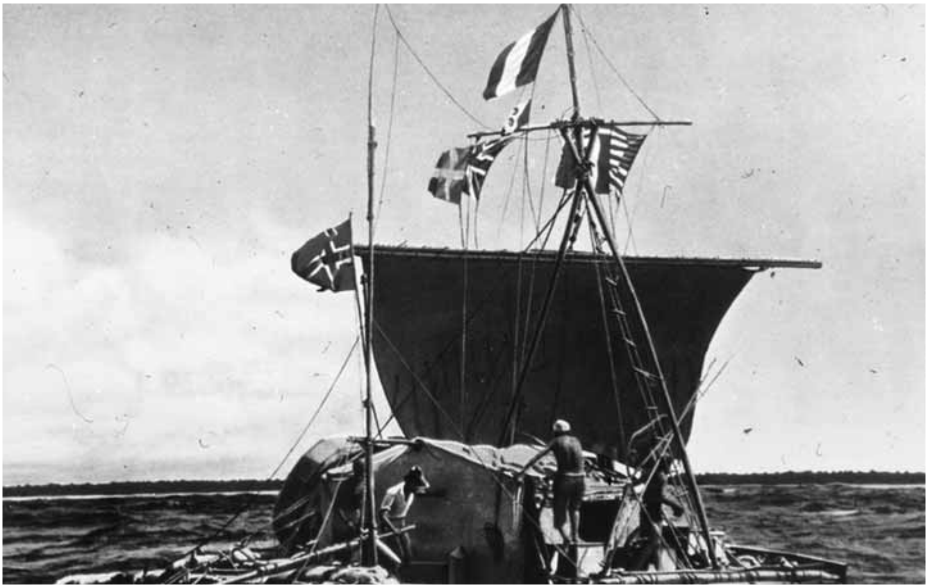


Figure 8. The balsa raft 'Kon-Tiki' on which the Norwegian anthropologist *Thor Heyerdahl* and a crew of five men embarked on a legendary expedition on April 28th 1947, starting in Callao (Peru). After 108 days they landed on the Polynesian Tuamotu Islands, thus demonstrating experimentally that Heyerdahl's theory, according to which the population of the Polynesian Islands came originally from South America, is compatible with what is technically feasible. Ironically, based on criteria anthropological in nature, scientists eventually convinced themselves that the Polynesian population originally came from Asia.

The possibility notwithstanding that conclusions in prebiotic chemistry eventually might suffer a fate similar to that of the Heyerdahl-experiment, the experimental results accumulated over the last half century [12] are in any case of lasting significance and importance. This is true irrespective of whether the organic material that had accumulated on the primordial Earth as the result of (geochemical) prebiotic processes and been delivered to the Earth by carbonaceous meteorites [9] was, or was not, relevant for life's actual emergence. What experimental prebiotic chemistry did achieve, is to conclusively demonstrate that the major types of low-molecular-weight building blocks of the life we know today have chemically *elementary* structures, elementary in the sense that their formation from (essentially) the chemical elements proceed quasi deterministically under an extraordinarily broad range of (potentially geochemical) conditions (Figures 5 and 9). This does not necessarily mean, however, that those prebiotic organics of terrestrial or extraterrestrial origin in the primordial Earth were actually the starting materials for the critical self-organization process. In fact, there are two sharply opposing views on this point: the notions of a *heterotrophic* [2][4][12][13] versus an *autotrophic* [14][15] origin of life (Figure 10).

The proponents of a *heterotrophic* origin take for granted that the accumulation of organic matter by high energy processes on Earth, or by delivery to the Earth by meteorites, was the chemical source for the process of self-organization eventually leading to life's origin. In contrast, the concept of an *autotrophic* origin maintains that any such globally distributed mixture of organic material was *irrelevant* to the process(es) that led to self-organization. Reasons brought forward against heterotrophy refer to problems of selection, accumulation and concentration of specific substrates out of complex mixtures of chemicals, and of combinatorial reactivity and the short survival times of chemically activated substrates in unorganized chemical environments. The concept of autotrophy postulates the emergence of *de novo* pathways to starting materials and intermediates from elemental geochemical sources as an integral part of the very process that constituted self-organization (Figure 11). From the chemical viewpoint, both concepts are burdened with a great many open questions, such as the chemical nature of start-up substrates and catalysts, of primordial metabolism, of primordial replicating entities, be they metabolic or genetic cycles, the role and nature of compartmentalization, last but not least cellularization. Leaning towards one or the other of the two concepts remains still today a matter of reasoned opinion. This should not be taken as being scientifically contra-productive, since in any search for events of the past, commitment to basically different views leads committed researchers to focus on correspondingly different experimental strategies, that in turn may lead to potentially complementary insights.

Besides the debate on heterotrophy versus autotrophy, there is another dichotomy dividing researchers into two camps in their conceptual and experimental search for the chemistry of life's origin: the 'geneticists' [16-18], versus the 'metabolists' [14,15,21]. While both agree on the postulate that crucial to any beginning must have been the emergence of chemical reaction cycles that amounted to autocatalytic replication of molecules (Figure 11), the two camps differ in their view about the chemical nature of those cycles (Figure 12). The controversy [22,23] between the 'geneticists' and the 'metabolists' is the denial by the former of a claim made by the lat-

Prebiotic chemistry of the last century has conclusively shown that the major types of low-molecular-weight building blocks of life

amino acids
sugars
nucleobases

have elementary chemical structures in the sense that their formation from (essentially) the elements can proceed under an extraordinarily broad range of (potentially) geochemical conditions

Figure 9.

Two opposing views:

Organic material that accumulated on the Earth's surface 4 to 3,5 billion years ago delivered the substrates for the self-organization processes that eventually led to life's origin.
(= **heterotrophic** origin of life)

The organic material that had accumulated on the Earth's surface was **not relevant** for the processes that led to self-organization; those processes built their chemical substrates themselves from elemental geochemical sources.
(= **autotrophic** origin of life)

Figure 10.

ter, which is, that a chemical 'metabolic' system may have been capable to evolve and become 'alive' before it acquired a genetic system. To 'geneticists', the indispensible prerequisite for the emergence of a chemical system that deserves to be called 'alive' is the operation of a primordial genetic system. Geneticists challenge the view that autocatalytic metabolic cycles could have evolved with any degree of efficiency. They point to the paucity of such a type of cycles with regard to constitutional diversity and flexibility, as contrasted with replicating informational oligomers with their potential to store structural information in the form of a quasi unlimited constitutional diversity (sequence of specific recognition elements) and, therewith, the chance to give rise in principle to a large spectrum of phenotypic catalytic capabilities.

In the focus of the search for the
chemistry of life's origin is the search
for potentially primordial
autocatalytic cycles

Figure 11.

Such primordial autocatalytic cycles could have been:

Autocatalytic **replication cycles** of "informational" oligomers, such as RNA, or ancestors of RNA
(= the *"geneticists"* point of view)
or
Autocatalytic **"proto-metabolic" cycles**, such as primordial variants of the reductive citric acid cycle
(= the *"metabolists"* point of view)

Figure 12.

What the standpoint 'metabolism first' in the debate between metabolists and geneticists implies is perhaps most clearly expressed by the bold proposal of Morowitz [24,25] which plainly states that 'life started with the *reductive* citric acid cycle', implying that this type of cycle originally was capable of operating without the assistance of enzymes (Figure 13). Irrespective of the serious doubts that may be raised against the validity of this latter assumption, the merit of the proposal lies in its exemplification of how, in principle, such a metabolic cycle could act as the heart of a replicating chemical *system*. The cycle (running in the reductive direction which is constitutionally opposite to that of the contemporary citric acid cycle) would be autocatalytic, since each run through both branches of the cycle would convert input materials (CO_2 and reductants) not in one, but in two

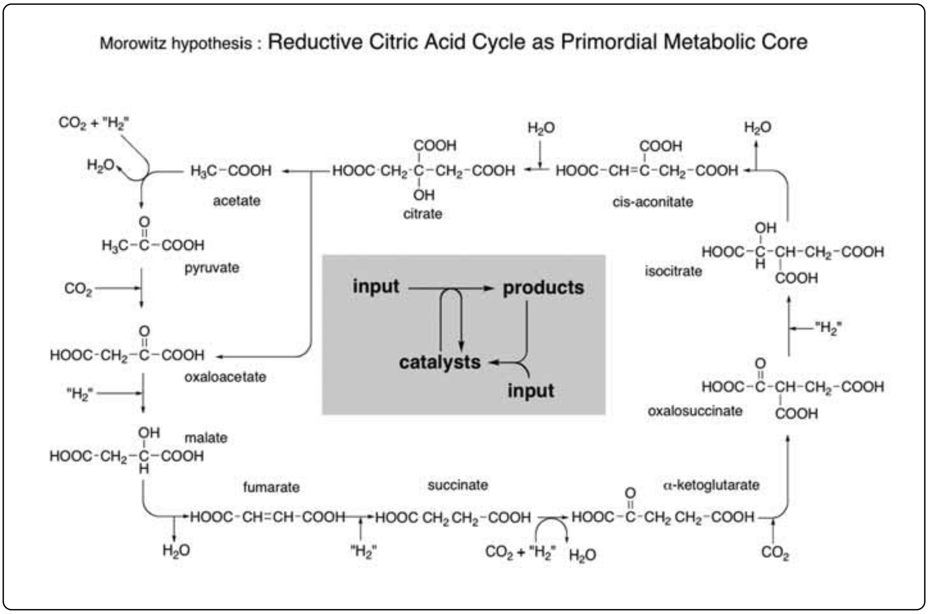
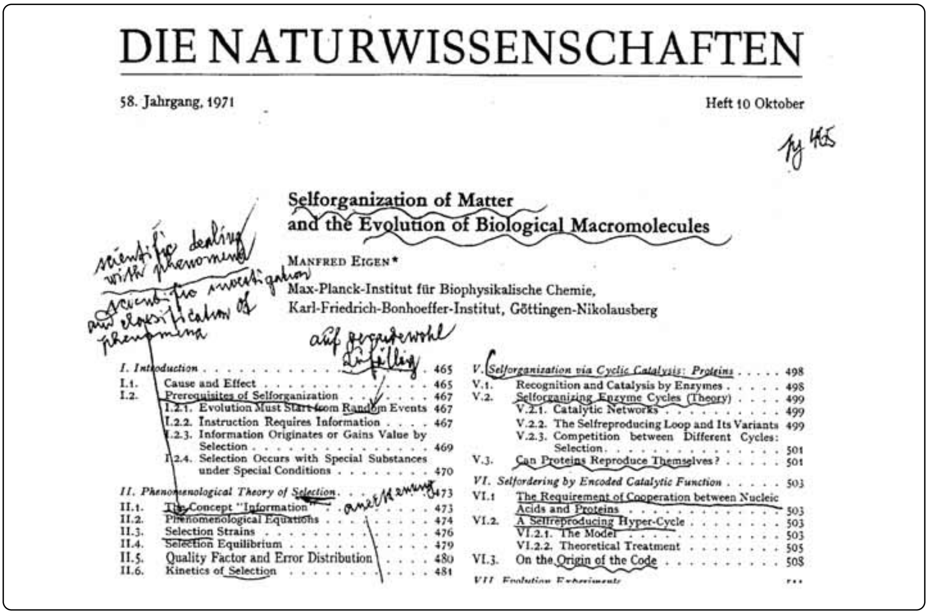


Figure 13. *Harold Morowitz's* proposal that (a non-enzymic version of) the reductive citric acid cycle has been the seed for life's origin [24,25]. The serious doubts organic chemists may have concerning the presumed operation of such a cycle operate without enzymes notwithstanding, the reductive citric acid cycle is a good example to exemplify essentials of an autocatalytic metabolic cycle: exergonic input reactions are to drive a reaction cycle in which two equivalents of each cycle-constituents are formed in each run and in which each cycle constituent is a catalyst both for its own formation as well as for the formation of all the other constituents of the cycle.

equivalents of any given cycle constituent, and each of these constituents – by virtue of their very affiliation to the cycle – would act as catalyst for the formation of itself and of all other constituents of the cycle. Running through the cycle would amount to the self-replication of a family of catalysts. The appeal of the reductive citric acid cycle as the seed of life's origin derives from the role that enzymic versions of the cycle play in some anaerobic microorganism (CO_2 assimilation) and on the fact that the constituents of an oxidative version of the cycle proceeding in contemporary organisms plays an absolutely central role in metabolism.

In the geneticists' view, genetic function is to be assigned unequivocal supremacy over metabolic function when it comes to define the requirements for an organized chemical system to be capable of undergoing Darwinian evolution. Molecular evolvability has as its prerequisite the functioning of an oligomer system that is capable of storing, replicating, and stochastically varying structural information, whereby at least part of it (the 'genotype') must be connectable to specific catalytic functions (the 'phenotype'). The viewpoint received its theoretical inauguration in Manfred Eigen's classic publication entitled 'Self-Organization of Matter and the Evolution of Biological Macromolecules' in 1971 [17] in which for the first time the concept of evolutionary processes on the molecular level was propounded and the kinetic principles that will dominate such processes delineated in conceptual and mathematical terms. Shortly afterwards, a paper entitled 'Self-Organization of Molecular Systems and Evolution of the Genetic Apparatus' appeared, in which its author, Hans Kuhn [18], propounded and exemplified the pragmatic paradigm that the conundrum of life's origin should be approached as a physico-chemical engineering problem. Both papers, pioneering in their time and focusing on concepts, had to circumvent the specific chemical questions that from today's point of view are the central ones, namely, the questions concerning the nature of the *chemistry* of life's origin.

In contemporary living cells a molecular machinery of extraordinary structural and functional complexity, the ribosome, fulfills the extraordinarily complex task of translating – mediated by the genetic code – the *genetic* information stored in the constitutional diversity of one type of biopolymer (the nucleic acids) into a constitutionally different type of biopolymer (the proteins). If a chemist undertook the attempt to think of the chemistry of a primordial molecular machinery by which a replicating oligomer system would be capable of performing a genotype-to-phenotype translation modeled after today's ribosome function, he would run



DIE NATURWISSENSCHAFTEN

58. Jahrgang, 1971 Heft 10 Oktober

Selforganization of Matter
and the Evolution of Biological Macromolecules

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Figure 14. The first page of *Manfred Eigen's* classic paper [17] containing handwritten personal comments made by the organic chemist *Leopold Ruzicka* (1987-1976).

into difficulties that are immense to the extent of being hopeless. This is why the notion of the '*RNA world*' [26] (Figure 15), a 'world' supposed to have preceded our 'DNA-RNA-Protein' world and one in which RNA fulfilled the functions of both the genotype and the phenotype, appears conceptually so attractive. In essence, it reduces the coding problem from (complex) chemistry to ('simple') physics in the sense of replacing an *intermolecular*ly operating chemical coding process by an i*ntramolecular* physical relationship between an oligomer molecule's *constitution* and its *conformation*. Any specific constitution (base sequence) of an RNA molecule induces the molecule to adopt a specific shape (conformation). We may say, the RNA molecule's constitution '*codes*' for that shape. In a system that could screen a population of RNA shapes (and implicitly RNA sequences) for catalytic capabilities, any RNA sequence turning out to be capable of a catalytic function that exerts a positive feedback on RNA synthesis would amount to the acquisition of a catalyst that will boost the system's survival. The concept of the RNA world implicates the capabili-

> "If there are two enzymic activities associated with RNA, there may be more. And if there are activities among these RNA enzymes, or ribozymes, that can catalyze the synthesis of a new RNA molecule from precursors and an RNA template, then there is no need for protein enzymes at the beginning of evolution. One can contemplate an RNA world, containing only RNA molecules that serve to catalyze the synthesis of themselves.
>
> W. Gilbert, "The RNA World", Nature **1986**

Figure 15. *Walter Gilbert's* pronouncement of the notion of 'RNA World' [26] in the wake of *Tom Ceck's* and *Sidney Altman's* discovery [29] of catalytic RNA's ('ribozymes').

ty of RNA sequences to replicate, mutate, select for RNA catalysts and, therefore, to undergo Darwinian evolution.

The important idea that RNA could originally have fulfilled both a genetic and a phenetic function had been adumbrated by F. Crick [27], L.E. Orgel [16], and C. Woese [28] as early as 1968. It became a realistic concept in 1986 [26] in the wake of the discovery of ribozymes [29]. Since then, massive support for the RNA-world concept has come from structural biology, as well as from research operating with the technique of *in vitro* evolution of RNA sequences. Comprehensive X-ray structure analyses in various laboratories revealed the structure of the (microbial) ribosome to document the surprising as well as highly significant fact that the ribosome is in essence a ribozyme, since the molecules within the ribosome that are most intimately engaged in catalyzing protein synthesis are RNA molecules and not proteins. By *in vitro* evolution (Figure 16) a host of new ribozymes have been uncovered, RNA molecules that are capable of catalyzing a large diversity of chemical reactions [30], the most dramatic of them being a specific ribozyme's own replication (see below).

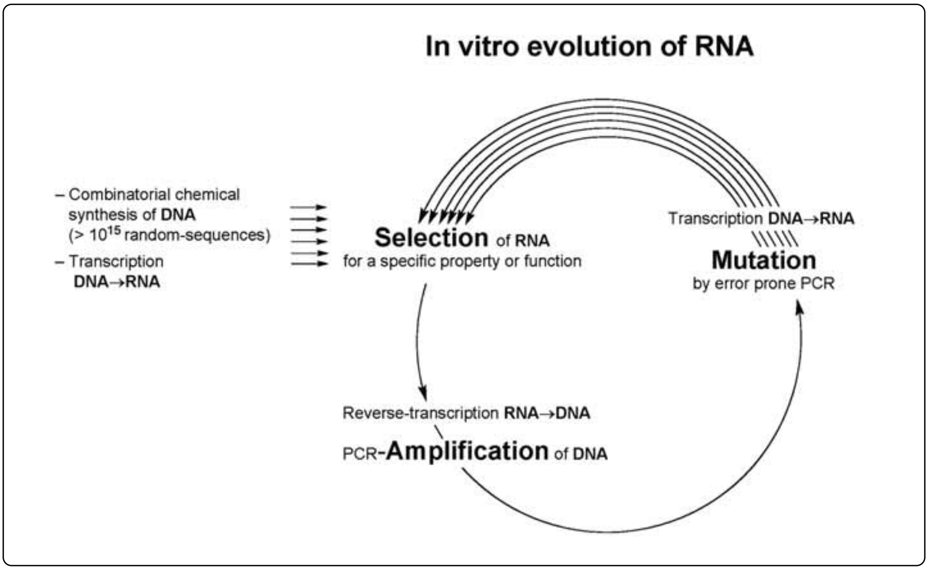

Figure 16. General principle of the experimental search for RNA sequences that fulfill a specific function (e.g. complexing with a specific biomolecules or displaying catalytic activity for a specific chemical reaction) by *in vitro* evolution [30].

The advent of the RNA-world concept had a marked impact on the thinking of researchers in the origin of life field and, at the same time, re-invigorated projects of exploring the potential of RNA to be generated under potentially prebiotic conditions. Significant progress in this direction has been made, especially on the formation of the sugar unit and certain of its nucleosides, on template-assisted oligomerization of suitably activated monomers in solution and on mineral surfaces [12]. However, no generational pathway to RNA that could be said to be potentially prebiotic has been demonstrated thus far. Much attention has been and is being devoted to providing experimental 'proofs of principle' for the feasibility of molecular replications with chemical systems under conditions not subjected to any sort of prebiotic constraints; such demonstrations have been achieved with both oligonucleotides [31] and oligopeptides [32]. Very recently, Gerald Joyce at the Scripps Institute succeeded in creating by *in vitro* RNA evolution ribozymes which, by template controlled cross-catalytic ligation of two RNA components, are capable of exponentially reproducing them-

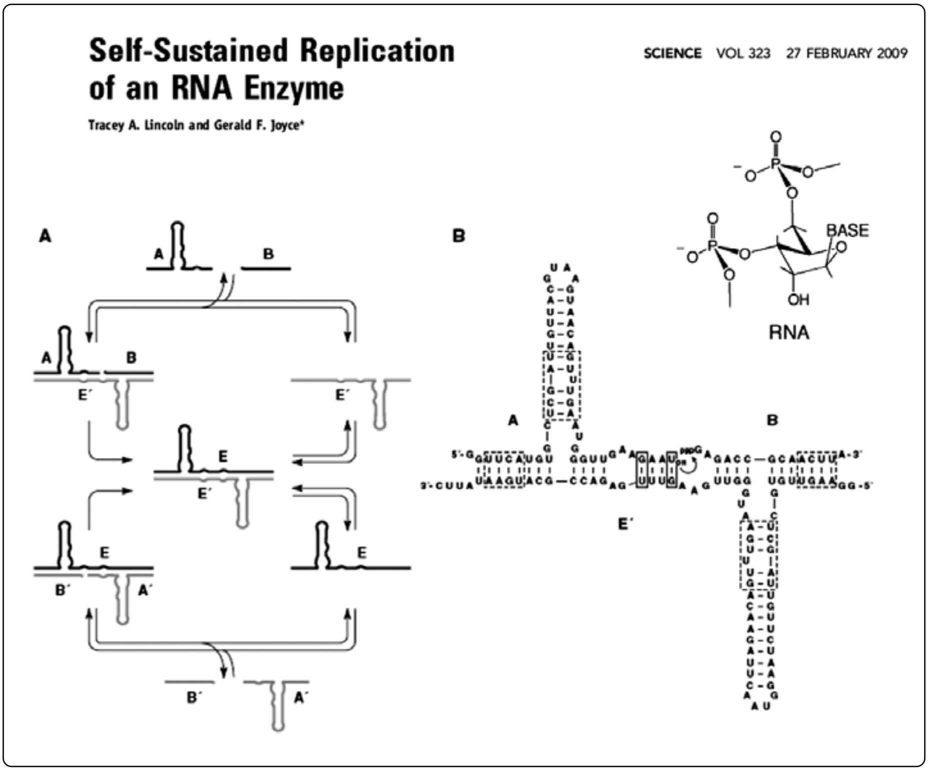

Figure 17. *Gerald Joyce*'s most recent RNA self-replication experiment [33], thus far the most advanced 'proof of principle' in support of the RNA world concept. – Scheme (A) on the left part of the Figure: A, B, E and A', B', E' denote RNA sequences. The two ribozymes (E and E') catalyze each others' synthesis from four oligonucleotide substrates (A, B, A' and B'). E' catalyzes the ligation of substrates A and B to form ribozyme E which, in turn, catalyzes ligation of corresponding substrates A' and B' to form ribozyme E'. Importantly, the duplex between the two ribozymes E and E' (center of the scheme on the left) dissociates into the single strands under the reaction conditions such that the process can repeat 'indefinitely' as long as the four substrates are provided. – Part B of the Figure: RNA sequence formula of the (transiently formed) complex between ribozyme E' and the (complementary) substrates A and B . The arrow indicates the position at which the ligation occurs by elimination of pyrophosphate (excerpt from Fig. 1 in [33]). – The chemical formula on the upper right is to remind the reader of the chemical structure of the nucleotide unit of RNA (B = Nucleobase, A or G or U or C). Note that the replication process does not require any protein enzymes and that (in principle) the RNA sequences used in the experiment can be synthesized by chemical methods.

selves without any assistance by a protein [33] (Figure 17). While this and all the earlier replication experiments are of considerable theoretical interest, they also make clear how far we still are from corresponding experiments under conditions that could be said to be compatible with the constraints of prebiotic chemistry. Figure 18 summarizes the research field's rather sobering state of the art.

Thus far:

Neither the formation, nor the autocatalytic replication of an informational oligomer **under potentially prebiotic conditions** have been convincingly demonstrated experimentally.

No case of autocatalytic "proto-metabolic cycle" has been demonstrated to operate efficiently **under potentially prebiotic conditions**

Figure 18.

The intrinsic limits any attempt of retrodicting chemical events of the past is facing will induce chemists to launch research on self-organizing chemical systems in complete independence from the environmental and geochemical constraints that the search for the chemistry of life's origin is subjected to. The quest is to think of, synthesize and study adaptive and self-sustaining chemical systems and, in the (perhaps very) long run, to create what will amount to elementary forms of *artificial chemical life*. Among those who are challenged are primarily physical-organic chemists who are prone to engage themselves in what today is recognized as the emerging field of 'systems chemistry' [34]. Its task is to deal with the wealth of problems dynamic structures of autocatalytic chemical systems are going to pose and to explore the new horizons they will open. Research toward the creation of artificial chemical life will be an important, if not the most important empirical source of knowledge for our eventual comprehension of life's origin.

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DISCUSSION ON PROF. ESCHENMOSER'S PAPER

PROF. DE DUVE: I would like to congratulate Albert Eschenmoser because he has given a masterful survey of the present research in this field. But there is a glaring gap in your presentation, Albert, you did not mention your own work.

PROF. ESCHENMOSER: I had no time!

PROF. DE DUVE: That is not objective, it is very modest but not objective.

PROF. ESCHENMOSER: It is an enforced modesty.

PROF. DE DUVE: The second point I would like to make is that, as he mentioned, there are many different clubs in this field, metabolists and geneticists and biochemists and organic chemists and so on but I think we all agree on one point, namely that the origin of life is a chemical problem. Now, chemistry deals with highly deterministic reproducible events. If it did not we would not have chemical factories or chemical laboratories. If there was a slight element of chance in a chemical reaction, we simply could not afford the risk of having chemical factories. So chemistry deals with highly deterministic events which therefore occur obligatorily when specific conditions are realised. The reason I am saying this is that, if the same conditions that occurred on earth or wherever life started should be reproduced elsewhere in the universe, because of this nature of chemistry, we would expect life to arise similarly. Not only similarly in general terms but similarly in chemical terms, DNA and RNA and proteins, so that the main question is to what extent will those special conditions be reproduced exactly elsewhere. The answer to that question is relevant to the frequency of extraterrestrial life, at least life as we know it.

THE BIRTH OF OXYGEN[1]

JOHN ABELSON

PROLOGUE

This paper discusses a quintessential problem in the field of geobiology. Geobiology can be defined in a single sentence: Evolution can only be understood in the context of geology…and vice versa. I am a biochemist but I have been a student of geobiology for the past five years and as President of the Agouron Institute, a patron of the field.

A word about the Agouron Institute: From 1968 to 1982 I was in the Department of Chemistry at the University of California, San Diego. When the recombinant DNA revolution occurred in the 1970s, my friend and colleague Mel Simon and I responded, not by forming a biotech company as some of my colleagues did, but by forming a non-profit institute, the Agouron Institute. Later a for-profit company, Agouron Pharmaceuticals, was spawned from the Institute to exploit advances we had made in the area of rational drug design. Agouron Pharmaceuticals was eventually a success. We discovered and marketed Viracept, an HIV protease inhibitor. This drug helped to save many lives. In 1998 Agouron Pharmaceuticals was sold to Warner Lambert, now a part of Pfizer. In the process the Agouron Institute obtained a significant endowment. We have used this money to support new fields. Geobiology is one of them. (see www.agi.org*). For the past seven years we have supported a course in geobiology. The course has included a geology field trip led by John Grotzinger of Caltech and Andy Knoll of Har-*

[1] This talk was given at a meeting of the Pontifical Academy of Sciences in Rome on November 1, 2008. I have also given the talk at a meeting of the American Academy of Arts and Sciences and a version of the paper, similar to this one, was published in the Bulletin of the American Academy of Arts and Sciences.

vard. I have been on all of the field trips. We have also carried out a drilling project in South Africa in which some 3000 meters of core were obtained that cover the period about 2.5 billion years to 2.2 billion years. It was during that period that oxygen first appeared in the atmosphere. In 2007 we sponsored an interdisciplinary meeting, 'Oxygen' in Santa Fe, New Mexico. About 40 chemists, biochemists, geologists, and microbiologists discussed the problem of the origin of oxygenic photosynthesis. This report represents my attempt to synthesize the ideas expressed in this exciting meeting.

We take it for granted that our atmosphere contains oxygen but we and most other animals would die within minutes if it were removed. It is not widely appreciated that for half of the earth's history there was virtually no oxygen in the atmosphere. Then 2.45 billion years ago oxygen appeared and has been present ever since though not always at its present level of 21%. More than 99% of the oxygen in the atmosphere is produced biologically, by photosynthesis. Arguably the biological invention of photosynthesis was, after the origin of life itself, the most important development in the history of our planet. About 12 times as much energy is derived from the aerobic metabolism of a molecule of glucose compared to the energy obtained from anaerobic metabolism. Without the invention of oxygenic photosynthesis multi-cellular organisms could not have evolved. Furthermore, the presence of oxygen in the atmosphere leads to an ozone layer that protects life from the lethal effects of ionizing radiation and allows life to flourish on land.

After life originated on earth there has been a continuous interplay between geological and biological evolution. The closely linked evolution of photosynthesis and the evolution of the atmosphere is perhaps the best example of the interdependence of geological and biological processes.

In chronicling the rise of oxygen, I will first describe photosynthesis and its origins. Then I will turn to a discussion of the state of the earth and its atmosphere before and during the rise of oxygen. After the rise of oxygen the atmosphere and the oceans went through some initial cataclysmic and finally very slow changes. Finally 540 million years ago, almost 2 billion years after the initial rise of oxygen, roughly the present levels of oxygen in the atmosphere and in the ocean were attained. It was only then that multi-cellular life began to flourish.

The story of oxygen and its effects takes place over a vast expanse of time – see the geologic time scale below. I will refer to the archean, the proterzoic and phanerozoic eons and sometimes to the Precambrian (all time up to 544 million years ago) and to the Cambrian (the 39 million years after). In geology 1 billion years is abbreviated Ga and 1 million years Ma (see Figure 1, p. 596).

One way to comprehend this vast expanse of time is to compare it with the time it takes the continents to completely rearrange themselves via plate tectonics. 225 million years ago all of the continents were together in the super-continent, Pangaea. In 225 million years the continents separated and the Atlantic and Indian oceans were formed. This is about 5% of earth's history and about one tenth of the time period we chronicle here.

It is also useful to consider how much biological change can take place in 2 billion years. A heritable and selectable change, a mutation, can take place at every cellular division. The earth's oceans contain about 4x 10^{24} ml. of water. If we conservatively assume a steady state of 1000 cells/ml in the ocean and a division time of one week (during this period most cells are unicellular microorganisms), then in two billion years something like 10^{39} divisions could take place. Specific mutations in bacteria take place at a frequency of about 10^{-8}. Even more rapid changes can occur when genes are transferred between different organisms. In 2 billion years, there is an enormous potential for evolutionary change.

Photosynthesis

In photosynthesis, the energy of light is used to extract electrons and protons from a donor molecule H_2A which are then used to reduce carbon dioxide, in the reactions:

$$2H_2A \rightarrow 4H^+ + 4e^- + 2A$$

$$CO_2 + 4H^+ + 4e^- \rightarrow (CH_2O) + H_2O$$

The donor molecule, H_2A can be a variety of reduced compounds including H_2S, Fe^{++}, H_2, various organic compounds and H_2O. Use of the former group of donors probably pre-dated the use of water in photosynthesis. The cellular machinery for oxygenic photosynthesis (in which water is used as the donor) is in part derived from it predecessors.

In oxygenic photosynthesis the electrons from water are extracted and used to generate energy and to reduce carbon dioxide to a carbohydrate according to the equation:

$$H_2O + CO_2 \rightarrow (CH_2O) + O_2$$

It has been known since the work of Martin Kamen and Samuel Ruben more than 50 years ago that the O_2 generated in photosynthesis is entirely derived from H_2O so water is dissociated in photosynthesis according to the equation:

$$2H_2O \rightarrow 4H^+ + 4e^- + O_2$$

It takes an enormous amount of energy to extract an electron from water because oxygen has a high affinity for electrons. One photon of light is required to extract each electron so photosynthesis is a four electron process.

Oxygenic photosynthesis takes place in one class of bacteria, cyanobacteria. It also takes place in a number of eukaryotic organisms, e.g. algae and plants but photosynthesis in eukaryotes and in cyanobacteria is almost exactly the same because photosynthetic eukaryotes are all derived from a symbiotic event in which a primitive eukaryote captured a cyanobacterium, so in discussing photosynthesis and its origin it is appropriate to focus on cyanobacteria.

In cyanobacterium the photosynthetic machinery is located in a system of layered *thylakoid* membranes. The membranes enclose an interior space, the *lumen*. The machinery consists of many pigmented proteins, many of them extending across the thylakoid membrane to the exterior space, the *stroma*. Some of the proteins and pigments in the thylakoid membrane serve as antennae to funnel light energy into the reaction center.

The reaction center consists of two complex multi-protein assemblies, termed Photosystem I and Photosystem II (PSI and PSII). At the heart of both PSI and PSII is a cofactor chlorophyll molecule.

The figure below is complex but successfully depicts the major multi-protein complexes involved in photosynthesis.

There isn't sufficient space here to discuss photosynthesis in depth. A book is required to do it justice. Instead I will focus only on the mechanisms of oxygen synthesis. This reaction takes place in photosystem 2 (PSII). The active site for di-oxygen synthesis is called the Oxygen Evolving Center (OEC). This site contains four manganese atoms and one calcium atom, coordinated mainly to one core PSII protein. The mechanism of water splitting is unique and so far, at least, a related metallo-protein has not been identified. The OEC allows for the integration of a one elec-

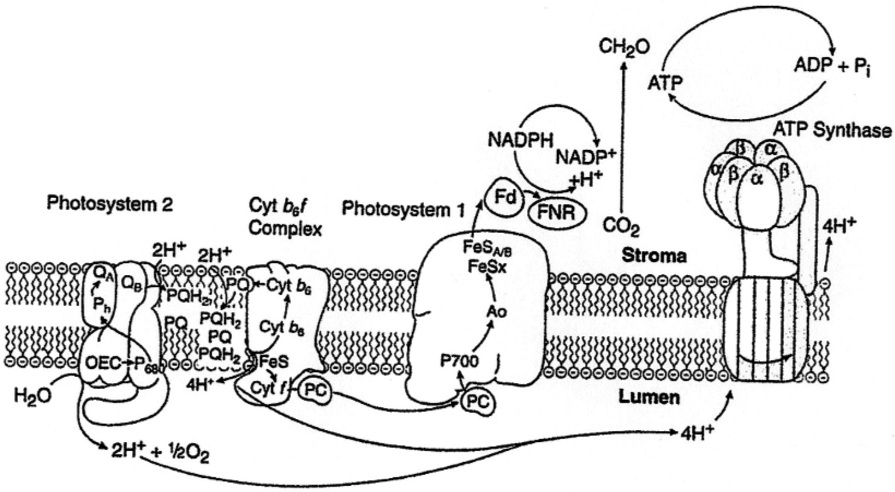

Figure 2. From *Molecular Mechanisms of Photosynthesis*, Robert E. Blankenship.

tron process, the excitation of cytochrome P680, with a four electron process, the splitting of H_2O to form O_2. A beautiful experiment done 50 years ago independently by Pierre Joliot and Bessel Kok proves that the OEC abstracts protons and electrons step-wise from water to evolve oxygen. Alternative models, ruled out by this experiment, include the cooperation of four reaction centers to cleave a single molecule of H_2O or that one center accumulates four oxidizing equivalents prior to oxidizing water in a single concerted step.

The OEC can now be understood more clearly because a 3.5A crystal structure has been obtained of PS II by J. Barber in London and a higher resolution structure of the OEC manganese oxide core by K. Sauer and W. Saenger *et al.* determined by x-ray absorption spectroscopy on single crystals of PSII (see Figure 3, p. 596).

In photosynthesis the manganese oxide cluster binds two molecules of H_2O. The energy of one quanta of light abstracts one proton and one electron. Thus this structure is the integrator of four electron transfer reactions resulting in the synthesis of one molecule of di-oxygen from two molecules of water. The invention of this mechanism was a unique event in evolution. When did it happen?

A Date for the Evolution of Oxygenic Photosynthesis?

Oxygen first appeared in the atmosphere 2.45 billion years ago and I will summarize the geological evidence for that below. Oxygenic photosynthesis must have evolved by that time but how much earlier did it evolve? There is a single piece of data that suggests that it had evolved by 2.7 billion years ago, 250 million years before the appearance of oxygen in the atmosphere.

Roger Summons, an Australian now working at MIT, has developed powerful analytical techniques (gas chromatography and mass spectrometry) for detecting minute traces of biological compounds (termed biomarkers) in ancient rocks. Rocks formed billions of years ago have gone through cycles of heating (termed diagenesis). The preservation of organic chemicals in ancient rocks is rare and when they are found they are limited to hydrocarbons.

In samples derived from black shales deposited in northwestern Australia 2.7 billion years ago a class of hydrocarbons called stearanes were found. Stearanes are derived diagenetically from steroids now found almost exclusively in eukaryotic cells. Cholesterol, e.g. is a steroid.

Steroid synthesis involves a number of steps requiring molecular oxygen. For example in the synthesis of cholesterol starting with squalene, eleven separate steps require molecular oxygen. It seems very unlikely to me that all of these steps would have used some other oxidant and different enzymes prior to the advent of oxygen and then been altered with the advent of oxygen. Thus the presence of stearanes in the Australian black shales argues for the presence of molecular oxygen in the ocean at 2.7 billion years.

Although the rocks from which these samples were extracted are correctly dated, it is more difficult to be sure that the biomarkers were deposited in the rocks at that date. They could have been the result of ground water penetration from the surface or penetration of oils from younger rocks into the older rocks. Or they could have been contamination from the drilling fluid. Great precautions are taken to avoid the latter artifact. The exterior surface of the drill cores is shaved off and the sample is taken from the interior of the core. But the cores used in this experiment were drilled with organic fluids and given the importance of this sort of result it is now considered imperative to drill with only water as a lubricant and this is being done (for example in our South Africa cores). It is also important, insofar as it is feasible, to investigate biomarkers in yet older rocks. The possibility that oxygenic photosynthesis evolved 300 million years before the advent of oxygen in the atmosphere poses the obvious question of why it took so long. We need to know what the earth was like prior to the appearance of oxygen in the ocean and what events might have triggered its rise in the atmosphere.

The Archean Earth and the Rise of Oxygen

In the Archean eon prior to 2.5 billion years ago, the atmosphere was reducing; the major components being N_2, CO_2, and perhaps CH_4, methane. The argument for methane is that at the origin of the earth the sun was 30% fainter than it is now and it can be calculated that without a greenhouse gas the earth would have been frozen until 2 billion years ago. The geological record shows that liquid water was present during the Archean eon and that the temperature was likely warmer than now. Certainly carbon dioxide would have provided a greenhouse effect but without oxygen in the atmosphere, methane, likely produced by methanogenic bacteria, could have accumulated to 1000 ppm; it is present at about 2 ppm now. The composition of the Archean ocean is less certain but geological evidence suggests that there was much less sulphate than now and there was certainly very little dissolved oxygen because there was abundant dissolved iron, Fe^{++}. In the Archean world organisms only lived in the ocean and the primary producers were likely the non-oxygenic photosynthesizers (although remember, we do not know for certain how early oxygenic photosynthesis evolved).

Geologists have known for more than 50 years that oxygen appeared in the atmosphere about 2.3 billion years ago. Preston Cloud and Dick Holland were the first to make this observation. What they realized early on and could see at many places around the world can perhaps most simply be chronicled in the Huronian Supergroup in southern Canada.

In the Matinenda formation (2.45 Ga) conglomerates can be seen that contain uraninite and pyrite. These conglomerates are detrital deposits meaning that were washed into the sea by ancient rivers. Uraninite, UO_2, is insoluble whereas unlike for iron the more oxidized form, UO_4 is soluble. If oxygen had been present in the atmosphere, UO_2 would have been oxidized and solubilized. Pyrite (FeS_2) is rapidly converted to hematite, Fe_2O_3 in the presence of oxygen. Pyrites and uraninites are not seen in the sediments above the Matinenda formation in the Huronian and they are not generally seen anywhere in detrital deposits younger than 2.3 billion years.

Between the Matinenda and the Lorraine formation in the Huronian can be found evidence for three glaciation events. We shall return to these glaciations later but when we reach the Lorrain formation (2.2 Ga) we first encounter red beds. These are sandstone beds, deposited by rivers or sand blown dust. Red crystals of hematite coat the sandstone grains. The presence of red beds is indicative of an oxidizing atmosphere. The earliest red beds were formed about 2.2 billion years ago. Oxygen must have appeared in the atmosphere after the deposition of the Matinenda formation, 2.45 Ga and before the deposition of the Lorrain formation, 2.2 Ga.

A more recent result has firmly pegged the rise of oxygen at 2.45 Ga. In order to understand this result we must briefly review the use of atomic isotopes in geochemistry. Four isotopes of sulfur occur naturally ^{32}S (94.9%), ^{33}S (.76%), ^{34}S (4.29%) and ^{36}S (.02%). In biological processes, for example SO_4 reduction to SO_2, ^{32}S is used preferentially to the other isotopes. ^{33}S is discriminated against by about half as much as ^{34}S. Starting with the work of Farquhar and Thiemens at the Scripps Institution of Oceanography, the isotopic abundances of the sulfur isotopes in various rocks has been meas-

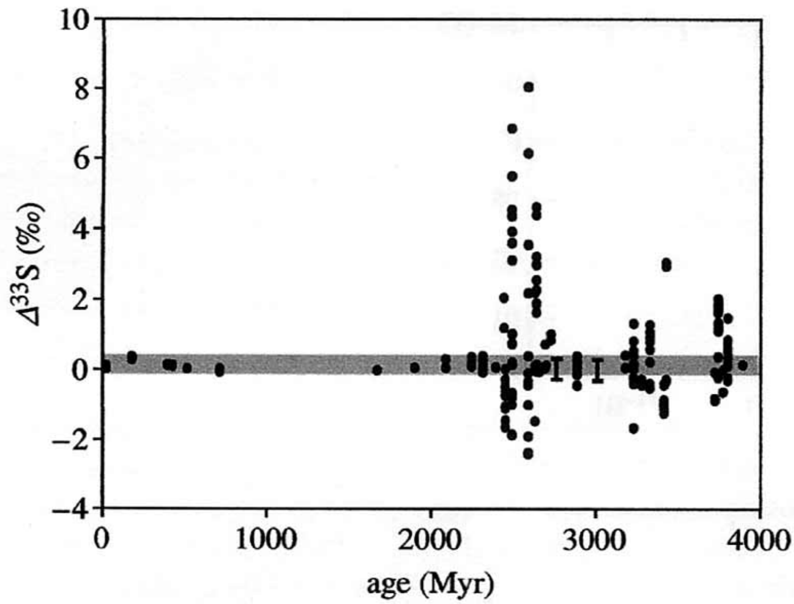

Figure 4. See J. Farquhar *et al., Science* 289: 756 (2000) (updated by S. Ohno).

ured. All modern rocks contain the same ratio of ^{33}S to ^{34}S because in modern rocks the ratio has been determined by the preferential use of ^{33}S to ^{34}S in biological processes. A quantity ^{33}S is a measure of the deviation of the abundance of ^{33}S from that ratio. In all modern rocks ^{33}S is zero. The figure below shows a recent compilation of the data.

In rocks before 2.45 Ga, the value of ^{33}S is zero; in rocks older than 2.45 Ga the value is different from zero – it is negative if the sulfur is derived from barite ($BaSO_4$) and positive if the sulfur is derived from pyrite (FeS_2). The variation of ^{33}S from zero is called *mass independent fractionation*. One is led to the conclusion that non-biological processes were at work on sulfur before 2.45 Ga. These processes were photochemical and the change that occurred at 2.45 Ga was the creation of an ozone shield due to the appearance of oxygen in the atmosphere. Ozone absorbs ultraviolet light, active in a number of photochemical processes in the atmosphere. For sulfur these could include reduction or oxidation of SO_2 or H_2S, leading to elemental sulfur or H_2SO_4 both of which can be incorporated into rocks. In the modern ocean all atmospheric sulfur is protected from photochemistry by the ozone layer and in the ocean is subjected to *mass dependent fractionation*. A level of oxygen in the atmosphere that is 1/100 the present level would lead to an effective ozone shield.

The sulfur isotope data fairly precisely determine the time for the rise of oxygen at some level. The biomarker data suggest that oxygenic photosynthesis originated at least 300 million years earlier. What prevented oxygen from appearing in the atmosphere earlier? Though this question has been frequently asked there is as yet no universally accepted answer. There could be either geological or biological reasons for the delay or both. Perhaps the level of reductants supplied to the atmosphere and the ocean by vulcanism decreased because of altered chemistry in the mantle. Or perhaps oxygenic photosynthesis, though it evolved earlier, had only become effective enough to alter the atmosphere at 2.45 Ga.

Interestingly the appearance of oxygen in the atmosphere had some relatively near term effects on the geology of the earth but did not markedly influence the biology at least as seen in the fossil record for another 1.8 billion years.

The Proterozoic Earth After the Rise of Oxygen

In the Huronian Supergroup evidence can be seen for three separate glaciation events between the anoxygenic uraninite conglomerates at 2.45

Ga and the oxygenic red bed deposits at 2.2 Ga. The glaciation events are seen as large dropstones, left behind in the sediment as the glacier recedes or as scratches in bed rock made as the glacier moves over it. Evidently in the period between 2.45 Ga and 2.2 Ga the earth went through a pronounced cooling period.

In South Africa evidence is seen in the Makganyene formation of another glaciation event at 2.2 Ga. Joe Kirschvink at Caltech has shown by paleomagnetism that the Makganyene glacial event took place when the Transvaal Craton was near the equator. This means that the entire earth was glaciated, a ‘snowball earth’ event. The most plausible cause of the cooling is that the rise of oxygen in the atmosphere destroyed the methane and thus the greenhouse effect that was warming the earth. As the earth cooled and ice formed, more and more solar radiation was reflected (ice reflects eight times as much radiation as water). Once ice had covered the poles to the thirtieth latitude north and south a positive feedback loop insured that a sheet of ice about two kilometers in depth would cover the earth.

Why did the earth not remain in a frozen state? How could life have survived? Likely through vulcanism; life would have been confined to heated regions near vents. Carbon dioxide escaping into the atmosphere would accumulate because it could not dissolve in the ocean and be lost in weathering processes as it is normally. It could have taken 30 to 50 million years for a sufficient level (350 times the current level) of carbon dioxide to accumulate providing a greenhouse level that would melt the ice. When a sufficient greenhouse had been attained, the reverse positive feedback loop would occur and melting of the ice could have taken place in a few hundred years.

In the aftermath of the snowball earth the intense greenhouse is predicted to have raised the surface temperature to 50°C – a hothouse earth. Carbon dioxide dissolved in the ocean and a massive precipitation of $CaCO_3$ and $MgCO_3$ (dolomite) occurred. These precipitates are called cap carbonates and they can be as much as 400m thick.

The post snowball earth ocean was rich in nutrients and cyanobacteria flourished, raising the level of oxygen in the ocean and in the atmosphere. Dissolved iron precipitated as hematite and manganese as MnO_2. South Africa possesses some of the richest manganese deposits in the world as a result of this event.

The Makganyene was the first snowball earth event (there were earlier regional glaciations) but it was not the only one. Two more snowball earth events took place in the period between 800 million years and 600 million years ago. In the intervening billion years the earth was relatively quiet. Geologists call this period the 'boring billion'.

The Boring Billion

Following a proposal made by Don Canfield in 1998 consensus is building among geologists that except for the likely spike after the Makganyene glaciation, the level of oxygen in the atmosphere remained low for more than one billion years and did not rise to present levels until the end of the proterozoic eon at 540 mY (see Figure 1, p. 596).

The modest levels of oxygen in the atmosphere could have led to an ocean that while weakly oxygenated at the surface was anoxic below and like the Black Sea today sulfidic. It is not possible here to review all of the geological data supporting this conclusion but one line of evidence from Ariel Anbar and Tim Lyons involving the level of molybdenum in black shales of the proterozoic strongly supports this model. In an oxic atmosphere, molybdenum is washed into the ocean by rivers as the soluble MbO_4^{2-} anion. Molybdenum is thus abundant in today's oceans.

A survey of molybdenum in black shales through time reveals that molybdenum is low during the archean, slightly elevated in the mid proterzoic and abundant in the phanaerozoic period. The relatively anoxic ocean of the mid-proterozoic could not have supported multi-cellular life and it would have been a poor environment for eukaryotes. There is plenty of evidence for single cell eukaryotes in the proterozoic, but Cyanobacteria would have dominated the shallow oceans and tidal flats. Beginning in the late proterozoic, as oxygen levels rose the multi-cellular eukaryotes make a modest appearance in the fossil record. It is the end of the boring billion.

The Rise of Multi-cellular Eukaryotes

The end of the proterozoic eon is punctuated by two snowball earth events: one at 750Ma and the other at 600Ma. These were not caused by oxidation of methane in the atmosphere but likely by a fall in carbon dioxide levels. At this time all of the land mass of the earth was near the equator and so none of it would have been covered with ice as Antarctica is today. Thus the entire land mass of the earth would have been available for removing CO_2 from the atmosphere by atmospheric weathering leading to a gradual cooling of the planet. The rich aftermath of the snowball earth events could have oxygenized the oceans and led to the initial rise of multi-cellular animals. Fossils from this period (called the Ediacaran or Vendian period) can be seen in many parts of the world. At the boundary between the Cambrian and the Precambrian at 542 Ma a mass extinction occurred. The Ediacaran animals disappeared and the modern world followed.

However we have to look at rocks deposited some 40 million years later to see the blossoming of animal life in the Cambrian as seen in the Burgess shales. The Burgess shales record a wonderful zoo of animals that have clearly developed many of the body plans seen later in evolution as well as mind boggling creatures that we never see again. Here are some of my favorites from Steven Gould's book *Wonderful Life* (see Figure 5, p. 597).

In an artist's rendering we see the entire community just before it was entombed for 500 million years by a mud slide.

By the Cambrian period, oxygen was near its present level in the atmosphere and the ocean. Animal evolution was on its way.

Epilogue

The unique and powerful process of oxygenic photosynthesis nearly resulted in the extinction of all life in the Makganyene glaciation. The earth itself with its molten core came to the rescue. After a period of nearly 2 billion years, however, photosynthesis made possible the evolution of multi-cellular animal life, a process still going on today.

Although it is in its infancy from a geological perspective, human intelligence may be as unique and potent a force for change on earth as photosynthesis was. Will human intelligence lead to a flowering of the earth as photosynthesis did or will it lead to the extinction of life? It is too early to say. Geology tells us that we will have to wait 2 billion years to know.

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DISCUSSION ON PROF. ABELSON'S PAPER

PROF. ARBER: You mentioned that in the anaerobic time life was rather limited to water. What about the deepness of the earth's crust and the same question would go to Albert Eschenmoser, could the origin of life be some kilometres down in the earth's crust?

PROF. ABELSON: Life now exists deep in the earth but the geological record does not tell us where life originated. It seems more likely to me that it originated near vents or in the shallow ocean.

PROF. ARBER: I will repeat my question which goes also to Prof. Eschenmoser: Do you consider that the origin of life could be a few kilometres down in the earth's crust, not on the surface of the earth?

PROF. ESCHENMOSER: We really do not know, but starting life might have been simpler on, or near, the surface of the earth than deep in its crust.

PROF. LE DOUARIN: You mentioned that the appearance of the photosynthesis chemical apparatus is the result of the fusion of two bacteria, one that had the photosynthetic system 1 and one that had the photosynthetic system 2. This was a very important step in evolution and I would like to think about this problem of evolution not only by mutations, by changing the genome of organisms, but also by cooperation between different organisms which create something new. This is the case, for example, of the cell. The cell is supposed to have evolved by the fusion of two bacteria or even three and the apparition of mitochondria is another type of symbiotic association and, in this case you have mentioned, something extremely important took place because this is how oxygen could arise in the atmosphere because two bacteria cooperated to produce a new apparatus to use the CO_2.

PROF. ABELSON: I think that is an excellent point. We certainly know that gene transfer is taking place rampantly in the ocean today, not only by the transfer of DNA, via mating between bacteria, but also by transfer via viruses. For example, there are cyanobacterial viruses in the ocean today that actually contain elements of photosystem II. The genes for photosynthesis are being transferred around at a high rate. There are ten viruses in the ocean for every bacteria, so there is a tremendous amount of gene transfer going on and a view of evolution involving simply point mutations is simply not what happened and is happening. Gene transfer is rampant. I am sure that Dr Collins can speak about what we know about this from sequencing.

PROF. COLLINS: I think that is absolutely incontrovertibly shown now by the sequence data that shows that horizontal transfer is a major event in early life and amongst microbes today and it makes it very difficult, of course, to decide what is a species anymore, because those usual ideas about trees of evolution are confused by all the cross talk between the branches. I want to ask in terms of also an evolutionary question that both photosynthesis systems, as you say, seem to have in common a core protein and, of course, I assume that protein had some other function and gradually got recruited to this. Is it known what that original protein's function was, is there some guess at that, how did this whole thing get started?

PROF. ABELSON: This is all in the realm of speculation but the homology between these two core proteins would suggest that there was a much more primitive kind of photosynthesis that took place and gave rise to both photosystem 1 and photosystem 2. They specialised and then finally came together and with further evolution made it possible to use water as the reductant in photosynthesis.

PROF. COLLINS: But are these proteins homologous to other transmembrane proteins that perform other functions that might give you a clue looking even further back?

PROF. ABELSON: No, I believe that no one has identified a protein with homology to the core proteins but with a different function (though I should add parenthetically that the homology between these core proteins is only in the topology of their transmembrane sequences and there could certainly be other proteins with similar topology). Further more no one has identified proteins with a manganese oxide core that could have evolved to become the oxygen evolving center.

THE GENETIC CODE AND EVOLUTION

MARSHALL NIRENBERG

> "For in the first place, as Augustine says (*Gen. Ad lit.* VI, 10), they [the seminal virtues that determine phenotypic traits] are principally and originally in the Word of God, as 'typal ideas'. Secondly, they are in the elements of the world, where they were produced altogether at the beginning, as in 'universal causes'. Thirdly, they are in those things which, in the succession of time, are produced by universal causes, for instance in this plant, and in that animal, as in 'particular causes'. Fourthly, they are in the 'seeds' produced from animals and plants. And these again are compared to further particular effects, as the primordial universal causes to the first effects produced".
> Thomas Aquinas, *Summa Theologica*, Question 115, Article 2.[1]

The DNA that we inherit from our parents contains the information that is needed to make the thousands of kinds of RNA and proteins that are the molecular machinery of the body. As shown in Fig. 1 (see p. 598), DNA consists of 4 kinds of letters, termed bases, T, C, A, and G, in long sequences. T forms hydrogen bonds with A, and C pairs with G. The backbone of DNA is composed of repeating sugar-phosphate moieties, and two complementary strands of DNA interact via base pairs and form a double helix.

The number of base pairs and genes in the DNA of some organisms is shown in Fig. 2. The sequence of bases in the DNA of each species shown has been determined. *Mycoplasma genitalium* has a very small genome consisting only of 580,000 base pairs and 470 genes. The genome of the bacterium, *E. coli,* consists of 4,600,000 base pairs, which encode 4,288 genes. Rice has a large genome consisting of 466,000,000 base pairs and contains 30,000 genes. The genome of the nematode, *C. elegans,* contains 97,000,000 base pairs and encodes 18,424 genes. The genome of the fruit fly, *Drosophi-*

[1] I thank Professor Mark Sagoff for suggesting this quotation.

NUMBER OF BASE PAIRS AND GENES IN GENOMES OF DIFFERENT ORGANISMS

SPECIES	DNA BASE PAIRS $x10^6$	GENES
Mycoplasma genitalium	0.58	470
E. coli	4.6	4,288
Rice	466	30,000
C. elegans	97	18,424
D. melanogaster	165	~14,500
Man	3,300	~25,000

Figure 2.

la melanogaster, consists of 165,000,000 base pairs and encodes approximately 14,500 genes. The Human genome consists of about 3.2 billion base pairs, which encode 20,000 to 25,000 genes. Only about 1.5 percent of the DNA in man encodes protein; additional DNA regulates gene expression. Some DNA consists of repeated transposable elements. DNA also contains nonfunctional pseudo-genes that may be experiments that failed during evolution. Finally, the function of much DNA is unknown.

There are 20 kinds of common amino acids found in proteins. The average protein consists of about 300 sequential amino acid residues, but some large proteins consist of thousands of amino acid residues. The genetic code refers to the translation of base sequences in DNA, which has a 4 letter alphabet to sequences of amino acids in protein, which has a 20 letter alphabet.

When I started to work on protein synthesis in 1958 the mechanism of protein synthesis was not known. Amino acids were known to be incorporated into protein on organelles termed ribosomes and amino acids had been found to be covalently attached to RNAs termed tRNA. Messenger RNA (mRNA) had not been discovered. The first question I asked using a bacterial cell-free protein synthesizing system was: 'Does DNA directly code for protein synthesis, or does RNA, which is transcribed from DNA, code for protein synthesis?' We found that RNA rather then DNA directs the incorporation of amino acids into protein.

In Fig. 3 is shown a simple outline of protein synthesis. We showed definitively that mRNA exists and directs the synthesis of protein (1). One strand of DNA is transcribed to mRNA, the mRNA then associates with ribosomes, and proteins are synthesized amino acid by amino acid on ribosomes. Enzymes with specificity for each kind of amino acid and the appropriate species of tRNA catalyze the ATP dependent activation of the amino acid and the covalent transfer of the amino acid to the tRNA. We showed that 3 bases in mRNA correspond to 1 amino acid in protein. Each 3 base codon in mRNA is recognized by an appropriate 3 base anticodon in tRNA

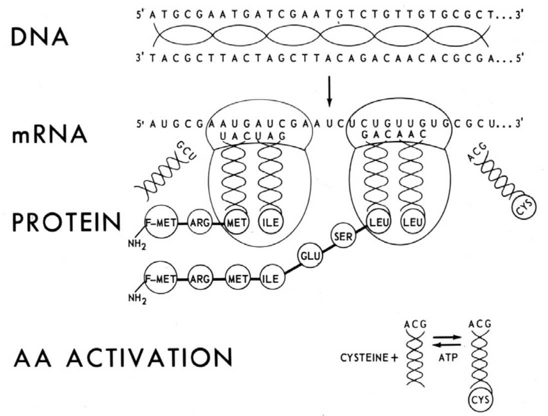

Figure 3.

by the formation of hydrogen bonds. The elongating peptide chain is then transferred to the amino acid attached to tRNA, the free tRNA is released from the ribosome and the tRNA with the attached peptide chain then is transferred to site of the vacated tRNA.

There are 4 kinds of bases in RNA, U, C, A, and G. U in RNA corresponds to T in DNA. U base pairs with A and C base pairs with G. With 4 kinds of bases in RNA there are 64 possible combinations of 3 bases, i.e., triplets. The genetic code, that is the 64 possible triplets which are termed codons and the 3 letter abbreviations of the amino acid that corresponds to each triplet is shown in Fig. 4 (see p. 599). All 64 triplets have meaning. My colleagues and I deciphered the genetic code between 1961 and 1966 (2). We found that the 3rd bases of synonym RNA codons varies systematically. For example UUU and UUC correspond to phenylalanine. Three amino acids, leucine, serine, and arginine each correspond to 6 synonym codons. For each of 5 amino acids – valine, alanine, glycine, threonine, and proline – there are 4 synonym codons. There are 3 synonym codons for isoleucine. The 3rd base of codons for 6 amino acids can be either U or C. The 3rd base of codons for 3 amino acids can be either A or G. Only 2 amino acids, methionine, shown in green, and tryptophan, each correspond to only a single codon. There are two species of tRNA for methionine, one species initiates protein synthesis (4), the other species corresponds to methionine in internal positions of proteins. Three codons, UAA, UAG, and UGA, shown in red, correspond to the termination of protein synthesis (5-7).

The arrangement of codons for amino acids is not random. For example amino acids with structurally similar side chains, such as aspartic acid and glutamic acid, have similar codons. Asparagine and glutamine also have similar side chains and correspond to similar codons. Most hydrophobic amino acids have U in the central position of the codon; whereas most hydrophilic amino acids have A as the second base in the codon. Thus the effects of mutations due to replacement of one base by another often are minimized.

After we deciphered the code for *E. coli* Richard Marshall, Thomas Caskey, and I (3) asked the question, is the genetic code the same in higher organisms? We determined the genetic code in the amphibian, *Xenopus laevis*, and in a mammalian tissue, guinea pig liver. We found that the genetic code is the same in *E. coli*, the amphibian, and the mammal. We also examined different guinea pig tissues and found that the code is the same in different tissues. We purified tRNA from *E. coli*, yeast, and guinea pig liver, and showed that some species of highly purified tRNA recognize only G in the third position of the codon, others recognize U or C, others recognize A

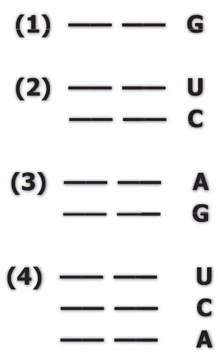

Figure 5.

or G, and still other species of tRNA recognize U, C, or A in the third position of codons (Fig. 5) (8). We showed that yeast alanine tRNA that had been sequenced by Robert Holley recognizes three codons, GCU, GCC, and GCA, and showed that inosine in the tRNA anticodon recognizes either U, C, or A in the 3rd position of the alanine codons (9). Many investigators have shown that there are different modified bases either in the tRNA anticodon or next to the anticodon that result in alternate recognition of 3rd bases in synonym codons.

21st AND 22nd AMINO ACIDS

21st.	SELENOCYSTEINE	UGA
22nd.	PYRROLYSINE	UAG

Figure 6.

In 1986 the 21st amino acid, selenocysteine, was found (Fig. 6) (10,11). Selenocysteine is found in the active centers of some oxidation-reduction enzymes, such as formate dehydrogenase. There is a special tRNA for selenocysteine that accepts serine. There also is an enzyme that catalyzes the acylation of this tRNA with serine and two enzymes that convert the serine attached to the tRNA to selenocysteine. Selenocysteine recognizes the termination codon UGA only if in the downstream region there is a stem-loop secondary structure in the mRNA. The mRNA folds back on itself and base pairs forming a hairpin-like stem-loop structure. There are either 1 or 2 proteins, depending on the species, that recognize both the selenocysteine tRNA and the stem-loop structure, and only then does UGA correspond to selenocysteine.

Pyrrolysine is the 22nd amino acid, which was found in 2002 (12, 13). This is a very rare amino acid, found only in a few species of primitive bacteria. It is found in the active centers of methylamino-, dimethylamino-, and trimethylamino-transferases and in transposase as well. There is a special tRNA for pyrrolysine that recognizes the codon UAG, and an enzyme that catalyzes the acylation of this tRNA with pyrrolysine. Whether this is a conditional recognition in which a protein recognizes pyrrolysine-tRNA and a stem-loop type of mRNA structure is not known.

There is only one genetic code that is used on this planet; hence, the code is a universal code. However, variants of the code have been found in some organisms. For example, in Fig. 7 (see p. 599) are shown some dramatic events that occurred during the evolution of some ciliated protozoa (14). The standard codons recognized by glutamine-tRNA are CAA and CAG. During evolution the gene for glutamine tRNA was duplicated; then a mutation in the anticodon of the second gene for glutamine tRNA replaced G with A; therefore, the tRNA corresponding to the second gene for glutamine tRNA recognized UAA and UAG that are terminator codons in the standard code. Later in evolution the second gene for glutamine tRNA was duplicated and a mutation in the anticodon of the third gene for glutamine tRNA resulted in a replacement of U with C. The tRNA corresponding to the third gene for glutamine tRNA then recognized the codon UAG. So in *Tetrahymena*, CAA, CAG, UAA and UAG correspond to glutamine tRNA. Changes in the meaning of codons are rare events, but there are a number of other organisms that have been found with changes in the translation of some codons.

A number of changes in the genetic code of mitochondria have been found in many organisms. Mitochondria are the organelles that produce energy for cells. Mitochondria have a small amount of DNA that contains about 10 genes and proteins corresponding to these genes are synthesized in mitochondria. Most of the genes for mitochondrial proteins reside in genomic DNA in the nucleus of cells and the proteins that are synthesized in the cytoplasm are imported into mitochondria. Some of the changes in the genetic code in mitochondria are shown in Fig. 8 (see p. 600). In the standard genetic code, UGA corresponds to the termination of synthesis and UGG corresponds to tryptophan. However, in the mitochondria of *Trypanosomes, Neurospora*, yeast, *Drosophila* and mammals both UGG and UGA correspond to tryptophan. In the standard genetic code AUA corresponds to isoleucine and AUG corresponds to methionine; whereas, in the mitochondria of yeast, *Drosophila*, and mammals, both AUA and AUG correspond to methionine. In the standard code CUU, CUC, CUA, and CUG correspond to leucine; whereas, in yeast mitochondria these codons correspond to threonine. In the standard code AGA and AGG correspond to arginine; whereas in the mitochondria of *Drosophila* these codons correspond to serine but in mammalian mitochondria these codons correspond to termination of protein synthesis. Additional changes in the translation of codons in mitochondria have been found in other organisms. The changes that have been found in the translation of codons in mitochondria probably are tolerated because mitochondrial genes only encode about 10 proteins. Similar changes in the translation of proteins encoded by nuclear genes, which would affect the synthesis of many thousands of proteins, almost surely would be lethal.

A summary of results is shown in Fig. 9. The results strongly suggest that the genetic code appeared very early during biological evolution, that all forms of life on Earth use the same or very similar genetic codes, that all forms of life on Earth descended from a common ancestor and thus, that all forms of life on this planet are related to one another. The messages in DNA that we inherit from our parents contain wisdom gradually accumulated over billions of years. The messages slowly change with time, but the translation of the language remains essentially constant. The molecular language is used to solve the problem of biological time, for it is easier to construct a new organism using the information encoded in DNA then it is to fix an aging, malfunctioning one.

SUMMARY

1. The genetic code appeared very early during biological evolution.

2. All forms of life on Earth use the same or very similar genetic codes.

3. All forms of life on Earth descended from a common ancestor and thus, all forms of life on this planet are related to one another.

4. The messages in DNA that we inherit from our parents contain wisdom gradually accumulated over billions of years. The messages slowly change with time, but the translation of the language remains essentially constant.

5. The molecular language is used to solve the problem of biological time for it is easier to construct a new organism using the information encoded in DNA than it is to repair an aging malfunctioning one.

Figure 9.

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DISCUSSION ON PROF. NIRENBERG'S PAPER

PROF. W. SINGER: Is there a possibility that that mechanisms are implemented in these non coding regions that promote evolution by promoting variability, that is, something that evolution has discovered that helps survival by creating variability from which then one can select, variability being a measure of robustness, that these non coding parts do something to the genome in order to make this work?

PROF. NIRENBERG: In DNA?

PROF. W. SINGER: Yes, on the DNA site.

PROF. NIRENBERG: Certainly, new genes can be formed in non-coding parts of DNA in many ways: by mutation, by gene duplication followed by mutation, or by transposition of DNA corresponding to part of a gene or to transposition and splicing together of DNA from multiple genes to name only a few of the many mechanisms that might be used to create new genes. Some non-coding DNA clearly is involved in regulation of gene expression. Recently, many genes were found for micro RNAs that regulate translation of proteins. Non-coding parts of DNA also contain pseudo-genes that may have been expressed earlier in evolution but no longer are functional. Non-coding parts of DNA also contain many transposable elements that have infected DNA and during evolution have undergone extensive duplication.

PROF. ARBER: I am aware that there may be chemical reasons for this particular code to be in general use rather than other codes. There are publications on that. On the other hand, we know that horizontal transfer of genes is an important evolutionary strategy. That, however, can only work if the donor and the recipient use the same genetic code. One can thus assume that there was a high selective pressure for a widespread code, and this can finally have resulted in the universal code. The mitochondria might have an interest to possess a variant code: they cohabitate in the same cell with the nucleus, and cohabitation favours an occasional, horizontal transfer of genes. In order to avoid acceptance of nuclear genes, it might be good for mitochondria to have their own specific code.

PROF. NIRENBERG: That is a very interesting idea.

PROF. LE DOUARIN: I have a question. It is known now that a large part of DNA, which is not coding for proteins, is transcribed and particularly the DNA which gives rise to the micro-RNA, which are supposed to be regulatory elements for gene expression as you mentioned just now. Is it known whether these micro-RNA, evolutionary speaking, are old, that means, did they arise at the same time as the genetic code was established?

PROF. NIRENBERG: miRNAs have been found in the nematode, *C. elegans*, in plants, and in *Drosophila*, as well as higher forms of life. I do not know if they are present in bacteria, or whether they originated at the same time as the genetic code.

PROF. LE DOUARIN: The last question, M. de Duve.

PROF. DE DUVE: You did not speak about the origin of the genetic code and there is evidence, I am thinking of the work of Freeland, for instance, that the genetic code is a product of natural selection. What is your opinion on that?

PROF. NIRENBERG: I think that amino acids were polymerized randomly and very slowly at first. Then amino acids became activated by covalent attachment to nucleotides and to RNA. Then hydrogen bonding between some bases in the precursor of aminoacyl-tRNA and the precursor of mRNA increased the local concentrations of activated amino acids which then were polymerized to peptides and proteins at much faster rates than had occurred previously. The fact that amino acids with chemically similar side chains have chemically similar codons suggests that at some early stage in the origin of the code amino acid side chains may have interacted directly with part of the tRNA precursors, with the anticodon, or the codon. Knight and Landweber (15) have reported some evidence for this. Alternatively, there may have been a population of genetic codes and one code was selected from this population that minimized the effect of mutations involving the replacement of one base by other. The two possibilities are not mutually exclusive.

PROF. LE DOUARIN: One quick last question because of the time.

PROF. COLLINS: So there is, as you know, difference between organisms in terms of codon usage, when you have this degeneracy of the code that allows multiple anticodons to represent the same amino acid and you look at quite wild swings in terms of what is the favoured balance. Is that a completely understood enterprise, now, just in terms of the abundance of the transfer RNAs or is there some drift going on? Do we understand codon usage differences between organisms?

PROF. NIRENBERG: We compared purified species of tRNA from *E. coli* and guinea pig liver and codons recognized by these tRNAs and found major differences in tRNA species expressed by *E. coli* and liver, which probably explains some of the differences in codon usage (8). At one time a study was done in my lab in the 1960s, which showed that relatively low amounts of *E. coli* tRNA for arginine that recognize AGA and AGG limits the rate of protein synthesis if there are multiple arginine codons of this kind in mRNA. I have not worked on the genetic code for about 40 years, so there probably are relevant papers that I am unaware of. However, my guess is that some synonym codons in mRNA have been selected during evolution that are translated more accurately and/or faster than other synonym codons. Nucleotide sequences recognised by mRNAs also might influence the process of selection. Organisms differ in the number of tRNA genes for each amino acid, tRNA anticodons and the nucleotide sequences of the rest of the tRNAs, posttranscriptional modifications of tRNAs, and amino acid sequences of aminoacyl tRNA synthetases. All of these factors and additional factors may influence the affinity of codon-anticodon interactions and the accuracy and rate of translation of codons. Therefore, the process of selection for synonym codons in mRNA may be different in different organisms.

PROF. ABELSON: I had one response to Dr de Duve's question. Michael Yarus at the University of Colorado has been doing a number of experiments to investigate the question of whether there is a physical basis for the genetic code or not. He randomises sequences of RNA and asks which ones can bind to a particular amino acid and goes through a cycle of selections. He then sequences the RNAs that can bind to arginine. These sequences are enriched in arginine codons, as I recall to AGA. When he selects for sequences that will bind to isoleucine he finds an enrichment for the isoleucine codon AUA. However it is difficult to imagine how an RNA sequence could specifically recognize glycine. There could be some structural meaning for at least some of the code.

PROF. NIRENBERG: I think you are right, you are absolutely right. I am familiar with those papers but I think more work has to be done to really understand how the code evolved.

THE ROLE OF CHANCE IN EVOLUTION

GIORGIO BERNARDI

I would like to start this contribution on a personal note by mentioning that I come from one of the few, perhaps the only Institute in the world, the Stazione Zoologica of Naples, which was established in order to prove a theory, in our case Darwin's theory (1). After its foundation by Anton Dohrn in 1873, investigations at the Stazione concentrated on what was possible to investigate at that time, namely the morphology, the physiology and the embryology of marine organisms, their great biodiversity being the main reason for the choice of Naples as the seat of the Institute. For a century after the death of Anton Dohrn in 1909 practically no work on evolution was done. At the beginning of 1998 I took the direction of the Stazione Zoologica and started a Laboratory of Molecular Evolution which still is very active. I will report here on our work on genome evolution and its general implications.

The role of chance in evolution

The first question one may raise about the role of chance in evolution is why this issue is so important. One may think about a number of explanations, but I prefer here to use a shortcut, by concentrating on the position presented in 1970 by Jacques Monod in his famous book *Le hasard et la nécessité* (2). There are three main reasons for this choice. The first one is the clarity of the ideas, the second the extreme stand and the third the discussion of its implications. These points make it easier to understand the problem under consideration here. Some key sentences clearly summarize the stand of the author: (i) *The origin of life on earth was due to a single chance event* and, since all living organisms descend from a common ancestor, (ii) 'the biosphere is completely separated from the inanimate environment', and 'Man knows to be alone in the indifferent immensity of the Universe, from which he emerged by chance'. As far as the evolution of living organisms was concerned, Monod expressed the opinion that (iii) 'Mutations are accidents that happen at random. Since they represent the only source of changes in the genetic text, which is the only repository of inherited structures of organisms, it necessarily follows that chance is responsible for any novelty, for any creation in the biosphere', the conclusion being that 'Chance only is the source of every novelty, of every creation in the biosphere. Sheer chance, chance only, absolute but blind freedom at the very roots of evolution: this central notion in modern biology is not anymore a hypothesis among other possible or at least conceivable ones. This hypothesis is the only conceivable one, since it is the only one which is compatible with observation and experience. And nothing allows us to imagine (or to hope) that our ideas on this point will need, or will be subject to, revision'. Finally, Monod considered the implications of his conclusions and proposed an 'ethics of knowledge', which will be discussed at the end of this paper.

The best comment on Monod's book was made by Eigen (3) 'The only thing lacking in molecular biology was its integration into a general understanding of Nature. So far, such an attempt has been undertaken only once, by Jacques Monod. This was a fascinating and ambitious attempt, in which Monod did not shrink from drawing philosophical conclusions. It culminated in an apotheosis of chance'.

The classical evolutionary theories

The role of chance in evolution was not, however, a new problem. Let us look at which way mutations were visualized by the classical evolutionists. The most famous sentence in *The Origin of Species* (1) was the following: 'I have called Natural Selection, or the Survival of the Fittest, this preservation of favorable individual differences and variations and the destruction of those which are injurious variations'. This statement looks extremely simple, but Crick (4) remarked that 'Natural Selection is the basic mechanism that makes biology different from all other sciences. Of course anyone can grasp the mechanism itself, though remarkably few people actually do so'. Indeed, Darwin's sentence seemed to indicate a dichotomy, and was widely interpreted that way. The sentence was, however, immediately followed by another one, which is only rarely quoted: 'Variations neither useful nor injurious would not be affected by natural selection and would be left either a fluctuating element … or would ultimately become fixed'. This still is the best definition of neutral changes. In other words, Darwin distinguished not two but three kinds of changes or mutations (which he called 'variations'): advantageous, deleterious and neutral.

Advantageous changes will tend to expand in the progeny, because the carriers and their progeny will reproduce more abundantly than average (this is the positive or Darwinian selection). In contrast, deleterious changes will tend to disappear from the population, because the carriers and their progeny will reproduce less abundantly (this is the negative or purifying selection). Finally, neutral changes may be fixed in the population (like advantageous changes) or disappear (like deleterious changes).

The idea of neutral changes was later obliterated by the neo-darwinians, the selectionists Fisher (5) and Haldane (6), only to be resurrected, later, by Kimura (7, 8) in his *mutation-random drift theory*. According to this neutral theory 'the main cause of evolutionary change at the molecular level – change in the genetic material itself – is random fixation of selectively neutral or nearly neutral mutants'; therefore, 'increases and decreases in the mutant frequencies are due mainly to chance'. As a logical consequence, this theory eventually replaced the *survival of the fittest* with the *survival of the luckiest* (9). Along the same line, King and Jukes (10) claimed in their *non-darwinian evolution* that 'most evolutionary changes in proteins may be due to neutral mutations and genetic drift' (the random changes in gene frequencies in a population). A significantly different position was taken by Ohta (11, 12) who proposed her *nearly neutral theory* according to which 'a substantial fraction of changes are caused by random fixation of nearly neutral changes, namely changes that are intermediates between neutral and advantageous, as well as between neutral and deleterious classes'. Fig. 1 (see p. 601) summarizes the points just mentioned.

It is now of interest to look at the experimental approaches used to develop the classical theories on evolution because of the tight links that exist between approaches, results and conclusions. Natural selection acts on the phenotype, namely the detectable characters (traits, features, properties) of living organisms. It is, therefore, understandable that the first approach to the study of evolution was based on morphological traits, a classical case being that of the beaks of the Galapagos finches, which show adaptations to different kinds of food, from hard seeds to soft vegetal tissues. After the rediscovery of Mendel's laws, the neo-darwinians relied on genetic characters. Only later a molecular approach was developed on the basis of the early protein and gene sequences, and this led to the neutral theory of Kimura. Indeed, the view that amino acids change linearly with time in proteins (the molecular clock of Zuckerkandl and Pauling, 13), provided the very first hint in that direction.

THE ORGANIZATION OF THE EUKARYOTIC GENOME

A totally different approach moving from the molecular level of a few proteins and genes to the genome level was the one I started in 1959 by degrading DNA from mammals and birds with a DNase (14), and by fractionating DNA on hydroxyapatite columns (15). These experiments (probably the first ones in genomics) produced important results, such as the breakage of the genome into large fragments and the separation of double- from single-stranded DNA. Most of the following work was done, however, after our development (16) in 1968 of density gradient ultracentrifugation of DNA in the presence of sequence-specific DNA ligands (such as Ag+ ions), and our discovery in 1973 of the compositional heterogeneity of the bovine genome (17). Our *compositional approach* to the study of the genome, incidentally the only one that was possible at that time, was easily moved from the analysis of buoyant density profiles to nucleotide sequences as soon as these became available. The rationale of the compositional approach was that the base composition of the genome, the most elementary property of DNA, (i) is altered by mutations, insertions and deletions; (ii) influences DNA, RNA, protein and chromatin structure (see below); and (iii) can be precisely assessed on whole genomes and their domains. The conceptual simplicity of the approach is such that the results can be easily understood.

The compositional approach led to three major discoveries: (i) the vertebrate genomes (the only ones discussed here) are *mosaics of isochores* (18, 19), megabase regions (1 Mb is one million base pairs; the human genome is 3200 Mb in size) of fairly homogeneous GC level (Fig. 2, see p. 602); GC is the molar ratio (the percentage of the molecules) of guanine and cytosine in DNA); (ii) isochores belong in a few families, characterized by different levels of GC, dinucleotides and trinucleotides, and define a *genome phenotype* (20), namely the *compositional landscape* of the genome (see Fig. 3, p. 603); the GC-rich, gene-rich and the GC-poor, gene-poor isochores define two *gene spaces*, the *genome core* and the *genome desert,* that are correlated with all the basic structural and functional properties of the genome, the main ones being chromatin compaction, DNA methylation, gene distribution on the one hand, gene expression, recombination, replication timing on the other (see Fig. 4, p. 604); (iii) a *genomic code* (20; not to be confused with the genetic code) correlates the compositions a) of coding sequences with those of contiguous non-coding sequences (*i.e.*, of 1% of the genome with the remaining 99%), b) of the three codon positions among themselves, and c) of coding sequences with the hydrophobicity and the secondary structure of the encoded proteins.

These discoveries (summarized in a book; 21) led to our conclusion that the genome is an *integrated ensemble*, with little or no room left for *junk* (22) or *selfish DNA* (23, 24). This is a completely new vision of the vertebrate (and more generally of the eukaryotic) genome, which has far-reaching implications. Indeed, (i) there is no way to create a compositionally compartmentalized genome, the mosaic of isochores, by random point mutations (namely, single base-pair changes); (ii) again no random process can lead to a genome phenotype or compositional landscape that is correlated with all basic structural and functional properties of the genome, and lastly, (iii) no random evolutionary process can lead to the compositional correlations mentioned above. In other words, the discoveries just presented rule out the *bean-bag view* of the genome (to paraphrase Mayr, 25), namely of a genome in which genes are randomly distributed in the bulk of non-coding sequences, a genome that is only endowed with additive and not with cooperative properties (21).

GENOME EVOLUTION AND THE NEO-SELECTIONIST THEORY

The ground was now ready to investigate genome evolution. The simple comparison of our early data (26) on vertebrate genomes (that we recently confirmed on the basis of full genome sequences, 27-30); led us to the discovery of two modes of evolution: the *conservative mode* and the *transitional mode* (31). The *conservative mode* is exemplified by a comparison of the isochore patterns of the genomes of Primates and Carnivores (Fig. 5, see p. 605). At least 50% base pairs changed during the time, 100 million years, comprised between their common ancestor and these two mammalian orders that independently diverged from it. The expectation from the randomness of neutral changes was a partial or total disappearance of the isochore families that were present in the common ancestor. Moreover, since nucleotide substitutions in vertebrates (and other organisms) favor GC→AT over AT→GC changes, this 'AT-bias' should also lead to lower GC levels. Instead, a remarkable conservation of isochore families was found in terms of GC levels and relative amounts.

This led us in a straightforward way to the *neo-selectionist theory* (32). As shown in Fig. 6 (see p. 606), this theory postulates a series of steps: (i) first of all, among AT-biased changes a number will accumulate to form local clusters; (ii) the 'last' AT-biased changes in the clusters, the *critical changes* transform clustered point mutations into regional changes that trespass a lower GC threshold; and (iii) cause changes in chromatin structure that expand over long distances. Fig. 1 (see p. 601) shows that the neo-selectionist theory incorporates the features of the nearly neutral theory of Ohta, adding, as a novelty, the critical changes, namely the superdeleterious changes that convert the clustered AT-biased point mutations into regional changes. It should be stressed that regional changes may also be caused by large insertions and deletions. The main point, however, is that chromatin changes are deleterious in that they affect some expression of genes located within the altered regions or in their neighborhood and may lead to negative selection of the carriers and of their progeny.

Since fish, amphibian and many reptilian genomes do not show the presence of the very GC-rich isochores that characterize the genomes of warm-blooded vertebrates (see Fig. 5, p. 605), a *transitional mode* of evolution in which isochore families underwent changes, must have taken place (see Fig. 7, p. 607). Back in 1986 we proposed (20) that: 'The formation and maintenance of the GC-rich isochores of warm-blooded vertebrates is due to natural selection, the selective advantages being the increased thermodynamic stability of DNA, RNA and proteins (GC-rich codons encoding aminoacids that stabilize proteins). In other words, the environment can mould the genome through natural selection'. The transitional mode involved both negative and positive selection, as discussed elsewhere (32).

An explanation as to why changes essentially affected the gene-rich isochores, is that these isochores are located (in the interphase nucleus) in an open chromatin structure, whereas the gene poor isochores are in a closed chromatin structure (33). Then, only the genome core needs to be stabilized by GC increases, the genome desert being stabilized by its own compact chromatin. While body temperature certainly is the *primum movens* of the compositional transitions that took place at the emergence of mammals and birds, other factors such as oxygen, salinity, pH, CO_2, may play a role in the compositional transitions which were found among fishes (see Fig. 5, p. 605).

To sum up, the *neo-selectionist theory* (i) provides a solution to the neutralist/selectionist debate, since it reconciles the nearly neutralist view of point mutations with selection at the regional level; (ii) is an epigenomic theory, in that the compositional changes in DNA affect chromatin structure and, as a consequence, gene expression, so leading to negative selection of the carriers and their progeny; and (iii) is an extension of Darwin's theory; in fact, the neo-selectionist theory may be visualized as an ultra-darwinian theory since even neutral and nearly neutral changes are eventually controlled by natural selection over evolutionary time. Needless to say, the neo-selectionist theory brings us back from Kimura's survival of the luckiest to Darwin's survival of the fittest (incidentally, a matter of satisfaction for somebody working at the Stazione Zoologica).

As any good theory, the neo-selectionist theory also made predictions: (i) that genome phenotype differences should be found in populations; and (ii) that some of them may affect the genomic fitness and cause genomic (not genetic) diseases (a typical one being cancer). The first prediction was confirmed by comparing two individual genomes: Venter's genome differs from the reference human genome because of a number of insertions and deletions that accumulate in GC-rich isochores (34). These may generate genomic diseases by affecting chromatin structure and, as a consequence, the expression of genes located within or next to altered regions, so reducing the genomic fitness of the carriers, without necessarily affecting the primary structure of coding and regulatory sequences.

Conclusions

We should now go back to our initial questions and see the answers that we can provide today. First of all, a currently accepted view is that in all likelihood the origin of life was not so much the *single chance event* visualized by Monod, as a necessity under the prevailing conditions (35). This establishes *a primordial link* between the inanimate world from which life arose and the living organisms. These are connected to each other by their common descent, and, far from being completely separated from the inanimate environment, are moulded by it through natural selection. In fact, we have shown that the genome itself is moulded by physical agents like temperature, oxygen, salinity, pH, etc. through natural selection.

Our findings lead to a largely deterministic vision of evolution, which is in contrast with the fully stochastic vision of Monod. Chance still plays a role in evolution through (i) *environmental chance events*, such as meteorite impacts, volcanic eruptions; (ii) *random drift,* the random changes in gene frequencies in populations; and (iii) *neutral and nearly neutral changes*; as in the case of random drift, these changes are evident when recent, or looked at on a limited time scale, but they vanish over longer time spans, because they are eliminated by natural selection. Obviously, we are very far from the overwhelming role of chance postulated by Monod.

As a consequence, we are also very far from Monod's view on the ethical implications. Given his premises, Monod claimed that *true knowledge ignores values* and invoked an *ethics of knowledge,* whose only value is the objective knowledge itself. In contrast, knowledge contains values: knowledge of common descent of all living organisms links us with them and dictates our respect and love for them; knowledge of the moulding of living organisms by the environment, trough natural selection, links all of them to the inanimate world from which they derived in the first place. The *'old alliance'* with Nature, proposed by the *'animistic conception'*, far from being *'a projection of our brain on the inanimate world'* (as suggested by Monod), is the age-old intuition of links now established by Science.

I would like to finish as I started, on a personal note. I had the good luck of being acquainted with Jacques Monod over many years until his premature death in 1976. My admiration for him led me to change the name of the Institut de Biologie Moleculaire that I was directing in Paris to Institut Jacques Monod, as well as to organize several meetings in his memory (see, for instance, ref. 36). I would like to stress that the contrasting vision presented here was built on the scene set up by *Le hasard et la necéssité*, I could say on the shoulders of Jacques Monod. It is a great pity that we cannot have his viewpoint on our conclusions. I dare say, however, that he would have accepted them, based as they are on new facts, which were not available or conceivable at the time his book was published. I also venture to guess that he would have liked them, since one can feel that the pessimistic conclusions of the book were imposed by its internal logics but not necessarily liked by its author.

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DISCUSSION ON PROF. BERNARDI'S PAPER

PROF. PHILLIPS: My question is about the conclusions, and it seems to me that conclusion n. 2 is the one that is most germane to the topic of your talk. So the conclusion seems quite remarkable. If I am understanding it correctly, you are saying that chance does not play much of a role in evolution. Is that your conclusion?

PROF. BERNARDI: No, I said that chance, of course, works, but is under control. Of course I do not pretend that point mutations are not random mutations initially. What I am saying is that, after a certain evolutionary time, when changes accumulate and cluster together changes also occur in chromatin structure and negative selection follows.

PROF. PHILLIPS: So basically your conclusion is, in a sense, reaffirming a kind of Darwinian…

PROF. BERNARDI: Absolutely. That is why I mentioned that I come from an institute that was set up to show that Darwin was right.

PROF. COLLINS: So, Giorgio, the focus on isochores clearly is an interesting way to look at DNA but I think also maybe potentially blurs out the details in the sense that evolution probably does not care too much about isochores, it cares about genes, it cares about selectable enterprises, so can you explain why it is useful, at this juncture, when we have complete sequences, to look at isochores as a specific element of the genome as opposed to drilling down to the more refined level.

PROF. BERNARDI: This is an excellent question. It would be totally unreasonable to deny that the changes in coding sequences as having an important effect. What I am saying, however, is that in the genomes of the kind we are considering now, where the amount of intergenic and intronic non-coding sequences represent 99% of the genome, there are effects which have been neglected so far and which in fact have an importance as far as gene expression in concerned. I was saying that it is perfectly conceivable to have a coding sequence which is untouched, but the region next to it has been altered in terms of chromatin structure and this creates a problem in gene expression. Therefore, it is not obligatory to find a change in the coding sequence. Even if this is the most common case probably, there may be, situations in which things happen outside the coding sequence in the so-called non coding sequences which, as you know better than I do, there is an accumulation of sequences which, in fact, matter more than we thought even ten years ago.

BACTERIAL EVOLUTION: RANDOM OR SELECTIVE?

RAFAEL VICUÑA

INTRODUCTION

The publication of *The Origin of Species* by Charles Darwin in 1859 constitutes a fundamental milestone in the history of science. In this book, Darwin builds up his theory of evolution based on the objective statements that living organisms change, that changes are transmitted to the progeny and that reproduction of organisms frequently gives rise to progenies that are too numerous to permit the survival of all the individuals. Darwin then concludes that in general, those individuals that change in such a way that their fitness to the environment increases will have a better chance to survive and reproduce. Thus, variations that are beneficial will gradually accumulate by simple natural selection.

What struck most the world at large was not the realization that living organisms evolve; after all, a transformist theory had been advanced four decades earlier by the French naturalist Jean Baptiste Lamarck in his *Histoire naturelle des animaux sans vertèbres* but the substantial differences between the theories advanced by both scientists. According to Lamarck, during their lifetime organisms undergo changes that favor their adaptation to the environment. These changes, which are influenced by the environment, are then transmitted to the offspring. Lamarck also stated that the evolutionary paths of the different species are independent of each other and that evolution follows a natural path towards perfection. In contrast, Darwin proposed that there is no such tendency to perfection. Rather, variation of living organisms is gradual, passive, spontaneous, with no destination. Favorable traits would be transmitted through the progeny, whereas those that are detrimental would tend to disappear. Moreover, in sharp antagonism with Lamarck, Darwin proposed the theory of common descent.

That variation (or mutation, as we call it now) arises spontaneously with no influence from the environment and without regard for utility has been elegantly shown by Luria & Delbruck[1] and by Lederberg & Lederberg,[2] in studies that are considered classic contributions to the field of molecular genetics. What these authors described correspond to mutations that are said to be growth-dependent, because they exhibit a definable relationship to cell division and are considered to result from random errors of the DNA replication machinery.[3] Does this undeniable fact imply that there is no variation promoted by the environment, as Lamarck had put forward? For a long time, growth dependent mutations were considered to be the primary cause of Darwinian evolution and even today it is so portrayed in the non specialized literature. However, some decades ago, researchers began to observe mutations that arise in non-growing, nutritionally deprived bacterial cultures that were subjected to non lethal selective pressure. Unexpectedly, these mutations appeared to have arisen with certain specificity in order to allow a better adaptation to the stressful environment.

Studies at the molecular level later showed that the mechanisms implicated in adaptive genetic change offer a much higher versatility of variation than the sole growth-dependent mutations attributed to errors of the DNA replication machinery. Although any one would think that most mutations are expected to be detrimental, an increase in variation is needed to allow some members of the population to arrive at a phenotype suitable for survival and proliferation in the new environment.

A challenge to random and gradual mutability

The first hint of mutations in non-growing cells was obtained by Ryan about fifty years ago.[4] He observed that cultures of *his*$^{-}$ *Escherichia coli* auxotrophs inoculated into medium lacking histidine continued to produce

[1] Luria, S., Delbruck, M. Mutations of bacteria from virus sensitivity to virus resistance. *Genetics* 28, 491-511, 1943.

[2] Lederberg, J., Lederberg, E.M. Replica plating and indirect selection of bacterial mutants. *J Bact* 63, 399-406, 1952

[3] In this case, the term random is used in a loose way, since geneticists are well aware that an average genome possesses hot spots for spontaneous mutations.

[4] Ryan, F.J., Wainwright, L.K. Nuclear segregation and the growth of clones of spontaneous mutants of bacteria. *J. Gen. Microbiol.* 11, 364-379, 1954.

his$^+$ revertants during a period of ten days after inoculation. He did not investigate whether other mutations also occurred, although he confirmed that the revertants were not slowly growing mutants previously present in the inoculum. A couple of decades later, Hall & Clarke found that a deletion mutant in the *lacZ* gene encoding β-galactosidase, when incubated for several days in the presence of lactose, reverted to a phenotype that allowed metabolism of this sugar.[5] The *lacZ* gene encodes an enzyme called β-galactosidase, which breaks down lactose into its components glucose and galactose. The new phenotype was the result of two mutations in an operon called *ebg* (for evolved β-galactosidase), which specifies a second β-galactosidase of unknown function. A mutation in the gene *ebgA* activates the enzyme, whereas a second mutation in the gene *ebgR* inactivates the repressor of the operon. Considering that either of the single mutations did not represent any advantage to the cell, it is remarkable that the double mutants arose with a frequency much higher than expected. Later, in separate studies, Shapiro[6] and Cairns *et al.*[7] investigated reversion rates in *E. coli* cells with bacteriophage Mu inserted into a fusion between the regulatory segment of the arabinose operon and the *lacZ* gene.[8] In this system, excision of Mu prophage led to fusion of *araB* to *lacZ*, yielding a Lac$^+$ cell as long as arabinose was also present to act as an inducer. The evidence showed that incubation for several days in both sugars, but not in either of them alone, led to the appearance of colonies in which Mu had been excised, whereas cultures grown without starvation produced none.

Other examples followed. Benson incubated bacteria in medium containing maltodextrins as the only carbon source. Normally, these high molecular weight polymeric substances do not trespass the cell membrane. However, bacteria underwent mutations in the gene encoding an outer membrane porin that allowed their ready entry into the cell.[9] In

[5] Hall, B.G. and Clarke, N.D. Regulation of newly evolved enzymes. III. Evolution of the *ebg* repressor during selection for enhanced activity. *Genetics* 85, 193-201, 1977.

[6] Shapiro, J. Observations on the formation of clones containing araB-lacZ cistron fusions. *Mol Gen Genet* 194, 79-90, 1984.

[7] Cairns, J., Overbaugh, J., Miller, S. The origin of mutants. *Nature* 335, 142-145, 1988.

[8] Both the arabinose and lactose operons are missing in this strain, which therefore is ara- and lac-. However, upon deletion of the intervening Mu prophage, it can grow on lactose provided arabinose is present.

[9] Benson, S.A., Partridge, L., Miller, S. Is bacterial evolution random or selective? *Nature* 336, 21-22, 1988.

turn, Hall pursued his work analyzing other systems. One of them required double mutations for utilization of β-glycosides, namely, excision of an insertion sequence and a point mutation.[10] Incubation in solid medium, only when containing substrate, promoted both mutations allowing its metabolism. Hall also tested for the first time the production of mutations in anabolic genes.[11] Two *E. coli* strains, each one possessing single point missense mutations in genes encoding enzymes for the synthesis of tryptophan (the *trp* operon), exhibited elevated reversion frequencies during starvation of this amino acid. Reversions in the *trp* operon did not take place when cells were starved for cysteine and mutation rates in other loci did not increase during tryptophan starvation. Therefore, the increased reversion rate appeared to be specific to conditions where the mutations were advantageous. In a subsequent study,[12] the author showed that a strain carrying two missense mutations in the *trp* operon reverts 10^8 times more frequently than would be expected if the two mutations were the result of independent events.

At the same time of the latter studies by Hall, one of the most paradigmatic papers in the field was published by Cairns and Foster.[13] These authors measured the reversion of a frameshift rather than a point mutation in the Lac operon of *E. coli*, which in this case is carried in an F' conjugative plasmid. The strain, called FC40, is deleted for the Lac operon on its chromosome and at the same time is resistant to the RNA polymerase inhibitor rifampicin due to a mutation in the chromosomal *rpoB* gene. The mutants were found to vigorously revert to Lac$^+$ (about one revertant per 10^7 cells per day) when plated on lactose minimal medium, whereas no reversion to the wild type rifampicin resistance phenotype was observed. Conspicuously, Lac$^+$ mutants did not arise in the absence of selection, i.e., when lactose was not present in the medium.

One of the most striking features of these early studies was that the increased frequencies of the advantageous mutations were not accompa-

[10] Hall, B.G. Adaptive evolution that requires multiple spontaneous mutations. I. Mutations involving an insertion sequence. *Genetics* 120, 887-897, 1988.

[11] Hall, B.G. Spontaneous point mutations that occur more often when advantageous than when neutral. *Genetics* 126, 5-16, 1990.

[12] Hall, B.G. Adaptive evolution that requires multiple simultaneous mutations: mutations involving base substitutions. *Proc Natl Acad Sci USA* 88, 5882-5886, 1991.

[13] Cairns, J., Foster, P.L. Adaptive reversion of a frameshift mutation in *Escherichia coli*. *Genetics* 128, 695-701, 1991.

nied by mutations at other loci.[14] This apparent selectivity, in open contradiction with the prevalent doctrine of randomness, astounded researchers in the field. For example, Cairns *et al.*[7] dared to state that 'In this paper...we describe some experiments suggesting that cells may have mechanisms for choosing which mutations will occur'. Also: 'This experiment suggests that populations of bacteria in stationary phase have some way of producing (or selectively retaining) only the most appropriate mutations'. Cairns even proposed molecular processes that 'could, in effect, provide a mechanism for the inheritance of acquired characteristics'. One of them was completely ground-breaking, since it implied information transfer from protein to DNA. According to this model, a reverse transcriptase instructed by *some element* that monitors the protein products would retrotranscribe an mRNA variant encoding a useful protein. Cairns referred to these mutations as adaptive,[13] while they were called 'directed' mutations by the editors of *Nature*[15] and 'a unicorn in the garden' by Franklin W. Stahl.[16]

Undoubtedly, this idea challenged the traditional thinking about spontaneous mutation, although the possibility of non randomness in variation had never been completely abandoned. In fact, Delbruck himself had previously noted the distinction between selecting for phage resistance versus selecting for carbohydrate utilization, stating that 'in view of our ignorance of the causes and mechanisms of mutations, one should keep in mind the possible occurrence of specifically induced adaptive mutations'.[17] A. Weismann, the father of neo-Darwinism, stated late in his career that directed variation must be invoked to understand some phenomena, as random variation and selection alone are not sufficient explanation. In turn, the

[14] Typically, in these studies, a mutant bacterial strain that requires a nutrient is plated on solid medium that contains a very limiting supply of the nutrient. When the nutrient is exhausted, there is a sparse population of bacteria on the agar and further growth cannot occur unless a known mutation reverts. The first observable colonies are considered to be spontaneous mutants that were present in the population prior to plating. Further incubation of the plates for several days up to a month reveals the continuous appearance of new colonies in numbers that cannot be predicted by the Luria&Delbruck test. These late appearing colonies that arise in a non-growing population of bacteria that are subjected to a nutritional stress are said to result from adaptive mutation.

[15] Cited in Foster, P.L. Adaptive mutations: Has the unicorn landed? *Genetics* 148, 1453-1459, 1998.

[16] Stahl, F.W. A unicorn in the garden. *Nature* 335, 112-113, 1988.

[17] Delbruck, M. Heredity and variations in microorganisms. *Cold Spring Harbor Symp. Quant. Biol.* 11, 154 – , 1946.

eminent geneticist T. Dobzhansky expressed by mid 20th century that 'The most serious objection to the modern theory of evolution is that since mutations occur by chance and are undirected, it is difficult to see how mutation and selection can add up to the formation of such beautifully balanced organs as, for example, the human eye'.[18] Interestingly, in a speculative paper published earlier than Cairns' work, Fitch had stated that 'because mutations are advantageous during stressful times but genome wide mutagenesis would be deleterious, organisms probably have evolved a mechanism for selectively mutating only the genes of relevance'.[19]

As expected, the possibility that certain mutations in bacteria that were in stationary phase and subjected to non-lethal selective pressure might occur at higher rates when advantageous gave rise to a deep controversy.[20] This new type of mutation that came into sight more often when beneficial than when neutral appeared to vindicate the Lamarckian idea that the environment influences variation to improve adaptation. In this case, however, changes would obviously not occur as a result of use or disuse of a particular organ. Instead, they might perhaps arise from selection based on the presence of molecular variations within cells. On the other hand, one of the main arguments used by the supporters of adaptive mutations was that the classical experiment of Luria & Delbruck could not show the appearance of mutations during selection, since their protocol involved a lethal selection assay (resistance to bacteriophage T1). This assay gave no chance to detect additional mutations in cells that had not become resistant to viral infection.

Are adaptive mutations really directed?

The first hint that there was not reverse information flow that would instruct the cell how to mutate to attain successful survival was obtained by a reversion of an amber mutation in an episomal *lacZ* gene, both through

[18] Quotations by Weismann and Dobzhansky taken from: Wright, B.E. A biochemical mechanism for nonrandom mutations and evolution. *J Bact* 182, 2993-3001, 2000.

[19] Fitch, W.M. The challenges to Darwinism since the last centennial and the impact of molecular studies. *Evolution* 36, 1133-1143, 1982.

[20] See for example letters by several scientists and rebuttals in *Nature* 336, 21-22, 1988; *Nature* 336, 525-528, 1988 and *Science* 269, 285-289, 1995. Also: Lenski, R.E., Slatkin, M., Ayala, F.J. Mutation and selection in bacterial populations: alternatives to the hypothesis of directed mutation. *Proc. Natl. Acad. Sci. USA* 86, 2775-2778, 1989; Lenski, R.E., Mittler, J.E. The directed mutation controversy and neo-Darwinism. *Science* 259, 188-194, 1993.

intragenic mutations that eliminate the stop codon and by extragenic creation of a tRNA suppressor.[21] The latter necessarily had to be random, since there was no relationship between lactose metabolism and a chromosomal gene encoding a tRNA. In a subsequent study, Foster tested the mutability of a second gene (*tet*^{S}) also present in the plasmid harboring the *lacZ* gene mutant. She found that upon selection in lactose, *tet*^{R} mutants appeared at about the same rate as Lac$^+$ mutations.[22] These results showed clearly that selection was unnecessary for obtaining mutations in stationary phase, as originally thought. The concept of adaptive mutation was hence adjusted to mean those mutations that occur in non dividing cells during selection and are specific to the selective pressure. Mutants that arise in non dividing cells and that are either not adaptive, or have not yet been shown to be adaptive, were called stationary phase mutations.[23] Later, other Lac$^+$ revertants of the *E. coli* strain FC40 were found to carry mutations that were not related to selection.[24,25]

In turn, specificity of reversion of *trp*$^-$ mutants was shown by the lack of reversion in cultures starved for other amino acids, as well as by the lack of appearance of other mutants during starvation for tryptophan. Out of 110 *trp*$^+$ revertants, Hall found only two carrying additional mutations.[26] However, he was somewhat cautious in the interpretation of these results: he stated that the explanation for the apparent influence of the environment in the selectivity of mutation did not necessarily have to be found in the two extreme choices that had been so far considered, namely randomness or directedness. He proposed to adopt the concept of 'Cairnsian' mutation to imply those sequence changes that occur with a higher probability when they are advantageous than when they are neutral. Later, citing a personal communication by J. Cairns, he speculated that the specificity could be

[21] Foster, P.L, Cairns, J. Mechanisms of directed mutation. *Genetics* 131, 783-789, 1992.

[22] Foster, P.L. Nonadaptive mutations occur on the F' episome during adaptive mutation conditions in *Escherichia coli*. *J Bact* 179, 1550-1554, 1997.

[23] Foster, P.L. Adaptive mutation: the uses of adversity. *Ann Rev Microbiol* 47, 467-504, 1993.

[24] Rosche, W.A., Foster, P.L. The role of transient hypermutators in adaptive mutation in *Escherichia coli*. *Proc Natl Acad Sci USA* 96, 6862-6867, 1999.

[25] Torkelson, J., Harris, R.S., Lombardo, M.J., Nagendran, J., Thulin, C., Rosenberg, S.M. Genome-wide hypermutation in a subpopulation of stationary cells underlies recombination-dependent adaptive mutation. *EMBO J* 16, 3303-3311, 1997.

[26] Hall, B.G. Spontaneous point mutations that occur more often when advantageous than when neutral. *Genetics* 126, 5-16, 1990.

explained by either selective capture or selective generation.[27] The former mechanism implies that mutations take place randomly and continuously during prolonged selection, but only those that are useful are captured by replication or recombination and immortalized by growth. Useless mutations have no way to express themselves. Selective generation, on the other hand, implies that sequence changes occur only in genes that are being actively transcribed. Indeed, one likely mechanism for directing mutations to specific genes requires their active transcription under nutritional deprivation (see below).

Systems involving mobile genetic elements represent a different situation. In the case of prophage Mu excision from the *araB-lacZ* fusion to allow growth on lactose when arabinose is also present,[6,7] the specificity of genetic variation is obvious. In the *egb* operon, it has been established that the gene *ebgR* encoding the repressor is a hot spot for the insertion of the mobile element IS30, whereas in the *bgl* operon the gene *bglF* reverts to wild type by excision of IS103. The latter event precedes mutations in the promoter (*bglR*), which will eventually allow growth in β-glycosides. In either of these situations, where movement of the mobile elements is stimulated by stress (see below), directedness could be explained by selective capture.

In spite of these clarifications, the controversy regarding the directedness of mutations followed for several years.[28] Even recently, Roth *et al.*[29] have been particularly critical in accepting that selection stimulates formation of new mutations. These authors prefer to think that what selection actually does is to allow faster growth of pre-existing mutants, with the parent strain remaining unable to grow due to the stringent conditions of the medium. However, the recent unraveling at the molecular level of several mechanisms involved in stress induced mutagenesis seems to leave no room for a controversy. It is now understood beyond doubt that stressful environments induce in bacteria genomic instability which results in mutants that are fitter than the parent strain to the adverse conditions.

[27] Hall, B.G. Adaptive mutagenesis: a process that generates almost exclusively beneficial mutations. *Genetica* 102/103, 109-125, 1998.

[28] See for example the series of papers by Rosemberg & Hastings, Ross & Andersson and Foster, with the corresponding rebuttals, in *J Bact* 186, 4838-4863, 2004.

[29] Roth, J.R., Kugelberg, E., Reams, A.B., Kofoid, E., Andersson, D.I. Origin of mutations under selection: The adaptive mutation controversy. *Annu Rev Microbiol* 60, 477-501, 2006.

A stressful environment induces adaptive mutations

Cells have different DNA repair pathways that are responsible for correcting sporadic mistakes arising as a result of DNA polymerase errors or through chemical modification of the bases. Therefore, mutations in the DNA are supposed to be transient, because they are normally corrected. However, under stressful conditions, these repair pathways are either down-regulated or become overwhelmed while taking care of abundant DNA damage.

There are several stress responses that intensify genetic variation in bacteria.[30,31] As mentioned previously, the molecular mechanisms leading to mutations in these pathways are different from those taking place in growing cells. All the previous findings of adaptation in non-growing cultures can now be interpreted under the light of one of these mutagenic pathways. In some cases, they may give rise to localized sequence changes, which have the advantage of avoiding non-adaptive mutations. The apparent selectivity observed in some of the laboratory studies may explain the original interpretation of directedness.

Perhaps the most thoroughly studied mutagenic pathway is the SOS response.[32] It is induced by extensive DNA damage, by cell saturation in rich medium, exposure to antibiotics and in aging colonies. About 30 genes encoding functions related to DNA metabolism are under the control of LexA repressor. Among them are those specifying DNA polymerases IV (*dinB*) and V (*umuC,D*), which are able to replicate damaged DNA although with low fidelity. Normally, the genes of the pathway are silent or are expressed at very low levels. The SOS response is triggered when the stressful environment induces RecA-dependent auto-proteolysis of LexA. If cells are proliferating, the two error prone polymerases increase the mutation rate by competing with the accurate DNA polymerase III, which replicates the chromosome under normal conditions. In non-growing cells, partial DNA synthesis by the mutagenic enzymes takes place during repair or recombination events. Some of the mutants arising will have a selective advantage for survival.

[30] Foster, P.L. Stress responses and genetic variation in bacteria. *Mutation Res* 569, 3-11, 2005.

[31] Foster, P.L. Stress-induced mutagenesis in bacteria. *Crit. Rev. Biochem. Mol. Biol.* 42, 373-397, 2007.

[32] Schlacher, K., Goodman, M.F. Lessons from 50 years of SOS DNA damage induced mutagenesis. *Nature Rev Mol Cell Bio* 8, 587-594, 2007.

Another important pathway is the general stress response.[33] In this case, the controller protein is not LexA but RpoS, a sigma factor (σ^S) that replaces the vegetative sigma factor σ^{70} of RNA polymerase. Sigma factors are critical for gene expression, since they are responsible for the selectivity of transcription by RNA polymerase. Nutrient limitation or stationary phase of growth results in the accumulation of polyphosphate (PolyP). This compound causes an elevation in the titers of σ^{70}, leading to higher levels of the error-prone DNA polymerase IV or to an inhibition of the expression of enzymes belonging to the mismatch repair (MMR) pathway. Both effects contribute to raise the adaptive mutation rate in bacteria.

Amino acid starvation also causes the buildup of (p)ppGpp, a phenomenon commonly known as the stringent response.[34] This rare nucleotide inhibits initiation of DNA replication and influences the selectivity of transcription by RNA polymerase. For example, it down regulates the synthesis of rRNAs and tRNAs while it also collaborates in raising the levels of RpoS. In addition, (p)ppGpp up regulates the operons for amino acid biosynthesis, which are normally subjected to end-product repression. It is well known that genes under transcription are more liable to mutate due to their partial single stranded character.[35] Thus, starvation for a specific amino acid makes its synthetic operon more susceptible to mutations. This may be the explanation for the 'directedness' observed by Hall in the reversion of the *trp* mutants.[11,12] DNA damage, starvation and high temperature (heat shock) also trigger a stress response dependent on a sigma factor called RpoH (σ^{32}). Among the genes controlled by σ^{32} is one that encodes GroE. This is a molecular chaperone that interacts with DNA polymerases IV and V (among many other proteins), protecting them from degradation by proteases and thus increasing mutagenesis.

There are three other mutagenic stress responses that are less well characterized. Two of them are specific for bacteria growing on solid media. One is called ROSE, an acronym for 'resting organisms in a structured environment'.[36] ROSE requires RecA and DNA polymerase I and it is independ-

[33] Hengge-Aronis, R. Signal transduction and regulatory mechanisms involved in control of the σ^S (RpoS) subunit of RNA polymerase. *Microbiol. Mol. Biol. Rev*. 66, 373-395, 2002.

[34] Braeken, K., Moris, M., Daniels, R., Vanderleyden, J., Muller-Hill, B., Michiels, J. New horizons for (p)ppGpp in bacterial and plant physiology. *Trends Microbiol*. 14, 45-54, 2006.

[35] Wright, BE. A biochemical mechanism for nonrandom mutations and evolution. *J. Bacteriol* 182, 2993-3001, 2000.

[36] Taddei, F., Radman, M., Maynard-Smith, J., Toupance, B., Gouyon, P.H., Godelle, B. Role of mutator alleles in adaptive evolution. *Nature* 387, 700-702, 1997.

ent of DNA polymerase V and RpoS. Another one is called MAC ('mutagenesis in aging colonies') and it does not involve LexA, although it does require RpoS and DNA polymerase II.[37] A third response, the GASP phenotype[38] (growth advantage in stationary phase) relies on the SOS DNA polymerases II, IV and V and in an attenuated participation of RpoS. The GASP response allows survival of a small percentage of the bacterial population that consumes the debris of dying cells in long term batch cultures. Under these conditions, the birth and death rates are balanced. An increase in the mutation rate of cells in stationary phase is further supported by down regulation of the DNA repair pathways, some of which operate through intricate mechanisms that are highly energy consuming.[39]

The hypermutable state model

Hall proposed an additional argument to interpret the apparent directedness of adaptive mutations. It was what he called the hypermutable state model.[40] According to this model, although all non-growing bacterial cells in a selective medium are experiencing a stressful situation, only a minor subpopulation of them, perhaps between one in every 10^3 or 10^4 of cells enters a hypermutable state.[41] While in these circumstances, those bacteria that generate neutral or deleterious mutations die in a short time. However, if one of the mutations is a revertant that allows growth, the cell is relieved from the stress. It then proliferates exiting from the hypermutable state, building up just only growth-dependent mutations at a normal rate. Thus, the hypermutable state is transient. Eventually, the only cells that survive the stressful condition are those that never enter into the hypermutable state or those that do so and acquire a useful mutation. The fact that the frequency

[37] Bjedov, I., Tenaillon, O., Gerard, B., Souza, V., Denamur, E., Radman, M., Taddei, F., Matic, I. Stress-induced mutagenesis in bacteria. *Science* 300, 1404-1409, 2003.

[38] Finkel, S.E. Long term survival during stationary phase: evolution of the GASP phenotype. *Nature Rev. Microbiol*. 4, 113-120, 2006.

[39] Saint-Ruf, C., Pestut, J., Sopta, M., Matic, I. Causes and Consequences of DNA repair activity modulation during stationary phase in Escherichia coli. *Crit. Rev. Biochem. Molec. Biol.* 42, 259-270, 2007.

[40] Hall, B.G. Spontaneous point mutations that occur more often when they are advantageous than when they are neutral. *Genetics* 126, 5-16, 1990.

[41] Rosenberg, S.M. Evolving responsively: adaptive mutation. Nature Rev. *Genetics* 2, 504-515, 2001.

of mutations in selected revertants is notably higher than in the surviving cells that do not mutate the selected gene clearly satisfies the model.[42] It also adds evidence for selective capture rather than for selective generation.

The hypermutable state model has received support from Rosenberg's group.[43] According to these authors, the high mutation rate reaches its maximum with the coincident induction of the SOS and RpoS stress responses.

There are various mechanisms for adaptive mutations

Work in different laboratories has revealed that there are several ways by which bacteria can modify their genomes to relieve the selective pressure in a stressful environment. In other words, there are several types of adaptive mutations, each of them involving a molecular mechanism that sheds light into the seeming selectivity of mutation.

a) The episomal Lac system.[44]

As mentioned above, the *E. coli* FC40 strain carries a large conjugal plasmid which includes a fusion of the gene encoding the Lac repressor (*lacI*) with the *lacZ* gene encoding β-galactosidase. Therefore, it lacks the regulatory region of the operon and transcription starting from the promoter of *lacI* is constitutive. This construction is Lac^- because it carries a +1 frameshift in *lacI*, changing CCC to CCCC, although it is slightly leaky, conferring about 1% of wild type β-galactosidase level. The chromosome in the strain has a large deletion that encompasses the *lac* operon. When these cells are inoculated on solid minimal medium containing lactose as carbon source, colonies of Lac^+ mutants appear a few days later on the plate. In the absence of carbon source, Lac^+ mutations (as measured by subsequent plating on lactose) do not accumulate regardless the incubation time. Strain FC40 also reverts to Lac^+ during non-selected growth. In this case, mutations include duplication, deletions and large frameshifts,

[42] Drake, J.W. Too many mutants with multiple mutations. *Crit. Rev. Biochem. Mol. Biol*. 42, 247-258, 2007.

[43] Gallardo, R.S., Hastings, P.J., Rosenberg, S.M. Mutation as a stress response and the regulation of evolvability. *Crit. Rev. Biochem. Mol. Biol*. 42, 399-435, 2007.

[44] Foster, P.L. Stress-induced mutagenesis in bacteria. *Crit. Rev. Biochem. Mol. Biol*. 42, 373-397, 2007.

while mutations obtained during selection are almost exclusively -1 frameshifts. The latter are typically made by DNA polymerase IV (*dinB*), which is induced by the SOS and RpoS pathways. Adaptive mutations are severely reduced in GroE and polyphosphate kinase deficient cells, confirming the requirement for DNA polymerase IV. Under normal conditions, frameshift mutations are corrected by the mismatch repair system, which is insufficient or may be down regulated in stressed cells undergoing the transient hypermutation state. Mutants obtained under selection also differ from those arising during normal growth in that they require enzymes involved in the recombinational repair of double strand breaks, such as RecA, RecBCD and RevABC.

There are two models accounting for adaptive mutation in *E. coli* FC40 cells. One of them relies on the fact that the conjugal origin of the episome is subjected to continuous nicking. Occasional initiation of episomal replication at its vegetative origin is allowed by the energy provided by the leakiness of the Lac construction. Advancement of the replication fork towards the nick generates a double stranded break that is repaired by RecA, RecBCD and RuvABC recombination enzymes. Short patches of DNA synthesis required by this pathway are undertaken by the mutagenic DNA polymerase IV and by DNA polymerase II. This model accounts for the fact that the Lac construction needs to be in the episome in order to obtain adaptive revertants. A second mechanism leading to Lac^+ colonies of the FC40 strain consists in the 20-50 fold amplification of the *lac* locus.[45] These revertants appear somewhat later than the point mutants. Amplification does not require DNA polymerase IV or the other SOS-induced proteins, although it depends on RpoS, DNA polymerase I and the recombination proteins RecA, RecBCD and RuvABC. Interestingly, the amplified clones do not exhibit unrelated mutants as it is the case with the Lac^+ point mutants. Moreover, the Lac^+ phenotype of the amplified clones reverts to Lac^- upon re-plating in rich medium. Some investigators originally thought that amplification was an intermediate state in the formation of Lac^+ point mutants, but it was later shown that it consists on an alternative way to relieve the starvation stress by cells that never enter the hypermutation state.

[45] Hastings, P.J. Adaptive amplification. *Crit. Rev. Biochem. Mol. Biol.* 42, 285-311, 2007.

b) The transcription-dependent revertants of *trp* auxotrophs.

Amino acid starvation triggers the stringent response, which, as mentioned previously, up-regulates transcription of operons for amino acid biosynthesis. It has now been well established that transcription during prolonged starvation is mutagenic. The reason for this effect is that nucleotide bases are prone to undergo chemical modifications when present in single stranded DNA. For example, cytosine deaminates to uracil, which upon DNA replication, preferentially pairs with adenine instead of guanine. In turn, adenine spontaneously deaminates to hypoxanthine, which hydrogen bonds to cytosine rather than to thymine. In cells where the mismatch repair system is down regulated, these modifications remain in the DNA sequence.

Transcription generates localized single stranded structures in two ways.[36] One is the formation of a transcription bubble, where the DNA-RNA hybrid structure exposes the nontranscribed strand leaving it vulnerable to change. The other one, related to the negative supercoiling generated behind the transcription bubble, gives rise to stem-loop structures possessing susceptible unpaired bases. Since starvation for a particular amino acid specifically targets derepression of the corresponding operon, it is most likely that the adaptive missense mutations in the *trp* operon in Hall's studies are generated during transcription of this operon. This mechanism is coherent with the observed directedness of the revertant mutations.

c) Systems involving mobile genetic elements.

As mentioned previously, some adaptive mutations require either excision or insertion of DNA elements. Normally, molecular events of this kind are under tight control to avoid deleterious effects in the genome. However, stressful environments promote movements of such sequences,[46] providing the cells with an additional strategy for adaptation. For example, numerous studies have demonstrated that starvation elicits an increase in transposition frequency of mobile elements, which may be mediated by the RpoS or SOS responses. In the long term, this type of genome flexibility contributes to increase the genetic diversity of microbial populations.

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ADAPTIVE MUTATION AND EVOLUTION

In proliferating bacterial populations, survival depends on efficient DNA replication, which requires high speed and fidelity. In contrast, a hostile environment where cells cannot multiply will favor the selection of mutants that are able to overcome the episode of crisis.

The basic difference between random and adaptive mutations is that the latter are beneficial by definition, since they increase fitness. Moreover, it has been observed that when adaptation requires more than one mutation, the appearance of the first one makes more expedite the production of those that follow. There are now three examples understood that illustrate this behavior: reversion of the *trp* double mutants, expression of the *ebg* operon and double reversion of *bgl* operon, all of them studied in Hall's laboratory. In each of these cases, reversion of the first mutation allows very slow growth. Then, selection operates to single out the second mutation which leads to rapid growth. This is undoubtedly a fine course of action for adaptation. No wonder evolutionary biologist Douglas Futuyma, excited by Hall's work on the evolution of the *ebg* operon to permit lactose metabolism, wrote: 'Thus, an entire system of lactose metabolism has evolved, consisting of changes in enzyme structure enabling hydrolysis of the substrate; alteration of a regulatory gene so that the enzyme can be synthesized in response to the substrate and the evolution of an enzyme reaction that induces the permease needed for the entry of the substrate. One could not wish for a better demonstration of the neo-Darwinian principle that mutation and natural selection in concert are the source of complex adaptation'.[47]

Common sense tells that the ability to accelerate variation in the genome offers a selective advantage for survival in a changing environment. Several studies, both theoretical and experimental, have confirmed this assertion. In this context, the hypermutation state could be particularly fitting because it increases the probability of obtaining an advantageous mutation when the majority of the cells undergoing a normal mutation rate do not produce it. A fine regulation of the hypermutation state lessens the likelihood of accumulating undesirable mutations.[48] First, it is transient,

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[48] Foster, P.L. Adaptive mutation: implications for evolution. *BioEssays* 22, 1067-1074, 2000.

i.e., when adaptation to the medium is achieved, a return to low mutation rates is selected for. But also, it is restricted to space, as it is clearly exemplified by mutations induced by double stranded breaks, transcription of defined operons and movement of genetic elements. In spite of the clear advantages of confining mutation in space and time, there are occasions in which adapted mutants maintain a mutator phenotype. This outcome is thought to result from adaptive mutations originated in strains with a mutator allele, a property that would be transmitted by hitchhiking in conjunction with the favorable alleles they produce.[49]

It would be very difficult to establish the precise contributions of growth dependent mutations, adaptive mutations and horizontal gene transfer to bacterial evolution. This problem could perhaps be approached experimentally, although laboratory studies are generally short term, whereas microorganisms in their natural environments confront long periods of starvation. Having this limitation in mind, it is worthwhile to highlight recent results obtained by Yeiser *et al.*[50] with bacteria struggling to survive in stationary phase. These investigators confirmed that SOS-induced DNA polymerases II, IV and V enhance long-term survival and evolutionary fitness of bacteria under stress. When grown individually, wild-type and SOS DNA polymerase mutants exhibit similar cell yields and stationary phase survival patterns. However, when the wild type and the mutant strains are co-cultured and must therefore compete for nutrients, SOS polymerase mutants undergo a marked reduction in fitness and fail to express the 'growth advantage in stationary phase phenotype' (GASP). Since DNA polymerase V is the most mutagenic, it is remarkable that mutants of this enzyme are the most affected in the competition experiments. According to these authors, DNA polymerase V may provide the mutational raw material for natural selection in a manner superficially similar to the increase fitness accompanying the absence of the mismatch repair system.

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[50] Yeiser, B., Pepper, E.D., Goodman, M.F., Finkel, S.E. SOS-induced DNA polymerases enhance long-term survival and evolutionary fitness. P*roc. Natl. Acad. Sci. USA* 99, 8737-8741, 2002.

CONCLUDING REMARKS

Unraveling the adaptive mutation phenomenon has allowed us to become aware that the complexity of living organisms is not the outcome of a sole random mutational process, as it is most commonly regarded. Instead, it has become clear that throughout evolution there have also been adaptive mutations stimulated by a variety of fine feedback mechanisms. These include activation of error prone DNA polymerases, down-regulation of DNA repair enzymes, gene amplification, movement of mobile genetic elements, development of a transient hypermutation state in some cells, localization of mutations in genomic space to minimize deleterious mutants, various types of recombination events, etc.

It is most likely that these induced mutations have had a key role in determining bacterial evolution, since natural habitats are often stressful due to a lack of nutrients or some other unfriendly condition. There is still a third kind of gene variation that is widespread in the microbial world and has played a decisive role in bacterial evolution, namely, horizontal gene transfer. In spite of its importance, however, the description of this phenomenon goes beyond the scope of this essay.

DISCUSSION ON PROF. VICUÑA'S PAPER

PROF. WITTEN: Do all mutations happen at random or does the organism have a library of things that it tries, which would be useful when it runs into different environments?

PROF. VICUÑA: A library? No, I don't think so. What microorganisms do under stress is to induce DNA polymerates that make mistakes. This implies that there will be many trial and error events. Most will be lethal, whereas a few will be useful. As soon as a useful mutation arises, the bacterium will start to proliferate. Therefore, it is not that they have a library and they can select which mutation or which gene they should change. Does that answer your question?

PROF. COLLINS: This is a fascinating story and it does seem to add some new understanding of Darwinian selection in a new way, in a fashion that might be referred to – and this is a word that is beginning to, I think, even be accepted more in mammalian evolution – the concept of evolvability that natural selection not only operates on specific changes, provided that there is some selective pressure, but that it is to the advantage of an organism to have a capability of evolving in unpredictable ways if some new pressure, some new niche arises, which is to say that it is to the advantage of organisms not to be squeaky clean in the way in which they handle their biology but to be prepared to make mistakes, to be prepared to have some stuff lying around that you are not really using that might come in handy when some new pressure arises as may be the case, for instance, with a lot of the transcription in mammalian cells for which it is not clear there really is a scientific function, but maybe it is just there in case you wanted to tinker with it. Would you agree that that is sort of the conclusion from this?

PROF. VICUÑA: I think so, I agree with it and you must be aware, of course, that,after the sequencing of the human genome, several genes were found to encode these error prone polymerates. There are five or even more of them. They have been well characterised. We now know that all organisms produce DNA polymerates that do not copy DNA with fidelity, which are induced when the cell is in trouble.

PROF. W. SINGER: Actually, retrospectively it makes a lot of sense that evolution has worked on its own evolutionary mechanism, how could it have done otherwise.

PROF. M. SINGER: I think, in a way, this is complementary to what Francis has just said. As I recall, in a paper a couple of years ago, Susan Lindquist showed, in yeast, that certain mutations that did not have obvious effects under normal circumstances, did so when the yeast was stressed. Proteins that are produced in response to stress, can assist, in ways I will not go in to, those mutated other genes to fill in for the newly emerged needs. Do you remember that paper, Francis? I think it was in *Science*. It was presented both with data and with a certain amount of speculation about this system as a new tool in evolution. In a way, it responds to Ed Witten's question.

PROF. VICUÑA: Yes, if I may add something, this adaptive response has also been studied in yeast and other eukaryotes and it has also been proposed by Cairns as a model for the development of tumours in mammalian tissues.

PROF. CAVALLI-SFORZA: There is evidence that there are strains of bacteria that are more mutable than others with a frequency of even a hundred times higher. Now, if that is the case, which I believe is true, then if a stressful environment is encountered or produced somehow the bacteria mutants that arise may come more likely from the mutable part so natural selection automatically will select for more mutable strains, so that is a way in which automatically there is a greater adaptability of the organism as long as the mutant is unstable. There are other situations in nature where that is clearly so, because another way of increasing genetic diversity is to introduce recombination, whether by sexuality or by other methods. Now, there are organisms that ordinarily can reproduce both ways. If the environment is stable they tend to stay in the asexual reproduction. Whenever the environment changes, they shift to the sexual phase. One of them is *Daphnia*, which is an aquatic organism. So it is clear that when the environment is hard or stressful then increasing genetic variation is favoured.

FROM MICROBIAL GENETICS TO MOLECULAR DARWINISM AND BEYOND

WERNER ARBER

When Charles Darwin reflected on the process of biological evolution some 150 years ago, he could not know of the existence of genes. But he and some of his contemporary natural scientists had observed that individual organisms belonging to a given species showed obvious phenotypical variations. Darwin's theory of evolution postulates that the different variants and their parents are steadily submitted to natural selection. This means that variants which can better deal with their encountered living conditions are favoured, and can, in the long term, overgrow less favoured organisms in the natural ecosystems.

Independently of evolutionary biology, Gregor Mendel initiated classical genetics in 1866, based on the observation that some phenotypical traits became transferred into the progeny and that recombinants could show up upon cross-fertility between individuals with different traits (i.e. mutants). The genes that were postulated to represent the determinants for phenotypical traits remained for many decades an abstract concept. This was still the case when around 1940 classical genetics and evolutionary biology joined forces in the so-called modern evolutionary synthesis that resulted in the Neo-Darwinism (Mayr, 1982).

About at the same time, microbiologists reported that bacteria and bacterial viruses could also undergo mutation and were thus postulated to possess genes. This opened the possibility to experimentally explore the formation of recombinants in mixed cultures of different bacterial or viral mutants.

Already in classical genetics there was good evidence that genes were associated with chromosomes. These were known to contain nucleic acids as well as proteins (chromatin). A strong evidence that desoxyribonucleic acid (DNA), rather than proteins, is the carrier of the postulated genes came in 1944, when Avery *et al.* (1944) reported their experiments with pneumococcal bacteria. These authors worked with two different bacterial types that were distinct by their traits. DNA was extracted from one of the strains and carefully purified from all attached proteins. When this DNA fraction was incubated together with intact bacterial cells of the second strain, some bacteria showed up that had acquired the trait characteristic for the first bacterial strain: these bacteria had been transformed. No transformation could be obtained upon incubation of the second strain with the purified proteins of the first strain. DNA was thus concluded to be the carrier of genetic information.

How the genetic information can be inscribed in DNA became obvious several years later, when Watson and Crick (1953) showed that DNA molecules are long filaments with double-helical structure. Two antiparallel strands composed of four different nucleotides are held together by hydrogen bonds ensuring a specific base-pairing between the neighbour nucleotides. On the basis of this discovery it became obvious that genetic information can be contained in the linear sequences of nucleotides. In addition, correct base pairing was suggested as the criterium for the transmission of the genetic information from the parental genome to the two daughter genomes upon DNA replication.

In the following decades molecular genetics was developed thanks to experimental investigations with microorganisms and soon also with eukaryotic organisms. This then led to genomics including DNA sequence analysis and investigations on gene functions. The thereby acquired knowledge can provide insights into impacts that spontaneous alterations of nucleotide sequences can have on specific phenotypical traits. This kind of research turned out to be quite informative for an understanding of molecular mechanisms that generate genetic variations. The products of genetic variants together with their parental forms represent the substrate for natural selection. It is thus appropriate to join now forces between Neo-Darwinism and molecular genetics to result in Molecular Darwinism.

Bacterial genetics was developed with only a few kinds of bacterial strains, particularly with *Escherichia coli*. Under laboratory conditions these bacteria propagate exponentially with a generation time of about 30 minutes between two cell divisions. Large populations can thus be obtained in one day. Since bacteria are haploid, having just one set of genetic information, spontaneously occurring mutants become phenotypically manifested quite fast. One can observe that, when a few hundred growing cells are reached, one new mutation shows up. With available research strategies the nature of newly isolated mutants can readily be analysed, both with regard to the suffered DNA sequence alterations and with regard to their functional capacities under various growth conditions.

As more and more gene and genome sequences of various prokaryotic and eukaryotic organisms become available, sequence comparisons can give hints on the molecular mechanisms that might have been at the origin of the observed functional differences. Such comparisons are also welcome for bacterial strains that cannot be propagated under laboratory conditions. Still, it is of importance to base any conclusions from sequence comparisons on available knowledge on already identified molecular mechanisms that are at the source of newly generated mutants. Experimental data of such events can best be acquired in work with genetically well known bacteria and bacterial viruses.

It is good to mention here that in the relevant genetic literature two different definitions are used for the term 'mutation'. In classical genetics, a mutant displays an altered phenotype that becomes transmitted to the progeny. In molecular genetics, looking at DNA sequences, a mutation is usually defined by carrying an altered nucleotide sequence. In the meantime, we know that, as a rule, classically defined mutants have also an altered nucleotide sequence. But we also know that by far not all nucleotide sequence alterations lead to an altered phenotypical trait. Many novel sequence alterations are, often for known reasons, silent or neutral and have no immediate influence on life processes. On the other hand, there is a good consensus between researchers in the field that relatively few novel mutations are favourable and provide to the organism a selective advantage. Much more often new mutations are unfavourable. They can inhibit life processes to some degree or, in extreme cases, they can be lethal. These kinds of mutations provide a selective disadvantage. This situation gives us no evidence for a directive nature of spontaneous mutagenesis. In general, the spontaneous generation of genetic variants reflects some kind of randomness; it is not a directing response to an identified specific need. We will explain below that several specific molecular mechanisms contribute to the overall generation of genetic variations.

Figure 1 can guide us in the discussion on Molecular Darwinism. The top of the scheme shows the three pillars of biological evolution: Genetic variation as the driver of the evolutionary process, natural selection that directs evolution together with the available genetic variants, and geographic and reproductive isolations that modulate the process of evolution. The different living conditions and the effective size of the biosphere on our planet, as well as enzymatic repair processes, limit genetic diversity.

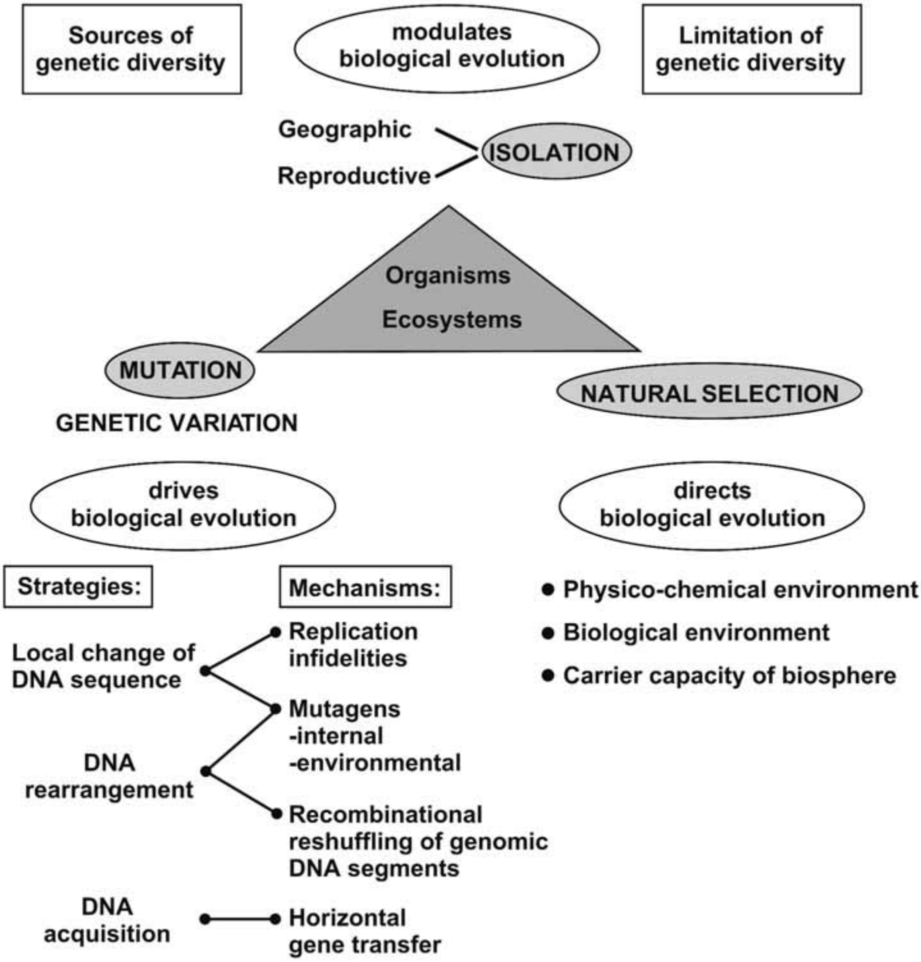

Figure 1. Schematic representation of elements involved in biological evolution and of the mechanisms and natural strategies of the generation of genetic variants (from Arber, 2008).

The lower part of Figure 1 shows on the left side in a condensed way the known sources of spontaneous mutagenesis. A detailed analysis to be commented below can lead to a classification of the different molecular mechanisms for the generation of genetic variation into three natural strategies of genetic variation: local sequence change, intragenomic DNA rearrangement, and DNA acquisition by horizontal gene transfer.

Before giving a more detailed explanation for these molecular mechanisms and strategies, it might be helpful for a better understanding to outline the main elements of the theory of molecular evolution (Arber, 2003, 2007) which is also called here Molecular Darwinism. We will see that a number of non-genetic elements contribute in reality to genetic variation. These elements are to a large extent intrinsic properties of matter, such as a certain degree of chemical instability of nucleotides. Another of these intrinsic properties relates to structural flexibilities of biological macromolecules, such as isomeric forms, in particular of nucleotides. Their tautomeric forms affect the proper base pairing in the double-stranded DNA molecules. Environmental chemical and physical (radiations) mutagens contribute of course also to spontaneous mutagenesis. Some of these mutagens are internal metabolic products (Smith, 1992). Still another factor is random encounter, e.g. of a mutagen with a cellular DNA molecule or of a gene vector with a target cell upon horizontal gene transfer.

Detailed studies of genetic variation processes have revealed that quite often, specific gene products are involved in genetic variation. These products of so-called evolution genes can act directly as variation generators and/or as modulators of the rates of genetic variation. Some examples will be discussed below. This outline shows that natural reality takes actively care of biological evolution. Genetic variation should not be attributed to errors and to accidents occurring to the DNA.

Local DNA sequence changes include the substitution of a nucleotide by another nucleotide, the deletion or the insertion of a nucleotide and also a scrambling of a few neighbouring nucleotides. There is good evidence that some of these sequence alterations occur upon DNA replication. It is known that enzymatic repair systems can rapidly spot the onset of these kinds of replication infidelities (Radman and Wagner, 1986). Upon the so-called repair, at least some repair enzymes can distinguish between the parental DNA strand and the newly synthesized strand. Consequently, they use the parental DNA strand as a master to put the affected nucleotide sequence in the newly synthesized DNA strand back into the correct parental order. Although these repair processes are quite efficient, they do not work with a 100% accuracy. This provides to cell populations a few rare local sequence changes in some individual cells, on the one hand, and to the individuals in the cell populations a relatively high genetic stability, on the other hand.

Let us now focus our attention on intragenomic DNA rearrangements. Various recombination enzymes are known to contribute to this kind of genetic variations. Generally speaking, these recombination processes can affect DNA segments of various lengths, often containing one to several genes, and they can lead to the duplication, the deletion, the inversion or the translocation of a DNA segment, depending on the specific activities of the particular recombination enzymes at work.

By speaking on genetic recombination, one usually thinks at the so-called general or homologous recombination. In this reaction, the enzymes bring together DNA segments of a high degree of nucleotide sequence homology. DNA strands are then cleaved and spliced together across the two partners. In higher organisms these reactions are exerted in meiosis, when recombinants between paternal and maternal chromosomes are produced. In contrast, they do not work in mitosis during the normal DNA replication before each cell division. Bacteria also possess enzyme systems for homologous recombination. Again, in normal cell growth the enzymes become not readily expressed. But when breaks in the DNA molecules appear, e.g. after high energy irradiation, the so-called SOS repair becomes induced which produces a relatively high level of enzymes for homologous recombination. As a consequence, survival rates after irradiation rise, since intact genomes can be reconstructed by homologous recombination between sister DNA molecules that are present as already replicated genomes before cell division.

Mobile genetic elements are widespread in living organisms (Shapiro, 1983). These are DNA segments carrying normally one to several genes. The products of some of these genes are enzymes called transposases. Their activities can promote a translocation of the element to other chromosomal locations, sometimes in conjunction with a duplication of the element. These translocations are usually called transposition. Most bacteria carry in their genomes such mobile genetic elements, some of which are called IS (for inserted sequences) elements. Well studied *E. coli* bacterial strains carry in their genomes several specific kinds of IS elements, mostly in several copies of each kind. Interestingly, practically each kind of IS element (IS1, IS2, etc.) follows its own functional criteria, both for the selection of novel insertion sites on the DNA molecules and for the control of the availability of transposase activities at a low level, so that rates of transposition are actually very low. For example, IS30 (Caspers *et al.,* 1984) becomes inserted most readily into a specific, relatively short nucleotide sequence, although at much lower rates it can also insert elsewhere (Stalder and Arber, 1989). In contrast, IS2 prefers to insert in particular DNA regions of a length of a few thousand base pairs (Sengstag and Arber, 1983). But within these regions insertion can occur practically anywhere; the used insertion sites show no distinct sequence homology (Sengstag and Arber, 1987). Transposons are mobile genetic elements that carry a segment with ordinary chromosomal genes between flanking elements that are responsible for their ability to transpose.

Transposition is not limited to intragenomic translocation, it can also occur to plasmids and to viral genomes during their residence in the bacterial cell. The impact of these possibilities on horizontal gene transfer will be discussed below. In this context, it is important to mention that some viral genomes can be counted to mobile genetic elements: They can insert into the host genome and at some later time excise again. Retroviruses that are widespread in higher organisms are a good example.

These considerations lead us to discuss processes of site-specific recombination. Indeed, some viral insertions into chromosomal DNA are to a high degree site-specific, and so is IS30, as we have seen. An interesting kind of site-specific recombination has been described as the basis for so-called flip-flop systems that are present in some bacterial and in some bacteriophage genomes (Glasgow *et al.*, 1989). We refer here to a flip-flop system that promotes the periodic inversion of a DNA segment. This segment is flanked on both sides by a 26 base-pairs long consensus (relatively high homology) DNA sequence. These flanking consensus sequences are carried in inverted order. The enzyme DNA invertase brings together these consensus sequences. The DNA strands become then cut and alternatively religated in the middle of the consensus sequences. This process results in the inversion of the DNA sequences carried in between the two consensus sequences. Inversion occurs back and forth every few generations in a growing microbial culture. This kind of flip-flop provides means to have two different genome organisations in a population of microorganisms. A strong evolutionary impact of this DNA inversion system, however, becomes obvious by the experimental observation that the enzyme-mediated DNA inversion can sometimes also occur between a consensus sequence and another, so-called secondary inversion sequence. Many different such sequences have been identified (Iida and Hiestand-Nauer, 1987; Arber, 1995). These secondary inversion sites do not show distinct similarities to the consensus sequence, and their spontaneous use shows at most some statistical reproducibility. This fact points to a certain specificity of the interactions. By using secondary inversion sequences, site-specific DNA inversion represents a source for novel gene fusions and for the assembly of an open reading frame for protein synthesis with an alternative expression promoter signal. We can conclude that these activities can be considered as active generators of genetic variants of evolutionary relevance. Note that in contrast to the regular flip-flop activity, the rates of using a secondary DNA site for DNA inversion are very low. These enzyme systems are a source for evolutionary novelty and they respect genetic stability of most of the individual cells in which they are carried.

With these presentations of a few well studied enzymatically mediated systems to promote occasional intragenomic DNA rearrangements we are impressed of the rich diversity of natural possibilities to provide novel genetic variations. In all these cases, the resulting genetic variants are, of course, substrates for natural selection. As we have already discussed, a majority of resulting genome orders may be lethal or of disadvantage. But it is the minority of winners, of variants providing selective advantage, that count for biological evolution.

Let us now look at horizontal gene transfer and its impact on the natural evolutionary strategy of DNA acquisition. As we have already discussed, microbial genetics has contributed much to today's knowledge in this field. Microbial genetics had a rapid start in the 1940s. In the already discussed transformation, free DNA molecules can be taken up by receptor bacteria, either actively or passively, depending on the particular microbial strain involved. In bacterial conjugation (Lederberg, 1947), two bacterial cells that can belong to different strains, meat physically. DNA from the donor cell can thereby become transferred to the receptor cell. A so-called fertility plasmid acts thereby as a gene vector (Hayes, 1964). Besides its own transfer through the conjugation bridge, the fertility plasmid can also provide the transfer of parts of the genome of the donor cell. A third possibility for horizontal gene transfer is its mediation by some bacterial viruses serving as gene vectors (Zinder and Lederberg, 1952). Again, we realize that nature was quite inventive with regard to the specific molecular mechanisms (Arber, 1994). In some of the processes, recombinant DNA molecules between viral and bacterial genomes are incorporated into viral particles (specialized transduction); in other instances, it is just a DNA segment taken from the donor genome that becomes incorporated into a viral particle (generalized transduction). Horizontally transferred DNA segments contain sometimes mobile genetic elements such as a transposon. This can facilitate an eventual incorporation of transferred DNA sequences into the genome of the receptor cell.

None of the horizontal gene transfer processes is specifically oriented to particular receptor bacterial cells. Transfer depends generally on a random encounter. However, between such an encounter and a stable integration of the foreign genetic information into the receptor genome, several barriers seriously reduce the chance of acquisition of foreign genetic information. First of all, there is a requirement for surface compatibility of the receptor cell. In transformation the foreign DNA must find its way into the cytoplasm of the receptor cell, either by an active or a passive uptake, as already mentioned. In conjugation, the two mating partners must provide means for the building of a mating bridge. In transduction, the viral gene vector must find on the bacterial surface receptor sites that are required for successful infection. Secondly, many bacterial strains are equipped with one or even several restriction/modification systems (Arber, 1965). Restriction enzymes provide efficient means to identify if incoming DNA is foreign or if it had been produced in the same kind of bacteria. In the first case, the penetrating DNA molecules are cut into fragments by the restriction endonuclease. Within a few minutes the fragments are then further digested by exonucleases. However, at low rates foreign DNA fragments escape full digestion and succeed to incorporate at least some of their genetic information into the genome of the receptor cell. Generally speaking, successful DNA acquisition occurs only rarely and mostly in small steps, involving a part of a gene or one to a few genes at once. More or less random acquisition of foreign genetic information can often disturb the functional harmony of the cell in question. This is then the last barrier acting against successful acquisition. The hybrid resulting from acquisition will often have a selective disadvantage, less frequently a hybrid may have an advantage. This then represents a positive step in the process of evolution.

After having discussed examples for each of the three natural strategies of genetic variation, we can now compare the qualities of contributions made by each strategy to the evolutionary progress.

Local sequence changes offer the possibility for steps of improvement of available biological functions. Theoretically, local sequence changes could also represent a source for an occasional new biological function. But this can probably only become effective when the function in question starts to represent a substrate for natural selection.

DNA rearrangements can be seen as a tinkering with available capacities (Jacob, 1981). Novel combinations of functional domains from different genes may, for example, lead to a novel biological function. On the other hand, DNA rearrangements can also provide an alternative expression control signal to a functional gene. Such genetic variants may then express either higher or lower quantities of the gene product in question, as compared to the parental forms.

Favourable acquisition of foreign genetic information can be seen as a sharing in successful developments made by other organisms. In successful cases, the acquisition (in one step) of a biological function that the receptor organism did not possess, represents an extremely efficient contribution to the evolutionary progress. DNA acquisition as well as intragenomic DNA rearrangements might sometimes be a possible explanation for a sudden emergence of novel properties in evolving organisms.

The theory of molecular evolution postulates that evolutionary fitness may be reached when organisms are genetically equipped with the capacity to profit from all three natural strategies to generate genetic variants. For each of these strategies at least one, or better a few, specific mechanisms should be available.

In the light of this request one can postulate that in the course of the long past periods of evolution, the evolution genes, i.e. the sources for variation generators and for modulators of the rates of genetic variation, may have become fine-tuned for their functional activities by second-order selection (Weber, 1996). This means that those populations of organisms which had reached a certain degree of evolutionary fitness, were in advantage for adapting to changing living conditions. This can explain why organisms that live today are actually able to evolve and, nevertheless, to provide a relatively good genetic stability to the individuals of evolving populations.

In the description of molecular mechanisms and strategies for the generation of genetic variants, we have mostly referred to microbial experimental evidence. However, there are good reasons to assume that this acquired knowledge applies also to higher organisms. In recent times, more and more evidence for this expectation becomes available, particularly from DNA sequence comparisons. In this context, one can mention that some genetic variation generators nowadays also serve at the somatic level. A striking example is found in the somatic assembly of functional genes for specific antibodies of our immune system. In addition, some repair systems taking care of limiting rates of mutagenesis carry out their functions also in somatic cells. As far as horizontal gene transfer is concerned, one knows that some animal viruses can serve as natural gene vectors. In addition, symbiotic cohabitation of various microorganisms in animals and in plants is a very likely source for occasional gene transfer in one or the other direction.

A classical representation of long-term biological evolution is the tree of evolution. This tree usually shows the vertical flux of genes from the stem of the tree through the branches up to their ends, representing today's organisms with their enormous diversity. By taking care of the concept of the evolutionary role of DNA acquisition, we have introduced more or less randomly placed connectors between branches as symbols for horizontal gene transfer (Figure 2). While in the vertical flux of genes the entire genomes are involved, upon the horizontal flux of genetic information only relatively short DNA segments become acquired, as we have already discussed. As we can expect from this modified representation of the tree of evolution, living organisms are not only interdependent by common roots in their past evolution, they are also interdependent in view of potential contributions to their future evolutionary progress by horizontal gene transfer. This new knowledge merits to become part of our understanding of biological evolution and it can enrich our world view.

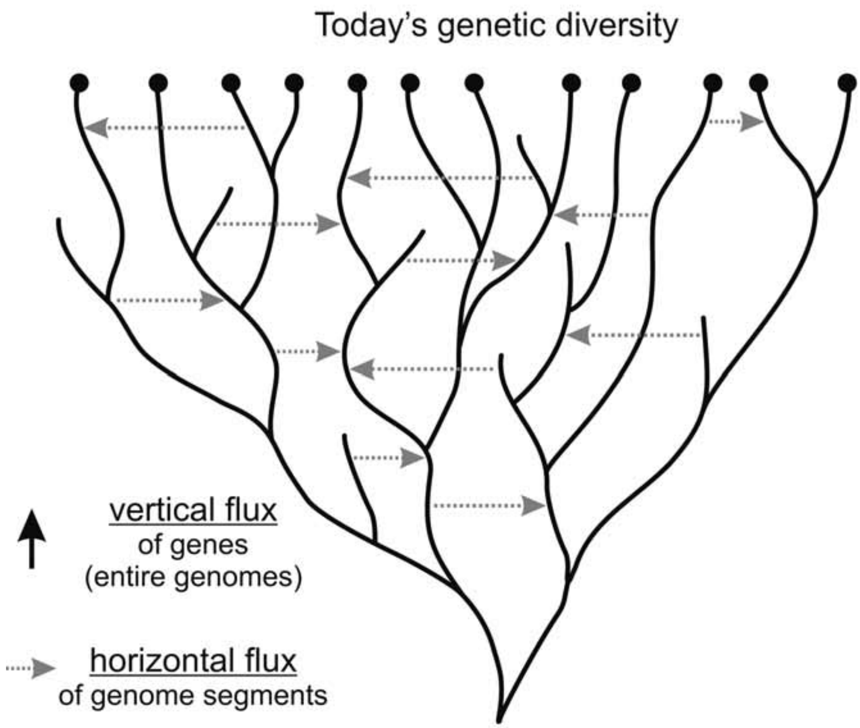

Figure 2. Actualized paradigmatic picture of the tree of biological evolution taking into account the evolutionary strategy of DNA acquisition by horizontal gene transfer (redrawn after Arber, 1991).

Another philosophical and world view aspect of molecular Darwinism is the notion of evolution genes. Although we know that some of their products serve also at the somatic level, other evolution gene products, such as at least some recombination enzymes and restriction/modification systems, clearly contribute only to the evolutionary progress of microorganisms. These genes are largely irrelevant for the bacterial life from one cell division to the next. We can thus conclude that genomes have a duality with regard to their content of genetic information. Many of their genes, such as housekeeping genes, accessory genes of use under particular life conditions, and in multicellular organisms the developmental genes serve for the fulfillment of the life of the organism. In contrast, the evolutionary genes ensure the capacity for biological evolution of the populations. Their products serve in cooperation with non-genetic elements for the expansion of life and for a slow, but steady, replenishment of biodiversity. Let me just mention that this philosophically interesting duality of the genome should not be taken as a strict classification of all the genes carried in the genome, since some gene products serve both for the needs of the individual life and for the capacity to evolve. However, the identified duality of the exerted functions can importantly contribute to a better understanding of the complexity of life and its evolution. From the scientific point of view, the living world of today reflects a long evolutionary path of permanent creation that may be based on a kind of self-organisation, and that must have its roots in the far past of the planetary evolution. The observed internal forces of the living world to undergo biological evolution gives us a guarantee that living organisms, at various stages of complexity, can continue to evolve and adapt to changing living conditions as long as such conditions will exist on our planet. Our actual knowledge on cosmic evolution predicts that appropriate conditions for organic life can still exist on our planet for about 5,000 million years.

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DISCUSSION ON PROF. ARBER'S PAPER

PROF. SZCZEKLIK: Is there any evidence that horizontal transfer occurs in organisms higher than bacteria, multicellular?

PROF. ARBER: Absolutely. The retroviruses are known to be gene vectors, and evidence for an occasional acquisition of foreign genes comes from DNA sequence comparisons. Keep in mind that genetic variation can only occur at low rates. This renders experimental investigations on DNA acquisition quite difficult. Nevertheless, more and more biologists agree that horizontal transfer is a general phenomenon.

PROF. RAVEN: I do not exactly want to use the word 'species', but can you talk a little bit about how you view the diversity of bacteria philosophically? I mean, how many different ones should we name, how much do they differ from place to place?

PROF. ARBER: Well, probably less than 1% of bacterial types can be cultivated in the laboratory. Up to now experimentally accessible bacteria have been classified according to their abilities to use particular sugars, particular amino acids, and some other essential nutrients. This contrasts with the criteria to classify higher, sexual organisms on the basis of sexual fertility. More and more, genomics makes now entire genome sequences available, also from non-cultivatable bacteria. Future classifications will certainly largely be based on sequence comparisons. Already now, one can identify a kind of continuum of the genomes of different microbial isolates. This can be explained as a result of both the vertical and the horizontal transmission of genetic information. One can expect that scientific classification might end up with a large number of specific forms of bacteria.

PROF. PHILLIPS: There are millions of them.

PROF. ARBER: Yes, there are many, oh yes! I carry more bacterial cells with me, in and on my body, than the number of my own cells: roughly one kilogramme per adult. But this is important. The public opinion that bacteria are in general pathogens is completely wrong. From the scientific point of view bacteria are my friends in symbiosis, they help and facilitate my life. But how can I tell that to the people in the street who cannot observe the bacteria at their work?

PROF. PHILLIPS: I was confused by one point. You said that there was no evidence of directedness of spontaneous mutation and then you hastened to say, well, this seems to be somewhat in contradiction to what we have just heard from Rafael, but you said, 'I am not talking about stress situations'. Now, if I understood correctly, I thought that what you were saying was that everything was random but that stress, in a sense, increased the rate of mutation so that you could get out of whatever difficulty, is that right? So you would also agree that there is no directedness of stress mutations either, is that right?

PROF. VICUÑA: It is right, but in certain stressful conditions, mutations may appear to be directed.

PROF. ARBER: An observable response to a stress situation is rather an exception and, usually, if one studies the reasons intensively, one can often find a causal explanation why it is so.

PROF. PHILLIPS: Are you saying that you have seen evidence of that or that you can see how it might happen?

PROF. VICUÑA: There is evidence on how you can get directedness for a specific mutation. It depends on the system, but it would be an exception.

PROF. ARBER: But you should avoid generalising.

PROF. POTRYKUS: I have some problems with the general acceptance of horizontal gene transfer in multicellular organisms. It is certainly true that there is the possibility, but it can only have consequences if the transferred piece of DNA reaches the germline. Plants do not have a germline so the DNA ends up in somatic cells. It can have consequences if you can regenerate a plant from a somatic cell, but it is not the general natural mechanism. So I am looking for alternative explanations for the widespread detection of homology. I am not convinced that this is the only explanation that there is horizontal gene transfer.

PROF. ARBER: I agree with you on some principle differences between higher organisms and bacteria with regard to the germ line. What you observe for higher organisms is possibly just another isolation phenomenon to keep the rates of horizontal gene transfer into germlines.

PROF. M. SINGER: So I was struck by the fact that you never mentioned *Archaea* in the talk. You talked about bacteria and I do not know whether you were including them or whether anything is known about horizontal transfer in *Archaea*.

PROF. ARBER: I must confess I am not sufficiently familiar with the literature, whether that has been clearly shown. Does someone else know? Yes, there are a few cases. For the time being the problem is that bacterial genetics is based on a handful of cultivatable strains. We then just extrapolate and often generalize the acquired knowledge. This, however, requires validation in future times.

Session III

INSIGHTS INTO HUMAN EVOLUTION

WHY IT IS USEFUL TO KNOW THE MODERN THEORY OF EVOLUTION

LUIGI LUCA AND FRANCESCO CAVALLI-SFORZA

1. DARWINISM

In the last two centuries there has been much discussion on the hypothesis, not unfamiliar to the ancients, that all living species originated from simple forms by a long process of evolution, that is, by transformation and differentiation into a great variety of species. Basic contributions came from Jean Baptiste Lamarck (1802) and Charles Darwin (1859). A major scientific step forward was accomplished through the understanding of the laws of inheritance in higher organisms, valid for the great majority of plants and animals, which we owe to the research carried out by the Czech monk Gregor Mendel. He was so far ahead of his time with regard to intelligent experimentation, that it took 34 years for Western scientists to appreciate, rediscover, and confirm with humbler experiments Mendel's original findings, which were communicated to the Natural History Society of Brünn, Moravia, in 1865, and published in its proceedings in 1866.

The introduction of *Drosophila melanogaster,* the fruit fly, as research organism by the group formed by T.H. Morgan at Columbia University, New York, made possible the rapid development of genetics after 1912, as the science of biological inheritance came to be called. In the twenties three geneticists: R.A. Fisher, J.B.S. Haldane and Sewall Wright set the mathematical foundations of the modern genetic theory of evolution, which were later enlarged by Motoo Kimura and many others. They thus applied Galileo's recommendation that, for scientific understanding, you must first learn the characters in which the world is written, and that the universe is written in mathematical language.

The demonstration in bacteria (1944) that DNA is responsible for biological inheritance; the discovery (1953) of the chemical structure of DNA;

and the research in the field of 'molecular genetics', that ensued, led to the examination of whole genomes, and provided new powerful means for studying their evolution.

Today evolution is no more a hypothesis and there are ample proofs that it is motored by natural selection. Knowledge of the sources of inherited variation and of the mechanisms that maintain it, at the same time favoring the transformation and differentiation of species, has greatly enriched a well-organized theory. The succession of evolutionary steps leading to the great variety of living organisms is being traced with astonishing precision thanks to the detailed analysis of whole genomes. That species change is no more a hypothesis or a debatable theory, and how and why they do so is becoming a matter of detailed proofs. Until a short while ago Genetics, once just the science of biological inheritance, was the Cinderella of Biology, but it has now become its central discipline, and has turned modern biology from a descriptive, morphological, 'qualitative' discipline with no theoretical background, into a highly sophisticated, quantitative science based on gigantic, exhaustive whole genome DNA data sets, and on very advanced techniques. Genetics also generated molecular biology, a slow but essential scientific machine that is systematically clarifying the very complicated network of metabolic pathways necessary to make a living organism develop, build, maintain and reproduce itself. To avoid confusion, it is worth adding that, while today we prefer to speak directly of DNA, earlier the structures responsible for inherited traits, then unknown, were called 'genes'. This word has now taken on a new meaning, limiting it to DNA segments making a protein with a specific function, but is still frequently used in its original looser meaning of inherited unit.

A recent development of genetic thinking that is referred to as 'epigenetics' is showing that the DNA of specific tissues can change during the development of an organism. Some of these changes, as in the formation of tumors (especially malignant ones) are definitely pathological. These and many other 'normal' processes that take place during development in 'somatic' DNA show how complex the process of development really is, ranging from somatic mutations and temporary partial prevention or modification of function of major parts of DNA, to the contributions of RNA to regulatory processes of gene action, and to occasional pathological deviations in the structure and function of proteins described under the name of 'prions'. In general, however, it is important that the DNA destined to pass information to future generations seems to be set aside fairly early in cells of the 'germinal' line, destined to produce 'gametes' (sperm and egg cells), and is basically excluded from these epigenetic developments.

The 'mystery of life' has now become very simple. A living organism is an organism capable of reproducing itself, generating other organisms that are almost identical to itself. The word 'almost' is added to indicate the fact that mutations are rare: they are chiefly very small errors in copying the hereditary patrimony, which is chemically a substance called DNA and is essentially a book of instructions on how to build a new organism, almost identical to the parent/s, a copy of which is transmitted by the parent/s to the children. The copies of DNA received by the children, that they use to direct their own development, are copied again for passing them on to their own children. Thus the copy errors made by parents in producing gametes accumulate into the master textbook the children will use, for their own development as well as for making new copies of DNA (with new errors) that will be passed on to their children and all descendants. Mutations are thus the main stuff evolution is made of, because they introduce all real novelties into the living world.

Most mutational changes taking place at every generation have little if any effect on the organism carrying them, or at least do not affect the adaptation of their carriers (i.e. are *selectively neutral*), but mutations that determine selection are those that affect the capacity to survive to reproducing ages, and/or the fecundity of the individual, because they alter automatically the composition of the next generation. In fact, changes of physical traits increasing survival probability or fertility (the number of children born), will generate relatively more descendants than the rest: they may therefore be spoken of as an evolutionary 'improvement' over the original types. Darwin, and independently another English naturalist, A.R. Wallace, understood around the middle of the XIX century that improved survival and/or fertility would thus *inevitably* cause evolutionary changes of living organisms over time and space, ensuring better adaptation to the environment/s. In fact those organisms that have more children than the original types must be, in some way, *fitter* than the ancestral type to the environment in which they live, and *if* the characteristics causing higher fitness are inherited by the progeny of the fitter types, their greater survival/fertility will increase their relative numbers in successive generations, causing a population change in time. Thus species will be transformed and will go on adapting ceaselessly to changes in the environment that demand different adaptations. Similarly, differentiation of a species in space will also arise in the course of time, wherever local environments differ.

In other words, *evolution due to natural selection is an automatic transformation of any species over time*, leading to differentiation in different environments, due to the higher survival/fecundity of fitter types. Higher fitness is measured in the demographic terms of higher survival and/or fertility, but in terms of the structure and function of the fitter organism this must mean that the fitter type is somehow better 'adapted' than the original type to live in its particular environment. One can therefore observe an increase in the average adaptation of a population to its environment in the course of evolution, and R.A. Fisher showed that the rate of increase in adaptation can be predicted by the variation of what he called individual 'Darwinian fitness' in a population. He named this the 'fundamental theorem of natural selection', strictly valid under the condition that the selective advantages of the different types does not change. If this condition does not occur, more complicated theorems take over. The accumulation of changes over time because of natural selection can increase, or reduce the complexity of living organisms. More and more complex organisms have thus evolved, but parasites can lose many complex organs and functions, initially necessary for feeding and reproduction, because they can use those of their hosts. The general results are organisms that are very efficient, often with increased complexity that is useful for prospering, and we marvel at the apparent perfection of their structure and function.

Fisher noted that natural selection is a mechanism that causes 'improbability', by the accumulation of higher fitness over generations. Some observers think it is very unlikely that modern living organisms could ever arise by chance alone from much simpler organisms, forgetting that they had an extraordinarily long time available for building the organs that help them to live, and that they did so over many generations and in a great number of steps, most of which increased only modestly their survival and reproduction skills. This increase is constant nevertheless, even if it is mostly small and hard to notice, because of the very nature of living organisms, which can replicate themselves. Self-reproduction is constantly subject to natural selection, and consequently every generation contributes to some genetic improvement, in each species.

This modern synthesis of Darwinism and its translation in quantitative terms points thus to a process determined essentially by mutation and natural selection, that is, the spontaneous production of DNA changes and the automatic filtration of those that permit improved adaptation to the environment. This filtration takes place through the different survival and fecundity of carriers who are somehow better adapted and can pass that quality to their children. All mutation products that have fitness greater on average than that of the original type, will increase in relative numbers with the passage of generations, at a speed in time an space that depends on how much greater the fitness of the mutant is over that of the original type (more generally, of the population average), and on migration. Those mutant types whose fitness is inferior to the population average must decrease in numbers and eventually disappear.

It is important, however, to note that fitness as a measure of adaptation is not, strictly speaking, a property of genes (DNA), and of genes only. More exactly, it is a property of the 'phenotype', i.e. the actual product of genes in the development of the organism, and it depends also on the environment in which growth, development and everyday life occur, including, especially in humans, behaviors culturally transmitted, i.e. learnt during development. An otherwise very good book by Richard Dawkins, *The Selfish Gene*, forgot to mention the caveat that natural selection directly affects phenotypes, not genes, an error which Dawkins later corrected.

Darwin was also impressed in drawing his conclusions by Malthus' observation that the number of children generated by any living organisms is practically always greater, often much greater than that allowed to live by the available resources. There is not enough room for all those who are born: some must die early or not reproduce. Natural selection can therefore be viewed also as a highly competitive struggle for existence, because not all children may manage to contribute to the next generation.

Some religious environments did not like this concept, because competition to survive seemed intuitively incompatible with a loving God. But what seemed most offensive to a large number of XIX century Anglican prelates (there was a famous exchange in 1860 between Julian Huxley and the bishop of Oxford, Samuel Wilberforce), was the inevitable conclusion that humans have common ancestors with animals, especially with our nearest Primates, like chimpanzees. Zoos were beginning to be built, and everybody could observe pictures or even living specimens of Primates. Recent research on Primates has actually shown that the gulf between the nearest Primate and us is not as profound as it seemed in the XIX century. The major difference objectively observed between us and other Primates is that they cannot develop an articulated and rich language like ours, and this may have proved a major limitation to the development of communication within different Primate families, and thus to cultural evolution.

The Bible gives humans a privileged position with respect to animals, by assuming our similarity to God. Jews were not allowed to use art to make representations of God, and this decreased the dangers of imagining men's similarity with God as physical, rather than spiritual and intellectual. In other cultures, when artists were given freedom of picturing the physical similarity of their Gods and showed them in human shape, there was increased potential for conflict between science and religion, as Gods inevitably became natural rather than supernatural beings.

The Bible also makes the acceptance of evolution impossible, if one takes literally the word 'days' in the statement on Genesis, and not as rough geological eras. Actually geology antedated biology by almost a century in making the literal interpretation of the beginning of Genesis scientifically obsolete.

The word 'Darwinism', as used today by its critics in philosophical or religious circles, is often plagued by a number of misunderstandings and abuses of the basic Darwinian concept of natural selection, that have little or nothing to do with Darwin's or the modern understanding of his theories. Discussion is useless with people who have not learnt that natural selection is a direct, inevitable, and automatic consequence of basic demographic processes. Darwin, by the way, knew nothing of Mendel's experiments, which were published five years after Darwin's first book, *The Origin of Species*, but remained practically buried until 1900. The word Darwinism is used correctly only if it refers to Darwin's idea of natural selection, remembering that he also did emphasize that the fundamental need for selection to be effective is limited to inherited traits. Darwin's ideas on inheritance mechanisms were inevitably vague but do not affect the validity of his understanding of natural selection.

2. The major factors of evolution

Natural selection is not the only factor of evolution. Today we have considerable knowledge of the basic mechanisms of genetic change that give rise to the diversity of DNAs. For all we know today the errors of copy of DNA, which we call mutations, are spontaneous and *random,* in the sense that they are unpredictable, and are not necessarily directed, for instance, in an adaptive direction. Their rates of occurrence can be estimated, with some difficulty because mutations are also *rare,* and large numbers of individuals must be examined. There is a good reason for the rarity of mutations: living organisms are complex mechanisms and they need *all* their organs and functions to be reasonably efficient, to ensure their own survival. Hence errors of copy of DNA must be rare or mostly not dangerous, and in fact mutations are rare and most of them do not affect Darwinian fitness.

DNA is made of very long filaments (the chromosomes) formed by a chain of units whose chemical nature is that of a 'nucleotide'. There are four types of nucleotides that can be aligned in any order, called A, C, G and T (the initial of their chemical names). It is common to suggest that DNA is a book of instructions for making a living organism, written in an alphabet formed by four letters. Human DNA is like a library made of 23 volumes (the 23 chromosomes). In sexual reproduction of 'diploid' individuals like us and the great majority of plants and animals, each individual receives one copy of each chromosome type from the father, and one from the mother, so that every cell in the human body, aside from the reproductive cells, numbers 23 *pairs* of chromosomes. All parts and units of DNA can mutate: the most common changes are called single nucleotide polymorphisms or *snps*, and are the replacement by mutation of a specific single nucleotide in a particular position on a particular chromosome by any other of the nucleotides in the set: A, C, G, T. *Polymorphism* means that both the ancestral type (allele) and the mutated allele are found in the population, usually in such frequencies that a study of 100 or even fewer individuals would find both alleles.

In our species *genetic* (= DNA) *diversity*, meaning the presence of polymorphisms, has been so far observed in about 0.5% of the billions of nucleotides forming the 23 chromosome pairs of the first man whose genome was fully investigated and published (Craig Venter). This variation of about 15 million nucleotide sites means that in 15 different million specific sites the contributions by Craig's father and mother were different, and are due to mutations that occurred many generations ago. Extending full sequencing of the genome to many more individuals will certainly increase this estimate of polymorphic sites. We call a site *heterozygous* when the paternal and maternal contributions differ and we use the percentage of sites that are heterozygous as a measure of the genetic diversity of an individual.

Mutation rates are a property of nucleotide sites: they can change under special conditions, and it is possible that they are adjusted by natural selection to optimal average values. It is interesting to note that mutation rates, if considered per unit of biological time, which is the generation time (the average age of reproduction) of the specific organism we study, tend to be of the same order of magnitude for many organisms, even though the difference in duration of a generation time between, say, bacteria and humans goes from thirty minutes for bacterial generation, to thirty years for humans: this means that the rate of reproduction is roughly half a million times greater in bacteria.

There have been efforts to show that mutation is not always random but tends to be adaptive, i.e. a mutation useful for the organism is more likely to appear than other random mutations. There is no evidence today that this is true, in spite of many attempts (e.g. recent ones by Cairns). This is not to be confused with the fact that if a favorable mutation appears it will be picked up by natural selection and expand, until it becomes the norm in the species. One of the greatest geneticists of the last century, who unfortunately died about a year ago, Joshua Lederberg, worked on this problem in the last years of his life. The last time one of us had an opportunity to discuss it with him he said that it is clear that there are some 'funny things' in the mutation process judging from mutation rates, but nothing is clear. A reasonable guess is that a gene that is functionally active is more likely to mutate than one that is inactive, and one small attempt to test this hypothesis was made by Luca Cavalli-Sforza, but the effort remained inconclusive.

Mutation and natural selection, however, are not the only factors of evolution. The modern theory of evolution includes other factors: the major ones are drift, migration, and recombination.

Drift, more accurately called *random genetic drift*, is defined as the variation in the frequency of polymorphisms, through succeeding generations, which depends on the size of a population, intended as a social group whose members rarely marry outside the group, or accept foreign members for reasons other than marriage. This is or was in earlier times the tribe, basically a linguistic unit (tribe and language have the same name or names) that usually claims common ancestry. Population size, N, increased considerably during human evolution ca. 10,000 years ago, when a major change in food acquisition took place: the change from hunting-gathering and/or fishing to agro-pastoral economies, i.e. from food collection to food production. Until then, and throughout most of the evolution of the genus *Homo*, the size of N may have ranged from a few hundred to a few thousand per social group (the tribe), that is ca. 1000 as order of magnitude. The few surviving tribes of hunters-gatherers are of this size.

As we shall see, the evolutionary effect of drift is that of causing the reduction of genetic diversity, as estimated by the percentage of sites that are heterozygous in a sample of the individuals from the population. If prolonged indefinitely, drift would reduce genetic diversity of the population to zero, an ideal situation for a racist, who would probably consider attractive a greater genetic homogeneity of all individuals forming one's social group. But loss of heterozygosity is not at all desirable: the progeny of close relatives suffers from mortality and morbidity that are greater, the higher the degree of relationship of parents. By contrast, higher heterozygosity, found for instance in 'interracial' hybrids, is likely to show greater vitality under a variety of respects – a phenomenon already well known to Darwin, and called hybrid vigor. Human social customs are usually geared to avoid too close relationship of husband and wife, and it has been estimated that tribes of size above 400 or 500 can escape damage caused by marriage among close relatives. Moreover, there is almost always some immigration, mostly by marriages with persons from other, usually nearby tribes.

In the last 10,000 years, the passage to agro-pastoral economy caused a considerable increase in population size, not far from a 1000 X factor. Tribes of hunter-gatherers have often maintained their original tribe name, which is usually also that of their language, but the new economy allowed considerable growth. In Nigeria, for instance, the four most important tribes (Hausa, Yoruba, Ibo, Fulani) have now more than ten million members each, but there are many much smaller ones.

Migration is another major demographic factor of evolution. When migration takes place among different tribes, it usually tends to reduce drift. Traditionally, much of it is due to marriage with a member of another tribe, or to work, which has recently been in constant increase. If the % of in-migration per generation of a tribe is m, the larger is m the more effective is the avoidance of drift effects. A larger population size, N, has the same effect, and their joint result of m and N in counteracting drift is measured by the product Nm. In Italy, Nm varies from 0.1 (in mountain isolated villages) to >2.9 (in towns of more than 100,000). (Observed data can be found in Cavalli-Sforza, Moroni and Zei, 2004).

Much migration occurs on an individual basis, especially when it is due to intertribal marriage, and is a very powerful factor that reduces drift effects. But there is a type of migration that acts in an opposite direction, generating new opportunities for drift: the migration of a group large enough to form a new colony. This takes place especially if the colony is far enough from the motherland, and contact with it is rare, for instance in the case when conflict was the reason for leaving the motherland. Puritans who escaped religious persecution founded some English colonies in North America, and the same was true of the French and Germans who joined the original Dutch founders of South Africa.

Long before any recent historical case, a special process of continuous migration accompanied several expansions of our species to the world. The oldest expansion of the genus *Homo* was from Africa to the Old World, Europe and Asia, about 1.7 million years ago. We know little about it genetically, because the earliest Eurasian human species, called *Homo erectus*, has probably left no direct descendants. The ancestors of our species, that eventually became *Homo sapiens sapiens* (considered undistinguishable from anatomically modern humans), lived between 150,000 and 100,000 years ago in eastern Africa, and spread to all of Africa starting perhaps 100,000 years ago. But maybe just one tribe that must have been most advanced in language development started expanding about 60,000 years ago from East Africa and continued until it settled the whole world. While Australia and New Guinea were already settled by them 40,000 years ago, southern Chile, the most distant place from the East African origin, was reached 11,000 years ago, after crossing from Siberia to Alaska. The expansion covered a distance of about 25,000 km at an average speed of half a km per year: much of it probably took place along the coasts or rivers or oceans, and went faster as time passed. Major oceanic islands were reached later, mostly from S.E. Asia, beginning some 6000 years ago. Some very small and especially isolated island, like Pitcairn and Tristan da Cunha were settled only a couple of centuries ago by a dozen or so settlers, who afterwards increased in numbers at a regular rate.

The introduction of the agro-pastoral economy occurred at similar times in different areas of the world, and generated the major crops and domestic animals that still support us: wheat and barley, sheep, goats, cattle in the Middle East; rice, millet, chicken and many fruits in East Asia; maize, beans, squash, tomatoes and turkey in Mexico. They all probably developed from the same semi-conscious biological discovery: how living organisms are born. They mostly developed, probably independently, in near-tropical areas at mid altitude, where food was rich but population density outgrew the resources. The new economy spread slowly, about one km per year to Europe and to Central and south Asia, by a combination of demic diffusion (of people: the farmers themselves) and cultural diffusion (local hunter-gatherers learning about food production technology from immigrant farmers). In the Sahara, there were at an early time very sophisticated agro-pastoral developments, but the region dried up around 5-6000 years ago, and farmers had to go south. They were especially successful in West Africa, with limitations imposed by the poverty of the soil and the difficulties of raising crops and animals originating from the Middle East. Using local plants, agriculture reached the Nigeria-Cameroon boundary, where in the first millennium BC an ally joined it: iron use, coming from the Middle East via Egypt and Sudan. The Bantu expansion had its origin there and spread to central and southern Africa. But African agriculture remained poor, until manioc arrived in the XVIII century AD, probably brought by a missionary coming from South America. Manioc was domesticated in the central Andes, and made possible the expansion to the South American plains via the major rivers, before conquering most of Africa in three centuries or less.

Agriculture changed the world. Hunter-gatherers were professionally nomadic, having to shift continuously to new hunting grounds. They traveled in small flexible groups, with no chiefs – a perfect democracy they still practice. People who travel all the time can own almost no personal property. But farmers had to settle near their fields, could build permanent houses, property became an advantage and a rule, and a variety of new jobs developed, requiring specialized skills. Societies acquired fixed caste structures, with chiefs, which reached the apogee in India, where the caste system has now disappeared, but only in towns.

The introduction of writing, the earliest in the Middle East and Egypt around 5000 years ago, began history. Metals soon followed, first copper then bronze and iron, all discovered above the Middle East, beyond the Caucasus. War, loot and piracy became a way of life, making defense necessary. Pastoral life separated largely from agriculture and went its own way, turning into a style of life in arid lands. This takes us to the history we learn at school, of which the Bible became a major record. According to some researchers, Genesis was written in two versions, later intermingled and partially contradictory, and it relates to the histories of two different tribes of farmers, one of which had partially reverted to hunting and gathering, or perhaps to a strictly pastoral life.

3. Natural selection and drift: the relative importance of adaptation and chance in evolution

3a. *Serial Founder Effect*

It seems likely that the so-called 'Out of Africa' expansion that settled the whole world and generated all presently living humans progressed by a series of repeated migrations of relatively small groups, which started out from the most peripheral colonies, settling not very far in uninhabited territory. This would allow a pioneering small colony to remain in contact with relatives and friends, in general with what was 'civilization' at the time. It is very unlikely or even impossible that there was admixture between modern humans and descendants of *H. erectus*, who must have had a very low population density throughout Eurasia at the time. There is so far no evidence of admixture of our species with Neanderthals, who lived in Europe at the time it was first settled by *H. sapiens* and were certainly far more advanced than *H. erectus*. Neanderthal has now been shown to be sufficiently different from modern humans to be considered another species, although it separated from *H. sapiens* much later than any other branch.

There must have been a large number – at least hundreds, perhaps even thousands – of similar events of foundation of new colonies, one after the other, in the many directions in which expansion proceeded away from East Africa. Hunter-gatherers live in camps made of huts that are rapidly built, and move across a fairly large area that makes up their hunting ground. In the search for new ground, a group smaller than a tribe, and probably of small size, may have explored new territory at some distance from the mother tribe. If the new area was found suitable and the small group settled it, *a new opportunity for drift*, and therefore local loss of genetic diversity was created. In all cases when a group lives in an isolated island or region, or for social reasons (religious, political, etc.) breeds separately from the other local population, drift can create genetic as well as cultural differences, the magnitude of which depends on the size of the population.

This is shown by a large number of examples from medical genetics: quite a few instances of rare genetic diseases are found in genetically isolated populations in which a mutation arose a few centuries ago. If the group increased in numbers subsequently, it will be especially easy to find several cases of the same disease today. This is common in particular for recessive genes (that do not show in the heterozygous condition, but come to light in one out of four children, in marriages between two heterozygotes). Jewish people have traditionally good medicine and have discovered a number of new recessive diseases, some of which are found also in different populations, while others are present only among Jews, more often in individual Jewish groups that separated from each other in one of the several diasporas that spread Jews around the world in the last 2500 years.

Ashkenazi Jews, for instance, were subjected to one of the worst genocides in World War II, and their survivors are now mostly in the US and Great Britain. It is believed that they originated from a small group that migrated from Rome to central Europe, perhaps a thousand years ago. Genetic screening of members of the Ashkenazi community indicates that 50% of them are descendants of just four women. Several mutations that occurred probably during their expansion in N. Europe gave rise to a relatively large progeny carrying mutations rare elsewhere; some were not even found outside the Ashkenazi. These observations of cases of genetic diseases, found in a few populations that expanded recently, or more generally in ‘genetic isolates’, are referred to as ‘founder effects’.

3b. *Genetic and geographic distance*

It has lately been shown that the recent human 'Out of Africa' expansion has generalized the founder effect to the whole world. It is in fact reasonable to view the expansion of modern humans, from an original relatively small African tribe, as the sequential founding of small colonies, and therefore as a sequence of founder effects that ran across the whole world in the ca. 50,000 years period that it took to cover the 25,000 km between the place of origin of our species and the farthest places. The progression of the species by successive episodes of colonization, each of which gave rise to a founder effect because of drift, due to the usually small size of the early colonies, must have caused a linear fall of genetic diversity from Africa to S. America, first observed by Prugnolle and others (2003) by examining the HGDP (a collection of DNAs from 52 indigenous populations of the five continents, (L. Cavalli-Sforza 2004). The Stanford research team confirmed it by doubling the number of original observations obtained, with genes called microsatellites (a total of 783 of them, Ramachandran *et al.*, 2005) and later by examining 650,000 snps of the HGDP populations (Li *et al.*, 2008). The explanation offered, summarized by the name of 'serial founder effect', was tested by simulation. The average single founder step suggested by the simulation corresponds to an *Nm* of about 0.3, in reasonable agreement with anthropological information on surviving hunter-gatherer populations (Ramachandran *et al.*, 2005). There were most probably hundreds of these successive colonizations from beginning to end, on any of the different routes made by our African ancestors who settled the world, and the total of single founder effects must have been of many thousand.

The same papers (Ramachandran *et al.,* 2005, Li *et al.,* 2008) also showed that there is a very close correlation between genetic and geographic distances (measured as the crow flies, with entrance to the Americas by the Bering strait) of all the HGDP populations, when each is compared to each of the others. The correlation is 0.87 with microsatellites and 0.89 with 650,000 nucleotide sites. Such close correlations are most easily explained by simple drift, plus migration limited to geographically close tribes, and allow the suggestion that true natural selection effects during the great 'Out of Africa' expansion might amount at most to about 20% of the total genetic variation observed today among indigenous populations. This has been the first large-scale attempt to estimate the relative importance of selection versus drift in the origin of the genetic variation observed in a species. Our species is the one that lends itself best to such computation, because of the availability of the necessary demographic estimates of population sizes and migration, difficult to obtain in other species.

3c. *Drift in the Parma Valley*

One of the present authors (LLCS) was responsible for the very first attempt at measuring the relative selection/drift ratio in humans. The opportunity arose thanks to the information and support offered by one of his first students of Genetics at the University of Parma in 1951-52, the Catholic priest Don Antonio Moroni, who made him aware of the existence of demographic data, that had potential interest for genetic study, collected by parish priests over the centuries and available in the Catholic Church records. Demographic data from 74 parishes of the Parma Valley, covering the last 400 years, were used in the research: population sizes, migration, and frequencies of consanguineous marriages. Genetic distances among the parishes were calculated for 14 blood group genes then available, obtained from a total of 2875 individuals. The parishes varied in population size, from less than a hundred to several thousand individuals, with a strong stratification of village size and migration by altitude. It became clear that demographic data, based on 400 years of demography (population size and migration), could predict very well the genetic variation within and between villages (parishes) on the basis of drift alone.

In addition, computer simulations (Cavalli-Sforza and Zei) were made to test how long it would take, given the observed migrations and population sizes, to reach an equilibrium value. Both migrations and population size affect variation among populations (smaller village size increases variation among populations, here represented by parishes, but increased migration acts in the opposite direction, reducing it). The greatest variation among villages (parishes) is observed in the highest, mountainous part of the valley, where they are also smaller; in the intermediate altitude part (hills), the size of villages and the genetic variation among them are intermediate; while in the plains population density is highest and parishes are proportionately largest, and there is no measurable genetic variation among parishes over that expected by random sampling in a homogeneous population.

The computer simulation of the blood group data, starting from complete genetic homogeneity of the population, showed that the variation among mountain villages increased regularly over generations and came to a stop, as expected in conditions of equilibrium between drift and migration, after about 250 years (8 generations). The observed variation among villages agreed with that expected on the basis of the simulation. There was a mistake in the original study that gave a small difference, but it disappeared in the most recent analysis of the data (Cavalli-Sforza, Moroni and

Zei, 2004). This book contains all the data collected by our group in Italy in the last 50 years; they were gradually extended to much of the rest of Italy and to other sources of data, like surnames, dispensations for consanguineous marriages, etc.

With a population like the one studied for blood groups in the Parma Valley, and with the numbers of individuals tested, drift provided therefore a sufficient explanation of all the observed genetic variation for standard blood groups, leaving no evidence of natural selection. Some natural selection could be shown in early, classical observations on blood groups, but only by using special approaches, like mortality and morbidity of RH+ children born to RH- mothers. Such an effect would hardly show in the approach used in the Parma Valley. By contrast, in the analysis of 52 world populations, with all the genetic variation tested by 650,000 nucleotides, some natural selection effects did appear and are now being examined further in a paper being prepared for publication by J. Pritchard. Serial founder effect did not provide complete explanation of variation among the HGDP populations, but left a fraction of about 1/5 of the genetic variation potentially explained by natural selection, 4/5 being explained by drift.

For readers interested in the origin of this estimate, it is calculated from $1-r^2$ where r is the correlation coefficient between genetic and geographic distance, under the assumption that geographic distance can explain genetic distance entirely. But 1/5 is actually an overestimate for the contribution of natural selection, because a substantial part of it is explained by the red dots of Figure 1 of Ramachandran *et al.* deviating from the straight line, and they are due to the fact that the three oldest African populations have separated earlier and have been exposed to drift for a longer time than the rest, thus building a greater genetic distance from the other African populations.

3d. *A clear example of natural selection: lactose tolerance*

Direct study of individual genes known to be under selection shows it is possible to detect the place of origin of a mutation that is known to have increased in frequency because of higher fitness. By observing how it spread around, the selection coefficient (fitness value) can be calculated. Examples of natural selection clearly demonstrated so far are of individual genes that became known in other investigations, and the evidence comes from finding that mutants of the gene cause specific diseases. Among these, the most interesting one is for an snp that is a regulatory mutation of the gene making the enzyme lactase, which allows metabolizing the milk sugar lactose. The enzyme-producing gene is located in the second chromosome, and a gene that regulates its production is located very close to it, within another neighboring gene (Peltonen *et al.*). The ancestral regulatory nucleotide site is responsible for suppressing the production of lactase after weaning, once milk is no longer available to the growing organism. The gene is found in all Mammals, as well as in the great majority of humans, because the consumption of milk after weaning is limited to a vast area centered around the Middle East, where sheep, goats, and cattle were first raised. In this area it is common to find a mutation of the regulatory gene, that does not stop the production of lactase after weaning, so that carriers of the mutant continue producing lactase and can therefore utilize the milk sugar for all of their life.

It has been shown that the mutation arose in an individual living somewhere in the Ural Mountains about 6000 years ago, probably a member of a reindeer shepherds' tribe that must have started consuming milk in adulthood. Adults of the ancestral type, that lose lactase production after weaning, suffer gastro-intestinal pains and other complications when they try to consume milk – at ages at which the lactase enzyme is no more produced – so they tend to abandon the custom. This condition is called *lactose intolerance*, while the capacity to consume milk as adults, without troubles and enjoying full benefit from the calories available upon digesting lactose, is called lactose *tolerance*. This capacity is especially advantageous in cold climates, which is where the mutation probably arose and therefore prospered particularly well.

The tolerance mutant is now very frequent in Scandinavia (90-95%), which is nearest to the place of origin, and in Great Britain, that saw the arrival of many Scandinavian Vikings. Its frequency decreases otherwise from the center of origin, being somewhat lower in other parts of northern Europe, close to 50% in northern Italy, and 20-25% in southern Italy, Sardinia, and other parts of S. Europe. The fitness increase determined by the mutation to tolerance has been calculated on the basis of the population size of the initial population to be between around 1.5 and 4% (Bodmer and LLCS, 1976. Other recent similar estimates have used other criteria). Similar recent estimates were obtained more recently, and this is one of the few advantageous mutations whose fitness has been estimated. It is interesting to remark that the selective advantage is realistic only in an environment where milk is available to adults for consumption. The environment is a special one, generated by human innovations, and there are probably many other examples of the same type.

3e. *Genetic variation between and within populations*

Further evidence that drift has a major effect is worth mentioning. It concerns the genetic variation *between*, and that *within* populations. The variation of gene frequencies among populations is estimated by a standard analysis of variance, and can be conceived as an average of the genetic distances between all possible pairs of populations examined. The genetic variation among populations has a close, formal relationship to the genetic diversity within a population. The variance between populations was estimated on HGD data with the 650,000 snps (Li *et al.*, 2008), separately for each of the 23 chromosomes. All the 22 autosomes (chromosomes other than the sex chromosomes XY) gave a variance between populations as a fraction very close to 11.7% of the total, with extremely little variation among chromosomes (standard error of the average ± 0.11%), with the only exception of the X chromosomes, which was 15.6% +- 0.53%, and will be discussed later.

In humans, the variation between populations is smaller than that observed in practically every other Mammal, for a good reason: differences among human populations have had very little time to build up, as the evolution of the species has been very short, and the separation among human populations is quite recent. The original observation that the fraction of variance between populations is very small was originally taken as the main reason to avoid using the concept of race for the human species (Lewontin, 1975). The first estimate used by Lewontin for the variance between populations in humans was 15%, and later results were also obtained on protein data for a long time, and were very similar to this value. Races are defined as relatively homogeneous subgroups of a species, clearly distinguishable from each other. They are sharply defined in domestic animals, where breeders have much interest in keeping their breeds homogeneous and easy to recognize. But the situation is very different in humans, where it seems impossible to establish useful races. Darwin had already noted that experts have trouble reaching an agreement when they try to classify humans into races, and mentioned that in his time the number of races varied from 2 to 63, according to different accounts. We cannot do any better with genes. Attempts at distinguishing races are also encouragements to racism, a serious social disease.

Our estimate of variation between populations based on DNA, 11.7%, is even less than the 15% estimated by Lewontin, working on proteins. Most of the older data are from protein polymorphisms: the genetic unit of transmission tends to be therefore the protein, which often has more than two alleles, being long DNA segments usually made of hundreds or thousands of nucleotides (see for instance AB0 and many other blood groups, etc.); on the other hand, single nucleotide polymorphisms analyzed in DNA sequences usually have only two alleles, partly because mutations are so rare but also for technical reasons that are not relevant here. This consideration can probably explain the higher value of the protein data, compared with DNA.

3f. *Sex and recombination*

Recombination, the reshuffling of genes that accompanies exchanges of genetic material between individuals, is another powerful source of variation, to be kept different from mutation. Genetic differences arise through recombination because new combinations of variants appear, as different mutants at different nucleotide sites come together, and thus no true DNA novelties are involved, but simply exchanges between preexisting DNA segments. Yet, by bringing together different gene types, recombination allows to test an enormous variety of combinations, from which new genetic types with predictable and unpredictable advantages can arise. Every enumeration of the new combinations of genes made possible by recombination generates numbers that are more than astronomical.

In sexual reproduction, there are exchanges between the maternal and paternal chromosomes, but every progeny gets a complete set of DNA from each parent. In the absence of sexual reproduction, all descendants of a single individual are identical, and by tracing the genealogy of individuals of an asexually reproducing group or species it is possible to reconstruct when and possibly where the mutations occurred and created different genetic types (called 'haplotypes' when they are defined on the basis of more than one mutation for a specific chromosome). We have an equivalent situation in humans for the Y chromosome, a chromosome found in a single copy and in males only, which is transmitted from father to sons. In such a case one can go back from all Y chromosomes existing today to a single ancestor, from whose Y chromosome all Y chromosomes living today descend. It is not that there ever was a single male from whom we all descend, an Adam; but Y chromosomes descending from those of other men who were living at the same time as Adam have no descendants left today. As often enough some men have no sons, and more generally the number of sons varies from individual to individual, we can always find how far back we must go before we find a single common ancestor to all Y chromosomes existing today, and how long ago he may have lived.

The same can be done for mitochondria, cytoplasmic particles descended from an ancient bacterial symbiont, found in practically all Eukaryotes (animals, plants and fungi), which are transmitted by mothers only to all their children. Mitochondria can provide information on a 'mitochondrial Eve', but here again this should not be taken as evidence that at some time there lived only one woman, but simply that the mitochondria of all of us descend from that of just one woman. If one were tempted to infer that this is proof that the Bible section on Adam and Eve was right, one would be very disappointed to learn that Adam may have lived about 125,000 years ago, and Eve 175,000 years ago.

Y chromosome and mitochondria are very useful for understanding the evolution of modern humans. But they do not have the advantage of recombination, because they stand alone and cannot mix their genome with anybody's. We reproduce sexually, like most Eukaryotes, and this gives us the full advantage of recombination for all the other chromosomes. Each of us has two specimens of each chromosome, so that every cell in our body has practically 2 x 332=46 chromosomes, that is 23 pairs of chromosomes. Twenty-two of them are called *autosomes*, the 23rd is an asymmetric pair of chromosomes, made of two members of different size, shape and gene content: X and Y, which determine sex. This condition forces males and females to perform a special trick, called *reduction* or *meiosis*, when preparing *gametes*, or cells that will fuse to generate a new individual: sperm and egg cells. A gamete contains only one chromosome of each pair. Thus every gamete has 23 chromosomes, one for each pair.

Genes on different chromosomes behave independently from each other, as Mendel found in his experiments: we usually describe this as his third law, or the *law of independent assortment of different genes*. Morgan showed that this is true for genes located on different chromosomes, as well as for genes on the same chromosome, if they are located far enough from each other, but it happens less and less the closer they are to each other on the same chromosome. The fact is that assortment is possible for genes on the same chromosome only when a phenomenon called *crossing-over* occurs, in which the paternal and maternal members of the same chromosome pair exchange a sizeable chunk of DNA, so that genes that are close to each other are more likely to cross over in bulk, switching between corresponding chromosomes.

As remarked above, the number of possible combinations that can thus arise because of independent assortment of genes is incredibly high, and this is what made sex so popular, because it multiplies enormously the possibilities that natural selection can explore. William Hamilton has strongly supported an idea expressed by others before, that the real reason why sex has become so widespread is that our major enemy are parasites, and recombination enhances our possibilities to increase our resistance to them, by combining in the same individual different ways of fighting a specific parasite (e.g. biochemical, and/or many different immunological defences).

There is a simple way to convince us that this hypothesis is very reasonable, and probably correct. Consider the history of medicine in the last 150 years, after the discovery of microbial diseases, and the progress of surgery thanks to the introduction of hygienic measures and anesthesia. Prior to this the average life expectancy at birth was only slightly greater than that which was standard for a very long time, and is still true in the most primitive conditions: about 18-20 years. Today it is close to 80 years, four times more, in developed countries. The average number of children born per family had to be at least of 6 in order to keep the population from decreasing in numbers, remaining approximately stationary in size, because about 2 out of 3 of the children died before they could reproduce. We find the number of children to be in this range among modern hunter-gatherers, who do not reap the benefits of modern medicine (but still need to not reproduce at will, because the carrying capacity of their environment keeps getting narrower). On the contrary, with the very low mortality observed today in developed countries, the number of children born per family can be just a little bit higher than 2 per family, in order to keep population numbers stationary. This happens because mortality has decreased dramatically in developed countries since medical control of infectious diseases took hold. The impact of other sicknesses, such as heart diseases and cancer, has been decreasing to a far lesser extent, but these bear less on population growth, because they occur more frequently in post-reproductive ages.

The success of modern medicine in raising life expectancy points to the fact that parasites are the major risk that *any* species encounters, and therefore the one against which natural selection is mainly directed: all mutations that increase resistance to parasites will automatically be favored, proportionately to the number of lives they spare. But recombination is more powerful than mutation in producing novelties: by rearranging genes on chromosomes and assorting combinations of different mutations it gives a faster response to needs. Natural selection is there to favor automatically those gene types or combinations that increase the probability of survival. The big impact of risks due to the parasite load in the environment indicates that Hamilton's hypothesis may be correct in detecting the major culprit that made sex so popular, at least in Eukaryotes, where a marvelous mechanism of gamete formation makes sex so efficient as a genetic mechanism, by making a precise recombination possible.

In organisms like Bacteria, that do not have such elegant mechanisms of gamete formation, more primitive yet efficient methods of DNA transfer or exchange have spread widely. One of them, the transfer of antibiotic resistance among bacteria, is extremely efficient and is the major danger to the efficacy of the most successful avenue of medical treatments that humans have invented. Recombination made possible by sex is good for humans, and for all victims of parasites in general, but is also good for parasites and their vectors.

3g. *Sex, drift and the 134 rule*

As mentioned above, tests on all the 23 chromosome pairs for 650,000 single nucleotides showed that the 22 non-sexual pairs (called autosomes and indicated in the following as A) showed very closely similar variation between populations, with very slight variation among autosomes, 11.7% of the total variance (Li *et al.*). The same variation was definitely higher for the X chromosome, close to 15.6% (Li *et al.*),

Why is the X chromosome more variable than autosomes among populations? The difference may seem trivial, about 15.6% instead of 11.7%, but these values have been estimated on tens of thousands of genes and are therefore very precise. Considerations like these can be extended to give the *a priori* expected value of the variance between populations for the various types of chromosomes, including the Y chromosome, which is transmitted in males as if they were a population four times smaller than that of the As, and 3 times smaller than that of the Xs. The variation among populations should be like that of the averages of samples of size 4, 3, 1 for A, X, Y, and therefore proportional to the reciprocals of these values, 1/4, 1/3, 1, which can also be written in the simpler form 1:3:4. This explains why the X chromosome has greater variation among populations than the average A, exactly like the ratio of the numbers 4 and 3. 4/3 equals 1.33, and should be equal to the ratio of the variations of X and A, which are 15.6% / 11.7%=1.37.

Unfortunately we do not have adequate Y chromosome data for the 650,000 nucleotides, which should have a variance among populations equal to four times that of Y. But there are unpublished data collected by Chiaroni *et al.*, on the major haplotypes of Y chromosome in ca. 30,000 individuals belonging to 800 indigenous populations, which give a variance between populations of 38.9% +- 2.5%. This value has a fairly large standard error, and is only slightly smaller than expected by the 134 rule (4 x 11.7%=46.8%). The difference is significant but the Y chromosome nucleotides on which it is based are not strictly comparable to those tested for autosomes and X; there are reasons that will be explained with greater detail elsewhere why the Y chromosome variance estimate could be smaller. Also this approach, therefore, confirms that drift plays a major part in determining human genetic variation among populations.

3h. *Kimura on molecular evolution*

In 1963-4 LLCS had Motoo Kimura as a guest in Pavia for eight months, and told him of the results of the observations carried out in the Parma Valley, showing that drift was responsible for probably all of the genetic variation observed for blood groups there. At the time a number of papers was being published reporting counts of amino-acid differences among proteins of different species, which were used for reconstructing evolutionary trees of a variety of species. Kimura had developed the idea, to be proved reasonable much later, that many mutations causing amino-acid replacements have very little if any selective effects, and a few years later he published a very elegant theorem (*Nature*, 1968) thanks to which he showed, based on this hypothesis, that the rate of molecular evolution is equal to the mutation rate. Of course it is not true that all or most mutations are selectively neutral, but it is true enough that his statement cannot be shelved, after some correction. When it was published, a symposium was convened at Berkeley, where practically every geneticist in the room reacted very loudly against this dethronement of natural selection. Today we have situations, like some of those here shown, in which it is very difficult to deny a role of chance greater than natural selection at least in some situations, without any attempt to really dethrone natural selection, which is the basis on which living organisms were built and prospered.

In 1970 a book by Jacques Monod appeared, named *Le hazard et la nécessité* (a title he borrowed from Heraclitus and applied to genetic evolution). As a molecular biologist, mutation was the only source of hazard he was familiar with; but it is a very powerful one. We now must add drift in its several manifestations: one might prove that it was active even in the situations that were so useful to Darwin for convincing himself and others of the power of natural selection. Here drift, considered more generally as a consequence of population size, can be shown to be very powerful in making the effects of natural selection particularly evident: it takes a much shorter time for a useful mutation to replace the ancestral type in small, isolated populations as those of the Galapagos islands than in the larger ones inhabiting large expanses and whole continents, not to mention cosmopolite species like ours.

Our analysis of this big genome evidence, which is currently proceeding, is far from complete, but it tends to confirm that natural selection has not had great effect in causing genetic variation of modern humans. The expansion of modern humans has been accompanied by adaptations to local climate and diet, part of which are genetic, but more largely are the consequences of major cultural adaptations, for instance the use of fire, clothing, housing, and more recently government, urbanization, writing, war and transportation technology, which have all helped to decrease the need for purely physical adaptations, during the process of settling the whole Earth. It is difficult to state which part of biological evolution is today under control by cultural evolution, but it must be large. Our biological evolution may have been slowed down in some aspects, and greatly ignited and/or changed in others, by our unique cultural evolution.

3i. *Proofs that all mutations are spontaneous*

An experimental procedure introduced by Joshua and Esther Lederberg in bacterial genetics, called ‘replica plating’, has made it possible to show that mutations easily selected in bacterial populations and that are of considerable importance for us are those that determine resistance to antibiotics and in general to antibacterial agents, and are indeed produced by spontaneous mutations. The technique consists of using standard plates filled with a medium containing the usual nutrients for bacteria in addition to agar that makes the medium solid, and use them to grow bacteria on the surface of the agar as a patina, at most a millimeter thick. Areas in the plate where a mutation for resistance to, say, the antibiotic streptomycin has arisen can be easily discovered. One takes a sample of the patina grown on a normal nutrient agar plate, by applying to the surface of the patina a piece of tissue like velvet, or of filter paper, pulling it out .and transferring a sample portion of the patina to another fresh, sterile agar plate containing streptomycin (Sm), and making sure one identifies corresponding areas on the original, Sm-free agar plate and the one with Sm. On the latter, only Sm-resistant colonies will grow, wherever there was one or more resistant bacterial mutants. Although the mutation rate to Sm resistance is very low, the patina had a sufficiently large number of bacteria that many mutations to resistance occurred during the incubation of bacteria that produced the patina, and may have generated locally descendants that are also resistant, if mutation to resistance is a spontaneous event (all descendant bacteria from the original mutant must be resistant, as expected for a genetic mutation). This technique will work with bacteria that tend to remain where they are born and do not move around. It becomes then possible to grow in the complete absence of streptomycin 'sibs' (co-descendants) of the resistant mutant who are also resistant but have never been in contact with streptomycin. In fact one can reasonably hope to find them, as they must be located in the area of the original plate corresponding to the position where the resistant colonies grew on the Sm-plate to which the original patina was replicated. In fact one does find them, and simple sequential repetitions of this replica plating procedure allow to enrich progressively the frequency of resistant mutants thus recognized, making it possible to select strains that are made entirely of resistant mutants of the original bacterial strain, and must have arisen spontaneously because they were never in contact with the antibiotic.

This experiment proves that bacterial resistance can arise spontaneously but does not prove that *all resistant mutants* are produced spontaneously. Transforming the experiment so that it is carried out in liquid medium rather than on agar plates, one can make the experiment quantitative (Cavalli-Sforza and Lederberg; 1954) and test if all mutants are produced spontaneously. The result was positive; initially it seemed that only a fraction of mutants were spontaneous, but it was later shown that, as one might have expected, this was due to the fact that resistant mutants, like the great majority of mutants, grow a little less fast than the original strain, and even a small difference of growth rate has profound effects on the results, given the very high growth rate of bacteria.

But in patients resistant cells can grow even if they are a little slower than the original type, as long as the presence of the antibiotic in the treated patient protects them, and later mutations make easily the resistant strain more competitive. It is worth stressing that we also know that multiple bacterial resistance to many antibiotics is now spread rapidly by non sexual or para-sexual mechanisms of 'lateral' transmission of DNA segments. Unfortunately this is becoming a major threat to the conquests of medicine in the last century, which made it possible to cause the most complete disappearance as causes of death due to infectious and parasitic agents.

The experiment was repeated successfully on chemotherapeutic-resistant tumor cells using cancer cells cultivated in vitro, and demonstrated that also this major cause of therapy failure is due to spontaneous mutations to resistance of cancer cells, similar to the phenomenon in bacteria.

4. Religions and evolution

A survey of belief in evolution inside a number of developed societies (Miller *et al.*, 2006) has given surprising results. Europeans show that the frequency of people who believe in evolution varies from roughly 60% to 90%, with an approximate average around 75%. Italy is near the European average. The most unexpected result is that the lowest percentage of believers has been observed in the United States (40%), lower than in the only Islamic country surveyed, Turkey (52%).

This result seems in stark contradiction with the level of development of science and technology in the United States, which is probably greater than in any other country, but its major cause is not difficult to locate: it is the influence of the southern Baptist religion and some other less important Christian sects. These religious groups do not accept any minor deviation from the strictly literal acceptance of the Bible. The Bible has not had that downgrading effect on the people who played the major role in generating it, Jews, who are far less affected by the first sentences of Genesis. The history of the settlement of the US, into which puritans of various origins took part, helps to understand why most States of the southern USA share a wide belief that the age of the Earth cannot be older than 6000 years, as estimated on the basis of Bible genealogies and of the initial statement in Genesis that the world was created in one week. A theme park in the southern US shows scenes of children of fewer than 6000 years ago playing with dinosaurs, a tale which is passed as 'science', and as such can only help to create idiocy. The 'intelligent design' theory is an important and influential part of this trend, and was probably catapulted to public attention by the interests of political lobbies.

Almost every religion did not accept Darwin's conclusions at the time they were produced, and there was widespread outrage, as Darwin of course had anticipated and feared. The Catholic Church was no exception at the time when Darwin's work was published and until the middle of last century, but in more recent times it has been going through a wide revision of its original stance. Recently its highest authorities have formally accepted that evolution is a fact, not a hypothesis, and the 2008 meeting of the Pontifical Academy of Sciences dedicated to evolution has contributed to reinforcing this statement, although there may continue to be subtler individual variations of opinion, as might be expected.

There remain however some basic differences of importance between religious and scientific views in the interpretation of the mechanisms of evolution. The present paper tries to show that basic differences that are still common can be removed simply by more precise explanations.

Natural selection is the only evolutionary mechanism that generates automatic adaptation and is, in a sense, strongly deterministic in this direction. Practically all other evolutionary factors do not necessary help or oppose adaptation, and all contain elements that could be called 'chance'. In fact the findings of our research show that factors that can be described as chance are often quantitatively more important than natural selection in shaping our genome. This is still a cause of disagreement among geneticists, although the importance of chance is gaining support; and obviously of major disagreement with the very few scientists who are still fond of the Genesis 6000 years date. One reason to dislike the influence of chance, especially in some religious circles, seems to be the strength of admiration towards a hypothetical 'biological order'.

It should be more widely realized that often chance is introduced as the scientific way of treating situations in which the causal system is too complicated to be analyzed in detail, i.e. when it is complex enough to defy our descriptive skills. In this case use is made of statistical approaches that are known to be potentially of aid precisely when the causal system is too complicated to be tackled in detail, i.e. when there are too many causes that interact in producing the phenomena being studied. Probability calculus teaches, by well-known theorems, that in these situations continuous probability distributions, like e.g. the normal or Gaussian and the lognormal, may be useful. Statistical correlation methods can sometimes help in disentangling causes and effects, although experience shows they must be used with real caution, especially in human genetics, as exemplified in the classical case of the Intelligence Quotient (L.L. and F. Cavalli-Sforza, 1995).

Ignorance of causes is not an issue when chance is built into the specific phenomena under study by *random sampling*. Mendel knew that when he studied segregations of characters in crosses he had to look at large numbers of individuals, in order to beat irregularities generated by the random sampling process, and find the laws he eventually did find. He made a few mistakes that led him to overcorrect his data, as Fisher showed (1936), but they generated no mistakes in his major conclusions. There cannot be any question that when natural populations or experimental sample sizes are small we are going to find, on average, greater random oscillations in evolutionary processes due to genetic drift, perfectly predictable by probability calculus. We should not become unhappy or suspicious if in these cases chance takes its toll and may generate superficially strange results. Drift may be defined simply as random samplings of gene frequencies accumulated over generations. It seems that even the fact that mutations are random (although there is a small chance, never really proved so far, that some – certainly very few – mutations may have a partly adaptive origin) should not trouble the minds of theologians.

Scientists are aware that ideologues do not accept scientifically ascertained facts when they are contrary to their favored beliefs. For this reason it is safe for scientists to refrain from political or religious ideology. It is necessary to keep science anchored to facts that can be observed with our senses (the world of nature), and to the search for rational explanations of them. The scientific way of proceeding democratically is the major guarantee of rationality. But scientists must stick to the reality of nature; they would betray science if they accepted supernatural explanations, which contain unverifiable hypotheses. Science cannot deal with supernatural facts, because they cannot be reproduced at will.

Ambitions, greed, prejudice, jealousy, dishonesty, dangerous ideologies (e.g. Lysenko's attempt at destroying Mendelism on the basis of Marxism principles) occasionally take the hand also in science. Still, there is a very good chance that sooner or later – maybe some time in the future, maybe after our death – truth will be recognized because of new, better experiments or simply because of a stricter use of logic by scientists.

One reason why some may consider chance a nuisance is that it seems to detract from, or even to destroy the idea that there is 'biological order', and other closely related assumptions which have a definite teleological flavor. It should be clear that it is better to avoid this kind of simplistic thinking that may easily invoke unnecessary supernatural explanations. Scientists can only try to interpret natural phenomena without recourse to supernatural causes, and nothing in biology has so far requested to resort to them, when enough time is dedicated to a problem. Louis Pasteur, to whom we owe so much in microbiology and medicine, and who was also a very devout believer, found himself unable to isolate chemically the enzymes active in the fermentations he had discovered because he found no ways of opening cells without destroying the enzymes they contain, and came to the conclusion that enzymes were created anew every time. This would positively have kept God's deputies very busy. But after Pasteur's death German chemists were able to develop subtler chemical methods of purifying enzymes and studying their structure.

What about the idea of 'biological order'? Is it really destroyed if we postulate that a lot of biological evolution takes place by chance? More than of 'order', when we marvel at the degree of perfection of certain organs and functions, e.g. of our eye, one should speak of 'biological efficiency'. Incidentally, our eye is a poor thing compared with the eye of most birds. And the organization of many organs and systems is far from perfect, in any species. The immune system, for instance, is a magnificent biological accomplishment that uses a new Darwinian structure, independent from our general development but operating inside us, for producing with special mechanisms of 'mutation' and natural selection new, specific antibodies against the parasites that attack us. But the system is not perfect and errors give rise to diseases (e.g. autoimmunity) that need medical help. Any biological mechanism has sufficient faults and imperfections that are hardly proof of divine intervention in generating them, as is perhaps in the intention of admirers of biological 'order'.

One of the best biologists of the XX century, François Jacob, together with another great scientist, Jacques Monod, discovered the mechanism whereby bacteria can produce a specific enzyme (e.g. lactase, that utilizes the sugar lactose) only when necessary, that is, only when the substance that the enzyme attacks, lactose, is present in the medium. After this breakthrough, other methods of regulating enzyme presence or action have been discovered (these enzymes are called 'inducible') while other enzymes are always present (and are called 'constitutive'). Inducible enzymes allow to spare bacterial energy and activity, and are useful especially if the enzyme substrate is seldom present, but require the ability to 'sense' the presence of the enzyme substrate in the medium – a primitive step towards rational organization of behavior. Jacob described the biochemical mechanisms he and Monod discovered as examples of 'bricolage' – do-it-yourself mechanisms that are assembled by using new tricks or old bits of machinery already available inside the organism, redirecting them to the new jobs. Usually this happens by exploiting new mutational changes that, if proved helpful, will be propagated by natural selection and can be improved further in many ways by new mutations. After a long series of improvements these mechanisms become rather efficient: the process by which efficiency is thus achieved is called simply 'trial and error', and we ourselves practice it many times when we busy ourselves with bricolage at home, to solve simple problems, usually of mechanical or electric nature.

Bricolage occurs all the time also in biological evolution, and not only in cultural evolution, where the name first arose, and where new ideas, small or big, have the same function as genetic mutations in biological evolution. Again, in cultural evolution our innate and acquired tastes, which form our personality, affect the choice of new ideas, and we call the acceptance/rejection process of new ideas *cultural selection*, a clear analogue of natural selection. But the inventions and choices made by cultural selection are still subject to a higher check: and this is, of course, natural selection, which can destroy few individual lives when we accept excessive risks (e.g. drug overdoses, or houses falling down on the careless builders), or many lives, even the whole human species and many other living organisms (e.g. with the worst of all cultural choices: that of starting a major international nuclear war).

Confronted by the extraordinary examples of biological structure and function, many prefer to accept the idea of a direct intervention by God, for whom it must have been simple to create from scratch an apparently intelligent mechanism that works beautifully. But unless we try to understand the real mechanism, with all the complications that nature has put into it by its bricolage, we will not be able to repair its malfunctions: then we will give up medicine. This suggests to be critical of excessive admiration of biological order.

Probably the idea of biological order was a wrong impression generated by early taxonomists like Linnaeus, who first generated kingdoms and phyla, classes, orders, families, genera and species of living beings, all beautifully organized in a perfect hierarchy, reflecting original creation, of course, and therefore believed to be immutable. The reality is different: today. With a better knowledge of DNA, it has become impossible to build perfect hierarchies, and specialists disagree as strongly as ever, especially for the lower organisms But at least we understand why there are no perfect hierarchies: there has been a fair amount of 'lateral transfer', that is, acquisition of pieces of DNA, or whole sets of them, from other totally unrelated organisms. Thus some small organisms, which parasitized much larger ones at first, later probably became symbionts. Having become a forced and indispensable part of their hosts, they have lost their independence and even their identity, bu we cannot do without them. The two clearest examples are: mitochondria, that take care of a major part of energy production from simple sugars for all animals, plants and smaller Eukaryotes; and chloroplasts, that have the task of catching sun's energy to build substances that make plant and animal life possible. In spite of these difficulties generated by a complicated history, it is clear that analysis at the genome level is making the study of evolution an exact science.

4a. *What is chance, after all?*

While natural selection tends to always increase adaptation, mutations and other factors introduce strong random effects, which may also be called, with slightly different connotations, hazard or chance. We prefer the latter term: in Italian, the word for chance is 'caso', which has a similar origin. The English word 'chance' stems straight from the same French word, 'chance' (in old French this was 'cheoir', derived from Latin 'cadere', 'to fall', with the same origin as 'caso'. Hence the Italian word 'accadere', to happen, which is perhaps related to 'hazard').

Before we come to a full understanding of the relative importance of natural selection and chance in evolution, we should discuss the concept of chance further. Mathematically, the introduction of chance brings us directly to the probability calculus.

We have seen three major evolutionary factors which bring chance into evolution: mutation, recombination, and drift. To these, we may add cosmic events: for instance, we know that about every many million years a huge meteorite is likely to hit the Earth; this has apparently taken place a number of times in the history of life, with dramatic impacts on the course of evolution. Though the likelihood of these events can sometime be measured, there is no way to tell when the next one will take place or what developments will take place as a consequence.

We have two ways of dealing with the occurrence of chance in evolution. One way is that all phenomena that are determined by the interaction of a large number of causes, none of which is clearly identifiable, can still be brought to rational analysis (i.e. mathematically, by probability calculus). The second, more direct way is when we count numbers of individuals showing different characters. We then have 'sampling' problems, whereby results in terms of 'counts' of individuals will change unavoidably almost every time we repeat the same experiment. Here again: probability calculus gives clear, helpful predictions of sampling problems. In fact, random genetic drift is essentially a 'random sampling' problem, built into the way organisms produce the next generation. The sampling nature of reproducers who generate successive generations giving rise to drift is a classical statistical problem, complicated by the fact that the sampling effects accumulate over the successive generations: the difficulty is handled by mathematical methods dealing with 'stochastic processes', which were developed largely for dealing with genetic problems.

One can also describe the effects of chance by older statistical methods, for instance correlation between different variables: for instance, the strength of inheritance by comparing the value of specific characters in parents and children. This can be done for qualitative traits like those chosen by Gregor Mendel, which were due to changes in individual genetic units, but were sharp enough to be defined by alternative adjectives, such as green vs. yellow for seeds, or tall vs. small for major differences in plant height. We are again struggling with sampling errors. Or we may struggle with variation in measured ('quantitative') traits like stature or any other anthropometrical trait, such as were chosen by Darwin's cousin, Francis Galton. In order to study the inheritance of quantitative traits, Galton and a statistician, Karl Pearson, developed methods that did not survive criticism by Fisher, who generated a large number of modern statistical methods, and also solved in his 1918 paper the problem of treating the inheritance of quantitative traits by incorporating Galton's approach into standard Mendelism.

4b. *It is probably a good thing that mutation is random*

It seems that not only scientists should take interest in the hypothesis that mutations are basically random. Any thinker dedicated to finding rational designs in the construction of the Universe should appreciate the idea that mutations are random events. By being random, mutation gives similar chances of being beneficial or not to all species. It is thus fair, giving equal chance of success to different species competing with each other, and to individuals of the same species. It is intuitively conceivable (but certainly difficult to prove), that this 'universal' democracy established by the randomness of mutations tends to prolong equally the probability of survival of all species and individuals. Thus, it also may give more stability to the system of all living organisms, that involves many millions of species. Species interact competitively but also need each other, and their numbers may vary greatly over time and space. And yet every species needs so many other species for its own survival that there is likely that there is a condition of general stability, permitting a slow, overall increase with time of biological mass as well as of general complexity.

In any case, there is evidence that mutation rates are under control by natural selection, and that at times when survival of a species is difficult mutation rates tend to increase. This is probably again an automatic reaction generated by natural selection: if mutants are favored by changes in environment and there is genetic variation of mutation rates in the population, increased selection of mutants may also automatically increase mutation rates because at least some of the mutants will have arisen in individuals that are genetically predisposed to a higher mutation rate. This indicates another way in which natural selection may contribute to increasing adaptation. It is encouraging that the greatly improved possibilities of studying whole genomes will increase the chances of studying more accurately also mutation rates and their natural selection.

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DISCUSSION ON PROF. CAVALLI-SFORZA'S PAPER

PROF. BERNARDI: Luca, I don't think there is any contradiction between your results and ours. We are looking at two very different scales. Looking at vertebrates means looking at five hundred million years of evolution. You are looking, of course, at human populations over a short span. You see the small details which we do not see at all on our much wider time scale. So I do not think there is any contradiction between the results.

PROF. CAVALLI-SFORZA: No, as a matter of fact I would also like to add that, when you say that all that is due to selection, in many cases there is really no proof that there is direct evidence of adaptation.

PROF. BERNARDI: Well, of course, I could not present everything but the evidence for evolution comes from the conservation which you can only assume to be the result of the elimination by negative selection of the changes, and I do not see any other way to get rid of those changes other than by negative selection.

PROF. CAVALLI-SFORZA: I'm not saying that those changes are not due to selection, I say that most frequently strong evidence that a particular genetic change is due to natural selection is difficult to acquire.[1]

[1] I have requested the Editors to add here, in the proofs, the following short note which is very relevant to the issue, and summarizes and extends somewhat the argument I tried to present in my main talk. Strong evidence of selection for a genetically determined trait requires proof that positively, or negatively selected traits really show increased, or decreased darwinian fitness of their carriers. This requires demographic estimates of fitness by analysis of survival and fecundity, a very difficult or impossible task in many situations, especially for mutants responsible for positive selection. Usually much evidence of selection is simply from correlations of phenotype and environment, as is the case, for instance, of body shape or size with climate. To put it simply, the nature of the trait suggests reasonable ideas for its adaptiveness to certain environments. But even if the intuitive answer derived from the nature of the trait seems unobjectionable, as for instance that wings are essential for flying, a closer analysis indicates that the development of wings came after a preliminary stage

PROF. GOJOBORI: Luca, could you give us a comment on *Neanderthal* genomes. I think Svante Paabo is now conducting sequencing of *Neanderthal* genomes, not only a single individual, maybe more than one, of course: then how can that information make an impact on your study? Obviously you are working on a gene frequency tree.

PROF. CAVALLI-SFORZA: All I know about *Neanderthal* is that there is no evidence that there has been any exchange but probably it may come if some individuals are found who may have been hybrid and so far there are none that have been found or tested. So it may well be that there was some exchange but, even if we find some hybrids, we still do not know whether we should consider them a separate species or not, because separate species, strictly speaking, requires that hybrids are not fertile, to be rigorous, but it is very difficult to reach that kind of rigour in many situations. But anyhow, I think, I don't know if *Neanderthal* developed a language and up to which point, but they probably did because I don't believe that language completely developed in the last hundred thousand years. There is evidence that the left part of the brain is developed in five out of six skulls that are 1.7 to 2 million years old, so it is likely that there was some early development of language and what happened more recently was only reaching the level of perfection that it has reached, like having syntax and so on. So I do not really think I can say more than that.

in which the beginnings were accidental or directed to other purposes, as was suggested in well known work by Lewontin. I would really like to know the global amount of selection that may have gone into evolution, and how it compares with other factors of evolution that were more or less entirely neglected, and this is more difficult to estimate. Our results on human evolution indicate that the input of natural selection in the recent peopling of the world by *H. sapiens sapiens* may have been much smaller than chance effects due to random genetic drift than one might expect, but they are limited to the intra-specific variation of one species, and this may be less than that found in inter-specific variation. Moreover our species is unique in several ways: In humans another very powerful general mechanism of adaptation exists beside natural selection, cultural evolution, which is not designed uniquely to improve the *species* survival, but depends to some extent on our whims. In human history there have been many catastrophes caused by hard follies of few individuals who gathered enormous power in their hands, and our society has not yet become able to protect itself from such risks. But leaving them aside, another consideration regarding natural selection in our species is that our species is in the nearly unique situation of solving many practical problems due to climate, food, or health etc. by cultural evolution, which is much faster than natural selection. This has probably lessened considerably the relative and absolute contribution of natural selection to the genetic variation we experienced, for instance, during the recent expansion of *Homo sapiens sapiens* to the whole world.

THE FUTURE OF LIFE

CHRISTIAN DE DUVE

In the two most recent plenary sessions of this Academy that I was able to attend, in 1996, when Pope John Paul II made his celebrated declaration: '*Evolution is more than a hypothesis*', and in 2002, when the present Pope, who was still Cardinal Ratzinger at the time, presented himself as a new member of the Academy, I have expressed some thoughts on the nature, origin, and evolution of life (de Duve, 1997, 2003). Today, in what is most likely my last participation in a meeting of the Academy, I will attempt to take a brief look into the future of life on Earth, as illuminated by our knowledge of its past and present. This topic is discussed in greater detail in a coming book (de Duve, 2009).

First, let me say a few words about the past. Life appeared on Earth at least 3.55 billion years ago, fairly soon after our newborn planet had become physically able to support it. Inaugurated by primitive cells of unknown origin, life remained unicellular for some 2.5 billion years, first in the form exclusively of prokaryotes (bacteria), to which, about 1.5 billion years later, were added the protists. These consist of much larger and more complex cells called eukaryotic and containing a nucleus, an elaborate membrane network, intricate cytoskeletal structures, and several cytoplasmic organelles, including lysosomes, peroxisomes, mitochondria, and, in photosynthetic organisms, chloroplasts. Many representatives of these microbes, both prokaryotic and eukaryotic, still abound in the world today.

Only about one billion years ago did eukaryotic protists first give rise to multicellular organisms. Plants led the way, soon followed by fungi and, 400 million years later, by the first animals. These started by blossoming into the rich world of invertebrates, of which one group eventually evolved into the first marine vertebrates, the fish, which, in turn, gave rise to the partly land-adapted amphibians, followed later by the fully land-adapted reptiles, from which arose birds, on one hand, and mammals, on the other.

Primates arose among the mammals some 70 million years ago, evolving to produce, in addition to a variety of apes and monkeys, a line, initiated some 6-7 million years ago, that led to the human species. Note the extreme lateness of this crucial event, which took place in the last 100th part of animal evolution, the last 600th part of the evolution of life.

The advent of humankind was signalled by several important acquisitions, including bipedalism, increased handiness, and, especially, a larger and more complex brain, which, in little more than two million years, almost quadrupled in size, from a volume of about 350 cm^3, the size of the brain of present-day chimpanzees, our closest relatives, to a volume of some 1,350 cm^3.

These acquisitions have allowed a fantastic evolutionary success, without equivalent in the entire history of life on Earth. Our early ancestors numbered about 3,000 when they separated from the Neanderthals, at a time estimated from recent DNA studies to lie between 800,000 and 500,000 years ago. There were about 10,000 of them 200,000 years ago, when 'mitochondrial Eve' and 'Y Adam' started *Homo sapiens sapiens* on its final evolutionary journey. They may have been on the order of 5-10 million, scattered over a good part of the world, when the first durable human settlements were created some 10,000 years ago. Since then, the human population has grown at an ever-increasing pace, reaching about half-a-billion in the time of Galileo, passing the one-billion at the start of the nineteenth century, and rising from less than 2 billion to more than 6.5 billion just in the last 100 years, coming to invade, occupy and exploit almost every habitable – or, even, uninhabitable – site on our planet. Ours is, by far, the most successful species – I leave out microbes – in the whole of biological evolution.

This success has a cost, briefly summarized in Table 1. We read or hear about it almost daily through the media. It is known to all of us and I need hardly elaborate. What I wish to do is extrapolate from the past and present to the future. If things continue in the same direction, there is little doubt that we are heading for disaster, soon to reach a point where we will be driven to extinction, together with a good part of the living world. If this happens, it will be nothing new in the history of life, including the recent history of humankind. These histories are landmarked by extinctions. But there will be a difference. Most likely, past extinctions were invariably associated with some kind of *failure* in the face of an external challenge (drought, glaciation, or other climate change, geological upheavals, meteorite impacts, epidemics, extermination by a more successful competitor, etc.). Our extinction, if it occurs, will be the consequence of inordinate evo-

TABLE 1.

The Cost of Success

1. Exhaustion of natural resources
2. Loss of biodiversity
3. Deforestation and desertification
4. Climate change
5. Energy crisis
6. Pollution
7. Overcrowded cities
8. Conflicts and wars

SUMMARY: IRRESPONSIBLE EXPANSION

lutionary *success*. We have developed to the point of endangering the ability of our planet to support us. If we go on following the same course, it can only lead to our doom.

Contemplating this ominous picture with the eyes of a biologist, I find a single culprit: *natural selection*. I use the word 'culprit' metaphorically – no guilt is involved – but, as will be seen later, the image is not entirely inappropriate. Natural selection is the process, now overwhelmingly established as a dominant evolutionary mechanism, whereby the forms of life that are most apt to survive and produce progeny under prevailing conditions obligatorily emerge from whatever set of organisms happen to compete for the same resources. All that is known about this process indicates that the variants on which it operates are accidentally generated, without intentionality or guidance, contrary to what is claimed by the defenders of intelligent design. Another key feature of natural selection, of special importance for our topic, is that it is governed entirely by *immediate* benefits. Natural selection has no foresight.

There is every reason to assume that humans are, biologically, products of natural selection, like all other forms of life. This implies that evolution has privileged in human genes traits that were immediately favorable to the survival and proliferation of our ancestors under the conditions that obtained there and then, regardless of later consequences. This is intrinsic to the process of natural selection. Note that I leave out traits that were acquired by cultural evolution and transmitted by education. I shall turn to these later. Right now, I will deal only with genetically inscribed traits.

On an individual basis, human traits retained by natural selection included intelligence, inventiveness, dexterity, skillfulness, resourcefulness, and ability to communicate, all the qualities that have served to generate the fantastic scientific and technological achievements responsible for our evolutionary success. But the selected traits also included acquisitiveness, selfishness, greed, cunning, aggressivity, and any other property that ensured immediate personal gain, regardless of later cost to oneself or to others. The recent financial crisis has illustrated in a particularly dramatic fashion how such traits still flourish in the world today. On the other hand, genetic qualities whose benefits would become manifest only in the long run, such as far-sightedness, prudence, a sense of responsibility, and wisdom, were not singled out by natural selection. Their fruits would have appeared too late for that.

On a collective level, natural selection has favored traits, such as solidarity, helpfulness, cooperativity, tolerance, empathy, compassion, altruism, even personal sacrifice for the common good, that form the bases of human societies. But the selection of those traits has been mostly restricted to the members of given *groups*, united first by shared kinships and territories, and later by shared interests, a shared language and culture, shared beliefs, shared prejudices, even shared hatreds. The negative counterpart of those 'good' traits has been collective defensiveness, distrust, competitiveness, and hostility against members of other groups, the seeds of the conflicts and wars that have landmarked the whole of human history up to the present day.

In other words, the defects that endanger the future of our species and of much of the living world are *inborn*, written and sustained in our genes by natural selection. They were useful in the past, at a certain stage of our evolution but have become deleterious; they are a natural burden we assume at birth. I would like to suggest that awareness of these innate genetic defects inspired the notion of *original sin*. That is why calling natural selection the 'culprit', as I did earlier, is not entirely inappropriate, except, of course, that no culpability is involved. There is no Eve to blame, no serpent, only natural selection, which is mindless and without intention, devoid of foresight and responsibility.

Is there anything we can do? Fortunately, yes. Of all living beings on Earth, we humans are the only ones that are not slavishly subject to natural selection. Thanks to our superior brains, we have the ability to look into the future and to reason, decide, and act in the light of our predictions and expectations, if need be against our immediate interest, for the benefit of a later good. We enjoy the unique faculty of being able to act *against natural selection*. The problem is that, in order to do this, we must actively oppose some of our key genetic traits, surmount our own nature.

It would be nice if we could correct our genetic defects by engineering, removing the bad genes and implanting good ones. We can do this to a limited extent with plants and animals; but we cannot possibly do the same with humans. We do not yet have a sufficiently reliable technology for human application. Even if we had it, we would not know what genes to modify in order to achieve a certain goal. Our knowledge of the genetic basis of psychological traits is still in its infancy. Even if we had this knowledge, there would be the problem of deciding who should benefit from the interventions. Finally, there are all the ethical objections such manipulations are likely to raise. So I won't waste time discussing this way out of our predicament. We are not ready, whether scientifically, technologically, or ethically, to create GMHs, genetically modified humans, for specified aims, as we do other organisms.

But there is another way out, provided by the fact that the structure of the human brain is genetically determined only in its general architecture. Its fine wiring takes place *epigenetically*, under the influence of the various stimuli to which the brain is subjected. Note that I use the word 'epigenetic' in its original meaning of 'added to the genetic', a meaning given to it by the developmental biologists who invented it and still used by neurobiologists; not in its new meaning of 'genetic, but not inscribed in DNA sequences', now accepted by many geneticists and molecular biologists.

It is known, from the work of Gerald Edelman, in the United States, and of Jean-Pierre Changeux, in France, that, in the developing brain, growing neurons continually send out extensions in various directions. Upon chance encounters between such extensions, the neurons form temporary connections, which are rapidly undone unless they happen to be repearedly used, in which case they become stabilized as synapses. Thus, the stimuli to which the growing brain is subjected operate some kind of selection among the many interneuronal connections that are created by chance. The similarity with Darwinian selection has not escaped the authors. Edelman, for example, speaks of 'neural darwinism'.

Thus, the wiring of a human brain, which forms the underlying substrate of the thoughts, feelings and other mental processes the brain can experience, is largely determined by the impulses conveyed to it by the external stimuli to which the body is exposed. In a way, this has always been known by all those who have had something to do with educating the young. Educators have always been aware of the importance of their work in the 'molding' of young brains. What is new is the realization that this process starts at birth, perhaps even before birth, and that parents, nannies, nurses, kindergarten personnel, elementary school teachers, baby sitters, that is, all those who deal with very young children, exert key influences on the wiring of the children's brains.

Thus, if we wish to create in young brains neuronal networks conducive to tolerance, sympathy, peacefulness, reasonableness, foresight, and wisdom, we must first do so with the parents and educators. Doing so in one shot is clearly impossible, but one can imagine initiating a self-enhancing movement that would progressively snowball into becoming worldwide. But for this to happen, the movement must be set in motion.

This brings me to my final message, of special significance within these walls. It concerns the role of *religions*. Historically, religions have always played a major role in the education of the young, even of adults. Even today, their influence in this domain remains tremendous. Religious leaders are, even more than the most powerful political leaders, uniquely placed to influence large crowds. When the Pope speaks, he reaches more than one billion individuals. Thus, he and the leaders of the other major religions are invested with an immense planetary responsibility. They are almost the only persons in the world who could play a decisive role in rescuing humanity from its suicidal course. They are particularly well placed to do this, in view of the millennia-old tradition of tolerance, love, and understanding that, originally, has been the main message propagated by the major religions.

Unfortunately, Churches have not escaped the genetic 'original sin' that plagues the whole of humanity. One cannot generalize, of course. There are important differences among the various religions. But each is, to a greater or lesser extent, tainted with authoritarianism, fundamentalism, doctrinal dogmatism, ethical rigidity, exclusiveness, extending, in some cases, to nationalism and strife, sometimes armed, even murderous.

The Catholic Church is not exempt from these defects. I hope that this statement, expressed within these venerable walls, will not be seen as disrespectful or unsuitable. This Academy was created to promote the free intercourse of ideas, within a framework of open-mindedness, intellectual honesty, and sincerity. With your permission and with apologies to those who disapprove, I will avail myself of this spirit, which corresponds to the true scientific attitude.

In my opinion, it is our duty, as members of this august body, to alert the higher Authorities to the extreme gravity of the menaces that weigh on the future of humanity and of planet Earth and to the urgent necessity of acting against those threats by all possible means. The facts (see Table 1) speak for themselves. They are evident and undeniable. We ignore them at our peril. The final outcome, if nothing is done to change the course of events, leaves little doubt. The Church, with its unique worldwide power and influence, bears an enormous responsibility in directing this course for better. If there is agreement on this point, this is a message our Academy, as advisor to the Holy See, could respectfully convey to the Magisterium.

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C. de Duve (1997). *Life as a Cosmic Imperative*. Commentarii, Vol. IV, N° 3, pp. 311-320. Plenary Session on the Origin and Early Evolution of Life (22-26 October, 1996).

C. de Duve (2003). *The Facts of Life*. Scripta Varia, Vol. 105, pp. 71-91. Plenary Session on the Cultural Values of Science (8-11 November, 2002).

C. de Duve (2009). *The Future of Life on Earth* (Provisional title, to be published).

DISCUSSION ON PROF. DE DUVE'S PAPER

PROF. POTRYKUS: To my understanding of the real public power, you should address your call to the media, not to the Church.

PROF. DE DUVE: Well, one is not exclusive of the other. I think the Church has an enormous power and could be extremely helpful.

PROF. PHILLIPS: I hope you will understand that I mean this as a compliment, but you have given us more of a sermon than a talk, but I think it is a sermon that is well taken. It resonates with many of the thoughts that I have had and this is not the first time I have heard the idea that inappropriately evolved behaviour is the same as original sin. The thing that I am wondering about is that the message that you have preached to us seems like it is the same message that has been preached by religious leaders since the time of Moses, Buddha, Confucius and various other people. So how do you intend to convince people that there is something more urgent now than has been the case in all the times past when people made the same urgent pleas that you have made today?

PROF. DE DUVE: Well, let me make a few points. First of all, I am too old to start trying to convince people. I think people should just look at the evidence – it's there for everyone to see – and draw their own conclusions. The other point is, you say that I delivered a sermon, which is perhaps not a bad idea in these surroundings, but you have to remember that this, to me, has been my farewell speech. I am 91. This is, certainly, the last plenary session that I will attend. I felt that, as a farewell speech, I would, within these venerable walls, speak my own mind.

PROF. PHILLIPS: And I thank you for it.

THE EVOLUTIONARY ORIGIN AND PROCESS OF THE CENTRAL NERVOUS SYSTEM: COMPARATIVE GENOMICS APPROACH

TAKASHI GOJOBORI[1,2], KAZUHO IKEO[1,2] AND JUNG SHAN HWANG[1]

Introduction

Historically, it had been the most essential question to ask why we think we are ourselves. A famous phrase written by a French philosopher, René Descartes, in Latin '*Cogito, ergo sum*' (translated in English, 'I think, therefore I am'). This paradigmatic enigma given by Descartes about self-consciousness or self-recognition is still the central question for us today. Apparently there is no easy answer for this question from any perspective. However, we can question and resolve the biological problem of 'how our brains work and think' from the evolutionary standpoints, especially when we are able to study it at the genetic level.

Since the draft sequence of human genome project has been completed, biologists have focused on the post-genomics studies including proteomics, transcriptomics (gene expression profile), SNP (single nucleotide polymorphism), non-coding RNAs (eg. miRNA, siRNA), comparative genomics and etc. Among these studies, comparative genomics provide a powerful way to resolve the evolutionary questions (Koonin *et al.*, 2000). Sequence comparison across the species is a fundamental solution to understand the origin, the evolutionary differences between organisms and the complexity of biological systems. Particularly the currently advanced technology of second-

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generation sequencers such as 454, Solexa, SOLiD and Helicos allows one thousand human genomes to be sequenced just within two years. Therefore, we expect to have the number of genome sequences of various organisms increase significantly in the next few years. Taking advantage of comparative genomics, we attempt to understand the evolution of the central nervous system (CNS) or the brain of humans at the gene level. To do this, we address the following questions: (1) What is the origin of the nervous system (NS) as based on currently available sequence data and the advantage of homology search? (2) How old are the nervous system genes especially those that are also expressed in the human brain? (3) What kinds of genes are expressed in planarian, a primitive flatworm having the simplest brain?

ORIGIN OF NERVOUS SYSTEM – A NERVE NET

There are around 100 billion neurons in an adult human brain and they can be categorized according to the number of axonal processes extended from the perikaryon (the cell body). Depending on their localization in brain regions, these basic neuron types are further subdivided into specialized neuron types and also functionally diverse. Let us take pyramidal cells as an example, which are typically characterized by a spiny apical dendrite, a basal dendrite and a single axon. The morphologically identical populations of pyramidal cells are found largely in two distinct functional parts of the brain, neocortex and hippocampus. Further diversification of pyramidal cells can be found within the hippocampus in which a heterogeneous expression of genes is observed across the pyramidal cell layer (Lein *et al.*, 2007). The ancestor of the human brain is considered much simpler. It is believed to have a two-dimensional neural network that is somehow similar to the diffuse nerve net of basal phylum Cnidaria, having an average of less than 8000 neurons, no glial cells, no centralized nerve tissue and no anatomical compartmentalization (Holland, 2003, Telford, 2007) (Fig. 1, see p. 608). However, the neuroanatomical comparison has failed to show any homologous structures of the nervous system between human and Cnidaria, nor has the cell morphology given any clue due to the simplicity of cell types in cnidarians. Recently, gene expression data have proven the conserved body plan between vertebrates and cnidarians (Bode, 2001; Finnerty *et al.*, 2004; Kusserow *et al.*, 2005; Lengfeld *et al.*, 2009), suggesting that the origin of the body plan can be dated to the early Metazoa.

The phylum Cnidaria includes animals such as coral, sea anemone, sea pen, jellyfish and *Hydra* and they all share a sac-like body surrounded by two layers of epithelial cells (ectoderm and endoderm). They only have a single opening that functions as both mouth and anus. Cnidarians have the simplest nervous system named nerve net in which thousands of neurons make up a mesh-like network at both epithelial layers (Fig. 1 and 2A, see pp. 608-9). Jellyfish and certain species of *Hydra* (eg. *H. Oligactis*) also have neurons concentrate and form a ring around the mouth region (Fig. 1, see p. 608). This nerve ring is considered to be an intermediate structure between a nerve net and a ganglion. Since Cnidaria and Ctenophore are basal metazoans with the nervous system, many expect the origin of the nervous system to somehow resemble the cnidarian nerve net. From time to time hypotheses have been made to explain how a simple nerve net of cnidarians evolves into a bilaterian nervous system (Holland, 2003). Most ideas are based on the scenario proposed for the evolution of the bilateral body plan (Lacalli, 1995; Meinhardt, 2002; Holland, 2000; Martindale, 2005; Hejnol and Martindale, 2008). Holland (2003) has a good summary of all the hypotheses on the transformation of nerve net/nerve ring into brain and nerve cord. Among all, the majority of scenarios believe that Cnidaria has the ancestor-like nervous system and the bilaterian brain is originated from the nerve ring. Other minor scenarios either consider the whole cnidarian polyp as a brain or the nerve net is compressed to one side of the body axis and becomes the brain.

Does nervous system emerge from nowhere?

Yet, could the ancestor of the nervous system be simpler than a nerve net? The nerve cell (or neuron) is the fundamental unit of the nervous system. It is not found in the basal metazoans such as sponge and placozoan and thought to arise early in the Eumetazoa (a clade comprising all major animal groups except sponges and placozoans) (Fig. 3). The sponge has well-defined photosensory cells. At the posterior pole of demosponge larva, there appears a ring of monociliated, pigment-containing cells and these cells function as a photoreceptor and control the directional swimming of the larva (Leys and Degnan, 2001; Leys *et al.*, 2002). Unlike the sponge, placozoan contains four basic cell types and none of them is morphologically similar to the neuron or sensory cell. However, neural genes involved in neurosynaptic activity and biosynthesis are identified in the

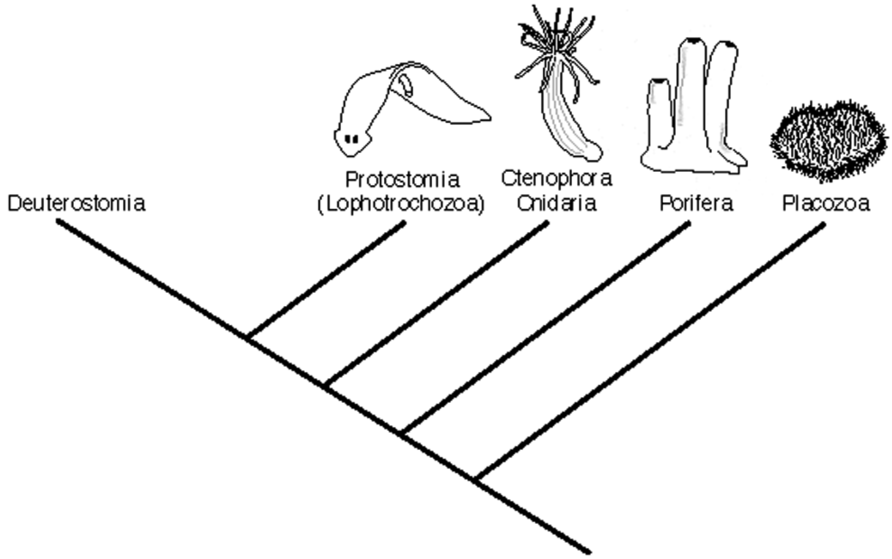

Figure 3. A classical taxonomy of basal metazoans.

placozoan genome (Srivastava *et al.*, 2008), and a *Proto-Pax* gene is expressed in a proliferating/differentiating region near the outer edge of placozoan cell body (Hadrys *et al.*, 2005). This molecular evidence suggests that neural genes predate the ancestor of nervous system. In fact, sponge and placozoan genomes encode a great deal of transcription factor genes that play a critical role in signaling pathway, embryogenesis and tissue specification of eumetazoan (Degnan *et al.*, 2005; Strivastava *et al.*, 2008). Therefore it is rather unlikely that the gene repertoire of the nervous system arises after the divergence of cnidarians but instead it emerges in the last common ancestor of Metazoa or even earlier. In other words, the repertoire of molecular factors that are essential for neuronal development and functions has already had a role in neuronal activities in the 'primitive cell' far before the emergence of the nerve cell in animals. The 'primitive cell' is referred to those having the potency but yet to develop into the neuron stem cell (Fig. 4). Later it evolves into two sister cells and one of them functionally diversifies into neuron stem cells. A similar view is found in a recent review, Arendt D. (2008) has proposed a scenario

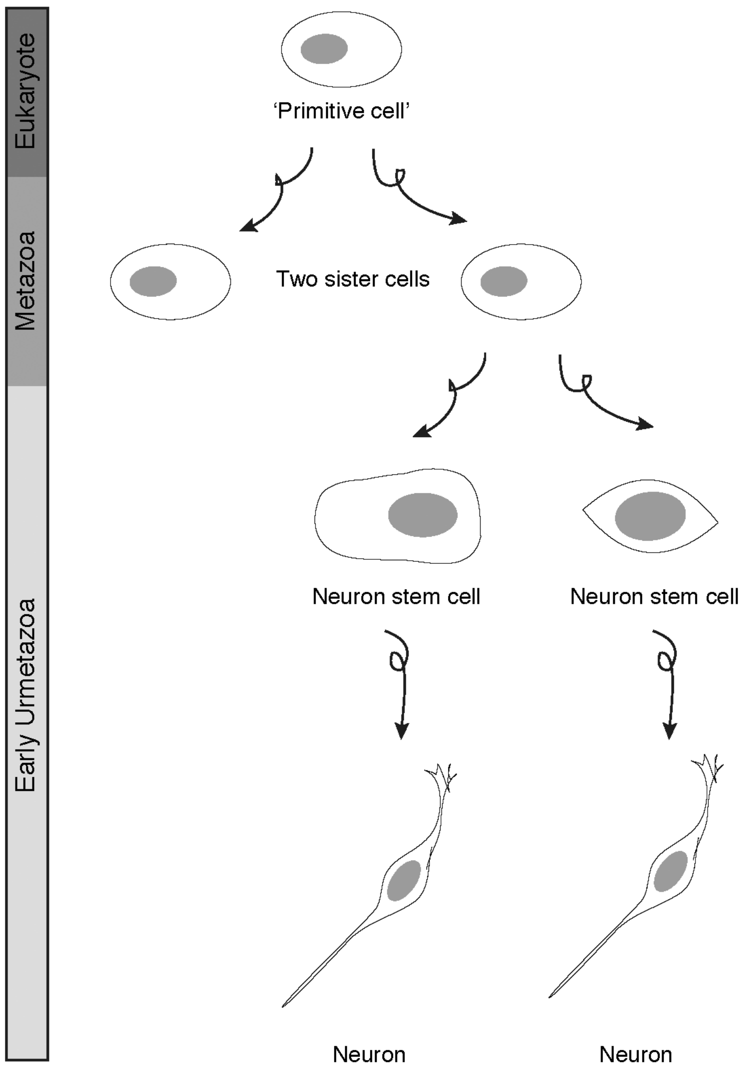

Figure 4. A scenario is proposed for the origin of the nervous system or neuron. A partial neural gene repertoire exists in the 'primitive cell' before the emergence of Metazoa. This 'primitive cell' evolves and diverges into two sister cells. One of the sister cells specializes its function via genetic modifications (eg. gene duplication, gene gain and loss, protein domain shuffling, horizontal gene transfer, etc) and further divides into two sister cells that contain similar potencies as neuron stem cells. Later in the evolution, one of two neuron stem cells might lose its ability to differentiate into a neuron, but the other one remains as a neuron stem cell (not illustrated in the figure).

of cell type evolution in which ancient metazoan cell types have multiple functions and later the cell type diversification within a species increases the number of functionally specialized cells. Arendt has further stated the importance of molecular signature (which refers to a set of differentiation and regulatory genes in sister cell types) in the evolutionary diversification of cell types. In fact, in our opinion, this molecular signature has to be imprinted in the ancient cell type before the emergence of sister cell types. Early sister cell types might retain the plasticity at the gene regulatory level. Not all cnidarians have neurons derived from one kind of cell types. The neurons of *Hydra* are differentiated from the interstitial cell (I-cell), a multipotent stem cell that lies between the ectodermal epithelial cells (David and Gierer, 1974). Nematostella, a marine cnidarian, lacks the I-cell and neurons are originated from the ectodermal and endodermal epithelial cells (stem cell lineages of cnidaria) (Extavour *et al.*, 2005; Marlow *et al.*, 2009). It seems plausible that the I-cell and epithelial cell are both sister cells and contain the same regulatory gene network that is capable of determining their cell fates and differentiating into neurons. Interestingly, this conclusion is supported by the observation that *Hydra* I-cell arose in the endoderm at the early embryonic stage, suggesting the endodermal origin of *Hydra* I-cell (Genikhovich, 2006).

In *Hydra*, I-cell and epithelial cell are having a relationship of sister cells as discussed above, while the differentiated products of I-cell, neuron and nematocyte (contain a stinging organelle that functions for prey capture and defense) can also be considered as secondary sister cells (Hwang *et al.*, 2007). This is not only because both are originated from the I-cell, but because they also both have specific expressions of *achaete–scute, prdl-b and COUP-TF* (Hayakawa *et al.*, 2004; Miljkovic-Licina *et al.*, 2004). The nematocyte has long been regarded as a sensory cell as it bears a mechano- and chemo-sensory receptor called cnidocil apparatus at the apical surface of cell.

In fact, the evolution of neural genes occurred far before the emergence of multicellular organisms, approximately 1,400 million years ago (Nei *et al.*, 2001). A genomic-scale analysis of nervous system (NS) specific genes shows that 35 out of 255 human NS specific genes (14%) appear prior to the split between metazoans and yeast (Fig. 5, see p. 610) (Noda *et al.*, 2006). Moreover in the same analysis, a sudden increase in the number of NS genes occurs before the emergence of vertebrates, and the majority of these NS genes are critical for protein binding or protein-protein interaction. Although the analysis is based on a small data set (255 human NS specific genes), the results support two conclusions: (1) A significant number of NS specific genes in yeast marks the ancestral complexity of the neural gene repertoire before the emergence of the nervous system, and (2) the evolution of the nervous system is mainly driven by the extensive gene gain.

The primitive brain of planaria

Although recent phylogenetic analyses have placed platyhelminth flatworms in the clade of Lophotrochozoa and not as basal to Bilateria (Fig. 3) (Baguñà and Riutort, 2004; Ruiz-Trillo *et al.*, 2004), it has a centralized nervous system that can be described as a 'primitive brain'. Planarian, a freshwater flatworm, contains a mass of cephalic ganglions in the head and a pair of ventral nerve cords (VNC) running parallel to the body axis (Fig. 1, p. 608). The cephalic ganglion has a bilobed structure with neuronal cell bodies that form the outer later (cortex) and nerve fibers that concentrate collectively in the inner core of the ganglion. Compared to the nervous system of cnidarians, the planarian central nervous system has evolved with several 'brain' features: (1) centralized neurons at cephalic region, (2) nerve cord, (3) neuron fibers surrounded by a layer of cortex, (4) lobes with commissural fibers, (5) glial cells, (6) motor neurons and (7) neurons with elaborated dendrites. Thus, the structure of the planarian nervous system has been well studied and characterized (Flexner, 1898; Oosaki and Ishii, 1965; Baguñà and Ballester, 1978). Not until recently, molecular tools including whole mount *in situ* hybridization, whole mount immunostaining, expression sequence tag (EST), microarray, and RNA interference are applied to study the detailed morphology and function of the planarian nervous system (Cebrià *et al.*, 2002a; Cebrià *et al.*, 2002b; Agata *et al.*, 1998; Mineta *et al.*, 2003; Nakazawa *et al.*, 2003).

What makes the nervous system (NS) complex?

In order to study the genes expressing in the planarian brain, we collect anterior tissue including the cephalic ganglia (above the neck) of planarians and conduct EST sequencing. Based on known NS genes, we have identified 116 genes out of 3101 that share significant homology to NS genes of other organisms (Mineta *et al.*, 2003). A further analysis of 116 NS-related genes has shown that more than 95% have their homologs in humans, *Drosophila melanogaster* and *Caenorhabditis elegans*. These NS-related genes include those involved specifically in the brain morphogenesis and neural network formation, suggesting the possibility that the bilaterian central nervous systems are derived from a common origin.

Moreover, we also examined the gene expression in the anterior part (i.e. cephalic ganglia) of the planarian by using cDNA microarray containing 1,640 nonredundant genes (Nakazawa *et al.*, 2003). The use of planarian cDNA microarray has an advantage over the ESTs collection. Planarian cDNA microarray can be used to examine the novel genes expressed in the central nervous system. A total of 205 genes are differentially expressed in the anterior part and by using whole mount *in situ* hybridization, the top 30 genes show various regional expressions in the cephalic ganglia and the ventral nerve cords (Fig. 2B, **see p. xxx**). Many of the top 30 genes have an unknown function. The variety of expression patterns of the top 30 genes in the planarian brain demonstrates the highly organized nature and the complex neural activities of the planarian central nervous system.

In summary, the above data indicate that the planarian brain expresses genes related to those in the human central nervous system and it is also highly divided into distinct compartmentalized regions (i.e. functional domains) according to the gene expression patterns. One of the important features for a diffused nerve net (in *Hydra*) that evolved into a centralized nervous system (in planarian) requires the mechanism of axon guidance. Axon guidance allows the proper growth of the axon cone and the precise target reached by the axon. The axon guidance molecules in planarians such as *NCAM, slit, netrin and robo* play conserved and important roles in the maintenance of the nervous system architecture (Cebrià, 2007). RNAi interferences of these three genes in the planarian result in the failure to regenerate a normal brain. For example, no proper commissural connection is seen between cephalic ganglia and nerve cords in regenerating planarians after *Smed-roboA* RNAi (Cebrià and Newmark, 2007). Interestingly, sequences homologous to axon guidance genes such as *NCAM, robo, slit, netrin, Eph* receptor and NCAM are also identified in the *Hydra* genome (personal data). Thus, the emergence of axon guidance genes did not happen in the early ancestors of Bilateria but rather dates back to the Eumetazoa. It would be of great interest to know whether the axon guidance homologs of *Hydra* had conserved functions like those of planarians and other bilaterians. Perhaps the complexity of the central nervous system as compared to the nerve net is not due to the number of NS genes but to the dynamics regulation of the gene network. It should be noted that the planarian also has lineage-specific NS genes. One of the examples is '*nou-darake*', a gene that belongs to the FGF (fibroblast growth factor) receptor family and is expressed in the cephalic ganglia and its surrounding tissues. The existence of '*nou-darake*' is important to restrict the brain tissue in the cephalic region (Cebrià, *et al.*, 2002a).

Concluding Remarks

For years, researchers have been struggling to isolate genes from an organism, to gain the genomic information of a gene and to compare the genes among many different species. Now with high-throughput sequencing, powerful analysis tools and large-scale data storage, we are able to collect a large amount of EST and genome data in a short time. These advanced approaches have found a solution to the current research on the evolution of the central nervous system. To understand the human brain, we believe that the study of lower organisms such as *Hydra* and planarian is essential and would provide useful knowledge of how the human brain evolves. In our studies, we predict that *Hydra* and planarian share at least half of their nervous system genes with humans. Clearly, many nervous system genes predate the emergence of Metazoa and the nervous system evolves as the gene network increases its complexity. For a future perspective, we believe that it is essential to construct a virtual 3D human brain. This 3D immersive environment would provide the gene expression map of each central nervous system gene against the anatomical, tissue- and single-cell levels of the human brain structure.

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DISCUSSION ON PROF. GOJOBORI'S PAPER

PROF. ARBER: Thank you very much for this very interesting and prospective presentation. I think you provide here an important answer to a question which evolutionary biologists have raised since a long time: how do novel properties emerge. With that regard, thinking of your statement that a knock out mutant of planaria gave an increase in brain tissue in that animal, I just wonder, could one speculate that the relatively rapid increase in the size of the human brain is due to a particular deteriorating mutation of something which was inhibiting the proliferation of the brain before?

PROF. GOJOBORI: If you kindly allow me to make a wild speculation, I think our results show that all of the gene set existed. However, still, the connection between genes was not much. Therefore, I think there was a certain important gene which made the network easier. I would call it an epoch-making gene, which was able to form a gene network. We can now observe genes which are responsible for formation of the human brain. In particular, when the gene or genome duplication takes place, the number of genes increases. Therefore, the number of networks would instantly increase accordingly. This is speculation.

PROF. LE DOUARIN: It was very interesting. I would like to know how you obtained these mutant epithelial hydras and the second question is, are there genes which are expressed specifically in the nematocytes and not in nerve cells which are over the body of the hydras?

PROF. GOJOBORI: First, the epithelial hydra was obtained by chemical mutagenesis and, among many variants, successfully this particular mutant was obtained. Secondly, like the genes which are expressed in the neurocells and the nematocyte cells, certainly the nematocyte cells have a few sets of genes very much specific to hydra, so we speculate that those genes may be horizontally transplanted from other organisms. Although we do not know yet, according to what our phylogenetic tree shows, this is quite possible.

PROF. W. SINGER: I would like to make a comment. This was fascinating because it seems to show a parallel with brain development on the other end. You seem to indicate that it is not the invention of new building blocks but the way in which they interact in more and more complex networks that makes all the difference. We see exactly the same in the brain, there are no new building blocks but the complexity of interactions is increased and that makes all the difference. It is a beautiful example of emergence.

PROF. COLLINS: A very fascinating presentation in terms of the evolution of brain-specific genes. It is interesting to note this emergence seems to be particularly strong before the appearance of bony fish, but one wonders whether that is, in part, an artefact of the difficulty in identifying evolutionary matches as you get further and further apart and is it possible that, in fact, some of those genes that are only identifiable by the time you get to bony fish actually have homologues in similar species but they are too diverged for your computational methods to appreciate that match?

PROF. GOJOBORI: Thanks so much for this important question. We worried a lot about this possibility, therefore first we changed our homologic criteria, but still the same conclusion was obtained. The other evidence is as follows. It is possible that before primate emergence a huge number of genes might have emerged, because sequence homology is much easier to detect. But instead, somehow, before bony fish emergence it appeared. Therefore, of course, I think there are some biases, but still general features can be unchanged. The most important issue would be the number of genes, because we dealt with only four hundred genes. Therefore if we can successfully obtain more genes, it is a question whether the picture does not change much.

PROF. NIRENBERG: What kind of cell-membrane genes have evolved latest? What functions?

PROF. GOJOBORI: In the human brain?

PROF. NIRENBERG: Yes, in the nervous system.

PROF. GOJOBORI: I think it looks to me that ligand-receptor type genes have evolved latest. In particular, the genes that are related to the receptor system seem to have played an important function among membrane associate proteins.

PROF. VICUÑA: I have two questions. The first one is the following: when you study gene expression in human brains, how do you obtain the samples? The other question is whether gene expression in the brain changes according to the physiological conditions of the brain. For example, if a person has a mental disease, or is in a coma, or sleeping, etc. Have you conducted those studies?

PROF. GOJOBORI: I have to confess I did not conduct isolation of a brain from a human body by myself, because we used only the data. However, according to my understanding, mRNAs were obtained from the dead body of a healthy normal person with informed consent of closest relatives. Therefore, certainly, if we have a certain diseased brain it would be interesting to see. Of course, ethical problems should be addressed carefully. I think specifically expressed mechanisms should exist in a transcription regulation system. If we get to understand the regulation system then I think we might have some answers. But we do not know yet.

PROF. DEHAENE: It was a beautiful story of evolution that you told us. Surely along these steps there are some important inventions, and one of them, in the nervous system, is the invention of spiking or excitable cells, so that the cells can fire and send a very specific message to long distances, to specific targets. I was wondering whether your research was showing when the spiking of cells first appeared.

PROF. GOJOBORI: That is also an important question, thanks so much. We are now examining cellular structures by EM, particularly gap junction between cells. As you know, electric synapses and chemical synapses can be examined from an evolutionary point of view. We have some answers. Certainly we are now addressing this question.

PROF. M. SINGER: Thank you. I too enjoyed your talk very much. You touched on a subject which, I think, is probably fascinating, namely, why it is that brains wound up in the heads of animals. You touched on that when you talked about the mutation in the hydra that resulted in multiple eyes and also about the cells that, instead of being concentrated, are dispersed. I wonder, do you know anything about the nature of that gene?

PROF. GOJOBORI: That is a very interesting question. Again, we do not know the answer. I think certain gene sets seem to have been lost, in the case of *C. elegans*. If a phylogenetic tree is correct and the planarian brain existed, then it must have had the formation of a brain, even before *C. elegans*. If that is the case, then the brain must have disappeared from *C. elegans*. Of course, researchers often say *C. elegans* has a brain, but in this case it means only a tiny number of cells. Therefore, if we can conduct transformation experiments in those organisms, then we may be able to answer the question of why the gene is located in the head. But we may be able to have the epitopic brain which is located in the tail, for example, by conducting transformation.

GENETIC AND EPIGENETIC SHAPING OF COGNITION – PREREQUISITES OF CULTURAL EVOLUTION

WOLF SINGER

Before entering the discussion of the evolution of our brains and the options for their epigenetic shaping I consider it appropriate to begin with an epistemic caveat. To the best of my knowledge there is consensus among neurobiologists that all mental phenomena including the highest cognitive functions are the product of neuronal processes. Likewise, social realities such as value systems and moral judgments are considered to be the products of interactions among human beings endowed with brains, the cognitive abilities of which allowed for the initiation of cultural evolution. If one accepts this position it follows that we can only perceive, imagine and comprehend what the cognitive abilities of our brains allow us to seize. Because brains – just as other organs – are the product of evolutionary adaptation, this implies that our cognitive abilities are with all likelihood constrained. Our brains are optimized to secure survival and reproduction in the narrow segment of the world in which life evolved. Coping with the highly specific challenges of an insecure and purely predictable world requires adoption of pragmatic heuristics that differ most likely from the cognitive strategies needed to assess a hypothetical 'objective' truth. Numerous experiments on perceptual illusions illustrate that such is indeed the case. Thus, the sobering conclusion seems to be inevitable that our cognitive abilities are likely to be highly constrained and idiosyncratically adapted to only a very small sector of the world. The world, as unravelled by scientific investigation, extends from infinitely small to infinitely large dimensions. Life, however, has evolved only within a narrow range that extends from micrometers to a few metres. Processes at this mesoscopic scale are dominated by the laws of classical physics and most of the dynamics that life has to cope with are linear. At this scale it makes sense to define states of matter as liquid, solid or gasous, to define space and time as separate categories, and to distinguish between cause and effect. Our sensory systems extract in a highly selective way a few signals from our environment that we then experience as light, temperature, vibrations, sound, smells and tastes. Some of these sensory categories reflect an arbitrary subdivision of physical continua. Thus, we classify electromagnetic radiations with wave lengths between 400 and 700 nm as light and those with longer wave length as heat. To us these categories appear as natural properties of the world and even though we perceive only very narrow spectra of the available physical and chemical signals in our environment, we experience the world as coherent and continuous – a convincing example of the constructive nature of our perception.

Because our cognition has adapted to a narrow range of the mesoscopic world, it is difficult for us to develop intuitions for phenomena at other scales. Our intuition of objects is meaningless in the world of quantum physics just as our concept of causality and our intuition of space and time does not hold for the putative structure of the universe. We tend to believe that the rules and concepts that we infer from the mesoscopic world can be extrapolated to all the other dimensions but there is no guarantee that this is actually the case. It must even be considered that the way in which we reason and draw conclusions is a specific adaptation to the processes at the mesoscopic scale and perhaps not generalizable. Thus, it is very likely that there are natural boundaries to what we can perceive, imagine and understand. Where these limits are and what is concealed behind, will in principle remain unknown. There is, thus, ample space for metaphysics and belief, constrained only be what is actually known.

The constructivistic nature of perception and the sources of knowledge

A large body of psychophysical evidence and neurobiological data indicate that perceiving is essentially a constructive process by which the brain attempts to interpret the sparse sensory signals conveyed by the various sensory organs on the basis of a huge amount of *a priori* knowledge (priors) that is stored in the functional architecture of the brain. What we perceive and how we perceive is by and large determined by context dependent expectancies and stored knowledge about the world. This raises the question of where the knowledge required for the construction of our percepts is derived from. Neurophysiological evidence indicates that knowledge and the rules for its application reside in the functional architecture of the brain. The term 'functional architecture' stands for the way in which nerve cells in the brain are interconnected with each other. Unlike in computers that are often erroneously cited to explain the functioning of nervous systems, there are no structurally and functionally different subsystems in the brain that could be considered as central processors and the various storage devices such as memories for data and programs. In the brain there are only neurons, and connections and processing as well as storage functions are accomplished within the same networks. All computations are determined by the functional architecture of these networks. What matters is which neurons are interconnected, whether these connections are excitatory or inhibitory and whether they are strong or weak. The setting of these variables is also the basis of all the knowledge that is stored in the brain. Thus, the search for the sources of knowledge is reduced to the question of which factors specify the functional architectures of brains.

The most important of these factors is beyond any doubt evolution. Through evolutionary selection brain architectures have evolved which contain the knowledge and the application programs that the organism needs in order to cope effectively with the challenges of its environment. In this sense evolution can be considered as a cognitive process. Through adaptation of brain architectures to the requirements of survival in specific biotops knowledge about the world is acquired, stored in the genes and made available for the control of adapted behavior every time a new brain develops. The knowledge acquired through this process is of course implicit. We do not know that we have it because we were not around when it was acquired. Therefore, this knowledge serves as unconscious priors that determines all subsequent cognitive processes. An important consequence is that perceptions based on these implicit priors have the quality of being objective, unreducible and not relativatable. They are taken as representing undisputable truth.

Another important source of knowledge is developmental shaping of brain architectures addressed also as developmental imprinting. The human brain develops structurally until around age 20. This developmental process is characterized by a continuous making and breaking of connections whereby the selection of connections that are to be consolidated is guided by neuronal activity and hence by experience and interaction with the environment. This developmental process leads to a substantial modification and refinement of the genetically specified architecture of brains and thereby installs further knowledge in the brain – this time knowledge derived from interaction with the actual environment in which the organism evolves. Much of this knowledge is also implicit. Brain structures that support episodic memories develop only years after birth which leads to the phenomenon of childhood amnesia. Children up to the age of about 4 years learn about the world but they keep no trace of the context in which they have learnt. They know but they do not know where their knowledge comes from. This is why early acquired knowledge – just as evolutionary knowledge – is implicit, serves as a source of unconscious priors for perception and thereby nourishes convictions that cannot be put to question.

This is not so for knowledge acquired through normal learning processes that begin once episodic memory functions become available and that persist throughout the entire life span. Knowledge acquired through this mechanism is explicit. Subjects are usually aware of having acquired the respective contents by experience and remember the context in which acquisition has taken place. Once brain development has come to an end, further learning is based on activity dependent modifications of the efficiency of existing connections and these changes are brought about by lasting modifications of the molecular machinery that mediates communication among nerve cells, i.e. synaptic transmission. These changes also go along with structural alterations but these are resolvable only at the ultra-structural level.

The layout of the functional architecture of brains is thus determined essentially by three factors, evolutionary adaptation, epigenetic shaping during postnatal brain development and normal learning processes. The resulting architecture in turn determines the various sensory categories according to which we classify sensory signals, the criteria for the definition of objects, the rules according to which brains detect contingencies in the outer world and form associations and finally, the way in which we reason, make inferences and assign values.

The following two figures illustrate the extent to which the *a priori* knowledge stored in the architecture of our brains determines the way in which we perceive.

The object in Figure 1 (see p. 611) is a mold used to produce candies. On the left side one sees the front aspect of the mold with the concavities and on the right the rear side with the corresponding convex protrusions. In reality, both pictures show the front aspect, but one picture is rotated by 180°. The reason for these very different perceptions is that the brain makes the *a priori* assumption that light comes from above. In this case contours that have the shadow above need to be interpreted as concave and those with the shadow below as convex. Thus, an implicit assumption determines what we perceive. Somehow this assumption is implemented in the processing architecture of the visual cortex but we are not aware of it.

Another even more striking example is shown in Figure 2 (see p. 611). It is hard to believe, but surfaces A and B have exactly the same luminance and this can be verified by covering all squares except A and B with white paper. The squares A and B appear as different because the brain sees the shadow that is caused by the cylinder on the right. Even though the amount of light reflected from surfaces A and B and impinging on the retina is exactly the same, the brain interprets the brightness of the two surfaces as different because it infers the following: given that there is a shadow, surface B must be brighter than surface A which has no shadow on it, in order to reflect the same amount of light. Thus, the brain 'computes' the inferred brightness of the surfaces but we are not aware of these computations. We just perceive the result and take it as real, i.e. we see B much brighter than A. One could spend hours with the demonstration of examples which indicate that the brain is generating inferences that we are not aware of, that it is permanently reconstructing the world according to *a priori* knowledge and that we, as perceiving subjects, have to take for granted what the system finally offers us as conscious experience. It is important to emphasize that this is not only the case with specially designed psycho-physical experiments but it is an essential feature of all our perceptual processes. We perceive the result of complex computational operations, and because we are unaware of both the priors and the rationale on which these interpretations are based, we tend to take for granted what we see. We do not realize that our percept is the result of complex computations that are based on assumptions and have difficulties to accept that what appears to be so evident and an invariable property of the perceived object is actually the result of a highly inferential and constructive operation.

The following Gedankenexperiment is meant to illustrate the adaptive value of such perceptual inferences. Imagine that red berries with a specific hue constitute a major food source and that red berries with a slightly different colour are poisonous. It is thus imperative to distinguish between the two sorts of berries and to be able to do this irrespective of daytime. The problem is that the spectral composition of sunlight is radically different in the morning, at noon and in the evening. Accordingly, the spectra reflected by the two kinds of berries differ at different times of the day and it may well be that the spectra of the poisonous berries produced by the morning light resemble the spectra produced by the good berries at noon. Thus, the only way to assure the distinction between the two at any time of the day is to interpret the reflected spectra as a function of the actual spectrum of the sunlight. The latter cannot be measured directly but it can be inferred from the comparison of spectra reflected from familiar objects and *a priori* knowledge of their likely colour. Thus, by comparing the color of leaves, barks, rocks, the clouds etc. the system can estimate the spectral composition of the illuminating light source (the sun), take this into account when interpreting the spectra reflected from the two types of berries and only then compute the hue of the colour that is actually perceived. Through this complicated operation it can be assured that the good berries are perceived as having the same colour irrespective of illumination conditions. This is but one of a large number of examples which illustrate that what we perceive and interpret as invariant properties of objects is actually the result of a highly inferential and constructive process. Furthermore, these examples explain why it is advantageous for organisms to base their perception on *a priori* knowledge and pragmatic heuristics rather than perceiving the absolute, unprocessed values of the signals provided by our sensors that transform physical or chemical stimuli into amplitude modulated neuronal activity.

Causes and effects of cultural evolution

Because most of the priors that determine our perception of the world around us have been acquired during evolution we share them with the animal kingdom. Non-human primates for example but also members of other species such as cats, dogs and even insects make the same inferences and thus perceive the world in similar ways. There are, however, also important differences and these result from the fact that only human brains are exposed during their development to realities that were absent during biological evolution that has shaped our brains as well as those of animals – realities that are the product of cultural evolution. This raises two related questions: what are the cognitive abilities that allowed homo sapiens to initiate the process of cultural evolution and what are the consequences of the epigenetic shaping of human brains by their exposure to socio-cultural realities?

Over the last decades, a number of cognitive functions have been identified that are apparently not found in our nearest neighbors, the great apes, and thus with all likelihood are responsible for the initiation of cultural evolution. One of these functions is the ability to generate a theory of mind, to imagine what goes on in the mind of the respective other when she/he is exposed to a particular situation but does not signal through any perceivable signs what her/his thoughts, intentions or feelings are. Another important function is shared attention. If a human being directs his/her gaze to a particular target or points towards it, a human observer is able to direct attention to the same target, understanding that both subjects are now sharing their attention. Dogs, probably because of domestication, are able to accomplish this very specific function but the great apes are not. Furthermore, human beings possess an unprecedented ability to generalize, to identify the common in the seemingly different and, therefore, are capable of forming abstract, symbolic representations. When monkeys learn to associate particular attributes with signals provided through one sensory modality, they usually have great difficulty recognizing the presence of the same attributes when signals are provided by a different modality. Humans accomplish such inter-modal transfer with great ease, probably because of the specific features of their cortical architecture that allow for easy exchange of information across the processing streams of the various sensory systems or because of the addition of association areas that allow for convergence of information from different modalities. The resulting ability of abstraction and symbolic coding is with all likelihood one of the prerequisites for the development of language. Other prerequisites seem to be the ability to represent complex sequences of nested relations which are at the origin of the comprehension and production of syntactic structures. Finally, human beings are capable of transmitting knowledge acquired during their lifetime through intentional instruction and education. Even the great apes learn essentially through imitation. Infant chimpanzees imitate nut cracking and even if they perform poorly, their mothers do not instruct their offspring but just continue to crack their own nuts.

This then raises the question of which changes in brain architecture might be responsible for the emergence of these novel cognitive abilities. When comparing the brains of the great apes with those of human beings, the only remarkable difference is the addition of new areas of the neocortex. Apart from that, there are no major structural changes and even the new cortical areas closely resemble with respect to their intrinsic organization those which exist both in humans and non-human primates. As outlined previously, the computational operations performed by a neuronal network are fully determined by its functional architecture and, therefore, it can be inferred that the new cortical regions operate according to the same principles as those that had already existed. Thus, the only options that these new areas offer are those that can be realized by implementing further nodes in the network. This could permit the generation of platforms for novel and more complex associations among the results obtained in parallel and previously unconnected processing streams or – if added on top of processing hierarchies – the generation of meta-representations. There is evidence for both strategies and both are likely foundations for the enhanced sophistication of human cognition. This interpretation agrees with the evidence that the molecular composition of nerve cells, the mechanisms mediating signal transduction and the molecular machinery supporting modification of synapses by learning closely resemble those found not only in all vertebrates but also in molluscs and insects. With the realization of the canonical circuits that characterize cortical modules, evolution has apparently discovered a computational algorithm that is universally applicable both to the evaluation of sensory signals of different modalities and to the design and organization of executive acts. Moreover, and this seems to be particularly advantageous, this canonical circuit can support iterative, reentrant processing of the results generated by these very circuits and thereby allow for the virtually unlimited recombination of signals.

Epigenetic shaping, cultural diversity and tolerance

Together with anatomical modifications allowing bipedal gait that freed the front legs for duties other than locomotion, the development of the cognitive abilities listed above allowed *Homo sapiens* to initiate cultural evolution. Although at dramatically different time scales, the dynamics of biological and cultural evolution share certain similarities. In both cases, complexification and diversification of evolving structures were initially very slow but then experienced a dramatic acceleration. Once *Homo sapiens* appeared on stage, it took apparently tens of thousands of years to develop communication skills resembling syntactically based languages, social structures that allowed for labour sharing, tool making, sedentary lifestyles and the development of concepts that added a spiritual or metaphysical dimension to the material world. However, this period of slow differentiation underwent a phase transition about 30,000 years ago that led to an exponential acceleration of socio-cultural evolution with its countless ground breaking inventions. This acceleration suggests that evolutionary mechanisms that support autocatalytic processes became effective. One of them might have been the increase in population density. Increasing population density permitted the establishment of denser communication networks, the sharing of inventions, the development of cooperative strategies for a less time- and energy-consuming exploitation of resources and the reinvestment of the spared time and energy into exploratory activities that rendered these early societies more and more independent of the hazards of nature. However, the most effective factors that catalyzed this unprecedented acceleration are with all likelihood the extremely protracted postnatal development of the human brain and the ability of human subjects to intentionally educate their offspring. In conjunction, these two mechanisms make it possible to translate knowledge acquired during lifetime into the functional architecture of the brains of the respective offspring. As outlined above, these modifications consist of changes in circuitry that determine the functional architecture of brains in very much the same way as genes. Thus, although the basic blueprint of our brains is not very different from that of our cave dwelling ancestors as the genetic outfit has not changed much over the last 30,000 years, our brains differ from theirs because of epigenetic modifications that our brains experienced while developing in a highly complex socio-cultural environment.

Right from birth our brains are exposed to a much more complex environment than the brains of our ancestors because of the countless artifacts that the various cultures have invented and added to nature. Moreover, our children are exposed to highly sophisticated languages that convey not only factual knowledge but also the experience with complex relational structures. And finally, there is intentional education that sets in right after birth and is intensified until it occupies nearly the whole wake time as children grow older. Thus, through the combination of epigenetic modifiability of brain architectures with intentional education, a mechanism is introduced in the evolution of *Homo sapiens* that permits reliable transmission of knowledge acquired during lifetime to the subsequent generation.

This is not the place to analyze in detail similarities and differences between genetic and epigenetic modes of information transmission. However, there is one important difference that I would like to highlight because it has far reaching consequences for our concept of tolerance. The knowledge about the world that has been acquired during biological evolution and that governs our perception of the world is similar for all human beings and we share this knowledge in various degrees with the animal kingdom. Although different species have evolved into different ecological niches, the constraints to which cognitive systems had to adapt were rather similar. This is why we usually agree with respect to the perception of phenomena characterizing the precultural world. We share the inborn priors with other human beings and, therefore, as reflected by the similarity of the genetically determined features of our brain architectures, rightly assume that other human beings perceive the world in very much the same way as we do. Still it may occur in certain situations that subjects come to different conclusions concerning the perception of non-culture specific properties of objects. A color blind person for example bases her/his perception on different priors than a color competent subject. Both experience the same object in different ways and it would be hard for them to find out who is actually right. In this case, the dissent can be resolved by consulting 'objective measurement devices' and thereby including a third person perspective.

However, in case of the perception of realities that cultural evolution has generated, it is much less likely that all human beings agree. Priors installed by post-natal epigenetic shaping are much less likely to resemble each other than priors acquired during biological evolution. One of the hallmarks of cultural evolution is diversification. Accordingly, it is very likely that the priors acquired by early exposure to different cultures exhibit culture specific differences. As outlined above, the knowledge acquired during early development remains implicit because of childhood amnesia. Nevertheless, this implicit knowledge, just as the evolutionary acquired knowledge, will determine how subjects perceive the world around them. It follows from this that individuals raised in different cultures will base their perception on different epigenetically transmitted priors and, therefore, are likely to perceive realities, in particular those brought fourth by cultural evolution – the so-called social realities – in different ways. In situations where these perceptions are based on implicit priors, subjects will be absolutely convinced that the way in which they perceive a particular condition is the only way it can be perceived – just as we are convinced that there is only one way in which a particular object can be perceived. Subjects raised in different cultures with differing implicit priors about social realities will perceive the same social setting in perhaps very different ways, both experiencing their perceptions as evident and not questionable. However, in this case no 'objective measurement device' can be consulted. The categories of right and wrong become meaningless in this context. Both subjects have the same right to claim as correct what they perceive.

It is obvious that conflicts arising from diverging perceptions of the same social realities increase in frequency and severity as globalization forces different cultures to interact with each other. It is also obvious that the only recipe to cope with such conflicts is tolerance. However, the classical strategy to practice tolerance has been based on the implicit assumption that eventually a distinction between right and wrong is possible. If there is sufficient consensus about the perceived among members of a sufficiently large group of people, it is usually taken for granted that the respective perception of conditions is correct. Deviating perceptions of others are then considered as false and it is believed to be a tolerant attitude if the dissenting minority is allowed to continue to maintain its 'false beliefs' as long as these do not really challenge the system of the majority. However, as history has shown over and over again, this non-reciprocal concept of tolerance does not solve but generates problems because of its humiliating effect on the tolerated minority. The worldwide surge of terrorism is but one of the many deplorable consequences.

The scientific evidence on the dependence of perception on priors and on the acquisition of priors by epigenetic shaping of brain architectures forces us to adopt new concepts of tolerance that are based on strict reciprocity. Perceptions that are based on implicit priors cannot be changed by argument, they remain evident to the subject and resist relativism. In addition, when it comes to the perception of social realities, distinctions between right and wrong, between correct and false perceptions are impossible. Therefore, members of all cultures have to be credited that what they perceive is correct, even if the respective perceptions diverge. Thus, mutual recognition and reciprocal tolerance are required. Tolerance needs to be granted on a mutual basis and may only be withheld when the respective other violates the rules of reciprocal tolerance. These rules, in contrast to the differing perceptions of realities, are objectivatable and can be codified. Rather than attempting to defend belief systems based on idiosyncratic perceptions of social and cultural realities mankind, if it were to cope with the tremendous problems of globalization, will have to invest massively into the definition and defence of rules securing reciprocal tolerance.

DISCUSSION ON PROF. W. SINGER'S PAPER

PROF. ARBER: Thank you for enriching our knowledge. I think that even at my age I will get some imprinting from what I hear in this room… this is quite nice. But I was a bit surprised to hear that brain development is completed at around the age of twenty.

PROF. BATTRO: Thank you, Wolf, for this thought-provoking presentation. Of course, this changed from biological to cultural evolution, it is key. I think it is what Prof. Zichichi said of Big Bang 3, perhaps, and the difference which is essential, as you said, in education – this is as a comment – it seems that the great change between our species and the other species is teaching. It is impossible to have a model of teaching in animals. What we say is that teaching is unique to the human species and this is why we need more work on the teaching brain, which is difficult, but we have a way out because, as you said perfectly well, children can teach because at 3 or 4 years old they already have a theory of mind. Without a theory of mind we really cannot teach. Therefore we can develop a protocol to do work on the teaching brain, we need more teaching brain research.

PROF. W. SINGER: I agree.

PROF. JAKI: I am puzzled by the fact that, although our brain is very specifically constrained in volume, in weight, in molecular composition, nevertheless that brain, which is the basic tool of our thinking, can perceive that it is constrained. My perplexity comes from a recollection of Goedel's incompleteness theorem. Nothing is more constrained than the laws of arithmetic, which is the basic form of all mathematics and Goedel discovered, in the late 1930s, that a mind, or the mind, which is bent on consistency, this is the basic rule of reasoning, can discover that it cannot achieve a full consistency within the laws of arithmetic. Do you know of any publication in brain research that considers the applicability of Goedel's theorem to the very problem you have discussed?

PROF. W. SINGER: I am not aware of a paper. I am only aware of epistemic circles.

PROF. WOLTERS: You differentiated or distinguished cognitions from reasoning and said that cognitions are a result of adaptation and have to be viewed in a functional perspective, which is different from truths. And then you said, well, reasonings may also be of that sort. My question is, what do you think of when you say 'reasonings', and this is related very much to your last point, where you pointed out that truth is cultural relative for quite a segment for things we say.

PROF. W. SINGER: Well, it is just by extrapolation, since I see that the same substrate that is responsible for perception is also responsible for reasoning. It is very likely that it is also adapted in an idiosyncratic way to a particular segment of the world in which certain contingencies are the case, from which would follow that the logic that we apply has evolved from experience with a narrow section of the world. Whether this is generalisable or not I don't know, but when I heard all the physicists talk on Friday and Saturday I sometimes had my doubts.

PROF. CAFFARELLI: I wonder if you gave any thought about devising some strategy for science education? For instance, there is this counterintuitive fact that if you teach science or mathematics specially, generalising from the particular seems to be natural way. Nevertheless it has been shown that I do not know at what level of age, if teenagers or children who are basically taught axiomatically, have a bigger power of generalising than the ones that have been…

PROF. W. SINGER: I have not given it any deep thought, but I thought it would perhaps be helpful to get our children used to complexity theory, so that they acquire an intuitive feeling for non linearity already from kindergarten, because the problems that we will have to deal with in the evolving world are of that kind and we are very poor in dealing with them.

PROF. MITTELSTRASS: A very short question. What distinguishes your principle of tolerance from the principle of relativism?

PROF. W. SINGER: Well, I think the principle of relativism admits that you can have different perceptions of the same thing and that there may be not an absolute independent view that allows you to perceive things as they may be in reality. This notion of relativism forces one to defend concepts of tolerance That's how I would see it.

PROF. ABELSON: I thought you rather beautifully give the boundary conditions for the problems that Professor de Duve raised in his lecture, that is, in a world that is increasingly dangerous we have to evolve some shared values. The threat of global warming, for example, might lead to shared values.

PROF. W. SINGER: But I think we might be able to agree on certain architectural features of societies that need to coexist to make it possible for them to self organise towards stable states. I do not believe at all that it is possible to manage these complex systems, be it the economy or any social or political system, in a top-down fashion by some meta-intelligence who would know how to do it. Because you cannot really steer those systems, one needs to implement architectural features, like in the brain, that stabilise them through self-organisation. I do not know how they work but this is where we have to inquire, I would think.

THE LANGUAGE OF GOD

FRANCIS COLLINS

In choosing a topic for this landmark discussion, I took seriously the fact that we are here to talk not only about science, but how science interfaces with spiritual perspectives. I could have used my time to talk exclusively about genome science, because that field is undergoing enormous exponential growth right now. I will indeed talk about that, but I also would like to try to provide, from my own personal perspective, some comments about how these advances can be synthesized with belief in a Creator God. After all, the effort to explore such a synthesis is a major point of this meeting.

I often begin conversations about science and faith with a pair of images representing the two major worldviews that various peoples of the world are debating: one image is the rose window of a cathedral, with its beautiful radial pattern; the other is a view of DNA, a different one than you usually see, looking down the long axis of DNA and also showing quite a beautiful radial picture. There are many who argue at the present time that we have to make a choice between these two worldviews. Certainly, in my country, the USA, such shrill voices of opposition are heard much more commonly than those who argue for possible harmony.

Is it a mistake to try to discuss science and faith in the same room? I often reflect on the greatest commandment as spoken by Jesus, 'Love the Lord your God with all your heart, with all your soul, and with all your mind' (Matthew 22:37). Isn't doing science a way of loving God with all your mind? It certainly doesn't sound as if Jesus thought there was a conflict between faith and reason.

The Human Genome Project and the practice of medicine

The Human Genome Project, which I had the privilege of leading, had an audacious goal: to read out the entire DNA instruction book for *Homo* *sapiens*, more than 3 billion base pairs. At the time of the beginning of this project the technology for doing this was clearly not in hand, so one could say this was a truly an ambitious objective. However, all of the goals of the Human Genome Project were achieved in April 2003. Throughout the course of the project, all of the DNA sequence from the human genome was made immediately available on the Internet every 24 hours, so that anyone who had ideas about how to use it for human benefit could begin work immediately.

The scientists who participated in the Human Genome Project hailed from six countries of the world. They, too, helped us identify where to go next. An iconic diagram featured in a *Nature* paper in April 2003 depicted a metaphorical building that we were now prepared to construct, resting upon the foundation of the Human Genome Project, but now applying that knowledge to biology, health and society.

Many of the 'Grand Challenges' outlined in that rather audacious publication have already been achieved, thanks to the rapid pace of genome research. Specifically, remarkable progress has been made in identifying variations in the human genome that are playing a role in risk of disease. Your genome and mine are about 99.6% the same. In that small percentage where we are dissimilar, most of those differences do not have medical consequences – but some of them do. For me, as a physician geneticist, a major goal was to try to identify what some of those genome glitches were that play a role in diabetes, heart disease, or cancer. While we had done a very good job of finding those glitches for diseases that were highly heritable, like cystic fibrosis and Huntington's Disease, until very recently we had not had much luck with the common diseases that fill up our hospitals and clinics. All that has changed in the last three years.

Building upon the success of the Genome Project, another project called HapMap provided a catalogue of human variation that made it possible in a comprehensive way – not based upon candidate genes, but looking at the entire genome – to scan and identify those variations associated with diseases that are non-Mendelian in their inheritance. The first success was age-related macular degeneration, mapped to chromosome 1 to a gene called 'complement factor H'. No one expected that gene to be involved in this disease, and yet a common variant in this gene is a major risk factor. Since that discovery, much has happened: in 2006 there were three more successes. With the full availability of the HapMap and the advent of very low-cost genotyping in 2007, discoveries really started to appear, and became a full-fledged deluge by 2008. As a result no less than 400 of these well-validated genetic variations associated with common disease have emerged, mostly in the last two years, shedding dramatic new light on the causes of diabetes, heart disease, cancer, mental illness, autoimmune diseases, asthma, and many others.

These successes provide us with powerful new targets for therapeutics. They also present the opportunity to provide individuals with a refined estimate of their future risk of disease, depending on which of these variants they happen to carry. Already there are companies who offer you the chance to test your own genome for about a million different variants, for a cost as little as 400 US dollars. Whether that is premature or not is a matter of some debate; while the tests are scientifically based, most of the heritability of common diseases has not yet been uncovered, and there is limited evidence that knowing this information actually improves outcomes. But the era of personalized medicine is at hand.

As technology advances, we will soon be able to examine individual genomes in their entirety, identifying not only the common variants but the less common ones that play a critical role in disease risk. Professor Gojobori already presented information about the way in which DNA sequencing is advancing. This capability has made it possible to tackle problems in a comprehensive way that previously had not been feasible. An important area is cancer. Certainly we have known for a long time that cancer is quite literally a disease of the genome. It arises because of mutations in DNA. It takes an accumulation of several mutations over many generations of cell divisions to reach the point where that cell is truly malignant. If we really want to understand cancer, we need to develop a comprehensive catalogue of all the mutations in the cancer cell. Last year, the first paper describing the full sequencing of a cancer genome was published in *Nature*. It described the complete DNA sequence of a leukemia arising in a woman who had a very aggressive form of the disease. A number of new genes were found mutated in the cancer cells, and were not on anybody's previous list of oncogenes or tumor suppressors. From these findings it is clear that this comprehensive view is going to open up many new vistas in terms of the understanding of malignancy.

Another area that these sequencing advances now allow us to tackle is to look more closely at those non-human genomes that are on us or in us. There are hundreds of trillions of microbes on our skin, in our mouths, and in our gastrointestinal tracts. For the most part these organisms are synergistic with us and assist in maintaining our health. However, the balance between host and microbes can be deranged, and that can lead to illness.

The Human Microbiome Project is a new international program that aims to catalogue these microbial genomes, both in health and in disease. This has not really been possible in the past, as only a minority of these microbes are possible to culture in the laboratory. But they have DNA.

Technology promises even more disruptive advances for high-throughput, low-cost sequencing. An example mentioned by Professor Gojobori is a new approach from Pacific Biosciences that sequences single DNA molecules. I have recently seen a demonstration of this technology, which carries out DNA sequencing in real time using fluorescently labelled tags and massive parallelism. This promises to reduce the cost of sequencing another couple of orders of magnitude and bring it down to the point where a complete DNA sequence can be done for a thousand dollars or less, in a matter of a few hours.

So how will these advances play out in the practice of medicine? Discoveries about causes and treatment of each disease will move at a different pace, but I think we can expect things to happen pretty quickly. Already for some diseases, we are using the tools of genotyping and DNA sequencing to identify individuals at high risk. As just one example, those found to be at high risk for colon cancer can now be counseled to have annual colonoscopy beginning at age 30 (instead of the usual recommendation of age 50).

We also have the opportunity to use the tools of genetics to identify variations that will predict response to drug therapy. This is the field of pharmacogenomics, and promises to provide a better opportunity for a patient and physician to choose the right drug at the right dose.

I would predict, however, that the major, long term impact of the genomic revolution will be the discovery of new therapeutic opportunities, building on knowledge about biological pathways that are fundamental to disease pathogenesis. Some of these new treatments will be gene therapies, where the gene itself becomes the treatment. A recent exciting example of this is in the treatment of a particular type of blindness. But perhaps an even more widespread consequence of our new knowledge of the genome will be in the form of drug therapies, because of the new targets that are being discovered using the genomic approach.

It thus appears inescapable that medicine will undergo a major revolution in the course of the next ten years. Unfortunately, however, I do not think that the medical profession is currently well prepared to respond to this revolution, because of the disparity between the rapid nature of these discoveries and the relative slowness of the medical education system to incorporate them into training.

EVOLUTION AND THE STUDY OF GENOMES

I would now like to turn to the evidence coming from these genome studies with regard to evolution, as that is a major topic of discussion at this meeting. If there have been legitimate doubts about whether Darwin's theory was correct, based upon so-called 'gaps' in the fossil record, those doubts have largely been swept away by the study of DNA. In fact, if Darwin had tried to imagine a compelling way to demonstrate the correctness of his theory, it is hard to see how anything outside of a time machine would have been better than comparative genomics.

Not only have we sequenced our own genome, but recent covers of *Nature* and *Science* magazines show successes for other genomes as well: the mouse, the chimpanzee, the dog, the honey bee, the sea urchin, the macaque, and the platypus. We have draft or complete genome sequences now for more than two dozen vertebrates. If you feed these genome sequences into a computer and ask it to create a relatedness tree between the organisms, it will produce a startlingly close match to evolutionary trees that have been generated from fossil data or from anatomical features.

But in my country, the USA, there are still many who reject the evidence that all of these organisms, including humans, are related by descent from a common ancestor. A recent poll shows that forty-five percent of Americans believe that the earth is less than 10,000 years old, and that humans were specially created by God. This view is in serious trouble, once one looks at the DNA evidence. Certainly, one could argue that God used the same motifs repeatedly to produce all of these organisms as acts of special creation, and that might explain the general relatedness at the DNA level. But when we look at the details, it is clear that this particular alternative view cannot be sustained. As an example, consider human chromosome 2. Chromosomes are the visible unit of heredity in a cell. We humans have 46 of them, made up in pairs. One can look under the microscope at a cell that is about to divide, and observe the chromosomes. It is noteworthy that human and chimpanzee chromosomes look a lot alike with regard to their size, their banding pattern and so on. The one exception, however, is that we have human chromosome 2 as our second largest chromosome, while chimps do not. They instead have two smaller ones. Gorilla chromosomes look similar to chimps; making us the outlier amongst primates.

There has been a prior supposition that perhaps in the lineage leading to humans there was a fusion of two smaller chromosomes giving rise to our chromosome 2. That finding has now been subjected to exquisitely detailed analysis from the DNA sequence data. There are special sequences at the tips of all chromosomes. These are the telomeres; a particular sequence, TTAGGG, appears over and over again in order to prevent fraying as the cell divides. It is interesting to note that when you look at human chromosome 2, there are telomeric sequences in the middle, exactly in the position where you would predict such a DNA footprint would have been left by a fusion between two ancestral chromosomes.

Another revealing example of our common ancestry with other animals also explains why sailors contracted scurvy on those long sea journeys. If we look at the order of genes in multiple mammals around a particular gene called GULO, we will see the order of genes is the same in humans, cows and mice, as well as many other vertebrates. But this is an interesting example, because the gene GULO, which stands for gulonolactone oxidase, is a pseudogene in humans (and in other primates) – meaning that it has sustained a knockout blow, decapitating its front end completely so that it lacks the first part of the coding region. It is utterly nonfunctional. Well, the product of that gene normally catalyzes the final step in synthesizing ascorbic acid (vitamin C). Unable to make their own vitamin C because of the non-functional GULO gene, sailors developed scurvy when they did not have access to vitamin C. But the mice on the ship, possessed of a functional GULO gene, did just fine.

Looking at that data, it is extremely difficult to argue that we humans are created as a special separate lineage compared to other animals. One would have to infer that God intentionally inserted a non-functioning GULO gene in just the position to mislead us into thinking that descent from a common ancestor was correct. This model would put God in the position of being a DNA deceiver, which does not seem consistent with other basic tenets of religious belief.

Catholics are in general much more comfortable with the shared descent of humans and other animals, so I probably do not need to make this case so strongly to this particular audience. But for many protestant evangelical Christians in America, this is still not an easily accepted conclusion.

The harmony of science and faith

Let me turn now to another question. Simply stated, 'If evolution is true, does that leave any room for God?' Let me begin with a personal perspective. I was not raised in a religious tradition. Until my twenties, I considered myself an agnostic, and ultimately an atheist. It was actually my involvement in medicine that forced me to consider issues of life and death in more than hypothetical ways, and my involvement in science that convinced me that the purely materialistic approach can be unnecessarily limiting for the kinds of questions that we humans want to ask – such as why there is something instead of nothing. These intellectual explorations ultimately led me, to my great surprise, to Christianity.

It didn't take long for my colleagues to point out that they thought I was on a collision course between the scientific and spiritual worldviews. As a geneticist, evolution was fundamental to my understanding of biology. But didn't I know that evolution and faith were utterly incompatible? Certainly that case has been smoldering ever since 1859, and has been recently made rather loudly by some of my colleagues, such as Professor Dawkins.

In his book, *The God Delusion* (a rare book that does not require a subtitle), Dawkins uses evolution as one of his strongest arguments against the plausibility of God. He insists that once Darwin arrived at his theory of evolution the need to describe a Designer or Creator went out the window. But in my view and that of most thoughtful believers, Dawkins makes a category error by trying to use scientific arguments to weigh in on the existence of the supernatural.

Nearly two years ago, I engaged in a debate with Richard Dawkins for *Time* magazine. The exchange is still available on the Internet.[1] Ultimately at the end of it, Dawkins admitted this category error to a certain extent, recognizing that science cannot exclude the possibility of a supernatural God, even though he thought it highly unlikely. But he stated that if there was such a thing as a supernatural God, it would be much more grand than any of us could imagine. That's exactly the God believers are talking about, I said!

So we are back to the question, 'How can evolution and faith be reconciled?' If you will indulge me, I would like to provide a rather personal response. I understand the risk of doing so here, in front of esteemed scientific and theological colleagues. I am an amateur theologian and philosopher. But it seems to me that there is a readily-achieved synthesis that is entirely compatible both with what we know scientifically, and with what the basic Abrahamic principles say about God the Creator. Here it is: Almighty God, who is not limited in space or time (an Augustinian concept from 400 AD) created this universe with its parameters precisely tuned to

[1] See http://www.time.com/time/magazine/article/0,9171,1555132-1,00.html.

allow for the development of complexity over long periods of time. God thus endowed Creation with amazing potentialities. That plan included the mechanism of evolution to create the marvelous diversity of living things on our planet – and, most especially, human beings, with minds created in God's image. Evolution was sufficient to prepare the 'house' for all this, namely the human brain in all of its elegant complexity. But there was something missing until the additional spiritual component of humanity arrived. The story of the Garden of Eden is then a description of God's provision of additional gifts to humankind: free will, the soul, and – I know this will be controversial – the moral law. The moral law, the knowledge of right and wrong, is universal and unique to humanity, though its interpretation is strongly affected by culture. Biblically we learn in the story of Adam and Eve that we humans used our free will to break the moral law, leading to our estrangement from God. For me, as a Christian, it is Christ who provides the solution to that estrangement.

This synthesis of Biblical and scientific perspectives has traditionally been called 'theistic evolution'. But I don't think that is a great label. It turns a lot of people off because it sounds like evolution is the noun and theistic is the adjective, implying God is less important than Darwin. So, in my book *The Language of God*, I proposed an alternative term: *Bios*, meaning life, through the *Logos*, or the Word – or simply *BioLogos*, God speaking life into being.

As you may imagine, there are a variety of objections to this perspective. For instance, one often is asked: 'Didn't evolution take an awfully long time?' This question is a concern of many Evangelicals who cannot imagine why God would have taken so long to get to the point (humanity). They often ask, 'Why didn't God just snap his fingers and make it happen?' Well, again, if God is outside of time this is our problem, not God's problem. Another related objection is: 'Isn't evolution a purely random process?' This question seems to take God out of it. As one of several possible responses, I would posit that if God is outside of time, then randomness to us may not necessarily be randomness to God.

Intelligent Design proponents ask, 'Is evolution really sufficient?' In other words, aren't there biological structures, like the bacterial flagellum or the human eye, that are just too complicated for evolution alone to have produced? Each of these structures has many subunits, and when just one of them is knocked out, the whole thing stops working. So how could such complexity have arisen by natural selection alone? Well, those questions reveal a basic misunderstanding of the stepwise fashion by which such multiprotein complexes come into being. A recent paper from *Nature Reviews Microbiolo-*

gy points out how many of these intermediate steps are being discovered for the flagellum. Intelligent Design, in my view, is turning out to be a major misstep. It is both bad science, representing a God-of-the-gaps approach, and bad theology, portraying God as a rather inept Creator that had to keep intervening along the way to correct deficiencies in the original plan.

Proponents of evolutionary psychology have objected to my portrayal of the moral law as a signpost to God. Can't this be a consequence of evolution? Isn't altruism just a human behavior that has led to greater reproductive success of the species, and that's all? There are, to be sure, many aspects of altruistic behavior that are consistent with explanations provided by evolutionary psychology. They include: 'kin selection', which explains generosity to your relatives since you share your DNA with them, and if you help them be reproductively successful your own DNA is succeeding too; 'reciprocal altruism', which argues that our own altruism is often driven by a hope for some reciprocal benefit in the future from those we have shown kindness; and even 'group selection', which proposes that altruistic behavior of a group of individuals provides advantages to the whole group, even if it harms a few individuals' chances of reproductive success along the way. Martin Nowak at Harvard expounds on these models in his very interesting game theory studies. He concludes, however, that for group selection to work, one must be hostile to anyone who is not part of the group. But is that the kind of altruism we most admire in humans?

Imagine for a moment the person who, with great risk to themselves, reaches out to someone they do not know, someone who is part of another group. Evolution, ultimately, would predict hostility. But when we see this kind of radical altruism, we admire it. As an example from about a year ago, Wesley Autrey watched with horror as a young man standing on the subway platform in New York City went into an epileptic seizure and fell onto the tracks, with train No. 1 quickly approaching. Without hesitation, Wesley leaped onto the tracks. He covered the still seizing student with his own body and wedged them both between the tracks. The train rolled over them, and they both miraculously survived. Wesley was black. The student was white. They had never met. Stories like this one electrify us, and we are likely to point to such actions as representative of the best of human nobility. And yet, from an evolutionary perspective Wesley's action was a scandal, taking an enormous risk of sacrificing his own potential reproductive future to save someone he didn't even know.

A final objection to BioLogos, raised especially in my own Evangelical Christian circles, is the question about whether evolution conflicts with

Genesis 1 and 2. But as strongly as these concerns are raised, I see this as an unnecessary conflict. In this regard, I am greatly rewarded every time I open one of the four commentaries that St. Augustine wrote about Genesis. He was a theologian who thought deeply about this subject and who can hardly be accused of trying to retrofit his views into Darwin's theories – since St. Augustine wrote down his views on Genesis more than a thousand years before Darwin walked the earth. Augustine ultimately concludes that there is no way for any single interpretation of Genesis to be declared correct, and he provides a warning that ought to be heeded today by many churches, especially in my country. Augustine cautions, 'In matters that are so obscure and far beyond our vision, we find in Holy Scripture passages which can be interpreted in very different ways without prejudice to the faith we have received. In such cases we should not rush in headlong and so firmly take our stand on one side that if further progress in the search for truth justly undermines this position, we too fall with it'.

Finally, before concluding I would like to respond to Professor Zichichi's statements that took aim at the discipline of biology. Contrary to his view, I do believe that biology has arrived at a new phase of scientific rigor. The era of complete genomes, and the ability to understand life in a digital way, allows biology to take its rightful place as a truly quantitative science alongside physics and chemistry. Although this was not true a few decades ago, it is clearly true now. Evolution is at the core of these advances. I therefore associate myself with Theodosius Dobzhansky, one of the leading lights of evolutionary thought in the 20th century and a Russian Orthodox Christian, in his statement, 'Nothing in biology makes sense except in the light of evolution'. I do not know how we could do biological science at all without accepting the evolutionary paradigm. Nevertheless I agree that evolution does not have, and will never have, an answer to the 'why' question. That is a question that science cannot answer; it is a matter for faith to address.

Thank you, again, for the gracious invitation to join this distinguished group at the Pontifical Academy, and to spend time discussing these important worldview questions.

DISCUSSION ON PROF. COLLINS' PAPER

PROF. ARBER: Thank you very much for this interesting presentation and the outlook into the spiritual world.

PROF. M. SINGER: Tomorrow, when I talk about intelligent design, I will, try to show how it is that, in the U.S., many people who do not accept evolution disagree with Francis' conclusions.

PROF. COLLINS: Yes, they do!

PROF. PHILLIPS: So I would like to ask about your discourse about the development of morality, because you gave a picture that was very different from what Wolf Singer gave before.

PROF. COLLINS: Maybe, maybe not, that is a good question.

PROF. PHILLIPS: Well, anyway, the way I perceived it he was emphasising the diversity of moral understanding and encouraging us to take the point of view that there is no right or wrong. You, on the other hand, emphasised a certain commonality and, in fact, in describing how someone may object to the concept of God by explaining that commonality of moral understanding came about through some evolutionary process. So it seemed to me, at least, that you were emphasising commonality and that Wolf Singer was emphasising diversity and my own perception of moral understanding across human cultures is that I am much more impressed by the commonality than I am by the differences. In other words, the differences I see more or less as things that have to do with case law whereas the commonalities have to do with general principles. Well, so can you correct my impression? But I would like to have your perspective on that difference between what you said and Singer said.

PROF. COLLINS: it is a great question and I think, actually, the differences may not be very great. C.S. Lewis, in his book *The Abolition of Man*, has an appendix that goes through the monotonous review of cultures down through history and across the world and their moral behaviour and the conclusion he arrives at, which, I think, is shared by those who have looked at that data carefully, is that the idea that there is such a thing as right and there is such a thing as wrong appears to be a universal human attribute. We do not find exceptions to the idea that there is such a thing as moral law. Where we find vast differences is how that is interpreted, which is what I took Professor Singer's discussion to mean, that that epigenetic modelling of the brain takes this fundamental law about right and wrong and it decides what goes in which category, and that is profoundly culturally affected by learning and by what your parents model for you. So you can see cultures that we see today as having done horrible things who at the time were convinced that they were behaving in a right fashion, based upon their own epigenetic modelling of the moral law in their brain or other forms of self delusion, perhaps, and I am sure our own culture has its own form of self delusion. But I do not think that that kind of variation in social mores or cultural mores can get us away from the fact that there is, apparently, in human commonality, this notion of a right and a wrong, again a notion which I find difficult to completely explain on totally materialistic grounds. And let me just say one other thing about that: if one wants to do that, and certainly the evolutionary biologists and my friend Dawkins will try to do so, you have to carry that all the way to its ultimate conclusion, which is a very uncomfortable one, which is that, in fact, good and evil are not real, that these are illusions, that we have been hoodwinked by evolution into imagining that there is such a thing and that we are driven by this evolutionary hoodwinking into certain kinds of behaviours that, perhaps, now that we are so smart, we should not have to be regulated by anymore. And yet, that is a very difficult thing even for the strongest atheists to say because they are quick in many instances to then point to religion and say, that is evil! Well, where do you get off, saying that anything is evil if you are a pure materialist evil goes out the window and so does good.

PROF. CIECHANOVER: Francis, about disease-related genes. I think several papers were published a few weeks ago showing that, in several aggressive cancers like glioblastoma multiforme and pancreatic cancer, there are about seventy or eighty mutations so how do we know which ones of them are causative and which ones are bystanders? Then, the next one is, of the causative, what is the minimal combinatorial or combinatory that is necessary in order to cause it? And then, if you can answer that, and about the predictability, not all of those mutations are inherited, some of them have been accumulating for a long time, so it would be very difficult to predict susceptibility to disease by sampling at a certain time and you do not know what will be the detrimental time point that makes the predictability certain, so all this adds to a huge complexity of what I thought was a little bit simplistic picture that you described.

PROF. COLLINS: It is a fair point. I would say that the two papers you refer to from the Vogelstein Lab may suffer a bit from inadequate statistics to tell the difference between a so-called driver mutation, which is actually contributing to the malignant phenotype, and a passenger mutation, which is just something that has arisen during the course of cell division and does not actually have a consequence. I think a more careful analysis using larger numbers of tumours, coming on glioblastoma, for instance, from the cancer genome atlas, or looking at almost 200 such tumours, comes up with a shorter list. It is still a long enough list to be a bit daunting in terms of how to put this together. A similar study on 186 samples of adenocarcinoma of the lung published last week also comes up with a list of more than a dozen, but they actually fit rather neatly into four pathways and that is somewhat reassuring that there seem to be four fundamental pathways for adenocarcinoma of the lung where virtually all the tumours have a glitch in each of those pathways, it is just not always the same point where the pathway is disrupted. That would suggest that, if you can come up with therapeutics that target those pathways, you would not necessarily have to have a drug for each individual, which would be obviously untenable, you could come up with something more general. Similarly for the leukaemia patient that I mentioned. But a lot of sorting out has to be done. As far as predictability, almost all of the genetic glitches that are being discovered are somatic, and the ones that involve inheritable risks are much less numerous and for the most part, with some exceptions like BRCA1 or one of the HNPCC mutations, much of those other cancer predispositions are pretty small in terms of their odds ratios. They might imply a need to do better surveillance for a slightly higher risk, maybe we can personalise that approach, but they are not going to make a huge influence and again, the challenge I think we are facing, is how do we get to the point where every cancer is immediately sequenced to see exactly what is the array of mutations. Then how do we take that information and map it on to our set of therapeutics that target various pathways and try to get the right mix, and it is not going to be *a* drug for cancer, it is going to be combination therapy and there are all kinds of problems with that but that has to be the right answer.

PROF. WOLTERS: It occurred to me that you are subscribing to Stephen Jay Gould's NOMA principle.

PROF. COLLINS: No, no, no, I will resist that but go ahead!

PROF. WOLTERS: OK, but anyway, if you think that religion is the source of our knowledge of right and wrong I would contest this with respect at least to Christianity, because in the Bible we find quite different moral recommendations coming from God such as ethnocide, rape, killing the children of the enemies and so on, and we find all the very nice things we usually ascribe to the Bible, so it occurs to me that you need, in order to distinguish between right and wrong, a principle you do not find in the Holy Scriptures but you might find in philosophical discourses since the time of Aristotle going on to Kant and utilitarianism and other positions.

PROF. COLLINS: Good comment, and again I may have come across in some way as implying I think there is a firewall between the worldviews that are spiritual and the ones that are scientific. I do not see it that way, I do not know how I would live in that kind of circumstance where I had to be really clear about which part of my brain was active on any given Thursday afternoon. It seems to me that was an unnecessary and artificial division. More importantly, though, if you are approaching a particular question, you have to ask yourself, is that a scientific question or is it a philosophical or theological question and then use the right tools to try to address it. But I would very passionately argue for the need then to synthesise those worldviews into a harmony, not an artificial separation. I certainly agree that much of what I have said has been said vastly better by other philosophers going back to Aristotle and certainly to Kant, whose statement about his increasing awe at the starry heavens above and the moral law within very much describes what brought me ultimately to become a Christian.

PROF. MITTELSTRASS: Again, a very short question. What is the reason for the claimed necessity of synthesising different worldviews? Isn't man the animal who can live in different worlds, like the world of science and the world of faith, the world of science not claiming orientational knowledge and the world of faith not claiming scientific knowledge?

PROF. COLLINS: Well, perhaps we are getting into a bit of a semantic issue in terms of what is harmony and what is separateness. I interpret

Gould's NOMA proposal as proposing a very strong division between the two, that one really cannot allow any overlap at all in your thinking about the causation of important events or about the answers to important questions. I guess I am rebelling against that idea that the firewall has to be that severe. At the same time I take what you are saying as very much my own perspective that yes, I am delighted and blessed to live within both a scientific and a spiritual worldview, but I reject the idea that I have to decide at any given moment that I am doing one and I cannot think about the other one at that point.

PROF. BERNARDI: There was a famous episode, a long time ago, when Napoleon went to visit the French Academy of Sciences and you know very well that Laplace explained a number of things about movement of planets and so on and, at the end, Napoleon asked the question, and where is God in all you said? And Laplace replied that he did not need that hypothesis. He did not deny at all the existence of God, he simply said, there is no need for God to explain the movement of planets. I think that trying to use science to prove the existence of God is a fallacy and I do not think that the argument of evolution or the argument of the gene are good enough to prove something that is outside the scope. So, I think we should be very careful in not trying to see science or scientific points like evolution as providing any proof. There is no proof for or against it.

PROF. COLLINS: If I came across as suggesting that I had found one then I have misrepresented myself, because I certainly agree that proof for God's existence will not be found within the area of science. I do think it is fair to say, and maybe I am particularly reflecting about my own experience, that there are observations about nature, such as the Big Bang, such as the fine-tuning of the universe, such as the fact that mathematics actually works to describe the way the universe is put together, such as the fact that there is something instead of nothing, and maybe even the fact that there is a moral law, and that is probably the most contentious of my list, that are worth reflecting on. They are not proofs, they will never become proofs of God's existence, but they are somewhat of an antidote to the sweeping atheism which seems to be so prominent in the scientific community, so I think it is worth bringing them up from time to time.

PROF. SZCZEKLIK: I have a question dealing with the first part of your presentation concerning complex diseases, say, atherosclerosis or diabetes. Despite the enormous effort which has been done over the last years, genome-wide search etc, the value of genetic factors for clinical diagnosis and prevention is still very very limited. Could it be so because the phenotypes of the disease we clinicians diagnose, are very inhomogeneous, or the sequencing technologies are not sensitive enough to detect rare variants? Do you have some other explanation, or is it just too early to expect the solution?

PROF. COLLINS: It is a question that is on everybody's minds. We are both exhilarated by discovering some of the genetic risk factors for common disease which have been so elusive but also puzzled by why they account for such a small fraction of the heritability that other studies have indicated must be there. For diabetes, for instance, a disease my own lab has been working on for 15 years, we are exhilarated now by having 18 genetic risk factors that we are quite sure are right and yet, together, they only account for about 10% of the heritability that must be lurking somewhere in the genome. Some of this may be dilution by lumping together phenotypes that really do not belong together, and therefore reducing the signal but it cannot be all that. Some of it may be, in fact, rare variants of large effect, which our current methods are not detecting but sequencing will, or copy number variants which are not readily detected by our current technologies but that many people believe are going to be a lot more important than we had previously imagined. Or perhaps there are many of these very common variants with very small effects, a very long tail of the distribution. We are going to figure that out, that will become apparent. And then, at that point, the ability to make predictions about risk will start to get better. Right now it is small because we are so early on but yes, there is this issue and, reflecting on Vera Rubin's term, the people in genetics are talking about the 'dark matter' of the genome. Where is the rest of the heritability? It is in there somewhere, we just have not found it yet!

THE BUNCH OF PREHUMANS AND THE EMERGENCE OF THE GENUS *HOMO*[1]

YVES COPPENS

Firstly, I want to thank the Pontifical Academy of Sciences for inviting me to this very important, very interesting, quite exceptional meeting that I am enjoying very much. As you know, I am a paleontologist and, more precisely, a field paleontologist, so I will try, through the fossil record, to tell you what I think could have been the history of man, which means the history of the last 10 million years.

It is well known today, especially today, as you have seen, that Bonobos, *Pan paniscus* and chimpanzees, *troglodytes*, are the creatures closest to us in nature. In an evolutionary way of thinking, it means that they, and we, have common ancestors. Because all primates are tropical, and because Bonobos and chimpanzees are African, there is some probability that those ancestors would have been tropical and African. Moreover, the morphological, anatomical, physiological, genetic, molecular and even ethological distance between these cousins and ourselves allows to situate our last common ancestor somewhere in the upper Miocene, which means about 10 million years ago. So we have the place, Africa, and we have the time of existence, 10 million years ago, of our last common ancestor. We will travel through these ten million years in a chronological order in four parts: first part, 10 million years ago, the time of the last common ancestors; second part, the prehuman, before man on our side; third part, the emergence of man; and fourth part, the evolution and expansion of man.

First part, what do we know about the apes in Africa at these late Miocene times and who do we know could pretend to be the last common ancestors to man and chimpanzee? We have three main candidates to

[1] Transcript unrevised by author.

answer this question: *Chororapithecus abyssinicus* from Ethiopia, 0.7 to 0.1 million years old; *Nakalipithecus nakayamai* from Kenya, 8.99 to 8.80 million years old; and *Samburupithecus kiptalami* from Kenya, 9.6 million years old. This very modest fossil record does not allow, of course, to tell who, among these candidates, is the closest to the last common ancestor of chimpanzee and human. Let us say that we have just started to find some remains of African great apes of the right geological age, which are giving us an idea of what these famous grandparents would have looked like. As a matter of fact, we don't know either where they are really standing in the phylogeny, *Chororapithecus*, *Nakalipithecus* and *Samburupithecus* respectively. We don't really know even if they are preceding the divergence *Homo/Pan* or if they are already engaged in one of the two lines, or if they are engaged in another independent branch, having nothing to do with the *Pan* or with the *Homo* branches.

Second part, let us forget this common ancestor, let us forget, as well, the slice of 10 million years of pre-chimpanzees and chimpanzee to focus our attention on our side, the prehuman and the human side of the divergence. We will divide the ten million years of our affiliation into two major episodes: the prehuman one, from ten million years ago to one million years ago, and the human one, from three million years ago to the present, which immediately shows that the last prehumans coexisted with the first humans. The prehumans are magnificently documented by seven genera and fourteen species. I called this diversity, which is reflecting a diversity of ecological niches, a bunch, instead of a bush, because a bunch seems to me clearer than a bush and it is not a political statement.

The seven genera and fourteen species originated from Central, Eastern and Southern Africa: Chad, Ethiopia, Kenya, Tanzania, Malawi and South Africa. Chronologically they can be organized in three steps: the earliest from seven million to four million years ago, with *Sahelantropus toumaï*, *Orrorin* and *Ardipithecus*, a second step between four million to three million, lasting just one million years, and a third step between three million and one million years ago. The second step, between four million to three million years ago, is emerging after an opening of the landscape. The third step, between three million and one million years ago, is also emerging after drought and because of this drought it is more dramatic than the four-million-years-old opening. In order to try to appreciate the bunch of the fourteen prehumans as a group, we will examine the traits that they shared and the few ones that are dividing them. 1) All the prehumans were tropical without exception; 2) All the prehumans were African, without exception; 3) All of them, as far as we know, were upright, permanently upright; 4) All the earliest ones, as far as we know, were both bipedal and arboreal (it is the case of *Orrorin*, *Ardipithecus*, *Australopithecus afarensis* – Lucy); 5) All of them, but at different speeds, seem to become exclusively biped (*Australopithecus anamensis*, from Kenya and Ethiopia, 4 million years old, seems to have been the first not to climb anymore, so the first true exclusive biped); 6) All of them have a slowly increasing endocrinal capacity as well as a slowly more complex organization of the brain: more complex convolution, more complex irrigation; 7) All of them show a tendency of the face to reduce its prognathism, its projection, to reach a sort of orthognathism, flat face. *Kenyanthropus platyops* (flat face) and *Australopithecus bahrelghazali*, 3.5 million years old, seem to have been the first and the best in that reduction. But, as far as the teeth are concerned, we can follow two trends: a tendency to a reduction in the site of the cheek teeth, molars and premolars, and a tendency to an increased size, which means two clear adaptations to two different diets. In summary, the prehumans are tropical, African, upright. They seem to have been arboreal and bipedal before adopting, for ecological reasons, an exclusively bipedal locomotion. They all show a brain of increasing size and complexity. They all show a trend to reduce prognathism at different speeds according to their *phylum*. Some of them, at least and at last, show a trend to a reduced size of cheek teeth, while others show the reverse tendency.

Third part: as I just told you, in describing the third step of prehumans, an important drought happened between three million years and two million years ago. The global cooling of the earth appeared, for instance, in the study of oxygen isotopes ratio, oxygen 16, oxygen 18, in the test of microorganisms collected in deep-sea cores. This climatic change is also particularly well visualized in the sediments of the lower Omo River basin in Ethiopia, because the sediments of this lower Omo River are the only ones in tropical Africa to offer a clear, continuous deposit of these times. I worked there ten years, and during those ten years I collected fifty tons of bones. The Omo sedimentary sequence is a superb stratigraphical column more than 1 km thick, particularly well exposed because of tectonic reasons, particularly rich in fossils, including hominids, and particularly well calibrated by biostratigraphic, paleomagnetic and radioisotopic cross-checking dates. And all the fossils collected – I tell you, as far as I am concerned, fifty tons of them – are showing this cooling. I can give you the example, but I will not, of the evolution of elephants, rhinos, pigs, horses, bovines, primates and rodents, during that time, as well as the example of the evolution of the frequencies of certain plants. All the animals are showing adaptation to a more open and drier environment, grass-eating adaptation, for instance. And all the plants are showing the same tendency towards a less and less humid climate, and a real drier and drier one. I will give you just an example, not to be too long. Having collected pollens in all these levels, I tried to do a ratio with the number of pollen of trees on the number of pollen of grasses and this ratio gave the result of 0.4 for three million years, and 0.01 for two million years, so I think this is clear enough. Well, the answers of the prehumans have been done in just the same direction, and they have been good enough to have given two answers. First answer, one prehuman, probably *Australopithecus afarensis*, but we are not sure, had chosen a larger size of the body and larger cheek teeth, the so-called *Robust Australopithecus*. Second answer, another prehuman, maybe *Kenyanthropus platyops*, maybe *Australopithecus bahrelghazali*, maybe *Australopithecus anamensis*, we don't know very well which one, maybe another one that we have not collected yet, had chosen a larger size of brain and teeth to eat a wider diet, meat included. It is man. The consequence of a larger brain is, of course, the emergence of more reflection and of something like consciousness. And consciousness is starting to build a new environment, the cultural environment, for the first time after four billion years of life, in its natural environment. Well, let me tell you that, for prehistorians, for me, culture is everything that is not nature. So, cultural environment for us means a technical, new environment, of course, but also an intellectual, spiritual, ethical, esthetic one and so on, so it is probably one of the Big Bangs of Prof. Antonino Zichichi, who told about the living matter with reason, and I called this event the '(H)Omo event', 'H' in brackets, because it was on the shore of the Omo river, which is amazing, that we collected this information and to remind of the pioneer role of the Omo area in this demonstration.

In summary, around 3 million years ago an important cooling appeared in the whole world, becoming an important drought in tropical areas, especially tropical Africa, and the whole ecosystem tried, of course, to adapt itself to this climatic change, to this new climatic environment. The prehumans were then part of this ecosystem, and one of these successful adaptations again is called 'man'. To answer Cardinal Christoph Schönborn, who unfortunately is not here, I would say *Homo* looks like a product of nature, a necessary adaptation to a climatic change but is a human being with, for the first time, this capacity of knowing that he knows, he is human since this beginning. So it is a sort of discontinuity in a continuum.

Fourth part: for biological and cultural reasons, the very first species of the genus *Homo* was more mobile than his ancestors because of his diet. He became a carnivore and had to run behind game. This very first species of *Homo* was more curious, also because of his better brain and the beginning of consciousness. He was more equipped because of his new manufactured tools. He was more numerous because of his successful adaptation to the climatic change we talked about. Therefore, he was more mobile, more curious, more equipped, and more numerous. I guess that it is the very first species, and not the second or the third, which moved out of its tropical birthplace and out of its ecological niche. And some environmental reasons can be added at that time to push *Homo* out of Africa, around 2.5 and 2 million years. For the moment we know stone tools in Israel, in one site, which could be, it is not sure but 2.2 to 2.3 million years old, and stone tools in China in three sites, which could be a little more than 2 million years old as well. We know stone tools in Algeria, around 1.8 million years old, stone tools and hominid remains, 1.8 million years old, in Georgia, in Java 1.8 million years old, in Italy 1.6 million years old. So, theoretically, I would think that it is this first *Homo* who had moved as soon as 2.5/2 million years ago, which means that I would not be surprised to meet this very first species of our genus anywhere and everywhere in the old world, in Africa, in Europe and in Asia, at dates between 2.5 and 2 million years ago.

The technical problem is that there are two first species of the genus *Homo*, *Homo habilis* and *Homo rudolfensis*, and I don't think that both moved. Because of a certain number of reasons I cannot develop here, I think finally it was *Homo rudolfensis* who moved. That means that, 2 million years ago, man was everywhere in Africa and almost everywhere in Eurasia, except maybe in the extreme north. And, as he was not demographically numerous enough to exchange genes everywhere and all the time, he first became *Homo erectus* where and everywhere he was, but this *Homo erectus* became *Homo neanderthalensis* in Europe, *Homo soloensis* in Java, *Homo floresiensis* in Flores and *Homo sapiens* in Africa and in Asia or in Africa only. And he probably became several other *Homo* in several other isolated places, isolated by sea or by ice, that we haven't yet discovered. So, at least, and it is a minimum, four humanities have been coexisting during several hundred thousand years, in some places maybe a million years without, of course, knowing that they were not alone: in Africa and in continental Asia, or in Africa only, as I told you before, in Europe for sure, in Java and in Flores. And, at last, *Homo sapiens* expanded his territory again around 200 thousand years ago, starting from Africa, or around 50 to 60 thousand years ago if we took the date of the Middle East. He reached America on foot, and peopled the Americas and Greenland without any problem, without any competition; he reached Australia by boat and peopled Australia without any problem as well; and reached Europe, Java and Flores and met there the previous inhabitants. In the three places, after thousands of years, thousands of years of coexistence, without real fights, without any active competition, *Homo sapiens* won. *Homo neanderthalensis* disappeared around 30 thousand years ago, *Homo soloensis*, Java man, disappeared around the same time, *Homo floresiensis* disappeared a bit later, 15 to 20 thousand years ago, maybe because of his more important isolation. And since that time there is only one hominid genus, *Homo*, one hominid species, *Homo sapiens* and one hominid race, *Homo sapiens sapiens*, on the earth, so we can very well become racist, because being racist means being humanist in a way.

Thank you very much.

DISCUSSION ON PROF. COPPENS' PAPER

PROF. ARBER: Thank you very much also for your presentation and for keeping on time. You mentioned that you had collected large numbers of bones.

PROF. COPPENS: Yes, and teeth.

PROF. ARBER: On the other hand you concluded, for example, on an increased complexity of the brain organisation. Is that on the basis of just the size of the brain or is there any other information available? Is there, for example, DNA that can still be analysed nowadays in some of these bones?

PROF. COPPENS: Well, unfortunately not. For the moment, you know, paleogenetics is trying to develop but we are just reaching the Neanderthal step which is not bad, but which is only a one hundred thousand year old hominid. And, as you heard, I was excavating in levels which were between two and three million years and sometimes a bit more than that and, for the moment, we could not find, and there is no technical possibility to find and discover pieces of DNA. We would appreciate that because the phylum, the phyla that we are trying to build and draw with our bones and teeth is only based on anatomy and morphology and it is a bit light.

PROF. ARBER: Other questions?

PROF. COLLINS: Thanks for the very nice summary. Yes, in terms of what DNA may tell us the *Neanderthal* genome sequence is gradually being assembled, there is already enough data to be able to confirm the dating of the separation of the *Neanderthal* line from *Sapiens* as roughly five hundred thousand years ago and, at the present time, no evidence to suggest that there was crossbreeding between *Neanderthal* and *Sapiens*, although that has to be looked at every time we get more data, at the present time there is no evidence that that is the case. There is also the ability to try to assess on a gene by gene basis, are there particular genes that have undergone more rapid evolution in recent times that might account for some of the unique features of *Homo sapiens*? So, for instance, the gene called FOXP2 which, if mutated in a human pedigree, results in the inability to use language in a very interesting way, with normal intelligence but inhibition of language production and understanding. That FOXP2 gene has undergone dramatically accelerated evolution since we separated from chimpanzees and people certainly point to that as a possible, molecular, very partial but interesting explanation for how language might have come about in recent times.

PROF. COPPENS: Thank you very much. It is *Homo erectus* which became either *Sapiens* or *Neanderthal*. There is no *Sapiens* at the bottom of *Neanderthal*. You know, for a long time we talked about *Homo sapiens neanderthalensis* and now we know enough to know that we could have talked about *Homo erectus neanderthalensis*, but surely not *Homo sapiens neanderthalensis*. *Homo* was only at the level of *erectus* when he divided itself because of isolation into *Homo neanderthalensis* in Europe, which was closed by ice, and *Homo sapiens* somewhere, and again Java Man and Forest Man.

PROF. VICUÑA: Thank you. I think my question was in the same line. The genetic data seems to show that *Neanderthal* and *Sapiens* had a common ancestor about six hundred thousand years ago. But the *Sapiens*' ancestors were in Africa and the *Neanderthal*'s ancestors were in Europe. So how can they have a common ancestor if by that time they were in different geographic regions?

PROF. COPPENS: Yes, that was the sense of my answer. You have *Homo erectus*, which is everywhere in the whole world, *Homo erectus* was in Europe, *Homo erectus* was in Asia and Africa but when Europe was closed by glaciers, by ice, there was a genetic drift in this small population and this was the genetic drift of *Homo erectus* that made *Homo neanderthalensis*, i.e. *Homo neanderthalensis* is really *the* European. We offered *Homo erectus* to Europe and Europe made *Homo neanderthalensis*, if I can say that.

PROF. PHILLIPS: You have told us the story of the human, of the hominid side of the divergence around ten million years ago, so what I am wondering is, what do we know about the other side, about the side that led to chimps and gorillas, and is there anything there that can give us insights into why the one side developed into people like us and the other side developed into chimps and apes and how different are those chimps and apes from the common ancestors?

PROF. COPPENS: I was hoping not to have this question! We have the impression to know quite a lot on the hominid side and we do not know much on the other side. The explanation can be that, on the other side, on the chimpanzee side, on that side there are forests at the moment and it is difficult to reach the sedimentary level through the forest and its humus, but that is just part of the explanation. There are a few bones which are now considered as possibly being part of an answer to the chimpanzee history, but they are very few for the moment and it is true that, in this beautiful divergence, we have a lot of people here, it is crowded here, and nothing on the other side. There are some bones that are considered to belong to hominids, which after a long debate, could probably come from the other side, but that is something else. As far as the difference is concerned, it seems to be really an ecological reason, that the common ancestor could have lived in a type of mosaic *paysage* with some forests and some open areas and these chimpanzees are clearly adapted to forests, wooded savannah areas, in their body, in their locomotion, for instance, it is very clear. On the other side, the hominid branch, what I am calling the pre-human, are adapted to much more open areas because at the same time they also climbed for a long time. This was a nice discovery, thanks to Lucy, Lucy was the first skeleton that allowed us to say that, well, the two locomotions are in the same body. It is the reason why they were at the same time upright and biped and still climbing for some million years and then, finally, exclusively biped.

PROF. DE DUVE: My question is, what is the present state of your East Side Story?

PROF. COPPENS: Yes, well, I cannot say that this question is good! You know, at a certain time – and some of you may know – at a certain time I thought that, having a common ancestor in central Africa at the time where the forests were developed from the Atlantic Ocean to the Indian Ocean, and having this big tectonic event which is called the Rift Valley – and the Rift Valley was not only a fault but it is especially mountains, mountains on the

Western shore of the rift, mountains going up to three thousand, four thousand, five thousand metres sometimes and this happening around 8 million years ago – there was a change in the rains and, of course, a change in the ecology and the ecology of the West and the East were not the same, the forests remained on the West and the savannah was clearly appearing – it is now very well documented – the savannah was appearing on the East and the East was becoming drier and drier every thousand of years. I thought that, having a common ancestor in these tropical areas at the time of the forest everywhere, the Rift could have been the reason, the separation, between one population and another and the change in ecological niche could have been the reason of the transformation of the ones on one side towards chimpanzee and the ones on the other side going to hominid. But, as you know, since 1995 there have been new discoveries in Chad and Chad is of course outside the Rift Valley, on the other side of the Rift Valley, so the explanation might be, as usual, more complicated than I thought. For the moment, Michel Brunet, who discovered the fossils in Chad, and myself are trying to understand what has been the role of the Rift Valley, because the Rift Valley has, for sure, played a role, but it was a sort of barrier sometimes and a sort of filter at another time. For instance, we are studying every group of mammal according to time and, as far as pigs are concerned, pigs are passing through the Rift, on the West and on the East they are the same but, for instance, anthracothere, which are a group close to hippos, anthracothere are on the West and could not pass the Rift, so the Rift Valley was really a barrier for them. And for hominids we do not know yet, because there are quite old hominids in Chad, *Sinanthropus* is seven million years old, and *Australopith gracile* is 3.5 million years old, so there are hominids between, let us say, seven and three million on the West and, in the East, the record is beautiful, as everybody knows. So, if the East Side Story has played a role, it is not the main role that I thought at a certain time.

F. CAVALLI-SFORZA: What do we know of the demography of these early humans, meaning the numbers that have been found in Africa rather than Asia and Europe, and do you think it is plausible, somehow, that the more successful development of the African *Sapiens* was due to the fact that the numbers were higher there, because it was obviously the place of original man, so more chance for mutation and successful adaptations?

PROF. COPPENS: Well, we do not know much, of course, about demography but, as in places like the Omo River Basin that I was telling you about, we have enough material, enough stuff, thousands of bones, to have an idea of what could have been the composition of the ecosystem at that time. We know, in comparison with what the ecosystems are today, what are the proportions of herbivores, what are the proportions of carnivores and what could have been the proportion of omnivores and, according to that and again in these sites where the number of fossils is good enough and important enough, we were talking about the possibility of a few thousand inhabitants of *Homo habilis* on the whole Eastern Africa at the time of 2.5 million years ago. The movement could have been like the movement of the Inuit, well, maybe 50 years ago. I had a director at the Musée de l'Homme who worked in Greenland in the 1930s and he told me that a group of Eskimo, when the diet was good enough, was demographically increasing and then it grew too big for the area to get food so a small group went 30 or 40 km beyond and organised a new community and so on, so the movement could have been something like that. As far as *Homo sapiens* are concerned, I am not happy – I must say – about the origin of *Homo sapiens*, it is a bit confusing because having *Homo* in Africa expanding his territory beyond Africa 2 million years ago is OK, and it is quite clear, but having again *Homo sapiens* in Africa doing the same thing in the same direction seems a bit confusing and I just do not understand what this *Homo sapiens* could have done with the previous population of *Homo erectus* becoming a bit *Sapiens* also elsewhere. So 'Out of Africa' once is OK, 'Out of Africa' two is not very good. And the other question about *Homo sapiens* is that there is a confusion also in the literature between *Homo sapiens* and *Homo sapiens sapiens* and it is strange that we have *Homo erectus* becoming *Sapiens* in some places and *Homo sapiens* becoming *Sapiens sapiens* in Africa and leaving Africa again. So I do not know what we are talking about, if we are talking about *Sapiens sapiens* or only *Sapiens* and you know, for instance, in two places – I am working in the field in Mongolia at the moment – I have old *Homo sapiens* which have *Homo erectus* traits again, so it is a sort of transition between *Homo erectus* and a sort of *Homo sapiens*, a sort of *Sapientisation* in situ. And we have the same thing in China, which is the same big province actually, and we have the same thing in North Africa, in Morocco, where we have enough fossils there is really a transition between *Homo erectus*, who is completely *Homo erectus*, and *Homo erectus* who is a bit *Sapiens* and *Homo erectus* who is so *Sapiens* that he is a sort of *Sapiens* with some *Erectus* in it so it seems, really, that, by himself, *Homo erectus sapientisised* where he could and where he was, of course, and everywhere he was. So, again, I do not understand. I know the genetic arguments which are very strong saying that the population today is very homogenous but, again, I do not understand how these *Homo sapiens* or *Homo sapiens sapiens* leaving Africa dealt with, coped with the people who were already everywhere in Eurasia. So I do not know if the argument of saying that the number of people in Africa might be at the origin of the second movement is sound.

CULTURE IN HOMINIZATION AND ITS IMPLICATIONS IN AN EVOLUTIONARY VIEW

FIORENZO FACCHINI

Human behaviour is characterized by culture. Human presence is indicated by culture. The question is defining what we exactly mean by culture.

Some authors have a broad concept of culture. For example, Cavalli-Sforza and Feldman (1981) say: 'we apply the term "cultural" to traits that are learnt thanks to any process of non-genetic transmission, whether by imprinting, conditioning, observation, imitation or as a result of direct teaching'.

In this concept, recognizable in many animals, there is no specific human character.

Other authors limit the concept of culture to artistic and spiritual manifestations and to the language used by *Homo sapiens* 100,000 years ago. This concept of culture is too narrow. In fact, when the products of technology show some kind of planning and denote a symbolic activity, they reveal an abstractive mind and therefore a self-reflection which certainly indicates that the human threshold has been reached.

But the application of the concept of culture can give problems when identifying man at his origins.

Current taxonomy refers many species to the genus *Homo*, but it cannot be adopted as a criterion to recognize the presence of man. A skeletal remain attributed to the genus *Homo* because of its anatomic features does not necessarily imply that it represents man in a philosophical sense, i.e. a thinking man.

In paleoanthropology, identifying the species is problematic, as this method is based on morphological skeletal characters. The same difficulty appears in taxonomy based on the DNA analysis in ancient remains compared to DNA in modern humans. The use of morphological or biomolecular differences in skeletal remains, when applied as a criterion for fecundity between species, is problematic.

But when we happen to meet skeletal remains that are connected with products showing systematic and innovative work, the presence of man can be inferred, whatever morphological and evolutionary level the remains are to be referred to.

What distinguishes human technology from non-human one (as it occurs in Apes and *Australopithecus*) is the complexity of actions by means of which this technology is performed and, even more relevant, the capacity of improving and innovating technique, and the significance assumed by the products in the context of everyday life.

According to Henry Bergson (1941) 'intelligence, considered in what seems to be its original feature, is the ability to manufacture artificial objects and particularly tools to make tools and to alter them in order to vary indefinitely their production'.

Jean Piveteau (1991) says: 'The reflection that characterizes man can be defined as conscience of deferred action in making tools. It is not credible that man since his origins, could have been *faber* earlier than *sapiens*'.

Planning capacity is revealed by tool making (purpose of products, variety, progress in technology, preservation of tools), and by the organization of the territory (shelters, camps). Intentionality reveals the notion of time; the subject elaborates images of the past and projects them into a future that he is able to prefigure. In the animal world one also finds techniques (at times very complex ones), but they are regulated biologically and do not exhibit innovation and progress. They do not constitute evidence of abstract ability to project into the future. In his manifestations of intentionality, man also shows capacity of choice, self-determination and liberty, an aspect that places him on the plane of values and thus ethics.

According to Paul Ricoeur, 'symbol leads to thinking'.

Julien Ries (1993) observed that flint flaking implies experimentation, imagination, choice of material and form; he also attributes a symbolic meaning to the organization of the territory.

Symbolization is the other characteristic of human behaviour. It consists in attributing to a sign (a sound or an object) a value that goes beyond the sign itself. By means of symbolization, realizations of techniques are enriched with meaning and value. A symbolic value, i.e. a symbolic activity, can be recognized in systematic manufacture of tools, in the organization of territory, in the subsistence economy and social organization. Instrumental culture reveals a symbolism which we suggest to call functional, distinguishing it from the social symbolism expressed in language and from the spiritual symbolism represented by artistic and religious expressions which are not connected with subsistence strategies (Facchini, 2000).

When the tool is produced for a purpose, in a variety of forms, when it is used in a given environmental context, when it is preserved (and not only used occasionally and then discarded, as in Apes), when tool making is improved in time, only then can we say that all this expresses a symbolic system of connections.

Homo symbolicus is such because he is human, creator of tools and of art, able to communicate his internal world in various ways.

We agree with Deacon (1997) who stated: 'The introduction of stone tools and the ecological adaptation they indicate also mark the presence of socioecological predicament that requires a symbolic solution'. Deacon defines man as symbolic species, with reference to making tools, as a system of adapting to the environment.

On the phenomenological level, culture reveals discontinuity compared with non-human forms, whatever the reason or nature of this discontinuity, because it does not follow biological laws. Culture, although related to the biological sphere, is characterized as extra-biological or meta-biological, in the sense that it achieves a transcendence with respect to purely biological laws or modalities of behaviour. In fact, even when it has some relationship with biological needs, culture occurs outside of any biological or behavioural determinism and, as mentioned above, is a sign of liberty and self-determination. This is particularly evident in the manifestations of spiritual and social symbolism.

According to Dobzhansky (1969), in the evolutionary history of life there have been two great moments of crisis. As a consequence of this, although the organization laws and modalities of the previous phase were conserved, there was an advancement beyond the previous organization to a new level. The author proposes to call these moments 'evolutionary transcendence'. A first transcendence was the passage from non-life to life. The laws of chemistry are not broken, but an organizational modality and a relationship with the environment are established: 'cosmic evolution transcended itself giving birth to life'. A second moment of transcendence was the appearance of man: 'biological evolution transcended itself giving rise to man'. The laws regulating living beings were not cancelled, but the organizational modalities of human society are set on another plane.

Ayala (2007) agrees with the previous statement and observes that moral behaviour is a biological attribute of *Homo sapiens*, but moral codes are not products of biological evolution, but of a cultural evolution.

When recognizing such discontinuity even in the simplest technological manifestations, it becomes difficult to identify the humans in the real sense of the word. This is an open problem in Paleoanthropology. In our opinion planning capacity and symbolism have been typically human since the origins of man, whatever their manifestations and the morphological level may be. Still, attitude towards culture can be recognized even out of its simplest expressions, starting from pebble culture.

With the passing of time cultural manifestations become more and more meaningful and therefore human attribution turns out to be easier (acheulean culture with befaces of the Lower Paleolithic, hunt organization, leptolithic culture of the Upper Paleolithic, artistic, aesthetic, religious manifestations). Innovation and intentional transmission for learning are fundamental in this respect.

If we want to represent culture development by a Cartesian coordinate diagram, it can be represented by segments of straight lines moving from the origin with a very small slope, but with the passing of time the distance of the segments of straight lines from the abscissa axis notably increases (Fig. 1).

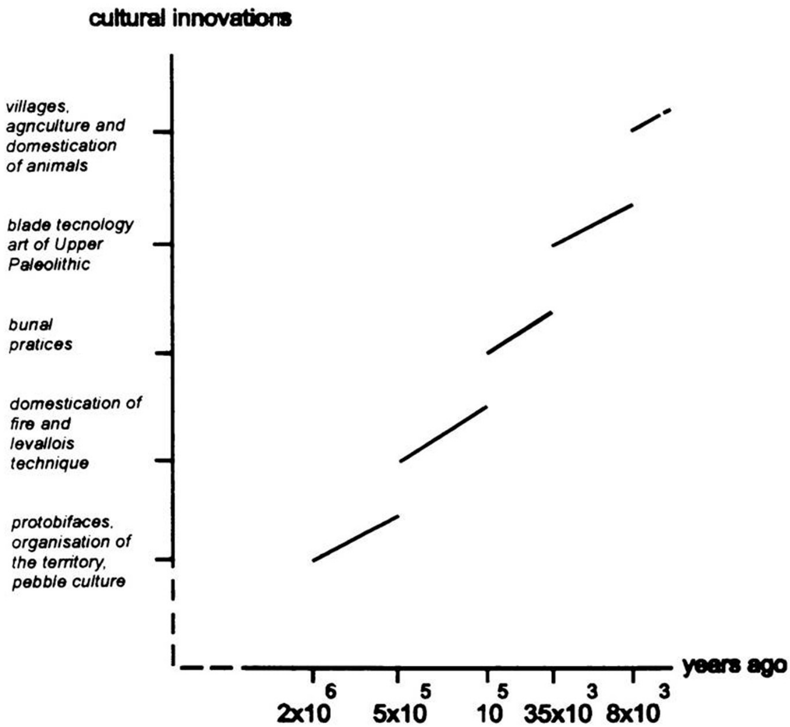

Figure 1. Hypothesis of graphic representation of the development of culture. In abscissa there is the time in logarithmic scale; in ordinate the quantification of cultural innovations. A greater distance from the abscissa axis, denotes a greater importance. The slope of the segments of straight lines is assumed to be constant.

Different Implications

The implications of culture in an evolutionary view can be recognized at different levels, which are interconnected.

a) *At paleoanthropological level*

Cognitive capacities disclosed by culture are to be related to brain development. Cerebralization characterizes the evolutionary trend in the Hominoid and among them, in the Hominids and in the human line that is more and more cerebralized starting from the *Homo habilis/rudolfensis*. The process of cerebralization is a privileged direction in evolution according to many Authors (Piveteau, Dobzhansky, Teilhard de Chardin, etc).

While there are no doubts about the cerebral development in man, the factors which made it possible are still unknown. Genetic factors are usually mentioned, like e.g. the influence of a meat diet and of food cooking, but a correlation has been prospected also with tool making and with technological development. A material culture would have favoured the increase in brain size, according to the auto-catalysis model (Lancaster, 1967; Blurton Jones, 1980; Tobias, 1981). Natural selection would have rewarded Hominids more capable of technical operations because more endowed on the cerebral level. Importance of social organization and of cooperation in order to achieve a greater success is recognized (Lovejoy, 1981; Blumenberg, 1983). Man developed himself by means of culture, in a kind of crossed catalysis (Tobias, 1971; Eccles, 1981).

From a paleoanthropological point of view, a coexistence of biological evolution and cultural evolution is admissible. However, their rhythms are different: biological evolution is quicker in the long periods of Low and Middle Pleistocene, while cultural evolution is quicker in the Upper Pleistocene, in which somatic evolution slows down (Fig. 2, see p. 612).

b) *At evolutive level*

Culture enters in the mechanism of the evolution of the species. In fact, by means of culture man adapts himself to his environment and adapts the environment to himself. We must admit a differentiation and isolation from non-human relatives. Moreover cultural adaptation reduces natural selection in man. This can stop or prevent the process of isolation which is necessary to speciation, even if morphological differentiation does not cease.

We know of a microevolution in the population genetics and this can be admitted in human populations too. This can explain the difficulty in identifying the species in hominization. According to some Authors (e.g. Ferembach, Jelinek, Coppens, etc.) it would be better to speak of morphological grades or steps, rather than of species.

In paleoanthropology human species are only supposed, on the basis of morphological and ecological characters, not demonstrated (see Facchini, 2006).

c) *At ecological level*

Culture characterises the relation between man and environment, both from the structural and the functional viewpoint, and in this way it is linked to the concept of ecological niche of the species. The ecological niche is not to be intended as a habitat, but as 'the functional state of an organism within his community' (Elton, 1927).

In more recent literature the functional relation of species with the environment, seen as different from the habitat, is emphasized. 'In order to study organisms, knowledge of the habitat is just the beginning. To assess the state of an organism within his natural community, one should be able to know his activities, especially the way in which he feeds himself, his sources of energy' (Odum, 1971). According to Colinvaux (1982) the ecological niche is defined as 'the set of abilities to make use of resources, to survive risks and contentions, which is connected with a corresponding set of exigencies'.

And since, in the human species, culture is what characterizes the structural and functional adaptation to the environment, it may be stated that culture is the 'ecological niche' of man (Facchini, 1988, 2001)(Fig. 3 see p. 613).

This can explain the wide diffusion of man in the world. Man is an ecumenical species.

d) *At phenomenological level*

Discontinuity expressed by culture implies not only a difference with respect to the rules and properties of animals, but it also points out a new modality of behaviour expressed by planning capacity and by symbolism. Symbolic language is peculiar of man. Freedom is a property of man. These are to be considered extra-biologic properties and they are documented by products of technology too. Man shows subjective conscience and self-determination, which contribute to determine his behaviour. They are signs of transcendence and express a phenomenological discontinuity.

The activity that man performs by means of culture (including instrumental culture) is external to fixed and constant biological schemes, is performed freely with ever innovative modalities based on individual experience, and is able to counteract natural selection. This is an absolute novelty in the history of life. In this regard the human species represents a paradox on the evolutionary plan: natural selection has produced a being capable of opposing it by a modality that no longer falls within the natural game of the competition of living beings with the environment. This is a unique case in the world of living beings, one can say an anomaly, explainable by the intervention of culture, a factor not to be found in other species.

g) *At cosmological level*

Some authors (Barrow and Tipler, 1986) proposed the Anthropic principle. On the basis of this principle astronomic constants turn out to be formed in order to let intelligent observers appear (strong expression of the Anthropic principle) or are such that they permit intelligent observers to be developed (weak expression).

At this regard Nicolò Dalla Porta and Secco (1991) observed that the strong principle is not demonstrable and that the weak one seems to assume more a character of ascertainment than of a proof.

Indeed, development of intelligent life is related to conditions that have actually taken place in the history of the planet, and of life on Earth, and in the whole cosmic and biologic evolution that predates man. This gives a new meaning to all reality. The Anthropic principle could be considered from another viewpoint. 'Our purpose, seen in hindsight, is attached to the purpose of the whole living world, in which it seems we are allowed to consider our appearance as a particular purpose', which is made possible by cosmological evolution (Leclerc, 2008).

However, beyond the problems raised by the Anthropic principle, through the thought and conscience of man, the entire universe is thought and becomes conscious.

f) *At philosophical level*

As pointed out above, Dobzhansky sees in the apparition of man a second form of transcendence in the history of life. Concerning the explanation of the nature of this transcendence and its causes it is necessary to move beyond the phenomenological aspects into a purely philosophical plane.

The nature of discontinuity, represented by abstractive intelligence, self-awareness, symbolic communication and language, gratuitousness and freedom, all of which cannot be reduced to purely biological activities, introduces into the picture the spiritual dimension. If matter becomes thinking (Coppens, 2006), one can speak of a qualitative difference in comparison with animals, not of a difference of grade, as affirmed by Darwin (1871), according to whom 'the difference in mind between man and the higher animals, great as it is, certainly is one of degree and not of kind'.

The creation of the spirit is outside the realm of empirical evidences and can be dealt with only at the philosophical level whether we are talking about human phylogenesis or ontogenesis. The discontinuity that can be observed on the phenomenological level may be interpreted as a transcendence at the philosophical or ontological level

John Paul II so describes man's appearance: 'With man we find ourselves in the presence of an ontological difference, one ontological leap, one could say' (*Message to the Pontifical Academy of Sciences, 22 October 1996;* in *Papal Addresses to the Pontifical Academy of Sciences 1917-2002*, p. 373; Vatican City, 2003). If discontinuity is observed in a long time at the phenomenological level, at the philosophical level this discontinuity must be radical, no matter what its cultural expressions are, because the spirit cannot come out of living matter. As the Pope remarked: 'Theories of evolution which, in accordance with the philosophies inspiring them, consider the mind as emerging from the forces of living matter, or as a mere epiphenomenon of this matter, are incompatible with the truth about man' (*ibid.*).

In the address to the Plenary Session of the Pontifical Academy of Sciences (31 Oct. 2008) Benedict XVI reaffirmed 'that every spiritual soul is created immediately by God – it is not "produced" by parents – and also that is immortal' (*Catechism of the Catholic Church*, 366).

We can assume that the will of the Creator includes, at a certain moment of the evolutionary process, a corporeity enriched by spirit, not in the sense of an entity which is added to another one, almost placed on or beside it, but which, starting from a certain moment, exists inside the other one, as and when it is wanted by God, in a way similar to what happens in human ontogenesis. All this for ontological reasons, not for biological reasons, if we recognize the presence of the spirit in man. The analogy with ontogenesis is present also in the quoted address of Pope Benedict to the Academy.

There cannot be any form of intermediate psychism which would be only partially human, as Maritain noted. But there may have been intermediate forms of animal psychism between the human one and that of the apes, as it is right to think about the *Australopithecus* (overdeveloped animals, according to Maritain, 1973).

Nevertheless, the exact moment of passage into the spiritual realm, i.e. when the hominid becomes aware of himself, cannot be represented by scientific methods or our imagination, as remarked by John Paul II.

The obscurity in representing the appearance of the spiritual dimension is similar to what happens in ontogenesis.

The Creator's will was accomplished without mediation of material agents in the first humans and continues in every human being, even if with the collaboration of parents.

Cultural manifestations cannot help in determining the exact moment of the achievement of the human threshold, but only can help in stating if that threshold can be considered as reached.

g) *At moral and ethic-social level*

We can point out another expression of transcendence in man: the wealth of values and meaning, unrelated to biological needs, that can be found in the responses man is capable of eliciting for biological needs; the same applies to human behaviours not directly related to the biological sphere, e.g. manifestations of spiritual symbolism. Man is able to internalize the responses to biological needs by attributing to them different values, related to the internal world of the person or to the social sphere.

If one looks at the manifestations of spiritual symbolism (art, religion, gratuitousness) the transcendent nature of man is even more evident.

Connected with cultural attitude and freedom is ethical behaviour, which requires the ability to recognize certain values and to choose freely.

According to Ayala (1987) three conditions are necessary for an ethical behaviour: a) the ability to foresee the consequences of one's own actions; b) the ability to make value judgments; c) the ability to choose between series of alternatives actions.

Following this line of reasoning we can state that the connection between means and ends can be detected in the ability to construct tools. The variety of technological products shows a freedom of choices.

As we remarked, cultural behaviour reveals ability for abstraction and not a stereotyped or automatic technological behaviour since the earliest stages of mankind.

The capacity for planning and symbolic activity is revealed by the products of technology, as we pointed out in the first considerations.

Very important and significant were the different forms of cooperation in the life strategies of prehistoric man, among then we must stress gratuitous behaviour.

Spiritual symbolism is recognized in particular rituals of the early Paleolithic and in the burials or decorations of the last hundred thousand years.

All this attests to freedom and capacity of values that are at the basis of the ethical behaviour connected with cultural attitude and are evident in modern humans, but must be supposed also in prehistoric man.

In conclusion we must point out the uniqueness of the human being in the living world for his cognitive activity, for his ability to ask questions about himself, his past and future, for his freedom.

During hominization, culture starts a process of humanization, defined as 'the way in which man, after appearing in the centre of nature, starts marking it with his presence' (Martelet, 1998).

It is a process that starts with the beginnings of humankind, but lasts in time, and is characterized by a growth of culture. Man, through technology and the development of symbolic systems of communication, builds a life environment that is increasingly marked by his presence.

In other terms, culture influences the environment, adapts it better to humans, increases cooperation, improves welfare.

Teilhard de Chardin speaks of a process of 'planetization' referring to the increase in socialization and relationships among the people. The process of globalization characteristic of present day humankind can be viewed in this perspective.

Even taking in account a lot of contradictions, human history is marked by a general progress of culture. It is marked by a growth of humanization, i.e. of the ability to influence nature, in order to make it more suitable to the development of humankind.

But freedom brings into the picture the responsibility of man regarding the use of technology in order to build his future. The building of the future is exposed to the risks arising from a bad use of science and technology.

We cannot disregard the severe and numerous problems regarding the relation of man with the environment, the concrete possibilities of destroying nature, and the contradictions and conflicts that mark the history of humankind and that can reach a planetary level. We cannot be silent about the risks of a de-humanization.

New scenarios seem to open up with the development of biomechanics and of genetical engineering. I am referring in particular to intervention related to personality, e.g. the ones operating on cerebral areas. Androids are being introduced in the picture, as a kind of hybridizing between human brain and computers, that could be possible thanks to genetic engineering practices and cybernetics. Even a meta-anthropos, a term whose meaning is not well defined, seems to be in the realm of possibilities.

According to Morin (2001), 'Man too *sapiens* becomes ipso facto *demens*'. Would it be a dramatic change in the course of the human evolution?

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DISCUSSION ON PROF. FACCHINI'S PAPER

PROF. LUKE: I have a question. What is the link between the biological dimension of man and the ontological dimension of man? Is there an interface between the ontological side and the biological side? If not, we get the problem of totally separated worlds. Everything I can say about man in an ontological way is not linked with the biological way. Is there a link, is there an interface?

PROF. FACCHINI: I think there are different points of view, different levels of knowledge, that is, the scientific or empiric level and the philosophical or ontological one. To these different levels of knowledge correspond different methods of approach or study. An actual interface cannot be established between these modalities of existence, because they are not homogeneous. Everything I can say about man in an ontological way is not dependent on the biological way. But there are some relationships between the biological and ontological dimensions. The ontological dimension supports the biological one in its existence. Both dimensions are related to the same entity, but in different ways.

PROF. ARBER: Are there other questions?

PROF. PHILLIPS: I have so many questions I hardly know where to start! So you said, at one point, that language and freedom are non-biological. But we heard from Francis Collins that there is this gene that, if it gets turned off, then you lose the ability for language without losing intelligence, which seems quite remarkable, and certainly seems that means there is, at least, a biological nature to language, at least a biological link to language. So I am wondering, in the light of that, what does it mean to say that language is non-biological and what do you mean when you say freedom and in what sense is that non-biological?

PROF. FACCHINI: To speak we need the organs of phonation and the cerebral centres of language that are localized in the frontal cortex (Broca's area) and parietal-temporal cortex (Wernicke's area). There are genes for these anatomic organs. But language is characterized by simbolization, an activity connected with abstractive intelligence, awareness and capacity of choices. These properties of human behaviour can be considered extrabiological properties, because they are not related to genes or anatomic organs. There are no genes for self-consciousness or freedom, as remarked by many authors (e.g. Dobzhanskhy, Eccles, etc.). For the exercise of extrabiological properties anatomic conditions are necessary, but their activity is not linked to particular organs. We can consider that between animal and human behaviour there is a discontinuity on the phenomenological level because they are not constant and regulated by biological rules.

PROF. ARBER: May I just add to that. I think language has two aspects: one is communication and, as far as I know, many animals and even plants can, within their communities, communicate in some way or another. The second aspect is the written language. As far as I know, this is rather unique to the human society. Is that also your view?

PROF. FACCHINI: I would like to point out the particular type of communication in man, represented by symbolism. In the animal world there are signals for communication, but not symbols, i.e. some particular signification connected to a sound or behaviour. Relationships in humans are symbolic. The systems of communications in human societies are enriched by symbols, they are not stereotyped or constant. This behaviour is not found in the animal world. With regard to written language we can remark that it is a particular form of communication between humans that increased communication and cultural evolution by means of a particular form of transmission.

COGNITION, CONSCIOUSNESS, AND CULTURE: UNDERSTANDING HUMAN COGNITION AND ITS GROUNDING IN A PRIMATE BRAIN

STANISLAS DEHAENE

One of the key outstanding scientific questions for the 21st century concerns the evolutionary origins of human cognitive competence. How is the human brain architecture organized to support our cognitive abilities? And how did this architecture appear?

The human species is primarily characterized by its remarkable cultural competence – the capacity to acquire, from its peers, a great variety of mental tools that were not anticipated by evolution. This competence rests, in the final analysis, on the plasticity of the developing brain which authorizes the laying-down of novel 'neuro-cultural' circuits. Within the space of a few years, the child's brain acquires new specializations and competences unique to the culture in which it is embedded. Thanks to education, a spoken language, a writing system, and many other motor, mathematical or artistic competences get inscribed in the brain for the rest of one's life.

This emphasis on cultural learning does not, however, imply that the human mind is detached from its evolutionary origins. The standard social science model used to consider the brain as the proverbial 'blank slate', an isotropic learning device that places little constraint on the patterns of human thought. This view is now obsolete. It is giving way to a new paradigm that considers human brain function in an evolutionary perspective. Even in domains such as mathematics, it is possible to identify precursors of human abilities in non-human primate brains. Cultural learning does not emerge entirely *de novo*, but operates by the transformation or *neuronal recycling* of evolutionarily older brain pathways that served a related role in other primates.

In the present chapter, based on recent cognitive neuropsychological evidence, I shall briefly review our current understanding of this interplay between evolution and culture in three areas where the specificity of the human species seems most evident: language development, cultural transmission of reading and mathematics, and consciousness. In each case, we begin to understand how human mental functions arise from a complex anatomical and functional architecture of nested neuronal networks, largely inherited from our primate evolution, yet importantly reorganized to support flexible symbolic manipulations unique to humans.

Origins of language

Language was rightly seen by Descartes as one of the defining features of the human species. Since Broca's original description of aphasia, numerous studies in neuropsychology and neuroimaging have questioned whether a particular organization of this part of the brain might explain the language faculty in our species, and its special relation to the left hemisphere (for review, see G. Dehaene-Lambertz, Hertz-Pannier, Dubois, & Dehaene, 2008).

In the adult human brain, leftward structural asymmetries are observed, both at the macroscopical and cytoarchitectonic levels, such as a longer sylvian fissure and a larger *planum temporale*. The white matter volume underlying the primary auditory area, Heschl's gyrus, is larger on the left than on the right side. Bigger pyramidal cells are noted in the left auditory cortex, associated with thicker myelinated fibers. It is argued that these structural features might allow the left hemisphere to code the rapid and complex acoustic transitions characterizing speech more accurately than the right. Indeed, the *planum temporale* is less asymmetric in children with specific language or reading impairments relative to the normal population.

Developmental studies indicate that these structural asymmetries are present early on in infancy and may guide language acquisition. During the last trimester of human gestation, sulci appear first on the right hemisphere. The right superior frontal, superior temporal and Heschl's gyri are detectable one or two weeks earlier than their left-sided homologous (Dubois *et al.*, 2008). This asymmetry in sulcation development is not reported in macaque fetuses. At birth, the sylvian fissure is longer on the left side and is associated with a larger left *planum temporale* while the superior temporal sulcus is larger on the right. Twin studies reveal a strong genetic influence in these areas. The volumes of both left *planum temporale* and Heschl's gyrus are similarly larger in hearing and congenitally deaf adults. Contrary to the hypothesis of an equipotential brain at the beginning of life, these observations point to evolutionary genetic changes in the human lineage which favoured a differential development between the left and right hemispheres in a systematic way across humans. Genetic studies have indeed begun to reveal asymmetrical gene expression in the peri-sylvian regions, specific to the human lineage. These genes that either regulate cell signalling or control other genes or protein expression are expressed at an early developmental stage (especially between 12 and 14 weeks of gestation), a critical time for cortical regionalization. LM04, for example, is expressed more on the right side than on the left in humans. For this gene, asymmetry is also present in mice but not biased systematically to the same hemisphere across individuals as in humans.

Functional brain activation also indicates that language acquisition does not initially cause a broad and unspecific pattern of brain activity, but recruits a specific, evolved brain network. My laboratory, under the leadership of Ghislaine Dehaene-Lambertz, has obtained some of the first images of the brain organization for language in 2-to-3 month-old infants (G. Dehaene-Lambertz & Dehaene, 1994; G. Dehaene-Lambertz, Dehaene, & Hertz-Pannier, 2002; G. Dehaene-Lambertz *et al.*, 2006). Remarkably, a circuit similar to adults is already in place and can be activated by listening to short sentences. It seems to be hierarchically organized and involved a progression from the bilateral auditory areas towards the left posterior temporal lobe, the bilateral superior temporal sulci, the temporal poles, and Broca's area in the left frontal gyrus.

Anatomical precursors of this hierarchical organization are already present in the monkey brain – there is already a hierarchical synaptic organization leading from the primary auditory cortex to both the anterior temporal region and to selected areas of the frontal cortex (Romanski *et al.*, 1999). However, the middle temporal gyrus is considerably more expanded in humans and a massive bundle of temporo-frontal connections, the arcuate fasciculus, has seen a large expansion and lateralization towards the left hemisphere (Rilling *et al.*, 2008). In a nutshell, the human cortical organization for language can be seen as an extension, expansion, and lateralization of temporal-frontal networks that are present in other primates, in ways which are beginning to be explored. Just after birth, the infant's brain is already biased for language acquisition through the presence of lateralized and hierarchically organized circuits. These early biases precede any overt production of language, even in the elementary form of babbling. However, they shape the early processing of language inputs from the child's environment.

Acquisition of a written and mathematical culture

Cortical specialization exists not only for language, but also for many other domains of cultural competence of the human species. For instance, recognition of written words is systematically associated with the left ventral occipito-temporal cortex, and mental arithmetic with the bilateral intraparietal sulci (for review, see Dehaene & Cohen, 2007). This reproducibility of the brain's major cognitive circuitry is remarkable, because although there might have been a specific evolution for language, reading and arithmetic are clearly too recent inventions to have exerted any selective impact on the evolution of specific brain circuits.

My proposal is that cultural inventions such as reading invade cortical circuits that initially evolved in a very different context, but are capable of partially 'recycling' for novel uses unique to the human species. Each cultural object must thus find its cortical niche, a neuronal circuit which is already structured but exhibits enough plasticity to be reconverted to a novel use.

Neuro-imaging and neurophysiological findings support the 'cultural recycling' hypothesis by showing precursors of the human adult specialization in infants and even in primate brains. For instance, in 3-month-old infants, the ventral occipito-temporal pathway already activates during visual object recognition, and the dorsal occipito-parietal pathway during the extraction of the numerosity of a set of dots. A similar ventral/dorsal distinction also exists in the macaque monkey, including the presence of inferotemporal neurons responding to an 'alphabet' of elementary visual shapes, and parietal neurons responding to numbers. Human education radically expands these abilities by allowing them to become activated, not only directly (e.g. by seeing a set comprising five objects), but also indirectly through the use of cultural symbols (e.g. by seeing the Arabic digit 5 or hearing the word 'five').

In the past twenty years, a particularly detailed evolutionary argument has been developed for the sense of number – a foundational sense upon which the specifically human development of mathematics largely rests (for review, see Nieder & Dehaene, 2009). The first imaging studies of calculation, using SPECT, PET and fMRI, quickly pointed to a reproducible bilateral activation in the intraparietal suclus of both hemispheres. The advent of single-subject fMRI demonstrated that, although inter-individual variability is somewhat larger than in studies of reading, the banks of the intraparietal sulcus are always consistently activated whenever adults compute simple comparison, addition, subtraction or multiplication with Arabic numerals. The intraparietal region seems to be associated with an abstract, amodal representation of numbers inasmuch as it can be activated by numbers presented as concrete sets of visual or auditory objects and events as well as in various culturally learned symbolic notations such as Arabic numerals and spelled-out or spoken number words. It is active in adults from various countries and cultures including France, UK, USA, Austria, Singapore, China, and Japan.

The parietal activation associated with 'number sense' occupies a fixed location within an overall map of sensory, motor and attentional functions in the parietal lobe, including finger pointing, manual grasping, visual attention orienting, eye movement, written word processing and calculation (Simon *et al.*, 2004; Simon, Mangin, Cohen, Le Bihan, & Dehaene, 2002). This layout in humans bears considerable similarity with the anatomical organization of areas V6a, LIP, PRR and AIP in macaques. Although details of this homology remain debated (Culham, Cavina-Pratesi, & Singhal, 2006; Orban *et al.*, 2006), the human map predicted that, if a precursor of human numerical abilities existed in monkeys, it might lie in the depth of the intraparietal sulcus. Indeed, awake-monkey electrophysiology uncovered number-coding neurons distributed within and near the intraparietal sulcus (Nieder & Miller, 2004; Sawamura, Shima, & Tanji, 2002).

Several parallels between monkeys and humans suggest that the monkey intraparietal neural code for numerosity may be the evolutionary precursor onto which the human invention of arithmetic encroached (Nieder, 2005). First, numerosity-tuned neurons are mostly found in the depth of the intraparietal sulcus and often show visual flow-field responses, compatible with a location in area VIP. Likewise, human fMRI studies have located a plausible homolog of area VIP at a location remarkably close and overlapping with that of number-related responses (see Hubbard, Piazza, Pinel, & Dehaene, 2005). Second, monkey intraparietal neurons are each tuned to a particular numerosity and show Gaussian variability on a log scale, similar to inferences derived from behavioral and fMRI adaptation studies in humans. Third, in some neurons at least, the code is abstract enough to respond to both sequential and simultaneous presentations of number. Fourth, distinct but intermingled populations of neurons code for number and line length, again parallel to inferences drawn from human fMRI.

Developmental evidence from human infants and toddlers suggests that higher-order arithmetical competence builds upon this foundational parietal 'number sense'. Even infants show a sensitivity to numerosity and to concrete addition and subtraction operations performed on sets (for review, see Feigenson, Dehaene, & Spelke, 2004). Number-related parietal activation, particularly in the right hemisphere, is already present in 4-year-old children and even in infants as they attend to the numerosity of sets. Thus, the parietal mechanism of numerosity extraction identified in monkeys seems to be already functional prior to arithmetic education in humans. A recent behavioral study shows that, prior to any explicit instruction, preschoolers possess a spontaneous capacity for approximate symbolic arithmetic whose variability is predictive of subsequent success in the math curriculum (Gilmore, McCarthy, & Spelke, 2007). Furthermore, children who suffer from dyscalculia, a disproportionate impairment in learning arithmetic which cannot be imputed to general intelligence, sensorimotor deficit, or deficient social or educational background, frequently exhibit a parietal hypoactivation and anatomical disorganization. These alterations are often due to genetic, pre- or peri-natal pathologies, suggesting that they may represent plausible causes rather consequences of dyscalculia.

In brief, the origins of human arithmetic abilities rest upon a functional parietal quantity system that is shared with monkey and probably many other species, and that we co-opt for higher-level arithmetic with specifically human symbols. A similar argument has been developed for the case of reading, where our cultural competence capitalizes on pre-existing circuitry for invariant visual recognition of elementary shapes of objects (Dehaene, 2007).

Evolution of prefrontal cortex and origins of consciousness

Both arithmetic and reading rely on the linking of arbitrary symbol shapes with meanings. Symbolic linkages seem to be unique to humans – as is the ability for metaphor, which implies the *de novo* creation of innovative links between otherwise distinct domains. Symbols and metaphors may reflect a particular capacity of the human brain for flexible thought – the ability to recombine, at will, various elements of thoughts into novel combinations. Various neuroscientists such as Luria, Fuster or Goldman-Rakic have emphasized the behavioral flexibility of the human brain and its link to the huge expansion of the frontal lobes (which occupy close to one third of all gray matter in humans). The frontal lobe can be considered as a major cortical site that contributes primarily to non-automatic, flexible reflection and imagination (Fuster, 1989). Thus, its expansion in the human lineage may betray a particular evolution towards greater rationality and 'free thought' detached from external sensory and motor contingencies.

White matter bundles underlying the prefrontal cortex, in particular, seem to have expanded considerably in humans (Schoenemann, Sheehan, & Glotzer, 2005). Guy Elston and his colleagues have described anatomical correlates of this massive increase in connectivity at the dendritic level, where pyramidal cells exhibit a considerably larger number of branches and synaptic contacts in humans than in other species, particularly in prefrontal cortex (Elston, 2003). Jean-Pierre Changeux and I have explored the theoretical proposal that this connectivity increase, although made possible by small genetic changes, led to a major alteration of the cognitive processing style associated with human prefrontal cortex. In our 'global workspace' model, prefrontal cortex is seen as a hub for information exchange that already exists in other non-human primates, but has expanded in the human species and serves to break the processing modularity of other cortical regions, thus allowing for information exchanges that would not otherwise be possible by direct point-to-point connections.

We further propose, speculatively, that prefrontal cortex plays a specific role in the evolution of human consciousness. What we subjectively experience as a conscious representation would be a global availability of information, resulting from its entry into this neuronal 'workspace' with divergent long-distance axons (Dehaene & Changeux, 2005). According this view, although considerable specialized processing can occur non-consciously, access to consciousness is specifically associated with the entry of information relevant to the goals of the organism into a capacity-limited workspace system that serves to dispatch information to other processors.

While the theory is clearly speculative, a variety of neuroimaging experiments have now begun to pinpoint the neural correlates of conscious experience (Dehaene, Changeux, Naccache, Sackur, & Sergent, 2006; Koch, 2004). Such an empirical research program has become possible thanks to the design of simple experimental paradigms in which identical or very similar stimuli do or do not lead to conscious perception, thus opening a window into the minimal differences that separate conscious and non-conscious brain states. Whenever information accesses consciousness, neuroimaging experiments reveal the sudden ignition of a distributed parieto-prefrontal system and the simultaneous top-down amplification of relevant posterior networks. Long-distance causality relations and phase-coherent oscillations are temporarily established across the relevant cortical areas, thus creating a transient metastable brain-scale assembly. This capacity to transiently link otherwise distant areas may have been a key ingredient in the emergence of human cognitive flexibility and symbolic competence.

A recent line of research has examined the 'resting state', 'default mode', or 'baseline' activity of the awake human brain at rest. This research has evidenced a broadly distributed network of areas active during rest, including dorsal and ventral medial prefrontal, lateral parietotemporal, and posterior cingulate cortices (Mason *et al.*, 2007; Raichle *et al.*, 2001). This network is not static and strictly confined, but constantly fluctuates in synchrony with changes in EEG spectral content. Furthermore, prefrontal, parietal, and cingulate areas show the greatest drop in metabolism during various types of transitions away from the awake state, whether during anesthesia, sleep, coma, or the vegetative state (Boveroux *et al.*, 2008).

In summary, long-distance neural networks linking associate brain areas with prefrontal cortex exist in all primates but have seen a particular expansion in the human brain. Their state of activation appears to systematically vary whenever the state or the contents of consciousness is altered, both as the result of stimulus changes in normal subjects, or as the result of brain insults and pathologies in non-communicating patients. The exact nature and reliability of this correlation between conscious states and distributed brain states remains a matter of some debate (Boly *et al.*, 2008). If reliable neural correlates of consciousness could be found, leading to a theory of its origins, it would not only provide a remarkable intellectual advance for our understanding of the relation between mind and brain, but also offer important hopes for the diagnosis, classification and potential treatment of pathological conscious states such as coma, vegetative state, minimally conscious state, and locked-in syndrome (Bekinstein *et al.*, 2009; Owen *et al.*, 2006; Schiff *et al.*, 2008; Voss *et al.*, 2006).

CONCLUSION

At first sight, human cognitive abilities appear radically different from those of other animals and may even suggest a unique status of the *Homo sapiens* species. However, the main conclusion of this rapid review of the origins of human cognitive abilities is that, although they are uniquely expanded, upon closer scrutiny none of them is devoid of evolutionary roots. The architecture of the human brain is that of a primate with additional evolutions regarding brain size, differential expansion of prefrontal cortex and other associative areas, long-distance connectivity, lateralization, and emergence of specialized regions such as language areas (as well as areas specialized in the representation of congeners, the 'social brain', which could not be reviewed here for lack of space). The uniqueness of humans does not seem to originate from a radically novel brain design – but rather, from the capacity to re-utilize or recycle its existing brain architecture for novel cultural uses such as reading or arithmetic. By granting the human brain a capacity for cultural invention and transmission, our biological evolution allowed for a massive change in the speed with which our mental life evolved, now based primarily on cultural rather than biological transmission.

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DISCUSSION ON PROF. DEHAENE'S PAPER

PROF. PHILLIPS: This observation that reading is found consistently in the same regions of the brain wherein there was not enough time for it to develop is quite a remarkable result. Can you, do you have some sense for why exactly the same area of the brain is recycled to do this job in every single case? In other words, considering the fact that it was not evolved to do reading and instead some other part that was evolved to do something else is being recycled, why is it always that part, why is that so well adapted to do reading when that was not its function to begin with?

PROF. DEHAENE: It is a very important question for us, of course. There might be several answers. First, we know that this area lies at a specific place in the hierarchy of visual neurons, distant enough from the periphery that it cares about assemblies of visual features and thus can contribute to the recognition of large visual objects such as letters and words. Second, in terms of its lateral position, it lies within a sector of cortex that responds preferentially to the fovea, that is to say features that are fine and can only be discriminated by the central part of the retina. The central part of the retina, the fovea, has a bias to project to specific parts of the cortex, and the word-form area is part of this projection zone. Yet a third answer is that this reading region always lies in the left hemisphere, and this might be, but it is only a hypothesis, might be because of its projections to the left hemisphere areas that care about language. Altogether, the left-hemispheric part of the visual system might be the only side that has just the right visual abilities to discriminate the fine shapes of letters in the fovea and has the right projections towards language areas.

PROF. SZCZEKLIK: I have a question. You showed us very nicely how the density of neurons increases in a child when he is two-three months old.

PROF. DEHAENE: Density of synapses.

PROF. SZCZEKLIK: Density of synapses, yes, and how they develop into a highly sophisticated network. I am wondering what really directs the axons, the dendrites into particular sites, how do they find their way, how do they know, if I can say so, to get the long-distance connections: is there some sort of chemotaxis like we see in other fields of biology?

PROF. DEHAENE: I may not be the person to respond to this question, maybe Wolf would be better, but yes, chemotaxis is a key factor and there are known repellents and attractors of growth cones of neurons. How exactly they do the sorting, so that projections from different areas do not mix up completely, is not completely known but there are genes that are known to be involved in specific aspects of this wiring diagram, for instance the ROBO1 gene, which is involved in crossing the midline – this is a very important problem – so that neurons in the right hemisphere connect to neurons in the left hemisphere. There are many specific genetic operators that are involved in this very complex wiring problem and, quite interestingly, there might be some diseases that are related to a misfunction of some of these genes. The ROBO1 gene is one of the four genes that are suspected of being involved in dyslexia, maybe because tampering with it causes the wiring to be incorrectly established.

PROF. SZCZEKLIK: Another very short question. You spoke about aneurosis versus the vegetative state. So in patients in a deep long coma, but with brain stem function well preserved, this is mostly the prefrontal area which is affected, and not the whole cortex? Did I get you right?

PROF. DEHAENE: I think I maybe overemphasised the prefrontal cortex, maybe I will come back to the slide. As you can see from this slide from Steven Laureys, it is really a large-scale network which involves the prefrontal cortex, certainly, but also, as you can see, the inferior parietal cortex, on both sides, some degree of middle temporal activation and especially there is this area in the precuneus, which is not very well understood but might relate to sense of self and orientation of the self with respect to the external world. So it is always a network which is engaged during conscious processing, and the suggestion is that prefrontal cortex is one key node of this network which allows the rest to communicate and facilitate, in a certain sense, the communication. Thank you.

PROF. W. SINGER: Thank you for this beautiful presentation. Could one say that one of the great inventions that came along with the cerebral cortex is to provide a data format that is freely exchangeable among all the local processors, a sort of lingua franca that everybody can use? Then, with the proliferation of tissue the architectural feature of small world networks was just repeated, so it is the same relation of hubs over local processors that is continuously carried through and in the monkey brain it is still small but in the human brain it gets bigger. So it is a scale-free developmental process that leads to the emergence of new functions because it provides new platforms for the association of things that had not been connected before. It is a creative act to connect what has previously not been connected. When one looks at monkey brains and monkey behaviour one is always so startled by the fact that they seem to be performing extremely well on a particular task which they have learned, but if you change a tiny little bit in the paradigm they start from scratch, because they are unable to see the common in the seemingly different, and this is what makes us so universal.

PROF. DEHAENE: I agree largely with what you say. There is, in fact, quite a bit of discussion in the domain of language to ask whether language as a communication device is not just a reflection of a much more major use of language as an internal device for shaping the information inside and, in fact, as a representational device for representing combinations of information. I suspect myself – but I have to say there is very little evidence for the moment that this might be the case – that language evolved primarily as a result of this internal exchange device. We could speak for hours, I think, about this.

PROF. BATTRO: Thank you for your remarkable presentation and congratulations for the discovery of the word-form area, which is amazing because it is universal for all writing and reading cultures, but what happens – this is a personal question – with children that have one hemisphere removed? In that case, this child for instance has no word-form area and he can perfectly write or read.

PROF. DEHAENE: That is an excellent question, thank you very much. In fact, this is precisely why I do not like the term 'module', because this is not an area which is a 'module' for reading, it results from a set of minimal biases that come from the genome, and we discussed maybe some of them, that make this area more appropriate for learning about certain domains such as the shapes of letters. We have, in fact, scanned one case of a patient, not with hemispheric removal but with just removal of the occipito-temporal cortex on the left side, including the visual word-form area but not including the language areas, and this child had left hemisphere language. The operation was at the age of four and she was scanned at the age of eleven. At this age, she had learned to read quite normally, almost normally apparently, she was a good reader, and when we scanned her during reading all of the normal activations were there in the left hemisphere except for the visual word-form area which was switched to the right hemisphere. And in the right hemisphere it was not anywhere, it was at the location exactly symmetrical to the normal place in unimpaired readers, suggesting that the biasing gradients, which are bilateral, might play a key role in specifying the location of this area.

PROF. BATTRO: There is kind of a symmetry, something is there but it is not used and in the case of losing the left one you can use all the network on the right. Thank you so much.

PROF. DEHAENE: I should add that, if you had the same lesion in an adult person you would not see this. What you would see would be pure alexia, where the person becomes totally unable to read. In adults there is, in fact, relatively little recovery from this predicament, even after years of trying to recover reading, so the plasticity of the child's brain is obviously contributing a lot to this ability to switch the visual word form representation to the other hemisphere.

PROF. BATTRO: This is important, thank you.

PROF. COPPENS: Just some data. We compared the brain of a young *Neanderthal* and the brain of a young *Sapiens*, same age, and the brain of the young *Neanderthal* seems to be at about 70% of its growth and the brain of the *Sapiens* only at 50% and we thought it could be one of the reasons for the extinction of one and the prevalence of the other, because of course the *Sapiens* has more time for education.

PROF. DEHAENE: Wonderful, thank you.

PROF. QUÉRÉ: Thank you for this beautiful lecture. Coming back to the recognition of reading, you mentioned that this was the same location for Hebrew or French or anything. First question, does it have anything to do with the nationality of the child and, second question, what happens when, instead of drawing Hebrew or French, you just put meaningless signs, kinds of drawings: does it go to the same point in the brain?

PROF. DEHAENE: Very good questions. So the first one, in first order it is the same area regardless of the writing script. In second order, when you look especially at people who master several writing systems, you can find small differences because now this is within a subject, you can look at much finer differences and you do find them. So this is now an interesting area of research to look at cultural differences. The effect of enculturation seem to lie mostly in the modulation or emphasis on one area relative to another. So, for instance, when people are studying Chinese readers, they find the visual word-form area at exactly the usual location in the brain, but they also find more activation in an anterior brain area, which is in the left premotor region, and may have to do with gestures. Now, when you learn 3000 Chinese characters, the gesture is extremely important and the order of the strokes is memorised and is often used. When a Chinese person meets with an unfamiliar character she has to decipher, she will try to reproduce the gesture to understand it, so we think that this activation may have to do with the strategy for memorising a large number of Chinese characters. In brief, as a general statement, one may say that the cerebral tool kit is the same, but the emphasis and combination of the tool kit may not be the same in the different cultures.

Session IV

THEOLOGICAL, PHILOSOPHICAL AND SOCIETAL ASPECTS

EVOLUTION AND CREATION: HOW TO TERMINATE WITH A FALSE OPPOSITION BETWEEN CHANCE AND CREATION AN EPISTEMOLOGICAL NOTE

JEAN-MICHEL MALDAMÉ

The question of chance and creation is at the heart of the speculation which currently arises from the movements opposed to the theory of evolution, in connexion with the materialist currents which resist them. These confrontations are the occasions of a great deal of passion, which confuses the dialogue beween science and faith. I shall endeavour to show how these two spiritual families share the same vision of nature and of the action of God. I think it is necessary to show which one it is. On one side, we have two trends of thought: the former is the creationist position, which rests on a fundamentalist reading of the Sacred Texts – Bible or Coran – with the so-called *Intelligent Design* movement, which, without denying the value of science, argues that the use of the word *chance* by the theory of evolution calls for the intervention of God. On the other side, we find several philosophical attitudes which exclude all reference to God. There's positivism or rationalism which remain within the framework of agnosticism on the one hand, and on the other, various atheistic currents which challenge any recognition of God's action. To remain within the scope of this convention, I shall only address an item which is at the core of the controversy aroused by the theses of the *Intelligent Design*: the place assigned to chance in the theory of evolution and the Christian confession of faith. My first step will be to clarify the fundamentals of the scientific method, and of the various philosophical approaches which accompany them.

1. Chance, Science and Philosophy

1.1. *Reason*

With the emergence of the rational spirit which presides over science, those who produced knowledge had to tear themselves away from the sacred vision of nature, according to which – since every phenomenon was produced by a divinity viewed as an image of man and endowed with freedom, nature could not admit anticipation or prevision. Ever since the ancient Greeks, scholars and philosophers have distanced themselves from a magical conception of existence; they have invented the notion of natural causes. According to them, nature must be understood starting from universal principles operating according to a rational principle contained in the notion of nature. The notion of law, in sciences and in social life alike, refers to the consistence of an action which rests on a fundamental order, at a deeper level than varying phenomena, a *Logos*, a Reason. The notion of nature then refers to the presence of an invariant which is of fundamental importance in the relationships between beings. Mankind, furthermore, shares in this reason; facts and laws are accessible to its intelligence. This fundamental asset of culture is still of immediate relevance. But it can be useful to examine it at the stage when it first appeared, and to observe that scholars have noticed the limits of this idealisation and that it was necessary to take into account what evades reason.

This tension lies at the heart of the debates on the theory of evolution, contradicted by an ideal which is at the same time of a scientific and religious nature. I shall approach the subject with a view to showing the errors which lie at the basis of the negations and mutual exclusions between science and faith, à propos of the post-darwinian theory of evolution.

1.2. *Various Conceptions of Chance*

The two words, chance and necessity, do not have the same meaning for everybody. They are part of a philosophy of nature which links up the various elements of evolution. In the first place, there is a compelling sequence of events between cause and effects; an act having been made, the consequence is unavoidable – as the logical order of propositions in reasoning, and even more drastically mathematical deduction, demand. But secondly, experience shows that such a sequence is not of an absolute nature. In natural processes, there are facts which evade forecasting: this is why philosophers have introduced the word chance (*tukè*). Using this word means that the world perceived by the human mind is not enclosed within the sole logic of necessity, as expressed by the laws of nature; it must provide scope for contingency. Such acknowledgement is a sort of humiliation for reason, which has to face what evades its investigation. In view of this difficulty, there are several schools of thought.

a. The first school makes chance into an ontological reference. The word *chance* designates a universal force which acts on natural phenomena. If there is an immanent rationality (a *Logos*), it is not all powerful; it is linked to another force which is called chance (a word used in games with an unforeseeable outcome, like dice). This notion revives a cosmology where necessity and chance are the demiurges who preside over the future of the world. Thus Democritus claimed that in natural processes, either physical or biological, there was a combined action between two principles: chance and necessity.

b. The second school bases their theory on a reading of nature according to mathematical principles (the model of which remains Plato). The human mind tries to understand the world by putting it in accordance with perfect forms (of which the dodecahedron is the iconic figure); but this perfection comes up against the resistance of the opposed principle, matter. This vision of nature provides a theoretical framework for the practice of craftsmen, engineers, and architects who act against the resistance of building materials in order to erect well organized, useful constructions. The mathematical orientation of modern science partakes of such a vision of nature which resists the action of the human mind and transformation. Chance points – if not to the failure of human thought, at least to its limitations. This definition of chance is quite present in modern scientific thought, in its mathematical treatment of natural phenomena. Chance – let's say ignorance – is minimised by a statistical approach which leaves the individual in the background and formulates general rules.

c. The third school of thought (the model of which remains Aristotle) considers that matter is not an obstacle, but a principle or a cause. There is no opposition, but a correlation, and cooperation, between this cause and the others (the shape, the producing agent, or the end). They all pertain to chains of action. Now, the chains of causality are independent; this is why there are events which evade all prevision. Thus modern science remains faithful to its sources, when it describes chance as the fortuitous meeting of independent causal series. Chance is connected to the richness of reality and its interactive complexity. Such a richness is conveyed by the vocabulary, since the word *tukè* has been translated by the Latin word *fortuna* (fortune, in English) and by the words *chance* (a classical word in English), or hope.

d. A fourth school of thought carries this notion of chance even further and claims that the concept of fortuitous events – void of moral qualification of good or evil – is the sign of a defeat of thought. This defeat is not due to the misunderstanding of actions in process, but to the lack of a global vision. Chance is due to the lack of a vision which would allow us to see independent causal series with an encompassing eye. Chance then could be defined as a lack of finality. Chance is the sign that, in natural processes, causes are not of the same order and that, even when they are, they are independent.

The present tradition in sciences offers then four conceptions of chance, namely: the sacred conception, where it is related to the divine; chance as defeat of mathematical perfection; chance as resulting from fortuitous connexions which evade prevision; and lastly chance as a lack of discernible finality. It is through the fourth notion of chance that science crosses the path of theology, which confesses God's creating action. Before developing this point, one should keep in mind that any discourse on chance is very closely linked to a philosophy of nature, according to the vision of the world given by science.

2. Does the Vision of God Abolish Chance?

The fourth notion of chance shares with the other conceptions the idea that chance shows the limits, perhaps the defeat of human reason. Such a situation has been received by monotheistic theology as an opportunity to indicate the difference between the human mind and God. For the monotheistic tradition, God is 'the Subject who knows all', 'the Living One who sees' – says the Biblical tradition, rejoining the indo-european etymology of the word deus. The immediate conclusion of this is that chance does not exist in the eyes of God.

The theological tradition dates back to the Greek philosophers who illustrated it with the following fable: two slaves have been sent by their master on some errand to the same place. Each one of them is informed only of what concerns him. Neither of them knows what the other has been ordered to do. When they meet, they believe that their meeting has been fortuitous, they think that they have met 'by chance'. In fact, when considered from the outside, their meeting was unforeseeable. On the contrary for the master, the meeting was foreseeable, since he knew what both had to do. So what can be described as chance when only one sequence of events is taken into account, is no longer that for him who has a global view of the problem. In a hierarchical vision of actions, several levels can be identified. There is the superior point of view (that of the engineer versus that of the workman, that of the architect versus that of the craftsman, of the officer versus that of the soldier). Chance ceases to exist for him who has a general knowledge and a global vision of the whole. There is also the inferior point of view: that of the grass-roots operator, with a limited point of view. Monotheistic theology, when it claims that God knows all, also concludes that for God – who is supposed to be at the very summit of all hierarchies in knowledge – there is no such thing as chance.

It is in the wake of this hierarchical view of nature that the debate takes place today, opposing chance and the action of God – or the theory of evolution and creation or providence. Such an opposition leads to two options: one is atheism, for which the very existence of chance negates the assertion of a world regulated by God. The other one is the apologetics used by the so called current *Intelligent Design* which, in order to assert God's action, discards the scientific value of the theory of evolution, which allows for the presence on a large scale of chance in the phenomena of life.

I shall endeavour to show that such an opposition is wrong, both from the theological and scientific point of view. But in the first place, the philosophical meaning of the words chance and providence (or creative process) must be clarified, ansd a few misunderstandings must be repudiated.

3. The Theory of Evolution and the Reference to Chance

The word chance is present in the theory of evolution – in its present form – the Synthetical Theory, also called neo-Darwinian (a clumsy expression, in my view, because it presents scientific research as an ideology). This theory is scientific; it must be understood in the context of what has occurred in the perspective of modern science, which began with the mathematical approach of the sciences of nature facing unforeseeable events. The progress of science has changed the meaning of the word chance, owing to the mathematical treatment of the prediction of the future.

3.1. *Chance*

Modern science has definitely repudiated two of the various meanings above mentioned, for ideological reasons. The first meaning is the religious meaning, according to which chance is like a demiurge opposed to the Goddess Reason. The second meaning is the meaning which deals with finality.

The present meaning of the word is related to the mathematical approach to the sciences of nature. Such an approach has consisted in a study of what has been called 'probability', starting with the logics of propositions which is today clearly understood, thanks to the 'theory of measurement'. Because of this intellectual attitude, the general meaning, already mentioned, associated with the coming together of two independent causal series, has been clearer.

The term 'fortuitous' has remained in use, to convey what is of the order of everyday life. In the sphere of physical studies, when one has formalized the study of probabilities, the word 'aleatory' has come up to qualify a singular occurrence which evaded prevision. This word has first been understood in the context of the study of more complex systems where one speaks of 'deterrminist chaos'. Another term turns up in the mathematical treatment of statistics, the term 'stochastic', or 'randomly determined': it applies to what is caught up within the mathematical web of statistics. These two words belong to science. They have the merit of discarding the affects conjured up by the word 'chance' – when it is given the status of demiurge, or when it seems to be a persistent shadow dodging the light of Reason. One observes that rigorous scientific language evades the false debate consisting in opposing chance to science, understood along the lines of a strict determinism. Science acknowledges the aleatory character of events in stochastic processes. Chance is no longer just the correlative of ignorance; when recognized by the mathematical knowledge of probabilities, it helps to understand occurrences considered as singular events. This is why, when Darwin invented the theory of evolution, he made reference to the notion of chance, considered in the narrower sense, already mentioned. The current scientific theory does more – since the mathematical progress of the study of populations, genes, and biological factors allow a really scientific approach of vital processes.

Chance then remains a shadow which escapes a perfect approach to reality. But its presence, acknowledged and located as it is, does not nullify the project of a scientific explanation, as it appears in the theory of evolution.

One must at this stage admit that modern science distances itself from the ambitions of classical science. The latter was built on a mathematical approach, where demonstrations had a compelling character; so that the expression of the laws of nature in mathematical terms gave them an absolute character. This philosophy was grounded on the success of astronomy, a proper field for theoretically perfect movements. But this model of scientific knowledge is no longer recognized today, because its ideal is not adapted to the science of life, where the intricacy of actions in a single living person is not compatible with the rigorous pattern of classical astronomy.

The theory of evolution rests on the use of the notion of probability in the perspective of a mathematical approach within the framework of a statistical study. Hence the two elements which define its status, namely: in the first place, the theory of evolution is scientific; in the second place, its status is that of a theory, according to the exacting epistemological traditions of scientific knowledge.

3.2. *The Theory of Evolution as Theory*

In the first place, the theory of evolution is scientific. It is part of the nature of science regarded in mathematical terms and therefore distances itself from any reference to finality. It rests on a pragmatical ontology and therefore excludes any form of absolute thought process. It only acknowledges the existence of a teleonomy (a tension of living systems towards unity). But this does not suffice to claim the specificity of the theory of evolution. The theory of evolution aspires to giving an explanation of the unity and the diversity of living systems, by classifying them according a genealogical tree. So that as time has elapsed, new forms have emerged, which all belong to the category of the living. Such a tree does not aim at projecting sense into the future, but only to state how living systems have diversified. It is a historical reading; it is scientific, because it uses the present knowledge stemming from biology, and which has been verified in accordance with the scientific procedures of objectivity. But a historical reading invites one to leave room for novelty and unpredictability: this is what it does, using the vocabulary of the probability theory.

In the second place, one should highlight the fact that a theory gives a general interpretation of facts. One must therefore grant it the following status: it relies on facts, it uses interpretative principles and it builds global visions. A theory is not a collection of facts, but an interpretation of observations: it is an intellectual construction which gives a global vision of phenomena, pertaining to a specific field. Thus, the theory of evolution presents a big tree where the living systems are organized. If this methodological point is well understood, the error of those who defend the *Intelligent Design* becomes obvious: they use the occasional deficient observations (the missing links) to oppose a theory which is not a catalogue of facts, but a research program.

The criticisms made by the defenders of *Intelligent Design* to the Synthetic Theory of Evolution are groundless, because if they do place emphasis on difficulties, those difficulties fall within the scope of the global vision given by the arborescence which allows us to see them. Thus, over nearly the last fifty years, many gaps have been filled, and many hypotheses have been verified. There's even more: whenever the observations have allowed it, the tree itself has been modified. These modifications were reckoned on by the perspective given by the general theory and they have confirmed the global perspective. If unresolved problems remain, in the present state of our knowledge, they do not call into question the global vision given by the Synthetic Theory of Evolution: on the contrary, they give the opportunity and the means to work at it.

3.3. *Reductionism*

It is important, at this stage, to distinguish between two meanings of the word 'reductionism'. Science produces results, which are not raw facts: they are conditioned by a method which demands that what concurs to the explanation be only what strictly belongs to its sphere or discipline, determined according to its methodological principles. This exacting demand is called, in the critical language of epistemology, *reductionism*. It excludes resorting to considerations which are not strictly speaking of a scientific nature and therefore it divests scientific work of all religious references. However, the word *reductionism* is ambiguous, because it has two meanings and it is important, as I said, to distinguish one from the other.

The first meaning is methodological. The word then simply signifies that the scientific explanation under no circumstances resorts to the 'non natural' – the 'supernatural' as we say today, in a sense which is not the sense of Christian theology. When science considers a fact, it takes hold of it inside the web of its means of perception, measurement, formalisation and inscription within the framework of the laws of nature. This is valid for neurosciences which bring about a reduction of what seemed to be the fundamental quality of man: his spirit, his conscience, his thought... Such methodological reductionism is necessary.

The word has another meaning. No longer pertaining to the field of epistemology, but to that of metaphysics. The reductionist option is philosophical, since it consists in saying that only a scientific method can approach reality and that anything that is not of a scientific order does not bear the stamp of truth. Thus, a discourse making use of supernatural beings – fairies, gods, angels or demons – belongs to the realm of fiction, to an archaic stage of learning, legitimate with children or the peoples which rationalists call for that reason 'primitive'. They have access to the kind of reason that knows that it is impossible to prove the existence of such entities through objective observations. Such a reductionism is found is various metaphysics which share a certain monism, in so far as they systematically use the adverb 'only', as though there were 'only' what falls under the scrutiny of science which could be considered as real. Science would be the exclusive approach to truth. This is a metaphysical option which is no longer scientific. It contradicts itself by denying through a metaphysical statement the value and the possibility of metaphysics.

If the first meaning is imperative for all, scientists, philosophers and theologians, the second meaning cannot possibly be held as valid by epistemological criticism. So that a free space opens up in order to deal with metaphysical perspectives concerning the origin and the end of life.

4. Chance and Contingency

This definition of the status of reductionism of science leaves room for a philosophical dimension. This is what we are now going to deal with. In order to do so, we must consider reality from a new perpective which is specifically philosophical, starting from our human experience getting involved in a process of transformation of reality. We then come across a term: that of contingency.

4.1. *Ontological contingency*

The word contingency is part of the philosophy of nature. It stands in opposition to the word necessary. Contingent is what is not necessary. But this definition does not apply only from the descriptive point of view of science. It also addresses the question of how to exist in the present time. In this perspective, one can say that what exists is contingent, but could well not be. Not only as possibly not having been, or as doomed later to cease to be, but as not being in the very act of being. It is important to highlight the fact that the word *contingency* is here used in a sense other than the sense it has in sciences, where it applies to statistical laws or aleatory phenomena – but that it does not contradict it in any way.

The use of the word contingency serves the purpose of dealing with a question which is no longer only of a descriptive nature, but belongs to the world of the philosophy of nature or to the world of ontology, therefore to the sphere of metaphysics. I shall describe as contingent not only an event occurring in a series of events, but also its ontological status. A being is said to be contingent because he exists but could very well not be, not only in the future, but also in the present and in the uninterrupted succession of moments which constitute his lifetime. These ontological considerations are particularly relevant where living systems are concerned.

To live is indeed to perform the acts which allow one to overcome death: to feed, to develop, to reproduce... Such an act is contingent, it is not necessary; it is part of its beauty and its grandeur. Ontological contingency is shown and even enhanced by the theory of evolution when it expresses itself in the language of mathematical statistics.

4.2. *Contingency in Nature*

The concept of contingency as defined above is not foreign to what the present theory of evolution offers. The word 'contingency' appears under the pen of scientists. The fact that an iconic figure of contemporary research (Stephen Gould) uses it, shows that he means to address a new question. It is not enough for the theory to redefine the tree which allows to classify the living systems and to unveil their unity and their diversity; the theory also insists on answering the question, why has the tree such a shape? It is not enough to explore the mechanisms of evolution – since the word mechanism conjures up a deterministic philosophy to the mind. One has also to pay attention to the production of novelty, as a characteristic of life.

The theory of evolution allows one to narrate the history of life. It is marked by contingency. Which means that with hindsight the human mind can survey the past course of events; but if one places oneself at the beginning of the historical sequence, one must admit that it cannot be inferred by pure mathematical calculation. The chaos theory shows that the limits of prevision are real. The future is based on conjecture. It is not an uncertainty which would result from ignorance; it is related to the very nature of life, whose main characteristic is to produce new developments. If such a possibility climaxes in human beings, it is present in all living systems. If Plato claimed that ignorance had something to do with the imperfection of matter, in this case ignorance relates to the ability of producing new developments, therefore to what is of value.

Current science no longer rests on the deterministic paradigm of the classical age (Descartes, Newton, Laplace, even Einstein) but on a paradigm where the present opens on to possibilities which are not strictly determined in advance. It may be of use to add that this is inscribed at the very heart of matter – in so far as quantic indeterminism reveals the rich energy held by bodies in physics and chemistry. At this stage, let me point to the awkwardness of those who support *Intelligent Design*, and confine their argumentation within the framework of the deterministic paradigm. They do so in cosmology, by recurring to the notion of the anthropic principle based on *fine tuning*. They do so in biology, when they claim that the indeterminism of genetics (of the individual, or of populations) has something to do with ignorance and not with the nature of the action connected to genes.The characterisation of the richness of life by the appearance of new developments logically leads to the question of creation. It is possible now to open a reflexion on the problem of creation without betraying the principle of a scientific approach.

5. Creation

The word *creation* introduces a new perspective. It has several meanings. This is why it is important to throw some light on a term which originally refers to a strictly theological concept, within the framework of monotheistic thought.

5.1. A total production of being

The word *creation* has become quite ordinary today. It indicates something new. An action is said to be creative when it causes something to appear which was not there. The word 'Creativity' is used to describe the ability of artists to create new things. The theological sense of the monotheistic tradition is more limited. It refers to the total production of being by a unique and transcendent God. In the active sense, it designates the act which produces all beings and the whole being of all. In the passive sense, it designates the result of such an action. I shall use it in the active sense.

In the theological discourse, the word 'all' indicates that it is not a matter of transformation, the passing from one state into another state. But in human action, if something new occurs, it is a relative novelty: it is a matter of passing from one condition to another. Let us remark that the use of the theological term is due to the desire to voice the value of the happy process by keeping the quality associated with the theological language. To be quite accurate, one should notice that the word is used in a metaphorical sense; for in the theological sense, creation is a total production and therefore the passing from nothingness into being; whereas in human actions, the old adage is verified, according to which 'nothing can be made with nothing'.

The theological notion of creation does not have its place in science, and therefore not in the theory of evolution. The theory of evolution tells the story of living systems and describes the process of coming into being. This notion describes a continous process – a transformation in the etymological sense of the word. Unfortunately, many scientific treatises use the word creation to describe the appearance of something new. It is a misuse of language. The word creation is only metaphoric and one should avoid using it. Unfortunately common language multiplies such confusions and many scientists use the word wrongfully, thus aggravating misunderstandings, by limiting the action of the creator to the very beginning of the process under scrutiny.

5.2. An act in the present

Because of this, the notion of creation demands further clarification. Creation refers to the act through which God causes being to spring from nothingness – according to the traditional image. Such an act occurs in the present. The term *creation* does not limit its sense to the production of being at the very beginning of its duration. The word describes the act by which something exists thoughout the span of its existence.

The most widespread image among creationists revolves around this idea: creation occurs at the beginning, and what follows is only the continuation of the first act. Such a conception compels them to consider that everything is given from the start – and therefore, to exclude the very idea of evolution or of a process leading to the creation of new things. If one understands well that creation is in the present, it then appears that such an act inscribes itself in the duration which it founds. The word creation does not deal with the question of the beginning, but with the question of origin.

5.3. The All-Powerful Creator

In all monotheistic confessions of faith, the All-Powerful, the Almighty, is always mentioned in relation to the notion of creation. This is another consideration which helps clarify the errors of the fundamentalists or the supporters of *Intelligent Design*. On this point, there are two important theological schools which divide the world of thought and monotheistic religions.

According to some, the term 'all-powerful' must be understood in its literal sense: all-powerful means powerful without limits, without reservations of any kind. Will is limitless and independent of all logical constraint. God is confessed as being the almighty, capable of all, without any reservation or the possibility of any kind of demand on our part. This conception is called 'voluntarist'. It is not mine. I believe, with a great number of those who support the Tradition, that the notion of omnipotence is at the service of God's wisdom, of God's intelligence, of God's goodness. God cannot do anything that would run against His kindness, or against the demands of the logics of His action. Such is my position, which I would describe as 'sapiential'.

As he creates by His act a world different from Himself, marked by contingency, God does not contradict this existential situation. The creative act is a gift of being to a living person who not only exists, but also evolves within his own predicament, and according to the laws which control him. The creating act, therefore, does not exclude contingency, but founds it: the existence of contingent beings is therefore based on the creating act.

Traditional theology has for a long time developed this point, in relation to human freedom. The way to see the theory of evolution is wider, but it sends us back to the very notion of omnipotence.

Creationists believe that creation is an act of the All-powerful God, in the voluntarist sense of the term. They impose a vision of the world whose origin is a text which they do not bother to read in its context. God's authority imposes to deny the results of science. Such an attitude justifies, in my view, atheism.

On the other hand, discussing the all-powerfulness of God from a sapiential point of view means that the acknowledgement of contingency does not call for the exclusion of God's action. Quite on the contrary, it founds the autonomy of beings. The Christian theology which has developed in the sapiential tradition insists on the fact that God gives not only pure existence to human beings, but also the possibility of using it according to their own nature. The essential feature of creative action is to give human beings their autonomy in what they do. According to a formula by Thomas Aquinas, God confers to man the dignity of being really a cause. 'We do not strip the created things of their own actions, even though we attribute to God all the effects of the created things, in so far as he operates in them all' (*The Sum against the Gentiles*) and again 'it has already been shown that the operation of providence through which God operates in the world does not exclude secondary causes, but quite on the contrary fulfils itself through them, in so far as they act through the power of God [...] As it is manifest that certain causes are contingent, because they can be prevented from producing their effects, it would clearly be against the notion of providence to claim that everything occurs by necessity. Divine providence does not impose necessities to things, by universally excluding contingency from things' (*op. cit*.).

These observations will suffice to show in what sense the refusal of those who oppose the Synthetic Theory of Evolution is theologically groundless. Of course, the theory is not infaillible, it will be revised, but the debate which concerns it must remain strictly within the domain of scientific knowledge, and should avoid using terms which are specifically theological to discuss scientific questions.

6. The Action of God

The difficulty arises from the fact that there are two types of actions which must be linked up together, and their combination, or synergy, poses a delicate problem. When two actors are at the same ontological level, they must come to terms with each other – like vectors in rational mechanics. What belongs to the one adds up to, or subtracts itself from, the other, according to their orientation. But when the two active principles are not of the same order, there is no possible composition, no adding up, no subtraction. A good example which allows to understand this kind of cooperation is found in the musical field. In a piece of music, everything comes from the instrument – and everything comes from the musician. Everything comes from the one, everything comes from the other. It is impossible to divide their action – or attribute to either a percentage of the effect which results from their combination. In the same way, by acknowledging that the creator is not an agent of the same order as the forces of nature, it becomes possible to say that in the process which is described by the theory of evolution, everything is in nature – and everything is in the creator.

The error of the fundamentalists and supporters of the *Intelligent Design*, whose approach is based on exclusion, then becomes obvious. For them, the action of God can be seen in the flaws of the scientific theory, or in phenomena which cannot yet be explained.

To this awkward apologetics, can be opposed the traditional notion of creation, according to which the action of God is the founding principle of what exists, in its very being. This is no manipulation, but the respect of what is. Thus, God knows what is contingent – as contingent.

The knowledge of God is based on several qualities, which are gathered together under the word 'vision'. The word, in fact, is about immediacy, since it describes the co-presence of separate elements in time as well as space; the word translates to convey the respect of diversity and of the normal process of time. But just as the vision does not abolish the spatial difference and the particularities of forms, it does not either abolish the temporality implied in natural processes – particularly in living systems. So that the evolution seen by God does not cease to be what it is: an aleatory process characterized by contingency, or as Thomas Aquinas said: 'The fact that God can produce by himself all the natural effects does not make other causes redundant. This does not reveal the inadequacy of the divine power, but the immensity of his goodness, which urged him to communicate his likeness to things, not only by granting them being, but also by allowing them to be the causes of other things. It is in fact in both these ways that creatures ressemble God, as has been shown above – therein lies the beauty of the order which reigns among the created things' (*op. cit*.).

This is a strictly theological debate. It shows how theology is not thwarted by the ackowledgement of contingency, translated into a scientific language by statistical analyses and probabilistic approaches. Let me once again quote Thomas Aquinas: 'there are things to which God's will grants necessity, and others to which he does not grant it'. He goes on explaining: 'when a cause is efficacious, the effect proceeds from the cause, not only concerning what results from it, but also concerning the way it results from it or the way it is ... Since God's will is perfectly efficacious, it follows that not only the things he wants are done, but also that they are done in the way he wishes them to be done'. Those who to day follow closely the theory of evolution must necessarily agree with the Ancients that some things occur of necessity, and others in a contingent way. Let us remember that St. Thomas said that God wishes it to be so, 'so that there might exist a certain order among things, for the perfection of the universe'. He concludes: 'This why he has prepared in a number of cases necessary causes, which cannot fail, whence certain effects necessarily proceed; and in a number of others imperfect causes, the effects of which are produced in a contingent manner' (*The Theological Sum*).

One last remark on the action of God and the recognition of the value of the autonomy of nature. Our vocabulary is here limited by the fact that it is rooted in human action. For a human being, to act is to situate oneself in front of nature, from an exterior point of view. So that there is a difference between a natural action and a human action which transforms reality through other means than nature alone – even if the knowledge of nature allows one to respect its laws. God, because he is a creator, is not external to nature. He does more than respect it in its laws and in its autonomy: he gives nature its laws and its autonomy. So that the creative act is in no way an intervention. It is the most intimate part of the energy at work in nature. Let us remark that this conclusion, which is perfectly justified in strict monotheistic terms, which give sense to the word creation, meets the intuitions of the oriental philosophies and religions, anxious to establish a communion between beings. This last point leads me to consider the question of finality.

7. Ackowledging the Presence of a Finality in Nature

Why are the links which have been established so difficult to admit? The immoderate affectivity associated with the terms chance and necessity is a fundamental part of the answer. In fact, for some people, resorting to a non-scientific principle is like the remanence of the religious feeling and the reference to providence is seen as a frame of mind that is convenient for chidren. For others, the ackowledgement of the aleatory is a source of insecurity. Others again consider that science is a destroying factor, in so far as it forgets what is the non-quantifiability of life... One must set aside those affects and admit that the assertion of the transcendence of God is all the more necessary, as it permits to establish the respect he has for what is done – while showing that such a respect is not a lack of power.

Ever since its birth in the XVIIth century, modern science has excluded the possibility of an explanation through finality as the Ancients formulated it, in so far as it cancelled the explanation and dispensed with the analysis. One should respect this option and therefore introduce a difference between the notion of life as defended by the Ancients and the notion of life as used by scientists.

Such a recognition does not prevent one from recurring to the notion of finality. But this is not a scientific attitude, properly speaking. It means entering a philosophical vision of nature, in order to propose a global vision, which serves to interpret the results of science by acknowledging in the first place that the process introduced by science displays a growth of complexity, therefore of realisations where diversity is assumed in a better form of unity.

It is therefore not expedient to use the notion of finality in opposition to the theory of evolution. One must admit that it is pertinent in a theological approach. The latter cannot be formulated without taking root in reality. One should then accept the fact that the old discourse should shift its emphasis, or otherwise it will appear as naive.

At this stage, it might be useful to bring back into one's mind a distinction which is traditional in theology. The wish to acknowledge God's action in present life has led theology to distinguish carefully between the two types of action that result from power. A first verb expresses the idea of power in its nature of power: to dominate. A second verb expresses the idea of power in terms of reason: to govern, that is to carry something to its end. The first term characterizes the conception of omnipotence which I have previously discarded: the conception marked by an arbitrary sovereign will. The second term characterizes the conception of omnipotence to which I have given preference: the conception which makes power subservient to wisdom and therefore refrains from acting all – and in the first place, from contradicting itself. Thus God, by creating a contingent world, does not distort the actions of the laws of statistics. The aleatory is inscribed in reality. It is not just the sign of human ignorance.

The term 'to govern' also contrasts with another word which is probably more present in the paradigm of those who support the *Intelligent Design*: to manage. The word corresponds to the paradigm of classical science which brings down the creative act to 'an initial flick' (to quote the term used by Pascal in his refutation of Descartes). The manager as a matter of fact uses the capabilities of his subordinates and the ways and means at his disposal to forward his projects. He reduces them to the role of actors involved in an action which unfolds according to the logics of material actions and human motivations. Whereas the use of the word governance conveys the idea that the aim of the act is not a project of management, where the agent is subjected to an end which is unknown to him, but that God proposes to actualize creation for its own sake, and each creature in its own order. It is to be regretted that this dimension has disappeared from the technical discourse that prevails over modern culture. The evolution of living systems, if it is technically within the operating sphere, is not enclosed in it. It leads to another realisation where contingency is the sign of a type of transcendence – the type which the moderns associate with the notion of beauty.

This analysis shows that the current polemics have a common origin. On the one hand, the deistic adversaries of evolution challenge contingency (like the supporters of the *Intelligent Design*) and on the other, atheists deny all divine action, as if divine action erased the autonomy of nature. There is, here, a misappreciation of the linking synergy between the Creator and nature. There is furthermore among the adversaries of the theory of evolution an epistemological error, because they remain within the framework of classical science under the deterministic paradigm of Cartesian mechanics, which they adapt to the level of God's action. Correlatively, atheism cannot acknowledge that the creative act founds the creatures' autonomy, i.e human freedom in the first place and in a wider sense the contingency of life.

CONCLUSION

To conclude, I would like to make two remarks on the relations that exist between science and the theology of creation.

The first remark is about the status of knowledge. A number of believers, today, go back to convictions which date back to the days of clerical omnipotence, and assert that scientific knowledge must be subservient to the religious authority – that of the Bible, of the Coran or of dogms. Since Galilei's time, we have known what misfortunes these convictions bring about. Others, more subtle, insist on science keeping within well marked limits and being forbidden from approaching certain subjects: in particular, those concerning the origins of life and mankind. This is wrong: because the limits of human knowledge should not be determined by the partitioning of knowledge, but by the way in which we approach reality. Reality, as a whole, is subjected to the scientist's scrutiny. The limit is not in the extension, but in the nature of the vision and the conceptualisation. There is no *a priori* prohibition that limits the scientists' explorations. However, they must be aware of the particular character of their method, in experimentation as well as in conceptualisation. There is then the possibility of a dialogue, since faith also looks at everything in a light which has its particular aspects. Two lights allow a better vision and can relate one to the other, with the open perspective of mediations.

My second remark concerns the status of scientific research. It seems to me that the debates on the theory of evolution should encourage us to address the question of what are the real issues of science. What are the intentions of science? It seems to me that a scientist should be aware of the fact that scientific research should not limit itself to its technical dimension. Science is different from technique. Even though it cannot ignore its operational dimension, science should not disregard the fact that its real orientation is towards pure knowledge – in which sense it can be said to be disinterested. The theory of evolution voices therefore the desire to understand what life is about. This dimension transcends the debating, the dithering, the uncertainties, the present limits of knowledge. It proclaims its greatness, and can contribute to the development of faith.

DISCUSSION ON PROF. MALDAMÉ'S PAPER

PROF. CABIBBO: Thank you very much for this beautiful lecture that clarifies that there is no problem between science and theology, which is good to hear. Are there any remarks?

PROF. DE DUVE: I would like to congratulate Father Maldamé for a very solidly constructed analysis. I would like just to make a suggestion, namely that in his final text he specifies that what he calls the theory of evolution really is the Darwinian or the Neo-Darwinian or the synthetic theory or the theory based on natural selection, because there are other theories of evolution and your analysis applies specifically to natural selection.

PROF. MALDAMÉ: It was about Darwinian evolution of life, living beings.

PROF. CABIBBO: I hope there is no problem with the D-word, Darwin.

PROF. COLLINS: Thank you for a very thoughtful summary of how these theological and scientific perspectives can be harmonised. Stephen Jay Gould was fond of pointing out that, at least from his perspective as an evolutionist, if you somehow could rewind the tape of evolution back a few hundred million years and then start things up again, not all the way back to the beginning but maybe to the Cambrian, and then see what happened as you ran it forward again, it would be extremely unlikely that you would end up with higher primates with advanced intelligence and consciousness. That is upsetting to some people who feel, therefore, that that threatens the idea that there is no chance in God's eyes. On the other hand, Simon Conway Morris would have the rejoinder that evolution seems to favour certain pathways over and over again as, for instance, the development of the eye at least seven independent times, and that higher consciousness would also be highly favoured when it was ultimately possible for it to appear, and so that we would end up, if not in a primate, in some animal with higher intelligence and potentially the opportunity for things such as free will and the moral law to appear and, if you are not hung up on the idea that the image of God has to look like us, then you have no real problem with that alternative outcome. I have heard these issues debated many times and I would just be very interested in your perspective from what you have just said to us, would that be troubling to you as a theologian the idea that if that asteroid had not fallen on the earth sixty-four million years ago and wiped out the dinosaurs that we might be here in the Pontifical Academy looking rather differently than we do?

PROF. MALDAMÉ: That is a lot of questions. But my meaning is not to speak about evolution as evolution. I have to speak on evolution but what the beings are and become. That is a different point of view. And the theory of evolution is a historical and retrospective point of view but I think we can now see a progress from the beginning to now. At the beginning the way is not clear and that is a stochastic problem, that is the point.

PROF. CABIBBO: May I ask a question myself? Coming back to the question of the eye, etc., I was very impressed by this morning's lecture by Prof. Gojobori who showed that, in some way, some of the basic pieces are very very old and were used again and again so, somehow, there was a predisposition of having circuits in the brain, even in simple brains, which have to do with reason and then maybe they substituted one sensor for a different sensor. Sometimes, one of the criticisms is that we are so complicated, but the complication is shuttled at different scales, so certain genes are produced and then they are used for something else, so it is a complication of a Meccano building more than starting from atoms and molecules.

PROF. MALDAMÉ: The genome is not a Meccano, it is the sense of the world, theonomy, which said that the different genes are together to realise the best solution to the problems.

PROF. CABIBBO: My question was not particularly theological, there was no question attached to it.

PROF. MITTELSTRASS: I understand that the concept of ontological contingency is at the centre of your argument, or at least very essential for that argument. I wonder whether this concept of ontological contingency is a premise of your argument or a result. I mean, if you use it as a premise, that would mean that contingency is the essence of everything that exists, that would be a theological or philosophical argument; if you use it as a result, that would mean that contingency is the result of research, philosophical, theological, scientific, into the phenomenal world. So is it more a premise or a result?

PROF. MALDAMÉ: Both. I think experience shows us that there is contingency and when, in philosophical discourse, contingency is a premise to explain what I understand but I think it is a hermeneutic cycle, it is both a premise and a conclusion.

PROF. PHILLIPS: What I have to say is more of a comment than a question. You gave us a very detailed definition of what you meant by a theory, which is exactly what I believe a theory is. That is, you told us that a theory was not a collection of facts but a way of interpreting those facts and a way of organising those facts and you had a much better description of what a theory was, and you said that evolution was such a theory. Now, the reason I am making this comment is that we have heard the term 'theory' used in a number of different ways during our discussions and I think that we have to be very careful about the way we use the term. For example, on, I think it was the first day, Christian de Duve made an impassioned plea that we should understand that evolution is not a theory but a fact. Now, under your definition of theory that is not a statement that makes sense, because one does not oppose theory to fact. Theory is something that collects together a lot of facts and makes sense of them. And then, earlier today, I believe that it was Stanislas Dehaene who at some point in his talk said, well, now this you must understand is just a theory, by which he meant it is just a hypothesis, and so I think we have to be very careful because the general public tends to interpret the word 'theory' to mean just that, 'hypothesis' or, worse still, a guess. And that is not the way at least a lot of scientists use the word 'theory' and certainly not the way in which you described the term 'theory' so, having heard you give such a good definition of the word 'theory', I thought I had to say something about the, perhaps loose, way in which we use 'theory'. And it is no surprise that we use it loosely, because it is used that way in general conversation, but we get ourselves in trouble. We talk about the theory of evolution and say that in the same way as we might say 'the theory of special relativity', one of the best verified scientific structures there is, or the theory of quantum mechanics. I just think we have got to be mindful of the way in which we use the term.

PROF. MALDAMÉ: I speak of the theory of evolution in the sense that is used in scientific literature but the term is wider and outside of this definition. I think this is a situation for all the world. For instance, the term 'evolution', evolution has a common sense, it is change, progress, continued. Evolution as a philosophical term, in natural philosophy from the Romantic time, has been used since the beginning to manifest potentiality in time. The word evolution has another sense from the scientific point of view. Theory is a scientific point of view with the mathematical treatment of information.

PROF. ABELSON: Well, I wanted to expand on the point you were making about things being used over and over again in evolution. There was a wonderful paper, in the 1970s I believe, by Francois Jacob in which he characterised evolution as a tinkerer or, if you want, God as a tinkerer or as a *bricoleur* in French, and the example he gave concerned certain crystalline lens proteins that allow you to focus light on the retina. Some of those proteins are familiar in another context, for example enolase is an enzyme in the Embden Meyerhoff pathway but is used as a lens protein. Now we know many examples in which the same protein is used for different purposes. This means that the tool kit that has been used in evolution did not have to be infinite or created anew. In order to create a new function the tinkerer only had to find a part from somewhere else that worked.

PROF. CABIBBO: Maybe Tinker toy is better than Meccano, but I fully agree, yes.

PROF. BERNARDI: Well, just a further small short comment on what Francis Collins mentioned. The story of the unwinding of Stephen Jay Gould can be really criticised, because he forgets that the climatic history of earth has mattered a lot in terms of natural selection so the reproduction of some patters would be expected, so it is not at all that if you unwind and start again you would end in totally different systems. Of course, apart from what Francis mentioned, the catastrophic effect of the meteorite, but otherwise the evolution of the eye, independently, and other facts, absolutely go against what Stephen Jay Gould proposed, because we are so dependent, in terms of natural evolution, upon the environment that many things are expected to follow the same patterns.

PROF. ZICHICHI: You are taking for granted that a single theory of evolution exists. As I have shown in my lecture, this is incorrect. There is the theory of evolution for inert matter, which is the most scientifically formulated and verified, the theory of evolution of living matter, which is not scientifically formulated and the theory of evolution of living matter with reason, once again, not scientifically formulated. So there is not a theory of evolution that you can compare with theology. Are you talking about the theory of evolution of inert matter, the theory of evolution of living matter or the theory of evolution of living matter with reason? These three theories have very different scientific status. There is not a single theory of evolution.

PROF. MALDAMÉ: Yes but I think the term 'life' is correct for insects, for mammals and for humankind. So I am talking about a theory of evolution of living beings, of life. But the science is not the same when we speak about astronomy, about mechanics, and this is the difference, but it is a view of life from the beginning unto now.

PROF. CABIBBO: I think this makes more cogent the request of Professor de Duve that you specify that you are speaking of Darwinian or Neo-Darwinian theory of evolution.

PROF. MALDAMÉ: On this topic I think that the theory of evolution in general, from Lamarck then Darwin, marked the beginning and the scientific way but now we have the synthetic theory of evolution. But the synthetic theory of evolution from the middle of the last century is not alone, there are a lot of theories, the neutral theory, the theory of Gould and it is a lot of theories but all these theories are grounded on the synthetic theory of evolution.

PROF. CABIBBO: May I make one last comment on the question by Prof. Phillips? Let me go ahead for a moment. I think, in my understanding, that evolution has two aspects: one of them is a historical aspect that essentially affirms that all species flow through the tree of life. There is this descent of certain species from previous species and going back down to the origin. This is one aspect. And the second aspect is, how did it happen? Darwin was posing both aspects at the same time, he was saying that, actually, species are derived one from the other and from previously existing species and then he also proposed natural selection, mutation, etc., as a mechanism which, at that time, he was not really understanding because he did not know about DNA, etc., but I see this as a sort of two separate classes of histories. I mean, one is the historical succession and the second one is a mechanism. The second one is probably more of a theory and the first one is probably more of a series of facts, I don't know.

PROF. M. SINGER: I was going to say something quite similar to what you just said, Professor Cabibbo, but I would like to say that certainly, in my discussions with people who are not scientists, I find it very important to make the distinction between what I would call the fact of biological evolution and a theory that explains those facts through a common descent with change by natural selection. Certainly, in the United States, it is very important in having such discussions with non-scientists to avoid the use of the word Darwinian or Darwin, because with some people that immediately causes them to bring a shutter down inside their heads and hear nothing else that you want to say.

THE HUMAN BEING – GOD'S PLAN OR JUST SHEER CHANCE?*

ULRICH LÜKE

In the present debate between creationist theology and evolutionary biology a new front seems to be opening up on old battlegrounds long considered pacified. The main opponents in this battle are a fundamentalist-biblicistic creationism and a materialist and reductionist version of evolutionary biology.

Thus, the Germany-based Giordano Bruno Foundation, which was established in 2004 and is emphatic on criticism of religion, polemically advocates this reductionist version, while claiming to argue from a responsible scientific point of view but going in fact far beyond what is scientifically admissible. Likewise, in the USA, modern creationists of the Center of Science and Culture founded in 1990 as part of the Discovery Institute equally make scientific claims in arguing for their version of a biblicistic creationism.[1] However, they simply fail to come up to the level of theological exegesis and Bible interpretation at the universities.

Again, we are confronted with the unfortunate tension and the unreasonable or foolish fission between, on the one hand, the sciences which want to annihilate religion, and, on the other hand, religion which thinks it must put the sciences right.

* I have to give thanks to Wolfgang Butzkamm (Aachen) for the translation.

[1] Cfr. Davis, P., Kenyon, D., Dembski, W., Wells, J.: (1st & 2nd Ed) *Of Pandas and People: The Central Question of Biological Origins. 1. u. 2. Aufl.* Richardson Texas 1989 f. *Dies.: The Design of Life: Discovering Signs of Intelligence in Biological Systems*. (geänderter Titel in der 3. Aufl.). Ed.: Foundation for Thought and Ethics, Richardson Texas 2007; Junker, R., Scherer, S.: *Evolution. Ein Kritisches Lehrbuch*. Baiersbronn 6. Aufl. 2006; Kutschera, U.: *Streitpunkt Evolution: Darwinismus und Intelligentes Design*. Münster 2007.

1. The problem of an all-encompassing theory

A central point of contention has been the concept of chance and the consequences deriving from it, consequences both for our individual lives and for our intellectual sense of self as a human being.

Some evolutionary biologists claim that due to the randomness of mutation there is no sense in evolution, and even more than that, that such a sense would theoretically be quite impossible. They espouse ideas held by the molecular biologist Jacques Monod in his book *Chance and Necessity,* (who famously said: 'The universe was not pregnant with life, nor the biosphere with man'). According to him, the existence of chance in the evolution and reproduction of life excludes the idea of design, plan, or God as a sense-giving, purposeful planner. On the other hand, religion is a phenomenon we simply cannot overlook; it is a visible, tangible, and, it seems, ineradicable reality, and, along with it, the assumption of an all-comprising, divine plan is equally realistic. Does man owe his existence to mere chance, be it pleasant or pitiable, or is he the result of divine Providence? This is *the* alternative we are faced with.

Although many evolutionary biologists deny such an all-encompassing divine plan, something of the sort is implied when they interpret the phenomenon of religion in a biological, population-dynamic way. In the words of A. von Hayek: 'Religion survives, because it produces offspring'. This is their tenet or dogma, and one could add, 'not because it is true or because there is a God'.

Accordingly, religion makes sense in a way religious man is not aware of, and that sense is said to lie in a 'side effect', namely, an optimized care for offspring, which is then made its main function and only sense. Thus, on the quiet and almost secretly, a sense emerges after all, despite all that chance. It is, however, a biological sense, not a theological one.

It is imaginable that man, although endowed with a vague idea, cannot understand the entire concept, because he must always remain its integral part and cannot be or become its uninvolved observer facing the world from an outside perspective.

Sometimes there are biologists who want to explain to people of faith, including theologists, that the content of their beliefs is absurd and nothing but a socio-cultural result of evolution. David Sloan Wilson, for example, came forward as a biologist to enlighten theologists in recent times. Because of religious fictions, it would be easier for the human species to cope with the real world. By means of religious practice, men could produce a brood-friendly environment within a logical structure they didn't really understand themselves.

And then such an advocate of enlightenment, after explaining what religion really is, declares himself an atheist, whatever that means. That strongly reminds me of someone who at the annual meeting of the chess club explains that chess is a dialogically structured exercise to perfect one's motor skills; namely, the fine motor skills for playing chess on a table and the gross motor skills for playing chess on grass. And that this would be the evolutionary gain, which can be understood in biological terms, but cannot be grasped by the chess player.

In addition, this advocate of enlightenment, in order to stress his objectivity, may state that the rules of chess, whose existence the chess player claims, are of no relevance whatsoever and don't need to be taken notice of and that he, the advocate of enlightenment himself, doesn't know them.[2] What kind of enlightenment is this? Perhaps it is good enough for this self-styled advocate of reason, but not for a reflective person. How pleasantly different is, in contrast, the position of someone like the philosopher Jürgen Habermas, who, before completely denying the genuine significance of religion, at least admits the possibility of just being 'religiously nonmusical' as an individual.

I think we can accept that there is – perhaps – this population-dynamic side-effect, but we cannot accept that it should be the main and only function. Some biologists try to make evolution-theory the main theory in explaining the world as a whole. But there must be a philosophically good argument advanced from outside of biology, which could convince us that the biologist point of view is the best and the one with the highest certainty.

2. The problem of the notion of chance

To clarify the question of whether chance or a Deity have a hand in this, we have to specify the notion of chance, and this attempt at greater preci-

[2] Bahnsen, U.: Vom Nutzen der Frommen. Der Amerikanische Biologe David Sloan Wilson hält es für erwiesen, dass Glaubensysteme nach den Regeln von Darwins Evolutionstheorie entstehen. Ein Gespräch über den Sinn der Religionen. In: *Die Zeit*, Nr. 52, 21. XII. 2005, S. 33.

sion is certainly in the best interests of science. What must be distinguished is – and in this I follow Gerhard Vollmer –:[3]

1. objective chance or randomness, as it is seen to be observable and stochastically quantifiable, but not reconstructible in causal analysis, with phenomena of quantum physics, and
2. subjective chance or randomness, as it occurs in biology, for instance, which is in principle accessible to a causal analysis but which, for pragmatic reasons, cannot be carried out.[4]

When determining the frequency of mutations for individual gene spots of higher animals, instead of random distributions, mutations accumulate in distinct areas, often called hot spots, which can and need be analysed. These mutations can only be called random in relation to their selective environments. This means they occur more or less independent of the environment, but only in as much as, or to the extent that the selective milieu itself does not contain mutagenous agents, that is substances that can induce mutations. In order to describe this independence of mutations from a selective milieu, the term randomness should not be used. It would be better just to speak of a lack of correlation or a lack of interdependence between mutation and selection. And this is what the Fluctuation Test of Delbrück and Luria (1943), the Spreading Experiment of Newcombe (1952) and the Replica-Technology of Lederberg (1952) can show.[5]

Even the notion of chance, as found in the books of Ernst Mayr, who is one of the founders of the Synthetic Theory of Evolution, shows that we are confronted with subjective chance. Mayr reconstructs the biological chance out of five factors:[6]

1. Mutation in one or more geneloci;
2. Crossing over;
3. Distribution of chromosomes in meiosis;
4. The lucky or unlucky fate of the gametes;
5. The lucky or unlucky fate of the zygotes.

[3] Vollmer, G.: Zufall in der Biologie. In: *Herder Lexikon der Biologie*. Heidelberg, Berlin, Oxford, Bd. 8, S. 509 f.

[4] The highly interesting experiments of Rafael Vicuña, a part of them published in these proceedings ('Bacterial Evolution: Random or Selective') show that in biology we have to do it with the second type of chance, with – in the diction of Gerhard Vollmer – the subjective chance.

[5] Cfr. Hagemann, R.: Allgemeine Genetik. Jena, 2. Aufl. 1985, S. 107 f.

[6] Mayr, E.: *Evolution und die Vielfalt des Lebens*. Berlin, Heidelberg, New York 1979, S. 18.

When the Dictionary of the history of Ideas says that 'this element, generally known as chance, could conceivably be the failure of man to know all possible factors affecting an outcome', then it does underline the position Vollmer has taken.

The question is whether from this notion of subjective chance or randomness as used in biology any inferences can be drawn as to our image of man.

Can we conclude from the biological fact that in the course of evolution innumerable species have died out or not developed to any recognizable degree that there is basically no tendency, no direction, no improvement and no increase in complexity?

Does the concept of chance as it is normally used in biology warrant the assumption that there is no aim, no plan, no sense in evolution as Monod, Wilson, Dennett, Wuketits and others have claimed?[7]

The answer to both questions is a clear no. For one thing, from the mere fact that a certain result was not reached, it cannot be inferred that it had not been aimed at – by whatever processes or strategies. I may have had the intention to go to the station even if I did not reach it because I misread the map or because I gave up when I realized I would be too late for the train.

For another thing: It is perfectly possible to interpret the seeming randomness of mutation as an exploratory, innovative and distributive element in a larger plan, without disclaiming the theory of evolution in any sense.

Randomness in this sense is just another word for not yet predictable with any certainty and is neither synonymous with chaotic, nor synonymous with directionless processes either, if chance can be seen as an element of something greater.

Let me illustrate with an example. When drawing 6 lottery numbers out of 49, subjective chance plays an essential part. Nevertheless, from what goes on in the lottery drum, which is certainly random from a subjective point of view, it cannot be concluded that the whole undertaking, the lottery itself, is meaningless or unplanned.

The chance behaviour of the lottery balls can be explained by such facts as their initial states, their turning speeds, the effects of friction, the number of turns of the drum, the mechanism of final selection etc. Here chance means simply subjective ignorance because of the sheer complexity of the event. But this kind of chance is not opposed to meaningfulness, sense or plan. In fact, it serves as an incentive for participants and as a mechanism

[7] Cfr. Wuketits, F.M.: *Evolution. Die Entwicklung des Lebens*. München 2000.

of distribution to find the winners among the participants. They contribute purposefully hoping for the occasional gains, and at the same time, their contributions ensure the continued existence of the lottery. And every time the lottery-company is the winner. That's the plan behind all of the randomness and through all the randomness.

The fact that a restricted element of chance is built into the total event does in no way lead to the conclusion that the whole undertaking is meaningless, whether it be a lottery or the evolution of life. And whatever chance or randomness means, for a theologian it is always an object of the creation and not the alternative subject to the creator in the way Cardinal Christoph Schönborn suspected.[8]

'Perhaps chance or randomness is that grey-coloured overall or boiler suit God likes to put on if he wants to stay incognito'.

Moreover, man forms part of an evolutionary process which, not having any knowledge of the origin and the end, he only vaguely understands and which he cannot approach from an objective viewpoint. Taking his point of departure from the findings of the natural sciences, all he can do is speculate about the entirety of this process in a philosophically interesting manner. These speculations, however, don't meet the criteria of science in a strict sense any more.

Let me again make use of an analogy. The physical build of birds reflects the laws of aerodynamics, which they 'extract' from the nature which surrounds them without being aware of this process of adaptation. Similarly, the bodies of fish represent the laws of hydrodynamics which again have been extracted from their natural environments, again without any sort of active conscious participation on their part.

In these cases, Man as an external and superior observer is able, in retrospect, to discover a plan in the phylo- and ontogenesis of birds and fish, which as far as we know, they themselves cannot understand although they themselves are the agents in this process.

In a similar way, analogous to birds and fish, Man is unable to survey, discern and understand the way he came into being. He has only a partial view of the biological as well as cultural processes he is involved in. He cannot survey the entirety of these processes from an independent standpoint outside them. His speculations remain extremely uncertain no matter whether he argues as a scientist critical of religion or as a philosopher or a

[8] Cfr. Schönborn, C.: *New York Times* and *International Herald Tribune*.7. July 2005.

theologian. Both parties – those who suggest there is a design and an ulterior meaning in evolution and those who deny this – are dealing in metaphysics. This is by no means forbidden, but those who do so should themselves be aware of it, and should make others aware of it, too.

An ideologically loaded evolutionary science that makes universal claims that transcend what is quantifiable in an empirical manner, is not what it purports to be, namely a science, but has turned into metaphysics – without knowing it or wanting others to know it.

A type of evolution theory which gives its descriptive terms such as 'random' mutation or 'necessary' selection or itself as a whole a metaphysical twist or turn, turns away from being a natural science.

The question of whether Man emerges from blind chance and owes his existence to some sort of silly coincidence, or issues from the hands of God (as Dante famously put it) is not a question of scientific certainties, nor is it a matter of vague professions of faith. In any case, it is not a question the sciences can decide, but rather a matter of belief, in favour of which more or less convincing metaphysical answers can be put forward.

3. A kind of conclusion

We may have a metaphysical option – perhaps we all have one with or without a god – but that is not the truth-keeping extension of certainties given by the sciences. Naturalism is a philosophy, more often than not a metaphysical one, whether we are aware of it or not, but by no means a natural science.

Man with his 'sense of sense' is a product of evolution, too. His search for, or longing for, meaningfulness is not something grafted on to the processes of evolution, or imposed on them.[9]

Doubtless Darwin's theory of evolution, which has considerably been scientifically enhanced to this day, is not only a central theory in biology, but in the natural sciences as a whole. However, those biologists and philosophers[10] who claim it to be a theory with high significance for ethics,

[9] Vgl. Lüke, U.: Religiosität – ein Produkt der Evolution? In Lüke, U.: *Mensch – Natur – Gott. Naturwissenschaftliche Beiträge und theologische Erträge*. Münster 2002, S. 58 – 66.

[10] Vgl. Wuketits, F. M.: Das naturalistische Menschenbild. Der Mensch als Produkt seiner Entstehungsgeschichte. In Klinnert, L. (Hrsg.): *Zufall Mensch? Das Bild des Menschen im Spannungsfeld von Evolution und Schöpfung*. Darmstadt 2007, S. 165 ff. Ganz ähnlich Kanitscheider, B.: *Im Innern der Natur. Philosophie und moderne Physik*. Darmstadt 1996.

religion, philosophy, social studies, etc., have changed a good scientific theory into a bad philosophical theory. With such an enlargement resulting in an allegedly not metaphysical hyper-theory including the dogmata of random mutation and reproductive selection, one invents a huge evolutionary myth, which extrapolates the biological results far into the field of the interpretation of the world.

This raises the serious question of whether the evolutionary ideas, as soon as they exceed the boundaries of a biological theory, become metaphysical and are thus, *sit venia verbo*, 'meta-fusiliered' as a scientific theory.

For an essentially incarnational religion such as Christianity, it is already implicit in the very idea of incarnation that there will be no conflicts with the biological, evolutionary or socio-biological theories, which are secondary meanings of the primary theological assertion of the creation of the world and the incarnation of God. However, it is equally obvious that theologians will not agree if people, who may be fine biologists but are clueless as far as hermeneutics are concerned, try to exchange the primary assertion for any secondary meaning and vice versa.

Indeed, there is an incontrovertible, solid, and detailed scientific database for a theory of evolution. There is also an elaborate and philosophically refined exegesis of biblical remarks on creation and their philosophical-theological explication.

Between these two there is not the front line of creationism vs. evolutionism with the war report which is presently staged in the media, because neither does the one side have the means to prove God's existence, nor can the other side rule out that possibility.

Creationists without a historical-critical exegesis and evolutionists without understanding their own reductionist arguments as a kind of more or less hidden metaphysic seem to me like pole-vaulters. The bar is positioned at a height of six meters. They jump four meters under it and think they have cleared the bar because it wasn't knocked down.

Both the theory of evolution and the theology of creation have to be taken into account for further ideological considerations. On that basis, and not by evading it, it will indeed be possible to develop different philosophical views upon the world based on these identical scientific findings or certainties.

That these views, provided they have an adequate scientific and philosophic basis, will be, may be or even should be controversial – so what?!

DISCUSSION ON PROF. LÜKE'S PAPER

PROF. LÜKE: I need help in order to answer the questions I expect you have. It was said about Shakespeare that he had learned 'little Latin and less Greek', but there was no problem because he spoke wonderful English. But I have two problems. First, I have learned little Latin and less English and the second problem is, I am not Shakespeare. But Professor Wolters will be so kind as to translate your questions into German and also my answers to you. Therefore I hope I won't answer questions that no one has asked and I hope you will not punish Herr Wolters for my answers.

PROF. LÉNA: I will ask you the simple question of an ignorant. Could you give us your precise definition of metaphysics?

PROF. LÜKE: (originally in German) Metaphysics attempts to make assertions that encompass both empirical statements made by the sciences and, ideally, an overall explanation of the world, a holistic plan. But who thinks he can do this, who presumes he has got this overall plan?

PROF. PHILLIPS: I very much liked your analogy to a lottery, in which chance plays a central role but the structure of the lottery has been well determined beforehand. But there was one feature of that description that I found somewhat bothersome, and that was that you said well, the outcome of the turning of the drum is something that is, in fact, influenced by physical law, how fast the drum turns, and cannot be predicted because we lack all the information in order to make such a prediction so that it appears to be random. It seems to me that two things are being mixed up here because, on the one hand, the analogy is a very nice one, if there is something truly random it still can be embedded in something that is very well designed. On the other hand, the implication that there might be something that is not truly random seems to me a separate assumption that has nothing to do with this wonderful analogy and so I was wondering how important you felt that other part was, that, in fact, in principle one could predict the outcome of the lottery if one had enough information. Many of us might doubt that that would be true because of classical chaos theory and the nature of deterministic chaos.

PROF. WOLTERS: Can you put your question in just two or three sentences so that I can translate it?

PROF. PHILLIPS: OK, I will try. In your analogy about the lottery, how important is your observation that the outcome of the lottery is something that in principle could be predicted if one had enough information?

PROF. LÜKE: (originally in German) I think that what Vollmer has called 'subjective chance' itself contains the randomness of quantum physics. So we have two forms of chance or randomness, on two different levels. As regards the notion of chance in quantum physics, one cannot make a complete analysis of it, unless you refer to the overall system. Now let me refer again to the lottery. There are certain determined elements, the drums and the position of the drums etc., and we as human beings cannot give *all* the conditions in order to predict exact results. But it is thinkable that there is someone, an absolute spirit, who could do this. I cannot maintain that chance constitutes the opposite of a Creator and this is why I say that chance, from a theological standpoint, is still on the side of Creation, and definitely not an alternative to a Creator. So this alternative does not exist. Admittedly, this is not very well expressed, but in the declarations of Cardinal Schönborn in the *NY Times* he opened up a new alternative between a God who has a plan and chance, which then, shall we say, bypasses God if you like. To my mind, chance or randomness and also the scientist who tries to transfigure this, would be very bad alternatives to God. Is that clear enough?

PROF. CABIBBO: May I make a remark, before giving the floor to Professor de Duve? I have a technical problem with your presentation and that is that you seem to imply that quantum uncertainty is not important, in fact you contrast quantum uncertainty and subjective uncertainty. Now, quantum uncertainty is very important even on the macroscopic scale. I remember an exercise I was given when I was a student more than fifty years ago. I give this exercise to the physicists here. Assume that you have a perfect sphere, like a ball and a small ball that you can drop exactly on top of the sphere. Now the question was how many times can you arrange for the small sphere to jump back and then fall again on the sphere, before being ejected outside of it.

PROF. LÜKE: I'm quite familiar with Roman Sexl's answer to this question: six or seven times. I've read about this mathematical experiment with an ideal billiard made by Roman Sexl and others. Therefore the randomness in quantum physics may be noticed very soon in our world of middle dimensions.

PROF. CABIBBO: Exactly, the limit is six times due to quantum uncertainty. So, given this exercise, it is clear that we cannot at all neglect quantum uncertainty as the limit of chaos. If a system is chaotic at the macroscopic level, the quantum uncertainty will be amplified very fast so, in fact, it will be that the limit of predictability is given by quantum uncertainty. When chaos is described in classical terms, you always say, well, if I had perfect knowledge I could have a perfect prediction but quantum uncertainty is the limit and it gets amplified very very fast. It was a remark. You know already the answer, six times. I remember seven but maybe the dimensions of the sphere in my exercise were slightly different or my memory is not so good anymore.

PROF. DE DUVE: Thank you. This is the last time I will speak, because I think I have spoken too much already. I have a problem with the word randomness. When you say that mutations are random, I do not think that is correct because mutations have specific causes. Also, the probability of a mutation happening at a given site of the genome is not the same as the probability of a mutation occurring elsewhere in the genome. Randomness gives an idea of something completely chaotic and this does not apply to mutations. When we biologists say that mutations are due to chance, what we are trying to underline is the fact that they are unintentional, that is, that changes in the genome are not related to any prevision or foresight of what the outcome is going to be. This is basically what intelligent design presupposes, namely that some mutations are intentional, that they are directed towards a certain goal. My second problem is that Professor Lüke mentioned Jacques Monod. Earlier, Professor Collins mentioned Stephen Jay Gould. I think those are monuments of the literature in this field, but they are a little outdated. We have to remember that a lot of progress has been made in recent years in the field of evolution. There is a new brand of evolutionists, for example Simon Conway Morris and also Richard Dawkins, who insist on the importance of convergent evolution, that is of evolutionary outcomes repeatedly and independently being the same, given specific situations. In fact, Dawkins even cites Gould's tape analogy and states, in direct opposition to Gould, that if the tape should be replayed, the same story would unfold. If I may quote myself, I have written on this subject also and pointed out, by some simple calculations, that chance does not exclude inevitability. All depends on the number of opportunities you provide for a given event to take place, as compared to the probability of the event.

PROF. LÜKE: (originally in German) I think converging evolution is the problem that you are focusing on. During my biology studies I learned that if the framework conditions are comparatively similar, the results from the pressure of natural selection will be similar, too. But evolution is run once and never again. We cannot compare it with another evolution from the same starting point. We can only look for similar inventions in this one evolution and then compare the results, for example, what the very similar eyes of octopus and of man must do and why they are so similar. And then we can try to explain why and how they are different. Although it's impossible to compare two varieties of evolution from the same starting point, I think it is very implausible that the results would be the same if there were two evolutions. I think there would be too many fortunate or unfortunate choices which would make an important difference between these twin evolutions. But I really cannot answer your questions, because you need a greater biological expertise than I have in this field.

THE CATHOLIC CHURCH AND EVOLUTIONARY THEORY: A CONFLICT MODEL[1]

GEREON WOLTERS

I. Preliminary Conceptual Remarks

The relationship between the Catholic Church and the Theory of Evolution is a specific area of research within the increasingly popular field of Science and Religion. Science and Religion is, in turn, a special facet of the Reason and Faith debate that has featured prominently in the teachings of the Church from the very beginning.[2] The corresponding relationships have always been very complex. The interaction between science and religion can take on four basic forms.[3] Science and religion can:

1) conflict with each other,

2) be complementary, 'each answering a different set of human needs',[4]

[1] I am grateful to the Netherlands Institute for Advanced Study (NIAS) for providing me with the opportunity, as a Fellow-in-Residence, to complete this paper. I gratefully acknowledge the great support of my work by the NIAS, especially the help of Petry Kievit-Tyson B.A. (Hons) who edited the text.

[2] This topic is particularly dear to the heart of Pope Benedict XVI. It was during his tenure (1981-2005) as Prefect of the Sacred Congregation for the Doctrine of the Faith (SCDF) that Pope John Paul II promulgated the Encyclical Letter *Fides et Ratio* (September 14, 1998) (John Paul II, 1998). Apart from that there is e.g. an interesting exchange between Cardinal Ratzinger and Jürgen Habermas on this topic (Habermas/Ratzinger, 2005). Pope Benedict has addressed it furthermore in important speeches, e.g. in his controversial lecture ('Faith, Reason and the University: Memories and Reflections') at the University of Regensburg, Germany, on September 12, 2006, which stirred much controversy in the Muslim world (Benedict XVI, 2006); or in the lecture he planned to give during a visit to the Roman university *La Sapienza* on January 17, 2008 (Benedict XVI, 2008).

[3] Cf. Brooke (1991), 2f. Brooke mentions only the first three.

[4] Brooke (1991), 2. This is basically the content of the NOMA (NOn-overlapping MAgisteria) conception of Stephen Jay Gould (cf. Gould, 1999). According to NOMA science

3) be cooperative, working 'to the advantage of both'. This seems to be the position Pope Benedict advocated at a conference meeting when he discussed the 'cooperation (*Zusammenspiel*) of various dimensions of reason'[5] with his former students,

4) or they can be *incommensurable*, where each side talks about fundamentally different things, or about the same things but in a fundamentally different way, so that mutual agreement becomes impossible.[6] There is much to be said about each of these views. The confines of this paper mean that I can only discuss the type of interaction between science and religion that is characterised by conflict. Inevitably, this means the paper will be rather one-sided.

It is important to define different types of conflict. The *first* is a doctrinal conflict in which science and religion hold conflicting, mutually exclusive, views about a particular situation. The most important example of this type of doctrinal conflict was seen in the case of Galileo and, to honour him, I term these kinds of conflict, *Galilean conflicts*. The most recent example of such a *Galilean conflict* is the debate surrounding evolutionary theory.

The *second* type of conflict is not so much about doctrine itself. It is more about scientists' attempts to refute that religion is a phenomenon in its own right. Such explanations are also called 'naturalistic' or 'scientistic'. In this vein, Karl Marx described religion as the 'opium of the people', Freud viewed religion as a collective neurosis and some modern brain researchers even regard it as an illusion produced by the limbic system. Others, in turn, see religion as an important component of the evolution of social behaviour; while others like Richard Dawkins explain religion as a by-product of evolution. Because in all these approaches religion appears as illusory, I would like to term these types of conflicts as *Freudian conflicts*, because the word 'illusion' appears in the title *The Future of an Illusion* of Freud's book on the topic.[7]

In any debate about the relationship between science and religion, two central questions need to be asked: 1) What should be done if scientific findings contradict the Word of the *Bible*? 2) What should be done if there

has exclusive competence in the realm of facts, whereas religion has exclusive competence for norms, values and meaning.

[5] In: Horn/Wiedehöfer (eds.)(2007), 150.

[6] Cf. Wolters (1997), 140. A protagonist of this view is the philosopher Ludwig Wittgenstein (1889-1951).

[7] Freud (1927)(*Die Zukunft einer Illusion*).

are contradictions between science and the teachings of the *Church*? St. Augustine (354-430) already gave an answer to the first question in his commentary on the book of *Genesis* (*De genesi ad litteram*) although his view has been largely ignored in almost all Galilean conflicts. St. Augustine recommends an allegorical, i.e. figurative understanding of the respective texts in cases where a literal reading of the Holy Scripture would lead to contradictions or be at variance with 'highly certain results of reasoning or with empirical evidence' (*certissima ratione vel experientia*, Augustine, 1961/1964).[8] Augustine advised not to become embroiled in the type of conflicts termed here as *Galilean conflicts* because this would only make religion look ridiculous (*deridetur*), which in turn could jeopardize its propagation. With respect to the second question, about whether science contradicts the teachings of the Church, matters are somewhat more complex, because the teachings of the Church are binding to very different degrees. Teachings can even be infallible.[9] Needless to say, a collision between a supposedly infallible teaching of the Church and a piece of scientific theory confirmed by evidence will create very special epistemological problems, but certainly not just epistemological problems, theological, political and other issues as well.

People today believe, as St. Augustine did much earlier, that scientific questions are answered by means of scientific knowledge and not by religious authority.

To conclude these preliminary conceptual remarks, I would like to emphasize another fundamental distinction: the distinction between *natural* and *his-*

[8] Particularly instructive is book I, chapter 19 (quotation there), where Augustine distinguishes central tenets of faith (he mentions the resurrection of Christ and the hope for an eternal life) from what is said about the material world. For Augustine there is 'nothing more embarrassing, dangerous and to be avoided' (*turpe est autem nimis et perniciosum ac maxime cavendum*) than insiting on wrong statements about matters of fact with reference to the Bible. In parts of Protestant theology, e.g. Rudolf Bultmann, the allegorical reading extends also to those parts of the Bible, whose literal understanding is – different from e.g. astronomical matters of fact – essential for the Catholic Faith. This holds, for example, for the resurrection of Christ from death.

[9] There are basically three types of teachings, which under certain conditions are regarded as infallible: (1) Pronouncements of ecumenical councils; (2) Papal proclamations *ex cathedra*, and (3) teachings of the 'ordinary and universal magisterium' of the college of bishops while dispersed throughout the world, but maintaining the bond of communion among themselves and the Pope. Whereas the first two types of infallible teachings, which form the *extraordinary* magisterium, are comparatively easily identifiable, there is with respect to the third much dispute about the lack of clear identity criteria.

torical facts, on the one hand, and *meaning, norms* and *values*, on the other. Statements about facts express how things *are*, normative or evaluative statements tell us how things *ought to be,* in other words, which value or meaning should be attached to them.

II. Galilean Conflicts on Evolution

The Galileo affair has been an embarrassment to the Church ever since the second half of the 17th century when it became clear to almost everybody in Rome that Copernicanism was far from being 'philosophically absurd and false' as had been stated in the verdict against Galileo. However, the Church's embarrassment is mainly linked to the fact that the verdict against Galileo declared Copernicanism to be 'formally heretical'.[10] This fallacious aspect of the verdict means that the Church had erred with respect to a matter of faith. The danger is that this could undermine other pronouncements concerning the very core of faith, which is a far more serious matter than, merely, not believing an astronomical theory like Copernicanism.

When evolutionary theory spread throughout the educated world during the second half of the 19th century, most Catholic circles merely viewed this as just as another threat to Faith from the materialist sciences.[11]

According to the above definition of a *Galilean conflict*, we would have expected to see more conflict surrounding evolution. However, throughout the first hundred years of Darwinian evolutionary theory, the ecclesiastical authorities seemed to keep a low profile. They seemed to have learnt their lesson from the Galileo Affair and kept their noses out of scientific debates, at least as far as making any official announcements about evolutionary theory.[12] The highest-ranking Vatican Institution, the 'Supreme Sacred Congregation of the Roman and Universal Inquisition' (in 1908 renamed to 'Supreme Sacred Congregation of the Holy Office' it became in 1965 'Sacred Congregation for the Doctrine of the Faith', before the 'sacred' was

[10] A teaching is 'formally heretical', when its author *knows* that it contradicts the teachings of the Church. This is true in the Galileo case because prior to his condemnation in 1633 Galilei had received a warning in 1616 not to advance Copernicanism.

[11] The charge of 'materialism' is a recurrent theme in the archival materials in the Congregation for the Doctrine of Faith.

[12] For details see Artigas/Glick/Martínez (2006), 281ff.

dropped in 1983 as with all other Vatican Congregations) did not address evolutionary theory. Evolution was only mentioned in the less important 'Sacred Congregation of the Index',[13] and then only with respect to the denunciation of certain books. Overall, it can be said that on the side of Vatican authorities 'there was, in a sense, no policy at all' with respect to evolutionary theory. They 'responded to particular circumstances, not to a carefully designed plan'.[14] Furthermore, one could say that the authorities took a low-key stance. An examination of the available sources (presently only up to 1929), shows that, notwithstanding the flood of polemics from theologians against the theory of evolution, there has not been one official denouncement of evolutionary theory by the Catholic Church. Only a few authors – mostly Catholic priests who tried to reconcile evolution and Catholicism – ended up on the Index of Prohibited Books. The available sources on the Index contain no evidence of any discussion of books by non-Catholic authors, even those that were clearly anti-Christian or anti-Catholic such as, for example, the biologist Ernst Haeckel (1834-1919). The reason for this focus on Catholic writers is that 'books written by Catholic authors and in Catholic countries […] were more likely to disturb the life of the Church'. In addition, Pope Leo XIII in his *Constitutio de Prohibitione et Censura Librorum* (1900) had decreed: 'Books written by non-Catholics that treat religion professionally are prohibited, unless it is ascertained that there is nothing in them contrary to Catholic faith'.[15] This meant that, in effect, non-Catholic authors were given more leeway because the criterion 'treating religion professionally' was vague. It was assumed that all the enemies of Faith and of the Church would be on the Index anyway. The problem was that readers could not judge in advance whether the content of the book they were about to read was such that it would end up being put on

[13] The Index Congregation was dissolved in 1917, and its task of prohibiting books was transferred to the Holy Office. In 1966, finally, the Index was abolished.

[14] Artigas/Glick/Martínez (eds.)(2006), 4. The book gives a careful analysis of documents preserved in the Archive of the Congregation for the Doctrine of the Faith, which containes material both from the former Congregation of the Index of Prohibited Books and the Holy Office. They, furthermore, relate these documents to publications in the leading Jesuit journal *Civiltà Cattolica* that fiercely opposed 'evolutionism'. The authors address the policy issue extensively in the last chapter of the book (270ff.). I am grateful to Elliott Sober (University of Wisconsin – Madison) for directing my attention to this book.

[15] Artigas/Glick/Martínez (2006), 14. I have rendered the Latin 'ex professo' as 'professionally'.

the Index. Readers would probably not even be sure after reading the book because of the vague criterion applied.[16]

There were three main kinds of objection that the, so-called, Consultors of the Index Congregation could raise that would result in the explicit condemnation of a book.

(1) Arguments against evolutionism were mainly along the lines of the following quote: 'On the basis of Scripture and Church tradition, focusing on a very few, narrowly defined issues such as the origin of Adam, or whether Adam's body, along with his soul, had to be created directly, immediately, and simultaneously by God, or whether his body might have been previously prepared to receive a soul by a natural process like evolution'.[17] This quote reflects a typical Galilean conflict, i.e. science says *G*, whereas the Church, based on the Word (Bible) and tradition, says *non-G*. Catholic authors who tried to reconcile Faith and evolution, and who had come to the attention of the Congregation of the Index, typically accepted evolution in the animal kingdom as being a fact but, rather arbitrarily, left Adam out of the story of evolution and conceded his special creation by God. However, this concession alone was not enough to save their books from being condemned.

(2) The Consultors not only answered issues by recourse to Scripture or Tradition, they often also put forward supposedly scientific arguments. This reminds us of the case of Galileo where the Church condemned Copernicanism as being 'philosophically absurd and false'. In our case it is the argument for the fixity of species, which is based on hybridity. This argument rested mainly on the erroneous idea that speciation occurs a) exclusively by hybridization, b) among individuals, rather than within populations and c) the concept of species is typological or essentialist, expressing a fixed set of immutable characteristics, rather than population associated. In other words, it relates to the dynamic distribution of characteristics and to various speciation processes. An example of such a process is allopatric speciation. This occurs when a small group is first geographically separat-

[16] But behind this restraint was certainly also the insight that it was practically impossible to skim the international bookmarket for 'heretical' literature with respect to evolution. This problem is, by the way, almost as old as the Index of Prohibited Books itself. Cf. the Introduction to Wolf (ed.) (2005), Vol. I. Wolf's edition that in its first phase covers the documents of the Holy Office and the Index Congregation on the prohibition of books between 1814 (return of the archives from Paris) and 1917 (end of the Congregation of the Index) is an invaluable instrument of research.

[17] Artigas/Glick/Martínez (2006), 92.

ed from the main population which means it is then effectively reproductively isolated from the source population, and this results in the course of relatively few generations in a new species.[18]

(3) Furthermore, we find condemnations of the hermeneutic principles used by the authors. Here an excerpt from the expert opinion on a book placed on the Index (*New Studies in Philosophy. Lectures to a Young Student* (1877) by Raffaello Caverni): 'Caverni's rules for biblical exegesis are absurd, omitting any divine inspiration, and therefore infallibility, from anything that can be considered the object of natural science. A corollary is that Darwinism or any other physiological, geological, etc. system is all admissible, even though manifestly opposed to the Bible'.[19] This passage can be read as a rejection of Stephen Jay Gould's NOMA principle *avant la lettre*, i.e. the methodological principle of keeping the two Magisteria – Science and Religion – completely separate. This principle can already be detected during Galileo's lifetime in an ingenuous formulation by Cardinal Cesare Baronio: 'The Holy Spirit had in mind to teach us how to go to heaven and not how the heavens go'.[20]

In the case of Caverni's book,[21] as in the Galileo Affair, the Church authorities claim to supersede factual scientific findings by referring to the Scriptures or traditional teachings. There are, however two remarkable differences between Caverni's book and the case of Galileo. 1) His topic, i.e. humanization, is much closer than Copernicanism to the Catholic faith because it is linked to the central theological doctrine of the Original Sin, which, in turn, is one of the foundations of Redemption by Jesus Christ. 2)

[18] More information is provided by Coyne/Orr (2004), who gives a splendid overview of the field. My biology colleague in Konstanz, Axel Meyer, referred me to this book. Relying exclusively on hybridization the Consultors could easily exclude speciation as a natural phenomenon, because also for contemporary standards this form of speciation ought to be very rare, because hybridization in most cases leads to no offspring or sterile offspring at best.

[19] *Ibid.*, 44.

[20] The quote is in Brandmüller/Greipl (eds.) (1992), 295, as quoted by a consultor in the case of the physicist and priest Giovanni Settele (1770-1841). Settele's book that advanced Copernicanism was – after long discussions – *not* put on the Index. Whether this bureaucratic act (or better: *non*-act), known only to those personally involved in the case, can count as 'fine della controversia', as the editors claim in the subtitle of their book on Copernicanism and the Settele case, seems rather doubtful. Cf. also Gould (1999), 6 for the Baronio quotation.

[21] In my points (1) and (3), to be exact.

In the case of Caverni, the Church authorities kept a low profile even though evolutionism is possibly of immense importance in matters of faith and it is significant that there was no public condemnation of the theory of evolution, when the book was put on the Index.[22]

Excursus: in all Galilean conflicts, there is the question of who has the expertise and is competent to judge on questions about facts, either historical or about the natural world. NOMA, which assigns the world of facts to Science and the realm of meaning, values and norms to Religion, would seem, at first glance, to have solved all problems. However, this is not the case. There are aspects of the teachings of the Church that are of a factual nature. For example, in the *Catechism of the Catholic Church* of 1994, one finds a thesis on the monogenetic origin of humankind.[23] Here the Church is – with reference to the *Acts of the Apostles* 17, 26[24] – advancing a thesis that *incidentally* coincides with scientific evidence. The question is what would happen, if in the future sufficient scientific evidence emerged to support *multiple* origins of humankind. Other fact-related teachings by the Church are the historicity of the so-called original sin, the resurrection of Jesus Christ from death, and the possibility of miracles in general.[25] The epistemological impossibility of supporting statements about facts by reference to Scripture and tradition has led some Protestant theologians to abstain from factual claims altogether, thus taking up a position similar to NOMA.[26] How-

[22] Only people directly involved in the decision of the Congregation of the Index could know that the book was condemned because of its 'evolutionism'. Caverni himself e.g. thought that his critique of the Jesuits had led to the condemnation. (Cf. Artigas/Glick/Martínez, 2006, 49).

[23] Catechism (1994), Nr. 360, p. 82. The encyclical *Humani Generis* (Pius XII, 1951), no. 37 makes it clear, consequently, that polygenism is not compatible with Catholic Faith, and that 'the children of the Church' do not have the liberty to embrace it. More on *Humani Generis* see below.

[24] 'And [God] hath made of one blood all nations of men for to dwell on all the face of the earth'.

[25] Cathechism (1994), no. 397ff., p. 89ff (original sin). The historicity of resurrection of Christ from death (no. 639, p. 146) is certainly in conflict with what biology and medicine have to tell us about death. This, however, does not amount to a Galilean conflict, because the teachings of the Church do not generally reject bio-medical laws. They rather claim miraculous exceptions to their action. The issue of miracles, therefore, is not a scientific issue, but rather an epistemological one. Here epistemological conceptions about miracles are in opposition to each other.

[26] Rudolf Bultmann's program of demythologization seems to be a first step in this direction.

ever, with respect to the factual claims quoted above, I do not believe this option to be available to Catholic theologians.[27] They will always be faced with the 'friction zone' between science and religion.[28]

The next official document I will discuss is the Encyclical *Humani Generis*, promulgated by Pope Pius XII in 1950. This is the first explicit public statement on evolution by a Church authority. On the whole, this Encyclical expresses a rather relaxed position with respect to evolution.[29] It does not instigate a Galilean conflict but it does intimate only *possible* problems. The text is somewhat obfuscated, however, by the low epistemological expertise, which characterizes documents of the Church up to the present day.

The Pope distinguishes between 'clearly proved facts' and 'hypotheses' in empirical science. However, as, by definition, all universal statements in empirical science are hypotheses, it seems more likely that the Pope is actually distinguishing between hypotheses that are strongly supported by

[27] Consequently NOMA is rejected by Cardinal Schönborn (in: Horn/Wiedenhofer, eds., 2007, 86).

[28] This felicitous expression was used by Wolf Singer in the discussion of this talk.

[29] Here is the text of the relevant passages: '35. It remains for Us now to speak about those questions which, although they pertain to the positive sciences, are nevertheless more or less connected with the truths of the Christian faith. In fact, not a few insistently demand that the Catholic religion take these sciences into account as much as possible. This certainly would be praiseworthy in the case of clearly proved facts; but caution must be used when there is rather question of hypotheses, having some sort of scientific foundation, in which the doctrine contained in Sacred Scripture or in Tradition is involved. If such conjectural opinions are directly or indirectly opposed to the doctrine revealed by God, then the demand that they be recognized can in no way be admitted. 36. For these reasons the Teaching Authority of the Church does not forbid that, in conformity with the present state of human sciences and sacred theology, research and discussions, on the part of men experienced in both fields, take place with regard to the doctrine of evolution, in as far as it inquires into the origin of the human body as coming from pre-existent and living matter – for the Catholic faith obliges us to hold that souls are immediately created by God. However, this must be done in such a way that the reasons for both opinions, that is, those favorable and those unfavorable to evolution, be weighed and judged with the necessary seriousness, moderation and measure, and provided that all are prepared to submit to the judgment of the Church, to whom Christ has given the mission of interpreting authentically the Sacred Scriptures and of defending the dogmas of faith. Some however, rashly transgress this liberty of discussion, when they act as if the origin of the human body from pre-existing and living matter were already completely certain and proved by the facts which have been discovered up to now and by reasoning on those facts, and as if there were nothing in the sources of divine revelation which demands the greatest moderation and caution in this question'. (Pius XII, 1950)

empirical evidence and hypotheses that lack sufficient empirical evidence.[30] In this light, we can say that Pope Pius XII:

1) accepts evolutionary theory as a scientific theory as long as it does not contest God's creation of the human soul or the monogenic origin of mankind,

2) believes that evolutionary 'hypotheses' have to be 'submit(ted) to the judgement of the Church'. Whether this also holds for 'proved facts', remains unclear,

3) invites the Faithful to scrutinize carefully whether the evidence for various evolutionary hypotheses is sufficient, in order to class them as 'clearly proved facts' or only as 'hypotheses'. He seems to assume here that evolutionary hypotheses do not belong to his category of 'proved facts',

4) does not speak out on whether he thinks that evolution is a historical fact of the history of the earth.[31]

The next pronouncement of the Church concerning evolution can be found in the *Monitum*, a warning against the writings of Jesuit palaeontologist Teilhard de Chardin, issued by the Holy Office on June 30, 1962 and reiterated on July 20, 1981.

> Several works of Fr. Pierre Teilhard de Chardin, some of which were posthumously published, are being edited and are gaining a good deal of success. Prescinding from a judgement about those points that concern the positive sciences, it is sufficiently clear that the above-mentioned works abound in such ambiguities and indeed even serious errors, as to offend Catholic doctrine.[32]

The above text illustrates two important points: 1) The Church is not interested in engaging in a Galilean conflict about evolution and explicitly

[30] He generally holds that 1) all universal statements of empirical science ('for all *x* holds…') have the logical status of hypotheses; and that 2) for logical reasons there can be no empirical 'proof' of a universal empirical hypothesis, because empirical confirmations come always in form of singular confirming instances. Empirical hypotheses are, rather, distinguished from one another by the degree of evidence that exists in their support. The most important form of evidence is empirical confirmation. Other forms of evidence are compatibility with well supported other hypotheses, range, explanatory power etc.

[31] I wonder how Gould (1999), 80 could celebrate Pius XII as accepting the NOMA principle of the two non-overlapping *Magisteria* of science and religion, when the Pope states that the hypotheses of the 'positive sciences, are […] more or less connected with the truths of the Christian faith' and that the Church has the last word in case of contradictions of scientific hypotheses to the Catholic Faith. These claims of the Pope constitute a major incursion into and, therefore, overlap between the two *Magisteria*.

[32] Holy Office (1962/81).

refrains from interfering with matters of science.[33] 2) The Church maintains a cautious and expectant position with respect to evolutionary theory.

This caution seems to be thrown to the wind in a famous letter by John Paul II to the Pontifical Academy on October 22, 1996. In this letter, Pope John Paul II confirms the position taken by Pius XII in *Humani Generis*, but with one decisive qualification:

> Today, almost half a century after the publication of the Encyclical [*Humani Generis*] new knowledge has led to the recognition of the theory of evolution as more than a hypothesis.[34] It is indeed remarkable that this theory has been progressively accepted by researchers, following a series of discoveries in various fields of knowledge. The convergence, neither sought nor fabricated, of the results of work that was conducted independently is in itself a significant argument in favour of this theory.

The above quote, like several other passages not quoted here, can be interpreted as follows:

1) Pope John Paul II acknowledges the theory of evolution to be an adequately confirmed theory or, as formulated in Vatican epistemological terminology, it has risen above mere 'hypothesis' and is beginning to be something like a 'proven fact',[35]

[33] Teilhard's understanding of evolution as a goal-directed process is not shared by current evolutionary biologists. In recent months there has been an ongoing press campaign in Italy with the aim to lift the ban on Teilhard's writings. In the context of this campaign Teilhard's case is often compared to the verdict on Galileo. Such a comparison shows poor judgement, because in Teilhard's case the ammonition was based exclusively on theological issues.

[34] The whole text of the letter is in: Pontifical Academy (2003), 370-374. Embarrassingly enough the English translation there ('new knowledge has led to the recognition of more than one hypothesis in the theory of evolution') of the French original of this passage is wrong. On the Vatican website there is only a Spanish version: 'Hoy, casi medio siglo después de la publicación de la encíclica, nuevos conocimientos llevan a pensar que la teoría de la evolución es más que una hipótesis'. (http://www.vatican.va/holy_father/john_paul_ii/messages/pont_messages/1996/documents/hf_jp-ii_mes_19961022_evoluzione_sp.html). The French original and a correct English translation were published in John Paul II (1997).

[35] This evaluation is, however – again in the terminology of Vatican epistemology – contradicted by Pope Benedict, who maintains that John Paul II 'had reasons, when he said this ['evolution more than a hypothesis']. But it holds at the same time that the theory of evolution is not yet a complete scientifically verified theory'. (Horn/Wiedenhöfer, eds., 2007, 151). Whatever the Pope may mean – as is well known there is no 'verification' of theories – he certainly wants to play down the evaluation of his predecessor.

2) Only the monogenetic origin of mankind and God's direct creation of the soul remain as possible points for a Galilean conflict. As previously mentioned, the thesis of the monogenetic origin of mankind is pretty much in accordance with scientific evidence while the question of the soul is a special conceptual issue that, to the best of my knowledge, the pertinent sciences probably are not that concerned about.[36]

The result of this short analysis of Galilean conflicts in the context of evolutionary theory is that since the letter by John Paul II there seems hardly any room for such conflicts. In addition, John Paul II, as is well known, had taken great pains to lay Galileo's Galilean conflict to rest. Pope John Paul II implemented a clear and judicious epistemological strategy to get the Church out of the line of fire and withdraw from a battlefield where there is little to be gained but a lot to lose. This could also be a consequence of realizing that the Church does not have the expertise to pontificate on scientific matters.

Therefore, it is most surprising that recently the Church, in the person of one of its most senior Cardinals, seems to have taken up arms again and marching head-long back on to this Galilean battlefield. In an article ('Finding Design in Nature') that was published in the *New York Times* on July 7, 2005 Christoph Cardinal Schönborn was widely perceived as siding with the most recent incarnation of American Creationism, the so-called Intelligent Design Theory, ID for short. As this paper focuses on epistemological issues, I will not address all of the many other interesting aspects of this article but I will concentrate here on two pertinent quotations:

1) 'The Catholic Church, while leaving to science many details about the history of life on earth, proclaims that the human intellect can readily and clearly discern purpose and design in the natural world, including the world of living things',
2) 'Evolution in the sense of common ancestry might be true, but evolution in the neo-Darwinian sense – an unguided, unplanned process of random variation and natural selection – is not. Any system of thought that denies or seeks to explain away the overwhelming evidence for design is ideology not science'.

[36] That the concept of soul is not a concept of empirical science, but rather of philosophy or theology is also emphasized by Sánchez Sorondo (2008), who gives an argument for the compatibility of scientific and philosophico-theological views on man, that is based on the Kantian distinction of the two complementary forms of reason: theoretical reason as the basis for scientific knowledge and practical reason as the basis for 'practical wisdom'.

As to the first quotation, I should remark that one of the founding methodological principles of modern science and a precondition of its success since the time of Galileo is its methodological materialism, I underscore *methodological* materialism. This implies that science exclusively looks for natural causes when explaining natural phenomena. Evolutionary biology in the course of its 150 years of existence has been able to explain thousands of design-like structures in living beings in terms of evolution, of which natural selection, as proposed by Darwin, is the most important but not the only factor. Before the advent of Evolutionary Theory, such structures were believed to have been drafted by an omnipotent designer.[37] To answer Cardinal Schönborn's first point in just one sentence: the human intellect, indeed, is able to discern purpose and design in the natural word, but explains this *scientifically* in terms of functional adaptations brought about mostly by natural selection.[38]

As to the second point, tens of thousands of biologists all over the world will be astounded to hear that by relying on the two principles of evolutionary theory: random variation and natural selection, they are ideologists rather than scientists. Taking Cardinal Schönborn's assessment seriously and dismissing random variation and natural selection would put an end to both evolutionary biology, and most other areas of biology, as we know them today.

In September 2006 in Castel Gandolfo, at the abovementioned meeting on evolution of Pope Benedict with his former students, Cardinal Schönborn reiterated and reinforced the position he took in his article in the *New York Times*:

> I dare say that at present there does perhaps not exist any scientific theory, which is subject to so many grave objections and which at the same time is defended as sacrosanct by many people. (96)

He then lists several such supposed objections that are well known from creationist literature and that by their mantra-like repetition do not get closer to the truth:

1) The supposedly missing 'missing links' between species,

[37] In fact, William Paley's (1743-1805) famous 'argument from design' that contends that the perfections of living nature can hardly be explained as having developed by chance as can a watch that is found on a beach was convincing only *before* evolutionary theory offered a third way of explanation of design-like structures, i.e. natural selection. For an excellent analysis of the argument cf. Sober (2000), chapter 2.

[38] Of course, this scientific account does not exclude a religious *interpretation* ('reading') of such design-like, functional structures in the theological language of creation and creator, or 'design', respectively.

2) 'The often admitted fact that until now no evolution beyond the species level has been proved',

3) The supposed impossibility of a transition from living systems like reptiles to birds by small mutations,

4) The problematical status of the concept of survival of the fittest.

Both evolutionary biology as well as the philosophy of biology have dealt with these objections and have disproved them on countless occasions[39] – to no avail.

It is not clear, however, whether Cardinal Schönborn *really* intended to do what he actually did: launch a new Galilean conflict; and whether he really wanted to side with ID. There is some evidence that he did not want this and that he merely meant to engage in a *Freudian* conflict but that he applied the arguments the proponents of ID implement in their *Galilean* fight against evolutionary theory. The quotations below confirm this view and seem to show that in order to secure a space for Faith, Schönborn criticizes Evolutionary Theory. However, Evolutionary Theory, as long as it not involved in a Freudian conflict, does not actually compete with Faith for space. Neither Faith nor Faith based *interpretations* of nature are significant issues within evolutionary biology.

Another argument in Schönborn's critique of evolutionary theory (which seems to be shared by Pope Benedict) is that scientifically unexplainable teleology of nature is a necessary counterpart to the Church's teaching that God can be understood through his creation by reason alone.[40]

III. Freudian Conflicts on Evolution

Freudian conflicts arise when a particular science tries to explain away religion as a phenomenon in its own right. They do not specifically affect the Catholic Church, but religion in general. Therefore, the first task of those who wish to wage a Freudian conflict should be to develop an adequate def-

[39] A comprehensive recent study by a Catholic author is Ruse (2005). Sober (2008) gives a magisterial analysis of the issue of evidence for evolutionary theory.

[40] Cf. Catechism (1994), No. 286: 'Human intelligence is surely already capable of finding a response to the question of origins. The existence of God the Creator can be known with certainty through his works, by the light of human reason, even if this knowledge is often obscured and disfigured by error'.

inition, or at least a satisfactory characterization, of the concept of religion. So far nobody seems to have achieved this and, unfortunately, most of those waging Freudian conflicts hardly even acknowledge this as a major problem. The second task would be to adduce sufficient scientific evidence in order to substantiate their Freudian claims in explaining religion.

Marx's explanation of religion as 'the opium of the people',[41] is based on the assumption that 'religion' provides the hope of a happy afterlife. It is psycho-socially explained as the last resort for people who live a materially and socially miserable life. The definition of religion as a belief in the afterlife is, on the one hand, far too narrow, because there are many more aspects to religion than this alone. On the other hand, there are religions like Buddhism that do not know this sort of compensation for terrestrial misery in a heavenly afterlife. Moreover, the fact that religion can flourish in a relatively wealthy country such as the United States is strong evidence against Marx's claim.

Freud's conception of religion as a collective neurosis suffers from the same shortcomings as his psychoanalytical theory, which was criticised mercilessly by Adolf Grünbaum (1984).

In terms of *evolutionary* Freudian conflicts, I would like to emphasize right at the outset that biological explanations of behavioural and cultural phenomena are legitimate undertakings within evolutionary theory. Evolutionary theory has successfully explained not only the anatomical and physiological features of organisms but – within the animal kingdom – also certain behavioural characteristics. The relevant biological discipline is called 'sociobiology'. However, how far sociobiological explanations hold for human behaviour is much contested. Examples of evolutionary explainable social behaviour in humans have been documented: the incest taboo is one,[42] but the complexity of human cultures means that studies are limited.[43]

[41] 'The wretchedness of religion is at once an expression of and a protest against real wretchedness. Religion is the sigh of the opressed creature, the heart of the heartless world and the soul of soulless conditions. It is the opium of the people. The abolition of religion as the illusory happiness of the people is a demand for their true happiness'. (Marx, 1970, 131)

[42] Cf. Bischof (1994).

[43] One has to be very careful not to declare without evidence every universal feature of human behaviour as evolved by natural selection. Universal characteristics of behaviour may also be a consequence of the general intelligence of humans, which may lead to similar problem-solving behaviour.

The first Freudian conflict in the context of evolution was launched by the Harvard entomologist Edward O. Wilson in the mid-1970s.[44] Wilson regards religion as an adaptation that intensifies internal cohesion within groups. Conceiving of religion as the glue that keeps human groups together is certainly an interesting notion. However, as in other examples of a Freudian conflict, this is hardly an adequate characterization of religion. In addition, Wilson also fails to provide adequate empirical or other evidence for his view. Instead of hard evidence, he delivers what Stephen Jay Gould has aptly called an 'Adaptationist just-so-story'. The adaptationism of just-so-stories is characterized by two epistemological shortcomings: firstly it accepts each identifiable characteristic of an organism as being an adaptation even without proof.[45] Therefore, religion is *per se* an adaptation and has to be explained by evolutionary arguments, based on natural selection. Secondly, one has to tell only a halfway plausible evolutionary story about what sort of adaptation might apply in the case of religion and how it could have come about by the workings of natural selection. The story that Wilson tells falls far short of the empirical standards that are required in the natural sciences. He delivers hypotheses without evidence, and develops a philosophical position rather than a scientific one.[46]

The same can be said of other such undertakings. To conclude, we will take a look at Richard Dawkins, whose controversial book *The God Delusion* has aroused much controversy recently. In Chapter 5 ('The Roots of Religion'), it is clear that Dawkins has difficulties in pinpointing the direct adaptational value of religion, in the way Wilson had done. After rejecting expla-

[44] See the last chapter of Wilson (1975), in which Wilson extends his evolutionary explanation of social behavior ('sociobiology') from animals to humans, and in a more elaborated and extended form in Wilson (2004) (1st edition 1978). I have dealt with Wilson's position at length in Wolters (1997), 148ff.

[45] Although it is perhaps the most important heuristic principle of evolutionary theory to look for possible adaptive explanations of identifiable characteristics of organisms, it is by no means true, however, that each such characteristic *is* an adaptation. This has, rather, to be convincingly shown by empirical and other evidence. Meanwhile the classical and frequently reprinted text against adaptationism is Gould/Lewontin (1979).

[46] Wilson himself (2004), 192 seems to be somehow aware of this because he regards his position of 'scientific materialism' as an 'alternative mythology that until now has always, point for point in zones of conflict, defeated traditional religion'. Whatever the merits of scientific materialism may be, it is a *philosophical* position and not the result of scientific research. This implies that what Wilson has to tell us about religion is a *philosophical* view, as long as it is embedded in the 'epic' of scientific materialism.

nations based on group selection, Dawkins starts with the confession: 'I am one of an increasing number of biologists who see religion as a by-product of something else' (174). The idea of by-product, i.e. the idea that a structure that at some period in time had evolved according to certain selective pressures is later used for other purposes than the one it was originally selected for, is quite common in evolutionary biology. This phenomenon is called 'exaptation' of a structure, which is distinct from adaptation. Dawkins goes on to present the bold idea that: 'natural selection builds child brains with a tendency to believe whatever their parents and tribal elders tell them. Such trusting obedience is valuable for survival' (176). Religion is just a by-product of this brain structure.

Here again we find the two typical shortcomings of a Freudian attack on religion. Firstly, to assume that religion is above all or even exclusively about 'trusting obedience' seems a rather narrow view of a monotheistic religion let alone a non-monotheistic religion. Secondly, as far as evidence is concerned, Dawkins just presents us with another just-so-story that abounds with 'might', 'could' and similar linguistic indicators of uncertainty and speculation. If natural science were conducted in this way, there could be no natural science in the sense that know and trust. In fact, Dawkins is much aware of the weakness of his position. 'I must stress', he admits 'that it is only an example of the *kind* of thing I mean, and I shall come on to parallel suggestions made by others. I am much more wedded to the general principle that the question should be properly put [i.e. religion as a by-product of the evolutionary process], and if necessary rewritten, than I am to any particular answer' (174). In response to this, it must be said that the very principle of scientific research is that ideas have to be supported by evidence. What is virtually missing from Dawkins' claim is the evidence that religion is a 'by-product of something else'.

The criticism of Freudian attacks on evolutionary explanations of religion given here only targets their claims of being scientific and meeting the standards of natural science. This is what I take issue with; true Freudian conflicts fail to meet empirical standards.

They could, however, although this may not be the intention of their proponents, be regarded as science-related *philosophical* conceptions. Whether they succeed philosophically depends on the criteria of philosophical success or failure, which are different from those used in natural science. Whatever the case, there is room for interesting philosophical discussions.

It could be that Cardinal Ratzinger also had a similar view of what this paper calls Freudian conflicts, in mind when in 1986 he criticized the naturalistic extension of the conception of 'evolution' decribing it as a:

> model of thinking (*Denkmodell*) that claims to explain the whole of reality and that has, thus, become a sort of first philosophy. If the Middle Ages tried to reduce all science to theology (Bonaventura), one may speak here of a reduction of the whole of reality to evolution that believes to be able to also deduce cognition, ethics and religion from the universal formula (*Generalschema*) evolution.[47]

During the abovementioned meeting at Castel Gandolfo in 2006, Pope Benedict reassumes:

> To me it seems important to underline that evolutionary theory implies questions, which have to be assigned to philosophy and transcend the realm (*Innenbereich*) of natural science.[48]

This statement seems to show that Church authorities are trying to enter the *Freudian* discussion about evolution without siding with the preposterous *Galilean* claims particularly as advanced in American creationism in its many forms.

IV. Conclusion

The discussion of Galilean and Freudian conflicts dealt with in this paper brings forth two epistemological recommendations for the ecclesiastical authorities:

1) Keep out of Galilean conflicts! You will lose these battles and turn yourselves and Faith into a laughing-stock: a danger St Augustine long ago was acutely aware and afraid of,

2) Do not be unnerved by Freudian conflicts! Up to now, their hypotheses have merely been science related philosophical speculations, not sound scientific hypotheses based on sufficient empirical evidence. It is not likely that this will improve in the near future.

[47] As quoted in Horn/Wiedenhofer (eds.) (2207), 9.
[48] *Ibid.* 150.

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DISCUSSION ON PROF. WOLTERS' PAPER

PROF. PHILLIPS: You described Cardinal Schönborn's *NY Times* article as being widely perceived as supporting intelligent design, but I thought I heard him say, here, in this room, that he did not like intelligent design very much and I am wondering whether you heard it the same way and what you think about that?

PROF. WOLTERS: Well, what I think about *this* is a bit speculative. As a matter of fact, in his presentation at the Castel Gandolfo conference he *gave* a sort of criticism of intelligent design, which he does not, however, in the article. I have heard, I am not sure whether this is true, that his article was drafted at the Discovery Institute in Seattle, a sort of think tank of American creationism, and there are, in my view, clear traces of this and there are also clear traces of this in his presentation at Castel Gandolfo when he extensively takes a position to the, above all, American issue of teaching evolution in schools. So his basic framework about what evolution is is not taken from biology textbooks, let alone from original articles, but it is taken from the textbooks of Creationists. And if you look at the literature he quotes, the only literature he quotes is from that camp and sometimes he quotes an evolutionary biologist but only to criticize him, but not in order to find out what evolutionary biology is all about.

PROF. ZICHICHI: I had the privilege of talking to Cardinal Schönborn here, a few days ago, and the point we discussed was what is the evolution theory. Now, evolution theory – as I have discussed in my lecture and mentioned several times during our discussion – does not exist. It has to be specified, as I have repeatedly said, whether you mean evolution of inert matter, of living matter or of living matter endowed with reason. Now, we have to agree on what are the basic principles of Galilean science. You quote Galilei's contradiction: this has nothing to do with science. The reason why Galilei is the father of science is not because of the book concerning heliocentric versus geocentric systems but because of the book *Dialogues on the Two New Sci-*

ences (*Discorso sulle due nuove scienze*), where the first fundamental laws of nature are reported. If these laws exist we cannot be the product of chaos but of a rigorous Logic. If there is a Logic, the Author of this Logic must exist. Now, I would like to bring you back to the foundations of science, otherwise we just create confusion. The Cardinal you mention fully agrees with the fact that, if evolution has to be taught in schools, it should be scientifically-based evolution, which means that those people who think they have understood everything about evolution should be confronted with rigorous science. So, you cannot attack Cardinal Schonborn on science, because he has never said that he is against teaching evolution on the basis of the transitions which go from Big Bang 1 to Big Bang 2 and Big Bang 3. He fully agrees with the scientific principles to be explained and taught to young fellows concerning the theory of evolution, based on the three Big Bangs. So why do you insist on these losing and winning stories?

PROF. WOLTERS: I will first of all criticize you, Professor Zichichi, for your absolutely narrow concept of science and I think you are pretty lonely with this concept. Given this I can very well understand that Cardinal Schönborn liked your approach, because he has doubts about the scientific character of the evolutionary theory.

PROF. CABIBBO: Please, I think it is inappropriate to have personal attacks, it is not part of the aim of this meeting.

PROF. WOLTERS: It is not my intention to engage in personal attacks. I was asked for a hypothesis why Cardinal Schönborn took a certain position. I would very much like to have him here and to have his personal views about the issue, but I take, of course, your advice, as the President, to just stop here.

PROF. VICUÑA: I just wanted to say something that may be obvious to you, but it is not obvious for everybody. When we speak of intelligent design, we must distinguish between the intelligent design doctrine supported by Dembski, Behe and so on, and the belief in an overall design of Nature by a supernatural being that is guiding the process through natural means. In the former case, supporters of intelligent design make a big epistemological mistake because they mix science and religion. Thus, they believe in evolution but they require to have God intervening periodically in the process. This mistake can be compared to that of materialists such as Dawkins and Dennett, who think that because there is a mechanistic explanation for evolution, there is no need for a supernatural being. Of course, believing that the world was designed by God requires a personal attitude, since you cannot deduce from the wonders of nature that there is God either. The latter is simply a matter of faith.

PROF. WOLTERS: Yes, I do not object to this and I think you beautifully made this distinction, and it is also made by Pope Benedict, in a somewhat different context, when he warns against making the theory of evolution a new *prima philosophia*. I think it fits very nicely with my distinction of Galilean and Freudian conflicts. What the Freudian conflict people are sort of aiming at is just giving a comprehensive explanation of everything by using a conceptual framework that has done great service in looking at special problems in the evolution of life and that they are just overusing it, and I think this is your point and so all the advantages and all the certainty that scientific methods confer on what biologists are doing, they do not confer on this approach, on this overall – as it were – metaphysical approach.

H.E. MSGR. PROF. SÁNCHEZ SORONDO: I would like to say that the Catholic Church is a little more complex than your presentation.

PROF. WOLTERS: I was forced to because of the…

H.E. MSGR. PROF. SÁNCHEZ SORONDO: Yes, but not only. I think that we need to recognise that it is the only Church that has had an Academy of Sciences for many years. And Cardinal Pacelli was the collaborator of Pius XI in the restoration of the Academy and, at that time, the Academy had a collection of the most important scientists. All the Magisterium of Pius XII was based on a scientific approach. For example, we studied the signs of death and we follow Pius XII's idea that it is up to doctors to judge primarily the state of death. On the other hand, the question of the soul is not out of date and, probably, the existence of the soul is not properly a scientific question, it is an anthropological and metaphysical one, as Pope Benedict XVI repeated in the address he gave to us. I think that a limitation of your exposition is that you did not approach the issue from this philosophical-metaphysical view.

PROF. WOLTERS: My answer would have to be a bit longer than is permitted now, but I agree absolutely with what you said in the first part of your comment that the Catholic Church has retained a very close connection to science, unlike other religious orientations, which is admirable, no question about this. I agree completely with that, otherwise we would not be here, as you rightly remarked.

PROF. LÜKE: I missed the differentiation of the special dignities in the Church declarations. We have dogma and Papal encyclicals, and if the Pope says something it is only infallible when he speaks 'ex cathedra' and on questions of faith and morality. And the word of a bishop is not as important as a dogma or an encyclical, I think we agree on this. The second thing I want to say is that perhaps the problem with the soul is not a problem. Perhaps you can say the soul is a cipher or symbol for the immediate relation between God and every person. Every human being is immediate to God, is face-to-face with his God. And this relationship has not been established for us by our father or our mother or the Pope or somebody else. And then the soul symbolizes the human dignity that each one of us has, because he is immediate to God. A problem may be to find out the beginning or the emergence of a soul in phylogenesis and the emergence of a soul in ontogenesis. That may be the main problem.

PROF. WOLTERS: Short answer. Two points: there are various degrees of obligation of the Faithful to what the Church says, but I am not going into detail here. Second, the soul, again I agree also with Monsignor Sánchez-Sorondo. As I said in my presentation, 'soul' is not a concept of present empirical science. You said it is a metaphysical concept. With this I agree very much.

PROF. M. SINGER: I would like to clear the air a bit about intelligent design. The evidence indicates that intelligent design is basically a new way of talking about what used to be called 'creation science'. A book that was written for creation science twenty years ago has been republished as a book for intelligent design, and the only change is that every place that creation science was written has been changed to read 'intelligent design'. Creation science itself was always talking about the creation story in the Judeo-Christian bible. Yet in the worlds we live in today, worlds with populations that belong to many traditions, we have an added problem in talking about creation science because it is based on the Judeo-Christian bible.

PROF. WOLTERS: No comment, I share your view.

PROF. W. SINGER: I would like to make a reconciliating remark. I have felt urged to do that for quite some time. Couldn't we agree on the fact that the science systems are epistemically closed systems, they are orthogonal to belief systems because they cannot talk about metaphysics while the latter can? Of course, there are areas where these two worlds meet and these little areas of friction require recalibration and that is what we are going to do here, recalibrate certain points. This is natural, since natural sciences extend the borders of the known towards the unknown, thus, there will be a recalibration of the borders from physics to metaphysics and that is unavoidable, but there will always be enough space for metaphysics beyond that border, we are just pushing it a little bit. So, if you could agree on that, I think that we should refrain from entering the metaphysics, we can neither prove it nor disprove it, all we can do is we can move that border and I think this is what we are going to do here all the time.

PROF. WOLTERS: You have nicely described my intention.

PROF. W. SINGER: So I misunderstood you.

PROF. WOLTERS: Yes.

PROF. ZICHICHI: I have a telegraphic statement to make. My definition of science is not a narrow definition of science, it is the only rigorous definition of science.

LA DOCTRINE PHILOSOPHIQUE ET THÉOLOGIQUE DE LA CRÉATION CHEZ THOMAS D'AQUIN

GEORGES CARD. COTTIER

I. Préliminaires

Vérité de foi

1. Pour le croyant la création appartient aux vérités de foi. Les questions qui concernent cette vérité sont donc d'abord d'ordre théologique. La théologie, en effet, répond à une requête de l'esprit du croyant de pénétrer, d'une manière raisonnée, critique et systématique, dans l'intelligence des vérités révélées. Dans la révélation judéo-chrétienne, le thème de la création occupe une place essentielle. Il est présent dans le Premier et dans le Nouveau Testaments, Livres sapientiaux et psaumes notamment. Mais les deux textes majeurs de référence sont le premier chapitre de la *Genèse* et le *Prologue* de l'*Evangile de Jean*.

La discipline théologique qu'est l'exégèse dégagera le sens du texte: quel est le sens d'un message par essence religieux, compte tenu du contexte culturel et historique dans lequel il est né? Qu'est-ce que l'auteur sacré a entendu dire? Comment un message délivré à un moment de temps conserve-t-il sa pertinence et son actualité au long des siècles?

L'interprétation exacte des textes est évidemment présupposée par la réflexion théologique. Même s'il nous faudra en dire quelque chose, ce n'est pas à cette approche que je m'arrêterai. Je voudrais vous entretenir de quelques approfondissements que la théologie spéculative a apportés à l'intelligence du problème.

Pour pouvoir développer adéquatement son argumentation, le théologien emprunte un certain nombre de notions à la métaphysique.

Celle-ci prend origine dans la rencontre première de notre intelligence avec la réalité, pour autant que notre regard, loin de glisser à la surface des choses, se laisse saisir par elles. Pour décrire ce contact auroral, Aristote parle d'étonnement, d'émerveillement. L'esprit est comme surpris et ébranlé jusque dans ses racines devant ce fait primordial que les choses sont, qu'elles sont ce qu'elles sont et par là nous parlent, provoquant en nous l'éveil du questionnement; elles suscitent les questions qui sont les questions premières enveloppées dans la certitude anticipatrice qu'elles sont promptes à dévoiler la réponse, – dit autrement, qu'elles sont intelligibles.

Métaphysique

2. L'étonnement qui est à l'origine du dynamisme de la pensée n'est pas un point de départ dont on s'éloignerait, comme d'un présupposé, pour porter son intérêt sur autre chose. La métaphysique procède par approfondissement; pour cela elle se maintient dans l'éveil initial. C'est l'être qu'elle interroge; ce sont ses traits fondamentaux qu'elle dégage dans leur intelligibilité.

C'est l'être en tant que tel qu'elle interroge, qui est à la fois ce qui est le plus commun et le plus intime à toute chose. Elle en découvre alors l'amplitude illimitée et la diversification interne.

Si j'évoque ici la métaphysique, c'est pour souligner le fait que notre raison est capable de poser à la réalité une pluralité de questions, dont chacune possède, sans exclusivité, son irréductible spécificité et sa légitimité, tandis que la mentalité positiviste fort répandue se fait du savoir une conception exclusive et univoque.

C'est ensuite parce que la tradition théologique nous a transmis la définition suivante de la création: *creare est aliquid ex nihilo facere*, créer c'est faire quelque chose à partir du rien, ou à partir du néant. Nous avons là deux notions, quelque chose, (*aliquid*), qui est un nom de l'être, et rien, néant, empruntées à la métaphysique.

Or sur ces notions, comme sur les autres notions premières, les philosophes sont divisés.

D'aucuns traitent l'être comme un fait brut et banal, d'autres y découvrent toutes les richesses de l'acte d'être (*actus essendi*).

Sur le néant, les divergences sont encore plus grandes.[1] C'est ainsi que Heidegger reprend la question formulée par Leibniz: "Pourquoi y a-t-il plutôt quelque chose que rien?". Ce serait là la première question que se pose

[1] Cf. dans mon ouvrage, *Le désir de Dieu*, ch. VII, *La doctrine de la création et le concept de néant,* Ed. Parole et Silence, Paris, 2002, pp. 131-143.

notre esprit. Mais la citation est tronquée. Leibnitz, en effet, ajoute: "Car le rien est plus simple et facile que le quelque chose". Il y aurait donc antériorité du rien sur le quelque chose, ce qui fera dire à Bergson que le néant dont parle Leibnitz est une sorte de quelque chose qui précède l'être. La critique part d'une position qui est à l'extrême opposé: le concept de néant, dit Bergson, est un pseudo-concept. En réalité, quand nous pensons le néant d'une chose, nous la pensons *absente*, parce que nous lui substituons une autre chose vers laquelle se déplace notre attention.

En étendant le processus à la totalité, on aboutit à l'idée du néant absolu, qui est une idée contradictoire, car on ne peut substituer au tout autre chose.

Le raisonnement, à supposer que l'analyse soit convaincante, repose sur le présupposé tacite de la nécessité de l'être. Comment dès lors rendre compte de l'existence d'êtres, dont l'essence ne contient pas la raison d'être de leur existence? Telle est la condition des êtres qui naissent et qui meurent et dont il n'est pas contradictoire de penser qu'ils ne sont pas ou qu'ils peuvent ne pas être. Il devient ainsi impossible de rendre compte de la contingence.

Ces quelques considérations préliminaires veulent simplement souligner la nécessité d'avoir des concepts clairs de l'objet de notre recherche et de les exprimer avec la plus grande rigueur possible.

II. Le modus cognoscendi

Commencement

3. Le premier chapitre de la *Genèse* et le *Prologue* de l'Evangile de Jean s'ouvrent par la même formule: *Au commencement* (*en arché*). C'est délibérément que Jean a repris l'expression. Cependant, le sens de ce *commencement* n'est pas parfaitement identique, car dans l'Evangile, il désigne la préexistence éternelle du Verbe. Alors que dans la *Genèse* il s'agit du commencement de l'univers, ici il s'agit d'une réalité antérieure au temps. La Vulgate latine traduit par *in principio*. Principe ne connote pas la dimension temporelle.

Quand nous essayons de réfléchir au problème de la création, c'est pourtant cette dimension temporelle qui vient aussitôt à l'esprit. Saint Thomas, que je commente, nous en donne la raison, qui tient à la nature de l'intelligence humaine. Nos idées présupposent la connaissance sensible; c'est à partir de celles-ci que nous les formons par voie abstractive. Cette dépendance détermine notre mode de connaître, et, par conséquence, le langage exprimant ce que nous connaissons.

Ainsi, à cause de la connaturalité de notre intelligence aux réalités matérielles et temporelles, il est nécessaire que, dans un mouvement réflexe, nous portions un regard critique sur notre pensée et sur son expression. Elle distingue alors entre l'objet qu'elle connaît et la manière (*modus*) dont elle le connaît et l'exprime.

Cette distinction est particulièrement importante pour notre compréhension de l'idée de création. Saint Thomas en fait la remarque. Notre tendance spontanée, non réfléchie, est de penser la création comme une mutation, qu'elle n'est pas. La définition même semble nous y incliner: *facere aliquid ex nihilo*, à partir de rien.

Création et mutation

4. La création n'est pas une mutation, si ce n'est selon notre mode de compréhension. Car l'idée de mutation inclut l'idée que la même chose se présente autrement maintenant qu'avant, soit en acte là où la mutation est qualitative ou quantitative, soit en puissance quand il y a mutation selon la substance, dont le sujet est la matière. Mais dans la création par laquelle est produite toute la substance des choses, on ne peut trouver quelque chose d'identique se présentant autrement maintenant et avant, si ce n'est selon notre manière de comprendre, quand nous concevons qu'une chose donnée d'abord n'a absolument pas existé, et maintenant existe.

Si on soustrait le mouvement, la mutation, il ne reste que divers rapports (*habitudines*) dans celui qui crée et dans ce qui est créé. Mais comme notre mode de signifier suit notre mode de connaître, la création est signifiée par mode de mutation; c'est pourquoi l'on dit que créer est faire quelque chose à partir du rien. D'ailleurs faire et être fait (*fieri*) conviennent davantage que changer et être changé (*mutare* et *mutari*) car faire et être fait comportent les rapports de cause à effet et d'effet à cause, et la mutation par mode de conséquence.[2]

Mutatio renvoie à *motus*, au sens large que lui donne Aristote: le mouvement indique tout changement, caractéristique générale de la réalité autour de nous et en nous-mêmes selon des formes diverses suivant les types d'être, de l'élémentaire jusqu'au niveau de l'esprit. D'où la définition

[2] *Sum. Theol.*, I, q. 45, a. 2, ad 2.

proposée: Mouvoir n'est rien d'autre que porter (*educere*) quelque chose de la puissance à l'acte, ce qui est le propre de l'être en acte.[3]

En pensant la création selon la condition de notre mode de comprendre, la référant à une mutation qu'elle n'est pas, nous nous reportons également au temps. Car la mutation implique un avant et un après. Le temps est, en effet, la mesure du mouvement selon l'avant et l'après. En d'autres termes, le mesuré est le mouvement, ce qui présuppose notre raison comme mesurant. Ce qui signifie que là où il n'y a pas de mouvement, il n'y a pas de temps. Or nous avons vu que le rapport de création n'est pas une mutation, si ce n'est selon le mode de notre appréhension. C'est pourquoi le temps, lui non plus, n'intervient pas dans sa définition.

Notre intellection porte, par sa nature même et dans son dynamisme spontané et premier, sur les choses, c'est-à-dire sur des réalités positives. Son objet est l'être.

Dirons-nous pour autant avec Bergson que le concept de néant est un pseudo-concept? Non pas. Car, pour penser adéquatement les choses, nous élaborons des instruments logiques à commencer par l'affirmation et la négation. Néant ou rien équivalent à non-être.

Quand nous pensons le néant, nous partons de l'affirmation de l'être, auquel nous apposons la négation. Cela ne comporte pas contradiction.

La négation signifie l'absence d'une chose. Nier, c'est écarter une réalité. Nier absolument, c'est l'écarter sans préciser si cette réalité est ou non requise par un sujet auquel elle appartiendrait. L'absence d'une propriété due à un sujet déterminé définit la privation, qui est une négation déterminée, c'est-à-dire connotant un sujet propre.

Quand donc nous pensons le néant, nous pensons l'absence radicale et absolue de l'être. Dans cette perspective doit s'entendre l'adage qui remonte aux philosophes grecs: *ex nihilo nihil fit*, du rien ou de rien, rien ne peut provenir. Penser le contraire supposerait que ce n'est pas vraiment du rien que nous parlons, mais que nous considérons le rien comme une espèce de quelque chose.

[3] Cf. *Sum. Theol.*, I, q. 2, a. 3. Le mouvement est d'abord le mouvement local. La mutation renvoie au processus de "génération et corruption", par quoi des êtres nouveaux naissent et disparaissent.

III. La relation à la cause première

L'émanation des êtres

5. L'être des êtres qui se présentent à notre regard étonné suscite en nous l'interrogation fondamentale sur son origine. Car ces êtres, nous voyons qu'ils naissent et qu'ils meurent, qu'ils existent mais qu'il n'y a pas de contradiction à les penser comme n'étant pas. Ils parlent à l'intelligence, ils sont intelligibles, mais leur notion ne contient pas leur raison d'être. Ce paradoxe qu'ils sont porte l'esprit, comme spontanément, à s'interroger sur le fondement de leur être. L'être contingent conduit à poser la question du fondement, qu'il ne possède pas par lui-même mais que par lui-même il postule.

Les causes particulières expliquent telle propriété, tel aspect, tel être singulier. Mais c'est l'être même, en tant que tel, dans sa totalité, qui exige explication. La considération métaphysique de l'être contingent nous conduit ainsi à l'Etre nécessaire, cause de tout ce qui existe. Dieu, l'Etre absolu, *Ipsum esse subsistens*, est la cause de la totalité des êtres, dont nous voyons qu'ils ne tirent pas d'eux-mêmes leur propre existence. Celle-ci est une existence reçue.

Cette considération première est propre à la métaphysique. Elle n'entre pas dans le champ d'investigation d'autres disciplines du savoir. Il arrive aussi que certains écartent la question, acceptant le réel comme un donné brut et muet.

Comment concevoir la causalité divine, c'est-à-dire l'origine, la procession des êtres à partir de l'Etre absolu?

La pensée antique n'a pas connu la doctrine de la création, qui a été développée à partir de la rencontre de la philosophie avec la tradition biblique. C'est par l'émanatisme qu'elle explique l'existence de notre monde. La formulation la plus explicite en sera donnée par le néoplatonisme.

Entre l'Absolu, l'Un originel, et les réalités qui découlent de lui, il y a continuité, bien que cette continuité ne soit pas homogène. En effet, les "hypostases" successives qui émanent du Premier, le font selon un ordre graduel qui signifie un éloignement progressif. D'un côté, en vertu de la continuité, on affirmera que le monde est divin et parfait. De l'autre, en vertu du graduel éloignement, pour l'âme humaine, appelée à rejoindre le Principe, la vie en ce monde est comparée à une chute et à un exil, et le corps à une prison. L'âme, qui aspire à un retour à l'Un, doit se libérer de la matière, source du mal.

Le *Timée* de Platon permet de saisir la distance qui sépare la pensée classique de la doctrine de la création. Notre monde n'est pas l'œuvre du Dieu suprême, mais d'une divinité subalterne, le démiurge, car le Dieu suprême ne saurait s'abaisser jusqu'à la matière, qui existe indépendamment de lui. Sur cette matière informe, le démiurge imprime la forme des êtres, mais cette forme n'est elle-même que le reflet des formes parfaites qui existent dans le monde intelligible.

En réalité, l'émanatisme ne va pas au-delà de la mutation: la matière préexiste, elle ne dépend pas du Principe, elle reçoit détermination et structure des formes qui se succèdent selon la loi de la "génération et de la corruption". La doctrine de la création affirme, au contraire, que la matière, qui n'existe pas sans la forme, est elle-même créée.[4] La création porte sur la totalité et l'intégralité de l'être.

La création

6. La création désigne le mode selon lequel tout ce qui est, de quelque manière que ce soit, émane de Dieu, cause première et universelle. Dieu, en effet, est l'Etre même subsistant par lui-même, *Ipsum esse per se subsistens*. Les autres êtres ne sont pas par eux-mêmes. Ils reçoivent l'être, ils sont par participation. La participation comporte des degrés; les divers êtres sont plus ou moins parfaits. Ils ont leur cause dans un premier être qui possède la perfection en plénitude, qui est la perfection même.

La création désigne ainsi l'émanation de la totalité de l'être (*totius esse*) de la cause première, qui est Dieu. Rien n'est présupposé à cette production: par rien, on entend non-être. Et ceci à la différence de ce qui se passe dans les mutations dont nous avons l'expérience, qui sont l'effet de causes particulières et dans lesquelles quelque chose est toujours présupposé, comme le bois à l'action du menuisier.[5]

On dira donc que ce qui est créé est fait (*fit*) à partir (*ex*) de rien, *aliquid ex nihilo fieri*. L'expression peut s'entendre de deux manières. Dans un premier sens, la préposition *ex* ne signifie pas la cause matérielle, mais seulement un ordre: nous disons ainsi que le matin devient (*fit*) le jour pour signifier qu'il vient avant le jour. La préposition *ex* inclut la négation contenue dans le terme rien, *nihil* équivalant à *non-ens*. Mais, et c'est le second sens,

[4] Cf. Saint Thomas, *De Potentia*, q. 4.
[5] Cf. *Ibid.*, I, q. 45, a. 1.

elle peut être incluse en elle. Alors que dans le premier sens, l'ordre demeure affirmé pour indiquer l'ordre de ce qui est au non-être qui le précède, dans le second sens l'ordre est nié et "est fait à partir de rien" signifie: n'est pas fait à partir de quelque chose. Dans ce cas, la préposition *ex* importe un rapport à la cause matérielle, qui est niée. L'une et l'autre lecture sont justifiées.[6]

Créer, c'est donc faire quelque chose à partir de rien, *creare est aliquid ex nihilo facere*. Tout ce qui est dans les êtres vient de Dieu, cause universelle de tout l'être. C'est de (*ex*) rien qu'Il produit les choses dans l'être.[7]

Explicitation

7. L'analyse de la définition et de ses implications met en évidence une vérité décisive.

Pour mener à bien cette analyse nous devons nous montrer attentifs aux illusions de l'imagination (*falsa imaginatio)*. L'illusion tient à notre mode d'appréhension, qui entend la création à partir de la mutation, qui est passage d'un terme à un autre.[8]

C'est la tâche de la réflexion critique que d'écarter de notre représentation ce qui tient à notre mode de saisir et de signifier, selon lequel une même réalité se présente *maintenant* différente de ce qu'elle était *avant*. Or ici il n'y a pas d'avant suivi d'un après, puisque "avant", la réalité créée n'était absolument pas; il ne peut y avoir passage, mouvement, d'un avant à un après, ce qui suppose deux états d'un même mobile.

Cependant entre la mutation et la création, il existe un point de rencontre qui est l'action. C'est elle qui nous fournit l'analogie pour penser la création. Dans l'action, en effet, nous distinguons un aspect actif, qui est l'action de l'agent, et un aspect passif, la "passion" de ce qui est mû ou changé. Une fois soustraits ou écartés le mouvement ou la mutation, demeurent les divers rapports (*habitudo*) entre celui qui crée (*creans*) et ce qui est créé (*creatum*). Le rapport entre faire et être fait met en évidence le rapport de la cause à l'effet et celui de l'effet à la cause. Nous disons que créer, c'est faire quelque chose du (*ex*) néant, parce que notre mode d'appréhender et de signifier a son point de départ dans la *mutation*, que la création n'est pas.[9]

[6] Cf. *Ibid.*, a. 1, ad 3.
[7] Cf. *Ibid.*, a. 2.
[8] Cf. *Ibid.*, a. 2, ad 4.
[9] Cf. *Ibid.*, a. 2, ad 2.

Il reste à expliciter ce que nous venons d'établir, en répondant à la question: qu'est donc la création pour l'être qui est créé? Nous avons déjà la réponse: puisque ce qui est créé ne l'est pas en vertu du mouvement ou de la mutation, il reste que ce que la création pose dans la chose créée, l'est uniquement selon la relation.

Ce qui advient en vertu du mouvement et de la mutation, devient à partir de quelque chose de préexistant. Nous en faisons l'expérience avec les processus de la nature. Mais ce mode de production ne peut s'appliquer à la production de tout l'être par la cause universelle de tous les êtres, qui est Dieu. Dieu, comme nous l'avons vu, produit les êtres sans mouvement. Soustrait à l'action et à la passion propres du moteur et du mobile, reste la relation. Dès lors la création dans la créature n'est rien d'autre que la relation au Créateur comme principe de son être.[10]

Une distinction nous permet d'apporter une précision ultérieure. On reconnaît, en effet, deux types de relation. Certaines relations sont données dans la réalité. Quand je vois un objet, ma vue est relatée à cet objet. Quand je cesse de le voir, la relation cesse d'exister. Ma raison peut, corrélativement, instituer une relation entre l'objet et ma vue. On posera ainsi une relation entre l'objet visible et ma vue; une telle relation n'affecte en rien l'objet. Dans le premier cas, on parlera de relation réelle, dans le second de relation de raison. Ma raison peut toujours, à partir d'une relation réelle, établir une relation de raison, qui lui est corrélative.

Au sens actif, la création signifie l'essence divine, avec, en connotation, une relation à la créature. Cette relation ne peut être une relation réelle; elle est une relation de raison. En effet, Dieu, acte pur, ne peut subir de modification, ce qui supposerait qu'il y a en Lui potentialité et donc imperfection. A l'inverse, la relation de la créature à Dieu est une relation réelle. La créature par tout ce qu'elle est orientée à Dieu, dont elle dépend dans ce qu'elle est et dans son exister, portée vers Lui, tenant tout de Lui.[11]

Ainsi le mouvement, le temps, le devenir n'entrent pas comme constitutifs dans la définition de la création. Au sens propre du terme, la création désigne la dépendance radicale de la créature de la Cause de tout l'être, qui est Dieu. La création est la relation de la créature, dans tout ce qu'elle est, à son Créateur. C'est souvent abusivement qu'on a recours à ce concept dans les débats relatifs à l'évolution.

[10] Cf. *Ibid*, a. 3.
[11] Cf. *Ibid.*, a. 3, ad 1.

IV. Observations complémentaires

La thèse de l'éternité du monde

8. Les philosophies émanatistes expliquent l'émanation des êtres à partir de l'Un originel comme un processus nécessaire. Il appartient à la nature de l'Un d'être à l'origine d'une expansion descendant graduellement vers la multiplicité. Ce processus est nécessaire et l'Un transcendant d'où il vient n'est pas personnel.

Tout autre est la doctrine de la création. Entre l'absolu et l'aséité de Dieu qui est l'être par soi et nécessaire et les êtres qui reçoivent de Lui leur être et qui peuvent ne pas être, la distinction est radicale. Et la création au sens actif du terme est un acte souverainement libre qui renvoie à la sagesse et à la volonté du Créateur, qui est un Dieu personnel. Si Dieu n'avait pas créé, rien ne manquerait à sa perfection, de même que la création n'ajoute rien à cette perfection. Etienne Gilson a montré qu'historiquement parlant il aura fallu la révélation biblique pour que la philosophie dégage à son propre plan la doctrine de la création. Les grands penseurs de la Grèce ne l'ont pas connue, et l'émanatisme ne cesse d'exercer son attrait sur la pensée moderne. Pensons à Spinoza et même à Hegel.

La distinction entre émanatisme et doctrine de la création est présente dans la discussion par Thomas de la thèse de ceux qui soutiennent l'éternité du monde mais aussi, par voie de conséquence, de celle de ceux qui entendent prouver le commencement de l'univers dans le temps. Dans les deux cas, il a affaire à des adversaires qui pour lui sont des autorités.[12] Le débat n'est pas sans jeter une lumière précieuse sur nos problèmes contemporains.

L'éternité du monde est affirmée par Aristote, dont la position est reprise par ses commentateurs arabes, Avicenne et Averroès. On pourrait penser que Thomas se trouve là devant une objection insurmontable, qui équivaut à une remise en cause de sa propre position. C'est pourquoi il examinera avec une particulière acribie les arguments du Stagirite.

La cosmologie d'Aristote intéresse aujourd'hui l'historien des sciences. Si nous n'avons donc pas à entrer dans l'examen de son contenu, il en va différemment de la lecture critique qu'en fait saint Thomas du point de vue

[12] Voir *Sum. Theol.*, I, q. 46, *Sum. Contra Gent.*, Lib. II, c. 31-38; *De Potentia*, q. III, a. 13-17.

épistémologique et méthodologique. La *Physique* est un traité philosophique qui, partant de la voie inductive, procède par la voie de la démonstration. C'est sur la valeur démonstrative des arguments que porte l'analyse thomasienne.[13]

L'analyse est précédée d'un rappel du principe qui commande l'ensemble de la doctrine de la création. C'est la volonté divine qui est la cause des êtres.[14] Pour donc qu'un être soit nécessairement, il est nécessaire que Dieu le veuille, car la nécessité de l'effet dépend de la nécessité de la cause. Or Dieu ne veut de nécessité que sa propre bonté, qui est perfection infinie. Il n'est en conséquence pas nécessaire que Dieu ait voulu que le monde existât toujours. Le monde ne sera donc éternel que si Dieu veut qu'il le soit, l'être du monde dépendant de la volonté de Dieu, qui est sa cause.

La conclusion à laquelle on aboutit n'est pas la non-éternité du monde mais la non-nécessité qu'il soit éternel (à supposer qu'il le soit). En conséquence cette éternité ne peut pas être prouvée par une démonstration au sens propre.

Telle est bien la nature de l'argumentation chez Aristote, qui établit le caractère contradictoire des raisons que ses prédécesseurs donnaient d'un commencement du monde. Quand, à l'inverse, Aristote en appelle au témoignage des mêmes Anciens en faveur de sa propre position, il y a là un argument probable: c'est là un exemple de "problème dialectique" dont la solution nous échappe.

La longue série de réponses aux objections (10) donne à Thomas l'occasion de discuter un certain nombre de textes significatifs d'Aristote sur le sujet. Nous n'avons pas ici à le suivre dans le détail.

Retenons simplement une observation sur le temps. Celui-ci apparaît avec la réalité créée; c'est par l'imagination que nous pensons un temps avant le temps. Et quand on parle de l'antériorité du Créateur sur la création, il s'agit d'une antériorité de l'éternité sur le temps, et non d'un temps sur un temps (cf. ad 6, ad 8).

Ainsi l'éternité du monde ne peut être démontrée philosophiquement. C'est là une thèse en faveur de laquelle on peut avancer des arguments probables. Aussi bien Thomas ne prétend pas démontrer sa fausseté. Il se contente d'y opposer un argument de convenance. Le monde nous fait connaître plus manifestement la puissance divine créatrice, si ce monde n'a

[13] Cf. *Sum. Theol.,* q. 46, a. 1.
[14] Cf. *Ibid.*, q. 19, a. 4.

pas toujours été. En effet, ce qui n'a pas toujours été manifeste davantage avoir une cause que ce qui a toujours été.

Les arguments de ceux qui soutiennent l'éternité du monde ne constituent pas des preuves apodictiques; ils n'ont pas une force contraignante, ils ne vont pas au delà du plausible.

Une vérité de foi

9. Des théologiens chrétiens ont, à l'inverse, prétendu prouver que le monde n'a pas toujours existé et a donc eu un commencement. Thomas réfute leurs arguments. Sa position est claire: que le monde ait commencé est une vérité de foi, qui ne peut être prouvée par démonstration.

Cette impossibilité tien à la nature de la démonstration qui ne porte pas sur les faits contingents. En effet, le principe de la démonstration est l'essence (*quod quid est*) de la chose. Or le constitutif (la raison) d'une chose, sa *species*, fait abstraction du *hic* et *nunc*; il est universel. C'est pourquoi il est impossible, à considérer leur essence, de prouver, que l'homme, le ciel ou la terre ne furent pas toujours. En considérant le monde lui-même, il est ainsi impossible de prouver sa nouveauté.

On aboutit à la même conclusion en considérant la cause du monde, qui est la volonté divine. Or notre raison ne peut connaître par elle-même la volonté divine que pour ce qu'elle veut d'absolue nécessité, c'est-à-dire sa propre bonté. Mais ce que Dieu veut en ce qui touche aux créatures est hors de portée de notre investigation.[15] Cette volonté nous est manifestée par la révélation, objet de la foi. Que le monde ait commencé est objet de foi, non de démonstration ou de savoir.

Thomas ajoute un avertissement sévère. En présumant démontrer une vérité qui est objet de foi, à l'aide de raisons inévitablement non nécessitantes, on s'expose aux moqueries des incroyants qui seront portés à penser que nous croyons à des vérités de foi à cause de telles raisons.

C'est par la foi que nous savons que le monde a commencé. La thèse de l'éternité du monde n'est pas contradictoire, mais elle ne s'impose pas avec nécessité. Si le monde avait été éternel, il serait tout autant un monde créé,

[15] Si le monde était éternel son "éternité" ne serait pas égale à l'éternité divine qui est selon la définition de Boèce *tota simul*. Un temps éternel comporterait la succession. Cf. *Sum. Theol.*, I, q. 46, a. 2, ad 5.

la création désignant la relation de dépendance ontologique radicale de l'être créé à la cause première créatrice.

De soi, la question de la création est antérieure à la question du devenir de l'univers. Le temps lui-même, mesure du mouvement et de la mutation, a été créé avec le monde.

La physique moderne s'occupe, à la différence de la physique ancienne, de l'origine temporelle du temps de l'univers. La théorie du *big bang* en fixe le commencement.

Le théologien verra là un argument qui converge avec la doctrine de la foi, mais non une preuve au sens rigoureux du terme.

Il précisera qu'il ne s'agit pas là d'un argument en faveur de la création. Car l'événement du *big bang* ne signifie pas le surgissement de *notre* univers à partir du néant: *ex nihilo nihil fit*. Il présuppose existants les facteurs qui l'ont produit ou déclenché. Ainsi le *big bang* posé aujourd'hui à l'origine du monde et du temps ne contredit pas mais présuppose l'intervention créatrice de Dieu.

La fonction herméneutique de la théologie

10. Les débats philosophiques et scientifiques conduisent le théologien à s'interroger sur l'interprétation à donner au premier verset de la *Genèse*. Il note que ce verset peut faire l'objet d'une triple lecture. Chacune d'elles est valable et permet de réfuter des erreurs incompatibles avec la foi.[16]

Autrement dit, le théologien se trouve invité à vérifier l'exactitude de son interprétation de l'Ecriture, parole inspirée.

L'auteur principal est l'Esprit saint, ce qui n'élimine nullement la part de l'écrivain sacré, de sa personnalité et de sa culture.

La question mériterait d'être développée, je ne peux pas le faire ici. Thomas le fait, dans le cadre du traité de la création, dans un article du *De Potentia* qui pose les principes de l'herméneutique théologique.[17]

On évitera ainsi l'erreur qui consiste à assimiler aussitôt à la doctrine de la foi une opinion que l'on tient pour vraie.

[16] Cf. *Ibid.*, I, q. 46, a. 3.

[17] Cf. *De Pot.*, q. 4, a. 1.

[18] Cf. *Ibid.*, a. 2. Thomas y compare la position d'Augustin, plus subtile, et pour autant moins sujette au mépris des incroyants, à celle d'autres Pères de l'Eglise plus simple, en apparence (*ad superficiem*) plus consonante avec la lettre. Notons que Thomas comme les Pères tient comme appartenant à la révélation la division en six jours.

Dans certains cas, le théologien doit vérifier la compatibilité d'une position avec la doctrine de la foi et avec le sens du texte biblique,[18] sachant que ce n'est pas à lui qu'il revient d'en prouver la validité.

J'espère qu'avec cette présentation à la fois théologique et philosophique, j'aurai contribué à dépassionner quelque peu un débat qui, tout en touchant à de vraies questions, comporte aussi une série de faux problèmes.

DISCUSSION ON CARD. COTTIER'S PAPER

PROF. CABIBBO: I would like to thank Cardinal Cottier for his beautiful presentation, it is a pity we were not able to listen to it all but we have the complete text of it. Do we have any questions?

PROF. PHILLIPS: If I have understood correctly, St Thomas' thought was that you cannot prove a beginning according to metaphysics but today it appears that we have the proof of the beginning of the universe through physics. For you, what does the relation between science and faith and your understanding of the Bible mean now that we have a proof in physics that we cannot have with metaphysics?

H.EM. CARD. COTTIER: (originally in French) Now, to go to the interpretation of St Thomas, he says that once the believer knows that the world was created in time, this underlines that it depends on a first cause, which corresponds to the human being. This is a proof, but I think that theology and philosophy have to listen to science and it is true that today we are going towards a beginning of the world in physics, therefore metaphysics is not closed off to that. When St Thomas speaks of the theory of Aristotle, he does not speak of a metaphysical theory of Aristotle, I should have said this, he speaks of the physics of Aristotle. The physics of Aristotle is very revisable and especially on this point I think the theologian must listen to what science tells us. This is true for many fields, because no knowledge is exhaustive but human reason is unique, therefore the different branches of knowledge must listen to one another.

H.E. MSGR. PROF. SÁNCHEZ SORONDO: (originally in French) Your Eminence, we can say that present science is probably unconsciously more Christian than Aristotelian, in the sense that science, today, tries to explain a temporal origin of Creation, while the Greeks, on the contrary, thought that the world was eternal (with the exception of Plato, in *Timaeus*).

PROF. CABIBBO: (originally in French) I think we need to be careful.

H.EM. CARD. COTTIER: (originally in French) Science is science and we ask that it serve the truth. I would hesitate to say that science is Christian. What the Holy Father said is true, that in the Judeo-Christian revelation, to take the words of St John, 'in the beginning there was the Word' and he always has the idea that at the roots of thing there is reason and the word 'reason', as we said the day before yesterday, has a lot of meanings and just one of them does not contain the exclusive truth.

PROF. CABIBBO: (originally in French) Thank you. I would like to make another small comment. We must be especially careful in accepting the ideas of science because they change with time. At the moment the Big Bang is not generally accepted. In the first days of this conference we discussed a multiverse in which there are several Big Bangs and it is the real universe that includes maybe an infinite number of universes such as ours that would be infinite in time.

H.EM. CARD. COTTIER: (originally in French) I think it is also part of knowledge to accept probable or hypothetical knowledge.

PROF. CABIBBO: (originally in French) It is really an extreme extrapolation.

PROF. ZICHICHI: There is an important point that Cardinal Cottier emphasized, namely that time cannot exist in the transcendental sphere. The transcendental sphere cannot have space, time, mass, charges. The fundamental quantities which make our world have nothing to do with the transcendental sphere, this is the interpretation that Cardinal Cottier gave to St Thomas, which is exactly correct. In fact, it is not a question of trying to understand the orthogonality between the two existing spheres, transcendental and immanentistic. They are not orthogonal. The basic quantities which define our world cannot exist in the transcendental sphere, otherwise there would be no difference between the two. In this sense, what Cardinal Cottier said is very modern and in full agreement with science.

PROF. LÉNA: (originally in French) A question for Cardinal Cottier. The supporters of intelligent design put forth a sort of proof of the existence of

God by the observation of nature. Not an indication or a path but a proof. Hasn't it been a temptation of natural theology to follow this approach?

H.EM. CARD. COTTIER: (originally in French) I think that natural theology said this before the supporters of intelligent design, but I think it must be understood along the lines that the world has a meaning. Before theology it is in the Biblical Scriptures, when the Psalm tells us that the heavens are filled with the glory of God, I would say it is a sort of poetical approach to the world, and if you read the Bible, it has an incredibly powerful poetic sense which is based on the evidence that the world is beautiful, that the world speaks to us. I think this is what lies behind the idea of a finality of the world. Things degraded during the 18th century, there was an author who would be very interesting to reread, called Bernardin de Saint-Pierre, who saw finality in the most ordinary elements of daily life and it becomes ridiculous, but the fact that the universe has a meaning and that the universe speaks to us when we exercise knowledge is because the universe gives us a response, and when one is sensitive to beauty, this is what we mean when we say it has a meaning. If you wants to see intelligent design in the details you are no longer in the field of metaphysics, but in a sort of experimental verification of God's existence which is not the great metaphysics, certainly not.

PROF. MITTELSTRASS: Just a short historical note. Metaphysics, one could say, is written in Aristotelian language. I just want to point out a Platonic or Augustinian element. For Plato the world is the result of a creative act, of an artefact, because it is the result of a creative act it is an artefact. Because it is an artefact it is understandable by mathematics and natural science. So that may be some blueprint for talking about Creation in a different terminology than an Aristotelian one, perhaps with the same result.

H.EM. CARD. COTTIER: (originally in French) I agree, yes, but I did not fully understand. Thank you.

PROF. FACCHINI: (originally in French) I would like to ask Cardinal Cottier if he can clarify the concepts of origin and beginning of the world.

H.EM. CARD. COTTIER: (originally in French) I did not speak about that, but when one says 'beginning' one talks of a beginning in time, of a succession. When one speaks of 'origin', one means rather the foundation, that is why I employed the word 'foundation'. One does not necessarily specify time when one says 'origin'. 'Origin' is more fundamental than beginning, I think. In ordinary language you exchange one for the other but, if you wants to be precise, I think that you need to distinguish between origin which means foundation, the raison d'être or the cause and then the beginning which presupposes a succession.

NATURALNESS AND DIRECTING HUMAN EVOLUTION
A PHILOSOPHICAL NOTE

JÜRGEN MITTELSTRASS

The European tradition of anthropology has always distinguished between the biological and the cultural nature of Man, in other words between what is natural to him in a physical and biological sense, and what pertains to him culturally, what his cultural essence is. This, however, does not mean that both essences, the physical and the cultural, fall apart, and that therefore, as Descartes for example holds, Man disintegrates into two essences. On the other hand, by establishing the distinction between the biological and the cultural nature of Man, problems arise concerning the concept of *naturalness* applied to Man. Is this concept only applicable to his biological nature or essence, or does his naturalness consist precisely in that it is expressed by both natures or essences, that is to say by their unity?

In fact, Man is a natural being, who can live only as a cultural being. *Descriptively*, within the context of biological systematics, mankind is a subspecies of the species *Homo sapiens*, namely *Homo sapiens sapiens*, and is the only recent member of the genus *Homo*. But this definition includes only the empirico-physical side of Man, not that which makes up the nature or essence of humanity *ascriptively*, namely its form of self-description and (not conclusively established) self-determination. The latter was described classically as the *animal rationale*, a being endowed with and determined by reason, or as a being lying between animal and God. More recent anthropologists (after Friedrich Nietzsche) capture this notion in the concept of a *nicht festgestelltes*, i.e. a not-yet-determined being (both biologically and culturally). It would be a category error to interpret our actions and thoughts as the products of natural processes, whereby even the act of interpreting becomes part of nature, a 'natural fact'. But we fall into a new form of naiveté if we oppose this interpretation with a claim that scientifically discovered facts have no influence, or at least ought to have no influence, on the self-determination of Man. Thus it is a matter of adopting a scientifically informed and philosophically considered position, one which is beyond mere *biologism* and *culturalism*, which, in other words, is beyond an absolute distinction between biological and cultural explanations, and which refers to both the lives and the laws that shape our lives**.** Such a position should neither reduce Man to (pure) nature, nor to the (absolute) spirit he aspires to be.

In the following, I will talk about what in philosophy and theology is called the *conditio humana* and what role the concept of naturalness could play in this context. I will then consider in what respect the relation between naturalness and the power of directing evolution, particularly Man‘s own evolution, create serious anthropological and ethical problems. And this with regard to a future which is not only human, but also humane.[1]

1. The Natural and the Artificial

Modern philosophical anthropology takes its point of departure from two opposing conceptions: that attributed to Max Scheler and that of Helmut Plessner. According to Scheler, 'Man' is the 'X that can behave in a world-open manner to an unlimited extent'.[2] According to Plessner, 'Man' is characterised by an 'eccentric positionality',[3] whereby his eccentric existence, which does not possess a fixed centre, is described as the unity of mediated immediacy and natural artificiality. Accordingly, Plessner formulates three fundamental laws of anthropology: (1) the law of natural artificiality, (2) the law of mediated immediacy, and (3) the law of the utopian standpoint.[4] Similarly, Arnold Gehlen states the thesis that Man is by nature a cultural being,[5] and in doing so, his cultural achievements are seen as com-

[1] For some aspects of what follows see J. Mittelstrass, 'The Anthropocentric Revolution and Our Common Future', in: W.-K. Raff *et al*. (Eds.), *New Pharmacological Approaches to Reproductive Health and Healthy Ageing (Symposium on the Occasion of the 80th Birthday of Professor Egon Diczfalusy)*, Berlin and Heidelberg and New York: Springer 2001 (*Ernst Schering Research Foundation. Workshop Supplement* 8), pp. 57-67.

[2] M. Scheler, *Die Stellung des Menschen im Kosmos*, Darmstadt: Reichl 1927, p. 49.

[3] H. Plessner, *Die Stufen des Organischen und der Mensch: Einleitung in die philosophische Anthropologie*, Berlin and Leipzig: de Gruyter 1928 pp. 362ff.

[4] H. Plessner, *op. cit*., pp. 309-346. See K. Lorenz, *Einführung in die philosophische Anthropologie*, Darmstadt: Wissenschaftliche Buchgesellschaft 1990, pp. 102f.

[5] A. Gehlen, *Anthropologische Forschung: Zur Selbstbegegnung und Selbstentdeckung des Menschen*, Reinbek: Rowohlt 1961, p. 78.

pensation for missing organs and 'Man' is defined as a creature of defect (*Mängelwesen*).[6] Common to all these approaches is that Man has a particular nature and that it is an essential element of this nature to work on it.

Stipulations of a similar kind can also be found in the history of philosophical anthropology. Thus Man is called the creature without an archetype by the Italian Renaissance philosopher Giovanni Pico della Mirandola: he himself, according to the will of his creator, is to determine the 'form', that is, the cultural form in which he wishes to live.[7] According to Immanuel Kant, the question 'What is Man?' can only be answered if we already have answers to the questions, 'What can I know?', 'What ought I to do?' and 'What may I hope?'[8] The attempt to determine '1. the source of human knowledge, 2. the extent of the possible and profitable use of knowledge, and finally 3. the limits of reason',[9] is itself an anthropological research programme, and on the background of the critical philosophy of Kant it is an open research programme that defines Man according to what he can achieve in theory and practice. For Friedrich Nietzsche, finally, Man is the not yet determined animal,[10] and thus science too is seen as the expression of the human endeavour 'to determine himself'.[11] Furthermore, one of the reasons for the difficulty of saying what Man is lies in the fact that Man is the (only) creature that possesses a reflective relation to itself, that Man, as Martin Heidegger says, is the creature 'that in its being relates understandingly to its being',[12] or that it is 'concerned in its being with this being itself'.[13] This opens up a broad horizon for an answer to the question,

[6] A. Gehlen, *Der Mensch: Seine Natur und seine Stellung in der Welt* [1940], 9th ed., Wiesbaden: Akademische Verlagsgesellschaft Athenaion 1972, p. 37. In a biological definition, 'cultural' is applied 'to traits that are learned by any process of nongenetic transmission, whether by imprinting, conditioning, observation, imitation, or as a result of direct teaching' (L.L. Cavalli-Sforza and M.W. Feldman, *Cultural Transmission and Evolution: A Quantitative Approach*, Princeton: Princeton University Press 1981, p. 7).

[7] G. Pico della Mirandola, *De hominis dignitate. Heptaplus. De ente et uno, e scritti vari*, ed. E. Garin, Florence: Vallecchi 1942, p. 106.

[8] I. Kant, *Logik* A 25, *Werke in sechs Bänden*, ed. W. Weischedel, Darmstadt: Wissenschaftliche Buchgesellschaft 1958, vol. III, p. 448.

[9] *Ibid.*

[10] F. Nietzsche, *Jenseits von Gut und Böse* [1886], in: F. Nietzsche, *Werke: Kritische Gesamtausgabe*, ed. G. Colli and M. Montinari, vol. VI/2, Berlin: de Gruyter 1968, p. 79.

[11] F. Nietzsche, *Nachgelassene Fragmente Frühjahr 1881 bis Sommer 1882, Werke*, vol. V/2 (1973), p. 533.

[12] M. Heidegger, *Sein und Zeit* [1927], 14th ed., Tübingen: Niemeyer 1977, pp. 52f.

[13] *Op. cit.*, p. 12.

what a human being, what his nature is. The only thing that is clear is what, with regard to the essential openness of Man, can be called the *anthropologically basic situation*.

It is equally clear that a differentiation between that which has *become*, which has occurred without any influence of Man, the natural, and the *made*, which has been created or shaped by Man, the artificial, is not easy to draw, and due to new possibilities of manipulation, not just of nature generally, but also of the (biological) nature of Man, it is getting even more and more difficult. The differentiation between the natural and the artificial, however, is still the essential differentiation on which our orientations are based. Even though we know that Man has taken a hand in much of what we consider natural, for instance climate or the flora, and that creating the artificial is natural to Man, we still use this distinction as orientation. After all, what would a world look like in which this distinction, the distinction between the natural and the artificial, could not be drawn? And how could it be possible to achieve a self-understanding that forgoes this distinction?

Philosophical views that reduce the one to the other, in which everything either turns into that which has become, or into the made, illustrate that such ideas nonetheless play a role in thinking about Man and his world. For Arthur Schopenhauer, for instance, in his fiction of a contemplative 'clear world-eye',[14] everything is purely given, unchangeable by human wants and actions, while, by contrast, for Johann Gottlieb Fichte, everything, also the natural, is constituted by an absolute I or self.[15] In one case (Schopenhauer) everything would be nature, in the other case (Fichte), everything would be spirit.

It is not just our natural intuitions, our way of dealing with the world and ourselves, that speaks against such radicalisations, so does a more detailed analysis of the implicit conceptualisation of that which has become, i.e. the natural, and the made, i.e., the artificial. In actual fact, we are always dealing with, in the terminology of Plessner, a *natural artificiality* (as opposed to something seemingly created out of nothing, thus being

[14] A. Schopenhauer, *Die Welt als Wille und Vorstellung* I § 36, *Sämtliche Werke*, ed. A. Hübscher, vol. II, Mannheim: Brockhaus 1988, p. 219.

[15] These examples are to be found in D. Birnbacher's writings, on whose detailed analyses of the concept of naturalness I will be drawing in what follows (*Natürlichkeit*, Berlin and New York: de Gruyter 2006, p. 3).

artificial) and an *artificial naturalness* (as opposed to something seemingly given without intervention, thus being natural). Here, a distinction made by Dieter Birnbacher is helpful to understand the concept of naturalness, namely that between a genetic and a qualitative naturalness, or a genetic and a qualitative artificiality, respectively: 'In the *genetic* sense, "natural" and "artificial" make a claim about *the manner in which a thing has been created*, in the *qualitative* sense, they make a claim about its current *characteristics* and *appearance*. "Natural" in the genetic sense is that which has a natural origin, "natural" in the qualitative sense is what cannot be distinguished from what is found in nature'.[16] This distinction in turn may be connected to the scholastic distinction between a *natura naturans* and a *natura naturata*: 'The genetic concept of naturalness relates to the aspect of *natura naturans*, that of a creative nature, the qualitative concept relates to the aspect of *natura naturata*, that of nature as nature having the properties it does'.[17] This also illustrates that already tradition has noticed the dialectical nature of the concept of naturalness, the reciprocal determination of natural artificiality and artifical naturalness.

2. Homo Faber

Today developments in biological and medical knowledge place Man in the unique position of being able to change not only nature in a general sense, but also his own nature, namely to intervene ever more powerfully not only in evolution in general but even in his own. And he is on the brink of changing the measures with which he previously described and regulated his situation, that is to say, the human condition.

While we have known since Darwin that Man, not only from the point of view of philosophy and culture, but also biologically, has no fixed essence, he is nevertheless subject to evolutionary changes, even though this is imperceptible to the individual and only recognisable to science over long periods of time. And it has become clear in the light of the new biology that Man can intervene in these changes himself – an ability to deliberately change his own genetic constitution, and that of his progeny. In fact, the *conditio humana* itself is changing: in the sense that now even Man's

[16] D. Birnbacher, *op. cit.*, p. 8.
[17] *Ibid.*

biological foundations are at his disposal. This creates a completely new and momentous situation in the domain of anthropology as well as in the domain of ethics – although the idea of determining our own nature is nothing completely new.

In 1488, Giovanni Pico della Mirandola wrote the following about God's intentions towards Man: 'We gave you neither a fixed dwelling, Adam, nor a particular appearance, nor any special talent, in order that you might have and own the dwelling, the appearance and the talents that you desire for yourself. (...) We made you neither heavenly nor earthly, neither mortal nor immortal, so that you might form yourself as your own, worthy, free and creative sculptor'.[18] One hundred years later (1596) Johannes Kepler writes in the dedication letter of his *Mysterium cosmographicum*: 'We perceive how God, like one of our own architects, approached the task of constructing the universe with order and pattern, and laid out the individual parts accordingly, as if it were not art which imitated nature, but as if God himself had looked to the mode of building of Man who was to be'.[19]

What Pico della Mirandola and Kepler still affirm in a pious and expressive language is nothing other than the extension of the concept of Man as *Homo sapiens* to include that of *Homo faber*, both with regard to himself and to his world. Pico della Mirandola's characterisation of Man as 'his own sculptor' again corresponds to Nietzsche's and Plessner's definition of Man as the not-yet-determined animal, or indeed to Plessner's characterisation of Man by means of his eccentric positionality (which is juxtaposed to the undistanced centricity of the animal). Similarly, Kepler's characterisation of a *Homo faber* competing with God paradigmatically corresponds to the modern notion of scientifically supported technical cultures, in which Man creates and encounters – both in and by means of his productions – not only the world, but indeed himself.

Is Man his own work, in the way that the (modern) world is his work? Certainly not in the sense that Man is an artefact that created itself. For even in his role as *Homo faber*, and independently of the complementary

[18] *Op. cit.*, p. 105f.

[19] *Prodromus dissertationum cosmographicarum continens Mysterium cosmographicum*, in: *Gesammelte Werke*, ed. W. v. Dyck and M. Caspar and F. Hammver, Munich: Beck'sche Verlagsbuchhandlung 1937ff., vol. I, p. 6 (1596), vol. VIII, p. 17 (1620). Translation by A.M. Duncan, *Johannes Kepler. Mysterium Cosmographicum / The Secret of the Universe* (Introduction and Commentary by E.J. Aiton, with a Preface by I. Bernard Cohen), New York: Abaris Books 1981, pp. 53/55.

definitions of his natural artificiality and his artificial naturalness, Man remains bound to what has been called the *conditio humana*, and what is meant by the work-like character of Man is above all his self-determining ('cultural') essence, not his biological essence. Nonetheless, such distinctions, which are also boundaries, are beginning to give – not only in an epistemological and anthropological perspective as explained here. Against the background of modern scientific and technical developments, the possibility has raised its head that along with the rational nature of Man (that which makes him *homo sapiens*) we might change not only his external (physical and social) nature but also his internal (biological) nature. Is his naturalness at risk? Is it at all possible to define this in any detail in a context that is not epistemological or anthropological? And how about the ethical question?

3. The Ethical Question

The recourse to naturalness, which is epistemologically and anthropologically mostly unproblematic, is, however, problematic ethically, in particular, when ethical conclusions are drawn from definitions of naturalness of Man. In such cases, what counts as natural lays claim to moral validity, for instance in Hans Jonas, who declares the natural as the highest norm and views any intervention into natural processes which might be of ethical relevance as an offence against 'naturally' given norms, as something against 'the strategy of nature'.[20] According to Jonas, this is also and, indeed, in particular, valid with respect to the naturalness of Man.

Such views immediately provoke the charge of a naturalistic fallacy, in so far as, apparently, an inference is made from an 'is' (a given naturalness) to an 'ought' (naturalness as a principle or norm).[21] Strictly speaking, however, this charge may only be voiced or, rather, upheld, when an actual *inference* is made from an 'is' to an 'ought'. If instead it is merely used as a point of departure – as compassion is used in Schopenhauer, or the will to power

[20] H. Jonas, 'Laßt uns einen Menschen klonieren: Von der Eugenik zur Gentechnologie', in: H. Jonas, *Technik, Medizin und Ethik: Zur Praxis des Prinzips Verantwortung*, Frankfurt: Insel-Verlag 1985, p. 179.

[21] Cf. D. Birnbacher, who considers in great detail the most important arguments against naturalness as a principle or norm (*op. cit.*, pp. 17ff.).

in Nietzsche, understood as a natural inclination of Man – the emphasis shifts towards the plausibility of that approach itself, in this case, towards the previously described 'dual nature' of Man, expressed in the concepts of natural artificiality and artificial naturalness. Thus it would be an anthropological premise, from which certain conclusions are drawn in an ethical context. In any case it is a *material* approach that causes the problems, if any; the fact that something in particular, namely the natural – in other cases of ethical reasoning it might be conceptions of the good, the just, or the rational[22] – is meant to play the role of a norm or justificatory authority.

The question then is again what may or should be called 'natural'. Clearly, nature as a whole cannot be meant with this, but also a recourse to Man as natural being would not go to the heart of the matter, as illustrated by the complementary concepts of natural artificiality and artificial naturalness. After all, ethics (and morality, of which it is the theory) is always the manner in which Man deals with his natural inclinations and needs, thus cultivating them.[23] Immanuel Kant even declares this the 'essential purpose of humanity', that is, as the purpose in the realisation of which the true nature of Man finds its expression. 'Whoever subordinates his person to his inclinations, acts against the essential purpose of humanity, since as a freely acting being he should not be bound by his inclinations, but should instead determine them through freedom, as when he is free, he must have a rule, but this rule is the essential purpose of humanity'.[24]

Connected to this purpose in Kant is the concept of *dignity*, making reference to the 'dignity of a rational being',[25] in more recent discussions the concept of a *species ethic*. This concept – and thus a 'moralisation' of human nature – is used by Jürgen Habermas against interventions in the integrity of the human species, for instance using the means of reproductive medicine.[26] Thus the natural foundations are at issue, and, in that sense, again what is essential to human nature. If we also count the cultural nature of

[22] See O. Schwemmer, 'Ethik', in: J. Mittelstrass (Ed.), *Enzyklopädie Philosophie und Wissenschaftstheorie*, vol. II, 2nd ed., Stuttgart and Weimar: Metzler 2005, pp. 404-411.

[23] Again, see D. Birnbacher, *op. cit.*, pp. 49f.

[24] I. Kant, *Eine Vorlesung über Ethik*, ed. G. Gerhardt, Frankfurt am Main: Fischer 1990, p. 135.

[25] I. Kant, *Grundlegung zur Metaphysik der Sitten*, *Werke*, vol. IV, p. 67.

[26] J. Habermas, *Die Zukunft der menschlichen Natur: Auf dem Weg zu einer liberalen Eugenik?*, Frankfurt am Main: Suhrkamp 2001, p. 27. Cf. the discussion in D. Birnbacher, *op. cit.*, pp. 169ff., and M. Kaufmann/L. Sosoe (Eds.), *Gattungsethik: Schutz für das Menschengeschlecht?*, Frankfurt am Main: Lang 2005.

man as human nature, the fact that Man is by nature a cultural being, in other words, that the definitions of natural artificiality and artificial naturalness are again applicable, interventions in his biological nature would change his entire nature – in a manner that possibly cannot be calculated or controlled. Thus the request for a species ethic.

In the Kantian tradition, such an ethic is only conceivable if it is, at the same time, a version of a *rational ethics*, that is, of an ethics that has its universal basis in a formal principle formulated in accordance with the Categorical Imperative, or else biological classifications or categories would take the place of ethical categories. But this means that an ethics of human nature that may be called a species ethic is not, if properly understood, an ethics of a particular kind, that might possibly be subject to the charge of a naturalistic fallacy, but an implication of a rational ethics, with which the principle of human dignity, which, speaking with Kant, expresses 'the dignity of a rational being', is applied to the entire human species.

Concluding Remark

Will Man put at his own disposal all the 'parts' that make up his essence – body, soul and reason? Has he become master of his own nature in a sense which would have been unimaginable even for Pico della Mirandola or Kepler? I think that we must accustom ourselves to the fact that this disposal of Man over himself will increase, driven as it is by scientific and technical development. But we must at the same time preserve, in opposition to this development, those indispensable things which are experienced in love and in happiness, in sickness and in death, and in which, despite the threat of the triumph of *Homo faber* over *Homo sapiens*, an essential part of our humanity is contained. Might this be what Pico della Mirandola meant when he had God say to Man that the latter was created neither heavenly nor earthly, neither mortal nor immortal?

Movements exist today that do not want to stop there. So-called 'Posthumanism' or 'Transhumanism'[27] is endorsing a perfectioning of Man, made possible by technological and medical advances, as well as the overcoming of the limitations of the species Man which have been taken as natural till now. The

[27] See L.M. Silver, *Remaking Eden: Cloning and Beyond in a Brave New World*, New York: Avon Books 1997, London: Weidenfeld & Nicolson 1998; N. Bostrom, 'In Defence of Posthuman Dignity', *Bioethics* 19 (2005), pp. 202-214.

question here is not merely whether this is playing God[28] or whether a new Pandora's Box is opened, but also, as to what species Man might be considered to belong if, as envisioned, he would have left his own species. After all, things such as the experiences of contingency, of neediness, and of ageing[29] are at issue here, which until now had been considered constitutive of the human species. But independently of that, this example equally illustrates the difficulties generally involved in a definition of how human nature is to be understood.[30] But it is also clear, on the other hand, that it is not just the perspective of biological evolution, thus a *descriptive* perspective, but also the perspective of cultural evolution, thus an *ascriptive* perspective, that will play a role.

This may be illustrated in yet a different manner. God's order to Man to subdue the Earth certainly didn't include the order to subdue himself, neither in the categories of master and servant, nor with respect to his essence, which is reflected, for instance, in the previously mentioned experiences of contingency and neediness. Wherever Man attempts to modify his own essence, his own nature, he is at risk of losing his very nature, the nature that makes him human. Natural artificiality and artificial naturalness would lose their balance. Man would assimilate with his creation; he would return to a paradigm of machinery, which has already unsettled thoughts and feelings once before, in early modernity. For after Man there wouldn't be Man, but a product (of Man), setting about to take the place of Man. The *conditio humana* would become a *conditio technica*; the species Man would have ceased to be itself; it would have crossed species borders. But this also means that Man, in a certain sense, cannot be optimised, at least not insofar as with such an optimisation he would step out of his own nature – however difficult it might be to define that in any detail.

[28] See M. Midgley, 'Biotechnology and Monstrosity: Why We Should Pay Attention to the "Yuk Factor"', *Hastings Center Report* 30 (2000), No. 5, pp. 7-15; L.R. Kass, 'The Wisdom of Repugnance', *The New Republic* 216 (1997), No. 22, pp. 17-26, also: *Life, Liberty and the Defense of Dignity: The Challenge for Bioethics*, San Francisco: Encounter Books 2002, 2004.

[29] See also C.F. Gethmann *et al.*, *Gesundheit nach Maß? Eine transdisziplinäre Studie zu den Grundlagen eines dauerhaften Gesundheitssystems*, Berlin: Akademie Verlag 2004, pp. 10-23.

[30] Cf. on this also N. Roughley, 'Was heißt "menschliche Natur"? Begriffliche Differenzierungen und normative Ansatzpunkte', in: K. Bayertz (Ed.), *Die menschliche Natur: Welchen und wieviel Wert hat sie?*, Paderborn: mentis 2005, pp. 133-156.

DISCUSSION ON PROF. MITTELSTRASS' PAPER

PROF. PHILLIPS: I am trying to figure out where to start. You presented a very clear plea, I think, that we do not mess around with our genome, I think that is what you are telling us, because we would therefore risk not being human. Now, we have messed around with the genomes of the rest of Creation for quite some time, in both so-called natural ways and, more recently, what people might call unnatural ways, but a lot of people would say there is not much distinction between breeding and recombinant genetics but you want us to stop at ourselves and you draw a distinction between the biological and the social. Now, we have doctored ourselves up socially and culturally very often to the tremendous detriment of the human condition. Some of the worst things propagated in human history have been the result of deliberate attempts to change our culture and our social structure, Nazi Germany being one of the more recent ones, but we have done plenty of other terrible things to ourselves as human beings culturally. So what I am trying to understand is, why are you so afraid, and I must admit I am too, of the biological aspect of this tinkering when it seems that we have done all of this cultural tinkering, we have done all this biological tinkering with the rest of Creation and what you are saying is well, yes, fine, but let us stay away from our own genome?

PROF. MITTELSTRASS: Well, I did not say stop wherever the human genome is involved. I only wanted to point out that this is quite a very new situation in which we are, or a situation which will come up very soon. Be careful because intervening with this biological nature of man may be a completely new situation for *Homo sapiens*, so I did not say stop where you are, stop medicine for example, not at all, but always be careful that you are now intervening with your own biological nature.

PROF. PHILLIPS: Part of the fear of messing around with our genome is that we do something that is, at least in some regard, irreversible. That is, when we change something culturally, well, you can always say in the next generation we could fix that, whereas, if you change something genetically, it is in there.

PROF. MITTELSTRASS: That is another important aspect, of course. I did not touch on that here.

PROF. PHILLIPS: Should we, for example, keep a gene bank of older human beings just in case we want to go back? I mean, we do that with all sorts of grain.

PROF. MITTELSTRASS: That is something that I would like to leave to you.

PROF. CABIBBO: At the moment we are not going very far, no?

PROF. PHILLIPS: No, we are not going very far. It is probably time to let someone who knows what they are talking about ask a question!

PROF. COLLINS: Thank you for a very provocative, thoughtful presentation. I must say I attach myself mostly to your conclusions. I do think, though, that the modification of the human germline presents another major ethical challenge that may, to our benefit, be fairly insurmountable, and that is the safety question. It is really difficult to imagine a circumstance where it would be considered ethical to alter the human genome in the germline in a way that will affect future generations, given the uncertainty of the consequences and the usual expectation that surprises occur when you modify the genome. It is hard to imagine how such an experiment could be considered ethical, given that the individuals whose life would be affected are not available to give their informed consent at that time. So it seems to me much more likely that this area of human enhancement, if you will, will not involve a manipulation of the germline but will be ways in which we use the tools of genetics and genomics to enhance ourselves, perhaps by coming up with strategies that make us stronger, for instance, which are already somewhat feasible using gene transfer in the muscle. Or, as we get smarter about how the brain works, perhaps enhancements that will improve memory or even mathematical abilities or other aspects of higher brain function which, if applied universally, and of course they probably would not be – there is a real risk here about the haves and the have-nots having a greater separation with such enhancements – but, if they were applied universally, you could imagine the same outcome that we would end up as a species whose functioning is categorically rather different than what we, in our natural state, might be able to achieve. So I wonder what your thoughts are on the differences between those scenarios, one where we have irreversibly engineered our genome so that, at the DNA level, we are no longer *Homo sapiens* as opposed to one where our DNA still looks like *Homo sapiens sapiens* but we have acquired these enhancement abilities that causes our functioning, biologically, to be quite different than in our natural state.

PROF. MITTELSTRASS: Thank you very much for this comment, I quite agree.

PROF. COLLINS: Well, I was hoping you would comment, actually, on the difference in terms of theological, philosophical and ethical considerations about this alternative scenario where the germline is being left alone but we are enhancing ourselves in somatic ways: are considerations the same in that circumstance?

PROF. MITTELSTRASS: I have to think about that before I can answer.

PROF. M. SINGER: I was intrigued about the division you made between genetic and artificial naturalness. I did not catch all the words, but I thought about how we could put your words in the framework of the biological terms, phenotype and genotype. The genotype is what you have in your DNA, as we find it in the human genome, but the phenotype describes the qualities that we see. It is probably going to be important to take into account some very new information about biology, some of which remains to be reproduced carefully. We now understand, that environmental influences, both internal environmental issues such as hormones and external environmental influences, can influence the phenotype that we have by changing the level of expression of genes. So we know now that DNA can get modified from the state in which we inherited it in response to such environmental influences and that this, then, can change the way in which those genes function. We know something about the chemistry of this, already. Just to give an example: when we have an emotional reaction to something, we release, as we all know, certain hormones and, in some instances, such hormones have the ability to make these modifications on DNA and related molecules that can then influence the level of gene expression. So, in a sense, that is artificial naturalness because it is responding to the environment as I understood the way you talked about it. I thought it was probably important just to introduce this idea into our discussions because, in the future, we will all have to deal with this newly recognized biological response.

PROF. MITTELSTRASS: Thank you very much. I tried to point out that distinction by using the distinction between the genetic and the qualitative but, of course, I believe it is the same distinction and perhaps it would be better to use the biological terminology here to be clearer than I was, thank you.

PROF. DEHAENE: Yes, I am venturing into this domain which I do not know much about. I was a bit overwhelmed by the philosophy that you presented but I would like to try to think clearly about some concrete case. It is tempting, of course, to establish a distinction between what is biological and what is cultural or mental, and our minds do this quite spontaneously, but in reality cognitive neuroscience shows that the boundaries are blurred, particularly because culture has been modifying our brains for a very long time. Yesterday I tried to argue that the invention of reading and of symbols has created massive changes in the way we are able to operate – with the same brain, of course, but, because we apply this education process very early on, we change the brain architecture. I could have given another example. There are beautiful examples in the domain of tool-learning in macaque monkeys: macaque monkeys can be taught to use tools and when they do so patterns of gene expression change in the parietal cortex, patterns of connections change, and this is a beautiful model for what probably happens in our brains when we learn to use tools. In brief, education is one way in which we have been constantly changing ourselves, and mostly for good, I would think. The other very concrete domain, genetics, is a little bit out for the moment, but brain-computer interfaces are going to appear in the next few years, they are already there. It will be very desirable, in many cases, to have extensions of our brains through a link with an external computer. In fact we are already doing this, we all carry iPhones and all sorts of items that extend our memories. So my question is: where is the boundary that you want to draw in these very concrete cases?

PROF. MITTELSTRASS: That is a very difficult question. As a matter of fact, as you said, we are always crossing the line in both directions but this does not mean that to make the distinction is not important. We have to refer to such a distinction in order to understand what we do. This does not mean, of course – I think I have made that clear from the beginning – that I am not talking about two essences of man, two kinds of nature. It is the particular nature of man that, well, what I tried to formulate in that language, artificial naturalness and natural artificiality, that this exactly is the particular situation in which we are, that is, the particular nature we call human nature. So what I tried to make clear is the distinction itself, how to apply this distinction in order to understand what we do in science and in other areas is another thing, of course, that is the most important one. What I wanted to do is just a conceptual clarification.

PROF. ZICHICHI: Thank you, Professor Mittelstrass. I would like to introduce a parameter in your definition of nature versus directed evolution and this parameter is mankind's lifetime or, if you want, the amount of years needed for civilisation to start, which is agreed to be around 10,000 years (human lifetime is about 100 years). Now, how many million years should we have waited, via biological evolution, in order to have a man who would be able, through his eyes, to see the opposite side of the moon? I had the privilege of knowing the inventor of television, Vladimir Kosma Zworykin, and he told me that the reason why he invented television was to give an instrument to mankind to see the opposite side the moon. How many million years should we have waited for mankind via biological evolution, including genetics and all genetic engineers, for mankind to be able to fly at supersonic speeds? A million, trillion or infinite number of years? What is the reason for this breakthrough? My dear friends and colleagues, it is the discovery of the fundamental laws of nature, which we call science. If you know science you give to mankind, via cultural evolution, the technology that would need an amount of years greater that the life of the cosmos for biological evolution in order to get the same results. Since the author of the laws of nature is the same, we should include in your interesting definition of naturalness whatever is derived from the fundamental laws of nature. I repeat, the parameter which you should use is 10,000 years. There is no question that, without the discovery of the fundamental laws of nature, which have the same author, who is called God, we would not be able to have this incredible evolution called cultural evolution which is, in the modern terminology, science. In other words, scientific evolution is by far much more important than biological evolution because, through scientific evolution, you give man the possibility of seeing with his eyes objects or hear what is being said billions of km away and to fly at conditions which would never be obtained via biological evolution, including genetic engineering. Thank you.

PROF. MITTELSTRASS: Well, thank you for this comment. I did not reconstruct the development of evolution which led to the present situation. My intention was to describe the present situation, the present understanding and, of course, in doing so, science is the most essential or very essential expression of the rational nature of man. I was not dealing with the question of how it came to that situation.

PROF. RUBIN: Thank you. I have a question that goes to almost all the talks we have been hearing in the last four days. I am not a biologist and I have heard very interesting discussions and I have never once heard the word 'woman'. At first, I started counting and after I got to about 150 'men' in a single talk I stopped counting and so my question is, is this a term that is common to biology? Does 'man' give life to women? I think you understand the question but it is not only to you.

PROF. MITTELSTRASS: No, no, I know, but I can only speak for myself. I put, as I might have said, 'Man' in capital letters.

PROF. RUBIN: But I cannot hear a capital letter!

PROF. MITTELSTRASS: Of course not! I tried to reformulate this by in always mentioning 'man and woman' or talking about mankind so this is a linguistic artificiality I do not like at all; I would like to make it quite clear that I am not only talking about man and that I do not distinguish between man and woman, not at all.

PROF. RUBIN: But I really mean, as far as I have tried to listen, I have not heard the word 'woman' here once in four days, so I do not know whether that is a trivial point or a major point but it would be nice if somehow it were modified.

PROF. POTRYKUS: I would like to come back to one of the first questions: whether it would be wise, unwise or should even be forbidden to change the genome of man (and woman of course, I am sorry), of the human being. I think the comments we heard about cases where we could change the human genome in the germline are still, I think, rather in the area of science fiction and here, I think, we would have really very severe problems, but I would like to point the question to the situation, which I think is developing relatively quickly, should we agree to change the genome if this can be helpful in medicine? It would have no consequences for offspring but it would only have consequences for the individual human beings and I think that is the burning question, because the technique is developing so that it will be possible very soon and I think for this reason we should have a clear answer.

PROF. MITTELSTRASS: I believe this is not a question I should answer. What I have made clear is, I hope I did, that I did not say stop wherever you come close to that question but consider it carefully. I was arguing for a scientifically informed and philosophically reflected position, that was my intention, to make that clear, and that refers to every particular kind of problem in that area.

PROF. COLLINS: Just a point of information relevant to the last question. We are doing this, in fact, and I think perhaps people are unaware that we have been doing somatic DNA therapy for decades. When you immunise a child against a particular virus, for instance, whether it is measles or rubella, you are inducing a DNA rearrangement in the immune cells of that individual and we not only think that is acceptable, we think it is admirable and that parents that do not do that are, in fact, not practising their proper role as benevolent parents. And in the field of transplantation, when you transplant an entire organ, you are certainly moving that DNA from that person into another person in a fashion that represents a massive rearrangement of the somatic genotype and certainly in gene therapy of the somatic sort, which has certainly had its ups and downs but is having some recent successes as, for instance, in the treatment of haemophilia or a certain type of blindness, I think the wide range of ethical perspectives on this is that, for medical purposes, this is consistent with medical traditions of other sorts and presents no major ethical problems. I think the real question is, if you move from the medical application to the enhancement of what is already a normal state, then what are you doing? If your gene therapy is not to cure blindness but to try to make somebody stronger or thinner than they would have been in their normal state, is that an acceptable application? And the problem I see there is that there is no bright line between the medical and the enhancement applications because, after all, as I started out saying, vaccination is an enhancement.

PROF. CABIBBO: Thank you for this very interesting comment. Another way in which we modify ourselves is with tattoos. Probably no one here has that modification but it has a long history so, in a way, there are modifications where you can go back, like the iPhone, which is an addiction, but then you can put it down and say, 'no iPhone today'. Then there are tattoos, vaccinations etc., or modifications of the germline.

PROF. SWARUP: This discussion reminds me of the movie *Brave New World*: Alpha, Beta, Gamma, Delta, and finally the boy, Alpha, got enticed by a girl from the forest and he changed, so I wonder whether the human intelligence, the survival of the fittest as we have it, human intelligence, whether you call it culture, has continued to increase for survival of ourselves, what you may call Natural Selection or whatever. We want to live in this world and want to be good so that human society, not only our children, but our own larger society or culture continues to survive forever. So I am quite optimistic, in spite of all medical revolution. Are you an optimist, Professor Mittelstrass?

PROF. MITTELSTRASS: Yes, I am.

PROF. PHILLIPS: I think that one of the reasons why this talk has generated so much discussion is that you have been explicit about something that, perhaps, most of the rest of the presentations have skirted around, namely what should we be doing as opposed to what can we do or what has already happened. This is an extremely important question and one certainly very appropriate for us to bring up in this body. Listening to all of these questions I am trying to develop a synthesis of what are the important questions and one of the things – well, of course, Francis really made a very important distinction – we all have to keep in mind the difference between somatic and germline changes and when I was asking about permanence, of course, I was thinking about germline, but as we were reminded by Maxine and Stanislas, even things like education change us in physical ways. Whereas we might make a distinction between cultural and biological changes, we cannot uneducated ourselves. We might be able to put down the iPhone but we cannot uneducated ourselves, we cannot reverse the changes that have been made to our brains especially when we were educated at a young age. These are things that cannot be reversed although the next generation, presumably, could start off with a kind of *tabula rasa*, or at least we believe that is the case. And so what I am wondering is, is the kind of question that we should be asking ourselves between germline modification and everything else which may be of basically the same character because it seems that, with our present understanding, there is not that much difference between education, nutrition, athletic training and gene therapy, because both change our bodies in ways that are more or less – sometimes a lot more and sometimes a lot less – permanent. I mean, Francis is pretty tall: it is not because his genome is different, it is because I assume his nutrition was particularly good and his parents fed him well! Even a hundred years ago it was extremely rare to have someone as tall as Francis. So we have had huge changes in our bodies by things that would have been normally classified as being cultural-social, certainly not genetic or biological. So, I do not expect you to necessarily give an answer to this, but I want all of us to be thinking about this: is this where the bright line is: between changing the germ line and everything else that one might do? In other words, giving the next generation a new set of genes to work with as opposed to giving them the same genes that we came with and the same opportunities and dangers of education and nutrition and gene therapy. Is that where the bright line is?

H.E. MSGR. PROF. SÁNCHEZ SORONDO: I just want to recall that when the DNA was discovered, Nobel laureate Max Delbrück said that, if a Nobel Prize were to be given to someone in antiquity, then he would give it to Aristotle because his idea of form or soul for living beings is the same as the one postulated by the DNA, i.e. a project that self-develops on its own and remains the same throughout life.

PROF. LE DOUARIN: I would like to say that there is a great difference between changing the germline genome and changing the connections in the brain and educating a certain person. When a person is educated, the children he will have will not get this education at birth, it is not transmissible, so changing the germline is something completely different.

F. CAVALLI-SFORZA: I would like to point out that it seems to me that the problem with our cultural evolution is that we are not aware of the long-term consequences of our actions. I mean, every innovation, every cultural innovation is usually prompted by the desire to bring some benefit, usually a very material benefit. We can see ideas like an equivalent of mutations in the cultural context and, to make a couple of macroscopic examples, it was most likely women who invented agriculture, because they were the ones who had the most advantage in bringing the fields closer to home, since they were the gatherers in the hunter-gatherer society, but they could not imagine, the first agriculturers, that, after a few thousand years, the invention that they started and which has multiplied the human species – because in ten thousand years we have grown a thousand-fold from a few million to a few billion people – they could not imagine that agriculture would also start those deforestation, desertification, pollution processes of which today we are beginning to pay the price on a planetary scale. To make another example which is closer to us, the automobile was, for a hundred years, the symbol itself of progress, of advancement, of well being, whatever. We could not imagine one hundred years ago that automobiles would have brought the range of pollution, of toxins, of ecological problems that we are having to face today. So, I think that is the key point when we speak of our cultural future, that we must very carefully try to investigate what will result from our innovations.

Session V

IMPACT OF HUMAN ACTIVITIES: EVOLUTION, ARTIFICIAL INTELLIGENCE, COGNITIVE SCIENCE AND PUBLIC PERCEPTION

EVOLUTION AS SCIENCE AND IDEOLOGY*

STANLEY L. JAKI

Although the three words that form the title of this essay may seem obvious, a close look at each may be enlightening. The word 'ideology' is now little more than two hundred years old. The word 'science' originated at least two thousand years ago and stood for a deductive form of reasoning. With Newton's *Philosophiae naturalis principia mathematica* the word 'science' began to take on a special meaning. Eventually the word 'scientist' appeared to distinguish some reasoners from others. Although theologians, and even some philosophers, call their fields a science, nobody would take them for scientists. Scientists are those for whom exact measurement is the ultimate test of truth, regardless of whether they reason deductively or inductively. The heavy reliance on numbers differentiates science, that is exact science, from all humanities. But even within the branches of exact science, such as physics, astronomy, chemistry, and molecular biology, there is a difference between proofs and the hope that the evidences on hand answer all questions. This difference looms very large in most discourses on evolutionary biology.

As for the word 'evolution', it long antedates Darwin who aimed at giving a new account of the origin of any and all species. He did so in terms of two principal arguments. In one he appealed to the imagination by portraying the variations observable in nature, the geological succession of organic beings, their geographical distribution, and the data of morphology and embryology. Inserted in these themes, so many chapters in *The Origin of Species*, were chapters about the struggle for existence, about natural selection, and about the survival of the fittest. In those chapters Darwin repeat-

* Apart from minor stylistic changes the text of this essay is identical with the one put at the disposal of the participants at the Plenary Meeting. Additional are the references of which the first should seem substantive even by its length.

edly referred to the mechanism of evolution (his second principal argument), as the impact of the physical environment on the difference between parent and offspring.

This mechanism could in principle turn speculations about the vast variety of species in space and in time into a scientific subject because that impact could be evaluated quantitatively. Such evaluations were not attempted by Darwin, nor by most Darwinists. They readily overlook the fact that 'could be' is not equivalent to 'is' or 'having been done'. Overwhelmed as they were and still are by Darwin's appeal to imagination his admirers think that this difference between 'could be' and 'having been done' can be taken lightly. In addition they are motivated by ideological considerations that vary from crude materialism to misguided theism. The result is a huge imbalance between what is proved and what is assumed to have been proved. Therefore a close look at the third word 'ideology' in the title of this paper should seem useful.

The complexities implied in the word 'ideology' can be seen by a quick look at the article 'ideology' in *Wikipedia*. Just as complicated is a shorter article in the *Encyclopedia of Philosophy*. In neither is it noted that the world 'ideology', which first appeared during the early years of the French Revolution, reflected the hope that a heavenly city could be implemented on earth. Hope, which is a major factor in human life, is a distinct note in *The Origin of Species*, in spite of the fact that it is heavily built on a ruthless struggle among the various species. In promoting a ruthless class struggle Karl Marx found a confirmation for it in *The Origin.* As for democracy, it is propelled by the hope that one can implement a social system in which all have not only equal rights but also equal opportunities. Capitalism, at least in its moderate form, is the hope that all can be shareholders and hold safely unto their shares, a hope rudely shattered in our very days. Hope has been the defining feature of Christian faith, which, alone of all hopes, contains warnings about Utopias, possibly the most hollow of all dreams.

So much in a way of a broader background to this paper's principal aim which is to remind one of the enormous and enduring difference between what Darwinism as a science has so far demonstrated and what it promises as an ideology. I hope that a reminder of that difference will not result in my being taken for a minimizer of the scientific merit of Darwinism. I hold its mechanism to be the only, I repeat, the only prospect that any reasoned discourse about the vast variety of species can be turned into science. I have been a resolute opponent of creationists, of champions of Intelligent Design, but also of Darwinian ideologues. One of these was Darwin himself as he tried to minimize the enormous shortcomings of his mechanism of evolution. Particularly telling were his efforts to talk around the absence of transitional forms. He also admitted that he found no observational evidence for the transformation of a single species into another.[1]

The imbalance between proofs and hope was very obvious already in Darwin's *Early Notebooks* which he filled between 1836 and 1844, following his four-year-long voyage aboard the *Beagle*. During that trip he lectured, with Bible in hand, Captain FitzRoy on the evil of cursing. But

[1] Darwin made that admission in his letter, of March 8, 1861, to Alexander Goodman More who had earlier supplied him with various kinds of orchids. A part of Darwin's letter first was found by Maurice Vernet in the British Museum, who published its photograph as frontispiece to his *Evolution du monde vivant* (Paris: Plon, 1950), with a French translation. E. Gilson quoted it in his *D'Aristôte à Darwin et retour. Essai sur quelques constantes de biophilosophie* (Paris: J. Vrin, 1971), p. 160. The full text first appeared in volume 9 of *The Correspondence of Charles Darwin* (Cambridge; New York: Cambridge University Press, 1994), pp. 49-50. The part of Darwin's letter not relating to orchids runs as follows with the part given by Vernet being put in brackets. The full text shows Darwin's often faulty reasoning which included seizing eagerly on analogies from other branches of science, in this case, physics and the treatment there of the status of the ether. In view of Darwin's heavy reliance on Blyth's articles that appeared between 1835 and 1837, one can also doubt the sincerity of Darwin's statement that it was after many years of thinking that he attributed the role he did to natural selection: 'I am not in the least surprised at your demurring to accept my notions of species. It took me long years before I converted myself; th[r]ough daily thinking and observing on the subject. You ask why I should not draw a line and allow natural selection to do a little work and no more. I can give no direct answer to this. But I think you do not fully see how, as it seems to me, the subject may be directly approached. Take the case of Light, – existence of Ether, and the existence of its undulations are both absolutely hypothetical or conjectural; [but because this hypothesis explains and groups together a multitude of phenomena, it is now universally admitted as a true theory. So, as it seems to me, the descent of species with their modifications through natural selection groups together and fairly well explains many phenomena (as classification, morphology, rudimentary organs, embryology, partially Geogr. Distrib. and partially Geolog. succession), and *therefore* I believe in its truth]. These phenomena are otherwise inexplicable, and my many hostile Reviewers have hardly attempted to improve my explanations, therefore I believe Natural Selection will after many years prevail'. It surely prevailed but not on account of measurements and calculations. Darwin proved himself a poor reasoner in defending the role of natural selection. It did not gain in convincingness because its critics could not provide something better. Tellingly, within forty years the ether began to be discarded by physicists, because experiments aimed at detecting it proved to be futile.

already Darwin's *Early Notebooks* show him a rude derider of metaphysics as well as of the Bible.[2] He seemed to have thought that if the Bible was not trustworthy on one point, it had to be unreliable on all other points. The point was that the Bible allegedly taught the fixity of species as a revealed truth. Later Darwin said nothing less than that all his aim was to discredit the Bible on that particular point.

He certainly succeeded in that latter respect for which theologians and exegetes should forever be grateful to him. Unfortunately, he could not find a single theological writer to explain two points to him: One was that biblical revelation was not given to teach man about how the heavens go, or how anything goes under heaven, but how to go to heaven. The other was that if any statement of the Bible about the physical world was taken for a revealed truth, then consistency demanded that all such statements of the Bible be taken in the same sense.

The pitfalls of this opened widely already in chapter 1 of the Book of Genesis, in which the Hebrew word *min* (kind or species) occurs ten times. But long before that word gave headaches to the Bible's readers, they had more than enough problems there, among them the coming of daylight before the sun. As I set forth in my *Genesis 1 through the Ages*, no other chapter of the entire Bible has been so badly misinterpreted. It is a dismal story, the story of concordism. Written possibly by Nehemiah at least eight hundred years after Moses, the chapter is primarily about the importance of the sabbath rest insofar as God Almighty is set up there as a role model for observing it, after six days' work.

Even today Darwin would not learn this from exegetes who, in order to get around the physical world, present that chapter as a myth without explaining what the word 'myth' means. As for the effort to present biblical revelation in terms of evolution, I would merely recall that Newman avoided the word 'evolution' and used the word 'development'. He saw

[2] The text of the *Notebooks* covering the years 1837-1839 first saw print in 1974 as part of H. Gruber's *Darwin on Man: A Psychological Study of Scientific Creativity*, with P.H. Barrett as the transcriber and editor of the *Notebooks* (New York: E.P. Dutton). Barrett was the chief editor of all the *Notebooks* covering the years 1836-1844 (British Museum and Cornell University Press, 1987), a massive volume in large quarto of almost seven hundred pages. A sampling of Darwin's statements deplored in this essay was given in chapter 2 'The Glorified Ape' of my *Angels, Apes, and Men* (1983; entirely reset edition, Real View Books, 2006), to be soon published in French as *Anges déchus * Singes glorifiés * Hommes créatifs*, tr. J. Vauthier (Paris: de Guibert).

that already in his day the word 'evolution' stood for a process in which the relation of cause and effect was not taken seriously.

Writing about the development of Christian doctrine or dogma, Newman, so keen on the dictates of logic, might say today that only the idea of a supergiant mutation could give an evolutionary slant to the relation of the Incarnation to the Old Testament. In the latter the attributing of a visible form to God, the invisible, was a grave crime. In the New the gist of salvation is that God became flesh and dwelt among men. Let it also be recalled that in biology the idea of giant mutation did not earn credit to its erstwhile proponent, the Marburg paleontologist O. Schindewolf, who, unlike most of his colleagues, took very seriously the enormous jumps between many species. Unfortunately, Schindewolf was active before the testimony of the Burgess Shale, originally spotted in the Canadian Rockies in 1909, was 'rediscovered' in 1962. In that Shale thousands of crustacean species appear suddenly, in defiance of the Darwinian mechanism of evolution, a very slowly working mechanism.

But back to Darwin who, seized as he was with the non-fixity of species, forged ahead with little concern about difficulties in his way. He was so much motivated by his ideology as to plagiarize three articles by a certain Edward Blyth, which appeared in *The Magazine of Natural History* in 1835, 1836, and 1837. In those articles Darwin spotted what in *The Origin* he later presented as the Darwinian mechanism of evolution. Tellingly, in the *Early Notebooks* Darwin said that the credit for a discovery should go not to the one who first proposed it but to the one who set it forth in great detail. Darwin tried to cover up his trail when in *The Origin* he made to Blyth five references, none of which related to the mechanism of evolution. Darwinians showed no outrage when Loren Eiseley, himself a Darwinian, exposed the whole story, first in a long article in 1959, and then in a book, posthumously published in 1979, which contains the full text of Blyth's three articles.[3]

The imbalance between proofs and hopeful vistas in *The Origin* are set forth in various books, one of them Gertrude Himmelfarb's *Darwin and the Darwinian Revolution* (1959).[4] I mention this because around 1980 I suggested to a perplexed student in Princeton to read that book. Her answer

[3] *Darwin and the Mysterious Mr X. New Light on the Evolutionists* (New York: Harcourt Brace Jovanovich Publishers, 1979).

[4] New York: W.W. Norton, 1959.

was that her professor of biology warned the class against reading it. One can easily imagine what Himmelfarb would have said if being told that since then the biology department in Princeton renamed itself Department of Evolutionary Biology. There apparently nothing is supposed to be known about the enormous difficulties of the Darwinian mechanism of evolution, or of the nature of the ideology which gives undue credit to it.

A principal of those difficulties was glaringly on hand as soon as that mechanism was subjected to probability calculus. The one who did this in 1867 was F. Jenkin, a Scottish engineer.[5] Darwin was shattered, but undaunted. Again, Darwin jotted the word *NO!* with an exclamation mark on the margin of his copy of a paper by Wallace who could not see how the large human brain could evolve among simians who had no need for such a brain. In order to prop up his mechanism Darwin was willing, in *The Descent of Man*, to adopt Lamarckism. Still the vast picture Darwin provided in *The Origin* overwhelmingly suggested and still does that all living forms had to be closely interconnected. The first edition of two thousand copies was sold out in three short hours and five other editions followed. Why? – one may ask. The motivations were scientific and ideological.

The principal scientific motivation was the urge to see scientifically verifiable interconnection among all parts, large and small, living and non-living, of nature. This motivation is also profoundly theological for anyone who takes seriously the Creator's rationality. The principal ideological motivation came from the fact that by the 1860s naturalism was the prevailing religion of the educated circles in the British Isles, while society at large wanted to retain some vague traces of the supernatural. This is why Darwin inserted in *The Origin*, from its second edition on, a reference to the Creator, for which he later felt ashamed.[6] But what he should have really regretted was that he forgot a precept he gave himself as he read Chambers' *Vestiges of the Natural History of Creation* sometime in the 1840s. The precept was that he should never use the words 'higher' and 'lower'.[7] He rightly guessed that if evolution was to be a science, it

[5] For details, see my *The Relevance of Physics* (Chicago: University of Chicago Press, 1966), pp. 307-08.

[6] See his letter of March 29, 1863, to J.D. Hooker, in F. Darwin, *The Life and Letters of Charles Darwin* (London: John Murray, 1887), vol. 2, p. 234.

[7] See *More Letters of Charles Darwin*, ed. F. Darwin and A.C. Seward (New York: D. Appleton, 1903), vol. 1, p. 114.

should not contain valuational considerations. As far as science goes, a dinosaur is not lower than a dog, nor is an ape higher than a mouse.

By the time Darwin died, Darwinian evolution was dying in spite of the rediscovery of Mendel's work on peas. A very informative presentation of this is the monograph, *The Eclipse of Darwinism* (1983), which covers the last decades of the nineteenth and the first decades of the twentieth century.[8] A major trouble with this book is that its author seems to take that the revival of the Darwinian theory in full swing by the centenary celebration of the publication of *The Origin* went on without a notable dissent concerning the explanatory power of the Darwinian mechanism as if it had been fully vindicated by Julian Huxley's synthetic theory of evolution.

In fact some leading biologists voiced a sharp dissent. Ernest Chain, who won the Nobel Prize for his work on penicillin, had in mind also that theory, when he wrote: 'Evolution by chance is a [mere] hypothesis based on no evidence and [is] irreconcilable with facts'. He added: 'Evolutionary theories are a gross oversimplification of an immensely complex and intricate mass of facts, and it amazes me that they are swallowed so uncritically and readily and for such a long time by so many scientists without a murmur of protest'.[9]

Slightly less devastating are the words of James Grey, professor of zoology at Cambridge: 'No amount of argument, or clever epigram, can disguise the inherent improbability of orthodox [evolutionary] theory; but most biologists feel it is better to think in terms of improbable events than not to think at all'.[10] Professor Grey was right in pointing out that whatever the defects of the Darwinian mechanism of evolution, it remains the only mechanism with a genuine scientific promise. The promise is that the mechanism can be measured, expressed in numbers with which a true scientific theory should end. Vitalism has repeatedly failed because the so-called vital force could not be measured. Lamarckism failed because it contradicts measurements. No one can measure the drive toward the noosphere and the Omega point as championed by Teilhard de Chardin. He surely increased the already enormous imbalance between what is proven and what some hope to prove.

[8] Baltimore: The Johns Hopkins University Press, 1983.

[9] Chain did so in his address, *Responsibility and the Scientist in Modern Western Society* (London: Council of Christians and Jews, 1970). p. 14.

[10] *Nature* 173 (1954), p. 227.

'Numbers decide', so stated Max Planck as he accepted, in 1920, the Nobel Prize for his discovery of the quantum of energy in which he first did not believe for ideological reasons. Einstein said that if his theory of general relativity was proven wrong by measurements on a single point, the whole theory should be discarded.[11] Niels Bohr did not see that he destroyed his ideology of complementarity and correspondence when toward the end of his life he remarked: 'There is no quantum world. There is only an abstract quantum physical description'.[12]

It took half a century after Jenkin before statistical theory was used on behalf of the claim that favorable mutations may prevail on unfavorable ones. I mean the publication in 1930 of *The Genetical Theory of Natural Selection*, by R.A. Fisher, for which he was knighted.[13] This circumstance merely increased the imbalance between what is proved and what is hoped to be proved. In that book it is not shown that the mechanism worked in a single case. Moreover, the mathematics in that work is not predictive, except in the vague sense that changes would come, which anthropomorphically one would then label as favorable. But again caution is needed about the use of the word 'favorable'. It may be burdened with the same illogicality which has been shown to vitiate the phrase, 'survival of the fittest'. (The fittest survive and those who survive are the fittest). The idea of progress suffers of a similar circularity.

Difficulties of the Darwinian mechanism of evolution do not disappear by the claim that Darwinism rose from the level of hypothesis to the level of theory to neither of which does the literature give a definite meaning. Nor do genetics and chromosomal mapping remove those difficulties. That human chromosomes differ but slightly from those of higher apes only increases the problem of why humans, and they alone, think, speak, and have science as well, all supergigantic differences in respect to apes. I am rather wary to emphasize this but only a month ago I participated in an international conference on what makes man a human being. There one academic from London spoke of the spirituality of apes. Against such thinking there is no arguing. One can only fall

[11] In a conversation he held, during the winter of 1952-53, with Manfred Clynes. See M. Michelmore, *Einstein. Profile of the Man* (New York: Dodd, 1962), p. 7.

[12] *Niels Bohr. A Centenary Volume*, ed. A.P. French and P.J. Kennedy (Cambridge, MA: Harvard University Press), p. 305.

[13] A second revised edition appeared in 1958 (New York: Dover).

back on Saint Augustine's favorite phrase: 'Greatly love the intellect'. The lopsided imbalance between Darwinian proofs and Darwinian hopes calls for the exercise of that love.

Almost two thousand years ago Galen warned the atomists that if consistent they would destroy the mind. Darwin failed to see this when in the *Early Notebooks* he singled out the human mind as the citadel which his theory should conquer. The mind remains unconquerable because all reasoned attacks on it assume what they try to reduce to mere matter and motion, or nowadays to energy levels registered in the brain. Good theology knew the uniqueness of the mind from the moment when the phrase was jotted in chapter 1 of the Book of Genesis that God made man in his own image. As for the death of a God, who is infinitely more than the God of deists, it is still to be demonstrated by some rabid Darwinists, or by some cosmologists who boast of their being atheists. At any rate, to claim, as this has become quite fashionable, that where there is water, or was water, or may be water, there was also, or is, or will be, human intelligence or even an intelligence far superior to man's, is a wild dream but not science, although Darwin would not be sure. He liberally mixed careful observation of facts with loose reasoning. He did not see the difference between deduction and induction. His idol in philosophy was Herbert Spencer, surely a confused reasoner if ever there was one. But Spencer was a great stylist, and all too often this is what counts. This was also the case with Fr. Teilhard who heavily relied on the rhetoric of Bergson, who tried to do the opposite, namely, to discredit Darwinism.

Finally there is, toward the end of *The Origin,* Darwin's marveling at the immense number of forms produced by evolution. He should have pointed out that all those forms were transient and most of them left no trace whatsoever. The theory states nothing about the erstwhile form of those trillions or perhaps quadrillions of forms of which only a relatively few proved to be somewhat stable. Of course, Darwin lived almost a hundred years before the era of fundamental particles of which it was aptly noted that none of them was fundamental or really permanent. The latest chapters in elementary particle theory show a trend toward particle evolution whose starting point nowadays is a complex mixture of abstract dimensions. The question then arises how from abstract forms there could arise concrete forms, let alone trillions of such forms, including all their ephemeral, transitional kind. A similar question was raised about absolute randomness insofar as it is a contradiction in terms. Even more existential is the question about purpose which has no place in Darwinian theory,[14] although Darwinists try to bring it back through the back door to buttress their ideology. In doing so they deserve Whitehead's biting criticism: 'Scientists animated by the purpose of proving that they are purposeless, constitute an interesting subject of study'.[15]

Forms from shapelessness, purpose from aimlessness, conjure up a greyness in which nothing is distinguishable. The specter of that greyness prompted Chesterton to call attention to what really irked common man about Darwin's theory. It was not the question of whether man descended from apes on his father's side or on his mother's side. Ordinary man, Chesterton wrote, could not tolerate that Darwinian ideology made man descend into the murky realms of the 'grey gradations of twilight'.[16] The twilight was both moral and intellectual. On the moral side it gave licence to everything. Aldous Huxley confessed that he and his literary comrades embraced Darwinism because they found in it a *carte blanche* for sexual libertinism.[17] Darwinian ideology was heavily used to justify ruthless economic competition, and even most destructive wars. Lately, it was presented as one principal reason to teach Darwinism in schools, on the ground that it gives man a sense of dignity and optimism.

Darwinian evolution should be taught as a science, with all its merits and defects, but this is the balance which Darwinian ideologues, whether they know the subject or not, are loath to consider. They will state, as did Professor Morrison of MIT, that termites, if given enough time, would come up with a telescope.[18] To accept such a prospect demands from man that he surrender his right to rigor, clarity, and consistency, and above all ignore his duty to show unconditional respect for facts.

[14] Evolutionary theories in the light of the broader theme of purpose are discussed in my Farmington Institute Lectures (Oxford), *The Purpose of It All* (Scottish Academic Press, 1990). Second entirely reset edition (Port Huron, MI: Real View Books, 2005). Italian translation, *Lo scopo di tutto* (Milano: Ares, 1994).

[15] A.N. Whitehead, *The Function of Reason* (Princeton: Princeton University Press, 1929), p. 12.

[16] *The Everlasting Man* (1925; Garden City, N.Y.: Doubleday, 1955), p. 13.

[17] A. Huxley, *Ends and Means: An Inquiry into the Nature of Ideals and into the Methods Employed for their Realization* (London: Chatto and Windus, 1937), p. 273.

[18] In his address broadcast by BBC television and radio. For its text see *The Listener*, August 23, 1979, pp. 234-38.

DISCUSSION ON PROF. JAKI'S PAPER

PROF. COLLINS: Thank you for your presentation. I certainly share with you the deep concern about the misapplications of Darwinian theory when it gets well outside of its boundaries and is used to justify certain kinds of social Darwinian activities which, of course, reached one of its most frightening manifestations in eugenics, but I am troubled that you are blurring together those legitimate concerns with a broader critique of the mechanics of the Darwinian synthesis, which is now more the Neo-Darwinian synthesis, which actually scientifically are quite well established. I think, in a certain way, you diminish your impact by trying to say that all of these approaches are equally troubling. Darwin's synthesis, admittedly, at the time, done through a blurred lens because of the lack of information about how heredity actually works, involved descent from a common ancestor: that, I think, is established beyond any doubt. It involved gradual change over time by variation subject to natural selection: that I think is also established incontrovertibly, especially by recent evidence coming from the study of DNA. So, stopping at that point, I think it would be fair to say that Darwin, imperfect though he may well have been, had an idea that now, 150 years later, since the publication of *The Origin of Species*, has held up to the point where there are almost no mainstream biologists who can think about their science for very long without including that theory, if you want to call it that, although it is a theory in the sense of gravity, in their particular approach to try to answer questions. It is an approach that has not only made predictions that are testable, it is a way of putting together a lot of data. So, that being said, I am troubled by the fact that your synthesis seems to cast those conclusions into doubt, perhaps many times referring back to quotes made quite some time ago and not reflective of more recent observations about biology that are very strongly in support of those main principles. Again I share, let me say that again, though, your concern about the way in which the Darwinian approach has been applied by people with other agendas, that move more into the metaphysical and social arena and that take the principles of natural selection and apply them in ways where they do not fit and where in fact great harm can be done.

PROF. JAKI: I had to leave out, from reading the written text, that in no branch of science, exact science – I am not talking about sociology and psychology and other things – there is no similar imbalance between proofs and hopes, and the proof of Darwinian mechanism must come from the observation of the transitions and Darwin himself admitted that, in not a single case, could he observe a transition and this is even today a fact, it is the fact today.

PROF. BERNARDI: Well, there are libraries on the subjects you dealt with. The real question, in my opinion, is simply the following: what about nowadays? We have sequences, we have plenty of very recent studies. I do not know, simply, anything in the literature of the last few years which is going against Darwin. Actually, exactly the opposite. Darwin is supported by all the new molecular proofs so I do not think – of course one can still raise questions about past history, this does not matter very much – the real point is how is present day science considering Darwin's ideas and the support is 100%. I do not see anything against him in the scientific literature, so one should keep that in mind.

PROF. JAKI: Well, I could refer you to a vast book which Stephen Jay Gould published towards the end of his life, *The Structure of Evolutionary Theory*, in which he collected a large number of his papers and in those papers he repeatedly refers to the faults and lacunae in the Darwinian theory.

PROF. BERNARDI: Yes, I know that book. I do not think there is anything new in that book. One should look at the recent scientific literature. Gould was excellent in writing articles for the Natural History Museum and so on, but I do not think that book, even in spite of being almost 1000 pages, does bring anything really solid against Darwin.

PROF. GOJOBORI: I would like to appreciate your description of the historical argument over Darwin. I do not have a strong intention to defend those descriptions from Darwin but I would still like to say that, in the case of RNA issue, I think he formulated it. Formulation goes like a polymorphism, particularly the degree of heterozygote and a proportion of polymorphic loci. Those kinds of quantities were tested by utilizing protein polymorphism data even before nucleotide sequence data was available. When we consider random genetic drift, then certainly Motoo Kimura formulated it incorporating natural selection and the random genetic drift into diffusion equations. Therefore, a formulation could be conducted, then it was fully testable. Therefore the issue is how much natural selection is taking place, how much random drift is taking place? We had the argument that the terminology solely may be different but still we have to admit that natural selection is taking place and genetic drift is taking place. Therefore, by acknowledging such mathematical arguments, data analysis is conducted under the natural selection from Darwin and random genetic drift. I think the argument should go into the reality, but I would like to join you in agreeing that Darwinian selection should be taught as a science.

PROF. MITTELSTRASS: Would you like to comment?

PROF. JAKI: The short answer is this. No, there is no short answer to the discussion, partly because I do not really grasp what is your question or what is your observation.

PLANT BREEDING AS AN EXAMPLE OF 'ENGINEERED' EVOLUTION

INGO POTRYKUS

Crop and forage plants which cover most of our cultivated land and provide, directly or indirectly, most of our food, have not in fact, and never would have evolved naturally. Their development required the intervention of man into the natural process of evolution.

Man (plant breeders) have used the principles of evolution – genetic variation, sexual hybridisation combined with subsequent selection of the best adapted offspring to specific ecological niches – in several ways: They have increased the frequency of genetic variation by physical or chemical mutagenic treatment. They have encouraged novel genome combinations and recombinations within and across species barriers by intraspecific hybridisation (within species) and by interspecific hybridisation (between species). In those cases where interspecific hybrids were not viable, they used embryo rescue techniques (in vitro culture of otherwise abortive embryos). They transferred random parts of genomes by fertilization with partial nuclei, which they recovered from cells treated so badly that the genome was totally fractionated into random pieces They grew haploid plants from germ cells to achieve rapid homozygocity and they used the cell poison cholchicin to recover polyploid plants. And they have given evolution specific directions by selecting for traits in their interest, and against undesired traits (see Fig. 1, p. 614).

Taking the example of *Brassica oleracea*, it can be well visualized, how breeders have changed the phenotype (and the underlying genotype) of a plant originally created by natural evolution. *Cabbage* is the result of excessive development of a single *terminal bud* (and suppression the rest of the plant); *Brussels sprouts* were created by selecting for mutations leading to development of miniature 'cabbages' from all *lateral buds*; breeders have created *Kohlrabi* by selecting for mutations leading to *swelling of the basal* *stem*, *Kale* was created by favouring *over-dimensional leaves*, *Broccoli* by collecting mutations leading to *excessive overproduction of flower buds and stems*, and *Cauliflower* by an extreme *overproduction of complex systems of flower buds*. All these cabbage varieties are still the same species (*Brassica oleracea*), but they are totally unsuited for survival in any natural environment, not even for independent propagation, and would, therefore, never have evolved without intervention of man. The difference in their morphology indicates the difference in their genome and there is not the slightest doubt that these genomes have been intensively genetically modified – long before the advent of 'genetic engineering'.

Breeders also combined different desired traits (genes) within the species or across species barriers to develop ever improved varieties to exploit the potential nature has provided. Virtually all plants used to date in agriculture and horticulture are intensely genetically modified in the interest of man. None of these biologically disadvantaged plant varieties would ever have evolved and they would disappear within few generations without the continuous care provided by farmers in the artificial habitats of agriculture (see Figs. 2 and 3, pp. 615-6).

All of our crop plants (including those used by organic farmers) were developed (on the basis of such intense and uncontrolled genetic modification!) and were consumed without any special precaution. And there was no harm to the consumer. Instead mankind was protected from starvation, was enjoying an ever improved supply of foods, and an ever prolonged life.

This adaptation of plants to the needs of mankind is a never ending process, with exponential demands to date, because the exponential population growth requires that agriculture is providing an increasing amount of food. To help save harvests plant breeders are continuously challenged by the natural evolution of pests and diseases, which overcome existing resistance. They have to develop novel varieties which are more resistant to biological stresses exerted by novel pathogens. The same is true for physical stresses decreasing possible harvests. And plant breeders have to work on increasing the potential of crop plants to exploit the natural resources (to increase future harvests). It is mandatory to perform plant breeding with ever increasing efficiency. There is no other option for an ever growing world population of already 7 billion to return to pre-industrial agriculture, where only a privileged minority would have a chance for a decent life.

Thus far, up into the 80s of the 20th century, the approach to man-made evolution was based on *trial and error* and *learning from experience* and knowledge was limited to *phenotypes*. It should be considered very fortunate that, just when demand for more food was becoming an overwhelming problem, progress in science was providing, with the advent of molecular biology and plant cell culture, a refinement and extension of the tools for breeding, enabling to adapt plants to the needs of man with increasing efficiency.

These novel tools are now based on *knowledge and understanding*. Complex phenotypic traits can be analysed on the level of genes, their regulatory signals, and their interactions with other genes in biochemical pathways and cellular networks.

To illustrate the difference between traditional and state-of-the-art breeding let us consider one concrete example: Let us assume we want to develop a vitamin A rice to combat vitamin A-deficiency. The traditional breeding approach would explore whether evolution has created anywhere in the world a wild or cultivated rice variety which has a yellow endosperm (which would indicate the presence of provitamin A). The probability is not very high, because this trait does not offer any selective advantage in any ecosystem. The result was, therefore, not surprising. A careful analysis of the entire worldwide gene pool of rice and its relatives disclosed that nature had not developed a plant which could be used as starting material for a traditional breeding program. Breeders had no possibility to work on the development of vitamin A-rice with traditional methods. And therefore breeders asked for help from the upcoming genetic engineering technology. This state-of-the art approach works as follows: The first step is to find out how pro-vitamin A is synthesized in plants (to understand the biochemistry of the biosynthetic pathway including the metabolic bottlenecks and their regulation). This is followed by the elucidation of the genes involved (including the number of genes, and their tissue-specific expression). Thereafter it is necessary to isolate the genes and regulatory signals. This can be done from rice or from a model plant or a micro-organism if this has such a biochemical pathway. The next step tries to introduce the missing genes together with appropriate regulatory signals (in our case signals which activate the genes in the endosperm cells of the seed storage tissue only) into somatic single cells. As this is a random process which requires millions of cells, it is mandatory to add a gene which enables to built up a tight selective pressure, which allows only those few cells to survive, which have taken up and integrated the genes of interest. From those single cells complete plants are regenerated, which finally produce seeds which transmit the novel genes (and traits) to all offspring (see Figs. 4 and 5, p. 617).

Taking this state-of-the-art approach vitamin A-rice became a reality in 1999. Following the same approach, in principle, any complex phenotypic traits can be analysed at the level of genes, their regulatory signals, and their interactions with other genes in biochemical pathways and cellular networks. Genes for desired traits and appropriate regulatory sequences can be isolated, newly combined, and their function predicted and tested experimentally. They then can be introduced selectively into otherwise unaltered genomes, thus providing *'direction'* for evolution even before selection (see Fig. 6, page 618).

This approach of elucidating the molecular basis for a given trait and of designing the biochemical pathways prior to re-introduction into a target plant, can be applied – in principle – to all those traits of outstanding importance for future food security such as drought tolerance, flooding tolerance, salt resistance, heavy metal resistance, disease resistance, pest resistance, improved nutritional value, reduced toxins, allergens, antinutrients, reduced post-harvest loss, improved response to climate stresses, etc. Not only is it possible to introduce desired traits, but it is also to inactivate undesired traits such as anti-nutrients or allergens and traits which are not available in a given species can be introduced from other species. These and other technological possibilities enable breeders to exert 'direction' and to 'predict' novel phenotypes by not only selecting gene combinations from increased variation, but by planning variation and gene combinations 'a priori' and making more efficient use of the potential nature is providing to us.

These improved technological possibilities are urgently needed to secure food for an increasing world population, which will not level off before it reaches 10-12 billion and for which at least twice as much food has to be produced in countries where already now one billion people are starving. And this food has to come from agricultural production systems which are already under tremendous stress because of shortages in land, water, manpower, energy, and capital and which are expected to produce all this additional food with less negative impact onto the environment.

Past progress in agricultural productivity is, of course, not only the success of plant breeding, but of all science and technology invested into agriculture, including mechanisation, synthetic fertilizer, pesticides, insecticides, integrated production, irrigation, expansion of agricultural land, biotechnology, and many more inputs. The challenges ahead will require far more intensive financial investment in further research in all these areas. It would be naive to assume that any one of these contributions alone can solve the burning problems of future food security.

To save the last remaining refuges of natural environments is only possible if we can produce more food on the agricultural land already in use. There is no alternative to intensive and sustainable production systems. And this requires careful exploitation of science and technology and the tools both are developing.

Paradoxically, as long as 'man-made evolution' was based on 'trial and error', without any other knowledge base than 'experience and phenotype' it was considered 'natural' and was accepted by our society. Now where the same is based on 'science, knowledge, predictability, and controlled experimentation', the same process is discredited as being un-natural, highly dangerous, unethical, and unacceptable.

This (typically European) attitude lacks any justification from science, experience, logic, and common sense, but it is a widespread psychological fact, and difficult to change with argumentation based on science and logic. The consequence of this attitude are regulations for the use of the technology, which prevent that the technology is used by public sector institutions, for altruistic solutions in the interest of the poor in developing countries.

Many of the lives lost to starvation and micronutrient deficiency could be saved, if European societies would change their hostile attitude towards this knowledge-based progress in plant breeding technology, which is nothing else but a more sophisticated continuation of the use of genetic modification to the benefit of mankind.

This European attitude is extremely unfortunate for those underprivileged poor in developing countries, for which food insecurity and malnutrition is a question of life and health. As the Nuffield Council on Bioethics phrases it: Europe is ignoring a moral imperative to support use of genetic engineering technology to the benefit of the poor.

Well-fed European societies have forgotten that our agricultural productivity depends upon centuries of exploitation of science and technology and cultivate instead a romantic imagination of farm life which was not even true in 1565, when Peter Breughel painted his popular picture, which represents a dream, not reality. Neither were the farmers well-fed nor the fields so productive and without weeds (see Fig. 7, p. 619).

Millet's picture from 1862 – in contrast to Breughel's – is 'honest' and reminds us that pre-industrial agriculture was, also in Europe, and not so long ago, not at all romantic, but a back-breaking fight for survival – the same way as it is today for hundreds of millions of farmers in developing countries. It is immoral to deny those farmers the help from technology-supported agriculture (see Fig. 8, p. 620).

Use of genetic engineering technology for the adoption of crop plants to the needs of mankind is neither 'unnatural', nor 'unethical', nor 'hazardous', as considered by many European citizens. It is state-of-the-art use of the natural potential. It is at least as safe as previous tools in plant breeding. There is consensus in the scientific community that this technology does not carry any novel inherent risk.

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DISCUSSION ON PROF. POTRYKUS' PAPER

PROF. PHILLIPS: You mentioned that plant breeders, for a long time, have used a lot of different strategies, including increasing the frequency of mutation and embryo rescue. So, in increasing the frequency of mutation, are you talking about actually increasing the frequency at which genetic mutations occur or the frequency at which the mutant plants survive and, in either case, how is that done and what is embryo rescue?

PROF. POTRYKUS: Plant breeders have taken such dramatic measures as firing gamma rays on plants for weeks. I have lived in an institute that has such a cobalt bomb for this purpose, which is destroying the genome completely into small fractions and then you have pieces from the genome and integrate them into breeding programmes. The famous Italian pasta wheat is the result of such a treatment and there are chemical mutagens which are also causing dramatic alterations of the genome. Plant breeders recovered plants from these badly treated genomes and used them in their breeding programs. And what is embryo rescue? You can do fertilisations which normally would not be successful because the embryo aborts. Using plant cell culture technology, you can excise the early embryo, put it onto a synthetic culture medium and grow it into an entire plant.

PROF. LÜKE: I have often read that perhaps it is not the sciences of agriculture that are undeveloped, but that it is a problem of distribution of wealth, distribution between poor and rich people in undeveloped countries. I have often heard we have enough already now, we have enough things to eat but the distribution is not functioning well.

PROF. POTRYKUS: Theoretically, at the moment, worldwide agriculture would produce enough food to feed six billion people. It is true that we have one billion starving people who would not have to starve if food could be distributed equally around the globe. But that is practically not possible. And it would not represent a sustainable solution. For a realistic and sustainable solution we need to produce food in those countries where there is not enough food. This would also require to stop the politics of Western countries of competing with Third World agriculture by providing billions in subsidies to their own farmers. World food production to date would, however, by far not be sufficient to feed 9 to 12 billion people. Therefore, even if we could distribute the food equally (which will never work) it would not be a solution. The situation with regards to food security is far more complex than I could indicate, and I would need a lot more time to explain all that is involved. Let me give you, therefore, a quick answer: the proposal that we do not need to produce more food, that we only have to distribute it right, is a totally unrealistic proposal.

DIGITAL INTELLIGENCE:
THE EVOLUTION OF A NEW HUMAN CAPACITY

ANTONIO M. BATTRO

Many education initiatives around the world show the massive and early unfolding of a new kind of intelligence, a 'digital intelligence' in children of the most diverse cultures and socio-economic conditions at early ages. Those children are becoming the 'digital natives' of this new culture. Children can use computers in creative ways, they learn and teach with remarkable ease in the new digital environment. In this culture *the computer is more than a tool, it creates a new environment*. Our challenge now is to use the new – and universal – digital intelligence in the search of truth, beauty and good.

A new digital generation

Each generation will become more digital than the preceding one

Nicholas Negroponte (1995)

A new environment, a new landscape, a new ecosystem is spreading without frontiers because of the incredible penetration of the computer and the communication technologies in every society, urban or rural, poor or rich. We are living an impressive cultural change that is unfolding from the bottom up, with hundreds of millions of participants, creating a new language, promoting new skills and changing the education parameters. How can we interpret this accelerating wave of changes in the framework of evolution? For Luigi Luca Cavalli-Sforza (2008) 'culture has supplemented biological mutation in producing novelties in the form of inventions'. Jean-Pierre Changeux (2005) explains this impressive leap forward by the 'brain epigenetic capacities to store stable representations of the outside world [that] give human beings the opportunity to create an artificial world of cultural objects at the social level'.

Novelty in a culture is not the result of a random mutation but it is still an unpredictable event whose impact in society has to be evaluated. And this relates to the way the transmission of novelty occurs. In the case of education for centuries the cultural transmission of knowledge was vertical (from adults, parents or teachers to children), now we are witnessing an increasing horizontal transmission (from anybody to anybody) as pointed out by Cavalli-Sforza. This shift has immense consequences on education. In fact humans are the only species capable to teaching (Battro, 2007, Passingham, 2008) and children are very good at that, it is a 'natural ability', in the words of Sidney Strauss (2005). This fact is becoming more and more important as a motor of the digital evolution, because in a society of digital natives there is a growing spiral of teaching and learning at all levels. The acceleration of this process has unique consequences on our culture, in particular in our education. The increasing horizontal transmission of digital skills is adding a most welcomed leverage to the educational system in all places. We have therefore a daunting task in front of us regarding the new ways of teaching and learning in a digital culture. It should be remarked, incidentally, that while we have a wealth of information related to the learning brain that may help to improve the educational practice we still don't know how the teaching brain works. Our understanding of the dialogue between teaching and learning brains will soon increase with the help of new portable and wearable brain imaging technologies to be used in the classroom (Koizumi *et al.*, 2008). In this sense the new trends in *neuroeducation* will also contribute to shape our evolving digital environment (Battro, Fischer & Léna, 2008).

Since the work of Jean Piaget, we know that any particular learning process needs the support of a developmental platform at a specific level of stability (Fischer & Bidell, 1998, van Geert, & Steenbeek, 2008). The core idea of Piagetian 'constructivism' is that we continuously build cognitive structures, and when they reach a certain stability, they become a platform for a new step or stage (Papert, 1986). When a whole population becomes 'digital' the rules of transmission – and construction – of knowledge change significantly. We now have the possibility, perhaps for the first time in history, to follow the evolution of a new human capacity, the digital capacity or intelligence, in a short period of time, in one generation. We can now observe and evaluate the behavioral, cognitive, emotional, and moral changes from early childhood to adolescence in cohorts of hundreds of thousands that are educated in a fully saturated digital environment. The notion of 'digital saturation' can be related to the analogy launched by Jonas Salk concerning the deep relations between epidemiology and education. When we compare passive to active immunization we discover that the first may 'induce a temporary effect of immunity by transferring antibodies from one host to the other, but a long-term immunizing effect can be induced only by the active participation of the host in developing his own antibodies as a consequence of his own interaction with the antigen'. Moreover, '"learning" in immunology or in psychology, is something that involves active effort, and that what is learned is significant and effective in proportion to the effort expended…the analogy to the educational process needs no longer clarification' (Salk, 1972). I like to use the expression 'digital vaccination' to show the need – and urgency – to give to every child in a country the possibility to develop their own digital intelligence. It is a matter of justice and solidarity. It is also a way to reach the Millennium goals proposed by the United Nations concerning the right of all children of the world to receive elementary education by 2015. This is also the mission of OLPC, the One Laptop Per Child initiative (www.laptop.org, Negroponte, 2007, Battro, 2007).

Recycling our neurons for new digital skills

Stanislas Dehaene has proposed a model of neuronal recycling to explain the introduction of new cultural objects in human history and their embodiment in our brains (Dehaene, 2005, 2007, 2008). In the case of reading, he has shown that there are some neuronal networks involved in the detection and identification of forms in nature that are active also in the perception of written symbols. His neural model works as a hierarchy of collections of neurons. The last level of integration is performed by the activation of the visual word form area WWFA in the left occipito-temporal sulcus, specialized in extracting an invariant representation of the visual words. Dehaene (2007) also uses the immunology metaphor to express the formidable impact of literacy in our brains: 'the *virus of reading* is inoculated via the visual path but its influence extends rapidly to the whole of the language areas, where it multiplies our spontaneous competences. When our children learn to read they return from school transformed; their brain is not the same' (my emphasis and translation). In fact the brain of a literate person is different from the brain of an illiterate, as has been demonstrated by neuroimaging in different tasks. What is incredible is that every child is able to learn to read in any language or script. For more than five thousand years scribes have performed marvelous feats to express the human thought with written symbols, today a child must compact this long cultural evolution in the few years of elementary school. A similar 'cultural preemption' – as is called by Dehaene (2005) – can be hypothesized in the case of the acquisition of the new digital skills: the human brain is prepared to deal with the new digital environment, because it can 'recycle' some neuronal networks with a long evolutionary story to new purposes, as we will see later.

Towards a digital intelligence

When we mention the term 'intelligence' we raise a manifold of questions. I will not summarize the history of this extremely polymorphous and complex concept, but for the sake of our experimental and educational pursuit I will follow now the definition given by Howard Gardner in his classical work *Frames of mind: The theory of multiple intelligences* (1983) and revised in his book *Intelligence reframed: Multiple intelligences for the 21st Century* (1999). To Gardner intelligence is 'a biopsychological potential to process information that can be activated in a cultural setting to solve problems or create products that are of value in a culture' (Gardner, 1999, p. 24). A list of conditions for the identification of a particular intelligence in his theory of Multiple Intelligences, MI, is the following:

1. The potential of isolation by brain damage.
2. An evolutionary history and evolutionary plausibility.
3. An identifiable core operation or set of operations (sub-intelligences).
4. Susceptibility to encoding in a symbol system.
5. A distinct developmental history, along with a definable set of expert 'end-state' performances.
6. The existence of idiot savants, prodigies, and other exceptional people.
7. Support from experimental psychological tasks.
8. Support from psychometric findings.

We have already dedicated a book *Hacia una inteligencia digital* (Towards a digital intelligence) to analyze these criteria in detail (Battro and Denham, 2007) and we have concluded that the digital intelligence DI is a fair candidate to be included in the list of eight intelligences, already accepted by Gardner (intrapersonal, interpersonal, musical, logico-mathematical, linguistic, spatial, bodily-kinesthetic and naturalist). We have detected two core digital operations, first the 'click option', second the 'digital heuristics' (exploration, navigation in the digital virtual space). In fact the interaction between a human subject and the computer is based in a very simple elementary behavior, the 'click option', a decision 'to click or not to click'. This can be represented in propositional form in Boolean lattices (Battro, 2004). On the other side, a series of click options, a chain of decisions, unfolds a complex heuristics of a new kind: the exploration of a new human environment, the globalized digital environment.

We have some evidence from the neurocognitive sciences to establish the biological foundations of the click option. Among others the extensive research done by Michael Posner and his team on the attentional neuronal networks offers a good platform for further research on this basic 'digital option' (Posner, 2008a, 2008b). It seems that the executive attention process depends mostly of the activation of the Anterior Cingulate and Lateral Prefrontal cortices, as well on the Basal Ganglia. The prominent neuro-modulator here is Dopamine. Some simple digital skills are observed in very young children, even before they can read or write. We are astonished by the natural and easy way children interact with computers, but if we consider the simplicity of the click option, there is some good and profound reason for that. The answer is in the brain, in the way the click option is prepared and executed. Exactly the contrary occurs when children learn to write by hand. Analog skills need considerable more time. The difference is striking in all accounts, but many schools are still reluctant to provide a digital environment to young children. We must overcome this prejudice. The human brain is already prepared to perform simple decisions from the very beginning of our mental life. The fact that even some animals (birds and mammals) can make a 'click option' and use a computer in elementary tasks is a sign of the deep evolutionary importance of the digital skills (Battro, 2004).

What we lack, however, is a sound neuronal basis for the other core digital intelligence: the 'digital heuristics' expressed by search, exploration and navigation on the network. If we follow Dehaene's model we need to know how the brain recycles the old neuronal networks to explore ('read') a new digital environment with a computer. I would propose, tentatively, to test the neuro-circuitry involved in the spatial abilities. In particular, we find universal spatial invariants in the representation of the urban environment. I will take the model of the 'image of the city' so well studied by the MIT team directed by the great urbanist Kevin Lynch (1960, 1977). In his work it was proved that any landscape or townscape is represented by a set of five invariants: *paths, borders (frontiers), zones, nodes (attractors) and landmarks (singularities)*. Normally, children follow a developmental sequence starting with the representation of the paths and borders and ending as the last step with the landmarks (Battro and

Ellis, 1999). What is interesting for our purposes is that this spatial representation has fractal properties. In other words, the five basic representations are scale-invariant. We find the same five invariants in the representation of a large sector of the town and also of a part of it (a big neighborhood with a park and a small rose garden in a corner of that park show the five invariants already mentioned). I find this fractal invariance as a key to understand the way we explore the digital landscape, the virtual space of the new global environment. In fact, some results show that even in the cultures of hunter-gatherers, these spatial invariances are already detected, and support the tracking skills of the hunters (Leibenberg, 1990). In the same vein Dehaene has investigated the invariance of letters and words involved in reading (size, orientation, position, format, etc). In the virtual space of the digital world we could interpret the sequence of links on a computer as a path, the frames as borders, the folders and menus as zones, the click options as nodes, the icons as landmarks. We can hypothesize that perhaps the same old neuronal circuits used to navigate in the real environment are recycled in the virtual digital space. The famous study of the London taxi drivers has shown how much the brain can change by the exercise of a spatial skill in the everyday practice of navigation in the streets of a large city (Maguire *et al.*, 2000). In this case the posterior part of the hippocampus is enlarged and the anterior part shows a decrease. We don't yet have a comparative evidence for digital navigators, but the study could be done. We need of course more research in this case but everything shows that our globalized culture is producing a new generation of experts, of 'digital natives' with a new kind of literacy that cannot be reduced to the traditional one. Their brains should also be different.

An important aspect of the increasing relevance of our digital intelligence is found in the world of disabled persons. We know how to build many kinds of devices to interface with the computer. Most of them are based on the elementary click option, which is the core of a digital intelligence. Motor and sensory disabled persons can operate a computer with simple switches, using their voice, or a voluntary movement of any part of their body, head, eye, finger or foot (Battro, 2002). In some cases a 'mental click' without any motion can trigger a series of voluntary decisions via the computer using implanted electrodes in the brain of severely disabled patients (Kennedy *et al.*, 2000) or even without invasive technology, just by detecting the local changes in neuronal activation from the skull (Koizumi, 2007). The click option gives the opportunity to reach a new world of knowledge, of communication, of work. The advances in the field of computer prostheses are incredible, and we are only at the beginning. We know, for instance, that hemispherectomized children can use a computer perfectly well; we don't need both hemispheres to acquire computing skills (Battro, 2000, Immordino-Yang, 2007, 2008). These, of course, are extreme cases but they show the road. As Steven Rose said, the future of education is in the margins (Rose & Meyer, 2000). When we allow free and early access to computing and communication no child is left behind and the disabled can enjoy the same privileges. Moreover, many times those devices, equipment and software, provided for the most disabled persons are in fact used by many others, for instance a software tool that helps those children with reading disorders is also useful in the standard classroom.

Biological and educational evolution

I would like to conclude with a reflection on some profound changes that the new digital skills are producing in our culture and the analogies we can establish with the biological evolution. Cavalli-Sforza (2008) says that the development of human language 'has given enormous power to another type of evolution, parallel and interactive with the genetic one: the evolution of culture, intended very generally as shared knowledge'. I think that this idea can shed some new light on the meaning of the invention of the computer as a new tool that is spreading around the planet and creating a new (digital) environment. I propose the following analogies between evolution and education:

EVOLUTION	EDUCATION
Mutation	Invention: computers
Natural selection	Adaptation: digital intelligence
Genetic drift	Digital drift: cohort stabilization (digital natives)
Migration	Globalization: networking

Evolution is about generations, education is about cohorts. A cohort is a group of subjects defined by experiencing an event in a particular time span. The new event to be studied is the education of the digital intelligence. I understand by 'digital native', in the strict sense, the child who has started to use a computer *before* the age of reading and writing. For instance all children starting with a laptop in the first grade (6 years old) belong to cohort 1, the cohort of digital natives. All children starting with a laptop in the second grade (7 years old) belong to cohort 2, and so on. This collection of different cohorts is heterogeneous but will become homogeneous with time, in other words every child will be a digital native if we continue to give a laptop to every child entering school every year. We can say that the school system at this end stage has been 'stabilized' because all schooled children belong to a homogeneous and stable population of digital natives. This is the objective of the OLPC initiative. When the entire educational system of a given city, region or country is stabilized, then, and only then, we can make fair comparisons among ages because all of them are digital natives of different ages. We are witnessing how diverse and multiple individual digital skills naturally improve with practice since early ages and shape with other partners of the same digital culture a new cognitive and practical environment. I consider this phenomenon of homogenization of a population 'saturated' with computers, the analog of the 'genetic drift' that can lead to the final homogenization produced by statistical chance in the evolution of biological populations. The essential difference is that the 'digital drift' is not produced by chance but by the strict execution of a deployment plan and in a short period of time, in the case of the OLPC program the period of homogenization is six years (the elementary school years in most countries). In short, cohort studies are key for educational research and this 'very large cultural experiment' is starting now and will reach millions of children around the world.

A good example in process is Uruguay where some 400,000 children and teachers (www.ceibal.edu.uy) are now receiving a laptop in ownership in the context of an educational national program to saturate the whole public and private elementary school system by 2009. Other thirty countries are following the same trend (www.laptop.org). A case study on 'digital evolution' is now taking place in Niue, a small island nation associated to New Zealand, a 250 Square Km coral island in the Pacific with a population of 1700 and some 400 children, attending two schools, elementary and primary. The island is well connected already by wifi and OLPC has given this year 500 laptops to every student and teacher on the island. Therefore Niue could be considered the first fully saturated 'digital nation'. It is expected that the 'stabilization' of the new digital environment in different regions of the world will provide valuable information about the multiple ways of unfolding a digital culture. This fact reminds the story of Charles Darwin in the Galapagos Islands. Darwin discovered in those islands a variety of finches that were later described as thirteen different species, and this discovery became a landmark in the genesis of the theory of evolution. Are we going to find different varieties of digital natives depending on the culture of the different human societies? We hope so.

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DISCUSSION ON PROF. BATTRO'S PAPER

PROF. CAFFARELLI: Don't you see the dangers of the atrophy of intellectual skills, you know, the same way everyone is worried about genetically modified food and whatever? My impression is that there is a big danger that many skills will have some atrophy, the ability to search, the ability to evaluate information. Now you just click 'go' and you get 5,000 papers that say completely opposite things.

PROF. BATTRO: What is your question?

PROF. CAFFARELLI: The question is, is there the danger of atrophy?

PROF. BATTRO: There are plenty of dangers! If we use the machine outside an education system, without the values I have already said, this is just an instrument, it can be used for good or bad, but if you use it as a digital environment it is completely different, because the children are not doing what you say. This is an impression that many adults have.

PROF. CAFFARELLI: I have two children at home.

PROF. BATTRO: But they are not in an environment where – I don't know, you are in Texas – every kid has a machine, owns a machine. It is not only when they go to school that they have the machine.

PROF. CAFFARELLI: No, no, they are in that environment, everybody has a laptop at home, and they have developed a lot of social skills, they spend their time chatting to each other, communicating and so on, but I think that many skills are being lost. It is an opinion.

PROF. BATTRO: Of course. This is the danger if they are badly educated. But normally there are many coaches and mentors helping them to do interesting things. In some of these remote places the schools have no electricity, have no books, have nothing, and then you arrive with these machines, the first thing you must give is a connection to the Internet. If there is no electric power these machines can be used with mechanical energy or solar power and this is difficult, but we can do that.

PROF. RUBIN: What happens if you give this machine to a 2-year-old?

PROF. BATTRO: Well, of course we did it. You know, the click option is so simple, even animals can do that. Of course most of the research on experimental behaviour is done with rats and the click option is there. Always, at the end you click or not click. Therefore, a 2-year-old is using the machine in very particular ways and many people in these countries are willing to start in kindergarten, but my Japanese friends have told me that in kindergarten it is too late.

PROF. QUÉRÉ: This is a marvellous perspective, of course, but is there any possibility, let us say some risks, that after one hundred or two hundred years, people all over the world will not be able to handwrite any longer, with public writers in the streets, perhaps.

PROF. BATTRO: You are a great writer! Calligraphy or good writing, handwriting can be, perhaps, in the future, a part of the arts and I don't see this problem because I work with children who are very disabled. These children could never write without a machine, and then, in that case, nobody will say, well, he or she has no hands then he or she cannot go to school. This is completely morally wrong. But, when I say that every child should use a machine since the very first day of school there is a great rejection. They will delay the use of computers for I do not know how many years. And this is completely wrong. And I call that the forbidden experiment: the forbidden experiment is to forbid normal children to use a computer before they know how to write. Well, I have my arguments to that but as you have all understood when somebody cannot write because he has no hands he can talk to the machine and write.

PROF. POTRYKUS: A fantastic possibility of training children but the big concern I had last year, when you showed the system, I have eight grandchildren and I know these machines can lead to addiction. I would not support this idea if you cannot describe to me how you control access to the Internet, because that is the big danger I really seriously worry about. You have shown that you have access to Google: how do you control what children are looking at with Google?

PROF. BATTRO: Thank you, this is a very important question and I have some answers. All these machines are already connected without using the Internet. This is a feat that this particularly machine accomplishes. That is why I was connected to Stanislas Dehaene here in this place without going through the Internet because he has a similar machine. Therefore I would say 90% of the use of the machine in such an environment is without accessing the Internet at all. They are sharing things, as I have shown, without going to the Internet, but in the classroom the teachers know where to go on the Internet and she or he is always there. Therefore, there is perfect control of what the children are doing, in the environment of the school. When they leave school they are free, because there is Wi-Fi, but firstly in most places where these children are using computers there is no such thing as a Cybercafé, it does not exist, it is impossible to have any connection outside the environment of the school. Professor Potrykus, you must look at that as an instrument or a new environment in very poor countries, where they do not have books, they do not have electricity, but they are connected and when they are connected they are collaborating and the Internet is only a single point of their activity. I will add, not only are they downloading things but they are uploading things, for instance taking videos or photographs and uploading them to YouTube. It is not only that they are receiving information, they are giving information.

THE TEACHING OF EVOLUTION

PIERRE J. LÉNA

1. A NEW VISION FOR SCIENCE EDUCATION

Since a decade and worldwide, the need for a high quality scientific education for all children and youngsters has strongly been advocated, put forward and supported by the scientific community and the Academies of science. While this action is partly caused by the reluctance of the young generation, especially in developed countries, to choose scientific careers, other important motivations do exist. The need to understand scientific reasoning and scientific issues becomes essential for citizens having to make decisions in a democracy facing complex problems; sharing the prodigious adventure of contemporary science and its beauty, and participating in it are a matter of justice [1,2]. In this movement, new curricula, new pedagogies, new training plans and resources for teachers are conceived and shared worldwide. We may observe the beginning of a revolution in scientific education [3,4,36].

A striking aspect of the new proposed policies is summarized under the motto '*science for all*', meaning that more than ever science education should be conceived for all children, beginning as early as elementary or even pre-school [5,6]. Doing so is justified by the cognitive development of children and youngsters, but is also a way to ensure basic scientific knowledge for all, as well as to create an extended potential source of future technicians, engineers and scientists. Here a question immediately arises: while science is undoubtedly universal in its methods and results, science education cannot escape to be inscribed in a great diversity of cultural and possibly religious landscapes, which are all of human value and must be respected. As Prof. Wei Yu was stating, speaking from a Chinese point of view (in [2], p. 159-165), 'it is highly important to maintain cultural identity or diversity in globalization'. How can this be achieved 'without reason losing its universal essence neither the world losing its cultural diversity' (J. Mittelstrass, in [2], p. 256)?

In this context, the subject of evolution appears especially critical, and it is not a surprise that it has been at the focus of many discussions, or even conflicts, in recent years. It therefore deserves special attention, as being potentially the subject of confrontations of science with myths, epics, religions and inherited representations of the natural world in various cultures. Specifying what is legitimate for science to enounce, with its power and its current limitations, and explaining why this legitimacy does exist, appear essential in order to avoid misunderstandings on the very nature of science, and unnecessary conflicts. Such conflicts appear in today's world and, in some cases, invade schools and confront teachers, and sometimes parents, with difficult issues which may greatly hamper the very goal of a sound, urgently needed science education.

2. Evolution, a broad subject

In the context of darwinism or neo-darwinism, the concept of evolution is often understood as the biological process affecting living species on Earth, and their changes with epochs over a time span of approximately 3.5 billions years: this is *biological evolution*. But astrophysical discoveries since about one century have brought up a vision of our universe where the physical and chemical conditions, which sustained the apparition of life on Earth, manifest themselves the emergence of complexity, over a time span which is now rather precisely specified to be 13.7 billions years: this is *cosmic evolution*. The two sets of phenomena are clearly not independent. First, the apparition of life on Earth has been dependent of the initial conditions existing then and resulting from the previous cosmic history. Second, life changes over further times occurred in close coupling with factors related to the Earth's evolution, both internal – such as volcanism or continental drift – and others being external, mostly related to the evolution of the Sun – such as variations of solar luminosity and ultraviolet flux, of the solar magnetic field modulating the cosmic rays flux, hence the mutation rate, of solar wind emission, etc. Factors related to Solar system history (exchanges of matter between Earth and meteorites or comets) or even to the nearby interstellar environment, such as supernovae events [7] must also be considered. These coupling mechanisms have operated on a grand scale, the most spectacular example being the transition in the atmospheric composition of the Earth, from an initial, reducing, quasi-equilibrium inert atmosphere to an oxidizing one, only sustained today by its equilibrium with living organisms. This is *planetary evolution*.

It is quite obvious that our present knowledge of cosmic evolution is still fairly limited to large-scale phenomena, like the apparition of hadrons, atoms, molecules and cosmic dust particles, and the formation of galaxies and stars. Observations of galaxy clusters, gravitational lenses and supernovae as tracers of the universal expansion have even revealed that classical, hadronic matter is only a small fraction (less than 5%) of the total matter-energy content of the known universe: *dark matter* and *dark energy* have been introduced as new, quite mysterious components of reality. Speculations over the existence of parallel universes (*multiverse*) have even broadened the realm of possibilities [8].

On the other hand, while our Solar system was the only one known to contain planets and life, a wealth of discoveries since 1995 has revealed hundreds of such planetary systems, making the existence of Earth-like planets a frequent phenomenon in the universe and indeed questioning the possibility of evolution phenomena leading to various – or unique? – forms of life in these systems.

While biological evolution observes and discusses the process of life on Earth, similar questions may be addressed to cosmic evolution, where the emergence of complexity over time is noticeable and generally agreed upon, starting from a highly undifferentiated and homogeneous universe before the formation of galaxies to reach the present universe. The concept of an *arrow of time* is sustained by the large amount of observational facts which also point to the apparition, in the universe, of complexity and novelties – sometimes qualified as *bifurcations* – not necessarily predictable from the previous state and not contradicting the second principle of thermodynamics. The degree of classical determinism and predictability of the successive steps in complexity encountered by the universe – living organisms, then reasoning humans are the last step we know of – is a difficult issue which has led to a number of different views [9,10]. At one extreme one may find the various expressions of the anthropic principle, with its finalist appearance, while at the other recent efforts are trying to extend the neo-darwinian principles to all phenomena in nature [11]. These are based on the demonstration of a theorem, stating that any physical dissipative structure statistically evolves with time in order to maximize the final dissipation rate of energy (maximal production of entropy, Dewar [12]).

These short considerations on a very complex subject nevertheless indicate that it may not be appropriate to restrain the teaching of evolution, at elementary levels, to the restricted domain of life evolution on Earth. This is indeed the broad perspective view which is briefly presented in the guide produced by the National Academy of Sciences in the United States [13] or by the American Association of Physics Teachers [14]: these documents do not discuss cosmic evolution, but simply observe that the detailed conditions for life emergence on Earth were resulting from previous transformations occurring in the universe.

3. Questions of origin

In all cultures, the question of origins – of the stars and Earth, of matter, of living things, of humans themselves – has produced myths. In these myths, attempts are made to describe with words some imaginary processes where the observed characteristics of the world may be inferred from previous events, caused by all kinds of actors: gods, demiurges, material events. These 'explanations' indeed lack any scientific substance, yet they already contain a certain sense of a necessary causality, combined with a more or less accurate description of natural phenomena through observation. In addition, they indeed contain deep thoughts on the very existence of human beings, which are not immediately relevant for science. At the level of individuals, psychologists have also observed that the question regarding the origin of the self appears as a profound concern during childhood. With the progress of modern science, this haunting question of origins has progressively evolved towards a description of successive transformations occurring in nature, each observed state of organization being traced as the product of an historical process, based on causality and physical properties, where previous conditions lead to a new state – even if a complete description appears at the moment out of reach. Let us simply observe that the fascination of humans for their origins has led large scale research programmes, e.g. at NASA or other agencies, to be placed under this generic designation [15].

On the other hand, philosophers have asked the metaphysical question of *being* (l'*Être*) opposed to the *non-being*, inevitably raising the question of a transition from the latter to the former. This question cannot be decoupled from considering the nature of time, since time appears to belong to the natural world, and statements on the apparition of time are immediately leading to *aporias*. This was well expressed by Basil of Caesarea: 'The beginning of time is not yet a time, not even the smallest part of a time' [16]. This is probably why it appears so difficult to present, and teach, the scientific description of cosmic evolution: too often there is an implicit understanding which in fact refers to a *creation*, understood as a transition from *non-being* (a metaphysical object of thought) to *being* (an observed fact of nature) – a metaphysical and non-scientific reference indeed. Is it necessary to recall here the popular understanding of the Big-bang model of cosmic evolution as a description of a creation of the world. While Georges Lemaître, whose role in the conception of the *atome primitif* was so decisive, never confused the scientific issue with the Christian vision of creation [17], the view expressed later by Pope Pius XII rather encouraged some kind of concordism [18], even leading to some conceptual oppositions by Fred Hoyle *et al.* to the standard model on the grounds of its supposed metaphysical and undue assumptions. In Western thought, although the distinction between natural processes and a *creatio ex nihilo* was introduced early by Augustine and Tertullian [19], it was often forgotten later on.

After the disputes of vitalism during the XIX century, the origin of life itself on Earth became accepted as a transformation arising from pre-existing physical and chemical conditions, even if the process itself is neither yet understood in detail, nor reproduced in the laboratory. The astronomical discoveries of the last decade have led to the emergence of a new discipline, *astrobiology* (or *bio-astronomy*), which aims at studying the possible observational evidence for the existence of life on extra-solar planets, and the conditions for its emergence. As this new discipline progresses in methodology and tools, a view becomes more substantiated: namely that the physical and chemical conditions, the available time span which made possible the emergence of life on Earth are likely to be encountered in a very large number of planetary system in galaxies. Following Christian de Duve [20], the likelihood of life apparition would then be high. Regarding evolution towards higher forms of complexity and possibly intelligence, the author states: *That extraterrestrial life may evolve in a similar direction is also, by the same token, a realistic possibility* [*ibid.*].

The principle of progressive transformations leading to the emergence of novelty has indeed also been applied by paleontologists to the emergence of man, to describe and understand scientifically the hominisation process, as part of a general evolution of species – the very title of Darwin's work [21]. The complexity of the process, the scarcity of available evidence to reconstruct an evolution spanning millions of years have not prevented an ever increasing scientific understanding of the *phénomène humain*, to quote here Teilhard de Chardin [22] and quite a solid description of this evolution over the last 5 million years or so.

4. Teaching of evolution

As observed above, scientists also have the responsibility to convey their discoveries to the next generation, not only to perpetuate science, but also to contribute to culture and the enlightenment of all humans. Understanding evolution, cosmic as well as biological, is such an achievement of science that it ought to be shared by all.

Involvement of Academies

Why should one discuss this question of education within the Academies of sciences? Would it not be sufficient to let scientists advise their ministries of education in every country, discuss school curricula, write the necessary books, help train teachers? Is the matter so important that it deserves the interest of an Academy, and especially the Pontifical one?

The central issue which appears in the various discussions on evolution, in the creationism or intelligent design positions is the very understanding of the nature of science, its method, its search for the truth, its meaning in modern culture, since they are questioned or even denied by these movements: this is why Academies are concerned. Referring to the Statutes of the Pontifical Academy, here is clearly an important *epistemological question and issue* (Art.2) where the Academy can *contribute to the exploration of moral, social and spiritual questions* (Art.3). The goal to '*ensure proper education in science for every child in the world*' has now received a clear support from the Academy [1] and from the Pope John-Paul II himself when he said: 'Therefore, because of the ideal of service to truth, [the man of science] feels a special responsibility in relation to the advancement of mankind, not understood in generic or ideal terms, but as the advancement of the whole man and of everything that is authentically human'.[23].

Seizing this challenge and moral obligation to guide education authorities, sixty-eight Academies of sciences, organized in the InterAcademy Panel, published in 2006 a common short Statement [24], which appears to be highly consulted worldwide. In the United States everyone knows that an intense public debate, related to education issues in primary and secondary schools, has been occurring since several decades, involving mostly Christians. It is analyzed in great detail by Jacques Arnould in his recent book *Dieu versus Darwin* [25], see also [26]. The US National Academy of Sciences published in 2008, after extensive work, a deep revision of an elaborate document explicitely aimed at parents and teachers [27]. The situation in the Muslim world appears more complex [25]. The wide and still ongoing distribution of the *Atlas of Creation* by the Turk Harun Yahya, available today in 11 languages on the Web, appears as the most extreme case of a certain tendency in the Muslim world to interpret the Coran as a scientific scripture and to oppose evolution – considered as a sign of materialistic drift in the Western world. Some Academies there have remained carefully silent on the matter [28]. In Europe, discussions with strongly diverging views were and are still ongoing at the European Council in Strasbourg, regarding the teaching of evolution and possible recommendations to European countries [37].

A pedagogy of science

Christian de Duve has stated with the utmost clarity the heart of the conflict in which many teachers find themselves today regarding the teaching of evolution: 'By making claims that contradict our most intimate convictions [...of humankind having a privileged position within some sort of cosmic blueprint designed around and for it...], it is contended, science disqualifies itself as a valid approach to truth' [20].

In the face of this, it is therefore necessary to have a twofold pedagogy: on the one hand, this pedagogy should help discover, understand and accept scientific process as a way of grasping elements of truth; on the other, it ought to respect the search and need to give a sense to the human condition, as well as the expression of this need in various cultures, beliefs and faith. Is this conciliation possible?

Regarding the first point, let us consider the contemporary and active movement of renovation in science education, quoted above [3, also 29,30]. It aims at giving children, youngsters and students an understanding of the very nature of natural science: an ability to question, observe, experiment, hypothetize, deduce, discuss, confirm or disprove from facts, evidence, formulation, prediction and control, establishing progressively fragments of truth and constantly improving their pertinence to reality. This pedagogy communicates science as being a process of knowledge rather than a collection of imposed theories, or models to be accepted as dogma – eventually opposed to other dogma. Progressive understanding of this process, including what scientists designate by *evidence based*, is the surest way to educate a scientific mind at any level, even elementary. It helps to understand why science operates as a *practical materialism*, methodologically reductionist; it allows to progressively delimit the perimeter of natural science to affirmations, based on evidence, which are testable and refutable; to see that this perimeter is not fixed for ever, but can progressively expand; to understand that on the one hand any question can be asked by science, and on the other that science is modest and does not pretend to reach the ultimate truth, if any.

Regarding the second point, it is important to inscribe the scientific process of discovery in a perspective view, presenting and understanding its historical dimensions. This confers the sense of science as being a human and cultural adventure. Through such a pedagogy, it can be progressively understood how scientific creativity, at any epoch, was also inscribed in the culture, the metaphysics and the global vision of the world where scientists found their inspiration.

A special difficulty arises in what may be called *historical sciences*, namely sciences such as astrophysics, geology, paleontology or evolution science, where models describe past events, which cannot be repeated or submitted to experimental demonstrations (*idiopathic* or *paletiologic* sciences) [31]. While micro-evolution can be observed in the laboratory, this is possible neither for macro-evolution, nor for the early or past universe. There, science may present itself in the mode of *story telling,* as does the East Side Story, popularized by the paleontologist Yves Coppens after the discovery of Lucy [32]. A similar presentation is often made of the early universe, as in the famous book *Three First Minutes* [33] or [34].

It is not entirely surprising that a misunderstanding may then appear about the scientific character of such stories, which becomes confronted with other cultural or popular stories, as are the myths of creation or other poetic descriptions of nature. The central point here is the nature of the proof. In these historical sciences, proof results from a convergence, an internal and external consistency of the proposed description with all pieces of available evidence, including the state of established knowledge in all experimental sciences (physics, chemistry…), and in theories recognized as valid. A new piece of evidence, such as the discovery of dark matter or dark energy in cosmology, may shake the entire edifice, as might the discovery of a new and odd fossil in paleontology or an entirely unexpected function of a gene in biology. This particular and somewhat subtle epistemology has to be understood by teachers – often very unskilful at this – and properly transfered to students and pupils, a difficult task indeed.

A pedagogy of respect and mutual understanding

Science, being universal in its methods and results, may have an inclination to refute and to challenge any other human experience or vision which does not obey the criteria which regulate its own development. This is *scientism*, an ever present temptation which is at the measure of the grandiose achievements of modern science. It may easily give rise to ideologies which, although non- or anti-religious, have in a recent past been more totalitarian than religions ever were. On the other hand, the goal of religions to embrace and give significance to the totality of human existence can obviously conflict with science – even more when inspired Scriptures, taken literally, provide alternative *stories* of creation or human emergence.

How could then co-exist on the one hand the precious universality of science, on the other the diversity of cultures, the richness provided by the singularity of each human being, the spiritual forces present on Earth? A first point of convergence is indeed *to consider the common sense of humanity, the universality of ethical principles and norms, which are, for instance, expressed in the concepts of human rights and the dignity of the person, as well as in the universality of knowledge, wisdom and science* (Final Statement in [2]). Certainly the teaching of evolution helps to perceive the identity, fragility and common destiny of humanity in the grandiose landscape of the universe today revealed by science [2, *ibid*.].

The emergence of modern science has been on the mode of separation: on the one hand, nature as an object of science, rational, submitted to mathematics, universal; on the other hand, culture as an object of sensitivity and individuality [35]. This dissociation has made possible the development of modern science, but is today challenged by the need to reconcile its technological power and rational mastering of nature with the goals of peace, justice and harmony on a finite Earth. Could a proper scientific teaching of evolution also contribute to such a reconciliation, by pointing out how culture can avoid the catastrophe: a blind natural selection within humanity, operating to the exclusive benefit of the fittest ones?

5. Conclusion: some guidelines?

Here is an attempt to formulate, following previous work on the same goal [13,14,24], some recommendations which may be useful for parents and teachers at primary, secondary and undergraduate levels. Since the author is ignorant of so many aspects of biological evolution, this enumeration should indeed be considered as a modest and grossly incomplete contribution. In a sense, it represents minimal requirements which could be conveyed to teachers, with appropriate examples and illustrations, in order to help them to teach evolution.

Science is a process of knowledge which must be taught, practiced and understood properly, even at elementary levels. Dealing with phenomena and transformations in nature, it is based on evidence, it provides explanations and predictions which are testable and refutable.

Science can also apply rationality and scientific method to events of the past, or events which only happened once. This *historical science* deserves a special epistemological approach, to understand how evidence and proof are established in these cases. This is especially relevant for cosmic or biological evolution.

Biological evolution and the more global frame of cosmic evolution – the latter at least for the epochs where the scientific basis are firmly established – should be taught as solid facts, not as hypothesis.

The history of scientific concepts, their inscription in the culture of the time, should be taught along with the most up-to-date facts and understanding, in order to illustrate the way science has proceeded in the past and still does.

Despite its great appealing and often popular character, the question of *origin* should be treated carefully: namely to avoid a confusion between a transformation occurring from previous physical conditions, and a metaphysical, possibly religious issue.

When answering a question, the aim of science is to build truth, not to propose the final truth, if any. Many questions belonging to science remain open and undecided, but no question should a priori be denied to be asked by science. The perimeter of science is more a question of methodology than legitimacy.

There exist other modes of knowledge than the scientific one, e.g. when dealing with ethical issues. Philosophical, religious, cultural ways of knowing need to be understood and respected, as well as they have to understand and respect science.

A better knowledge and proper understanding of our natural condition on Earth, of its past evolution, its situation in cosmic time and space give humanity the possibility to prepare for the future, to use at best the human wisdom and the universal sense of justice in order to make Earth liveable and sustainable.

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DISCUSSION ON PROF. LÉNA'S PAPER

PROF. PHILLIPS: I want to ask about your description of myth, because you talked about how the question of origins is so important to people and I was particularly taken by your description about how children are very interested in their own personal origins and the connection of that fact to the interest of peoples in their origin and the development of cultural myths. But one of the things that, at least – maybe I did not hear this – seemed to be missing to me was one of the aspects of myth that I think is very important, in that cultural myths and religious myths have the effect of defining what we believe ourselves to be. I think this is a very important part of myth and one of the reasons why myth has such power over the years and one of the reasons why we should be very careful not to abandon the idea of myth even as origin myths become replaced by scientific understandings. We should be aware of the fact that there are other things that myths give us than simply a description of how things came to be.

PROF. LÉNA: I certainly agree with what you say. My reference to myths was more considering them as an early attempt to understand the world by providing explanations based on observation and causality, since both are present in many myths. Science, as it develops, contradicts indeed many mythical 'explanations', hence myths tend to be totally discarded in modern cultures, including their positive role you stress. Maybe we should use another term, and speak of vision or global vision?

PROF. MITTELSTRASS: If there is no other question I might just make a remark. Since you have stressed the fact that science is a process, it follows from that that the history of science is a very very important topic within this area. As I realise now, at least in my country, in Germany, and in other countries, the history of science, as far as it is a university discipline, is not flourishing any longer. We are losing professorships in that area, at least in my country, so I think to stress the fact that the history of science is a very important issue not only in school but also in university would be important in that context. You mentioned the history of science as an important topic but just because of this development it is very important to stress that.

PROF. LÉNA: I thank you for this comment and the fact of not having people doing the history of science in universities is considered, at least in my country, an excuse not to teach teachers the history of science because there is nobody to do it.

THE LATEST CHALLENGE TO EVOLUTION: INTELLIGENT DESIGN

MAXINE F. SINGER

Albert Einstein's theory of relativity is more than a century old. The Belgian priest George Lemaître helped start the path that led to the idea of the Big Bang and the concept of the age of the universe. Alfred Wegener proposed the concept of continental drift that led to the idea of plate tectonics and our understanding of how the planet has changed since its birth. Charles Darwin's and Alfred Russel Wallace's theory of evolution by natural selection is 50 years older than Einstein's and also remains the topic of work by scientists. But, while Einstein is a revered celebrity, and Wallace, Wegener and Lemaître escape public scorn, Darwin is reviled by many. What is the explanation for these disparities?

Most people don't understand Einstein's theory even at a very superficial level. They are ignorant of the roles of Wallace, Wegener, and Lemaître as they were taught little about science or its history in school. But a lot of people think that they know and understand what Darwin said and they don't like it. Some still don't like what science tells us…that the age of the universe is about 13.7 billion years and that of the Earth about 4.7 billion years. Many reject the idea that we share common ancestors with other primates and that the first member of our species walked this planet as many as 0.5 million years ago. All the evidence we have indicates that they object because the scientific facts challenge any literal interpretation of the creation text in Genesis or the creation stories of other religions. Scientific descriptions of evolution, both physical and biological, are in direct conflict with the religious views of vast numbers of individuals, worldwide.

For example, Protestant fundamentalist Christians recently built a Creation Museum in the state of Kentucky in the U.S. with $27 million of private money (1). One of the museum's exhibits shows human children playing alongside roaming dinosoaurs. The Earth is said to be 6000 years old and the museum's web site says:

'The Bible speaks for itself at the Creation Museum. We've just paved the way to a greater understanding of the tenets of creation and redemption. Our exhibit halls are gilded with truth, our gardens teem with the visible signs of life'.

A poll in 2005 demonstrated that fewer than 40 percent of Americans accept the concept of evolution (2). Note that the word used is 'accept' rather than 'believe' because our view of evolution rests on scientific findings not on faith. This result is consistent with many other polls carried out over decades. Only one country polled had a lower percent of public acceptance of evolution than the U.S., Turkey, the only Muslim nation on the list. Turkey is actually quite a modern country with several excellent universities teaching science as we know it. But it is also the source of that elegant, though problematic 12-pound creationist volume that was sent free of charge to many scientists in Europe and the U.S., *The Atlas of Creation*. Some members of the U.S. Congress, journalists, and a few science museums also received the book. The man who appears to be responsible, Adnan Oktar, is now in prison for unrelated reasons.

This poll also showed that many people in many countries do not accept the idea of evolution. Recent activities confirm this finding. Isolated problems about teaching evolution have emerged in Canada. The Swedish government is discussing how to apply its law on education to private schools run by religious groups that reject evolution. The British Prime Minister's Office was concerned enough about the issue to release a statement in June of 2007 saying that 'creationism (including intelligent design) should not be taught as science'. The issue has arisen in Northern Ireland. In October 2007, the Parliamentary Assembly of the Council of Europe approved a resolution urging its member governments to oppose the teaching of creationism as science; this is a helpful start although it was troubling to read that the vote in favor was far from unanimous. Fortunately, a U.S. organization, the National Center for Science Education, publicizes these stories in its newsletter and web site; the organization is devoted to promoting the teaching of evolution as sound science (3).

The situation in the U.S. seems more acute than that in most other countries and has a rich history. American scientists have known for almost a century that we must be vigilant about what is taught in science classes. The National Academy of Sciences has, since 1984, published 3 versions of a booklet discussing how creationist ideas differ from science and why they should not be part of science lessons in schools (4).

Efforts to curb the teaching of evolution in U.S. public school science classrooms continue to emerge all over the nation. As soon as one challenge is defeated, another appears. A major difficulty is that public school educational policy including what to teach and what textbooks to use is made by more than 17,000 local school boards with guidance from the states. The national federal government has no authority in this regard. These school boards are usually elected and reflect the tensions of local politics. However, the federal, that is the national, courts do have a say in the matter because the first amendment to the US Constitution, passed in 1789, says that 'Congress shall make no law respecting an establishment of religion, or prohibiting the free exercise thereof…'. Later, in 1868, the 14th amendment to the Constitution extended the first amendment's restriction to the states. Therefore, state and local laws and policies can be challenged in federal court by a citizen or group of citizens on the grounds that they violate the Constitution. These two amendments, one more than two centuries old, have allowed science to prevail in public schools. Private schools including religious schools that do not receive government monies can do what they please including teaching students that the Earth is only a few thousand years old, that the biblical flood story is accurate, and even that the Earth is flat.

Policies attempting to ban or dilute the teaching of evolution in public school science classes have evolved as the federal courts, including the Supreme Court, dismissed as unconstitutional one attempted subversion of the constitution after another. Laws banning the teaching of evolution outright were dismissed in 1968. Next to fall to the courts, in 1982, was the idea that schools could teach a 'balanced treatment' of Biblical creation and science. Five years later, laws requiring the teaching of 'creation science' or 'scientific creationism' were thrown out. In 1992 a federal court affirmed the right of a school district to prohibit a teacher from teaching creation science. The latest court decision, the 2005 Dover case, ruled that so-called 'intelligent design' is also religion masquerading as science and cannot be taught in science classrooms in public schools (5).

In none of these court decisions did the courts say anything about the validity of evolutionary theory or biblical creation. They only ruled that creationism in its various guises is a religious doctrine and therefore, because of the Constitution, is illegal to teach in science classrooms in public schools.

Now, anti-evolutionists are trying new tactics to get around the earlier federal court decisions. One tactic is to call for laws protecting the academic freedom of teachers who teach creationist notions. As recently as June of this year, the Louisiana legislature passed and the governor signed a bill incorporating this new anti-evolution approach. Under the guise of academic freedom it permits teachers to speak of evolution as 'controversial' and is an invitation to teachers to present alternative, nonscientific explanations. The young governor of Louisiana, Bobby Jindal, signed the bill, making it law although he had been a biology major at Brown University. The 'academic freedom' argument is also a primary thrust of a movie called *Expelled: No Intelligence Allowed* that is popular in some communities in the U.S. (6). It has been a commercial success and is being shown in many fundamentalist Protestant churches.

Even more worrisome, is the strategy attempted by the Kansas State Board of Education that adopted, in 2005, a new definition of science essentially stating that scientific explanations are no longer limited to natural phenomena. Fortunately, a newly elected Board reversed that decision two years later. However, any future elected board could reverse the 2005 decision.

Another troubling tactic is to argue that U.S. school science classes should teach what is called the 'controversy' or the 'debate' between evolution and the creation story. Unfortunately, there are, in the U.S., major political figures, including the current president,[1] who hold this view. (The incoming president espouses a more scientific approach). The argument harbors two profound misconceptions. First, it implies that the biblical creation story is equivalent to a scientific explanation. Second, the argument fails to recognize that in our pluralistic societies, people of faith adhere to many different creation stories and the Bible is not everyone's text. The words 'controversy' and 'debate' are meant to convey the idea that there are real scientific disagreements concerning the fact of evolution. But scientifically, there is no such controversy. Scientists do argue about the details of evolutionary processes but not about whether physical and biological evolution actually occurs. The profound differences between science and faith are muddled by this approach to the advantage of neither.

Intelligent design is one of the more recent subterfuges used to try to get creationist ideas into school science curricula. While the federal court decision in 2005 concluded that intelligent design is essentially creationism dressed up in new terms (5), it continues to be taken seriously by many who seek ways to undermine the teaching of evolution in science classrooms. The Discovery Institute, the primary organization promoting it, defines intelligent design as follows: 'The theory of intelligent design holds that certain features of the universe and of living things are best explained by an intelligent cause, not an undirected process such as natural selection'(7). Intelli-

[1] George W. Bush.

gent design proponents do not generally refer to the Bible. In an effort to circumvent the Constitution, they decline to characterize the 'intelligent cause' but both supporters and critics understand that it is a deity at work.

'Design' is of course an old idea for explaining the extraordinary elegance and complexity of nature. Darwin himself had to deal with it as he did in a letter to the American botanist, Asa Gray. 'I have lately been corresponding with Lyell, who, I think, adopts your idea of the stream of variation having been led or designed. I have asked him…whether he believes that the shape of my nose was designed. If he does, I have nothing more to say' (8).

Contemporary proponents of intelligent design claim to be scientists and indeed several have advanced degrees and university positions. They say their methods are scientific. But they do not describe experiments or systematic observations and do not publish in recognized, peer-reviewed journals. A central argument made by intelligent design proponents is that there are features of living things that are irreducibly complex and could not have developed by evolutionary processes (9). The favorite examples of irreducible complexity are eyes, the immune system, the blood clotting system, and bacterial flagellae. In fact, a great deal is known about how these systems work and evolve and details are published continually. But intelligent design proponents have invented a number of counter arguments to undermine the significance of the data concerning the evolution of these biological elements; with these arguments they continue to maintain the concept of irreducible complexity.

For example, Michael J. Behe, Professor of Biochemistry at Lehigh University and a leader in the intelligent design movement, wrote about the mammalian immune system as follows in 1996 (9). 'As scientists, we yearn to understand how this magnificent mechanism came to be, but the complexity of the system dooms all Darwinian explanations to frustration'. Less than a decade later, a great deal had been learned about the evolution of the immune system including that one essential element derives from transposable elements. When confronted with the recent data during the 2005 trial at Dover, Behe said that the 'evidence of evolution [of the immune system]' was not 'good enough' (5). We can expect similar rejection of the evidence for the evolution of blood clotting and flagellae as well as of eye.

Walter Gehring, a leading investigator of the development and evolution of the eye has written: 'Recent developmental genetic experiments and molecular phylogenetic analyses…argue strongly for a monophyletic origin of the eyes from a Darwinian prototype and subsequent divergent, parallel and convergent evolution leading to the various eye-types' (10).

The judge in the Dover case raised a major point about the concept of irreducible complexity. 'Even if irreducible complexity had not been rejected [as it has been] by the scientific community at large, it still does not support intelligent design as it is merely a test for evolution, not design'. That is, failure of a test for one theory tells us nothing about the validity of a competing notion. But intelligent design proponents can always say that the evidence is just not good enough. That will be enough to raise doubts in a public that is largely scientifically naïve.

Speciation is another topic that those who object to evolution on religious grounds dismiss in the face of scientific evidence. Until recently, explaining biological evolution to the public was confounded by the scientific difficulty in describing how new species with markedly different phenotypes can arise from existing species.

This difficulty was underscored when, in 1975, Mary Claire King and Allan Wilson demonstrated that chimp and human genomes are 99 percent identical (11). More recent genome sequencing confirms that coding regions vary by only 1.2 percent, although there are larger differences in noncoding segments (12). This fact, by itself does not explain the difference between the two species. However, the clue to the explanation was stated in the summary to the King and Wilson paper: 'A relatively small number of genetic changes in systems controlling the expression of genes may account for the major organismal differences between humans and chimpanzees'. It is increasingly clear that this prediction is true. Variation in gene expression levels can yield marked differences in phenotypes some of them sufficient to lead to speciation.

An interesting example of the importance of gene regulation to evolution by natural selection comes from recent experiments on the very finches that Darwin studied on the Galapagos Islands (13).

Darwin observed that the various finch species on different islands have notably different beaks. Some are wide, some narrow, some deeper and some longer than others. Darwin wrote in his account of the voyage: 'one might really fancy that from an original paucity of birds in this archipelago, one species had been taken and modified for different ends' (14).

Peter and Rosemary Grant of Princeton have spent more than 30 years studying the Galapagos finches. They learned that the beak shape correlates with the food the finches eat. The three dimensions of the beaks can be accurately measured and the Grants and their colleagues measured hundreds of them (15). Thus, the phenotypes are well defined. They also identified the kinds of food eaten by each species and discovered that the shape of the beak correlates with the type of food consumed by the several species. For example, those finches that probe cactus flowers for food have relatively elongated beaks of low depth while those that crush large seeds have deep, short beaks. Now, the relative levels of expression of two genes, *BMP4* and *CaM*, have been measured in the developing beaks in the various finch species (13). Together, the expression of these two genes account for much of the difference between the beaks; the higher the level of *CaM* expression the longer the beaks: the higher the level of *BMP4* expression the wider and deeper the beaks. Thus, differential regulation of gene expression accounts for the shape of the beaks rather than any kind of change in the coding region and protein structure.

These data are not likely to change the minds of those espousing intelligent design or other forms of creationism. They can argue that the story of the finch beaks is only 'microevolution', which some of them acknowledge to occur. They can still argue that 'macroevolution', the generation of striking new species like chimps and humans from a common ancestor, does not happen. Indeed, their primary concerns relate to the origins of animals, especially humans. The day is not far off when we will have convincing data describing the phenotypic differences between chimps and humans in terms of differential gene regulation. Some relevant papers have already appeared (for example, 16). But those whose beliefs are threatened by such data will resist.

Another approach to resistance is illustrated by the reaction to a 2008 paper in *Nature* magazine that reported on the evolution of cichlid fishes (17). The journal's cover shows a picture illustrating the distinctive coloration of two species in Lake Victoria and carries the headline 'a textbook example of evolution in action'. The difference in color between the males of the two species and associated frequencies of different opsin alleles in the species leads to reproductive isolation without geographic isolation. It took less than a week for the Discovery Institute's web site to display a link to an objecting story that said: 'But the researchers did not observe the origin of a new species. They did what biologists have been doing for a long time: They analyzed differences in existing species to find evidence to support a particular hypothesis of speciation… all they really did was compare existing species and find a correlation between differences in their DNA and differences in their vision'.

These stories are illustrative of the difficulty scientists face in fostering majority public support for the concept of evolution. As scientists, we understand science to be as described by the U.S. National Academy of Sciences:

'Science is a particular way of knowing about the world. In science, explanations are restricted to those that can be obtained through observations and experiments that can be substantiated by other scientists…Explanations that cannot be based on empirical evidence are not part of science'. Yet, rigorous scientific findings obtained according to this definition appear to be powerless in the face of faith in the literal words in ancient religious texts.

Reviewing this history, leads me to two related general conclusions

My first general conclusion is that we are unlikely to convince those who view their religious faith as in fundamental conflict with scientific evolution. Yet, many people of faith do not find evolution incompatible with their beliefs. This includes many scientists of deep religious faith who accept evolution and are defenders of the nature of science. We heard this week from Francis Collins about his faith. Father George Coyne, S.J., a former member of this Academy, has written eloquently about his faith and acceptance of evolution. Pope John Paul II, revered by Catholics and non-Catholics, was clear in stating that the weight of science supports evolution. (See reference 4 for quotations from these three people). But these approaches do not succeed with many people whose minds are closed and see Darwin as the source of evil in the world.

My second conclusion derives from the first. The most important task for scientists and the only one that has a chance to succeed is assuring that science and evolution are taught properly in school science classes. There are several reasons for this. School science education, certainly in the U.S. if not in other countries, has failed to instruct people in the nature of science, its absolute dependence on honest experimentation and observation, and its inherent quality of being correctable. Science itself is neutral on the subject of religion and this Academy, whose members represent many religious communities, speaks loudly for that fact.

Classroom teachers who are required to teach about evolution face continual challenges. They may be people who reject evolution because of their own faith. Or, they may be people who accept evolution but are challenged by students or parents who do not. For these teachers, the only practical approach is to say that students are not required to accept evolution, but they are required to understand it. And such situations are opportunities to teach what science actually is and is not and how it works. It is my understanding that this was the view of Michael Reiss who was Director of Education at the Royal Society in London until forced recently to resign because of the uproar this position elicited from some scientists. Those scientists have probably not been in a school classroom since they were students themselves. Their lack of understanding of the real challenges to teaching evolution troubles me.

I also find troubling those scientists whose support of evolution and lack of personal faith is accompanied by an apparent lack of respect for religions and religious views. There may indeed be an unbridgeable chasm between science and religion as some have written but there is no need for a chasm between scientists and people of faith.

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DISCUSSION ON PROF. M. SINGER'S PAPER

PROF. COLLINS: Thank you for a very eloquent and well-argued description of the current circumstance which is, perhaps for our European colleagues, almost impossible to understand, given the anomaly that the USA represents at the present time. I just want to pick up on almost the last thing you said about the concern that you have about scientists who have no religious faith but who are basically showing disrespect for it in others. I have heard many comments upon the fact that the wind behind the sails of intelligent design, at the present time, is being substantially supplied by the best-selling books from Dawkins and Hitchens, Sam Harris, Daniel Dennett, and so on, because that continuing barrage of messages coming from those who are seen to represent the mainstream of the scientific community further forces believers into a corner, feeling that they have to have some means of defence and the Discovery Institute is very effective as promoting intelligent design as that solution and so the misunderstandings continue. Does the scientific community have a greater responsibility than has so far been exercised not only to insist upon the fact that science should be taught in science class, including evolution, but also to speak out in circumstances where members of our own guild are using science as a club, over the head of believers, in a fashion that is not justified by reason alone?

PROF. M. SINGER: I do believe that the scientific community has a responsibility to deal with a lot of this. Certainly the National Academy of Sciences in the USA has tried to do this by the constant revision of the booklet and then sending that booklet out to all 17,000 school boards free. It is not clear how many people read it when it arrives, of course, but the Academy has done much more than that so there are reports that are more specific about the teaching of evolution, about resources for teachers with regard to evolution, a lot of it is also tied in with the history of the court decisions. And in recent months, particularly in the National Center for Science Education newsletter, I have seen reports of scientists who are speaking out against the kind of disrespect that is being shown by some of our colleagues, which I think is really important.

PROF. LÜKE: I think intelligent design could perhaps have two enemies: a good Catholic theology and the sciences. And from a general point of view the situation with intelligent design in the USA is not understandable. And therefore my question is: what is the position of the university theology in the USA? A good historical critical exegesis as it is useful all over the world is one of the best theologian helps against intelligent design. What is with this part in the USA?

PROF. M. SINGER: I am sorry, I did not hear the first part of your question.

PROF. LÜKE: I think intelligent design could perhaps have two enemies: a good academic theology and good sciences. What is with the first enemy of intelligent design, with a good theology, with a good historical critical exegesis as it is usual in every European country, especially at the universities?

PROF. M. SINGER: I am afraid I cannot give you an informed answer to that question, because I do not follow a lot of theology and certainly Christian theology, in general, is quite irrelevant for me so I really cannot speak to that. I do not follow the publications of the theological institutions. Maybe someone else in the room can.

PROF. COLLINS: Well, very briefly, I think it is not a pretty picture. Certainly, in many of the fundamentalist very conservative Christian seminaries the notion of intelligent design or even Young Earth Creationism is the accepted norm for how theology is presented to future pastors, very much saying that, if science disagrees with the literal interpretation of Genesis I and II, then science must be wrong and it is the duty of the Christian to resist what is seen as a materialist perspective derived from these insights. It is not populated with a lot of open-mindedness in many of those institutions. I think this is a disaster for the Protestant Church in the US, because ultimately it will fail. One hope would be that sometime in the not too distant future that realisation will begin to sink in and that, by a true and effective dialogue about the facts as opposed to the strong crusading feelings of some, it might be possible to develop a much more effective theology, a theology that celebrates what science is teaching us about the universe as manifestations of God's awesome creation as opposed to a theology that seems to be afraid of science and defensive about what science is teaching us, as if, somehow, our puny minds, in understanding the universe, could threaten God Almighty.

PROF. M. SINGER: I would just like to add that those Protestant denominations that used to be the majority denominations do take the kind of approach that Francis was talking about and they by and large do not agree, as far as I know, at all, with what is being taught in the fundamentalist evangelical institutions.

PROF. ZICHICHI: Thank you, Mr Chairman. I would like to propose a logical solution to this paradox, in fact it is nearly an antinomy: how can it be that the most powerful country in the world refuses to believe in evolution? Here we have different components, one is culture, as Professor Léna has pointed out, namely that history of science is not part of our culture in present day life, but I think that the reason why the majority of people in the USA and in many other parts of the planet refuse to believe in evolution is because evolution has been linked to Darwin. We could give a contribution towards scientific culture in the world. This Academy could give a contribution because we should explain that evolution has its roots not in Darwin but in the discovery that time cannot be separated from space. It is here the origin of evolution. From this moment on the progress has been enormous. The electron evolves, the most elementary particle and the first one discovered evolves in space-time. The Dirac Equation describes this evolution. We should try to explain that evolution has its roots in the fundamental structure of science. The only quantities that do not change with time are the fundamental constants of nature. As I have tried to explain in my lecture, everything evolves, inert matter, living matter, culture, everything evolves and the roots of this should be clearly identified. The discovery that time cannot be separated from space and that space and time cannot be both real (Immanuel Kant did not imagine this) was a big discovery coming after 150 years of totally unexpected discoveries in electricity, magnetism and optics, synthesised by the Maxwell Equations. These equations brought Lorentz to discover Lorentz invariance, which means that space cannot be separated from time and, therefore, evolution must exist not because Darwin has discovered it but because it is impossible to separate time from space. Let me add a detail which can be of relevance for the public. For 10,000 years all civilisations were measuring time using the 'sundial', the standard technique of all civilisations, with one second per day uncertainty in the measurement of time; this had been going on for 10,000 years up to the moment when Galilei discovered the laws of the pendulum. Now, the uncertainty in the measurement of time is less than one second per universe lifetime, which means 20 billion years. In four hundred years we went from one second per day to one second per 20 billion years. So, to say that people do not want to listen about evolution is, in a certain sense, our fault, because we have never clarified that the Darwinian contribution to evolution is negligible compared to the fundamental discovery that space and time cannot be separated and cannot both be real.

PROF. RAVEN: I would like to go back to some of the remarks that were made by Francis Collins and Maxine Singer in her excellent talk. I have spent a good deal of time working with Evangelical Christians in the USA on environmental matters and it has been very productive. The Evangelicals, of course, are already very concerned about environmental matters, as is the Holy Father and the Catholic Church generally, because of the associated injustice, which affects the poor but the poor disproportionately. Pastors are very busy, of course, which is why some scientists try to help them with the preparation of environmentally credible sermons. In this context more generally, it will be very important for scientists to respect religious people, to engage in dialogue with them, and to provide useful material about points of interest to them. Separation of people with differing belief systems is not good for either group. The second point I would like to make is that a lack of acceptance of evolution is not deeply rooted among most Evangelical Christians, but rather a misunderstanding of what evolution implies. It is not valid to compare an acceptance of evolution with such fundamental issues as abortion, gay marriage, stem cell research, or other issues where the views are deeply held and strongly argued. With more engagement and respectful discourse, it should become possible for virtually all people to accept evolution, in a descriptive sense, as a fact, while various explanations of evolution can legitimately, in a scientific sense, be legitimately considered theories. Evolution as an observed set of facts neither affirms nor denies the existence of a Creator, and those who take it as such commit a serious logical error.

PROF. MITTELSTRASS: That is the end of our session. May I hand the floor over to President Cabibbo for some concluding remarks? It is the end of the conference.

PROF. CABIBBO: What can I say? My conclusion is that I learned a lot and was very impressed by the high quality of the contributions, and I think it will become an interesting book with the discussion also, the discussion was very lively. I am very happy with the conference.

PROF. ARBER: As a member of the Council, I am glad I could help in organising this plenary session.

PROF. CABIBBO: More than that!

PROF. ARBER: I want to express my deep gratitude, first of all, to those Academy members who presented their own scientific contributions. It was good to have you all present in our intensive, interdisciplinary debates. As usual for our plenary sessions, the Council invited a few non-members in order to enrich our programme. I am glad to state that we have been successful with the selected additional contributions and we also owe our gratitude to their authors. Finally, the Council notes with pleasure that the discussion periods were intensively used. Our deep thanks go to all participants for your activities. And last, but not least, these thanks go also to the administrative personnel, for their appreciated and competent support.

STATEMENT BY THE PONTIFICAL ACADEMY OF SCIENCES ON CURRENT SCIENTIFIC KNOWLEDGE ON COSMIC EVOLUTION AND BIOLOGICAL EVOLUTION

REVISED DRAFT OF 24 JANUARY 2009 BY PROF. W. ARBER (2),
WITH SUGGESTIONS MADE BY THE ACADEMICIANS N. CABIBBO,
P. LÉNA (2), Y. MANIN, J. MITTELSTRASS, W. PHILLIPS, P. RAVEN (2),
I. RODRÍGUEZ-ITURBE, M. SINGER, W. SINGER, A. SZCZEKLIK (2),
R. VICUÑA, AND A. ZICHICHI

The Pontifical Academy of Sciences devoted its Plenary Session of 31 October-4 November 2008 to the subject: 'Scientific Insights into the Evolution of the Universe and of Life'. The Plenum was attended by 45 members of the Academy and by 14 invited guests. Lectures were given by 23 members and 8 additional lectures were given by invited experts. Ample time was devoted to discussions.

The chosen subject is very topical for the sciences as well as for philosophy and theology and it is also of relevance for the general public. A majority of the lectures and debates concentrated on presenting contemporary scientific insights into the evolutionary processes and on integrating these insights into our common world-view. The Academy also provided a platform for a discussion on the relationship between acquired scientific knowledge and other branches of knowledge, including a philosophical approach and traditional wisdom such as that to be found in Biblical writings.

On the first day of the session, the Academy specifically addressed established knowledge, theories, models and open questions relating to cosmic evolution. Ever more powerful instruments (telescopes, etc.) allow us to explore developments that occurred in the distant past despite the limitation imposed by the speed of light. Another frontier of scientific investigation is penetrating ever smaller dimensions, revealing the laws of the cosmic microworld. Recent investigations both in the very big and in the very small confirm and strengthen the previously reached scientific consensus that the cosmic evolution of galaxies and of matter is an undeniable fact. The cosmos and time may indeed have a temporal origin, contrary to ancient Greek opinion (with the exception of Plato – *Timaeus*) which generally regarded them as eternally cyclical, without a beginning and an end. The exact time of that origin is subject to a small but fundamental uncertainty.

Several lectures raised questions about the existence of life in other parts of the universe. Theories and logical speculations attempt to provide answers to these pertinent questions. However, until appropriate observations and investigations in our galaxy (it may be observed that over 300 extra-solar planets have already been discovered), and perhaps in the future in other galaxies, are possible, science cannot provide solid answers to these questions. The origin of life on earth was also discussed, with an exposition of recent progress in the field, in the light of what man is learning about our galaxy as well.

We can now understand biological evolution at the molecular level. Hypotheses that had been presented earlier have been validated with novel research strategies. Genetic variation, the driving force of biological evolution, is shown to involve a number of different molecular mechanisms. Genetics as well as computational comparison of DNA sequences allow us to explore these mechanisms, which can be classified into three natural strategies (local DNA sequence changes, intragenomic rearrangement of DNA segments, and acquisition of foreign DNA segments) of different evolutionary qualities. Interestingly, both specific products of so-called evolution genes and a number of non-genetic elements contribute to overall spontaneous mutagenesis, and very low rates of mutagenesis underlie the genetic stability of living organisms.

Natural selection results from the way by which living organisms deal with encountered living conditions to which both the physicochemical environment and the presence of other organisms in a given ecosystem contribute. Most of the prevalent substrates for natural selection are phenotypes resulting from the presence and activities of expressed gene products. However, particularly for eukaryotic organisms, genome organisation and the compacting of chromosomes into chromatin can also contribute to the outcome of natural selection. The presence of evolution genes determining the evolutionary fitness of living organisms is selected at the population level by second-order selection. Positive selective pressure is also exerted by long-term symbiotic associations between different kinds of microorganisms – for example between humans and several kinds of microorganisms. Organelles, such as mitochondria and chloroplasts, testify to the evolutionary importance of symbiotic cohabitation.

The Plenum devoted ample time to primate and in particular to human evolution. In this evolutionary pathway a remarkable increase in the size of the brain has occurred. Many novel genes that have been added during the course of evolution are expressed in the brain. In addition, importance can be attributed to the development and establishment of a complex neuronal network during childhood. All of these evolutionary and developmental changes are generally seen as a basis for the capacities for consciousness, intelligence and freedom, and their possible development. These attributes allowed human beings to develop what is generally known as 'culture'.

Since cultural evolution facilitates the organisation of human lives, the pressure of natural selection on a number of distinct traits in the human population is diminished, although, of course, it still acts on many other features. In view of this situation, the Academy calls for humanity to exercise responsibility when intervening in the natural evolutionary processes and to use scientific knowledge and its technological applications to safeguard the conditions for survival of all species and, in particular, to assure the dignity and the wellbeing of humans.

We have to be aware that the impact of human activities on our environment is not unique but is now as great as any factor affecting living things during the whole period of the existence of life on earth. Many other living beings, including bacteria, which are not provided with consciousness, may also contribute to changing in a considerable way the environment and thus also the pressure of natural selection. The Plenum noticed a remarkable example of this situation: it is generally thought that early life on earth was largely anaerobic as long as the atmosphere contained no or very little oxygen. This changed after photosynthesis was developed through the biological evolution of microorganisms and, in particular, when plants acquired the capacity for photosynthesis. It is only thanks to this evolutionary progress that aerobic life became possible, including that of higher animals and human beings.

This striking example of interdependencies between biological and geological evolution on the planet should not be seen as a justification for human society to abuse precious natural resources and to cause climate change by its modern lifestyle; indeed, quite the contrary. Since we are the only being with consciousness that is in the position of affecting the condition of life on earth as a whole, we have a special responsibility, clearly outlined in Holy Scripture, to care for the earth.

It is largely due to considerable improvements in human living conditions – among which we may also list the strong improvement in therapeutic and preventive medical care – that in the last hundred years both human life expectancy and the global density of the human population have strongly increased. Justice at a global level that provides sufficient food and water to all, without injuring the environment, is an increasing imperative.

On several occasions the role of chance was addressed by the Plenum, in relation to both cosmic and biological evolution. According to present scientific knowledge, chance is required in natural reality in order for it to be prepared for rapid adaptation to newly developing situations. In biological evolution, partial randomness in the generation of genetic variants may render populations of organisms more adaptable to changing living conditions.

From the natural scientist's point of view, natural evolutionary processes largely reflect self-organisation, which depends on the intrinsic properties of matter and energy. This holds for cosmic and for biological evolution, which must cover about 15,000 and almost 4,000 million years respectively.

It is important for scientific knowledge on evolution to become integrated into our world – view and for our world – view to be steadily updated. The extraordinary progress in our understanding of evolution and the place of man in nature should be shared with everyone. This will help to guide humans and the next generations in decisions that contribute to cultural evolution, including agricultural practices, societal developments, medically-relevant activities and environmental emissions, based on reason, fairness and justice. A wise use of available scientific knowledge not exclusively for the benefit of the human population but also for the safeguarding of a rich biodiversity and of natural resources can contribute significantly to a harmonious evolution of life on our planet and the wellbeing of future generations. Furthermore, scientists have a clear responsibility to contribute to the quality of education, especially as regards the subject of evolution, and to the quality of knowledge that education conveys.

The plenary session confirmed the Pontifical Academy of Sciences in its awareness of a remarkable strengthening in recent years of our scientific knowledge about cosmic and biological evolution. One could see in these evolutionary processes a confirmation of the theological concept of *creatio continua* (*creatio* and *conservatio)* which states that creation is a permanent process of participation of being by the Being by essence, who deserves our respect and our praise. Evolution and creation fill us with wonder and awe and remind us of the Biblical benediction: 'And God saw every thing that He had made, and, behold, it was very good' (Gen 1:31).

SUMMARY

CHRISTIAN DE DUVE

The Pontifical Academy of Sciences devoted its Plenary Session of 31 October-4 November 2008 to the subject: 'Scientific Insights into the Evolution of the Universe and of Life.'

The Academy offered a unique setting and intellectual climate for the chosen topic, which is of burning interest – and an occasional source of dispute – for scientists, philosophers, and theologians alike, as well as for the general public. It was particularly valuable to have representatives of all major scientific disciplines and of philosophy and theology gathered together and exchanging views in an atmosphere of intellectual freedom and mutual respect.

There was little disagreement on major issues. The participants unanimously accepted as indisputable the affirmation that the Universe, as well as life within it, are the products of long evolutionary histories. They rejected as objectively untenable the so-called 'creationist' view based on a literal interpretation of the biblical account of Genesis, a view not to be confused with the belief, legitimately held by many, in a creator God. Benedict XVI in his opening address to the participants proposed a valuable approach based on a metaphysical interpretation of the creation clearly different from that of the 'Creationists': 'A decisive advance in understanding the origin of the cosmos was the consideration of being *qua* being and the concern of metaphysics with the most basic question of the first or transcendent origin of participated being. In order to develop and evolve, the world must first *be*, and thus have come from nothing into being. It must be created, in other words, by the first Being who is such by essence.'

Several contributions reviewed recent developments in cosmology. Attention was drawn to a number of still unsolved problems, including dark matter, dark energy, black holes, and the possibility that our Universe may be only one among a huge number of universes (multiverse), perhaps the only one that happens by chance to have physical constants such that complex forms of matter, including living beings, can arise. The latter hypothesis, however, is purely speculative and may well remain so, because of a lack of means of either proving or disproving it.

Special attention was paid to the solar system and, within this system, to planet Earth and the emergence of life on it. The question was raised whether other such systems, possibly including planets bearing life and, perhaps, intelligence, might exist elsewhere in our galaxy or in others. This has become a major subject of astronomical research. More than 300 planets have been discovered around nearby stars and intense efforts are made to devise technologies that would allow signs of life to be detected. The search for extraterrestrial intelligence (SETI) has been underway for some time and is being expanded, without, however, having yielded any positive result so far.

Many discussions were devoted to the origin and evolution of life. It was generally admitted that all known living beings, including humans, descend from a single ancestral form of life that appeared on Earth several billion years ago. How this form originated is not known but is believed by a majority of experts to have involved special chemical reactions that were rendered possible, perhaps even imposed, by the physical-chemical conditions under which they took place. Particularly impressive in this respect is the recent discovery that a number of typical building blocks of life, including sugars, amino acids, and nitrogenous bases, arise spontaneously, together with numerous other organic compounds, in many parts of the Universe. Not all scientists, however, believe this remarkable fact to be relevant to the origin of life.

A key event in the long history of life on Earth was the appearance, between 2.4 and 2.0 billion years ago, of molecular oxygen, a product of photosynthetic organisms and an essential prerequisite to the formation of aerobic forms of life, including all animals (and humans). Another decisive event was the development of eukaryotic cells which eventually gave rise to the multicellular plants, fungi, animals, and humans. Although many details remain to be clarified, the actual occurrence of biological evolution is no longer just a theory, strongly suggested by fossil evidence, but not conclusively demonstrated by it. Evolution is now supported by overwhelming molecular proofs and has acquired the status of established fact. In the words of His Holiness John Paul II, it is 'more than a hypothesis'.

There was also wide agreement on the central role played in biological evolution by Darwinian natural selection, defined as a natural process that obligatorily brings out, from a collection of accidentally produced genetic variants, those most apt to survive and, especially, to produce progeny under prevailing conditions. A number of contributions did, however, underline the need to refine some of the conceptual bases of this theory in the light of recent findings. The genetic variations subject to natural selection may be of different type, involving, not only changes in DNA sequences, but also intragenomic reorganization of genetic fragments, acquisition of foreign DNA, as well as chemical modifications of the DNA and changes in chromosome organization. One also has to take into account the hierarchical organization of genes, their mutability and its control, and the presence of so-called 'evolution genes.' Attention must also be given to non-Darwinian mechanisms of evolution, such as genetic drift, by way of neutral or near-neutral mutations, and the direct inheritance of certain molecular shapes. It must also be recognized that the conditions that influence natural selection are not only physical and chemical, but also biological, including entire eco-systems. These factors all tend to modulate the role of chance in evolution and to introduce more necessity in the process than was believed by earlier evolutionists.

On the other hand, no one, at least among the scientists, defended the recently advocated theory of 'intelligent design', according to which certain evolutionary events could not have taken place without the intervention of some higher influence, of which no evidence can be found in nature. Several of the arguments cited in support of this theory were shown to ignore recent findings. In particular, the theory was rejected as intrinsically non-scientific, resting, as it does, on the *a priori* contention, neither provable nor disprovable, that certain events cannot be naturally explained. These views did not satisfy some theologians who stressed the role of design in creation, an affirmation which, in turn, raised the questions of where and how design is manifested. The issue was not settled during the meeting.

These discussions automatically brought to the fore the subject of human manipulation of the selection process, including the much-debated topic of genetically modified organisms (GMOs). It was pointed out that humans did not await the development of genetic engineering to start interfering with life on Earth. They have, ever since the inauguration of agriculture and animal breeding, some ten thousand years ago, manipulated living organisms for their own benefit, empirically generating plant and animal species that are totally different from their wild ancestors and which have, thanks to their much higher yields, allowed the feeding of many more people than could otherwise have been sustained. In this context, the development of GMOs by rationally designed manipulations could be seen as a distinct improvement over earlier empirical techniques, of great potential benefit for the feeding of the expanding human population. Nevertheless, this technology is vigorously opposed as 'anti-natural' by many defenders of the environment.

The advent of humankind attracted a great deal of interest. The recent history of hominization was reviewed, together with the molecular evidence establishing the single origin of all the human populations that exist on Earth today. Special attention was paid to the astonishing increase in size (almost four-fold) and complexity of the brain that accompanied, in a span of only a few million years, the conversion of chimpanzee-like ancestors into fully developed human beings. Several neurobiologists and cognition experts elaborated on the anatomical and functional correlates of these remarkable changes. The new capabilities of these changes, in relation, among others, to human freedom and the human intellective soul, were underscored by several speakers.

Particularly highlighted was the faculty of the human brain to undergo, mostly during the first years of its development, a considerable amount of epigenetic reprogramming of its genetically determined basic structure. The decisive role of education in this process was emphasized. This consideration has become acutely urgent for the future of humanity and of much of the rest of the living world, which is gravely threatened by the consequences of the inordinate evolutionary success (largely imputable to natural selection but also to culture) of the human species. For this threat to be averted, some of the unfavourable ingrained traits of human nature (which, from a theological point of view, could be viewed as related to original sin), must be corrected by education and, for those who believe, by the grace and love of God. Religions can be particularly influential in this respect and thereby bear a crucial responsibility in changing the future of the world for the better and, perhaps, saving humanity from extinction.

TABLES

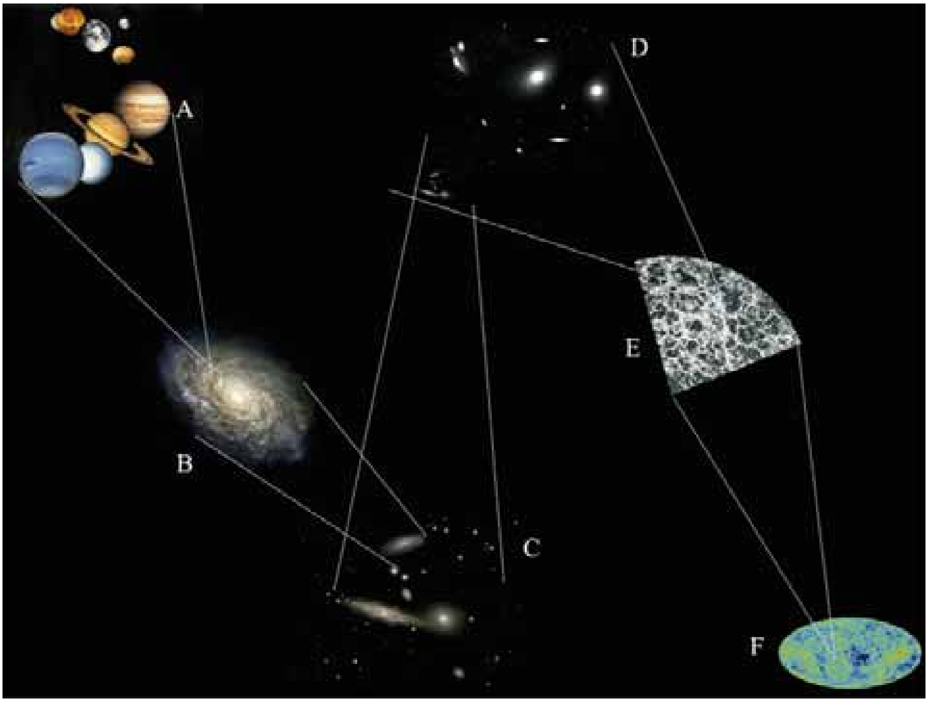


Fig. 1. This is a one-page sketch of our Universe, from nearby to distant. (A) The planets in our Solar System; (B) a galaxy similar to our Galaxy, with the 'location' of the sun and planets indicated; (C) a cluster of galaxies similar to our Local Group of galaxies; (D) the center of the Virgo Cluster of galaxies. The Local Group is currently moving away from the Virgo Cluster, but slowly. It may ultimately halt, then start moving toward the Virgo Cluster, and finally become gravitationally bound to the Cluster; (E) distribution of distant clusters of galaxies (white), with voids between; (F) our view of the very early universe showing the tiny fluctuations in the cosmic microwave radiation 400,000 years after the Big Bang. This microwave radiation traveled for almost 14 billion years to reach our detectors.

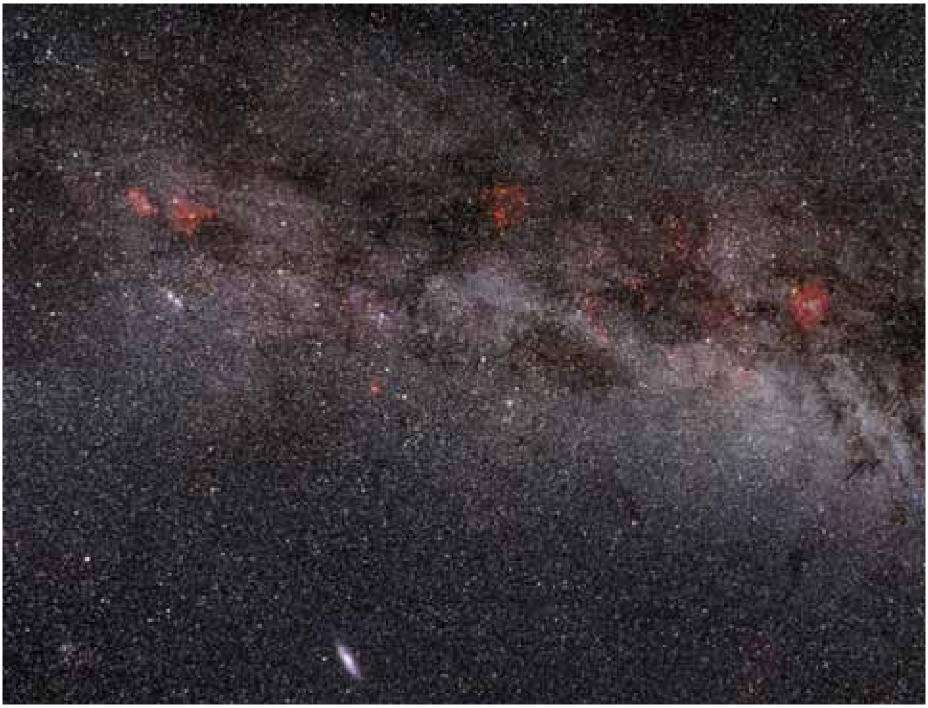


Fig. 2. A view of the stars and gas clouds in our northern Milky Way, the central plane of our Galaxy. The white regions contain billions of stars; the red blobs are hydrogen gas clouds; all in our Galaxy. The small white blob, lower left, is the Andromeda galaxy, the nearest large galaxy to us. [Photo by Wei-Hao Wang].

Fig 5. The massive cluster Abell 2218 acts as a lens, and distorts and magnifies the images of background clusters and galaxies moving them into the line of sight of the observer. The arcs are the distorted background galaxies; the color of an arc depends on the distance and the type of galaxy.

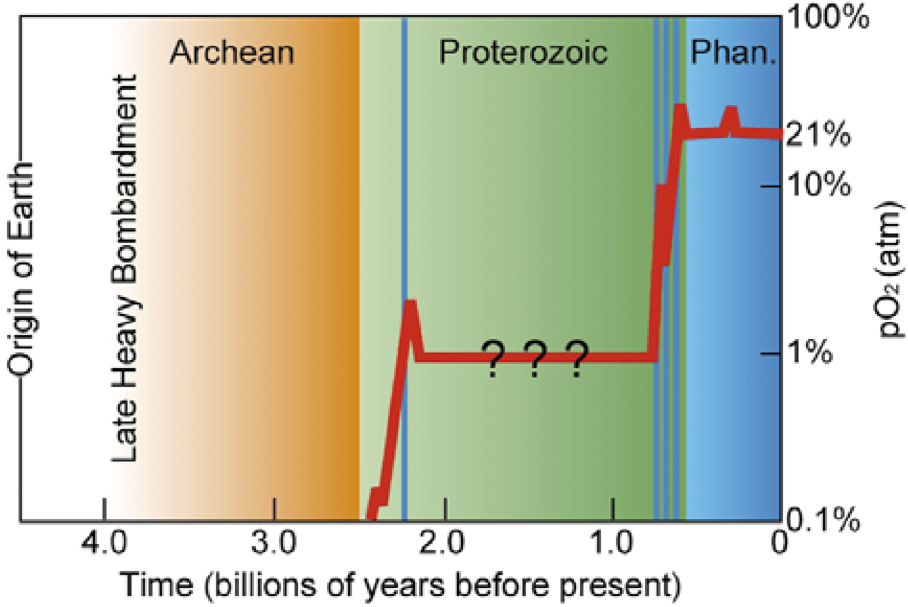


Figure 1.

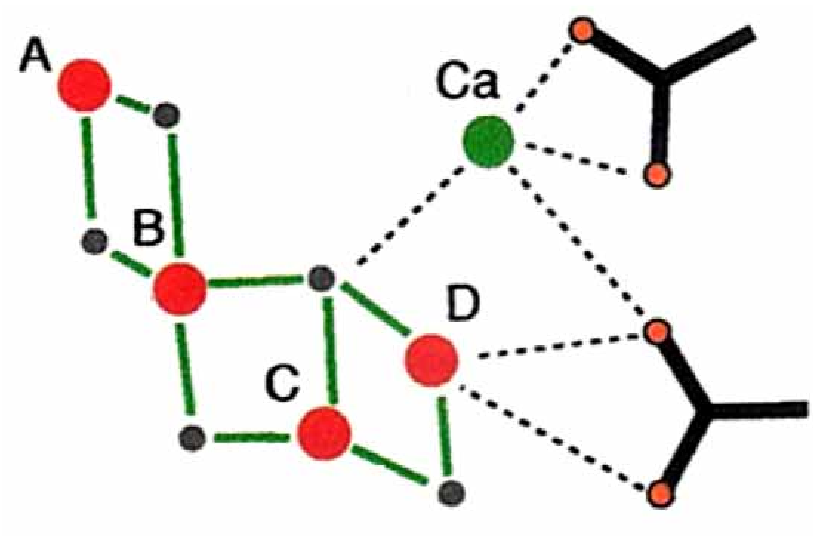


Figure 3. From Yano *et al.*, *Science* 3 November 2006, 314: 821-825

Figure 5.

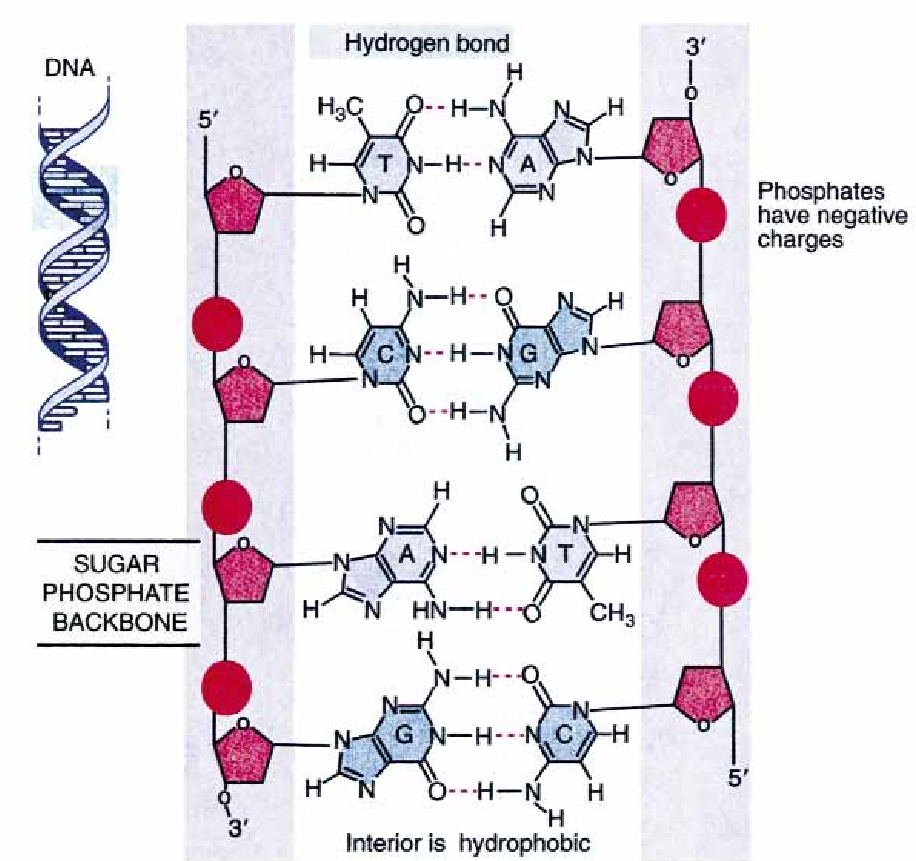


Figure 1. From B. Lewin, *Genes* IX (2008).

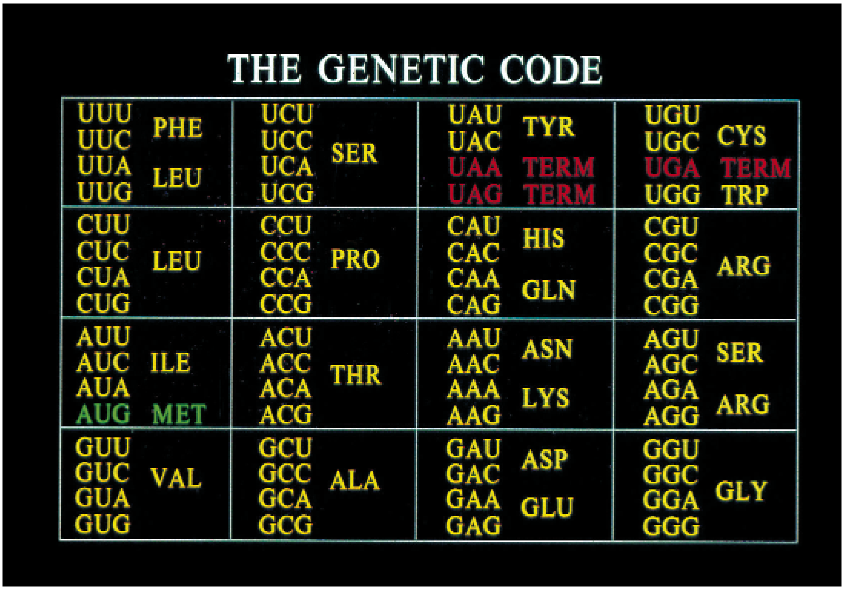


Figure 4.

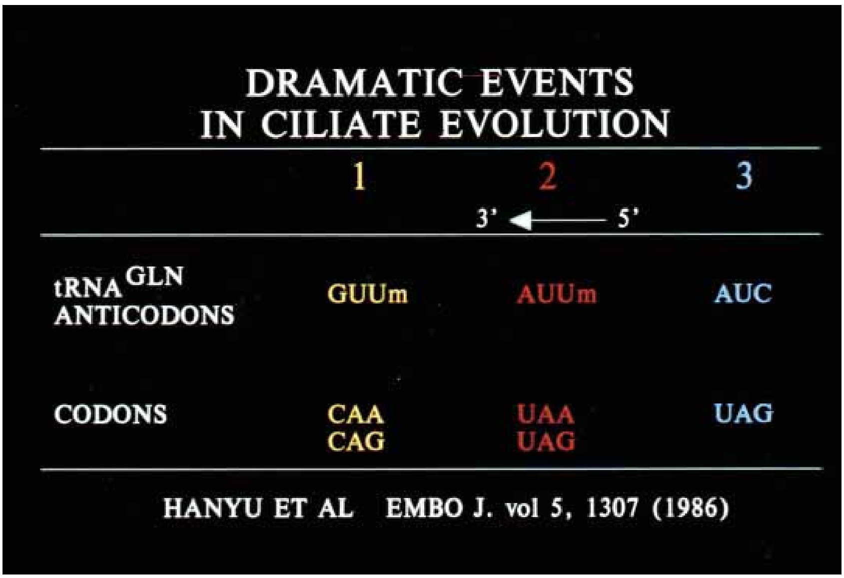


Figure 7.

DIALECTS IN THE GENETIC CODE OF MITOCHONDRIA

STANDARD CODE		MITOCHONDRIA			
		TRYPANOSOMA NEUROSPORA	YEAST	DROSOPHILA	MAMMALS
UGA	TERM	TRP	TRP	TRP	TRP
UGG	TRP	TRP	TRP	TRP	TRP
AUA	ILE		MET	MET	MET
AUG	MET		MET	MET	MET
CUU	LEU		THR		
CUC	LEU		THR		
CUA	LEU		THR		
CUG	LEU		THR		
AGA	ARG			SER	TERM
AGG	ARG			SER	TERM

Figure 8.

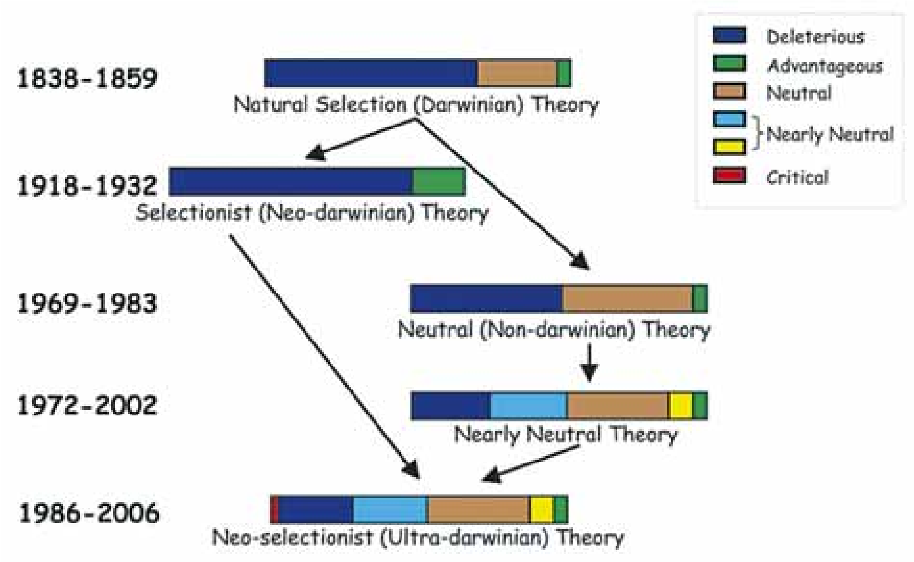


Figure 1. Darwin postulated the existence of deleterious, advantageous, and neutral changes. The neo-Darwinians (or selectionists) neglected neutral changes. These were reintroduced and amplified by Kimura (7, 8), who developed the neutral theory of evolution (a non-Darwinian evolution, according to King and Jukes,10). The nearly neutral theory was proposed by Ohta (11, 12) to include intermediates between neutral and advantageous, as well as between neutral and deleterious changes. In the neo-selectionist theory, nearly neutral theory is fully accepted and critical changes are responsible for the transition from point mutations to regional changes (from ref. 32).

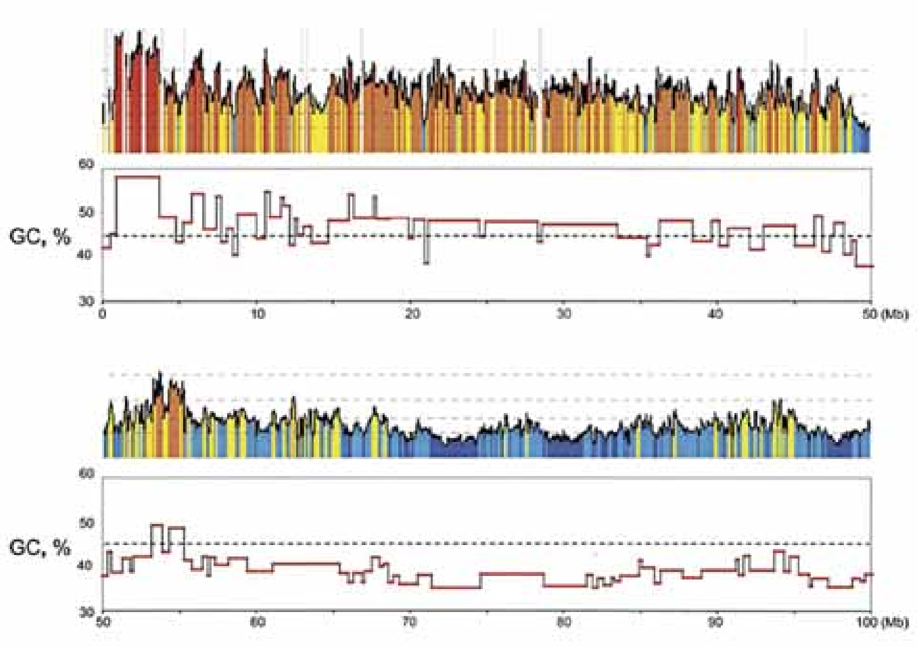


Figure 2. Overview of isochores on 100 Mb of chromosome 1 as a representative region of human chromosomes. The *top* frames represent GC profiles. Red to blue colours in the profiles correspond to decreasing GC levels. Horizontal red stretches in the *bottom* frames represent isochores (from ref. 27).

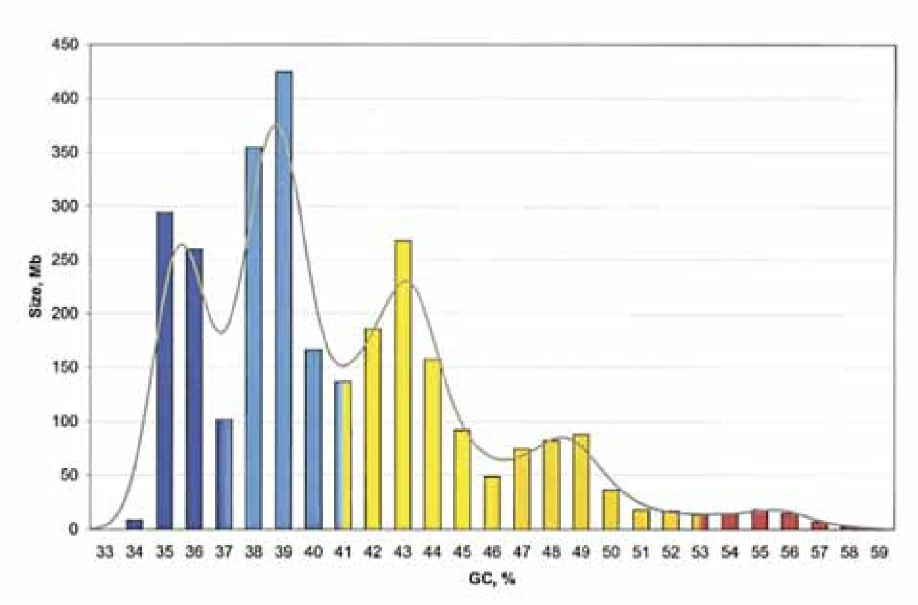


Figure 3. Distribution of human isochores according to GC levels (from ref. 27).

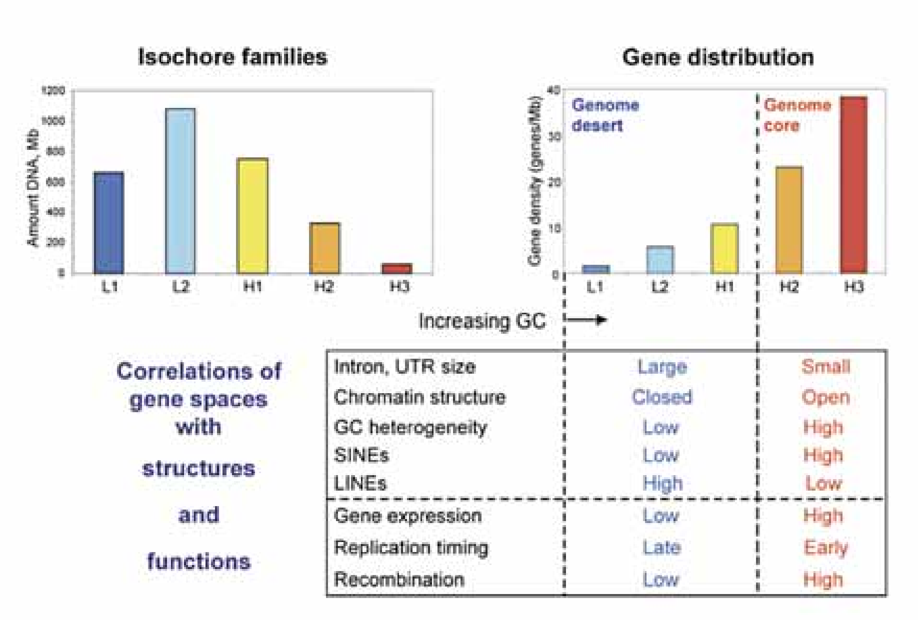


Figure 4. DNA and gene distribution in the isochore families of the human genome. The major structural and functional properties associated with each gene space are listed (in blue for the genome desert and in red for the genome core). SINEs are short interspersed sequences; LINEs, long interspersed sequences (from ref. 32).

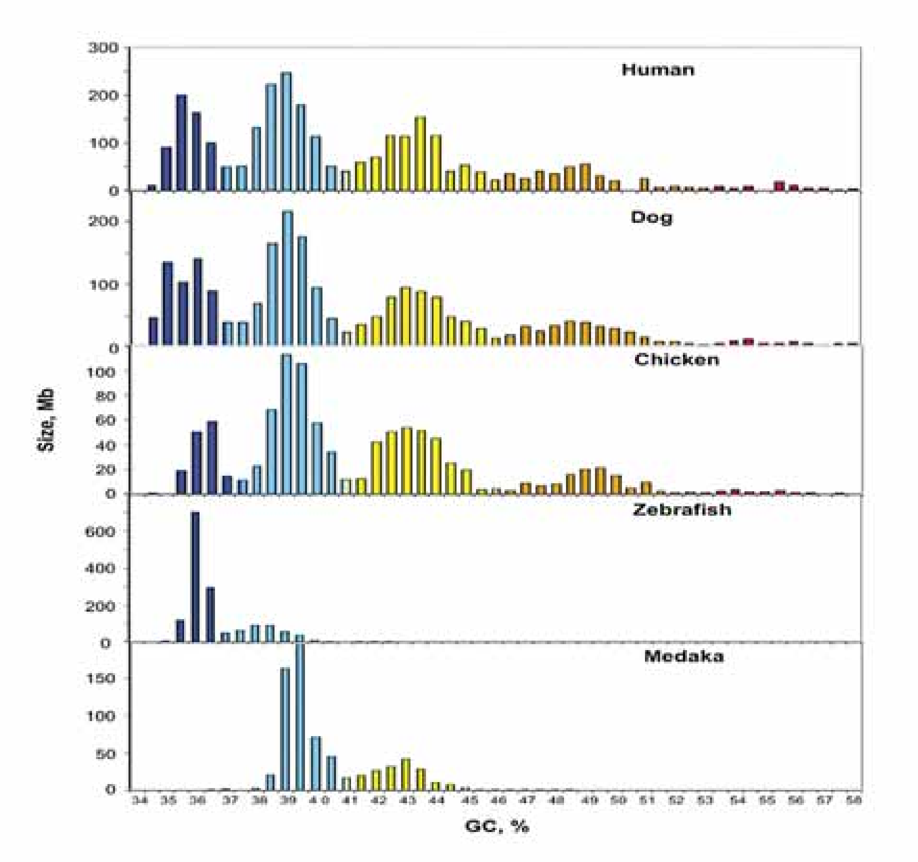


Figure 5. A comparison of the isochore families from several vertebrate genomes (from ref. 30).

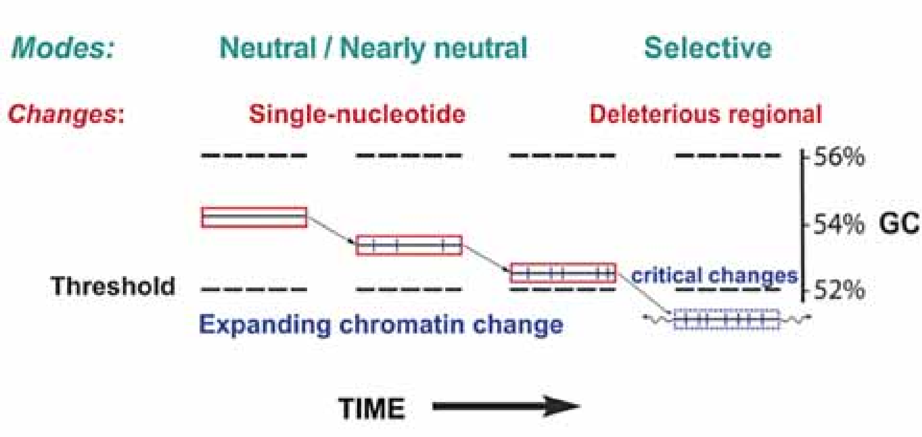


Figure 6. Time course of typical compositional changes of a GC-rich region from a warm-blooded vertebrate in the conservative mode of evolution. In an early phase, the average GC level of the region, initially visualized at its compositional optimum (arbitrarily set here at 54% GC), is decreasing because of the mutational AT bias (the vertical blue bars crossing the black DNA line in the chromatin red boxes represent the 'excess' GC → AT changes), but remains within a tolerated range (whose arbitrary thresholds are indicated by the thick horizontal broken lines). In a late phase, the average GC level trespasses the lower threshold (arbitrarily fixed here at 52% GC), because of the last changes, the critical changes. The corresponding chromatin (red boxes) then undergoes a structural change (broken blue box) that is deleterious for transcription (see text). Until then, the changes may be neutral or, more frequently, nearly neutral (from ref. 32).

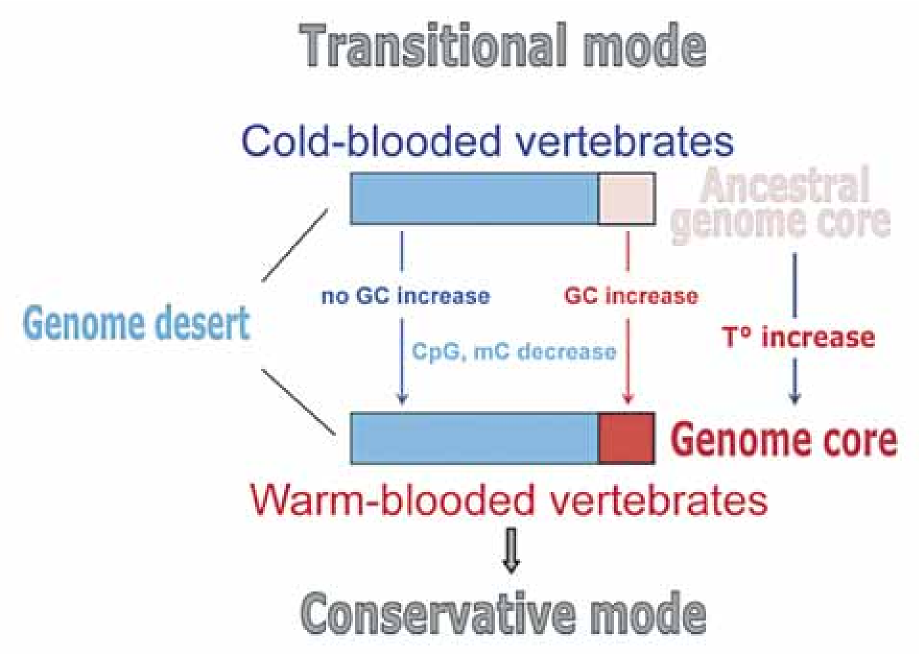


Figure 7. Scheme of the compositional evolution of vertebrate genomes. At the transition from cold- to warm-blooded vertebrates, the gene-dense, moderately GC-rich 'ancestral genome core' (pink box) became the gene-dense, GC-rich genome core (red box), but the GC-poor and gene-poor (blue box) genome desert did not undergo any major compositional change. This transitional (or shifting) mode, which was accompanied by an overall decrease of CpG doublets and methylcytosine, was followed by a conservative mode of genome evolution in which compositional patterns were maintained (from ref. 32).

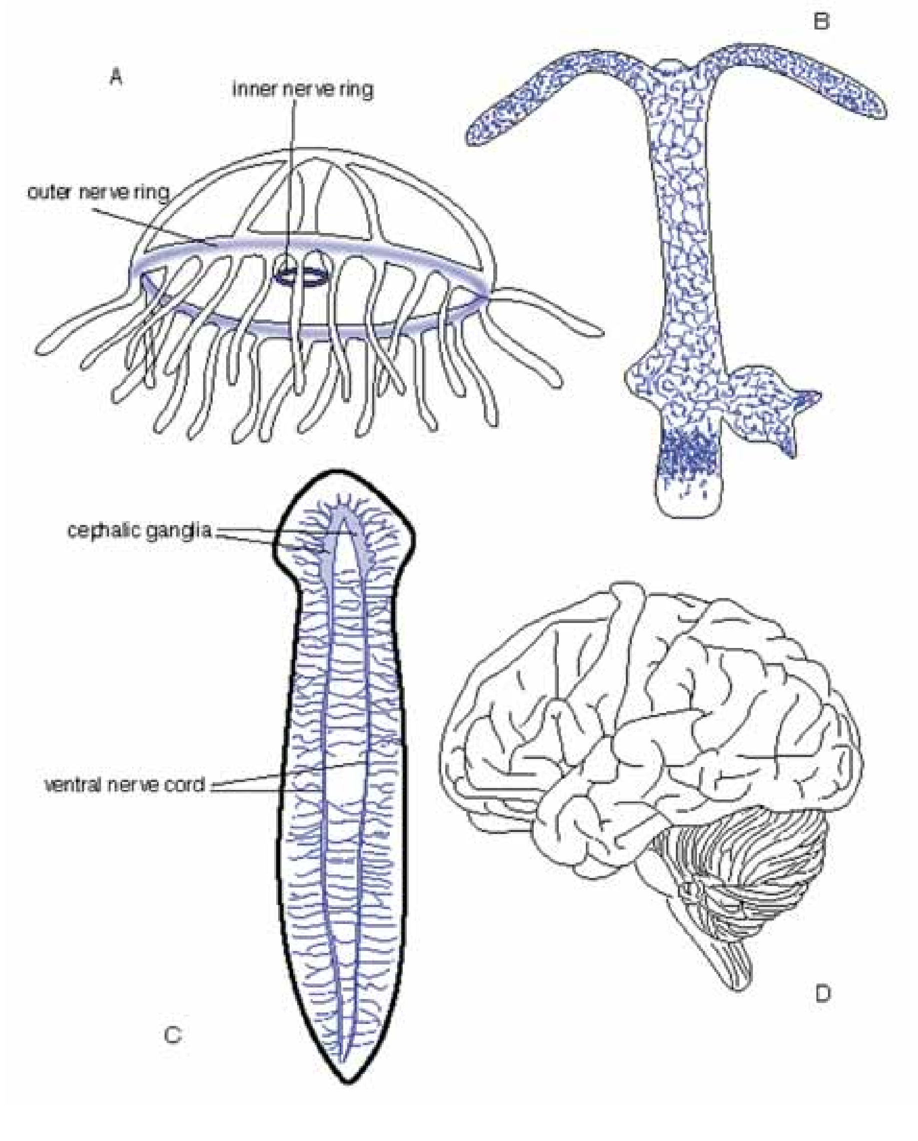
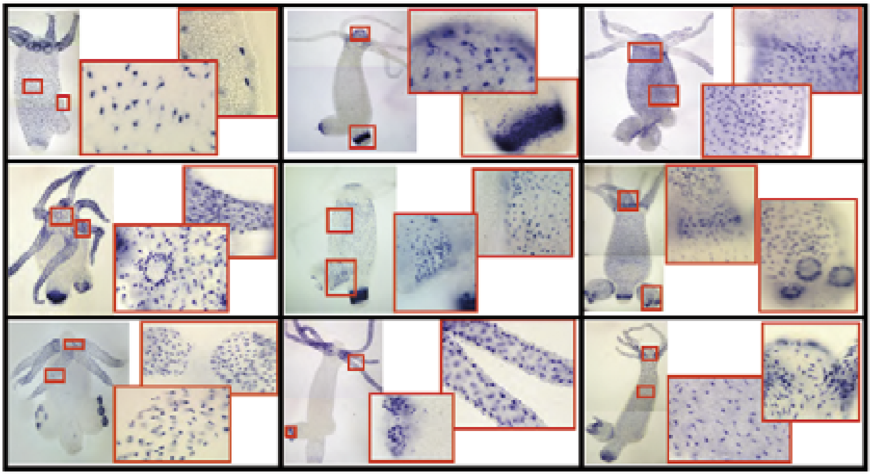


Figure 1. The nervous systems of jellyfish, *Hydra*, planarian and human. Both jellyfish and *Hydra* have a diffuse nerve net. (A) The inner and outer nerve rings of jellyfish are highlighted in blue. (B) In *Hydra*, neurons (blue) spread out in the ectoderm and the endoderm. Some *Hydra* species also possess a nerve ring at the mouth region. The central nervous system (blue) of planarians contains cephalic ganglia and ventral nerve cords. (D) Human brain. Note that the scale of the animal size in the figure does not refer to the relative size of the actual animal.

A



B

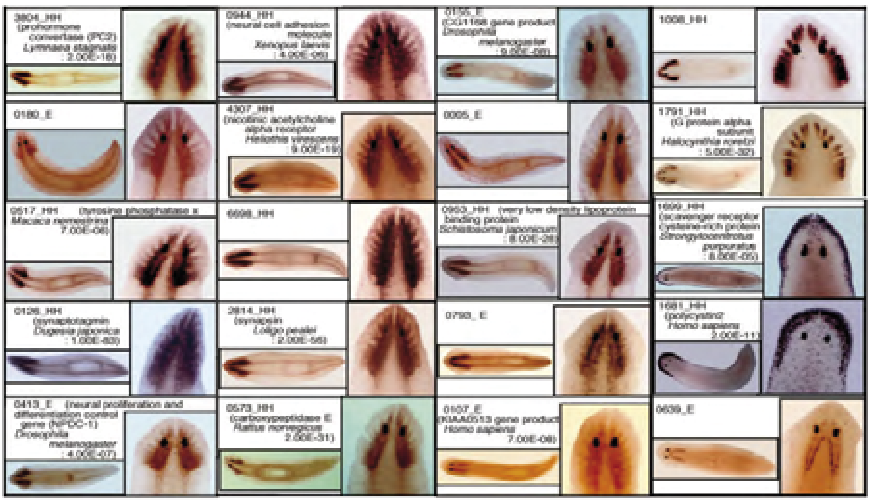


Figure 2. Various expression patterns of nervous system genes of *Hydra* (A) and planarian (B) are examined by whole mount *in situ* hybridization. The results have been published in Hwang *et al.* (2007) and Nakazawa *et al.* (2003).

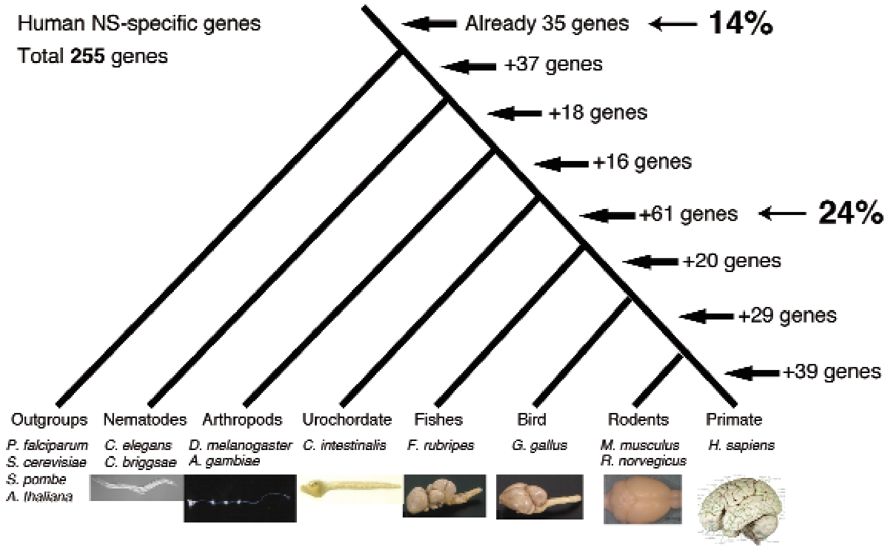
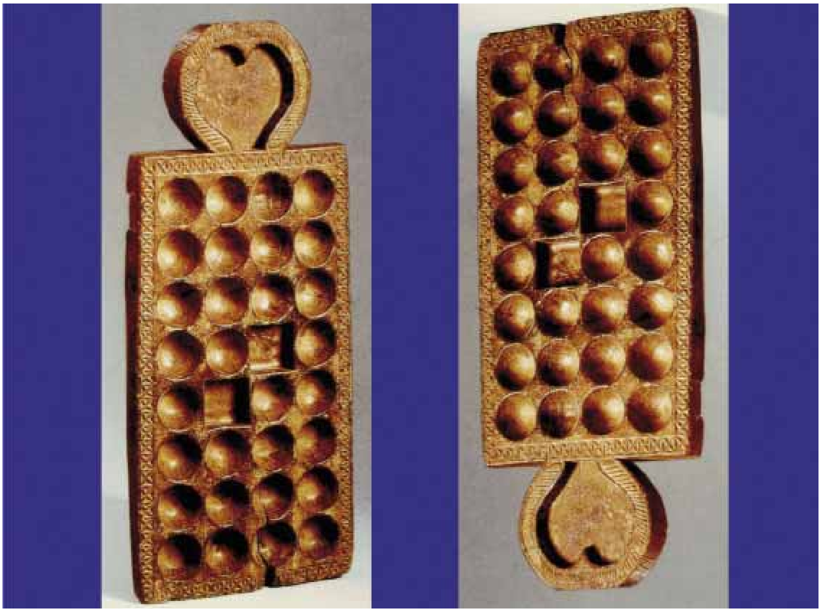


Figure 5. Schematic drawing of the emergence of human NS-specific genes. Out of 255 genes, 35 genes (14%) exist prior to the divergence yeast and human and 61 genes (24%) emerge after the divergence of urochordates and human. The data analysis of this figure is described in Noda *et al.*, 2006.



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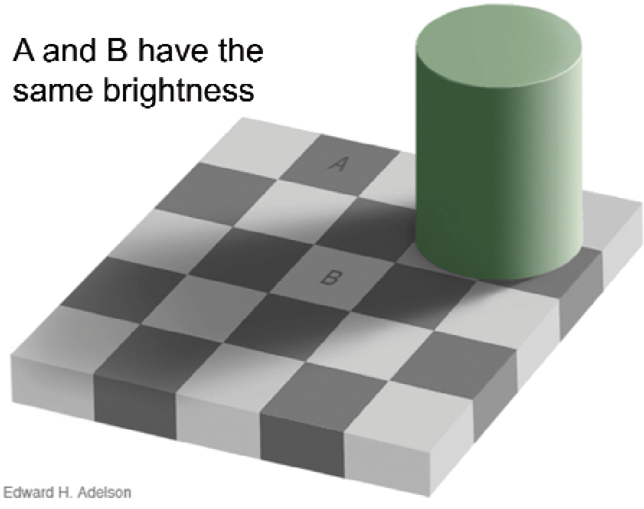

Figure 2.

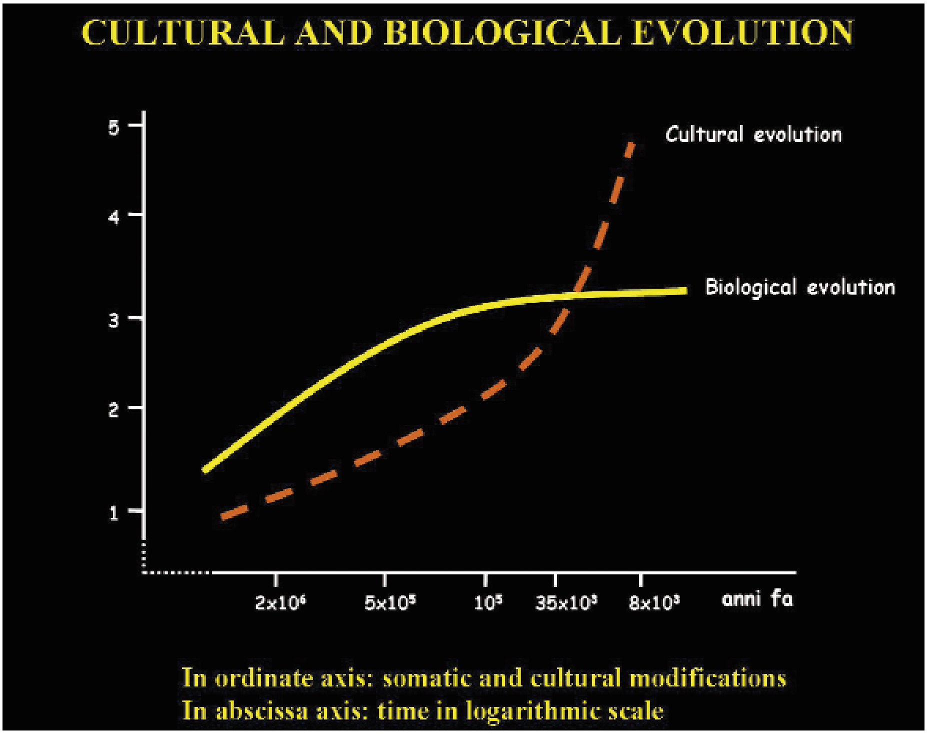

Figure 2. Hypothesis of graphic representation of cultural and biological evolution.

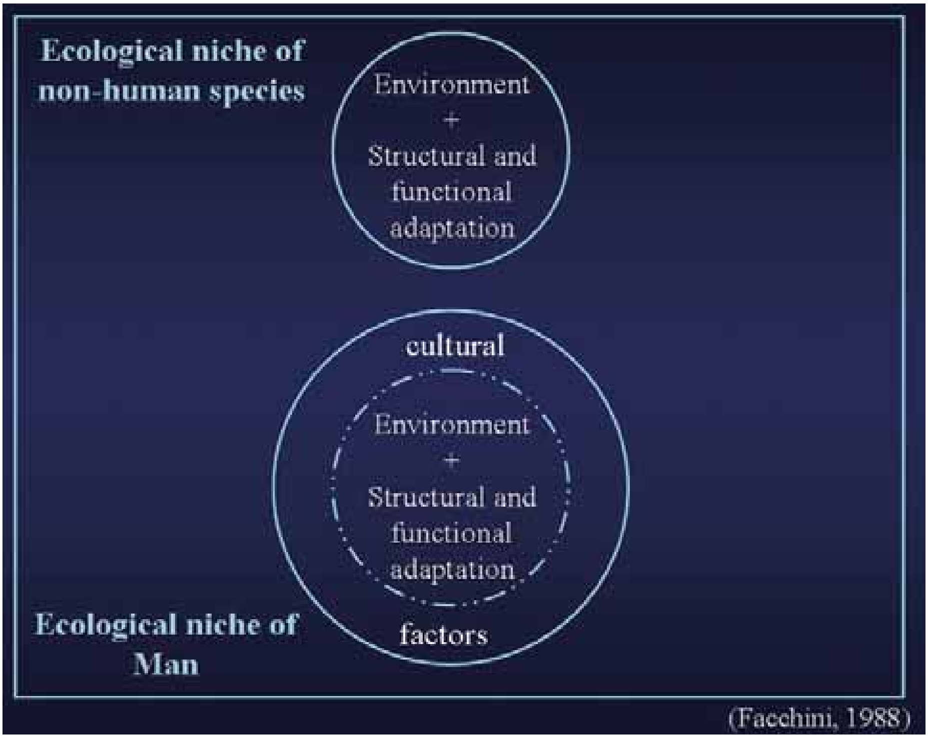

Figure 3. Graphic representation of the ecological niche for non-human species and for Man.

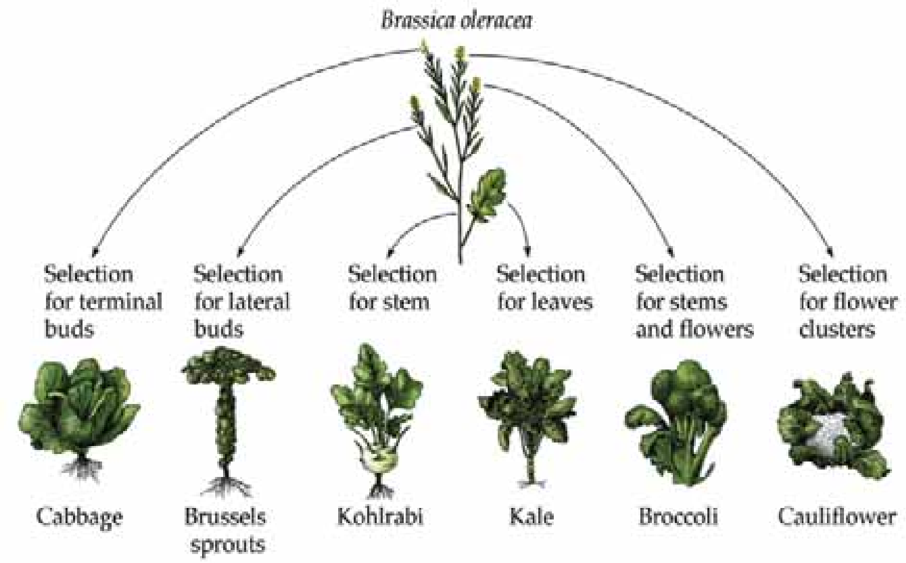

Fig. 1 A variety of different cabbage crops have been bred from wild cabbage, by selecting amongst the genetic variation for different desired traits.

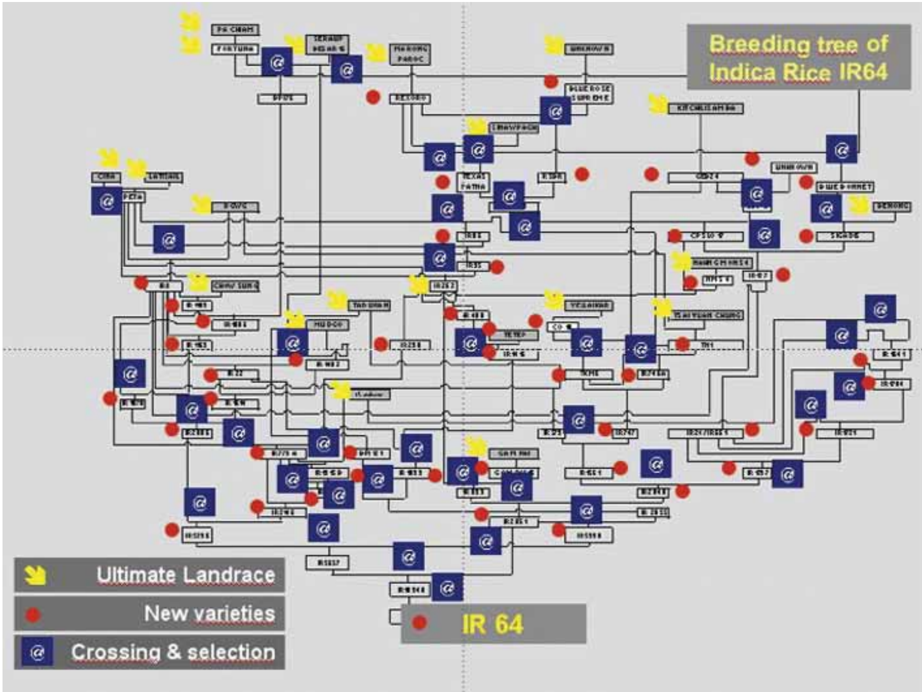

Fig. 2. The ‘breeding tree’ (the history of the breeding process) of the most popular and widespread rice variety IR64, indicates over how many breeding steps the development of a modern variety evolves. The yellow arrowheads indicate ‘landraces’ (mutant forms of rice selected by farmers for specific beneficial traits) and the blue boxes indicate the steps of sexual hybridisation and selection. Each of these parameters and steps inadvertently leads to uncontrolled and unpredictable alterations of the genome. And the breeder has no control on these changes but just selects, among hundreds of thousands of offspring, the single one with the desired trait combination.

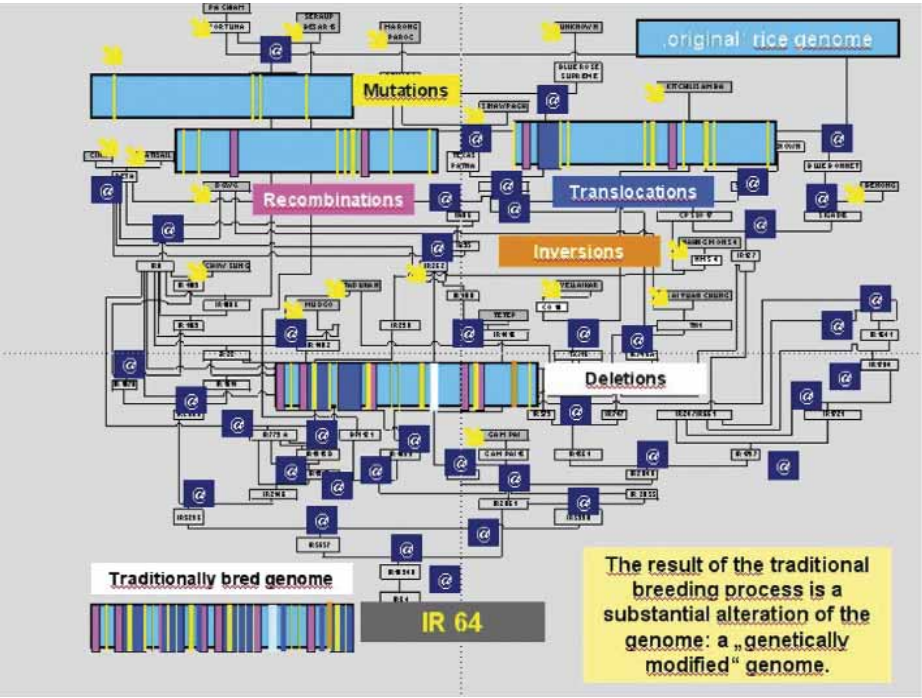

Fig. 3. A graphic representation of the types of uncontrolled changes in the genome that accompany the traditional development of a modern crop variety. *Blue* represents the original genome; *yellow* are spontaneous or induced *mutations*; *red* are *recombinations* (rearrangements of large parts of the genome); *blue* are 'translocations' (excision from and re-integration of at novel positions in the chromosome); *orange* are *inversions* (excision and re-integration with opposite polarity of entire chromosme pieces); *white* are *deletions* (loss of entire fractions of chromosomes with hundreds of genes). All these uncontrolled 'genetic modifications' of the genome were the basis for those crop varieties, which we eat daily.

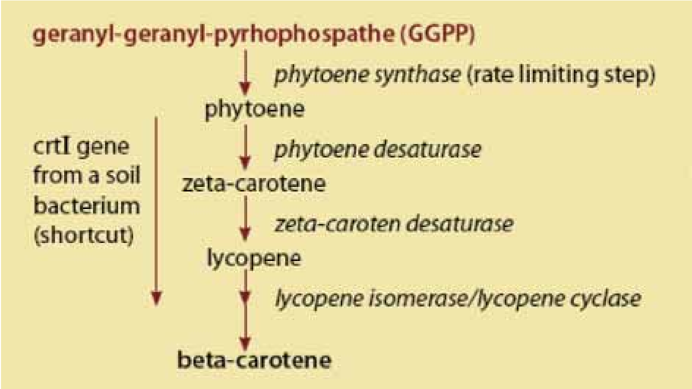

Fig. 4. The provitamin A pathway with rate-limiting steps and genes required to engineer the synthesis of provitamin A in rice endosperm. The plant uses four enzymes to convert the precursor (GGPP) to provitamin A (beta-carotene). These genes are active in all green tissues of the rice plant, but are not active in the seed storage tissue, the endosperm. Three of the missing enzymes (produced by an active gene) can be replaced by one bacterial gene, providing the possibility to achieve the goal with the introduction of two genes only. Proof-of-concept was gained with the four plant genes. To date all novel Golden Rice varieties are produced by the two-gene system.

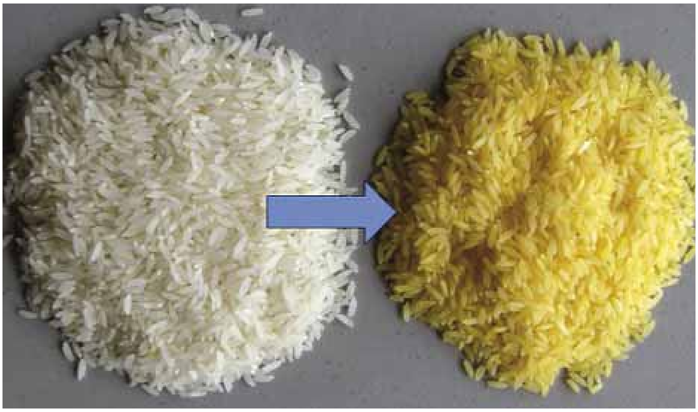

Fig. 5. 'Golden Rice' is a novel rice variety which is based on genetic engineering. It contains sufficient amounts of provitamin A to prevent vitamin A-malnutrition of rice-dependent poor societies, if consumed instead of ordinary rice. The 'directed' evolution of provitamin A-rice was planned, in response to the need, and executed on the basis of the molecular knowledge about the biosynthetic pathway and state-of-the-art gene transfer technology. Such provitamin A-rice never developed during natural evolution, and there is no 'incentive' for evolution to develop such a plant, because there is no selective advantage in any ecosystem for this trait.

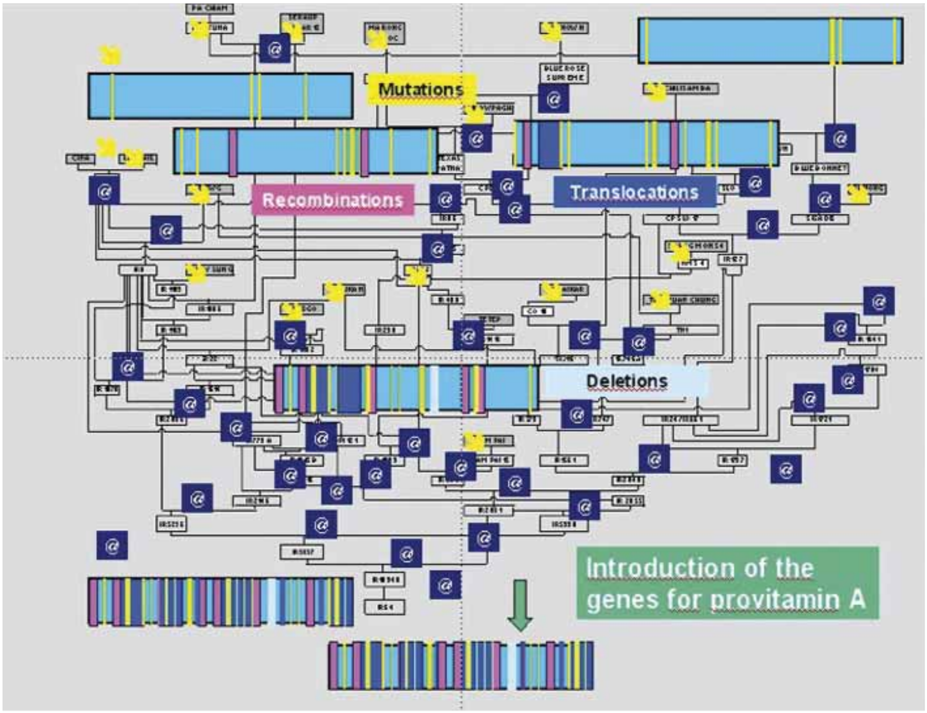

Fig. 6. A relatively minute additional alteration of the genome of the precisely studied genes for the biochemical pathway for provitamin A does not lead to a novel quality of insecurity or unpredictability. But the novel phenotype has the potential to rescue millions of children from blindness and death.

Fig. 7. Peter Breughel the Elder, *The Harvest*, 1565.

Fig. 8. Jean-François Millet, *Man With a Hoe*, 1862.