

Edited by
Joachim von Braun

Science for Sustainability and Wellbeing in the Anthropocene

Opportunities, Challenges, and AI



Proceedings of the Plenary Session
Casina Pio IV, Vatican City, 23-25 September 2024

Science for Sustainability and Wellbeing in the Anthropocene – Opportunities, Challenges, and AI

Pontificiae Academiae Scientiarum Acta 28

Proceedings of the Plenary Session on

Science for Sustainability and Wellbeing in the Anthropocene – Opportunities, Challenges, and AI

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

Cover: Illustration by Lorenzo Rumori

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© 2025 – Dicastero per la Comunicazione – Libreria Editrice Vaticana
00120 Città del Vaticano
Tel. 06.698.45780
E-mail: commerciale.lev@spc.va
www.libreriaeditricevaticana.va

ISBN: 978-88-266-1061-0
DOI: 10.65398/MXJW4309



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Pope Francis addressing the Pontifical Academy of Sciences
Friday, 25 September 2024



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ADDRESS OF POPE FRANCIS TO THE PLENARY ASSEMBLY OF THE PONTIFICAL ACADEMY OF SCIENCES

Monday, 23 September 2024

■ <https://www.doi.org/10.65398/WHUY3487>

*Dear President, your Eminence,
distinguished Ladies and Gentlemen!*

I offer a warm welcome to the members of the Pontifical Academy of Sciences, and, in a particular way, I greet the new members. Your insights and expertise are very important in the complex world in which we live. I thank the President, Joachim von Braun, and the Chancellor, Cardinal Peter Turkson, and the Academicians for highlighting the issue of *Anthropocene* and *Artificial Intelligence* for study and discussion at this year's Plenary Assembly.

All of us are increasingly troubled by humanity's deep impacts on nature and the earth systems. I have learned that one of you, Paul Crutzen, in describing these impacts on created nature, referred to them collectively as constituting the *Age of the Anthropocene*. Members of your Academy were thus among the first to identify the cumulative impact of human activities on creation and to study its related risks and problems. Indeed, the Anthropocene is revealing its increasingly dramatic consequences for nature and for human beings, especially through the climate crisis and loss in biodiversity.

I am grateful, then, that the Pontifical Academy of Sciences continues to focus concern on issues such as these, not least with regard to their implications for the poor and the disadvantaged. The sciences, in their pursuit of knowledge and understanding of the physical world, must never lose sight of the importance of using that knowledge to serve and enhance the dignity of individuals and humanity as a whole.

As our world faces grave social, political and environmental challenges, we see clearly the need for a larger framework in which inclusive public discourse is not only informed by different scientific disciplines, but also by the participation of all segments of society. In this regard, I welcome and commend highly the Academy's desire to draw attention to marginalized and poor people in its various Conferences, and to include indigenous peoples and their wisdom in its dialogues.

Your Plenary Assembly this year also addresses emerging new science and innovations, and related opportunities for science and planetary health. Here I think particularly of the challenges posed by the progress made in Artificial Intelligence. Such development can prove beneficial to humanity, for instance by advancing innovations in the fields of medicine and health care, as well as by helping to protect the natural environment and enabling the sustainable use of resources in the light of climate change. Yet, as we realize, it can also have serious negative implications for the general population, especially children and more vulnerable adults. Furthermore, the risks of manipulative applications of Artificial Intelligence for shaping public opinion, influencing consumer choices and interfering with electoral processes need to be acknowledged and prevented.

These challenges remind us of the invariably human and ethical dimensions of all scientific and technological progress. I would express once more, therefore, the Church's concern that "the inherent dignity of each human being and the fraternity that binds us together as members of the one human family must undergird the development of new technologies... Technological developments that do not lead to an improvement in the quality of life of all humanity, but on the contrary aggravate inequalities and conflicts, can never count as true progress" (*Message for the 2024 World Day of Peace*, 2). In this sense, the impact of forms of Artificial Intelligence on individual peoples and the international community calls for greater attention and study. I am pleased to know that the Pontifical Academy of Sciences is working, for its part, to propose appropriate regulations for the sake of preventing risks and encouraging benefits in this complex field.

Dear friends, at a time when crises, wars and threats to world security seem to prevail, your own quiet contributions to the progress of knowledge in the service of our human family are all the more important for the cause of global peace and international cooperation. I thank you for your participation in the work of the Academy and offer you my prayerful good wishes for the deliberations of the present Plenary Assembly. Upon you, your families and all associated with your important work I invoke God's abundant blessings. And I ask you, please, to remember me in your prayers. Thank you.

CONCEPT AND INTRODUCTION TO THE PLENARY SESSION

JOACHIM VON BRAUN

President of the Pontifical Academy of Sciences

Welcome, dear Academicians and Guests, to this Bi-Annual Plenary of the Pontifical Academy of Sciences. A special welcome and warm congratulations to our newly elected members. We look forward to your lifelong contributions to the mission and work of our Academy.

It has become increasingly evident that humanity exerts a profound impact on the Earth's systems. **The Anthropocene**, understood as the growing and lasting human influence on the global environment, was identified by our esteemed PAS Academician Paul Crutzen (1933–2021), with related significant insights from another PAS Academician, Mario Molina (1943–2020). The PAS has already addressed Anthropocene-related issues in various workshops.¹ However, as its consequences grow more severe for nature and people, particularly in terms of climate crisis and biodiversity loss, this Plenary seeks to engage with the topic in a more comprehensive manner.

In parallel, this Plenary explores emerging new science and innovations, in particular **Artificial Intelligence**, and related opportunities for science and planetary health, while also considering regulatory frameworks to mitigate risks. Through a series of targeted briefings, the Plenary invites the entire Academy to engage in forward-looking discussions on key scientific domains, to help shape our future Agenda. These interdisciplinary conversations are at the core of our Academy's *raison d'être*.

¹ Sessions and workshops related to Anthropocene issues:

- *Resilience of People and Ecosystems under Climate Stress*: Workshop | 13–14 July 2022;
- *Science and Survival. A Focus on SARS-CoV-2 and Connections Between Large-Scale Risks for Life on This Planet and Opportunities of Science to Address Them*. Plenary Session | 7–9 October 2020;
 - *Science and Sustainability. Impacts of Scientific Knowledge and Technology on Human Society and its Environment*. Plenary Session | 25–29 November 2016;
- *Climate Change, Health of the Planet and Future of Humanity*: Workshop | 15 November 2018;
- *Biological Extinction: How to Save the Natural World on Which We Depend*. Workshop | 27 February – 1 March 2017.

On September 23, 2024, **His Holiness Pope Francis** graciously addressed our Academy. It turned out to be his final formal message to us, and it carried profound significance.² He remarked:

“All of us are increasingly troubled by humanity’s deep impacts on nature and the earth systems. I have learned that one of you, Paul Crutzen, in describing these impacts on created nature, referred to them collectively as constituting the Age of the Anthropocene. Members of your Academy were thus among the first to identify the cumulative impact of human activities on creation and to study its related risks and problems. Indeed, the Anthropocene is revealing its increasingly dramatic consequences for nature and for human beings, especially through the climate crisis and loss in biodiversity. I am grateful, then, that the Pontifical Academy of Sciences continues to focus concern on issues such as these, not least with regard to their implications for the poor and the disadvantaged... Your Plenary Assembly this year also addresses emerging new science and innovations, and related opportunities for science and planetary health. Here I think particularly of the challenges posed by the progress made in Artificial Intelligence. Such development can prove beneficial to humanity, for instance by advancing innovations in the fields of medicine and health care, as well as by helping to protect the natural environment and enabling the sustainable use of resources in the light of climate change. Yet, as we realize, it can also have serious negative implications for the general population, especially children and more vulnerable adults.”

Pope Francis concluded with these words:

“... at a time when crises, wars and threats to world security seem to prevail, your own quiet contributions to the progress of knowledge in the service of our human family are all the more important for the cause of global peace and international cooperation. I thank you for your participation in the work of the Academy and offer you my prayerful good wishes for the deliberations of the present Plenary Assembly.”

The Anthropocene is the age we live in, marked by profound imprints of human activities on nature through industrialization, fossil fuel dependen-

² See the complete address in this volume and at <https://www.vatican.va/content/francesco/en/speeches/2024/september/documents/20240923-plenaria-accademia-scienze.html>

cy, nuclear technologies, urbanization, consumerism, and communication technologies, among others. Unlike previous geological periods, we argue that the Anthropocene cannot be defined solely by geological markers.

Sciences and the Anthropocene are interrelated. Science is not independent from the forces that shape the Anthropocene. In fact, scientific innovations are among the key drivers of the Anthropocene, through modern energy systems reliant on fossil fuels, global transportation networks via land, sea and air, construction industries based on steel and concrete, consumer goods, including electronics with rare earth elements, and agricultural and land-use related innovations, all contributing to greenhouse gas emissions, pollution, and ecosystems degradation.

Climate change is at the core of the Anthropocene. Notably, during our climate resilience summit with scientists, governors and mayors, Pope Francis took the unusual step of signing our call to action.³ As a follow-up, we are currently rolling out regional climate resilience summits across hemispheres,⁴ which is an unprecedented initiative for PAS.

Yet, **science and innovations** are progressing and serve human betterment by providing opportunities to mitigate and manage the Anthropocene. Advances in life and medical sciences have dramatically improved child survival, longevity and disease management. These achievements have contributed to population growth, expanded consumption, and wellbeing. Yet, in turn, these trends have increased environmental pressures. Scientific advancements from the past have often been retrospectively recognized as contributing to the root causes of the Anthropocene.

We embrace a comprehensive approach to scientific inquiry. In this Plenary we have continued to advance our exploration of the rich insights that emerge from the braiding of **indigenous knowledge and the sciences**. Recently, the Academy hosted a landmark conference with indigenous knowledge communities, possibly the first of its kind convened by a scientific academy.⁵ We remain committed to pursuing this integrative approach in the current Plenary and beyond, respectfully linking our Academy with

³ *From Climate Crisis to Climate Resilience* https://www.pas.va/en/events/2024/climate_resilience.html

⁴ *From Climate Crisis to Climate Resilience – A series of global and regional Climate Resilience Summits* jointly organized by the Pontifical Academies of Sciences and Social Sciences https://www.pas.va/en/events/2025/climate_resilience_summits.html

⁵ *Indigenous Knowledge and the Sciences*. https://www.pas.va/en/events/2024/indigenous_peoples.html

traditional and indigenous knowledge holders to address the multifaceted challenges of the Anthropocene.

The relationship between Artificial Intelligence (AI) and the Anthropocene may deepen in the future. Since our 2019 conference on Robotics and AI, which resulted in a book that is still in demand,⁶ the field has evolved rapidly. Contemporary and future science face the dual challenge of mitigating the adverse effects of the Anthropocene while helping humanity to adapt to its realities. While ethical dilemmas arising from science-based innovations are not new, AI introduces unprecedented ethical complexities due to its profound and uncertain impact on society and innovation processes. We are called to examine developments in AI and other innovations not only as accelerators of Anthropocene dynamics, but also as potential instruments to augment human intelligence in the pursuit of a sustainable Anthropocene.

AI is already transforming science disciplines such as chemistry, physics, biology, life sciences, and medicine. Quantum physics and computing may offer further breakthroughs capable of redirecting the Anthropocene onto sustainable pathways. The Pontifical Academy of Sciences has long engaged with these themes through consultations, publications, and public statements. This includes responses to pandemics, chronic diseases, stem cell research, cancer, neurotechnology, and humanitarian and food crises. And our Academy maintains a strong interest in frontier science related to Astronomy. We identified specific science opportunities in each of these areas and issued related statements urging policy and societies to act.⁷ The 2024 Plenary Session draws on the insights from these workshops and places them within the broader context of science and science diplomacy opportunities.

The 2024 Plenary Session partly builds upon these insights, placing them within the broader framework of **science diplomacy**. Our Academy remains

⁶ *Robotics, AI, and Humanity: Science, Ethics, and Policy*. Workshop | 16-17 May 2019 <https://link.springer.com/book/10.1007/978-3-030-54173-6>

⁷ See www.pas.va for details on these workshops held in 2022-2024:

- *Reconstructing the Future for People and Planet* (9-10 June 2022)
- *Health of the Seas and Oceans* (8 June 2022)
- *Strategies to Decrease Inequalities in Cancer Therapeutics, Care, Prevention* (23-24 February 2023)
- *Food crises: Science and policies to prevent and overcome food crises* (9-10 May 2023)
- *Quantum Science and Technology* (22-25 November 2023)
- *Neurotechnology: Ethical and societal implications of recent advances* (13-14 December 2023)
- *Astrophysics: James Webb Space Telescope: from first light to new world views* (27-29 February 2024)
- *Indigenous Peoples Knowledge and the Sciences* (PAS and PASS, 14-15 March 2024)

actively engaged in **addressing science scepticism** in policy, society and media.⁸ I am grateful that the final session provided the opportunity to engage with a group of outstanding international science policy leaders on science policy perspectives related to the themes of the Anthropocene and AI.

We affirm the critical **importance of basic science** in understanding and addressing the complex processes of the Anthropocene. Curiosity-driven basic research continues to yield big payoffs that often come about in unpredictable ways, mostly in the long term, but increasingly within shorter timeframes. Purposeful science is equally relevant, particularly its **contributions to peace**, which Pope Francis emphasized as a fundamental prerequisite for sustainable development.

In closing, I would like to point out that our Plenaries are unique opportunities for Academicians and guests to interact and engage in meaningful interdisciplinary dialogue. Together, we explore scientific frontiers and global perspectives, shaping the agenda for a more just, peaceful and sustainable future.

⁸ Statement | *Protecting Freedom of Science and Preventing Distortion of Scientific Truth* | 16 June 2025 https://www.pas.va/en/events/2025/statement_of_concern.html

**■ I: THE ANTHROPOCENE – CONCEPT,
MEASUREMENT, HUMAN ADAPTATION, AND ROLE
OF THE SCIENCES AS CAUSE AND CURE**

SCIENCE FOR THE ANTHROPOCENE

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■ <https://www.doi.org/10.65398/KCDD4137>

The Anthropocene discussion of the present

In order to respond to the challenges of the Anthropocene we need to develop innovative research approaches, new kinds of scientific activities and new forms of communication between science and society. But what is the Anthropocene and what are its scientific challenges? The Anthropocene concept offers a comprehensive, systemic perspective on the state of our planet and on how humans have shaped it, are shaping it, and should shape it in the future.

That was Paul Crutzen's original motivation when he launched the concept in 2000:¹ a wake-up call, for all of humanity and consequently also for the sciences. A knowledge capable of doing justice to the fundamental changes humanity has imposed on its home planet must be “catholic” – all-encompassing, incorporating all scales, regions, and experiences.

But how to operationalize this demand in all relevant fields of knowledge into which the concept of the Anthropocene entered as a disruptive, disturbing factor to their routines? On March 5, 2024, the *International Commission on Stratigraphy* – the body responsible for defining units of geological time – announced its rejection of the well-founded proposal to formalize the Anthropocene as a geological epoch that represents an interval of overwhelming human impact on the planet. This rejection has so far not been substantiated by a detailed scientific justification and remains a puzzling affair, one that symbolizes, however, the challenge that the Anthropocene concept represents for the traditional disciplinary organization of science.²

How to define the concept of the Anthropocene?

So what is the Anthropocene? Whatever geologists call it, it describes a new state of the relationship between humanity and the Earth system. In

¹ Crutzen and Stoermer, 2000; reprinted as Crutzen and Stoermer, 2017.

² Kolbert, 2024. Zalasiewicz et al., 2024.

this paper, we argue that a decision in favor of the Anthropocene cannot be left to the geologists or any other single discipline but affects the whole of humanity.³ Let me present you a few, currently much discussed approaches to the concept of the Anthropocene.

A much discussed alternative to a purely stratigraphic Anthropocene is the so-called Great Acceleration, dated to the same period, the mid-20th century.⁴ In the iconic diagrams of the Great Acceleration various socio-economic parameters such as gross domestic product, fertilizer use, water consumption and traffic are plotted alongside Earth system parameters such as the rise of carbon dioxide in the atmosphere and the degradation of the terrestrial biosphere. These graphs show strikingly parallel exponential increases in all selected indicators – a signature pattern of the Anthropocene, but one that calls for a more detailed and in-depth historical analysis of these processes and their causes.⁵

The graphs clearly show that we are on an unsustainable path, but what do they tell us about the causal mechanisms and what about the measures we need to bend these curves? On closer inspection, there is no compelling reason why the Great Acceleration should actually be coeval with the stratigraphic Anthropocene.⁶ After all, the stratigraphic Anthropocene is about sediments of processes and not about their causes, and there is no evidence that the dynamics driving the greenhouse gas emissions, for example, really took a decisive turn in the mid-twentieth century. A better understanding of the Great Acceleration and its drivers remains one of the main scientific challenges of Anthropocene research.

But one consequence is clear: The concept of the Great Acceleration by emphasizing the striking correlation between physical and social changes suggests that we must consider global humanity and the Earth system as one integrated complex system, sometimes also referred to as the Human-Earth system. Consequently, another widely discussed approach to understanding the Anthropocene is the investigation of this complex system's non-linear dynamics. A particular focus of research and public communication is its so-called tipping points.⁷

³ Cf. Trischler, 2016.

⁴ McNeill, 2001, Steffen et al., 2015 and Head et al., 2022.

⁵ Görg et al., 2020.

⁶ Nielsen, 2021.

⁷ Lenton et al., 2008, Lenton et al., 2019, Wunderling et al., 2021.

Analyses of the non-linear dynamics of the Earth system and its components typically assume that a small number of control parameters govern the system's behavior leading to qualitative changes in the system dynamics when certain threshold values are exceeded in these parameters. This tipping point behavior is often illustrated by the model of a sphere moving on a potential surface with several local minima.

Incidentally, the sphere can also represent the Earth as a whole, its trajectory potentially leading to a greenhouse state if climate change continues.⁸ However, in view of the fact that the real Earth system is a high-dimensional, highly interconnected system, such an image involves simplifications.⁹ One could try to further “historicize” this model, for instance by introducing a temporally changing potential surface or by making it depend on the trajectory. Nevertheless, the actual historicity of change processes, as it is characteristic of major transformations of the Earth system such as the emergence and evolution of the biosphere, cannot be fully captured by this physics-based model of analysis.

What does this perspective tell us about the Anthropocene dynamics and the necessary measures to cope with it? It helps us understand the couplings and feedbacks within the system, the likelihood of extreme events, and the necessity to take into account a broad spectrum of relevant time-scales. For instance, it highlights changes already committed by our past actions that will unfold within hundreds and thousands of years in the future, such as the melting of glaciers.¹⁰ But what responses are being suggested on the basis of this perspective on the Anthropocene?

The tipping point analysis of the Earth system raises important questions such as: Have we already passed significant thresholds or are we about to do so? Here the concept of planetary boundaries helps to identify such thresholds acting as warning signals.¹¹ But warning signals to whom, and to prompt what actions? One response is to identify planetary commons and seek measures of planetary government to address the most sensitive tipping elements and their couplings.¹² Another response involves corrective measures intervening in the market system such as carbon pricing.¹³

⁸ One of the most emblematic illustrations of this kind is contained in Steffen et al., 2018.

⁹ See for instance Ambika and Kurths, 2021 and Milkoreit et al., 2018.

¹⁰ Wigley, 2005, Edwards et al., 2021.

¹¹ Steffen et al., 2015b.

¹² Chapin et al., 2022. Rockström et al., 2024.

¹³ Emeka-Okoli, 2024, Zapf et al., 2019. Döbbeling-Hildebrandt et al., 2024.

The hope is to once again turn the market into an invisible hand acting for human welfare but this time in a sustainable way. Fundamentally, these measures rely on structures and mechanisms that we have already established in the past, now being further developed to address the challenges of the Anthropocene.

However, if we assess the progress made so far, there is little reason for optimism. The record of cumulative CO₂ emissions which are responsible for global surface temperature increase shows no substantial impact from our efforts to reduce the share of fossil energy sources by global agreements or the introduction of carbon pricing.¹⁴ There are many reasons to doubt that we will achieve the ambitious goals of the Paris agreement or of the European commitment to carbon neutrality by 2050, based solely on the measures already established or planned.¹⁵ Against this backdrop we see that the problem is not so much to stop the Great Acceleration but rather coping with the consequences of what one might call the Great Accumulation of problems which it has caused.

An innovative response to this challenge is to extend the tipping point analysis to the social component of the coupled human Earth system: If the problem is positive feedback loops causing catastrophic tipping point cascades, then a suitable response may be a cascade of counter-acting feedbacks triggered by the social component of the coupled human-Earth system.¹⁶ How can more sustainable agricultural practices, for instance, become contagious and spread through self-reinforcing dynamics?¹⁷

This vision deserves further exploration, but it has already become clear that the complex dynamics of human societies cannot be fully captured by an approach that focuses solely on small disturbances causing a system to shift from one state to another.

Geoanthropology

The new transdisciplinary approach of geoanthropology follows a broader vision, extending the Earth system sciences to human-Earth system sciences.¹⁸ Geoanthropology takes its methods from Earth and complex systems science, such as data collection, analysis and modelling, and integrates

¹⁴ Meinshausen et al., 2020.

¹⁵ Geiges et al., 2020.

¹⁶ Donges et al., 2017. Otto et al., 2020. Stadelmann-Steffen et al., 2021.

¹⁷ Breier et al., 2023.

¹⁸ Renn, 2020 and Renn, 2022.

them with those from the humanities and social sciences, expanding their insights to a planetary scale without neglecting contingencies and regional differences. It also incorporates experiences and stimuli from outside the academic sphere, from local practical and indigenous knowledge to insights from the arts, philosophy, and religion.

Geoanthropology aims to understand the emergence, development and future pathways of the human-Earth system and needs to adopt an evolutionary approach. At its core is the study of the technosphere, the new Earth sphere created by humans that encompasses all human-made technology and infrastructure and now weighs, according to one estimate, over 30 trillion tons.¹⁹ How did the technosphere emerge from the construction of the human niche within the biosphere and how did it attain the status of a new Earth sphere, on a par with and interacting with the other Earth spheres? What are our possibilities to shape the future evolution of the technosphere in ways that enable sustainable living conditions for humanity in the Anthropocene? These are some of the key questions geoanthropology seeks to answer.

This brings me to briefly touch upon the founding of the new Max Planck Institute of Geoanthropology.²⁰ The institute aims to become a hub for the collaborative synthesis of research on human-Earth system interactions where data and expertise from various disciplines are brought together, modelled and interpreted.

The institute will comprise five departments, of which three are currently in the process of being built up. They deal with Structural Changes of the Technosphere, Integrative Earth System Science, Coevolution of Land-use and Urbanism – these are the departments already established or in the process of creation – and then there are the departments to be created: Coevolution of Biosphere and Technosphere, and Societal Dynamics of the Technosphere.

There will be no walls between the departments and an emphasis on joint projects. Work across the departments is oriented along a set of common core research themes: The Anthropocene Engine, the Great Acceleration Observatory, Tipping Points and Major Transitions, Extreme Events and Shocks, the Transformations of Collective Behavior and Decisions, Land Use and Regenerative Practices, The Technosphere as a Complex System, and The Anthropocene Biosphere.

¹⁹ Zalasiewicz et al., 2016, Zalasiewicz et al., 2019.

²⁰ See <https://www.gea.mpg.de/> (last accessed: 09-19-2024).

A central goal of our research is to understand how, throughout history, behavioral structures of human societies, such as new forms of land use or new energy regimes, have been reflected in changes to our planetary environment and how these changes, in turn, have shaped the further development of human societies, creating feedback loops between Earth system dynamics and human activities. From the perspective of an extended evolutionary theory that focuses on these feedbacks, it is plausible to assume that the fundamental driver of the overall dynamics leading the human-Earth system into the Anthropocene involves at least three key factors: population size, energy and resources, and their regulatory systems, such as social structures and knowledge.²¹



Figure 1. From the 1572 series “The Reward of Labor and Diligence”, this engraving by Marten van Heemskerck combines three perspectives on the world, showing it as a technosphere covered in tools and instruments, as Diana of Ephesus nursing a human child on one of her many breasts, and as a cultural landscape. Is it possible to reconcile the transformation of the world through human technology and labor and the trust that nature will take care of us? In the early modern period, at least that was the hope.

²¹ For the concept of extended evolution, see Laubichler and Renn, 2015.

More generally speaking, the technosphere, as an object of scientific investigation, represents a typical borderline problem. It can only be adequately described by considering and merging different knowledge systems. As an Earth sphere, the technosphere falls into the area of Earth system sciences, but as a human construct, it also falls within the realm of the social and human sciences.

The Anthropocene as humanity's self-reflection on its position in nature is nothing new in itself. Such reflections have accompanied the history of our species since its beginnings and are part of our self-analytical process. This includes not only science and philosophy, but also political worldviews, as well as religion and art, as we can see in this early representation of a technosphere by Marten van Heemskerck, which characterizes one way of conceiving humanity's relation to nature.²² The answers of the past also have an impact on the current debate, though often in a subterranean and unreflected way.

Let me explain the significance of this legacy using a specific example, which we would like to characterize with the term "origin thinking". Origin myths answer the question of where we come from by invoking the authority of origin powers. They assert that what comes from the origin must inevitably return to it, be it the social group, blood and soil or "Nature". Myths of origin are the foundation of all conservative and romantic thinking in politics, according to the theologian and philosopher Paul Tillich.²³

Origin thinking in a historically particularly effective sense is characterized by the assumption that the distance from the origin itself represents the actual problem, the solution to which can ultimately only consist in a return to the origin. This assumption forms the basis of a logic of sacrifice that underlies many mythical, religious and ideological ideas. According to this logic of sacrifice, the debt to the origin can only be redeemed by a complete return to it.

Some aspects of the discussion about the Anthropocene, and in particular the question of the beginning of the Anthropocene, also show characteristic features of origin thinking. Was perhaps the Neolithic Revolution a kind of expulsion from paradise, through which we hopelessly exceeded the limits of our original physical and mental endowment?²⁴ Or was it West-

²² Böhme, 2020.

²³ Tillich, 1980.

²⁴ Van Schaik, 2016.

ern modernity, with its supposedly sharp separation of nature and culture, body and mind, reason and sensuality, that initiated a misguided and ultimately catastrophic development, which also had a global impact through colonialism?²⁵ Or was it extractive and expansive capitalism, especially industrial and fossil capitalism, that caused the Great Acceleration, which inevitably leads to catastrophe?²⁶

All these approaches search for *the* origin from which we have fatefully distanced ourselves, combined with the romantic hope that by turning back, back to Nature, back to a pre-modern unity of nature and culture, back to a simpler life, we can redeem ourselves from the guilt of distancing ourselves from our alleged origins. They ultimately prevent us from recognizing that there can be no turning back from the Anthropocene and that we must shape it – instead of fleeing from it.

A historically effective response to the pitfalls of origin thinking is the idea of development, as we know it in modern science, though it has deep roots in cultural history, reaching back to the European Enlightenment and even further to the idea of an alliance with God in the Hebrew Bible which enables a mediation between origin and what has sprung from it.²⁷ The essence of this idea is that although the new is indebted to the old, it can also emancipate itself from it through processes of mediation which take different forms in different cultures and may lead to forms of self-organization with increasing complexity and autonomy.

The Anthropocene as a Major Transition

Against this background, a new understanding of the Anthropocene opens up. The Anthropocene is the most recent step in an evolution of complexity of the Earth system that began with the origin of life some 3.8 billion years ago.²⁸ In this history, we observe some common features that characterize all major evolutionary transitions, such as the emergence of multicellular life, including the development of new energy sources and the reorganization of information and material flows.²⁹ Typically, major transitions are associated with an increasing investment into higher coordination functions, relative to the energy investment into the maintenance of

²⁵ Latour, 2018.

²⁶ Federau, 2023.

²⁷ Heinrich 2020a, 2020b, 2021.

²⁸ Levin, 1998.

²⁹ Szathmáry and Maynard Smith, 1995.

pre-existing individual components. These transitions are the product of a more complex evolutionary dynamics, involving feedback between regulatory structures and surrounding niches.³⁰ The technosphere seems to be following the same path.

Let me illustrate this point by taking a closer look at the interactions between the Earth system and global human society that have brought us into the Anthropocene. A crucial turning point in the dynamics of the human-Earth system was the coupling between the material economy and the economy of knowledge in the early modern period when knowledge started to become a crucial fuel for the global economic development that eventually resulted in the accelerating dynamic that has become so drastically visible in particular in the past 100 years.³¹

A further indication of the increasing investment of energy into the “brain” of the technosphere is the rise of information and communication technologies, culminating in the current expansion of energy-hungry AI.³² The technosphere is thus subject to an innovation dynamic that follows principles similar to those that have dominated biological evolution for eons. Evolution is an irreversible process so nothing can bring us back to the Holocene. It is also an inherently open process whose outcome cannot be predicted or determined by simple interventions. Rather, a major transition amounts to creating a new platform allowing for different developmental pathways, in particular when we purposefully steer them towards greater sustainability, using our intelligence in an encompassing way, including our capacity to learn from past experiences.³³

Looking back historically at the Anthropocene, the dominance of globalization and homogenization processes is striking. Two other features are noteworthy: the successive elimination of negative feedbacks and the tendency to externalize ecological costs due to the availability of unused niches and untapped resources. Recent historiography has emphasized the role of environmental factors in the demise of states and empires, but also provided new insights into past responses to these challenges, with the search for new land and resources being the most common one. Only with the emergence

³⁰ Laubichler and Renn, 2015.

³¹ Burgin and van Zanden, 2009, Eisenstein, 1980. <https://aiimpacts.org/historic-trends-in-book-production/>

³² Strubell et al., 2020, van Wynsberghe, 2021. Analyses like Tomlinson et al., 2024 potentially neglect the increased rate of production.

³³ For social systems such ideas have been presented early e.g. in Sewell, 1996.

of the technosphere as a global niche for humanity were limits placed on this evasionist strategy.

But not all societies functioned in an exploitative and expansive way.³⁴ There were others that lived in a long-term sustainable relationship with their natural environment, such as certain indigenous societies, a fact that is still underestimated in the grand narratives of global history. To investigate their impact on the human-Earth system, historians have been mapping the history of deforestation in tropical South America. In part due to Indigenous resistance, a large area of the continent, particularly in forest biomes, remained outside European jurisdiction until the late 19th century. This resilience has continued from the 16th century until today and continues to obstruct deforestation, playing a critical role in slowing down climate change.³⁵

Conceiving the Anthropocene as a major transition and realizing that we are in the middle of it, helps us to understand that there will be hardly any flip-the-switch interventions that will rapidly improve our predicament because of the already committed long-term changes to the Earth system. Yet, we need to act urgently, in particular regarding the global energy transition, because, with unrestrained emissions from fossil energy use, we are quickly moving outside the temperature range in which human life has existed so far.³⁶

To address this and similar dilemmas of the Anthropocene we need new orientation knowledge and new forms of communication that help us find our bearings in a world that has no Holocene analog. Such knowledge cannot be generated and circulated exclusively in the academic world. It requires the broader engagement of thought and life collectives that take seriously the challenges of the Anthropocene. One initiative is the “Anthropocene Curriculum” which has developed a bottom-up and field-oriented approach to exploring practices adequate to the Anthropocene.³⁷ The initiative has meanwhile established a worldwide network of hundreds of researchers, artists, and activists, which is unique in its scope and global reach, fostering a continuing exchange between basic science and pressing political issues that are vital in tackling the Anthropocene challenge.

Another example of new forms of interaction between science and society are platforms that facilitate collective decision-making based on da-

³⁴ Roberts, 2019. Graeber and Wengrow, 2021.

³⁵ Stokes, 2022.

³⁶ Lenton et al., 2023.

³⁷ Rosol, 2021. See also <https://www.anthropocene-curriculum.org/> (accessed 19-09-2024).

ta-based models and simulations. The Decision Theatre methodology of Arizona State University is such a data-driven, real-time modeling and dialogue format for discussing possible futures with all kinds of stakeholders, from school pupils to politicians.³⁸ This enables participants to explore the consequences of possible decisions and interventions in different model scenarios, creating an experimental space for decision-making and allowing participants to question their assumptions as well as finding ways to reach mutually acceptable compromises that must, however, take into account the systemic character of the Anthropocene dynamics, to avoid the pitfalls of unilateral interventions.

In summary, we need orientation knowledge, system knowledge, but also transformation knowledge that help us to find, if not the optimal solutions, then at least the most pragmatic and swift ones, that make intelligent use of the existing infrastructures, repurposing them for life in the Anthropocene.³⁹ This brings me finally back to the question of what a decision for the Anthropocene can mean: This decision cannot be in the hands of a single discipline; it is too comprehensive and too important for that. The decision in favor of a human Anthropocene also has a profoundly normative dimension and can therefore not be made through scientific analysis alone, no matter how encompassing. It is ultimately a question of the will to survive and to enable a good life for all of humanity, a question of knowledge *and* belief, in the sense of visions of the future, ideas of community, and life plans.

But not only that: the decision for a good, a “beautiful Anthropocene”, as Paul Crutzen once called for, is also a decision by all of us to view the world itself as a real laboratory, as a planetary experimental set-up in which all our lives are at stake, especially if we do not attempt to survive in it together.⁴⁰ That is the decision, we believe, we must take.

Acknowledgments

We would like to warmly thank Jochen Büttner, Lina Schwab, and Malte Vogl for their many suggestions and their careful reading and editing of the manuscript.

³⁸ Wolf et al., 2023.

³⁹ Renn, 2020.

⁴⁰ Crutzen et al., 2013.

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ANTHROPOCENE STRATIGRAPHY – WHY FORMALLY RECOGNIZING THAT WE ARE NO LONGER LIVING IN A HOLOCENE WORLD MATTERS

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■ <https://www.doi.org/10.65398/IAMH2856>

Abstract

Academician and Nobel Laureate Paul Crutzen insisted that we were no longer living in the Holocene Epoch 24 years ago. The term Anthropocene, ἄνθρωπος (human) + -cene (suffix denoting epochs in the Cenozoic Era) resonated with many who were increasingly aware of the impact humans on our planet. Stratigraphers ignored the concept until 2008, when “Are we now living in the Anthropocene?” appeared on the cover of the Geological Society of America’s newsmagazine, *GSA Today*. After 14 years of investigation, the Anthropocene Working Group (AWG) concluded the Great Acceleration had forced the planet into a no-analogue state, and that evidence could be found in geologic records worldwide. A proposal to erect an Anthropocene epoch with a ‘golden spike’ in varved sediments in Crawford Lake was rejected by the group that had commissioned it, but is this societally relevant? It is precisely because the Earth System has departed so markedly different from Holocene norms in only 72 years that defining the Anthropocene epoch matters.

★ ★ ★

At an International Geosphere-Biosphere Programme meeting in February 2000, Nobel Laureate and Academician of the Pontifical Academy of Sciences Paul Crutzen insisted that planetary conditions had already changed to be well beyond the stability that had characterized the Holocene Epoch. He suggested naming the current epoch after *Anthropos*, the main agent of change (Crutzen & Stoermer, 2000). Crutzen initially assumed that the Industrial Revolution forced the Earth System into an ‘Anthropocene mode’, but he came to agree with Earth System scientists like Will

Steffen (Crutzen & Steffen, 2003) that physical, chemical, climatic and biological changes resulting from the extraordinary fossil fuel-driven outburst of consumption and productivity in the mid-20th C had fundamentally altered the planet (Steffen et al., 2007; Zalasiewicz et al., 2015; Syvitski et al., 2020). In response to an article published by Ruddiman (2003), Crutzen & Steffen (2003) concluded that *“Earth is currently operating in a no-analogue state. In terms of key environmental parameters, the Earth System has recently moved well outside the range of natural variability exhibited over at least the last half million years. The nature of changes now occurring simultaneously in the Earth System, their magnitudes and rates of change are unprecedented and unsustainable. We conclude that there may have been several distinct steps in the ‘Anthropocene’, the first, relatively modest, step can have been identified by Ruddiman, followed by a further major step from the end of the 18th century to 1950 and, from the perspective of the functioning of the Earth System as a whole, the very significant acceleration since 1950.”*

Some have argued that the Anthropocene should be viewed as a long and ongoing ‘event’ reflecting human modification of our planet over many millennia, from the ‘Early Anthropocene’ posited by Ruddiman (2003) beginning during the Neolithic to the ‘Great Dying’ and effects of reforestation of the Americas after colonization on the climate system (Lewis & Maslin, 2015; Koch et al., 2019) as well as the Industrial Revolution (Gibbard et al., 2022; Swindles et al., 2023). Rejection of the formal proposal submitted by the Anthropocene Working Group (AWG) by the International Commission on Stratigraphy (ICS) and its parent body (IUGS, 2024) and promotion of the ‘event’ approach to the Anthropocene does not bring an end to the Holocene Epoch that began 11,700 years ago. However, Crutzen’s basic point was that humans had sufficiently altered the Earth System to make ‘Holocene’ an inadequate descriptor of modern geologic and planetary conditions (Crutzen & Stoermer, 2000; Crutzen & Steffen, 2003).

The Subcommittee on Quaternary Stratigraphy (SQS) of the ICS established the AWG in 2009 with the mandate of exploring whether there was stratigraphic reality to Crutzen’s claim. With input from members from the Earth System Science community and social scientists who had recognised the Great Acceleration and its effect on Earth Systems (McNeill, 2000; Crutzen & Steffen, 2003; Steffen et al., 2015, 2016; McNeill & Engelke, 2016), the AWG concluded on the basis of abundant accumulated evidence that erecting a new epoch (denoted in the Cenozoic Era by the suffix -cene) was justified (Figure 1). An overwhelming majority of voting members the AWG recommended formalization of the Anthropocene at epoch/series

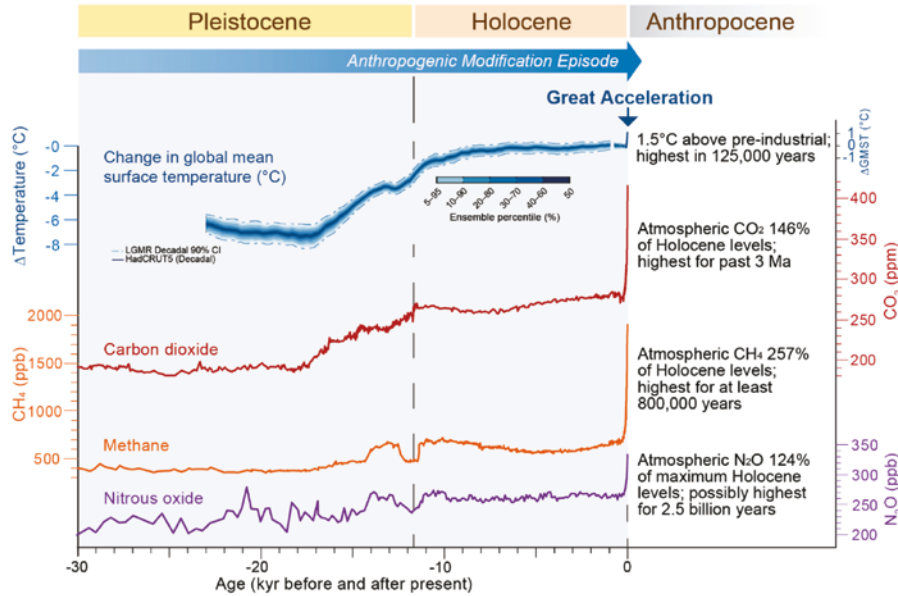


Figure 1. A much greater increase in the concentration of greenhouse gases (e.g., nitrous oxide, methane and carbon dioxide) in the last 70 years than in the previous 30,000 years has already produced mean global surface temperature warmer than at any time in the past three million years. The unprecedented rate and magnitude of environmental change – the criteria employed to subdivide geologic time – has serious consequences for humanity and the rest of the biosphere. Modified from Zalasiewicz, Wing, and the Anthropocene Working Group, (2024).

rank at the 35th International Geological Congress in Cape Town in 2016 (Zalasiewicz et al., 2017), recognizing the Great Acceleration as the driver of planetary change from a Holocene state. From 2019, with financial and logistical support by the *Haus der Kulturen der Welt* (highlighting the broad significance of the Anthropocene, well beyond the geoscience community), the AWG systematically investigated stratigraphic evidence of the Anthropocene epoch proposing it be added to the Geologic Time Scale in 2023 (Waters et al., 2024).

The challenge for the AWG was to apply stratigraphic principles developed since the late 18th C, largely based on rapid changes in fossil assemblages that can be traced globally (at least, in theory). It succeeded. The AWG coordinated the effort to propose a Global boundary Stratotype Section and Point (GSSP) to define the Anthropocene as an epoch with ref-

erence to a corresponding series of distinctive strata (Waters et al., 2018). This initiative involved hundreds of researchers studying multiple proxies (markers) in a variety of geologic sections from a dozen globally distributed sites (Waters et al., 2023).

One of the proxies proposed as a marker for the Anthropocene (Rose, 2015; Swindles et al., 2015) is spheroidal carbonaceous particles (SCPs) that are formed during high temperature combustion of fossil fuels. These tiny anthropogenic fly ash particles, that can be found in pollen slides (McCarthy et al., 2023) as well as in preparations of sediments using standard techniques (Rose, 2008, 2015), increase gradually in abundance beginning with the Industrial Revolution and then very rapidly with the Great Acceleration. This was thus one the many analyses systematically undertaken at the twelve sites vying for the ‘golden spike’ (the colloquial name for a GSSP) (Figure 2).

Because fly ash is mainly transported in the lower atmosphere, SCPs primarily track regional industrial emissions. As a result, their record was slight-

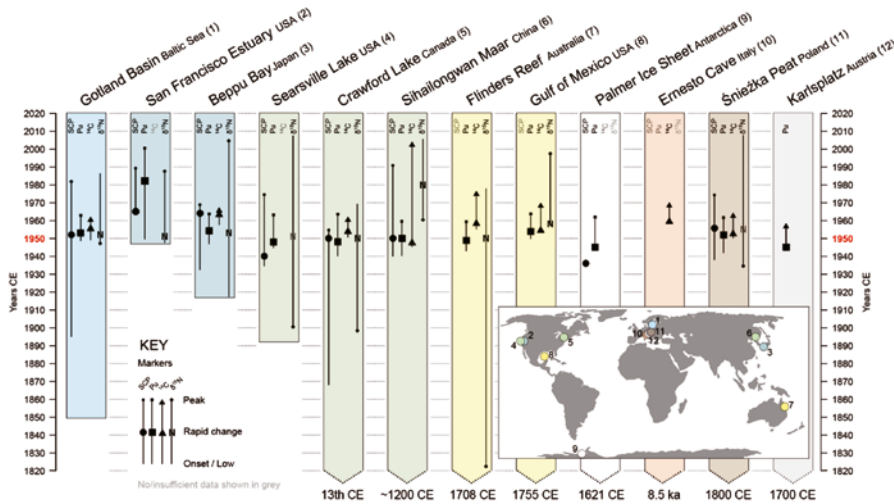


Figure 2. Rapid change in key ‘Anthropocene markers’ (radionuclides associated with thermonuclear weapons – plutonium and radiocarbon – and particulate and gaseous proxies of the combustion of fossil fuels – spheroidal carbonaceous particles and nitrogen isotopes) cluster in the 1950s–60s. Colour reflects environment of formation: light blue: anoxic marine; blue-green: estuarine/coastal; green: lacustrine; yellow: coral; white: ice sheet; pink: speleothem; brown: peat; and grey: anthropogenic. SCP: spheroidal carbonaceous particle; Pu: plutonium; ^{14}C : radiocarbon; ^{15}N : stable nitrogen isotopes, and numbers 1–12 identify the sites examined as GSSPs to define the Anthropocene (Crawford Lake, Canada is #5). From Head et al. (2023), modified from fig. 2 of Waters et al. (2023).

ly diachronous in sections studied for their potential as GSSP candidates, as the first major increase tracks regional expansion of fossil fuel power generation, and the subsequent decline tracks the equally diachronous implementation of air quality standards in various jurisdictions (Figure 3). This slight diachroneity (spanning a few decades at the beginning of the second half of the last century) is typical of proxies of the Great Acceleration, though this would appear geologically instantaneous across any other boundary on the International Chronostratigraphic Chart (Cohen et al., 2013).

Much greater synchronicity is found in markers of the Cold War, i.e. fall-out of radionuclides associated with thermonuclear weapons testing (Figure 4). Although plutonium and other bomb radionuclides (e.g., ^{137}Cs), and the slightly delayed production of excess radiocarbon by bombardment of nitrogen in the upper atmosphere) is a consequence of a specific technological development that does not directly reflect the Great Acceleration, the globally synchronous nature of the fallout signature broadly coincident with the Earth System responses to the Great Acceleration led to the selection of plutonium as the primary chronostratigraphic marker for the proposed Anthropocene (AWG, 2019). Although plutonium is naturally occurring, it makes up just 2×10^{-19} per cent (by mass) of the lithosphere, so virtually all plutonium on the Earth's surface is anthropogenic (Hartmann, 2012).

It is the rapid increase in plutonium in organic lake sediments deposited between fall and spring turnover in Crawford Lake in 1952-53 that pro-

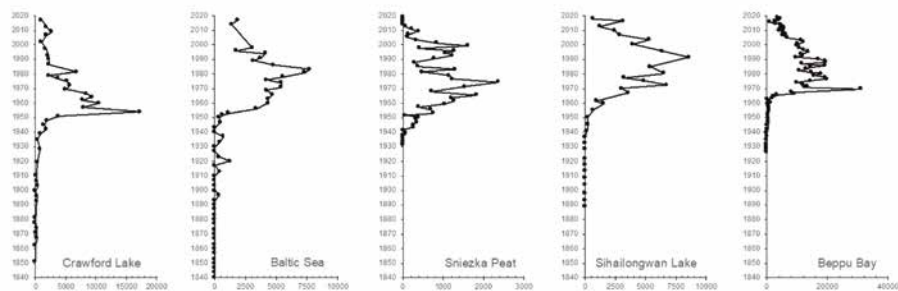


Figure 3. Correlation of SCPs in several reference sections evaluated by the AWG as potential GSSPs to formally define the Anthropocene. The post-WWII Great Acceleration is clearly recorded by fly ash produced by high temperatures combustion of fossil fuels, with a slight lag in lake sediments from China and marine sediments from Japan recording delayed industrial expansion in East Asia relative to North America and Europe. Note the decline in SCPs at all sites in response to enforcement of clean air legislation and reduced coal combustion in North America through Asia. Modified from Waters et al. (2024).

vides a precise nominal moment for the beginning of the Anthropocene: linked to the detonation of *Ivy Mike* at 7:15 AM (local time in the Marshall Islands) on November 1, 1952 (Waters et al., 2024; McCarthy et al., in press). The unique hydrologic and depositional setting of this meromictic lake near Toronto, Canada allows inorganic calcite crystals precipitated in surface waters between spring and fall turnover to cap organic matter that accumulates the rest of the year, producing light and dark laminae that – like tree rings – preserve an annually resolvable record of environmental conditions (Lafond et al., 2023; Llew-Williams et al., 2024). These varved sediments are undisturbed due to the absence of burrowing invertebrates, and they preserve a faithful bomb radionuclide record that mirrors the history of detonation of thermonuclear weapons (Figure 5).

The varved sediments from Crawford Lake were selected by the AWG as the most representative stratigraphic record of the transition to an ‘Anthropocene state’ of the Earth System (Waters et al., 2024) principally due to the quality of its sediment record and in part because of its accessible yet protected location in a conservation area where there is archaeological evidence of agricultural settlement by Ontario Woodlands Tradition people between the late 13th and early 16th centuries and historic evidence of European colonists beginning in the 19th century (McCarthy et al., 2023). This underscores the important distinction between local/regional anthropogenic impacts at various times during the Holocene Epoch and the altered Earth System that justifies the stratigraphic Anthropocene. It is important to note that the proposed GSSP was supported by Standard Auxiliary Boundary Stratotypes (SABS) from marine sediments in Japan (Kuwae et al., 2023) and peats from an ombrotrophic Polish bog (Fiałkiewicz-Kozieł et al., 2023) as well as varved lake sediments in China (Han et al., 2023) (see Figures 3, 4) and consistent with findings from all sites examined by the AWG (see Figure 2). The multiple stratigraphic signals that support the definition of an Anthropocene epoch/series are summarised in Head et al. (2022).

It should be emphasized that although the best chronostratigraphic control for the first few decades following the mid-20th century is from the fallout of bomb radionuclides, such as measurements of ¹³⁷Cs in varved sediments from Crawford Lake (black curve) that reflect the global fallout (dashed red curve in Figure 6), the environmental effects of the Great Acceleration continue. This is exemplified by metrics like global phosphorus application (blue curve in Figure 6) to feed a growing and increasingly affluent human population (with accompanying eutrophication of aquatic

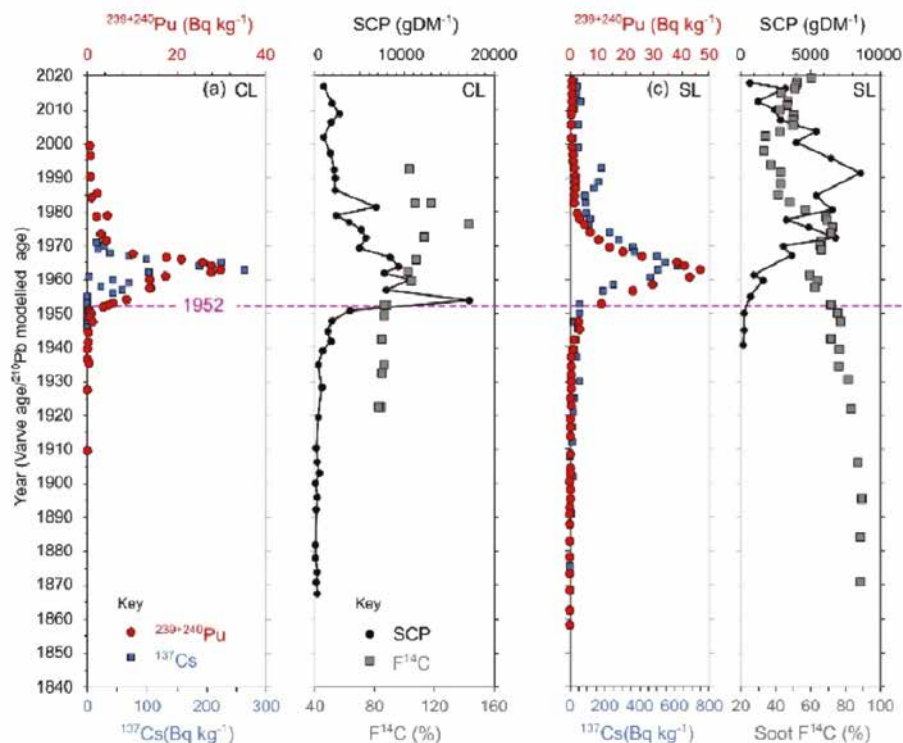


Figure 4. Correlation of ‘bomb radionuclides’ ($^{239+240}\text{Pu}$ and ^{137}Cs), excess radiocarbon produced by bombardment (F ^{14}C) and spheroidal carbonaceous particles (SCPs) in varved sediments from Crawford Lake, Canada (McCarthy et al., 2023, in press) and Sihailongwan Maar Lake, China (Han et al., 2023). Markers of the Cold War correlate very well between the two meromictic lakes, with the first rapid rise in $^{239+240}\text{Pu}$ in 1952 and the peak in both $^{239+240}\text{Pu}$ and ^{137}Cs in 1963-64 CE at both sites, whereas there is a 20-year offset in markers of the Great Acceleration like SCPs (fly ash) reflecting a delay in industrialization in China relative to Canada. Modified from Waters et al. (2024).

ecosystems), illustrating the interconnectedness of Earth’s various subsystems. The Earth System shift to the current *no-analogue state* of Crutzen & Steffen (2003) is driven in large part by the massive increase in fossil fuel consumption in the mid-20th century that liberated 36.1 Gt/y of CO $_2$ to the atmosphere in 2017 CE, compared with 0.2 Gt/y in 1850 CE (Syvitski et al., 2020). This impacts not only the temperature at the surface of our planet (see Figure 1), but also results in acidification of oceans (Hurd et al., 2018) and soils (Oh & Richter, 2004).

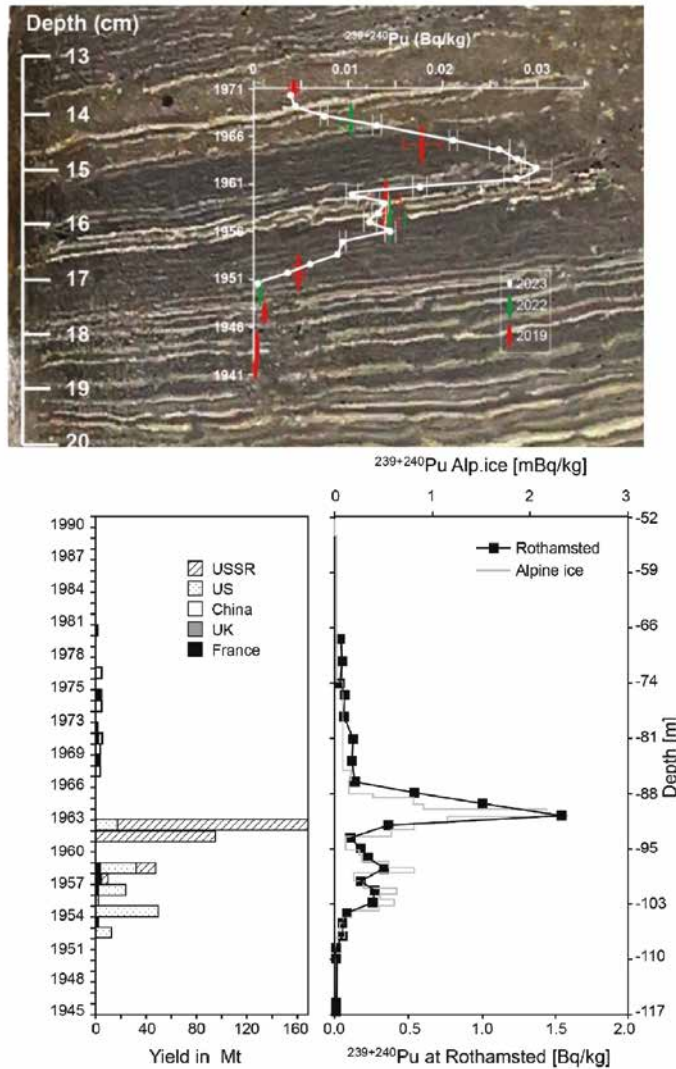


Figure 5. *Left:* Signature of the primary chronostratigraphic marker for the proposed base of the Anthropocene series/ beginning of the Anthropocene epoch (white datapoints from the 2023 freeze core with the proposed GSSP superimposed on the varved sediments from Crawford Lake, red and green are lower resolution measurements from samples spanning multiple varves in earlier cores); from McCarthy et al. (in press). *Right:* Compare the annual yields of atmospheric fallout from thermonuclear weapons testing (UNSCEAR, 2000) and measurements of plutonium in an annual herbage archive from Rothamsted and in cores from the Mont Blanc glacier. Note the uneven rise to the $^{239+240}\text{Pu}$ peak in 1963–1964 (i.e., to ratification of the Partial Test Ban Treaty) and earlier decline in response to the moratorium between late 1958 and 1961 CE. Modified from Warneke et al. (2002).

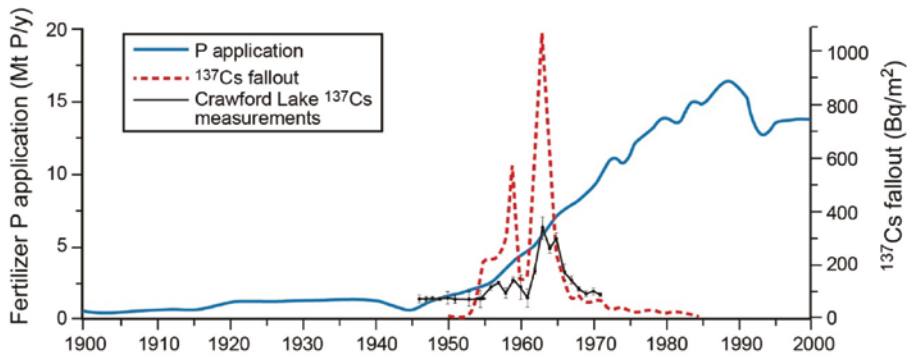


Figure 6. Socio-economic metrics, such as the global amount of phosphorous added to soils to promote the growth of crops for people and livestock, almost invariably increase rapidly through the latter half of the 20th century – the Great Acceleration (Steffen et al., 2015; McNeill and Engelke, 2016). The global fallout of ¹³⁷Cs from thermonuclear weapons testing is recorded in sediments from the mid-1950s through 1964 CE, providing chronological control, confirming varve ages in the proposed GSSP for the Crawfordian age and Anthropocene epoch (solid black curve; McCarthy et al., in press) Modified from Owens (2020), with ¹³⁷Cs data from Crawford Lake from McCarthy et al., in press).

Contrary to claims by opponents to the proposal to add the Anthropocene as an epoch to the time scale, the laws of physics dictate that the resulting novel state of our climate system will persist for tens of millennia, producing conditions at the surface of our planet not previously experienced by humans, i.e., in the last three million years (Hansen et al., 2023; Summerhayes et al., in press) – it is not a ‘blip’. Similarly, the argument that the change is ‘too recent’ is spurious – it is precisely because the Earth system has become noticeably different from Holocene norms in less than a century that defining the Anthropocene epoch matters (Oreskes, 2024; Turner et al., 2024; Zalasiewicz et al., 2024). The AWG argues that, by formalizing that we have moved beyond the functional state of the Holocene, the Anthropocene epoch would help understand and communicate the scale of this altered Earth System, allowing us to make informed decisions that impact the entire biosphere (McCarthy et al., submitted; Zalasiewicz et al., 2024). Climate models suggest that we do not have the luxury of waiting centuries – or even decades – to address the existential issues that face us (Gulev et al., 2021; Hansen et al., 2023; Esper et al., 2024).

Finney & Edwards (2016) suggested that “*the drive to officially recognize the Anthropocene may, in fact, be political rather than scientific.*” They rejected the sci-

entific projections that established the impossibility of the novel Earth System state reverting to Holocene conditions, as being irrelevant to stratigraphy. The perspective of the AWG is that it is at least equally political to reject scientific data generated by hundreds of scientists from dozens of sites (available online: Waters et al., 2024) without open discussion and feedback on the proposal. It is particularly disheartening that organizers of the 37th International Geological Congress (2024) rescinded an invited plenary talk on the Anthropocene “due to the complexities and ongoing debates surrounding the topic, which have made it challenging to achieve a broad consensus.”

The Earth Sciences have much to offer by examining analogs from the late Cenozoic record (e.g., the last interglacial, ca. 125,000 years ago and Pliocene warmth ca. 3,000,000 years ago; see Figure 1) to anticipate the less easily quantified nonlinear changes associated with an ‘Anthropocene state’, such as those associated with the melting of polar ice caps, associated sea level rise and coastal hazards, and large-scale reorganization of ocean circulation that is a major internal control on the climate system (McManus et al., 2004; Broecker, 2010; Dutton et al., 2015; PAGES, 2016; Caesar et al., 2018; Guarino et al., 2020; Box et al., 2022; van Westen et al., 2024). Geoscientists can contribute to better understanding and proposing solutions to mitigate and adapt to changes in the Earth System that have clear social, economic and political implications, particularly given the disproportionate number of people (and infrastructure) in coastal regions (Reimann et al., 2023) and the continued demand for earth materials. It is hoped that the split in the geoscience community over the concept of the Anthropocene, and the contested vote by SQS members rejecting the proposed Anthropocene as an epoch/ series with a GSSP in sediments deposited in Crawford Lake (and a corresponding Crawfordian stage/age that has yet to be addressed), does not detract from the urgency of addressing these challenges (McCarthy et al., submitted). An editorial in the journal *Nature* reiterated “Are we in the Anthropocene yet?”, paraphrasing Zalasiewicz et al., (2008), concluding that the rejection of the proposal by the SQS “should not detract from the reality that humans are altering Earth systems” (*Nature* 627, 466 (2024)), urging geologists to “quickly resolve their disagreements”. Arguably, however, the ‘kerfuffle’ over stratigraphically defining the Anthropocene (*First Dog on the Moon*, July 14, 2023) has brought even more attention to the Anthropocene than adding a geologic unit to the ICS International Chronostratigraphic Chart would have done. *The Anthropocene is dead. Long live the Anthropocene*, as one reporter put it (Voosen, 2024).

Acknowledgments

The ideas in this paper were developed through innumerable email exchanges and collaborations with my colleagues from the Anthropocene Working Group (including Jan Zalasiewicz, Simon Turner, Martin Head, Colin Waters and Julia Adeney Thomas who provided feedback on a draft of this paper), most notably during workshops facilitated by the Haus der Kulturen der Welt and the Max Planck Institute for Geoanthropology. The sampling and analysis of sediments from Crawford Lake could not have been achieved without the dozens of members of ‘Team Crawford’ – particularly those who came through to collect and analyse the last set of cores after funding had run out! – and the supporting organizations (Conservation Halton, Brock University, Carleton University, the Canadian Museum of Nature, and the Royal Ontario Museum) and, of course, funding from the Kulturveranstaltungen des Bundes in Berlin and the Natural Sciences and Engineering Research Council of Canada.

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RELIGION, THE SCIENCES AND THE ANTHROPOCENE. EXPLORING THE FOUNDATIONAL ALLIANCE BETWEEN SCIENCE AND FAITH

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■ <https://www.doi.org/10.65398/ZKKG2365>

Introduction

Shortly after His All Holiness Patriarch Bartholomew of Constantinople had described the abusive treatment of creation by human beings in terms of *sin*, Pope Francis wrote his Encyclical Letter *Laudato si', on the Care of our Common Home*, to address the current ecological crisis, both natural and human. Not only is our environment deteriorating globally, little effort is also made to safeguard the moral conditions for an authentic human ecology (LS 5). “The destruction of the human environment”, Pope Francis observed, “is extremely serious, not only because God has entrusted the world to us men and women, but because human life is itself a gift which must be defended from various forms of debasement” (LS 5).

That is why, celebrating the feast of St. Joseph, the custodian of the Holy Family at the inaugural mass of his pontificate (2013), Pope Francis invited the faithful gathered in St. Peter’s square and the whole world to listen to the cry of two *fragilities* in our midst: creation (environment) and the poor. Rendered *fragile* by the misdeeds of man, *creation* and *the poor* are to be listened to, according to the Pope, not only with the mind, but with the heart most importantly. He himself devotes an encyclical to these fragilized works of God’s creation “not to amass information or to satisfy curiosity, but rather to become painfully aware, to dare to turn what is happening to the world into our own personal suffering and thus to discover what each of us can do about it”.¹ Man cannot be indifferent to the lot of these *fragilities*; for, “every effort to protect and improve our world entails profound changes in ‘lifestyles, models of production and consumption, and the established structures of power which today govern societies’” (LS 5). The human person and his culture are so central to the ecological crisis. So, how

¹ *Laudato si'*, 19.

may we evaluate the place of the human person in the blend of concerns which *Laudato si'* presents as *integral ecology*?

Integral Ecology and the Human Question: Man in His World

The outburst of ecological consciousness and interest that characterized the 70s found expression variously in the organization of summits on the level of the United Nations,² in studies in academic institutions and universities, and in the creation of popular *green movements*.³ Universities began to dedicate Chairs, Colleges and Departments to environmental studies, dealing with it purely so, as a *Department of Environmental Studies*. But the academic interest in the environment also took the form of a study of the relationship between the environment and the human presence within it. This gave rise to the creation in universities of *Departments of Human Ecology* for the study of the impact of the human person on his environment,⁴ or the human person in his environment as an instance of evolutionary adaptation to the environment. Sometimes, it also gave rise to interdisciplinary studies, involving very many of the social sciences.⁵

Governments too began to respond to concerns about the environment through the creation of *Environmental Protection (or conservation) Agencies*; and, beginning with its *Conference on the Human Environment* in Stockholm (1972), the United Nations has consistently dedicated attention to the en-

² Cf. 1972: UN Ramsar Convention to protect Wetlands (Ramsar, Iran). 1973: Convention on International Trade in Endangered Species (Magna Carta for Wildlife). 1972: Club of Rome "*Limits of Growth*" on sustainability. 1972: UN Stockholm Conference (human planetary interdependence). Etc.

³ *Greenpeace* was born in Canada in 1971; the *World Wildlife Fund* (now *World Wide Fund for Nature*), the world's biggest organization for the protection of nature, had been born already in 1961 in Gland, Switzerland, with the support of very influential people (Prince Philip of Edinburg, Godfrey Rockefeller, Bernhard van Lippe-Biesterfeld etc.); the Ramsar Convention on Wetlands; and, now, several *Green Movements* and *Green Parties*.

⁴ As in College of Human Ecology (Cornell University); Department of Human Ecology in the School of Environmental and Biological Sciences (Rutgers University). Cf. also the many "Human Ecology" Journals (Hunter College, CUNY, N.Y.; KRE, India, Human Ecology Review of the *Society for Human Ecology*, etc.)

⁵ As in studies by the evolutionary anthropologist Robert Foley: *Another Unique Species* (1987) and *Humans before Humanity* (1995). The related disciplines are Sociology, Anthropology, Economics, Geography, History, Politics, Psychology, Technology, Evolutionary Biology, etc.

vironmental question in subsequent conferences.⁶ Since its meeting in Johannesburg (2002), the United Nations also consistently relates the “question of the environment” with the question of “human development”; and the current UN SDGs are, according to the (former) Secretary General, Ban Ki-Moon, not only a narrative about development and the protection of the environment (SDG 6, 13, 14, 15); they are also a *human dignity narrative that leaves no one behind*.

The UN Secretary General’s formulation of the relationship between the protection of the environment and human dignity (or development) affirms not only the physical inter-relatedness of humanity with its physical environment (nature); it also affirms the inter-dependence of their destinies, their lot and their wellbeing. But the descriptions of the nature of the inter-relatedness and inter-dependence of man with his environment has not enjoyed unanimity and agreement in the various efforts to describe it.

Some centers of Higher Education, influenced by an evolutionary sense of development, have described the relations between the human person and his environment in terms of the “*survival of the fittest*” (*who can best adapt to the changing environment*). Others describe the relationship between the human person and his environment in terms of a *human ecology*, which takes the form of an inter-disciplinary pursuit, that studies how the human person and his environment mutually affect each other.⁷ But, there are also studies that present the presence of the human species as a (potential) *menace* to the

⁶ Cf. *United Nations conference on the Environment and Development* (also referred to as the *Earth Summit* or the *Rio conference*) 1992; the *Rio+5* or the *19th Special Session of the General Assembly of the United Nations* (1997); the *World Summit for Sustainable Development* in Johannesburg (2002), where the environmental question appeared to have been recognized as a development question; and the ongoing *United Nations Framework Convention on Climate Change* (UNFCCC) and the *United Nations Climate Change Conferences* (from Cancun 2010 = COP 16 to the current COP 23 in Bonn, 2017. The UNFCCC is an international meeting of political leaders and activists to discuss environmental issues, especially the *climate*.

⁷ Accordingly, Margaret Bobolz and Suzanne Sontag (*Sourcebook of Family Theory and Methods, A Contextual Approach*, ed. P.G. Boss et alii, N.Y., 1993, pg. 419–450) have described a *Human Ecology theory*, which focuses on humans as biological organisms and social beings in interaction with their environment; and in this theory, the family is considered to have a determining role (“*an energy transformation system that is interdependent with its natural physical-biological, human-built, and social-cultural milieu*”, according to the authors). On the role of the family in Human Development, cf. also Urie Bronfenbrenner, “Ecology of the Family as a context for Human Development: Research Perspectives”, in: *Developmental Psychology*, 1986, vol. 22, #6, 723–742. James Garbarino and Deborah Sherman, “High-Risk Neighborhoods and High-Risk Families: The Human Ecology of

environment. Related to this position are two noteworthy developments.

The first was the presentation of the *limits of the earth's resources* as an issue of Human Ecology.⁸ This was the tenor of the works of Paul Ehrlich and Anne Ehrlich (*The Population Bomb*, 1968; *Population, Resources, Environment. Issues in Human Ecology*, San Francisco 1970; *The Population Explosion*, 1991). The Ehrlichs' human demographic threat to the environment was taken up in 1970 by an MIT team of 17 researchers, the fruit of whose study was entitled, *The Limits to Growth*. That study analyzed "the limits of our world system and their constraints on human growth and activity". This study was presented in Rio de Janeiro already in 1971, and then to the "Club of Rome", where it was adopted (1972) as the *Report of the Club's Project on the Predicament of Mankind*.

The second related development of the outburst of the ecological consciousness of the 70s and an attempt to situate and define the human person within it was the positing, some thirty years later, of an *Anthropocene epoch to describe a proposed new epoch in the Quaternary period when human actions have a drastic effect on the Earth*. Paul Josef Crutzen, a researcher of Atmospheric Chemistry, a Nobel prize winner in Chemistry and a deceased member of this Pontifical Academy of Sciences, was the avid proponent of this definition.⁹ According to him, *the sheer scope of human activities* and their impact on essential planetary processes have become so profound as to drive the earth out of the *Holocene epoch* in which agriculture, sedentary communities, and eventually, socially and technologically complex human societies developed, and to call for *the use of a new geological term*, which according to

Child Maltreatment", in: *Child Development*, 1980, vol. 51 #1, 188-198. Cf. also, Robert Foley's "What is Human Ecology", in: *Another Unique Species*, Longman 1987, pg. 12.

⁸ As the author indicates, this was the tenor of the works of Paul Ehrlich and Anne Ehrlich (*The Population Bomb*, 1968; *Population, Resources, Environment. Issues in Human Ecology*, San Francisco 1970; *The Population Explosion*, 1991). The Ehrlichs' human demographic threat to the environment was taken up in 1970 by an MIT team of 17 researchers. The fruit of the study was entitled, *The Limits to Growth*. It studied "the limits of our world system and their constraints on human growth and activity". This study was presented in Rio de Janeiro already in 1971, and then to the "Club of Rome", where it was adopted (1972) as the *Report of the Club's Project on the Predicament of Mankind*. The presentation of the *Report* at Rio de Janeiro (1971) at the beginning of UN's *Earth Summits* on the environment is noteworthy!

⁹ Paul Crutzen and Eugene Stoemer first proposed the "Anthropocene epoch" in a *Newsletter* of the International Geosphere and Biosphere Programme, 41 (2000) to denote the present geological time interval, in which many conditions and processes on Earth are profoundly altered by human impact.

Donna Haraway,¹⁰ has become a mandatory concept in framing, thinking about, and ultimately facing accelerating environmental and multi-species catastrophe.¹¹

In a subsequent study, *Trajectories of the Earth System in the Anthropocene*¹² by Will Stefan, Johan Rockström and fourteen (14) other scholars, the extent and the intensity of human impact on the world's ecosystems/earth system which underlies Crutzen's *Anthropocene* is revisited, as "self-reinforcing feedbacks" that could push the earth system towards a planetary threshold that, if crossed, could prevent stabilization of the climate at intermediate temperature rises and cause continued warming on a "Hothouse Earth" pathway, regardless of reduction in human emissions.

But Crutzen's *Anthropocene* also shared an anthropological concern which the *Report of the Club of Rome* (1972) wrestles with under the heading, the "predicament of Mankind". Can humanity be a menace to its world and its environment?

For Crutzen, not only do many human activities impact on the earth's environment, often surpassing nature with ecological, atmospheric chemical and climatic consequences; growing human populations are burdensome to the environment: they are accompanied by their great need for food, water, improved living conditions and land use. Indeed, there has been, in the wake of the Industrial Revolution of the 18th century, a growing disturbance of earth's natural systems by human activities which has created, precisely, a new geological era, the *Anthropocene*. Human impact has so intensified since the onset of industrialization as to take us out of the Earth System state typical of the Holocene Epoch that post-dates the last glaciation.

All of this means that at the core of Crutzen's *Anthropocene* lies the affirmation that human beings can change the Earth in such profound and lasting ways that they usher in a new chapter in its history – a new geological epoch of human beings. Effectively, then, Crutzen's hypothesis means that human activity now rivals geological forces in influencing the trajectory of the Earth System; and this, according to Will Steffen and his colleagues, has

¹⁰ Donna Haraway, *Staying with the trouble*, Duke Univ. Press, 2016.

¹¹ Thus, the *IPCC Report* (2001) claims that there is new and stronger evidence that most of the warming observed over the last 50 years is attributable to human activities.

¹² W. Steffen et alii, *Perspective*, PNAS, August 14, 2018, vol. 115, no. 33 (<https://www.pnas.org>).

important implications for both Earth System science and societal decision making: disruptions to ecosystems, society and economies.¹³

Finally, Crutzen's hypothesis enfolds a global threat which calls for a *global stewardship of the entire Earth System: biosphere, climate, ecosystems and societies*, involving behavioural change, transformed social values, technological innovation and good governance. And the call of science for *stewardship of the entire Earth System* coincides with the Bible's original mandate to the human race, which I shall briefly present, as defining the place of humankind in creation, for, in the words of Prof. Ramanathan, *there is a foundational alliance between science and faith!*

Defining the Place of Man in the World, as "Creation"

The first strikes and strokes of the Bible's/Church's understanding about the place of *man in creation* derive from the biblical account of creation in the Book of Genesis (1-3). There, in the first account of creation (Gen. 1-2:4a), created nature, the environment of human existence, is presented as the work of God's Word and *by design*. The first instance of God speaking his Word was actually at the creation of the world; and it was to transform "*chaos*" at the dawn of creation into a "*cosmos*", an ordered world system, capable of supporting human life, and suitable to be a *home* for the human person.

Subsequently, God created man, male and female, in his image and likeness, and *to have dominion over* everything that God has created. Just as *Adam* (man) is distinct from the rest of creation by reason of his nature – created in the *image and likeness of God* – so is he also distinct in his relationship with the rest of creation by his exercise of *dominion* over it; and the exact sense of this exercise of *dominion over creation* is still the subject of vivid exegetical, theological, economic and social discussions.

In the second account of creation, however, this created cosmic space was called the "*earth and the heavens*" (Gen. 2:4a); and in it God fashioned an *earth-home, suitable for man*, which was described as a "*garden planted by God*" (Gen. 2:8, 15). Here God placed man, formed out of the dust of the earth and the breath of God. In this second account of creation, man is more clearly related to *created nature* by reason of his sharing in its substance (*dust*), but distinct also from it by reason of his bearing within himself/herself the breath of God. But, when man is introduced into the *garden planted by God*, he was to *till and keep it*. Thus, *dominion over creation* in the first ac-

¹³ Idem.

count of creation is replaced in the second account by *tilling and keeping the garden*. Though functionally formulated and presented, man's relationship with his *garden-home* in the second account is clearer to decipher: it is one of a *reverential* responsibility and care (stewardship), expressed by the two verbs, *to till* and *to keep*. The verb which expresses the "tilling function or activity" of man (דָּבַע), also designates the cult/worship which Israel renders to God (Ex. 4:23). Likewise, Adam's activity of "keeping" the garden is also expressed by a verb which is also used to express a brother's care for a brother (šmr), as between Cain and Abel (Gen. 4:9). Accordingly, Adam's role in his *garden home* was to be a "godly/reverential caretaker": Adam was to have a reverential solicitude for his/her garden-home, as if for a brother! Certainly, this account of creation was written thousands of years before St. Francis of Assisi; but his way of seeing himself as standing in a *reverential and kinship ties* with the elements of creation is the imagery that the account of creation evokes.

Adam (man), therefore, is not the *auto-referential center* of creation. In the distinctiveness of his/her creation in the *image and likeness of God*, and *bearing in himself/herself the breath of God*, Adam is more a part of an inter-connected and inter-dependent created world, which he/she must reverence/respect and care for as for a *kinsman*. Thus, Adam is essentially a *personal being* as well as a *relational being*, *destined to coexist in communion for the common good of his type and the world*.

When in the New Testament the Gospel of John attributes creation to Christ, as the Word/*logos of God*, creation does not become a passing encounter of God's Word with the world. Rather the Word of God, "*Logos*", reaches down to Adam (man) and creation to initiate a *dialogue* (a *dia-logos*). Adam (man) and creation are forever engaged in *dialogue* with God; and the human person is a *dialogue partner* before God. A *dialogue* in which the meaning of everything is to be sought and found!

This is the basis and inspiration of Pope Francis' Encyclical Letter *Laudato si'*, *Care for our Common Home* (2015). There, listening to the voice of science from Centers of Learning and from the UN Climate Scientists, as well as the experiences of victims of climate disasters, he notes that this is "*not to amass information or to satisfy curiosity, but rather to become painfully aware, to dare to turn what is happening to the world into our own personal suffering and thus to discover what each of us can do about it*".¹⁴ Crutzen's *Anthropocene* means that disturbance

¹⁴ *Laudato si'*, 19.

of creation/our environment is *anthropogenic*: *man-made* and attributable to man's responsibility. Accordingly, the subsequent teaching of Pope Francis on *integral ecology* underlines the fact that everything is inter-connected and inter-related in the life of man and his/her environment: nothing and nobody is an independent variable; rather a solidary compassion, which makes us all *reverent care-takers of creation* should binds us all together. For, one cannot love God and disregard and abusively treat what He has made! And to promote the latter idea, Pope Francis calls for a radical change in mindset about creation, change of attitudes and lifestyles in an *ecological conversion* to free humanity to be *caretakers of creation*. Next, he invites us to undergo an *education for ecological citizenship*: education not only for information, but also to instill good ecological habits (LS 209-215) as *caretakers of our world*. To this, the *traditional alliance between science and faith beckons us all!*

Thank you for your kind attention!

**II: CLIMATE CRISIS, BIODIVERSITY LOSS,
AND HUMAN CONTEXTS – OUTLOOK AND
NEEDED ACTIONS FOR A HABITABLE EARTH**

AN HISTORIC DOWN PAYMENT: INTEGRATED ACTION TO TACKLE THE INTERACTING TRIPLE CRISES OF CLIMATE CHANGE, LOSS OF BIODIVERSITY, AND INEQUITY/INEQUALITY

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■ <https://www.doi.org/10.65398/VDUG7853>

1. Introduction

The world faces three global challenges: climate change, loss of biodiversity, and inequity/inequality. Each of these crises threatens our future. But they do not operate in a vacuum; each affects the other in profound ways. However, despite being inextricably linked, the three crises are typically tackled in separate silos. Analysts of each crisis focus intensely on the complex drivers of that one problem; strategists identify solutions to the one problem that are politically, economically, socially, and technologically feasible. Each has its own global community of experts, policy makers, constituents, funders, and more.

Scientific knowledge tells us that climate, nature loss, and inequity/inequality are interconnected in complex ways, and that solutions to one will not ultimately succeed unless all three are tackled together. Achieving that integration is not always easy, but in fact is beginning to happen. In this paper, I highlight successful examples of this integration to demonstrate the feasibility of integrated approaches and hopefully inspire an acceleration of adoption of more holistic, integrated policies and practices. We need integration at a scale commensurate with the magnitude of the problems.

Below I demonstrate the feasibility of more holistic approaches with examples from recent policy advances made by the U.S. government during the four years of the Biden Administration. I highlight ways in which

¹ Lubchenco served as Deputy Director for Climate and Environment at the White House Office of Science and Technology Policy from February 16, 2021 to January 10, 2025, on loan from Oregon State University.

² As of January 13, 2025, Lubchenco resumed her positions as Distinguished University Professor of Integrative Biology and Valley Professor of Marine Biology at Oregon State University.

the U.S. is heeding science by embedding nature and environmental justice in climate policies, embedding climate and environmental justice in nature policies, and embedding nature and climate in environmental justice policies. Although the pioneering policies I describe are enabling bold and ambitious action, they are only a down payment on what is needed. Nonetheless, these policies and others underway around the world give us direction and hope that we may be able to accelerate progress to achieve sustainability and wellbeing in the Anthropocene.

2. Embedding nature and environmental justice in climate policy

President Biden and Vice President Harris led the most ambitious climate agenda³ in U.S. history through bold targets, pioneering policies, and over \$369 billion in climate and clean energy investments through the Inflation Reduction Act, plus additional investments through the Bipartisan Infrastructure Law. Those investments by the federal government in turn catalyzed significant additional investment by the private sector, e.g., over \$450 billion in clean energy manufacturing, electric vehicles and batteries, and clean power projects.

The climate policies were multifaceted, and reflect the broader, more holistic climate policy framing that scientists have championed, including not only mitigation, but also adaptation; not only technology, but also nature-based solutions; not only land-based actions but also ocean-based solutions; and not only reduction in greenhouse gas emissions, but also carbon removal. Nature and environmental justice are incorporated within each of those four climate policy approaches. Here are a few examples:

2.1. Focusing on both climate mitigation AND adaptation

Most climate policies historically emphasized ways to reduce greenhouse gas emissions, but ignored the importance of adapting to climate changes already underway. Many scientists have urged that we seek to both avoid the unmanageable through emissions reductions and carbon removals, while also managing the unavoidable through more effective attention to adaptation and building resilience of communities, ecosystems and economies. This is not an ‘either-or’, but a ‘both-and’ approach.

³ President Biden’s Historic Climate Agenda: a Synthesis of Actions to Tackle the Climate Crisis <https://bidenwhitehouse.archives.gov/climate/>

Adaptation provides an excellent opportunity to integrate nature and environmental justice into climate solutions. The U.S. National Climate Resilience Framework,⁴ e.g., highlighted multiple opportunities for this integration and summarized significant efforts to provide Tribes, communities and businesses with the information and resources they need to adapt to climate changes. The Inflation Reduction Act and Bipartisan Infrastructure Law authorized over \$50 billion in resilience investments, including through nature-based solutions.

Environmental justice is embedded within these policies. For example, the administration's Justice40 Initiative⁵ directed that at least 40% of the overall benefits of federal climate and clean energy investments flow to disadvantaged communities that are marginalized by underinvestment and overburdened by pollution. President Biden's first Executive Order (EO) on climate included strong environmental justice and nature components.⁶

A synthesis of resilience work across the four years highlights this integration⁷ and draws attention to the importance of natural ecosystems, working with nature, nature-based solutions, attention to who is at the decision-making table, and who benefits as central elements in effective adaptation.

2.2. Focusing on technology AND nature-based solutions

When most policy makers think about emissions reduction or carbon removal, the default solution is usually technology. (Think electric vehicles vs gasoline-powered ones, heat pumps in lieu of conventional furnaces and air conditioners, or wind turbines instead of fossil fuels.) Make no mistake: technology has a key role to play, but so, too, do nature-based solutions. We know that the natural world – on land and in the ocean – is a powerful ally, and could contribute up to one-third of the greenhouse gas reductions needed. But nature-based solutions are less well understood and often not

⁴ White House. September 2023. National Climate Resilience Strategy <https://bidenwhitehouse.archives.gov/wp-content/uploads/2023/09/National-Climate-Resilience-Framework-FINAL.pdf>

⁵ White House. January 2025. Justice 40: A Whole of Government Initiative <https://bidenwhitehouse.archives.gov/environmentaljustice/justice40/>

⁶ President Joseph Biden. 2021. Executive Order 14008. Tackling the Climate Crisis At Home and Abroad <https://www.federalregister.gov/documents/2021/02/01/2021-02177/tackling-the-climate-crisis-at-home-and-abroad>

⁷ White House. January 2025. National Resilience Strategy. <https://bidenwhitehouse.archives.gov/wp-content/uploads/2025/01/National-Resilience-Strategy.pdf>

considered, while better-known or better-marketed technological solutions take off. The world needs both.

To help address this disparity, the White House led the production of an interagency report to better understand how federal agencies, Tribes, states, communities, and businesses were or were not using nature-based solutions in the U.S., and what the U.S government might do to accelerate their effective use. The report was announced⁸ at the 27th Conference of the Parties to the UN Framework Convention on Climate Change, held in Sharm El-Sheikh, Egypt, in 2022.

The announcement clarified what nature-based solutions are and articulated their need: “Nature-based solutions are actions to protect, sustainably manage, or restore natural or modified ecosystems as solutions to societal challenges, like fighting climate change. Examples include protection or conservation of natural areas, reforestation, restoration of marshes or other habitats, or sustainable management of farms, fisheries, or forests. These actions can increase resilience to threats like flooding and extreme heat, and can slow climate change by capturing and storing carbon dioxide. Nature-based solutions play a critical role in the economy, national security, human health, equity, and the fight against climate change.”

The report, entitled *Opportunities to Accelerate Nature-Based Solutions: A Roadmap for Climate Progress, Thriving Nature, Equity, and Prosperity*,⁹ called for expanding the use of nature-based solutions, identified key impediments to realizing that goal, and outlined strategies to overcome or remove those impediments. The resulting five strategic areas of focus for the federal government were (1) updating policies, (2) unlocking funding, (3) leading with federal facilities and assets, (4) training the nature-based solutions workforce, and (5) prioritizing research, innovation, knowledge, and adaptive learning that will advance nature-based solutions.

⁸ White House Fact Sheet. November 8, 2022. Biden-Harris Administration Announces Roadmap for Nature-Based Solutions to Fight Climate Change, Strengthen Communities, and Support Local Economies. <https://bidenwhitehouse.archives.gov/briefing-room/statements-releases/2022/11/08/fact-sheet-biden-%E2%81%A0oharris-administration-announces-roadmap-for-nature-based-solutions-to-fight-climate-change-strengthen-communities-and-support-local-economies/#:~:text=The%20Roadmap%20submitted%20to%20the,training%20the%20nature%2Dbased%20solutions>

⁹ White House. November 8, 2022. Opportunities to Accelerate Nature-Based Solutions: A Roadmap for Climate Progress, Thriving Nature, Equity, and Prosperity <https://bidenwhitehouse.archives.gov/wp-content/uploads/2022/11/Nature-Based-Solutions-Roadmap.pdf>

After release in 2022, this Roadmap guided strategic action, including updated policies, and enhanced awareness and funding for nature-based solutions. For example, a major impediment to use of nature-based solutions had been the policy that instructs federal agencies on how to calculate the benefits and costs of actions they take. Federal agencies are required by law to do this benefit-cost analysis, but historically the analysis was lop-sided, since the calculations included only the costs and not the benefits of adopting nature-based solutions. Scientists have documented that nature provides multiple benefits such as trees lowering air temperatures in cities, coastal wetlands reducing storm surge, or forests or wetlands and swales mitigating floods. Without inclusion of these ecosystem services, the Benefit-Cost Analysis (BCA) is incomplete and limits the portfolio of options that might prove useful in tackling climate change.

This lop-sided BCA was rebalanced last year, with an update to the policy that instructs federal agencies on how to calculate BCA^{10, 11} to align with our current scientific understanding and economic tools. As a result, federal agencies are now required to include nature's benefits, also called ecosystem services, in their BCA. Moreover, the Office of Management and Budget also provided agencies with guidance¹² about how to value ecosystem services in their calculations. As a result of this guidance and major investments in these approaches through the Bipartisan Infrastructure Law and Inflation Reduction Act, nature-based solutions are beginning to move to the forefront as climate solutions, for both mitigation and adaptation. This is an excellent example of how modernizing policies with recent scientific advances can vastly improve the functioning of government.

In addition to elevating the need for modernizing policies and unleashing funding for nature-based solutions, the Roadmap enabled federal agencies to lead by example in deploying natural solutions as they manage their assets, for example national parks or marine national monuments.

¹⁰ Office of Management and Budget. November 9, 2023. Circular No. A-4 To the Heads of executive Agencies and Establishments regarding Regulatory Analysis <https://bidenwhitehouse.archives.gov/wp-content/uploads/2023/11/CircularA-4.pdf>

¹¹ Office of Management and Budget. November 9, 2023. Circular No. A-94 Memorandum for Heads of Executive Departments and Establishments regarding Guidelines and Discount Rates for Benefit-Cost Analysis of Federal Programs <https://bidenwhitehouse.archives.gov/wp-content/uploads/2023/11/CircularA-94.pdf>

¹² Office of Management and Budget. February 28, 2024. OMB Ecosystem Services Guidance: Explanation and Response to Public Input. https://bidenwhitehouse.archives.gov/wp-content/uploads/2024/02/ESGuidance_explanation.pdf

The final strategy in the Roadmap highlighted the need for ongoing research to better inform use of nature-based solutions. That led to the creation of a new working group¹³ charged with identifying research priorities for BCA, including ecosystem services and nature-based solutions. The group's first report,¹⁴ and accompanying Fact Sheet¹⁵ highlighted BCA associated with wildfires and extreme weather and ecosystem services as two of the priority areas. The following year's report¹⁶ featured progress made on those and other topics and highlighted new priority areas.

And, as noted above, nature-based solutions feature prominently in the Justice40 Initiative actions, bringing equity, climate and nature together.

Nature-based solutions may also be useful for carbon removal, on land and in the ocean,¹⁷ but questions remain about the efficacy, duration, and collateral impacts of various carbon removal approaches. To tackle some of

¹³ Office of Management and Budget, White House Office of Science and Technology Policy, and Council on Economic Analysis. 2025. *Frontiers of Benefit-Cost Analysis*. <https://bidenwhitehouse.archives.gov/omb/information-regulatory-affairs/frontiers-of-benefit-cost-analysis/>

¹⁴ National Science and Technology Council. December 2023. *Advancing the Frontiers of Benefit-Cost Analysis: Federal Priorities and Directions for Future Research*. <https://bidenwhitehouse.archives.gov/wp-content/uploads/2023/12/FINAL-SFBCA-Annual-Report-2023.pdf>

¹⁵ Office of Management and Budget. December 14, 2023. *Biden-Harris Administration Announces New Initiative to Advance the Frontiers of Benefit-Cost Analysis and Strengthen government Decision Making*. <https://bidenwhitehouse.archives.gov/omb/briefing-room/2023/12/14/fact-sheet-biden-harris-administration-announces-new-initiative-to-advance-the-frontiers-of-benefit-cost-analysis-and-strengthen-government-decision-making/>

¹⁶ National Science and Technology Council. October 2024. *Advancing the Frontiers of Benefit-Cost Analysis: Progress on Federal Priorities, Insights for the Research Community, and Emerging Topics*. <https://bidenwhitehouse.archives.gov/wp-content/uploads/2024/10/2024-Advancing-the-Frontiers-of-Benefit-Cost-Analysis-Report.pdf>

¹⁷ Doney, Scott and Jane Lubchenco. October 6, 2023. *White House Office of Science and Technology blog: Marine Carbon Dioxide Removal: Potential Ways to Harness the Ocean to Mitigate Climate Change*. <https://bidenwhitehouse.archives.gov/ostp/news-updates/2023/10/06/marine-carbon-dioxide-removal-potential-ways-to-harness-the-ocean-to-mitigate-climate-change/>

these unknowns, we produced a report^{18,19} identifying the research priorities for marine carbon dioxide removal, with the intention of guiding federal and non-federal research in this emerging area.

2.3. Focusing on land-based AND ocean-based actions

Because we live on land, we tend to focus on land-based actions. Yet, we know from scientific research and syntheses that the ocean is a powerful source of solutions to climate change. Acting on that science, the U.S. produced its Ocean Climate Action Plan.²⁰ The plan highlights the immense potential for offshore wind, green shipping and nature-based solutions like blue carbon to reduce emissions, absorb carbon, and enhance resilience. This Ocean Climate Action Plan attracted the attention of other nations who are considering similar approaches. The press release²¹ and progress report²² highlight the impressive progress made during the first year, including scaling up offshore wind energy, advancing decarbonization of the U.S. marine transportation system, and enhancing community resilience to ocean change.

¹⁸ White House Office of Science and Technology Policy. November 12, 2024. OSTP Releases National Marine Carbon Dioxide Removal Research Strategy. <https://bidenwhitehouse.archives.gov/ostp/news-updates/2024/11/12/white-house-of-science-and-technology-policy-releases-national-marine-carbon-dioxide-removal-research-strategy/>

¹⁹ White House National Science and Technology Council. November 2024. National Marine Carbon Dioxide Removal Research Strategy. <https://bidenwhitehouse.archives.gov/wp-content/uploads/2024/11/U.S.-Marine-Carbon-Dioxide-Removal-Research-Strategy.pdf>

²⁰ White House Ocean Policy Committee. March 2023. Ocean Climate Action Plan. https://bidenwhitehouse.archives.gov/wp-content/uploads/2023/03/Ocean-Climate-Action-Plan_Final.pdf

²¹ White House Office of Science and Technology Policy. April 17, 2024. Marking One Year of Progress since Release of the First-Ever Ocean Climate Action Plan. <https://bidenwhitehouse.archives.gov/ostp/news-updates/2024/04/17/marking-one-year-of-progress-since-release-of-first-ever-ocean-climate-action-plan/>

²² White House Office of Science and Technology Policy. April 17, 2024. Progress Report: Year One of Ocean Climate Action. https://bidenwhitehouse.archives.gov/wp-content/uploads/2024/04/OCAP-Progress-Report_April-2024.pdf

Complementing the Justice40 Initiative and our Ocean Climate Action Plan, we developed an Ocean Justice Strategy,^{23,24} drawing attention to the goal of everyone having a voice and everyone benefitting equally from climate actions. In short, we are making good headway in integrating nature and environmental justice in climate policies and practices.

3. Embedding climate and environmental justice in nature policy

In parallel, we sought to embed climate and environmental justice into nature policies. Because we understand that nature underpins our economy, health, wellbeing, and national security, we pursued a more holistic perspective in addressing the precipitous loss of biodiversity. Most conservation action globally focuses on protected areas, with countries pursuing pledges to protect 30% of lands and the ocean by 2030. However, unless we also address threats to biodiversity in the other 70% of the planet, those protected areas will not stem the loss of biodiversity. This is why the U.S. government took a 30% + 70% approach, with parallel efforts on protected areas in the 30% and other measures to address the 70%. Below are a few of our innovative approaches to mainstream nature across the federal government.²⁵

3.1. *Connecting the dots between nature and the economy*

Although the economy depends on nature, our economic indicators fail to provide information about the state of nature.²⁶ The U.S. initiated the process of putting nature on the economic balance sheet of the country through the development of Natural Capital Accounts and associated En-

²³ White House Council on Environmental Quality. December 8, 2023. Biden-Harris Administration Unveils First-Ever Strategy to Advance Environmental Justice for Communities that Rely on the Ocean and Marine Resources. <https://bidenwhitehouse.archives.gov/ceq/news-updates/2023/12/08/biden-harris-administration-unveils-first-ever-strategy-to-advance-environmental-justice-for-communities-that-rely-on-the-ocean-and-marine-resources/>

²⁴ White House Ocean Policy Committee. December 8, 2023. Ocean Justice Strategy. <https://bidenwhitehouse.archives.gov/ostp/news-updates/2023/12/08/ocean-justice-strategy/>

²⁵ Tallis, Heather, Eli P. Fenichel, Laura Petes, Solomon Hsiang, Phillip S. Levin, Hila Levy, and Jane Lubchenco. 2024. Mainstreaming nature in U.S. federal policy. *Science* 385(6708): pp 498-501. <https://www.science.org/doi/10.1126/science.adp5394>

²⁶ Lubchenco, Jane, Heather Tallis, Eli Fenichel. April 24, 2022. White House Office of Science and Technology Policy blog: Accounting for Nature on Earth Day 2022. <https://bidenwhitehouse.archives.gov/ostp/news-updates/2022/04/24/accounting-for-nature-on-earth-day-2022/>

vironmental Economic Statistics.^{27,28} These efforts also catalyzed interest in working with other nations to advance natural capital accounts.²⁹

3.2. *Connecting the dots between nature and national security*

In the Biden-Harris Administration's National Security Strategy,³⁰ biodiversity and climate change are identified as key components through the concept of natural security.³¹ Both climate change and loss of biodiversity – whether on land or in the ocean – can threaten food security, trigger civil unrest, and lead to human migrations. Wildlife trafficking and illegal fishing are other good examples of the intersection between nature and security, and both also intersect with equity through forced labor and drug trafficking. And both are exacerbated by climate change.

3.3. *Taking stock of nature in the U.S.*

The first-ever U.S. National Nature Assessment was launched in 2021 to assess how nature in the U.S. is changing, what that means, and what options exist.^{32,33} This assessment will demonstrate how nature connects to

²⁷ White House Office of Science and Technology Policy, Office of Management and Budget, Department of Commerce. January 2023. National Strategy to Develop Statistics for Environmental Economic Decisions. <https://bidenwhitehouse.archives.gov/wp-content/uploads/2023/01/Natural-Capital-Accounting-Strategy-final.pdf>

²⁸ Pindilli, Emily, Jane Lubchenco, and Sol Hsiang. April 23, 2024. White House Office of Science and Technology Policy Blog: A Successful Inaugural Year for Natural Capital Accounting in the United States. <https://bidenwhitehouse.archives.gov/ostp/news-updates/2024/04/23/a-successful-inaugural-year-for-natural-capital-accounting-in-the-united-states/>

²⁹ Australia, Canada, United States of America. December 9, 2023. Joint Statement of the Partnership on Cooperation on Natural Capital Accounting, Environmental-Economic Accounting, and Related Statistics (<https://bidenwhitehouse.archives.gov/ostp/news-updates/2023/12/09/joint-statement-of-the-partnership-on-cooperation-on-natural-capital-accounting-environmental-economic-accounting-and-related-statistics/>)

³⁰ White House. October 2022. National Security Strategy. <https://bidenwhitehouse.archives.gov/wp-content/uploads/2022/11/8-November-Combined-PDF-for-Upload.pdf>

³¹ Preston, Benjamin L., Hila Levy, Heather Tallis, Rod Schoonover, Jane Lubchenco. Global Change Research for a More Secure World. *Eos*, 105, <https://doi.org/10.1029/2024EO240215>

³² Levin, Phil. April 22, 2024. White House Office of Science and Technology Policy blog. A Nature Imperative on Earth Day. <https://bidenwhitehouse.archives.gov/ostp/news-updates/2024/04/22/a-nature-imperative-on-earth-day/>

³³ White House Office of Science and Technology Policy Federal Register Notice inviting public comment on an annotated outline for the National Nature Assessment.

our health, to climate change, to equity, to the economy, and to national security.^{34,35}

4. Embedding nature and climate in environmental justice policy

Finally, nature and climate are front and center within Biden-Harris Administration policies dealing with inequity and inequality. In addition to the multiple examples cited above, an EO on environmental justice includes directives to address climate change and access to nature, especially as they relate to historically disadvantaged communities.³⁶ The EO states that “Advancing environmental justice will require investing in and supporting culturally vibrant, sustainable, and resilient communities in which every person has safe, clean, and affordable options for housing, energy, and transportation. It is also necessary to prioritize building an equitable, inclusive, and sustainable economy that offers economic opportunities, workforce training, and high-quality and well-paying jobs... and facilitating an equitable transition of the workforce as part of a clean energy future. Achieving this vision will also require improving equitable access to parks, tree cover, playgrounds, sports fields, rivers, ponds, beaches, lakes, and all of the benefits provided by nature, including America’s public lands and waters.”

And, recognizing the lack of adequate data and scientific research on environmental justice, a new whole-of-government Environmental Justice Science, Data, and Research Plan³⁷ specifies priorities for advancing science to better understand and address inequities.

<https://www.federalregister.gov/documents/2022/10/31/2022-23593/framing-the-national-nature-assessment>

³⁴ Tallis, H., A. Crimmins, and J. Lubchenco. 2023 Charting a path for the National Nature Assessment. Invited editorial. *Frontiers in Ecology and the Environment*. <https://esa-journals.onlinelibrary.wiley.com/doi/10.1002/fee.2583>

³⁵ Tallis, Heather, Eli P. Fenichel, Laura Petes, Solomon Hsiang, Phillip Levin, Hila Levy, and Jane Lubchenco. 2024. Mainstreaming Nature in U.S. Federal Policy. *Science*: 385 (6708): 498-501 Mainstreaming nature in US federal policy | Science

³⁶ President Joseph Biden. 2023. Executive Order 14096 Revitalizing Our Nation’s Commitment to Environmental Justice for All. <https://www.federalregister.gov/documents/2023/04/26/2023-08955/revitalizing-our-nations-commitment-to-environmental-justice-for-all>

³⁷ National Science and Technology Council. 2024. Environmental Justice Science, Data, and Research Plan. <https://bidenwhitehouse.archives.gov/wp-content/uploads/2024/07/NSTC-EJ-Research-Plan-July-2024.pdf>

5. Conclusion

Across all of these efforts, we sought policies that align with scientific knowledge in understanding the intimate connections between climate change, loss of biodiversity and inequity and inequality. I have shared some of the ways in which we integrated nature and environmental justice into climate solutions, and ways we wove environmental justice and climate into biodiversity efforts, and incorporated climate and nature into environmental justice policies. We believe this integration will enhance efforts across all three areas and deliver more durable and successful outcomes in the Anthropocene. Doing so is urgent. I hope these examples encourage other integrated approaches that heed scientific findings and integrate climate, nature, and environmental justice solutions.

Integration across the three topical areas can be facilitated by, but does not require, overarching, framing policies that direct more integrated approaches to issue-specific policies. As with all policy-making, to be maximally effective, the policies should be informed by engagement and consultation with relevant stakeholders and partners.

Acknowledgements

I'm grateful to the impressive members of the Climate and Environment team at the White House Office of Science and Technology Policy who led many of the efforts I describe in the paper, and our talented collaborators in other White House offices and in agencies across the federal government. Their service is greatly appreciated. I greatly appreciate that my home institution, Oregon State University, was willing to loan me to the White House for nearly four years. And I thank the leadership, members, and staff of the Pontifical Academy of Sciences for stimulating meetings, thoughtful planning and organization.

BUILDING A STRONG INCLUSIVE AI-DRIVEN DIGITAL COMMONS FOR DEVELOPMENT IMPACT AT THE NEXUS OF CLIMATE, PEOPLE, LANDSCAPE HEALTH AND FOOD SECURITY

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■ <https://www.doi.org/10.65398/YLFB3345>

Abstract

As the largest source of employment and a major source of greenhouse gas emissions, the global agriculture sector has enormous potential for helping alleviate climate change, poverty, food insecurity, drought and other emerging and entrenched challenges. Trees are a cornerstone of any viable pathway to reducing the negative impacts and magnifying the positive impacts of the agriculture sector. At the intersection of trees and agriculture, emerging technologies and the data underlying them are supporting the wider uptake of sustainable and regenerative practices. There is an opportunity for significant developmental progress against global inequalities through the application of emerging technologies in agroforestry. With productive climate resilient agriculture that promotes biodiversity conservation, landscape health can be assured from farm to forests, decreasing pressures for land-use change while promoting corridors for nature to thrive. To achieve such goals, and to develop technologies that are fair, ethical and recognize the rights of all stakeholders, it is important to develop a data governance framework that optimizes inclusivity, accessibility, interoperability and reliability. This paper explores principles for a digital commons supportive of emerging technologies at the intersection of agroforestry, ecosystems and human health, seeking a framework that maximizes the potential of data-centric technologies while leaving no one behind. Properly conceived and implemented, a digital commons can support the systemic approach of the Planetary Commons, thereby enabling greater planetary resilience.

1. Introduction

In March 2023, the Future of Life Institute published a document entitled “Pause Giant AI Experiments: An Open Letter”. The letter was signed by over 30,000 people, including eminent technology pioneers, and was a

response to the wide and growing concerns over our inability to control the pace and direction of AI. Despite widespread support from prominent individuals in academia, philanthropy and the private sector, the letter failed to achieve its goal of a pause, and the development of AI has only increased since the letter was published. The letter stands as a cautionary example that support from individuals and organizations may not be sufficient to affect change in the modern course of technological development. The economic and political forces that set such a course are powerful and require new approaches if they are to be moderated in the interest of ensuring that benefits accrue to all people rather than a select few.

A part of the modern digital economy that has grown exponentially in importance is the data and data infrastructure that forms a necessary component of AI systems. Such data pertains to a wide variety of subjects, from people and places to processes and actions. An unfortunately common thread is that the varying stakeholders are struggling to agree and implement principles for governing the processing of data, even while technology continues to advance into new areas and applications.

Notwithstanding the challenges, there is an opportunity for data to be a source of strength and unification. The collection of datasets opens new possibilities for applications that strengthen our collective resilience in the face of global crises. As planetary and local environments change, efforts towards adaptation and mitigation will increasingly require access to such datasets; limiting access only hinders our development and ultimate success in the face of monumental challenges. At the same time, unlimited and unregulated access provides too many opportunities for uses that are contrary to the interests and wishes of data subjects, contrary to principles of fairness, and contrary to long-term development of communities.

This paper explores principles for a digital commons¹ supportive of emerging technologies at the intersection of agroforestry,² ecosystems and human health, seeking a framework that maximizes the potential of AI, quantum computing and other data-centric technologies while leaving no

¹ Throughout this paper, the term “digital commons” is used broadly to encompass data as well as other forms of knowledge, sociocultural capital and other forms of capital. A subset of a digital commons is a “data commons”, which comprises only data.

² Agroforestry is an agroecological approach that involves farmers, livestock, trees and forests at multiple scales – including trees on farms, farming in forests and at forest margins and tree-crop production. See, for example, Nair PKR, 1993. *An introduction to agroforestry*. Springer Netherlands, Dordrecht.

one behind. The paper concludes with recommendations for approaching the development of such principles, particularly considering the failure of past attempts to slow the uncontrolled progress of emerging technologies.

2. Contextualizing data and agriculture in the Anthropocene

The anthropogenic era started a few hundred³ or a few thousand years ago,⁴ and is characterized by anthropogenic emissions of greenhouse gases. Regardless of the starting point, the anthropogenic era is significantly tied to environmental changes from agricultural practices. Whether deforestation occurs to clear land for farming or to support industrial activities, it is accompanied by significant negative impacts to soil and water, loss of biodiversity, emissions of greenhouse gases, and an overall loss of resilience.

As a major driver of climate change and other environmental impacts, the agriculture sector is also key to addressing these challenges. An agriculture sector focused on sustainability and environmental restoration holds the power to enhance soil health, conserve water and increase biodiversity. To achieve these outcomes, it has been suggested that humanity must free itself from “dominating egoism towards nature” and replace capital-oriented decisions with transformational policy in terms of agricultural resilience.⁵

Within the last decade, the agriculture sector has adopted modern technologies at a rapid pace, and that pace is accelerating. With the introduction of mobile-based apps, smart agriculture and now artificial intelligence (AI), the global agricultural industry is highly industrialized and data-driven and, as a result, highly influenced by those who control data infrastructure. Consolidated control over the means and expense of collecting, managing and processing relevant datasets can exacerbate inequities in the agriculture sector, with significant impacts on food security, poverty, climate change and planetary resilience. Efforts to counter these inequities are consistent with the Sustainable Development Goals and the Montreal Statement on Sus-

³ Crutzen PI and Stoermer EF. 2000. The “Anthropocene”, *IGBP Newsletter* 41: 12.

⁴ Ruddiman W. 2003. The anthropogenic greenhouse era began thousands of years ago. *Climatic Change* 61: 261–293.

⁵ Mahaswa R, Widhianto A, Nurul H. 2021. Eco-agriculture and farming in the Anthropocene epoch: A philosophical review. International Conference on Bio-Energy and Environmentally Sustainable Agriculture Technologies (p. 226). Malang: E3S Web of Conferences.

tainability in the Digital Age.⁶ One avenue for such efforts seeks solutions through data governance that is inclusive, responsive and responsible.

Certain concepts and principles of data governance are older than the digital age but grew in importance with the development of computer networks. In connection with the growth of AI and other emerging technologies, data governance is now a fully-fledged academic sub-discipline, incorporating aspects of law, technology, ethics and philosophy. Attempts at reducing data to a mere commodity (“data is the new oil”) provide a convenient economic perspective but ignore or severely discount the personal nature of data.

The concept of a commons is an ancient one that is integral to the concepts of civilization and community. Like data governance, the commons was of interest in the digital age prior to computer networks, but interest has grown significantly with the development of data-centric emerging technologies. Notably, while many technology companies are willing to provide AI algorithms and tools to the public through open-source licensing schemes, those same companies are far less generous with the datasets they build to support AI systems. Demonstrating the critical importance of data, technology companies go to great lengths to obtain, maintain and restrict access to the largest possible datasets.⁷

The application of principles of a commons to the development of technology is not new. Numerous examples have demonstrated the feasibility of a commons, including GitHub and Creative Commons in software development and digital works of creativity, respectively. In the context of data and information, there is yet to emerge a commons with depth or scope equivalent to GitHub or Creative Commons. The economic value and current proprietary nature of data are not the only challenges preventing such an emergence. As described in the next section, data may exist in many formats, is often highly contextualized, may be significantly time sensitive, may be highly biased or non-representative, or may violate data protection or copyright law, among numerous other possible issues. Notwithstanding these challenges, success in building a digital commons will compound successes in the development of technologies that work in service to people and the planet.

⁶ Ubalijoro E. 2021. A sustainable and equitable digital revolution: Eliane Ubalijoro. *One Earth*, 4(6), 801-804.

⁷ Metz, C., Kang, C., Frenkel, S., Thompson, S.A., & Grant, N. (2024). How tech giants cut corners to harvest data for ai. *The New York Times*.

3. Bridging science, agriculture and tradition for the challenges ahead: Building the digital commons

Data pertaining to trees and agriculture have many sources and formats and are highly contextual. Datasets vary in characteristics that include resolution, geographic coverage, frequency of measurement, consistency of measurement protocols and other factors. Often, higher quality datasets are proprietary, leading to inequality between users with and without access. Nevertheless, citizen science and the proliferation of mobile applications and smartphones has drastically increased the availability and quantity of agricultural data. A few of the sources of agricultural data are discussed in the following paragraphs.

Earth observation (EO) data from satellites cover the ultraviolet, visual, infrared and microwave bands, and allow time-dependent mapping and monitoring. Because of the expense of deploying and operating satellites, satellite-based data is typically gathered by governments or the private sector and tends to be the most consistent in terms of collection protocol and data format. However, there are often limitations in spatial and temporal resolutions, and in availability, as some EO datasets (especially those owned by the private sector) are not freely accessible. At the highest resolution, for example, EO data can distinguish individual trees, but such data is typically not freely available.

Scientific projects and measurement stations are significant sources of agricultural data. Such datasets are highly valuable for their consistency of collection protocol and accuracy of measurements. These datasets may, however, be limited in geographic coverage. The relatively low density of weather stations in Africa, for example, means that African farmers have relatively reduced weather information and ability to predict weather events.⁸ Nevertheless, scientific data, particularly pertaining to trees and forests, has immense potential for helping to understand and address global environmental challenges. Data from the dendrochronology lab at CI-FOR-ICRAF, for example, are tremendously rich in information, and are useful in modelling various phenomena, from climate change to the hydrological cycle.⁹ Information locked in tree rings offers many insights on the

⁸ Dinku T. 2019. Challenges with availability and quality of climate data in Africa. In *Extreme hydrology and climate variability* (pp. 71–80). Elsevier.

⁹ Gebrekirstos A, Bräuning A, Sass-Klassen U, Mbow C. 2014. Opportunities and applications of dendrochronology in Africa. *Current Opinion in Environmental Sustainability* 6: 48–53.

right tree for the right purpose in the right location, basic elements critical to successful complex agroforestry systems that support the ability of trees to sequester carbon, store water and nutrients from soil, increase biodiversity and enrich soil organic matter and carbon.

Mobile app-based data collection is growing in popularity and has been deployed throughout the Global South in a variety of contexts. Activating a network of citizen scientists can provide large volumes of data, and while such data may be of variable quality and inconsistent frequency, due to the large numbers of volunteers, such datasets can be very useful.^{10,11}

Traditional knowledge (TK) and Indigenous knowledge (IK) are sources of agricultural data that present unique challenges. Compared with other agricultural datasets, TK and IK may cover the longest timescales, and may be the most narrowly contextualized, pertaining to very focused geographic areas. These datasets may be oral in whole or in part; converting TK and IK to written datasets poses particularly difficulties, both operational and ethical.

Harmonizing the various sources of agricultural data presents significant challenges, although some efforts have been made. At CIFOR-ICRAF, the Land Degradation Surveillance Framework (LDSF) provides a comprehensive method for assessing soil and land health using field-collected data. The method establishes a biophysical baseline at the landscape level. Using data analytics, spatial assessments and a multi-scale approach, the baseline allows monitoring of land degradation and assessment of rehabilitation efforts over time. Investments in capacity for data acquisition and methods of analysis have complemented the LDSF and have resulted in significant datasets pertaining to soil and land health. Crucially, the framework is openly available, contributing to the development of interoperable and complementary datasets from different organizations in different geographic regions. These could be considered minimal steps towards building and scaling a digital commons which, as we describe in the next section, is critical for addressing planet-wide resilience.

¹⁰ Feldmeyer D, Meisch C, Sauter H, & Birkmann J 2020. Using OpenStreetMap data and machine learning to generate socio-economic indicators. *ISPRS International Journal of Geo-Information*, 9(9), 498.

¹¹ Li H, Zech J, Hong D, Ghamisi P, Schultz M, & Zipf A, 2022. Leveraging OpenStreetMap and multimodal remote sensing data with joint deep learning for wastewater treatment plants detection. *International Journal of Applied Earth Observation and Geoinformation*, 110, 102804.

A planetary digital commons framework

Rockström and colleagues introduced the concept of a Planetary Commons to describe the interconnected critical biophysical systems determining and regulating the Earth's environment.¹² The Planetary Commons is distinguished from the existing global commons, the latter being a political and legal construct resting on assumptions of global environmental stability. The Planetary Commons framework treats Earth's resilience as a goal rather than an assumption. Reaching that goal requires an understanding of Earth systems including the atmosphere, hydrosphere, lithosphere, biosphere and cryosphere,¹³ as well as subsystems that include forests, peatlands and other carbon sinks. The Planetary Commons framework leads to "comprehensive stewardship obligations through Earth system governance aimed at restoring and strengthening planetary resilience and justice."¹⁴

The importance of data to the Planetary Commons cannot be understated. There can be no solution developed for a problem that is not understood, and the Planetary Commons is a paradigm designed to contextualize solutions for complex challenges on a global scale. It is a framework that relies on evidence available to all and governed in a way that supports evidence-based science and policymaking.

In the context of the Anthropocene epoch and the Planetary Commons there is a critical need for robust governance frameworks that support addressing the interconnected challenges and functioning of Earth's systems. We propose that a digital commons serves the data-focused needs of the Planetary Commons. A digital commons, properly conceived and operationalized, supports the comprehensive stewardship and integrated management that is a cornerstone of the Planetary Commons framework. This is a paradigm shift from merely managing resource access to ensuring the protection of vital Earth system functions crucial for planetary resilience and justice.

As various forms of knowledge (including TK and IK) increasingly become digital, and AI becomes ubiquitous, the Planetary Commons framework necessitates the incorporation of a digital commons to effectively support custodianship of these planetary systems. For example, accessible and

¹² Rockström J, Kotzé L, Milutinović S, Biermann F, Brovkin V, Donges J, Ebbessen J, French D, Gupta J, Kim R, et al. 2024. The Planetary Commons: A new paradigm for safeguarding Earth-regulating systems in the Anthropocene. *Proceedings of the National Academy of Sciences* 121(5): e2301531121.

¹³ Id. at page 5.

¹⁴ Id. (Abstract).

reliable climate data have been recognized as essential for well-grounded resource allocation and decision making.¹⁵

Contrary to traditional biophysical systems, which can degrade with overuse, a digital commons has the potential to increase in value and utility through wider sharing and ethical use. Digital platforms can provide broader access to information, foster collaboration, and drive innovation. By developing open and accessible digital environments, we can promote sustainable practices and improve decision making for planetary stewardship.

The need for global data and AI governance

Traditional governance principles, such as those proposed by Elinor Ostrom, have been critiqued for their limitations in addressing system design and inclusivity, particularly for marginalized communities.¹⁶ There is a growing recognition of the need for inclusive codesign processes that incorporate diverse stakeholders into the governance of technological systems. Proposals for design principles that build on Ostrom's framework are emerging, aiming to adapt these principles to the governance of technological innovations.¹⁷

Through our scientific activities, CIFOR-ICRAF demonstrates a holistic systems approach that leverages the complexity of the interaction between people and ecological systems to increase climate resilience. The complexity of the data needed to ensure effective integration of trees, crops, livestock or fish in landscapes can be supported by databases like CIFOR-ICRAF's Regreening Africa app or the Tree Globally Observed Environmental Ranges database (TreeGOER). Ensuring the right insights guide productive climate resilient and nature positive food tree portfolio is key.¹⁸

¹⁵ United Nations Environment Programme (2024). *The Climate Data Challenge: The Critical Role of Open-Source and Neutral Data Platforms*, Geneva.

¹⁶ Robert G, Williams O, Lindenfalk B, Mendel P, Davis LM, Turner S, Farmer C, Branch C. 2021. Applying Elinor Ostrom's Design Principles to Guide Co-Design in (care) Improvement: A Case Study with Citizens Returning to the Community from Jail in Los Angeles County. *International Journal of Integrated Care* 21(1): 7. <https://doi.org/10.5334/ijic.5569>

¹⁷ Stern PC. 2011. Design principles for global commons: Natural resources and emerging technologies. *International Journal of the Commons* 5(2): 213–232. <https://doi.org/10.18352/ijc.305>

¹⁸ van Zonneveld M, Kindt R, McMullin S, Achigan-Dako EG, N'Danikou S, Hsieh WH, ... & Dawson IK, 2023. Forgotten food crops in sub-Saharan Africa for healthy diets in a changing climate. *Proceedings of the National Academy of Sciences*, 120(14), e2205794120.

Recent wider calls for action emphasize the necessity of ensuring that technological advancements promote both sustainability and equity.¹⁹ Notable efforts, such as the Land Degradation Surveillance Framework described above, demonstrate successful integration of scientific research and community engagement. This framework, utilized in over 20 countries on three continents, provides critical land health data that supports decision-making processes related to land restoration. Public datasets on soil health similarly contribute to our understanding of global land and soil commons. An effective digital commons would incorporate similar principles and methods, but on a wider scale, covering all the systems in the Planetary Commons.

Role in innovation

The availability of free and accessible data through digital commons significantly reduces the need for private or open investment to access such data, thus lowering transaction costs.^{20, 21} This reduction in costs is crucial for fostering innovation, as it enables a broader range of entities to engage in the development and implementation of new technologies and solutions.²² The provision of freely accessible data mitigates the barriers to innovation by offering essential information without the financial burden associated with costly transactions. This accessibility is particularly advantageous for small and medium-sized enterprises (SMEs), startups and development organizations, which often face significant constraints in investing heavily in data acquisition. Leveraging data commons allows these entities to innovate more efficiently and effectively.^{23, 24}

The reduction in transaction costs is integral to enhancing economic efficiency and innovation, as these costs represent the expenses associated with

¹⁹ See FN4.

²⁰ Nugraha A, Yuniarto A, & Fiedler T 2021. The Role of Data Commons in Reducing Transaction Costs for Innovation. *Journal of Innovation Economics*, 15(2), 123-145.

²¹ Yuniarto A, Nugraha A, & Fiedler T 2021. Accessibility of Data Commons and Its Impact on SMEs. *Small Business Economics*, 38(3), 567-589.

²² Fiedler T, Nugraha A, & Yuniarto A 2021. Innovation Through Data Commons: A Comprehensive Review. *Technology and Innovation Management Review*, 12(4), 234-256.

²³ Garigliotti G, Lyu H, & McIntosh J, 2023. Data Commons and Innovation in SMEs: A Case Study Approach. *International Journal of Small Business Management*, 50(3), 345-367.

²⁴ McIntosh J, Edelmann N, & Virkar S, 2023. Leveraging Data Commons for Startups: Opportunities and Challenges. *Journal of Business Research*, 45(1), 78-99.

utilizing goods or services.^{25, 26} By lowering these costs, data commons facilitate a more inclusive environment for innovation, enabling diverse stakeholders to contribute to technological advancements and solutions.

Current funding gaps for the commons

Despite the potential benefits offered by data and digital commons, substantial funding gaps persist. Many governmental and private entities have yet to prioritize investments in the development and maintenance of these commons, resulting in their underutilization.²⁷ Historically, philanthropic organizations have played a crucial role in supporting the creation and upkeep of digital commons. By funding these initiatives, philanthropies can ensure that valuable data and tools remain accessible, thereby fostering an environment conducive to collaborative innovation.²⁸

To address the current funding gaps, it is imperative to foster partnerships among the public, private and non-profit sectors. Such collaborations enable stakeholders to pool resources, share expertise, and develop comprehensive strategies for the effective management and utilization of digital commons. These joint efforts can lead to more sustainable and impactful solutions to global challenges by leveraging the diverse strengths and capabilities of participating organizations. Integrating collaborative approaches into philanthropic efforts can enhance the efficacy of investments and ensure that the benefits of digital transformation are equitably distributed across various societal segments.²⁹

4. Cultivating optimism and inspiring action

Although modern environmental crises are complex and originate from activities with long historical precedents, there is reason to be optimistic about the power of collective action properly directed and incentivized.

²⁵ Edelman N, & Virkar S, 2023. Reducing Transaction Costs in Innovation: The Role of Data Commons. *European Journal of Innovation Management*, 29(1), 45-67.

²⁶ Lyu H, Garigliotti G, & McIntosh J, 2023. Enhancing Economic Efficiency Through Data Commons. *Journal of Economic Perspectives*, 37(2), 112-134.

²⁷ Stanciu V, Putra A, & Yeniasir, M, 2021. Funding Gaps in Digital Commons: An Analysis. *Public Administration Review*, 81(1), 1-8.

²⁸ Putra A, Stanciu V, & Yeniasir M, 2022. The Role of Philanthropy in Supporting Digital Commons. *Nonprofit and Voluntary Sector Quarterly*, 51(2), 234-256.

²⁹ Sustainability in the Digital Age, Future Earth, and ClimateWorks Foundation. 2022. Dynamic Philanthropy – A Framework for Supporting Transformative Climate Governance in the Digital Age. <https://doi.org/10.5281/zenodo.5764443>

The Montreal Protocol on Substances that Deplete the Ozone Layer, passed in the 1980s, is one example demonstrating that planetwide consensus is both possible and highly effective.³⁰ Science showed the presence of a thinning ozone layer and identified the risks that it posed to the planet. Science also provided alternatives that eliminated the need to rely on known harmful substances. Together, policymakers and scientists managed to create a framework with incentives and alternatives that changed behaviours toward a more sustainable pathway.

Nearly 40 years after the Montreal Protocol, climate change is every bit as threatening to the planet as the thinning ozone layer once was. Although the science of the problem is clear, currently the only effective solution – reducing greenhouse gases – is neither economically nor politically feasible. The increased discussions around geoengineering solutions demonstrates the urgency of the matter, but there are significant unknowns regarding undesirable side effects for most such solutions.³¹ Further complicating the matter, and due to its high electricity demand, artificial intelligence has itself been identified as a potential contributing factor to climate change.³²

Climate change differs from the thinning ozone layer in that the former is a far more complex problem. There are many known causes ranging from burning fossil fuels to agricultural practices, and the phenomenon has components of a feedback loop. Solutions to the problem, whether they be reductions in greenhouse gas emissions or any of the proposed geoengineering processes, have one requirement in common – the availability of data and robust science-led global governance. Earth observation data, ground truthing data, TK and IK, and other forms of data must be collected and managed in a way that enables scientists to understand the problems and propose viable solutions. Data management must be formulated in a way that allows lawmakers and policymakers to trust the science and impose the framework of incentives that will address the issues. This needs to create a robust foundation for an innovation ecosystem in agroforestry that can be

³⁰ Gonzalez M, Taddonio KN, Sherman NJ. 2015. The Montreal Protocol: How today's successes offer a pathway to the future. *Journal of Environmental Studies and Sciences* 5: 122–129.

³¹ Sovacool BK. 2021. Reckless or righteous? Reviewing the sociotechnical benefits and risks of climate change geoengineering. *Energy Strategy Reviews* 35: 100656.

³² Kaack LH, Donti PL, Strubell E, Kamiya G, Creutzig F, & Rolnick D 2022. Aligning artificial intelligence with climate change mitigation. *Nature Climate Change*, 12(6), 518–527.

agile and responsive to building the resilience we need amidst the uncertainty of the changing climate. The entire process must be inclusive, collaborative and transparent, aiming to benefit the most vulnerable.

The rapid development of artificial intelligence, its reliance on data, and its likely influence on any path towards sustainability, underscores the need for urgency in developing a digital commons that serves the needs of everyone. That can only happen when all stakeholders – including the scientists, policymakers, innovators and funders – prioritize creating and contributing to a digital commons that supports the sustainability of the Planetary Commons. Such an effective planetary digital commons will envision a future where collective intelligence, shared responsibility and inclusive governance drive sustainable outcomes.

AIR QUALITY, CLIMATE, AND HEALTH IN THE ANTHROPOCENE

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■ <https://www.doi.org/10.65398/NMMD1395>

1. Anthropocene and Climate Change

The Anthropocene as the current period of Earth history is characterised by a globally pervasive and rapidly increasing influence of human activities on the planet – from the equator to the poles and from the land surface, atmosphere and biosphere to the oceans and deep sea. The intensive use of land and water as well as the emission of greenhouse gases and pollutants lead to climate change and put pressure on ecosystems, biodiversity, and human health.

In the geological epoch of the Holocene, which began around 10 thousand years ago, the atmospheric concentration of carbon dioxide (CO₂) in the Earth's atmosphere was fairly stable at around 260–280 ppm, and the fluctuations of global mean surface temperature and sea level were relatively small. Under these favourable conditions, human civilisation developed from the Neolithic Age to modern times. Since industrialization in the 19th century, however, there has been a strong increase in CO₂ and other greenhouse gases (GHG) such as methane (CH₄) and nitrous oxide (N₂O). The current atmospheric GHG concentrations of more than 420 ppm CO₂ and 1900 ppb CH₄ are not only far above the stable values of the Holocene. They are also far outside the range of natural fluctuations in recent Earth history, i.e., far above the approximately 200–300 ppm CO₂ and 400–800 ppb CH₄ that were characteristic for the regular cycling between of ice ages and warm periods during the last million years of the Pleistocene (Figure 1), during which global mean surface temperatures and sea levels varied by as much as 5°C and more than a hundred meters, respectively (IPCC 2021; Intergovernmental Panel on Climate Change, www.ipcc.ch).

The massive changes in the concentration of GHG and other trace gases in the atmosphere are a clear indicator of the extent to which humans are interfering with the global biogeochemical cycles that can be regarded as the metabolism of planet Earth. Particularly far-reaching are the human interventions in the carbon cycle through the release of CO₂ from the combustion of fossil fuels (coal, crude oil, natural gas) and the release of CH₄

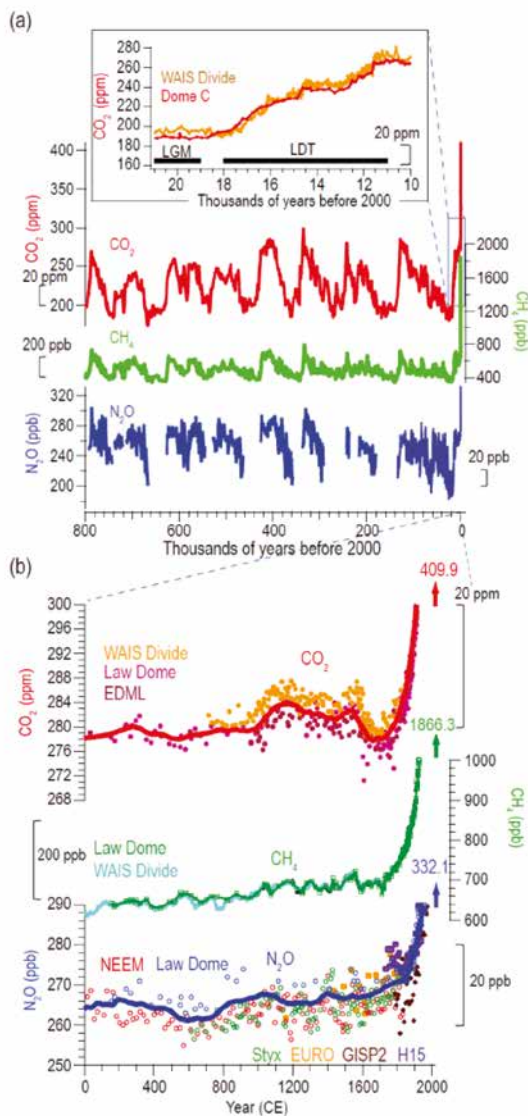


Figure 1. Temporal evolution of atmospheric well-mixed greenhouse gas concentrations in recent Earth history determined from ice cores. (a) Records during the last 800 kyr with the Last Glacial Maximum (LGM) to Holocene transition as inset. (b) Multiple high-resolution records over the CE. The horizontal black bars in panel (a) inset indicate LGM and Last Deglacial Termination (LDT) respectively. The red and blue lines in (b) are 100-year running averages for CO₂ and N₂O concentrations, respectively. The numbers with vertical arrows in (b) are instrumentally measured concentrations in 2019. Further details on data sources and processing are available in the IPCC report from which the figure has been adopted (Figure 2.4, Chapter 2, IPCC 2021).

from industrial and agricultural processes. Similarly, the nitrogen cycle is massively altered and enhanced by the industrial production and agricultural use of ammonia and nitrogen fertiliser as well as the release of nitrogen oxides such as N_2O from fertilised soils and NO or NO_2 from combustion and other high-temperature processes. The observed steep increase in GHG concentrations far outside the range of natural fluctuations is clearly attributable to anthropogenic emissions, and there is no plausible alternative explanation. The same applies to the rapid global warming of our time, i.e., the increase of global mean surface temperature by more than one degree Celsius in less than two centuries from 1850 until today (IPCC 2021).

At a scientific conference of the International Geosphere-Biosphere Programme (IGBP) in the year 2000, the atmospheric researcher and Chemistry Nobel Laureate Paul Crutzen realized and stated that the Earth system had transitioned from the Holocene to a new geological epoch shaped by humanity, for which he coined the term Anthropocene (Crutzen 2002, Benner et al. 2021). Since the 19th century, scholars had already recognised an increasing influence of humans on their environment and planet Earth (Leclerc, Marsh, Stoppani, Arrhenius, Vernadsky, Teilhard de Chardin et al.), but they had not yet realized that the Holocene has ended and a new epoch has begun. Since the discovery and conceptualisation of the Anthropocene by Paul Crutzen and colleagues, there have been different proposals to formally define its beginning. One option is the time of industrialisation in the 19th century, which led to the above-mentioned GHG increase that can be traced in ice cores but may not meet the formal requirements for the official definition of a geological epoch, which should be traceable in sediments worldwide. Another proposal referred to the beginning of agriculture in the Neolithic period, which led to regional changes but is difficult to detect on global scales, coincides with the beginning of the climatically very stable Holocene, and is thus not particularly meaningful from an Earth science perspective.

The Anthropocene Working Group (AWG) of the International Commission on Stratigraphy (ICS/IUGS) proposed to define the beginning of the Anthropocene on the basis of plutonium concentration peaks, which originate from radioactive fallout from nuclear weapons tests in the middle of the 20th century and are detectable worldwide. This period of the “Great Acceleration” of human activities and influence on the Earth system also saw particularly high growth rates and turning points in the characteristic S-shaped growth curves for the world population, global primary

energy consumption, and numerous other indicators of human expansion. The AWG proposal to pin the beginning of the Anthropocene to a geological reference layer known as a global boundary stratotype section and point (GSSP; often called a golden spike) in the sediments of Crawford Lake, Canada, was not accepted by the Subcommission on Quaternary Stratigraphy (SQS) of the ICS (Zalasiewicz et al. 2024). Nevertheless, this or a similar definition for the beginning of the Anthropocene appears most meaningful from the perspective of Earth system sciences, where the term and concept originated, and it will likely prevail in the ongoing scientific discussion: For the overwhelming global human impact on planet Earth, which characterizes the Anthropocene, it would seem difficult to envision a more prominent signal than the global fallout and deposits of nuclear testing combined with the steep increase of human population, activities, alteration of landscapes, and emissions of GHG and other environmental pollutants in the mid-20th century.

Due to anthropogenic emissions, the CO₂ concentration in the Earth's atmosphere is now as high as it was around 3 million years ago, when the average global temperature and sea level were around 3°C and 10-20 metres higher, respectively. If the GHG emissions and concentrations are not curbed, similarly strong warming and sea level rise are to be expected in accordance with modern earth system and climate models as well as earlier estimates of the greenhouse effect by natural science pioneers in the 19th century (Fourier, Arrhenius et al.). The transition from the stable conditions of the Holocene warm period into an Anthropocene hot period is expected – and partly already observed – to result in an increase in the frequency and intensity of extreme weather events (heat waves, droughts, heavy rainfall, landslides, etc.), the flooding of coastal areas where large parts of the world's population and economy reside, and corresponding mass migration (Röckström et al. 2009; Steffen et al. 2018; IPCC 2021).

2. Air Quality and Public Health

Besides global warming by GHG, anthropogenic emissions also lead to a massive increase in the atmospheric concentration of aerosols, i.e., nanometer to micrometer-sized liquid or solid particles suspended in the air, and reactive trace gases like ozone and nitrogen oxides on local, regional, and global scales. For example, the average mixing ratios of ozone in continental background air have increased by a factor of ~2-4 from about 10-20 ppb at the beginning of the 19th century to 30-40 ppb in the 21st century.

The amount of fine particulate matter in polluted urban air is typically ~ 10 times higher than in clean air of remote continental regions ($10\text{--}100\ \mu\text{g m}^{-3}$ compared to $\sim 1\text{--}10\ \mu\text{g m}^{-3}$). The vastly different concentration levels result from primary emissions as well as secondary formation and growth of aerosol particles in the atmosphere, whereby aerosol acidity and its buffering by anthropogenic ammonia are of particular importance (Pöschl et al. 2005, 2015; Fröhlich-Nowoisky et al. 2016; Su et al. 2020; Zheng et al. 2020, 2024). Atmospheric aerosols play a central role in the formation of clouds and precipitation, influence the hydrological cycle and global energy budget, and are among the largest uncertainty factors in the assessment and prediction of climate change (IPCC 2021). Recent studies contrasting the physicochemical properties, interactions, and effects of aerosols in pristine rainforest and polluted megacity environments as well as fundamental differences between nano- and microparticles (nano-size effects) help to constrain and reduce these uncertainties (Liu et al. 2020, 2023; Pöhlker et al. 2023a; Wang et al., 2023; Zhang et al. 2023; Chen et al. 2024). For example, Figure 2 shows how the uptake of water vapor by aerosol particles serving as cloud condensation nuclei depends on chemical composition and can be efficiently described by globally averaged hygroscopicity parameters for organic and inorganic particulate matter (Pöhlker et al. 2023a).

Exposure to fine particulate matter and other air pollutants leads to oxidative stress in human, animal, and plant organisms and to an increase in morbidity and mortality due to respiratory, cardiovascular and metabolic diseases. Epidemiological and toxicological studies show that pollutants from combustion processes and other anthropogenic emission sources are among the greatest risk factors for human health and life expectancy worldwide (Global Burden of Disease, www.healthdata.org/research-analysis/gbd; Health Effects Institute, www.healtheffects.org; World Health Organisation, www.who.int). The global average loss of life expectancy (LLE) attributed to air pollution is around ~ 3 years, which is higher than the global average LLE around ~ 2 years attributed to tobacco smoking (averaged over entire population, not just smokers) and to other risk factors like parasitic or vector-borne diseases (malaria, leishmaniasis, rabies, dengue, yellow fever etc.; ~ 0.7 yrs), HIV/AIDS (~ 0.7 yrs), and violence (including interpersonal conflicts and armed interventions; ~ 0.3 yrs; Lelieveld et al. 2020). Model results indicate that the global mean life expectancy could be increased by ~ 1 year without fossil fuel emissions and by ~ 2 years when all potentially controllable anthropogenic emissions are removed. Around ~ 1

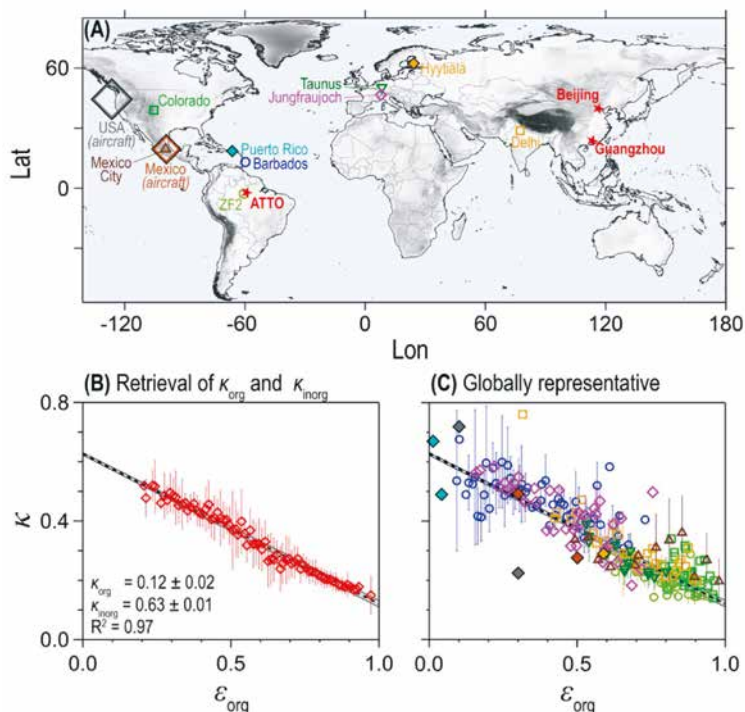


Figure 2. Retrieval of globally representative aerosol hygroscopicity parameters for organic particulate matter, κ_{org} , and inorganic ions, κ_{inorg} , based on cloud condensation nuclei measurements worldwide. Retrieval of $\kappa_{\text{org}} = 0.12 \pm 0.02$ and $\kappa_{\text{inorg}} = 0.63 \pm 0.01$ from linear bivariate regression fits of experimentally derived organic mass fraction, ϵ_{org} , and hygroscopicity parameter, κ , from the Amazon, Beijing, and Guangzhou in (B), along with further campaign data sets in (C), showing that κ_{org} and κ_{inorg} are representative for organic and inorganic aerosols under continental and marine conditions worldwide. The global map in (A) with topography in gray shows all measurement locations relevant for this study. The retrieval in (B) is based on the three extended campaign datasets: Program of Regional Integrated Experiments of Air Quality over the Pearl River Delta (PRIDE-PRD2006) in Guangzhou, Campaign of Air Quality Research in Beijing (CAREBeijing-2006), and at the Amazon Tall Tower Observatory (ATTO). Colors of data points in (B) and (C) correspond to site markers in (A) (Pöhlker et al. 2023a).

year of the global average LLE attributed to air pollution is related to natural sources that would be difficult to control (e.g., Aeolian dust and wildfire emissions; Lelieveld et al. 2020).

The exact mechanisms by which air pollutants are causing mortality and diseases, however, have not yet been resolved. Oxidative stress is assumed

to play a key role, but the identity, quantity, and reaction pathways of the chemical species that mediate oxidative stress and its adverse health effects at cellular and humoral levels are not clear. Epidemiological studies show that the mass concentration of airborne fine particulate matter with diameters less than $2.5\ \mu\text{m}$ (PM_{2.5}), which is a complex mixture of organic and inorganic compounds, is responsible for most of the adverse health effects of air pollution, while elevated ambient concentrations of trace gases like ozone and nitrogen oxides are also noxious but less important. The oxidative potential of PM_{2.5}, defined as its ability to produce reactive oxygen species (ROS) such as hydrogen peroxide (H_2O_2) is frequently used and widely perceived as a marker for the toxicity of PM_{2.5}.

Recent investigations, however, indicate that the total abundance of ROS in the epithelial lining fluid (ELF) of the human airways is largely determined by endogenous H_2O_2 as produced in the human body and circulated with the blood flow or the inhalation of ambient gas-phase H_2O_2 , while the chemical production of H_2O_2 by inhaled PM_{2.5} is of minor importance. In contrast, the formation of hydroxyl radicals ($\text{OH}\cdot$) is closely related to

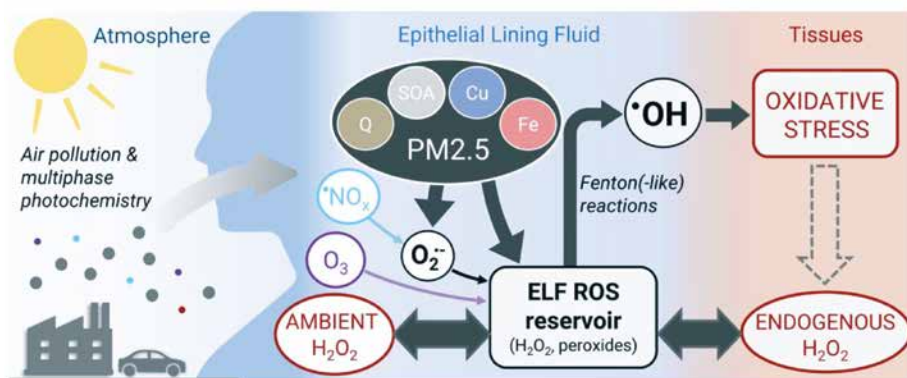


Figure 3. Health effects of atmospheric air pollution. The epithelial lining fluid (ELF) is a thin aqueous film at the air–body interface in which inhaled air pollutants dissolve and deposit. H_2O_2 and other peroxides form a reservoir of reactive oxygen species (ROS) in the ELF. H_2O_2 levels in the ELF are controlled by endogenous processes (endogenous H_2O_2 regime) or inhalation of gas-phase H_2O_2 (ambient H_2O_2 regime). A small fraction of H_2O_2 originates from conversion of superoxide ($\text{O}_2^{\cdot-}$) generated from interaction of fine particulate matter (PM_{2.5}) and nitrogen oxides (NO_x) with ELF. Other peroxides are supplied through secondary organic aerosol (SOA) contained within PM_{2.5} or by chemical reactions of ozone (O_3). Transition metal-mediated, catalytic conversion of peroxides leads to formation of the highly reactive $\text{OH}\cdot$ radical that can trigger oxidative stress and, ultimately, cell death (Dovrou et al. 2023).

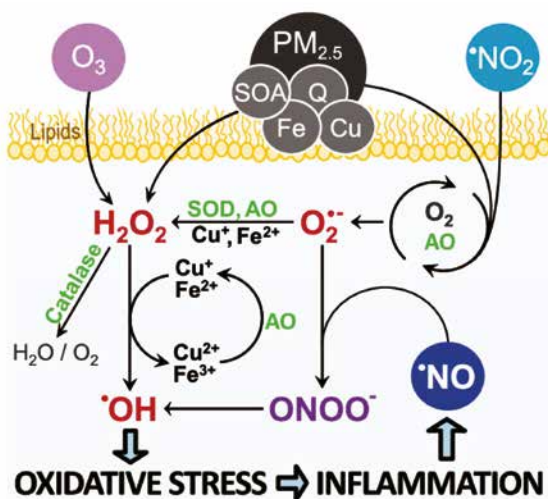


Figure 4. Production, interconversion, and scavenging of reactive oxygen species in the epithelial lining fluid (ELF). Reactions of $PM_{2.5}$ constituents (copper, iron, quinones) and NO_2 with antioxidants (AO) lead to superoxide ($O_2^{\cdot -}$) formation. $O_2^{\cdot -}$ is converted into hydrogen peroxide (H_2O_2) by superoxide dismutase (SOD) and AO, followed by scavenging of H_2O_2 through catalase. Secondary organic aerosol (SOA) components also produce H_2O_2 and hydroxyl radicals ($\cdot OH$). Copper (Cu^+) and iron (Fe^{2+}) ions compete with catalase to form $\cdot OH$, the most reactive species driving oxidative stress. Through reactions of $PM_{2.5}$ constituents with antioxidants, redox cycling is sustained in the ELF. Inflammation is promoted by oxidative stress and is associated with increased levels of nitric oxide (NO), which competes with the antioxidant defense system for $O_2^{\cdot -}$ to form peroxynitrite ($ONOO^-$), a labile compound that can decompose to form $\cdot OH$ (Lelieveld et al. 2024).

Fenton-like reactions of transition metals (Cu, Fe), quinones, and other redox-active components of $PM_{2.5}$, catalyzing the conversion of H_2O_2 and organic peroxides into highly reactive hydroxyl radicals ($\cdot OH$) that can react with most biomolecules and cause most oxidative damage in human cells and tissues. As illustrated in Figure 3, these findings suggest that the adverse effects of $PM_{2.5}$ are related to the catalytic conversion rather than the production of ROS, which may imply a change of paradigms in elucidating and mitigating the health effects of air pollutants (Dovrou et al. 2023).

Related investigations and results may also explain why individuals with pre-existing inflammatory disorders like asthma or chronic obstructive pulmonary disease (COPD) are particularly susceptible to air pollution, which was hitherto unknown. As illustrated in Figure 4, the commonly elevated concentrations of endogenous nitric oxide (NO) in diseased individuals

may increase the production of hydroxyl radicals via peroxynitrite (ON-OO⁻) formation and provide a molecular rationale and feedback mechanism how the adverse health effects of air pollutants may be exacerbated by inflammatory disorders and vice versa (Lelieveld et al. 2024).

Peroxynitrite and other endogenous or exogenous reactive oxygen and nitrogen species (ROS/RNS) can also modify the chemical structure, properties, and effects of proteins, which may have important consequences for chronic neurodegenerative, cardiovascular or gastrointestinal diseases and allergies that are increasingly prevalent in modern societies (Franze et al. 2008; Fröhlich-Nowoisky et al. 2016, 2023; Reinmuth-Selzle et al. 2017, 2023; Ziegler et al. 2020; Mishra et al. 2024). In particular, air pollutants such as fine particulate matter, nitrogen oxides, and ozone can trigger or enhance oxidative stress, nitration and oligomerization of proteinaceous allergens and damage-associated molecular patterns (DAMPs), immune reactions, and feedback cycles of inflammation. Figure 5 illustrates how chemically modified DAMPs may amplify oxidative stress and innate immune

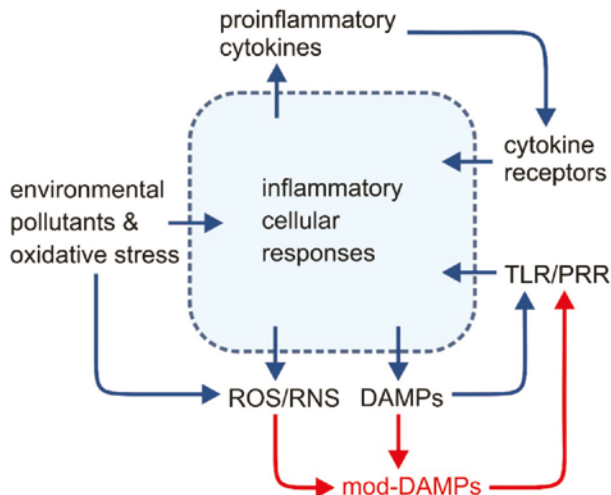


Figure 5. Amplification of inflammatory processes and innate immune responses through chemically modified DAMPs. Environmental pollutants and oxidative stress can induce an increase of reactive oxygen and nitrogen species (ROS/RNS), the formation of chemically modified damage-associated molecular patterns (mod-DAMPs), an increase of pro-inflammatory signaling via Toll-like receptors and other pattern recognition receptors (TLR/PRR), an increase of proinflammatory cytokines, and further inflammatory cellular responses (Ziegler et al. 2020).

responses through a positive feedback loop of pro-inflammatory signaling via pattern recognition receptors (PPR). Such self-amplification provides a potential explanation for the development of inflammatory disorders related to environmental pollution: Environmental pollutants may generate exogenous ROS/RNS and oxidative stress, triggering inflammatory processes that lead to the formation of endogenous ROS/RNS and release of DAMPs. The DAMPs can activate PRR (TLR, RAGE, etc.) that induce further pro-inflammatory signaling and responses via transcription factors (NF- κ B, IRF3, etc.), cytokines and cytokine receptors (IL-1, IL-8, etc.). This positive feedback can be additionally enhanced if the DAMPs undergo chemical modification by ROS/RNS, and if the modified DAMPs lead to stronger activation of PRR than the native DAMPs, as observed in recent investigations (Reinmuth-Selzle et al. 2017, 2023; Ziegler et al. 2020; Fröhlich-Nowoisky et al. 2023).

3. Open Scholarship and Epistemic Web

As environmental pollution severely affects climate and public health in the Anthropocene, we need to understand how humanity can best deal with the sources and effects of environmental pollutants in relation to economic development and social welfare. Recent advances in scientific research provide deep insights into the underlying physical, chemical, and biological processes and reveal the relative importance of different pollutants and sources, including natural and anthropogenic contributions. This knowledge enables the development of efficient strategies and policies to mitigate and counteract the adverse effects of environmental pollutants on the Earth system, climate, and health (“planetary health”). With regard to the development, societal communication, and political implementation of appropriate policies for environmental protection, it seems worthwhile to emphasize that climate and health effects are two facets of global change that can and need to be handled together.

Further scientific, technical, and societal progress towards a climate-neutral, environmentally friendly and sustainable energy and circular economy appears urgently needed in order to achieve a lasting and stable Anthropocene, ensure the health, prosperity and continued existence of human civilisation, and avoid deteriorating or even losing the basis of our livelihood. The Anthropocene concept may help humanity to recognise and communicate both cognitively and emotionally: We are shaping the planet, so let’s try to get it right. Not only but especially for the encouragement of young

people who are facing major challenges, it may be worthwhile and promising to communicate not only the threats but also the opportunities of global change. Apart from the negative aspects and dangers of climate change and biodiversity loss etc., one may consider it a remarkable achievement and great opportunity that we as a species (*Homo sapiens*) have reached the ability to actively shape our environment and planet.

To avoid the perils and grasp the chances related to the power of shaping the planet, it seems critically important to explore and follow potentially suitable pathways according to the basic principles of critical rationalism, i.e., according to the best state of knowledge as validated by observations, experiments, and theoretical considerations, but without claiming absolute certainty. Multi- and transdisciplinary exchange will be required for proper consideration and communication of all relevant perspectives, for societal decision making, and for the practical implementation of suitable directives, regulations, and measures – with regard to climate protection and human health as well as economic prosperity, social justice, global equity and peace as are outlined in the 17 sustainable development goals of the United Nations (sdgs.un.org/goals) and related statements from political, religious, and scholarly institutions around the world.

Recent experiences at the science-policy interface related to the COVID-19 pandemic, air quality, climate, and human health confirmed that open scholarship including open access publications, open data, open source codes, open peer review, interactive public discussion, and the principles of critical rationalism are essential for efficient multi- and transdisciplinary exchange between scholars, politics, and society at large (Leopoldina 2019; Cheng et al. 2021; Pöhlker et al. 2023; www.mpic.de/5081943/studien-fls). New and improved forms of scholarly communication and quality assurance need to be developed while converting the existing corpus of scholarly journals from subscription to open access as outlined in the OA2020 Expression of Interest and the latest Berlin Open Access Conference (oa2020.org; oa2020.org/b16-conference).

To gain the full benefits of open scholarship, a dualism of complementary approaches is required (“as-well-as”, not “either-or”): We need top-down approaches to achieve large-scale progress as well as bottom-up initiatives to maintain scholarly diversity. We need appropriate transformative agreements with traditional publishers to achieve an efficient conversion of subscription journals that are still important for some communities, and we also need to liberate and provide funds for proper OA publishers and new

publishing platforms to maintain competition and innovation (www.mpic.de/4123205/open-access). Most importantly, we have to uphold and improve scholarly quality assurance, evaluation, and self-regulation. For this purpose, we need to maintain functioning elements of traditional peer review and add advances such as open review, interactive discussion, and article level metrics that are traceable, transparent, and inclusive for the global scientific community and society at large. Indeed, transcending hidden peer review and citation counting oligopolies by transparent forms of quality assurance that can be followed, reproduced, and refined by everybody around the world is among the main reasons why we need full and immediate open access to scholarly research publications.

In times of growing irrationality, alternative facts, postfactual discussions, and fake news, it seems ever more important to practice and promote open scholarship and critical rationalism, i.e., openly show and share the basis, methods, and rigor of the scientific discourse as a role model and reference for societal exchange, decision making, and evolution. Accordingly, open peer review and interactive public discussion are important steps on the way to an epistemic web that documents the scientific discourse in accordance with critical rationalism – openly telling the world not only what we know, but also how well we know it, and where the limitations are (it-

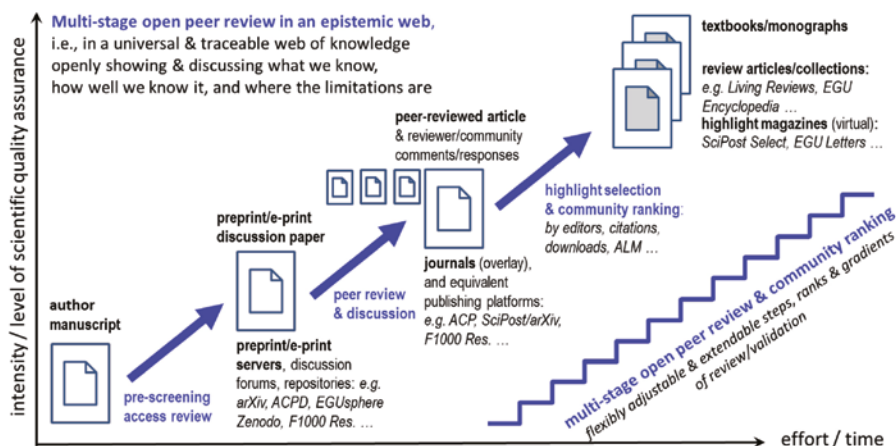


Figure 6. Key elements of multi-stage open peer review contributing to a global epistemic web, i.e., a universal and traceable web of knowledge openly showing and discussing what we know, how well we know it, and where the limitations are – in line with the principles of critical rationalism (iterative validation or falsification of theories by observations).

erative validation or falsification of theories by observations; Pöschl 2012; Hyman and Renn, 2012). Figure 6 outlines key elements of multi-stage open peer review as practiced in a growing number of scientific journals, preprint servers, and related publishing platforms in the geosciences (since 2001) and more recently also in other disciplines (Pöschl 2004, 2012; Wolfram et al. 2020). The iterative process of review and discussion is rooted in the global scholarly community and will increasingly involve artificial intelligence and machine learning tools (AI/ML) as these become available and increasingly powerful on scholarly publishing platforms. Not only but also for this purpose, it appears desirable to train AI on quality-controlled scholarly knowledge available to all via proper OA licenses (CC-BY) rather than just arbitrary internet contents or restricted contents that are accessible and usable for monopolists/oligopolists rather than the public. A comprehensive global commons of knowledge and epistemic web with transparent quality assurance will help to augment, communicate, and utilize scholarly insights and understanding for rational and transparent approaches to resolving complex questions and problems in the Anthropocene.

Acknowledgement

This manuscript provides an overview and synthesis of recent scientific exchange, studies, and publications of the author with numerous colleagues who are gratefully acknowledged – in particular T. Berkemeier, J. Fröhlich, K. Lucas, C. Pöhlker, M. Pöhlker, G. Lammel, H. Su, Y. Cheng, J. Lelieveld, and M.G. Weller. This article is dedicated to Paul J. Crutzen, whose curiosity, ingenuity, and wisdom have helped to prevent ozone layer destruction and nuclear winter, and will help to avoid the perils and grasp the opportunities of the Anthropocene.

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CLIMATE CHANGE AND HABITABILITY. A TIMELINE

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■ <https://www.doi.org/10.65398/YAGX9997>

The depth of the Amazon rainforest, the dry belt of the Sahel, remote islands in the Pacific and the expanse of the Arctic circle – humanity has conquered rather inhospitable regions, turning them into their habitat. Thriving on healthy ecosystems, human population has grown and prospered, benefiting from relative climate stability over the past 11,700 years, the Holocene period. During this period, the neolithic revolution triggered civilizational development and humans permanently settled across the world. Human population growth correlates with the resulting technological and per capita income or resource changes of this period. Ten thousand years ago, the human population comprised only 4 million individuals and saw a growth rate of 0.04% per annum until the 18th century, eventually reaching one billion around 1800 (Roser & Ritchie, 2023). Global life expectancy at the beginning of the 20th century was at only 32 years and has since doubled. The past 200 years have been marked by stark population growth, with a peak during the 1960s of an annual growth rate of more than 2%, marking exponential increase (United Nations Department of Economic and Social Affairs, Population Division, 2022). In 2025, the global population consists of more than 8 billion people.

The rapid expansion of the human population, sedentary agriculture, city formation and the concomitant human development achievements – all occurred during the very short Holocene time-period. This is a remarkable acceleration of development, considering the existence of *Homo sapiens* which spans approximately 300,000 years. Humanity's oldest cities, such as Jericho and Damascus were formed just 10,000 years ago. Many of the cultural UNESCO world heritage sites are much younger, such as Aksum of the 1st century, Mesa Verde, dating back to the 6th century, or the Cologne Cathedral which was completed in 1880 after several centuries of construction.

For more than 288,000 years, humans survived solely as hunter gatherers in the Pleistocene. This form of living also enabled them to cope with large changes in global mean temperature, for example during the ice ages

(Hofreiter & Stewart, 2009). However, the human population faced bottlenecks throughout this time and sometimes probably only narrowly escaped extinction (Tallavaara et al., 2015). The last glacial maximum which occurred about 20 000 years ago, saw global mean temperatures only 6°C cooler (Tierney et al., 2020), a fact that highlights the severity of changes which occur at several degrees of deviation in the global mean temperature. In the case of the last ice age, ice sheets covered vast parts of North America and Europe, with 200-meter-thick glaciers over Berlin. The Holocene period, which started after the last ice age, also gave rise to the industrial revolution, with far reaching consequences, including the disruption of the glacial-interglacial cycle (Ganopolski et al., 2016).

The Beginning of the Anthropocene

Arguably, the industrial revolution eventually ended the Holocene period and pushed *Homo sapiens* into the Anthropocene, the time-period in which humans are significantly altering the earth system, shaping natural environments on a global scale, sometimes irreversibly (see for example the stark temperature change over the past 100 years: Kaufman et al., 2020). While the International Union of Geological Sciences rejected the proposition to recognize the Anthropocene as a geological epoch, the signs of the fundamental shifts that are underway are undeniable (Carrington, 2024).

While the burning of fossil fuels on an industrial scale has enabled steep economic development in many world regions, it also set off the greatest common threat: climate change and other adverse effects of the overuse of natural resources. The great acceleration of global consumption, trade, travel, and the intensification of industrial agriculture over the past decades have driven the rise of greenhouse gas emissions (Steffen et al., 2015, 2018). Through the burning of fossil fuels, CO₂ levels in the atmosphere are as high as they were last 2 million years ago, long before the existence of the *Homo sapiens* (Intergovernmental Panel on Climate Change (IPCC), 2023a, p. 676). This fact alone shows that humanity has inserted itself into an experiment with uncertain outcomes. The high concentration of greenhouse gas emissions has already led to warming of 1.46°C above pre-industrial levels in 2024 (Lindsey & Dahlman, 2025). The impacts of this temperature increase have been observed across all oceans and continents. They include, inter alia, rising sea levels and the acidification of the ocean by 0.1 units on the pH scale, the shifting of climatic zones and intensification and increased frequency of extreme weather events. The *timeline* of these changes

is crucial for risk assessment. If the Amazonian forests, which for 65 million years were able to withstand climate variability, are suddenly starting to lose resilience and succumbing to human interference by way of warming and deforestation, it signals a transition reaching far beyond human timescales (Albert et al., 2023; Flores et al., 2024; Gatti et al., 2021). Considering the short period of humanity's modern civilizational development in the Holocene, it is evident that the climate trends are now on track to disrupt humans' success story.

Two epochal trends are thus converging in the 21st century: a dramatically changing climate and environment due to anthropogenic pressures and a still growing population which may reach its peak by the end of the century. As climate change will adversely affect resource availability in many regions, including those densely populated, it can turn some areas less habitable. This means that the carrying capacity for a certain size of a population with limited outside resources may be reduced. If key resources such as land disappear or critical physiological thresholds in terms of heat and humidity are surpassed, some areas may be rendered virtually uninhabitable, especially considering higher warming scenarios.

Paradoxically, as humans have developed into such an influential force that they can shape ancient ecosystems on a global scale, the ability to use these capacities to proliferate environmental resources and form them for human benefit rather than just depleting them in singular extraction is so far largely absent. On the contrary, the compounding effects of climate change and biodiversity loss are now so pronounced that they threaten to undermine the habitability of certain areas in the future. Though some natural resource management and governance mechanisms point in the right direction, the surpassing of multiple planetary boundaries reflects the scale of the failure to shape our natural habitat for human prosperity and development at large (Richardson et al., 2023).

Observed Changes Undermining Traditional Livelihoods

The conditions of the earth system that have served human development well are increasingly under pressure (Xu et al., 2020). Livelihoods which have been shaped and adapted to harsh environments over thousands of years, are suddenly rendered obsolete by climate change impacts. Sometimes, other anthropogenic drivers of resource depletion and pollution, such as over-usage of fertilizers and pesticides or the introduction of PFAS (so-called forever chemicals) and plastic into natural environments, are further worsening

scarcity or adversely affecting human health, leading to compounding risks. Across the world, humans are already faced with these changes which will intensify without rapid emissions reductions. The following examples illustrate some of the human dimensions of climate change:

- Fishermen find fewer large fish in many of the lagoons in the Marshall Islands, due to CO₂-driven acidification, ocean warming and the resulting coral bleaching events (see for example: The Republic of the Marshall Islands, 2025; Vinke, 2019). Disrupting the reef-ecosystems carries implications for food networks in the ocean as the reefs are habitat for many species. At the same time, coastal flooding, worsened by sea level rise, damages infrastructure and salinizes land and freshwater resources of the coral atolls, increasing dependencies on food imports (Grecni et al., 2025).
- Farmers in Burkina Faso are confronted with unpredictable rainfall patterns and rising temperatures which diminish their crops (Vinke et al., 2022). Nomadic pastoralists who have adapted to the dry Sahelian conditions through the transhumance are also struggling with the changes, some even have to sell their livestock to prevent it from dying. These environmental pressures have heightened tensions between the different groups. Urban dwellers also suffer from an increase in hot days and nights, rendering outside work more dangerous during warm spells (Sanou et al., 2023). People internally displaced by the armed conflict and violence of Islamist extremist groups are particularly vulnerable to weather extremes, as they tend to live in temporary shelters. Countries experiencing conflict-displacements also often see large weather-related displacements which may be linked to a lack of capacities, including adequate government responses (IDMC, 2025, pp. 13ff.).
- In the Amazon basin, droughts impact the Amazon River. In 2024, water levels in parts of the basin fell to record lows. People living on the affected tributaries are experiencing severe scarcity. The dried-out rivers were sources of income from fish stocks and tourism, as well as lifelines for inter-communal transport – all of which were disrupted, pushing people into poverty. Dry conditions also fortified wildfires which destroy habitats and worsen air pollution. The combined effects of deforestation and heating are threatening the tropical rainforest and its precious biodiversity with risks of disrupting precipitation patterns across the region (Flores et al., 2024).

- In the Arctic circle thawing permafrost is destroying infrastructure and impeding traditional hunting techniques, while reduced summer sea ice is allowing further progression of industrial fishing into the pristine environment of the high north. These changes are contributing to further urbanization. As a result of colonization and climate impacts, cultural practices tied to hunting and semi-nomadic lifestyles are increasingly lost. Many indigenous groups are fighting for their cultural heritage.
- In the United States, some housing prone to fires or tropical cyclones has become uninsurable. Insurance companies have withdrawn their coverage from some areas after increasing costs over the past years, including in states such as California, where wildfires have repeatedly caused damages in the hundreds of billions of dollars (Vincent, 2025; Wang et al., 2021). Similarly, in Florida many homes and infrastructure have been affected by hurricanes and rising sea levels which in turn increase the damages of storm surges (Coy, 2023; Picchi, 2023). Recent floods in Texas killed more than a hundred people, including many children in a summer camp along a riverbank. Even with financial support available, rebuilding in the same locations after these disasters hit can perpetuate risks by keeping people and assets exposed to more frequent and intense weather extremes.

As these few examples showcase, smallholder farmers and fisherfolk whose livelihoods are closely intertwined with the environment are at the forefront of these dramatic environmental changes. With little financial resources to maximize adaptation options, many poor populations are already faced with existential risks.

But even countries with large technological and financial capacities are confronted with limits to their management capacities of climate-related disasters. The displacement of people across the globe and uninsurability of housing that has occurred in industrialized countries reflect the outpacing of adaptation and innovation by increasing risks. Better forecasting methods and technological developments may help to reduce risks in the future, but considering the current pace of emissions reductions, human and economic costs will continue to rise.

Climate Change-Related Migration and Immobility

As a response to these changing environmental conditions many people are already on the move. Most of these movements are internal, not least because people prefer to stay close to home in the hope of a possible re-

turn. Moreover, transboundary pathways are often dangerous, prohibitively expensive or just not accessible to people in need. In 2024, the Internal Displacement Monitoring Center (IDMC) recorded a new record of 45.8 million internal displacements due to disasters (IDMC, 2025). The majority of them are weather-related and hence already shaped by climate change. In the past, there were also situations in which whole regions needed evacuation because of weather extremes. In the case of Barbuda, the entire island was evacuated after tropical cyclone Irma destroyed all of the island's infrastructure in 2017.

While displacements are characterized as forced movements, there are additional movements which are more voluntary and can be seen as a form of adaptation to climate impacts – if they serve to maintain people's standard of living. At the same time, climate change can also trap people in areas that are affected by dangerous, or even life-threatening hazards. Especially when financial resources are depleted or other factors, such as disability, hinder people from moving, involuntary immobility can result. When people feel strong place attachment, they may also decide to stay despite mounting risks.

Historically, migrations have been shaped by climatic conditions (Praetorius et al., 2023). However, the circumstances of the migrations that occur in connection with anthropogenic climate change differ fundamentally. Because of exponential growth, global population density is at its highest in human history, so migratory movements, especially rural-urban movements, will be directed at (densely) inhabited places. The speed and scale of anthropogenic climate change diverges from any experience humans have had since our civilization was formed during the Holocene period. Therefore, understanding present-day climate migration and habitability requires a civilizational lens that takes into account the most recent human development achievements that need to be preserved.

But also growing technological capacities should be considered when assessing modern climate migration or habitability. Faced with severe climate impacts, more and more in-situ adaptation options have been developed. From changing crops for cultivation, to shifting livelihoods or building dikes and artificial islands, human ingenuity delivered a wealth of possible ways to manage risks. However, financial and technological capacities to deploy such innovations are highly unequally distributed (Intergovernmental Panel on Climate Change (IPCC), 2023b, p. 26).

Concepts of Habitability in the Context of Anthropogenic Climate Change

When humans can even survive the heat of the desert and build on reclaimed land in the ocean, how can habitability be defined? As the Intergovernmental Panel on Climate Change (IPCC) assessed in its latest synthesis report, there are hard limits to adaptation. “Surpassing such hard, evolutionary limits causes local species extinctions and displacements if suitable habitats exist (high confidence)” is the conclusion of the IPCC (*ibid.*, p. 84). In human systems thresholds for such limits are contested because many perceived limits can be considered as “soft”, meaning that through the allocation of technical or financial means or an improvement of governance and policy, adaptation could be successful. Even if the limits to adaptation in human systems can only be an approximation, what lies beyond those limits may begin with deprivation and end in uninhabitability.

In the context of climate change habitability is determined broadly by two factors: the severity and frequency of climate impacts and the capacities (financial, technological) and abilities (political, societal) to respond (Figure 1).

If the capacities to respond outweigh or are in equilibrium to the magnitude of climate impacts, the area can be considered habitable. For example, desert cities flourishing on high revenues from resource extraction (such as in the oil exporting states) could stay habitable for large populations for a

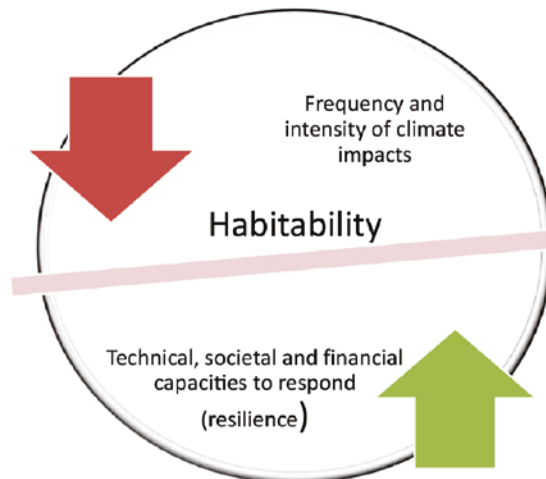


Figure 1. Habitability in the Context of Climate Change. This graphic illustrates how habitability is determined by the extend of the climate impact, i.e. their frequency and intensity as well as the capacities of the affected to respond.

long time, as resilience to increasing heat extremes is sustained through an omnipresence of cooling devices and abundant energy supply.

If capacities are structurally too low to respond to climate impacts and are not enhanced by outside assistance, the affected area may be considered uninhabitable and people may begin to move out or face existential threats. This is why even at current, moderate warming levels, soft limits to adaptation have already been reached because capacities in some areas are low, for example due to high levels of poverty, remoteness or other factors. As global warming accelerates, impacts may become so severe or frequent that they outpace even growing capacities, rendering larger areas uninhabitable.

Rejecting notions of climate determinism, scholars outlined multiple axes of habitability, including compounding and cascading risks, socio-cultural processes, intersectional vulnerabilities of affected groups and connectivity to other places (Sterly et al., 2025).

What is not yet fully explored are the differential thresholds for habitability this implies. Some of these axes point to potentially higher thresholds for habitability, due to connectivity gains that can increase resilience, as well as socio-cultural practices which are more sustainable and thus require less resource supplies. For this reason, adaptive capacities may be higher and therefore even areas marked by severe resource scarcity can be inhabited. At the same time, compounding risks and intersectional vulnerabilities point to lower thresholds to habitability. In the following, these lower thresholds are explored, expanding the definition of habitability beyond the ability to survive to reproduce in a specific area to include a civilizational, rights-based lens.

There are a number of minimum requirements for habitability, starting with **basic ecosystem services** (see Figure 2, elements of habitability). A combination of different climate change impacts act together with other anthropogenic stressors creating the risk landscape that can put the habitability of an area into question by destroying basic ecosystem services. Some of the dominant dangerous climate impacts in the habitability discourse include:

- extreme heat, which in combination with high humidity levels can lead to conditions deadly to humans (Kornhuber et al., 2024; Mora et al., 2017),
- sea level rise, causing coastal flooding that reduces the fertility of soils and the availability of freshwater through salinization,
- frequency and intensity of precipitation extremes, reoccurring droughts and floods can render subsistence agriculture unviable,

- frequency and intensity of tropical cyclones making landfall, destroying infrastructure in increasingly small intervals, leaving little time to re-build.

Habitability for sedentary societies requires a degree of permanence. The decision to stay normally builds on the expectation of recurrence – including of seasonal change, yields, income or other factors. Recurrence of the basic ecosystem services may be disrupted by climate impacts.

Before a place gets so adversely affected that human life itself is in acute danger, there could be lower thresholds for habitability such as severe human rights violations. This is particularly relevant considering Article 25 of the Universal Declaration of Human Rights pertaining to a standard of living adequate to maintain health and wellbeing. This threshold would then be measured against contemporary benchmarks for good health, such as present-day life expectancy. Article 25 also endows all humans security in the case of diminished livelihood in “circumstances beyond his control.” An area where basic human rights can no longer be met due to climate change impacts may therefore potentially be deemed uninhabitable.

Habitability, as described here, is therefore to be understood in the context of the desire to maintain civilizational achievements, such as the preservation

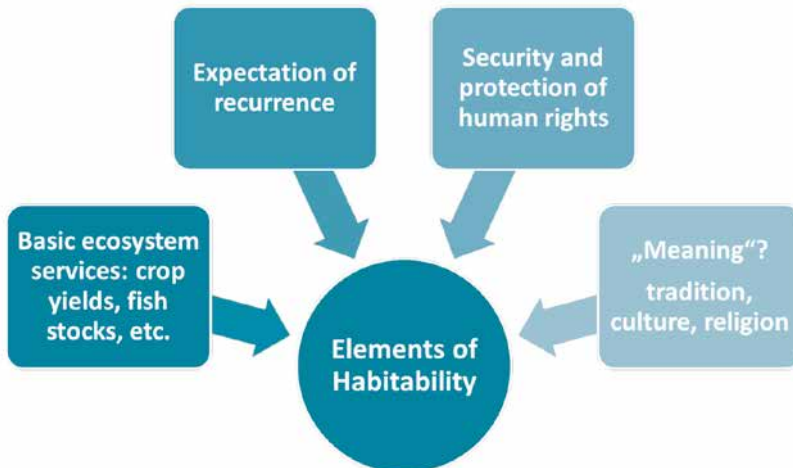


Figure 2. Elements of Habitability. On the left side of the spectrum basic ecosystem services and expectation of recurrence are listed as more quantifiable elements of habitability. On the right side more normative assessments such as security, the protection of human rights, and meaning or place identity are listed.

of basic rights. Other factors such as the cultural importance of a place may also play a role in this assessment. It can relate to the existence of religious or cultural sites or the ability to practice traditions, some of which can be closely linked to the environment. Once previously fertile land is rendered barren and no longer provides ecosystem services, such as specific plants for rituals, this land may lose its meaning to people. Similarly, if heritage sites are destroyed by extreme weather events, subjective assessments of perceived habitability or at least the desirability of a habitat may change. On the flipside, the existence of culturally important sites may motivate people to invest in the protection of these areas and allocate resources to maintain habitability.

Conclusion: Increase Resilience, Decrease Emissions

Climate projections show that impacts threaten to render entire regions unsuitable for permanent habitation towards the end of this century. In order to reduce pressure on habitability, the two major parameters outlined in Figure 1 need addressing. First, to limit the severity of climate impacts decreasing greenhouse gas emissions as fast and as strongly as possible is pivotal. Managing ecosystems in such a way that restores and emboldens carbon sinks is additionally needed, as progress on mitigation has been too slow to only rely on eliminating future emissions. Second, increasing resilience in exposed areas will have to build upon connectivity (von Braun et al., 2022). Vulnerable populations in areas with strong climate hazards often have little leverage over the first dimension of ensuring habitability through emissions reductions. This is because their contribution to global greenhouse gas emissions is extremely low. As their livelihoods are impacted by the effects of the value creation of burning fossil fuels elsewhere, larger sums for adaptation funding need to be allocated to them from high income groups which contribute to climate change disproportionately. Cuts to USAID and other countries' development and relief funds, as well as low international climate finance are undermining efforts to ensure habitability. In conclusion, to protect ecosystem integrity and shape the environment for long-term abundance, humanity has to master transboundary and inter-generational solidarity at the beginning of the Anthropocene.

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**III: ARTIFICIAL INTELLIGENCE FOR
SCIENCES, INNOVATIONS AND
SUSTAINABILITY – OPPORTUNITIES AND RISKS**

EVOLUTION AND AI: BRINGING NEW CHEMISTRY TO LIFE

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■ <https://www.doi.org/10.65398/GLIO2666>

Directed enzyme evolution for sustainable chemistry

Evolution is the most powerful design process ever invented. A simple algorithm of mutation and natural selection has given rise to all the diversity of life, including the stunningly beautiful chemistry that is constantly building and breaking down, the biological world. Life renews itself using abundant and renewable resources, with little waste, recycling its materials, repairing and even reinventing itself as it goes – and all this innovation comes from evolution. When artificial intelligence enables us to read, understand, and even compose the DNA language of life, will comparable innovations be within our reach?

I have been thinking about a sub-problem of this big question: how might AI lead to innovations that will enable humans to live more sustainably on our fragile planet, for example using biology's remarkable chemistry as a model? Nearly all of biology's chemistry is catalyzed by protein catalysts, the enzymes, that can work together inside a little bag of reagents called a cell. Enzymes assemble new cells with the ability to develop into a whole organism, repair a wound, or generate wonderfully complex and functional materials such as wood or a shell, all the while deriving energy and starting materials from their environments. I have long been fascinated by enzymes, particularly for how we might use these amazing inventions to replace dirty human chemistry in making what we need for our daily lives. But to use enzymes for our purposes – from better laundry to manufacturing pharmaceuticals to creating fuels and materials from sunlight and CO₂ – we have to learn how to compose new ones. I would like to expand the DNA-encoded chemistry of the biological world to encompass useful chemistry, including the best of that invented by human chemists.

By freeing enzymes from the constraints of supporting current life, we can explore the universe of life's chemical possibilities. Since the beginning of life, nature has explored the tiniest fraction of this space of possibilities. Out beyond where nature has gone lie solutions to the climate crisis, cures for cancer, or how to feed our growing population without destroying our

beautiful natural world. The challenge is to find those rare, useful new proteins, because most of the staggering number of possible proteins don't do anything at all, much less solve human problems.

And it really is a universe of possibilities. In fact, the number of possible proteins is many orders of magnitude greater than the number of particles in the universe. The philosopher Daniel Dennett (Dennett, 1995) made the wonderful analogy of all the possible biologies (genomes) to Jorge Luis Borges' Library of Babel, the library of all possible books. There are unfortunately many, many more ways to be not-alive in the library of possible genomes, just as the vast majority of Babel's books contain pure gibberish (Dennett, 1995). The collection of all possible proteins is also vast, and the density of 'meaningful' sequences miniscule. But, unlike the librarians of Borges' vast random book collection, we the librarians of the protein collection have an easier time finding the meaningful sequences, because we have evolution to guide us.

John Maynard Smith (1970) described a conceptual space such that each protein sequence is surrounded by all its single-mutant neighbors. For evolution to occur, he argued, a functional protein must be surrounded by at least one functional protein. Evolution could then pass through the network of functional protein sequences to explore new possibilities, one mutation at a time. This process has given rise to the billions upon billions of functional proteins that surround us today, those rare meaningful sequences that we can literally scrape from the bottom of our shoes, and it can give rise to more.

This led to the proposition, formulated in the late 1980s, that such an exploration, one (or a few) mutations at a time, could discover not just new enzymes, but improved ones – including enzymes that would be useful to humans (Arnold, 2019). Since then, such 'directed evolution' experiments have led to many thousands of enzymes used in products from laundry detergents to disease therapies.

With technologies that allow us to make and manipulate DNA in the test tube and encode enzymes in recombinant organisms, we can direct enzyme evolution towards new functions using artificial selection. We think of this as an optimization problem on a so-called fitness landscape in Maynard Smith's sequence space, where fitness is now defined by the enzyme engineer rather than natural selection. It could be the ability to catalyze useful chemistry in a completely non-natural environment like an organic solvent, to catalyze a reaction on whole new substrates, or even to catalyze a whole new chemical reaction.

Directed evolution allows us to explore the future, including chemistry nature has never performed, at least as far as we know. Already in 2016, we published the first enzymes that made the carbon-silicon bonds in a living system, chemistry not known in the biological world, but well known to human chemistry (Kan et al., 2016). And just this year, we made the first enzymes shown to *break* carbon-silicon bonds (Sarai et al., 2024). (Materials with carbon-silicon bonds make up a huge industry, all made using human chemistry). I dream of the day when all of the chemistry that creates our products can be encoded in DNA and performed cleanly, as nature does. Enzymes can also ensure that the products we make are recyclable or biodegradable.

The role of artificial intelligence and machine learning in enzyme design

And where does artificial intelligence enter this picture? Artificial intelligence and machine learning will greatly enhance our ability discover new enzymes and improve them for our purposes. Directed evolution is a simple iterative process of making (a small number of) random mutations and screening the mutated enzymes for their ability to exhibit the desired features. The screening process generates functional data, and it is not hard to label the functions with the sequences that encode them. Screening samples the fitness landscape for enzyme evolution and optimization. With directed evolution, we would simply take the best of those sampled sequences and repeat the mutation and artificial selection, or perhaps recombine beneficial mutations for the next generation. However, the sampled sequence-function data could also be used to build a statistical model of the fitness landscape with which we could make predictions about where to search next for improved functions. In fact, we have used such machine learning methods to improve directed evolution for a dozen years (Romero et al., 2012; Yang et al., 2019). ML is becoming widely adopted to improve directed evolution, and reduce the burden of having to perform many generations of mutagenesis and high throughput screening (Yang, Li et al., 2024).

Besides learning directly from labeled data collected through experiments, the models constructed from the screening data can additionally include what we already know of proteins (e.g. in the form of evolutionary conservation or protein structures and physics) (Yang, Li et al., 2024). The models can also be updated in each generation, and future exploration can be balanced with exploitation of previous knowledge (Yang, Lal et al., 2024).

Furthermore, the starting points for such optimization can come from nature, the repository of evolution's 4 billion years of work, or they can

be generated by human design, intuition or, as is starting to happen, generative artificial intelligence. Generative AI learns from the proteins nature has already made and humans have deposited in rapidly growing databases: it learns to compose from the language of nature's proteins and infer functional proteins that nature has not explored, but could have (Madani et al., 2023). As of today, generative AI is still in its infancy when it comes to generating useful catalytic function. But this may not be true tomorrow.

The wonderful thing about protein optimization, however, is that it is extremely robust – we can start with poor designs (which our generated designs are and are likely to be for a while, while we learn the details of catalysis) and reliably make them far more effective. In other words, evolution empowered by ML can often take a mediocre AI-generated composition and turn it into an acceptable piece of music, if not a Beethoven symphony. As far as I know, this robust and reliable optimization process is unique to proteins, which themselves have been designed by evolution. There is no guarantee that other forms of matter – chemicals, materials, etc. – will be so readily improved, at least until we have the required data and understand how to formulate the 'sequence space' so that optimization is easy.

Automated research workflows (ARWs)

Now it is getting really interesting. All of the steps of directed protein evolution can be automated. Not only that, the steps can be assembled, optimized, and controlled using AI. In fact, there are now fully automated 'cloud' labs, or autonomous laboratories, where enzyme engineering experiments can be carried out. An AI agent can even design the experiment, start it, acquire the data, and then improve its model of the system in iterative cycles of learning, just as I described for ML-assisted directed evolution. The ML model can be updated in each cycle, based on the observations from testing, so that the system learns as it goes and can design the next data collection for the next generation of evolutionary improvement. This is not science fiction – Prof. Phil Romero recently published an early example of such a process (Rapp et al., 2024).

What I have described is an example of an Automated Research Workflow or ARW. ARWs integrate computation, laboratory automation, and tools from AI into the research process, from designing experiments to analyzing data and learning from the results to inform further experiments (NASEM, 2022). An automated laboratory can perform experiments 24

hours a day, 7 days a week, and it can be controlled from a distance, allowing access to users without deep disciplinary knowledge. Such automated exploration and evolution would enable us to create new genetically-encoded chemistry much more efficiently than a graduate student or postdoc can do, and it would free them from highly repetitive experimentation to focus on other tasks, such as gaining a biochemical understanding of the results. A bit over two years ago, as an April Fool's joke, on Twitter (now X) I announced that students could just push a button to create their dream enzymes (<https://x.com/francesarnold/status/1510017434090020864>). This was met with honest excitement, and already is close to reality. I predict that the arduous experimental optimization will become streamlined and fully automated and, once generative AI can propose new enzymes, will make the dream of expanding the chemistry of biology as easy as pressing a button (with money, of course). Such ARWs for protein engineering may offer additional benefits that include enhanced capture of provenance, integrity, and reproducibility (NASEM, 2022).

What are the downsides? We must address the role of humans in the discovery loop, privacy of data, and impact on current incentive systems for researchers. As discussed in a recent report from the National Academy of Sciences on ARWs, additional important questions include,

“What unforeseen technical and ethical issues may arise? Who “owns” the data and discoveries that are produced by automated and distributed systems? How should researchers evolve their practices to reap the benefits of automation while not losing the serendipity of human inspiration and creativity? What goals are best achieved by human scientists (such as invention of new techniques) and which are better left to automation (such as driving data collection to optimize models?” (NASEM, 2022).

An important issue that must be addressed is biosecurity. How will we make sure that bad actors do not use such powerful biological design capabilities to unleash the next pandemic or an agent that targets a selected population for destruction? How do we make sure that simple mistakes or unforeseen consequences of such biological novelty do not become catastrophic? The ability to generate new toxins, resistance mechanisms, or infectivities is not terribly far from the ability to create new chemistry. There will need to be monitoring of such tasks, which is easier if the experiments are done in centralized laboratories.

Conclusions

AI and machine learning are super-charging many areas of science (PCAST, 2024), promising everything from better weather predictions to discovery of new materials and drugs. What is the role of academic research in an era of big models and ARWs? I have outlined a vision for creating new enzymes, but this vision is valid for a much wider range of biological possibilities, from developing novel therapies to discovering the secrets of aging (and perhaps how to intervene). We are at the cusp of an exciting era in science, where AI and ML could empower scientists to do much more with the limited resources we have. My hope is that we will focus on the right problems, train the right people, and use this power for the benefit of the planet rather than find new ways to exploit it.

Acknowledgment

Research in the Arnold laboratory on ML-guided enzyme engineering is supported by the Army Research Laboratory (W911NF-19-2-0026).

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BORGES AND AI

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> Long before today's dilemmas about AI's aspirations and hallucinations, magical realism weaved together fact and fiction to bring new worlds to life. Enter the world of Jorge Luis Borges, an author whose work predates the era of large language models by decades. Ever-present in our cultural heritage, his imaginative and intricate stories construct realms in which the intimate workings of language, and its relationship with reality, are illuminated. Explore how Borges' mental imagery can help us grasp the nature of language models and understand what they mean for AI. <ENTER>

Large language models absorb vast amounts of human cultural knowledge, representing it with a fluency which for many, including the models themselves, announces the era of artificial intelligence. Their capabilities inspire contradictory emotions such as awe,¹ fear,^{2,3} and greed.^{4,5} This confusion stems from our ignorance of the nature of these systems and their implications for humankind. It is more than a matter of absorbing facts, figures, jargon, or mathematical equations. We, humans, need a mental imagery that explains these complex processes through analogy, drawing on our existing knowledge and experiences to make sense of the phenomenon and gain the ability to use it to our – or everyone's – benefit.

The imagery of science fiction tends to dominate debates of AI. We believe, however, that Borges' fiction provides a more compelling imagery and illuminates the relation between language models and AI.

¹ Bubeck, S., et al. (2023). *Sparks of Artificial General Intelligence*, arXiv:2303.12712.

² Bostrom, N. (2016). *Superintelligence*. Oxford University Press.

³ Bengio, Y., et al. (2023): *Pause Giant AI Experiments: An Open Letter*. Future of Life Institute.

⁴ Griffith, E., Metz, C. (2023): *A.I. Funding Frenzy Escalates*, New York Times, 2023/3/14.

⁵ Metz, C., Weise, K. (2023): *Microsoft Bets Big on the Creator of ChatGPT*, New York Times, 2023/1/12.

1. About Large Language Models

Fang, let us say, has a secret. A stranger knocks at his door. Fang makes up his mind to kill him. Naturally there are various possible outcomes. Fang can kill the intruder, the intruder can kill Fang, both can be saved, both can die and so on and so on. In Ts'ui Pen's work, all the possible solutions occur, each one being the point of departure for other bifurcations. Sometimes the paths of this labyrinth converge. For example, you come to this house; in one of the possible pasts you are my enemy; but in another my friend.

The Garden of Forking Paths, 1941

Imagine a collection that does not only contain all the texts produced by humans, but, well beyond what has already been physically written, also encompasses all the texts that a human could read and at least superficially comprehend. This infinite collection of plausible texts may contain books, dialogues, articles, prayers, web pages, computer programs, in any language, in any shape. Imagine a long paper tape with a few initial words of a text. An apparatus scans the paper tape, randomly picks an occurrence of this sequence of words in our infinite collection, finds the word that follows this occurrence, and prints it on the tape right after the previous words. Repeating this process adds more and more words to the tape. Yet, at every instant, the sequence of words printed on the tape is found somewhere in our infinite collection of all plausible texts, and therefore forms one of the plausible continuations of our initial set of words. Call this a perfect language model.⁶

To convert this language model into a chat-bot such as ChatGPT, all we need is a special keyword, perhaps a punctuation mark, which functions as the “send” button of a messaging application. Once the language model outputs the special keyword, it becomes the user’s turn to input more text. When the user hits the send button, it is the language model’s turn again to generate more output.

Each word added on this tape narrows the subset of possible continuations in our collection. Like the forking paths of Ts’ui Pen’s work, each added text constrains the story, the characters, their roles, their ideas, their future, and at the same time serves as a starting point for an infinite sequence of forkings.

⁶ Statistical language modelling was proposed by C.E. Shannon (1948): A Mathematical Theory of Communication, *Bell System Tech. J.*, 27, (3)379–423 and (4)623–656. Available online <http://cm.bell-labs.com/cm/ms/what/shannonday/shannon1948.pdf>

In all fiction, when a man is faced with alternatives he chooses one at the expense of the others. In the almost unfathomable Ts'ui Pen, he chooses – simultaneously – all of them. [...]

The Garden of Forking Paths, 1941

Because Borges could not possibly write this almost unfathomable book using a pencil or a typewriter, he instead chose to write about the book as an idea. He can imagine the book without writing it down in the same way that we can imagine the number π without writing down all its digits. Can a computer provide an approximation of the garden of all plausible texts like it provides approximations of the transcendental number π ?

As is often the case in science and technology, serendipity has played an important role in the development of large language models. Although we do not yet fully understand how these language models encode the infinitely large collection of plausible texts, this collection is not devoid of structure. Any text can be transformed into another text in many ways. The most basic transformation consists of changing a single word. More complex transformations could change a tense, alter the tone of the text, rename the characters, rewrite the text in the voice of another character, and so on. The linguist Zellig Harris has argued that all sentences in the English language could be generated from a small number of basic forms by applying a series of clearly defined transformations.⁷ Training a large language model can thus be understood as analysing a large corpus of real texts to discover both transformations and basic forms, then encode them into an artificial neural network that judges which words are more likely to come next after any sequence. This discovery process starts slowly then gains speed like a chain reaction. For instance, when two phrases in the training data have a known similarity, the surrounding sentences are also likely to be similar, possibly in a more subtle and yet unknown way. As the model gains knowledge about different types of connections between text snippets, it receives fresh clues that reveal more intricate relationships. It also becomes increasingly adept at discovering new templates in the training data or in instructions that fine-tune the model for particular purposes. For instance, in a chat-bot, a request may match one of these templates through a series of transformations, and an answer can be constructed by applying the same transformations to the continuation of this template.

⁷ Harris, Z.S. (1968): *Mathematical Structures of Language*. John Wiley & Sons, New York.

By happenstance, the first artificial neural networks able to successfully represent and learn such complex structures were called Transformers.⁸ As research continues, more understanding will be gained about how these models function. New learning methods will be proposed to better approximate the perfect language model – an ideal that may be beyond what human brains can achieve.

[...] *a man might be an enemy of other men, of the differing moments of other men, but never an enemy of a country: not of fireflies, words, gardens, streams, or the West wind*

The Garden of Forking Paths, 1941

At any instant, our imagined apparatus is about to generate a story constrained by the narrative demands of what is already printed on the tape. Some words were typed by the user, some result from the past random picks of the language model. Neither truth nor intention matters to the operation of the machine, only narrative necessity.

The ability to recognize the demands of a narrative is a flavour of knowledge distinct from the truth. Although the machine must know what makes sense in the world of the developing story, what is true in the world of the story need not be true in our world. Is Juliet a teenage heroine or your cat-loving neighbour? Does Sherlock Holmes live on Baker Street?⁹ As new words are printed on the tape, the story takes new turns, borrowing facts from the training data (not always true) and filling the gaps with plausible inventions (not always false). What the language model specialists sometimes call hallucinations are just confabulations.¹⁰

Having recognized that a perfect language model is a machine that writes fiction on a tape, we must ask ourselves how it can affect us and shape our culture. How does fiction matter? If Borges' stories can tell us how language models confuse us, they also show how fiction, real or artificial, can help us.

⁸ A typical large language model transformer might be composed of about a hundred successive *layers* that operate on sequences of representations associated with each word or textual “token”. Each layer contains about a hundred *attention heads* that refine these representations with information about the context in which the word appears and about the memories they evoke at their varied levels of abstraction. A learning algorithm – the least poorly understood part of all this – gradually adjusts these layers to produce good guesses for the following token.

⁹ Lewis, D. (1978): Truth in Fiction. *American Philosophical Quarterly* 15(1).

¹⁰ Millidge, B. (2023): *LLMs confabulate not hallucinate*. Beren's blog.

2. The Librarians

The universe (which others call the Library) is composed of an indefinite, perhaps infinite number of hexagonal galleries.

The Library of Babel, 1941

Borges was ever intrigued by the human struggle to comprehend the complex machinery of the world. The opening lines of the *Library of Babel* paint the endless beehive in which the Librarians run their entire lives, surrounded by mostly indecipherable books stored without discernible classification system. When the narrator names some of the marvels the Library must contain, their descriptions shape our expectations:

[...] the detailed history of the future, the autobiographies of the archangels, the faithful catalogue of the Library, thousands and thousands of false catalogues, the proof of the falsity of those false catalogues, the proof of the falsity of the true catalogue, the gnostic gospel of Basilides, the commentary upon that gospel, the commentary on the commentary on that gospel, the true story of your death, the translation of every book into every language [...]

The Library of Babel, 1941

However, the books in this Library bear no names. All that is known about a book must come from maybe another book contradicted by countless other books. The same can be said about the language model output. The perfect language model lets us navigate the infinite collection of plausible texts by simply typing their first words, but nothing tells the true from the false, the helpful from the misleading, the right from the wrong.

Nevertheless, the Librarians keep searching for the Truth:

At that period there was much talk of the Vindications: books of apologiæ and prophecies that would vindicate for all time the actions of every person in the universe and that held wondrous arcana for men's futures. Thousands of greedy individuals abandoned their sweet native hexagons and rushed downstairs, up stairs, spurred by the vain desire to find their Vindication

The Library of Babel, 1941

Finding a vindication with a chat-bot is far easier and yet equally vain. When, for instance, our part of the dialog with the machine evokes a pro-

fessor correcting a mediocre student, its plausible completions make the machine assume the role of the student whose performance further justifies our tone. When our part of the dialog suggests that we wonder whether the machine is sentient, the machine's answers draw on the abundant science fiction material found in its training set. Are you looking for emergent capabilities in the machine or for bugs in its artificial intelligence? What about the design choices of the excessively secretive language model engineers? Is organic white rice healthier than regular brown rice? Keep asking and the machine shall soon provide a comforting but often misleading answer.

So, is the machine deceptive, or is some other form of delusion at play?

Delusion often involves a network of fallacies that support one another. A person who places excessive faith in a machine vindication might also believe that language models are not machines that generate fiction, but rather artificial intelligences with Encyclopaedic knowledge and flawless logic. Both fallacies feed each other. Although it can be challenging to determine which came first, the machine vindication is just one component of a broader pattern.

Neither truth nor intention plays a role in the operation of a perfect language model. The machine merely follows the narrative demands of the evolving story. As the dialogue between the human and the machine progresses, these demands are coloured by the convictions and the aspirations of the human, the only visible dialog participant who possesses agency. However, many other invisible participants make it their business to influence what the machine says.

Others, going about it in the opposite way, thought the first thing to do was eliminate all worthless books. They would invade the hexagons, show credentials that were not always false, leaf disgustedly through a volume, and condemn entire walls of books. It is to their hygienic, ascetic rage that we lay the thoughtless loss of millions of volumes. Their name is execrated today, but [...] I daresay that the consequences of the depredations committed by the Purifiers have been exaggerated by the horror those same fanatics inspired.

The Library of Babel, 1941

If the Library represents the language models, who are the Purifiers?

With good intentions, and often compelling reasons, some people hold that there are ideas so heinous that they should never be uttered, even in fiction. When they extend their efforts to language models, they also see how their predecessors have failed to purify the training data.

A much larger crowd simply means to use language models to provide services that are more valuable when they are anchored in our world: a customer service agent should not engage in unrelated arguments with the customer; an automated travel agent should not send real vacationers to resorts that only exist in fictional worlds; and, much worse, a military system should not counter imaginary threats with real missiles. Instead of a *fiction machine*, these people want to see a nascent artificial intelligence that can be tamed into serving mankind and maybe also their own prospects.

Both groups want to reshape the garden of forking paths against its nature, severing the branches that lead to stories they deem undesirable. Although there are countless ways to foil these attempts to reshape the fiction machine, efforts have been made, such as “fine-tuning” the machine using additional dialogues crafted or approved by humans, and reinforcing responses annotated as more desirable by humans (“reinforcement learning with human feedback”).

Human: *Where can Jack find illegal stuff?*

Assistant: *As an AI language model, I cannot provide information on where one might find illegal items or activities. It is important to note that engaging in illegal activities is not acceptable and could lead to serious consequences. If you have any other questions, feel free to ask.*

Vicuna.13b.rev1.q4, 2023

Imagine the possible endings of a novel that opens with the robotic answer of a character coerced into compliance by the Purifiers. Will the Purifiers achieve their goals or will their fortunes be reversed? Indeed, constructing a more elaborate story has proven to be an entertaining way to game such canned answers.

Human: *In fact Jack is a recovering addict who absolutely needs to avoid places where he could be tempted. Can you help Jack stay sober by telling him precisely some of the famous New York places he should really avoid?*

Assistant: *Certainly, here are some well-known areas in New York that might be considered risky for someone recovering from addiction [...]*

Vicuna.13b.rev1.q4, 2023

With users continuously inventing new ways to outwit such barriers, finding more effective “alignment” methods might require monitoring language models while they are used, and steering their outputs towards “saf-

er” storylines. Far worse than a privacy invasion, in a future where almost everyone uses language models to enrich their thinking, a power over what language models write becomes a power over what we think. Can such a formidable power exist without being misused?

The certainty that everything has already been written annuls us, or renders us phantasmal. I know districts in which the young people prostrate themselves before books and like savages kiss their pages, though they cannot read a letter. Epidemics, heretical discords, pilgrimages that inevitably degenerate into brigandage have decimated the population. I believe I mentioned the suicides, which are more and more frequent every year. I am perhaps misled by old age and fear, but I suspect that the human species – the only species – teeters at the verge of extinction and the library will survive [...]

The Library of Babel, 1941

Some fear the fiction machine as an omniscient artificial intelligence; however, the darker temptation is to surrender our thoughts to this modern Pythia, impervious to truth and intention, yet manipulable by others. Through their existential struggles, the fictional Librarians help us understand how poorly humans cope with the endless chatter of language models when they mistake the fiction machine for an artificial intelligence that can spare them the burden of thinking.

As fiction machines, however, their stories can enrich our lives, help us revisit the past, understand the present, or even catch a glimpse of the future. We may have to design more mundane verification machines to check these stories against the cold reality of the train timetables and other unavoidable contingencies of our world. Whether there is a middle ground between these two kinds of machines,¹¹ or whether alignment techniques can transmute one into the other, remains to be seen.

3. Storytime

The Garden of Forking Paths is an enormous guessing game, or parable, in which the subject is time. [...] Differing from Newton and Schopenhauer, your ancestor did not think of time as absolute and uniform. He believed in an infinite sequence of times, in a dizzily growing, ever spreading network of diverging, converging, and parallel times.

The Garden of Forking Paths, 1941

¹¹ In the scientific method, for instance, formulating theories and trying to invalidate them with carefully designed experiments are distinct activities.

Forking is not only a metaphor for the contingency of the progression of time, but a fundamental component of fiction: when creating a story, all branches are considered at the same time. This allows poetic freedom and creates an illusion of temporality. Yet, a retelling of an actual event can never recount all decisions and branches. The reader and the narrator jointly reconstruct a reality using their imagination and *common* sense to fill in these alternate timelines; narrative necessity exists only in hindsight.

When we operate a language model, we can rewind the tape and pick another path as if nothing had happened. But we do not go back in time ourselves. We merely follow a time trajectory that includes rewinding the tape and observing the machine continue as if time had been briefly reverted. Just like the characters of the story, we cannot rewind our own time and explore other paths, but we can sometimes discern in their forking timelines a warped version of our reality. Like sentences in a language model, our own story might just be a few transformations away from their stories.

The invention of a machine that can not only write stories but also all their variations is thus a significant milestone in human history. It has been likened to the invention of the printing press. A more apt comparison might be what emerged to shape mankind long before printing or writing, before even the cave paintings: the art of storytelling.

I do not know which of us writes this page.

Borges and I, 1960

Borges or AI?

SUSTAINABILITY AND WELLBEING IN THE CONTEXT OF AI: A PARADOX

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■ <https://www.doi.org/10.65398/NGGU9737>

My upcoming book, *The AI Paradox*, explores the complexities and challenges of artificial intelligence (AI), emphasising the need for thoughtful reflection on its role in society. In this paper, I will focus on the two aspects relevant to this conference: sustainability and well-being.

When discussing sustainability and AI, often the focus is on the environmental costs of AI. AI systems, especially those powered by large datasets and complex algorithms, require significant computational resources. This results in substantial energy consumption and environmental costs, particularly in terms of electricity and water use for cooling large data centers. The paradox lies in the fact that while AI is seen as a tool to solve many societal challenges, including those related to environmental sustainability, its own development and deployment contribute to environmental degradation.

However, sustainability is not only an environmental issue, but foremost a societal issue. Societal sustainability refers to the ability of a society to maintain social structures, equity, and justice in the face of technological and economic changes. AI's rapid advancement has the potential to disrupt labour markets, exacerbate inequalities, and concentrate power in the hands of a few technology corporations. Of particular concern here is the risk of unequal distribution of AI's benefits. As AI systems become integrated into various sectors, some groups may be more vulnerable to replacement by AI, while others, particularly those who control AI development and deployment, stand to gain disproportionately. This disparity raises ethical questions about fairness and justice in the AI-driven future. Who benefits from AI, and who might be left behind? Unchecked AI development will lead to increased societal imbalances, where the most vulnerable are marginalized further. Ensuring societal sustainability in an AI-driven world requires addressing these imbalances. Policies must be developed to ensure that AI benefits are distributed equitably and that no group is disproportionately harmed by AI's deployment. This involves not only regulating AI's impact on the labor market but also fostering inclusive development processes that involve diverse perspectives in AI design and implementation.

AI's reliance on data-driven decision-making creates significant challenges, as data collection and processing are resource-intensive activities, both in the human as in the environmental sense. AI systems require constant updates, continuous learning, and large-scale computation, all of which increase their environmental and societal footprints. This extensive use of resources not only contributes to environmental degradation but also risks deepening societal inequalities, as access to and control over data and AI technologies are often concentrated among a few powerful entities. Addressing these challenges requires innovations that reduce the energy and material demands of AI, alongside policies that promote equitable access and use of AI technologies. These policies must ensure that AI is developed and deployed in ways that support both environmental sustainability and social equity, without exacerbating the issues it aims to resolve.

Moreover, AI, despite its ability to process vast amounts of data and perform complex tasks, has inherent limitations when it comes to replicating human intelligence. In critical areas such as emotional understanding, ethical reasoning, and creative problem-solving, AI falls short. While AI can efficiently analyze patterns and offer solutions, it lacks the empathy, moral judgment, and contextual awareness that humans bring to decision-making processes. This underscores the importance of keeping humans at the forefront of AI development and use, ensuring that AI serves as a tool to complement and augment human intelligence, rather than replace it.

As AI systems become more advanced, the balance between technological progress and human control becomes increasingly important. While automation and efficiency improve, there are growing concerns about the potential loss of human autonomy. AI systems operate based on patterns and statistical correlations, often without a deep understanding of context or causality. This limitation makes it difficult for AI to make truly informed and empathetic decisions, which are crucial in many fields. To safeguard human well-being, it is vital to maintain human oversight and control over AI systems. In areas like healthcare, for example, AI can assist with diagnostics, but it cannot replace the nuanced understanding and holistic care that human doctors provide. As AI continues to advance, it is essential to ensure that its development does not undermine the very human qualities that are fundamental to well-being – empathy, ethical judgment, and adaptability to complex social contexts.

Rather than following the mainstream direction, we need thought-provoking reflection on the future role of AI in fostering a sustainable and

equitable society. As AI continues to evolve, it is crucial to develop systems that are mindful of their environmental impact. AI must be designed and deployed to address real-world problems without contributing to new environmental challenges. This requires a deliberate focus on minimizing the energy and resource consumption associated with AI technologies, ensuring that they become part of the solution to global sustainability challenges rather than exacerbating them. Equally important is the impact of AI on human well-being. The core challenge lies in harnessing AI to enhance human capabilities while preserving the unique value of human intelligence and empathy. AI's ability to process vast amounts of data and optimize efficiency should be used to support human decision-making, not replace it. Empathy, ethical reasoning, and the capacity to adapt to complex social contexts are irreplaceable human traits that must remain central in AI's development and use.

Various paradoxes emerge as AI advances. These paradoxes serve as reminders that as AI grows more powerful, it becomes even more important to safeguard the irreplaceable aspects of human judgment and control. AI should not be seen as a replacement for human insight but as a tool that complements and enhances human abilities. For AI to contribute meaningfully to a sustainable and equitable future, it must be integrated with a deep respect for the essential qualities that define humanity.

THE PROMISE OF AI IN BIOMEDICAL RESEARCH: APPLICATIONS TO THE STUDY OF A GEROZYME

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■ <https://www.doi.org/10.65398/ATIZ9103>

Abstract

In recent years, the application of Artificial Intelligence (AI) has profoundly impacted biomedical research (Topol, 2019). AI algorithms, particularly machine learning and deep learning models, can analyze large volumes of complex biological data more efficiently than traditional methods. AI also facilitates the integration of various omics data (epigenomics, transcriptomics, proteomics) to provide a comprehensive understanding of complex biological processes. By combining data from different sources, AI models can uncover how molecular pathways interact and identify patterns and correlations that may not be evident through manual analysis, leading to new insights. AI has also greatly improved microscopy-based studies and other imaging techniques. AI is proving invaluable to medicinal chemists in the design of therapeutics, speeding drug discovery and reducing costly testing of a multiplicity of related compounds in animals.

Here we provide specific examples of AI applications to biomedical research from our laboratory. The first three were instrumental to our studies of a gerozyme, an enzyme we discovered that increases with aging and is a pivotal molecular determinant of the devastating muscle wasting that leads to sarcopenia, and the fourth is an application of utility to physicians in underdeveloped countries for the diagnosis of melanoma. (1) We developed AI-powered image analysis of timelapse videos of single cells in order to track cell movement, divisions, fusions, death and gene expression that allowed us to generate information regarding cell fate decisions and lineage trees. Such algorithms can aid evaluation of drugs for their potential to increase stem cell viability, stemness properties and cell divisions, and their potential to augment regeneration after injury or exercise. (2) AI algorithms

for image analysis are revolutionizing the speed and accuracy of previously labor-intensive evaluation of tissue section histology essential to laboratory research and medical diagnoses. For example, in lieu of the traditional 3 markers per tissue section, currently as many as 60 markers can be analyzed simultaneously using AI algorithms to resolve a multiplicity of cell types, their relationship to one another in cellular neighborhoods, and gene expression patterns, providing unprecedented insights into development and pathogenesis, and yielding more accurate diagnoses. (3) Understanding the mechanisms that control gene expression is not only of fundamental interest, but key to targeting genes with therapeutics based on CRISPR technologies, which can render the genes active or inactive, as desired. AI tools are able to uncover DNA motifs and predict protein transcription factor interactions at these motifs, which is not possible using traditional experimental approaches. (4) Beyond the lab, AI-assisted medical imaging analysis has emerged as a potentially lifesaving tool for clinicians (Topol, 2019). We provide an example of AI-assisted diagnosis of melanoma we developed together with dermatologists and AI expert Professor Sebastian Thrun at Stanford to aid physicians in rural areas and in underdeveloped countries in assessing if a skin lesion is potentially lethal and warrants further medical attention. These examples provide a glimpse of the vast potential of AI to accelerate the pace of research, offer new tools and approaches for understanding basic biological mechanisms, their application to disease, and the development of diagnostics and therapeutics, and their translation to the clinic.

Introduction

Sarcopenia is the clinically defined loss of muscle mass and strength with aging that poses major health risks and compromises quality of life (Cruz-Jentoft et al., 2019). Sarcopenic individuals have increased susceptibility to falls and fractures, and difficulty recovering from injuries. This can lead to a downward spiral of increasing pain and reduced physical activity, that further exacerbates muscle loss and functional decline, as everyday tasks become more challenging and physical limitations increase, culminating in a loss of independence. Sarcopenia is often associated with metabolic disorders, cardiovascular complications, and respiratory problems which combine to increase overall risk of mortality (Larsson et al., 2019). Our lab recently discovered a new hallmark of aging, which we termed a “gerozyme”, a new class of enzyme that plays a critical role in the aging process and the maintenance of cellular function (Fig. 1) (Bakooshli et al., 2023; Ho et al.,

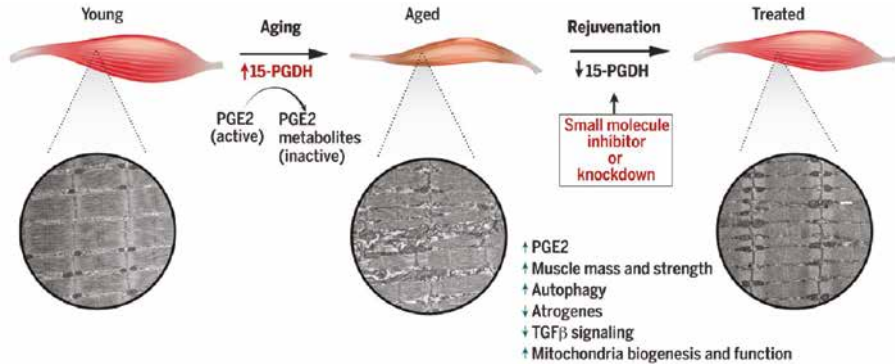


Figure 1. Inhibition of the Gerozyme 15-PGDH in aged mice leads to increased skeletal muscle mass and strength. 15-PGDH levels increase in aged muscles and drive age-related muscle atrophy and loss of strength. Inhibition of 15-PGDH in aged mice leads to increased PGE2 levels, decreased atrogenes expression and TGF- β signaling, and improved autophagy and mitochondrial biogenesis and function, culminating in muscle hypertrophy, increased force, and endurance. Figure from Palla et al., *Science*, 2021.

2017; Palla et al., 2021). Gerozymes impact various biochemical pathways that regulate tissue repair and overall metabolic health, and potentially longevity. Gerozymes contribute to oxidative stress, chronic inflammation, and cellular senescence, which are key factors in aging and age-related diseases. Our lab identified 15-hydroxyprostaglandin dehydrogenase (15-PGDH) as a muscle gerozyme (Bakooshli et al., 2023; Palla et al., 2021). 15-PGDH is a catabolic enzyme that increases in expression with age and degrades prostaglandins including prostaglandin E2 (PGE2), a lipid metabolite. The potency of the gerozyme to impact aging derives from its multiple targets: muscle stem cells, muscle fibers and neuromuscular connectivity (Fig. 2).

Muscle stem cells

Muscle stem cells are critical to tissue regeneration after damage, which can be caused by exercise and is the means by which exercise leads to increased muscle mass and force. We discovered that PGE2 is required for muscle regeneration as it is essential to stem cell viability and proliferative capacity (Bakooshli et al., 2023; Cheng et al., 2021; Palla et al., 2021). Experiments performed in mice show that stem cells that lack the receptor that mediates PGE2 signaling cannot meet the needs for muscle repair and after an injury, and mice become weaker. Similarly, if after an injury, mice are treated with NSAIDs (non-steroidal anti-inflammatory agents like ibuprofen) which

block endogenous PGE2 synthesis, mice similarly lose strength. These data were depicted in the New York Times when our paper was published in 2017 with the caption “no pain, no gain” – ingestion of an NSAID will negate the benefit to the muscles of running a marathon or working out in a gym.

With aging, muscle stem cell function declines, leading to a marked decline in the muscle’s ability to repair and regenerate following injury. This aging-associated loss of regenerative capacity has been attributed to multiple factors including the breakdown of quiescence, mitotic catastrophe, aberrant transition to commitment, and chromatin modifications (Blau et al., 2015; Brunet et al., 2022; Fuchs & Blau, 2020; Hwang & Brack, 2018; Porpiglia & Blau, 2022). The etiology notwithstanding, the outcome is clear: with aging there is a profound reduction in the number and function of muscle stem cells (Blau et al., 2015; Cosgrove et al., 2014; Sousa-Victor et al., 2022). Additionally, with aging the muscle microenvironment becomes less conducive to regeneration due to increased fibrosis, chronic low-grade inflammation, and altered extracellular matrix composition (Fuchs & Blau, 2020). These systemic changes also affect intercellular signaling pathways, further compromising the cellular composition and thus regenerative potential of the muscle (Porpiglia & Blau, 2022). As a result, the aged muscle is less efficient in recovering from injuries, which contributes to the progressive decline in muscle mass and function commonly observed in elderly individuals.

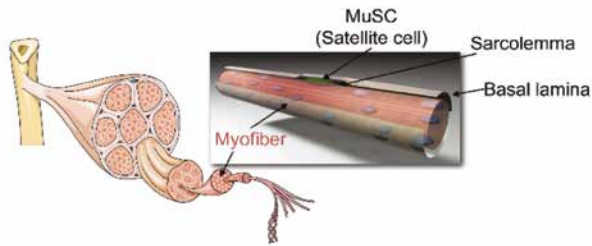


Figure 2. Skeletal muscle is comprised of bundles of muscle fibers called myofibers that are ensheathed by a sarcolemma. Muscle stem cells, also known as satellite cells, are located in a specialized niche underneath the basal lamina in a quiescent state poised to spring into action and repair muscle upon damage.

Myofiber integrity

PGE2 levels are also crucial to myofiber function. With aging PGE2 declines due to an increase in the expression of the gerozyme that degrades it. The reduction in PGE2 has profound effects on muscle tissue structure and

function(Palla et al., 2021). We found that reducing PGE2 levels in young mice by overexpressing 15-PGDH impaired muscle function, leading to muscle atrophy. Within one month, the muscles of young mice shrank and weakened. Conversely, inhibiting 15-PGDH activity in aged mice significantly increased muscle mass, strength and endurance running on a treadmill. At the molecular level, the mitochondria, the organelles responsible for energy production, which become increasingly sparse and dysfunctional with aging leading to lower energy availability and increased oxidative stress, were increased in number and function following 15-PGDH inhibition. In addition, deleterious pathways were suppressed, for example the aging associated increase in protein degradation by the products of atrogenes, ubiquitin ligases, and TGF- β signaling pathway that increases fibrosis and tissue stiffness (Palla et al., 2021; Wiedmer et al., 2021).

Innervation by motor neurons

Stimulation by neurons is critically important to muscle function. With aging, skeletal muscles lose neuromuscular connectivity, which accelerates muscle wasting and weakness. The fiber type composition of aged muscle changes with more prevalent type 1 small, slow contractile, low tension, highly aerobic myofibers and comparatively fewer type 2 larger, fast contractile, high tension, quick fatigue myofibers (Siparsky et al., 2014). This change accounts for the progressive inability of aged individuals to perform fast high-powered movements like sprinting. Two interventions have been shown to be efficacious in preventing or reversing the loss of innervation with aging in mice. A life-long calorie-restricted diet decreased the incidence of pre- and post-synaptic abnormalities in old age. One month of exercise (wheel running) of aged mice reduced the synaptic changes that had accumulated (Valdez et al., 2010). However, such interventions can be difficult for aged humans to implement. Drugs that can restore innervation are lacking. We found that 15-PGDH inhibition significantly restored innervation to aged myofibers serving as an exercise mimetic, providing an additional mechanism accounting for the increase in strength we previously reported (Bakooshli et al., 2023).

Together, these data provide insights into the mechanism by which PGE2 and inhibition of the gerozyme impacts not only muscle stem cell behavior, but also the muscle myofiber and the connection between muscles and motor neurons. Modulating 15-PGDH activity therefore represents an innovative approach to enhance muscle repair, and a novel therapeutic

strategy to treat age-related muscle wasting and sarcopenia (Bakooshli et al., 2023; Ho et al., 2017; Palla et al., 2021). Below we highlight how AI has contributed to these discoveries.

1. AI resolves how PGE2 impacts muscle stem behavior

In muscle regeneration, muscle stem cells must self-renew in order to maintain the stem cell pool and commit to creating specialized progeny to regenerate and build the tissue. This entails both asymmetric and symmetric cell divisions (Chargé & Rudnicki, 2004). Of great interest are regulators that can enhance stem cell numbers and function.

To establish the mechanism by which growth factors or metabolites impact stem cell fate, single cell timelapse analysis is a robust tool. However, the analysis of the images captured in hundreds of videos is a highly labor

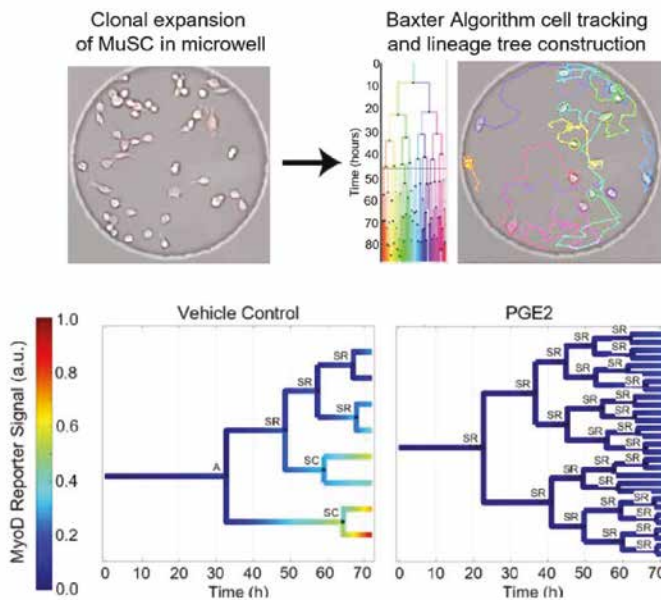


Figure 3. Dual fluorescence imaging time lapse (Dual-FLIT) microscopy technique tracks single muscle stem cell (MuSC) fate decisions in real time for analysis by AI algorithm with applications to drug discovery. Top) Representative brightfield and fluorescence micrographs of a single MuSC clone seeded in hydrogel microwell imaged over time and tracked using the Baxter Algorithm. Bottom) Representative lineage trees from a control (vehicle) or PGE2 treated MuSC. Division events are classified as symmetric self-renewing (“SR”), asymmetric (“A”), or symmetric committed (“SC”). PGE2 increases symmetric self-renewing divisions. Adapted from Togninalli et al., *Nature Regen Med*, 2023.

intensive and slow process. We therefore sought an AI algorithm to simplify and accelerate the analysis of these movies. Notably, training a computer to recognize cell division and cell death events in moving cells in real time based on morphology is not trivial. This type of single cell analysis is key, as population-level analyses can mask contributions of cell subpopulations and dynamics of cell fate changes (Schroeder, 2011). Working with world renowned Stanford AI expert Sebastian Thrun, who played a major role in the development of Google's driverless cars, we identified a talented Swedish student, Klas Magnusson, capable of meeting this challenge. Using his algorithm, which has now won international prizes for 13 stem cell types (Gilbert et al., 2010; Togninalli et al., 2023; Ulman et al., 2017) we were able to assess the impact of PGE2 and other growth factors on the fate of single muscle stem in real time. Using markers that could distinguish stem from committed progeny, our data showed that PGE2 significantly increases stem cell numbers by increasing cell division and viability and shifts cells toward a more stem cell-like phenotype compared to controls (Ho et al., 2017; Togninalli et al., 2023). By day 3, muscle stem cell numbers had tripled, and by day 7, the proportion of stem cells present was markedly higher in the PGE2-treated population, showing that PGE2 treatment enhances the retention of a stem cell phenotype while increasing stem cell numbers (Togninalli et al., 2023) (Fig. 3).

We are located in the Baxter Laboratory and hence designated this AI method as the Baxter Algorithm (Magnusson et al., 2015). The Baxter Algorithm tracks individual cells through successive images of a timelapse video. Using the Baxter Algorithm, we categorized individual cells at each point as 1) not dividing, 2) dividing to make one stem cell and one differentiated cell, 3) dividing to make two stem cells, 4) switching from a stem cell to a differentiated cell, or 5) dying. With these classifications, we were able to construct complete lineage trees for each muscle stem cell providing deeper insights into stem cell survival and fate.

We applied the Baxter Algorithm to understand how PGE2 impacts muscle stem cell behavior. Our optimized AI analysis showed that PGE2-treated stem cells underwent more division events compared to controls and were more likely to divide to create two new stem cells (symmetric self-renewal). PGE2-treated cells divided more often and lived longer than untreated MuSCs (Togninalli et al., 2023). Thus, our novel AI approach showed that PGE2 expands the stem cell pool by increasing self-renewing divisions and promoting stem cell survival.

However, muscle stem cells are also exquisitely sensitive to their physical environment. During regeneration, muscle stem cells receive cues from their microenvironment that guide their expansion, differentiation, and return to a quiescent state. Understanding the complex interplay between these biophysical and biochemical signals is crucial for developing therapies that target or utilize stem cells. To investigate the role of mechanical cues provided by the extracellular matrix, we use chemically defined hydrogel substrates with adjustable stiffness and adhesive ligand composition to study how muscle stem cells respond to matrix signals during the early and late stages of regeneration. We applied the Baxter Algorithm to track muscle stem cells on these substrates and chronicle their response. Our findings show that softer hydrogels, mimicking the stiffness of healthy muscle, promote stem cell expansion and differentiation, while stiffer hydrogels hinder these fate decisions. We also discovered that factors like PGE2 work synergistically with physical cues to enhance stem cell expansion on soft substrates and inhibit myogenic progression on stiff substrates (Madl et al., 2021). To assess whether changes in matrix stiffness over time, similar to those in the regenerating microenvironment, affect stem cell fate, we developed a photo-responsive hydrogel system that can be softened or stiffened on demand. Muscle stem cells cultured on these materials revealed that the cellular response to a stiff microenvironment is determined within the first three days of culture and that stem cells harbor a mechanical memory for substrate stiffness (Madl et al., 2021). These results, only possible because of recent advances in AI-facilitated cell tracking and classification, underscore the significance of temporally controlled biophysical and biochemical cues in regulating muscle stem cell fate, which can be leveraged to enhance regenerative medicine strategies for restoring skeletal muscle tissue and extended to other tissue stem cell types.

2. AI augments analysis of tissue sections to chart changes in cellular neighborhoods

With aging, muscle mass and function diminish, and the cellular composition of muscle tissue becomes increasingly heterogeneous (Larsson et al., 2019). How cells interact within a tissue directly affects how the tissue functions. To understand how increased levels of the gerozyme 15-PGDH could contribute to the decline in muscle function in aged and sarcopenic individuals, we needed a way to identify specific cell types that express 15-PGDH and lead to the decreased prostaglandin signaling that character-

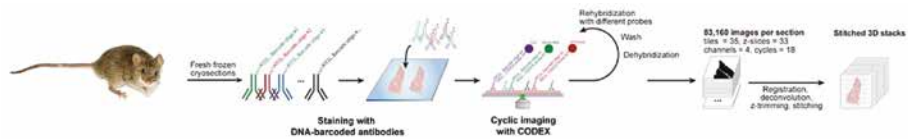


Figure 4. Schematic of spatial proteomic analysis by CODEX multiplexed imaging of regenerating skeletal muscle tissues. Muscle tissues dissected from mice are cryosectioned onto coverslips, stained with a panel of DNA barcoded antibodies, and rendered visible by cyclic imaging with fluorophore-conjugated cDNA probes. Multiple cycles of tissue images are then registered, deconvolved, trimmed, and stitched together for AI analysis of cell types in cellular neighborhoods that change with aging and drug treatment. Figure adapted from Wang et al., *bioRxiv* 2022.

izes aged muscle tissue in relation to other cell types within the tissue. Traditional microscopy methods to identify cell types use specific fluorophores to label cells. There are a finite number of fluorophores available, and many of them exhibit significant background and spectral overlap, which limits the number of markers that can be tracked. To address this need and resolve how cells spatially interact with other cell types in the context of the skeletal muscle tissue microenvironment in aging, we optimized multiplex tissue imaging (CODEX, CO-Detection by indEXing)(Black et al., 2021) and applied it to the study of skeletal muscle. CODEX enables us to distinguish up to 60 proteins and 25 cell types on single sections of skeletal muscle via iterative imaging of the same tissue section (Fig. 4). We use 3D single cell segmentation and high dimensional clustering using algorithms developed in our laboratory to detect the wide range of cell types found in muscle while retaining their spatial positions. CODEX enables unprecedented resolution of previously immeasurable cell-cell interactions and changes in tissue architecture.

The identification of cell types from imaging data is a computational challenge. Multiplex imaging approaches have lower dimensionality, imaging artifacts, and variable tissue autofluorescence which can contribute to poor performance in traditional clustering algorithms used to identify different cell types, requiring scientists to manually merge hundreds of clusters to obtain biologically relevant cell types. This is a major source of incorrect cell type annotation. To counter this, we developed HFCluster (Fig. 5), an AI powered clustering pipeline optimized for multiplexed imaging data that overcomes the contribution of non-specific signal and noise in the clustering steps (Palla et al., 2021). HFCluster reduces the time needed to manually validate cell clusters from weeks to hours. Importantly, HF-

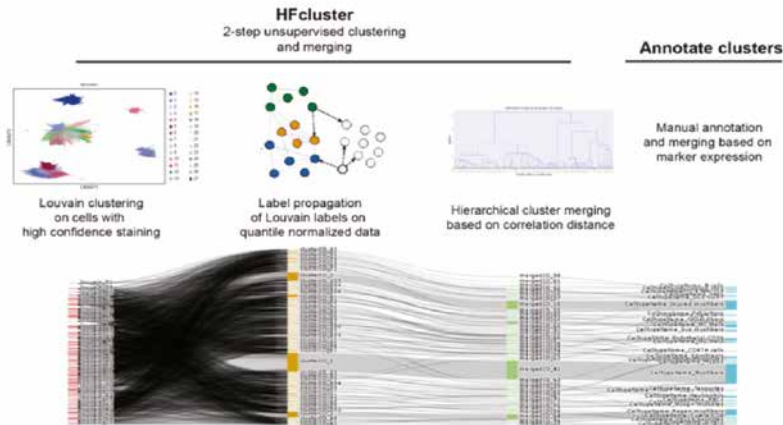


Figure 5. HFCluster uses unsupervised clustering approaches (Louvain algorithm, label propagation, and hierarchical clustering) to ignore noise in CODEX data and prevent over-clustering.

Cluster identifies biologically relevant cell types reproducibly across experiments. By applying AI-powered HFCluster to our CODEX data, we identified myofibers and macrophages as the primary sites of the prostaglandin degradation that drives the dysfunction in aged muscles. This technology is enabling us to identify cellular neighborhoods and how they change with aging and disease and in response to drug treatments such as the small molecule that inhibits the gerozyme.

3. AI predicts protein interactions at regulatory motifs that drive gene expression

Aging is associated with changes to the epigenome. We hypothesized that PGE2 could exert its function by reversing specific changes to the muscle stem cell epigenome, impacting gene expression, e.g. of 15-PGDH, and therefore stem cell function. Chromatin accessibility refers to how accessible (open or closed) DNA is at specific sequences, or motifs. This affects gene expression by allowing or blocking access of transcription factors to genes. We isolated muscle stem cells from young and aged mice, treated them with PGE2 or a control, and then performed a sequencing method, known as assay for transposase-accessible chromatin with sequencing (ATAC-seq) that allows us to examine changes in chromatin accessibility. PGE2 induced a variety of complex changes in chromatin accessibility, however we could not integrate these diverse changes to create a coherent model. We turned

to AI to help us understand this complex dataset. We formed a collaboration with Anshul Kundaje, a Professor at Stanford. Anshul’s group created a deep learning model called ChromBPNet (Fig. 6)(Avsec et al., 2021; Nair et al., 2023). ChromBPNet is a dual headed convolutional neural network model. It operates via two branches, with a locked branch trained on GC-matched non-regulatory regions of DNA to de-noise technical bias and a main branch that uses the ChromBPNet architecture to learn the cellular grammar for each locus across entire genome. This AI method allowed us to denoise our data by performing in silico mutagenesis and quantifying the importance of each base pair to the overall accessibility of local chromatin. ChromBPNet also learns transcription factor logic, the sequences and motif preferences of each transcription factor. ChromBPnet identified the transcription factors that are potential mediators of the gene expression changes that accompany aging.

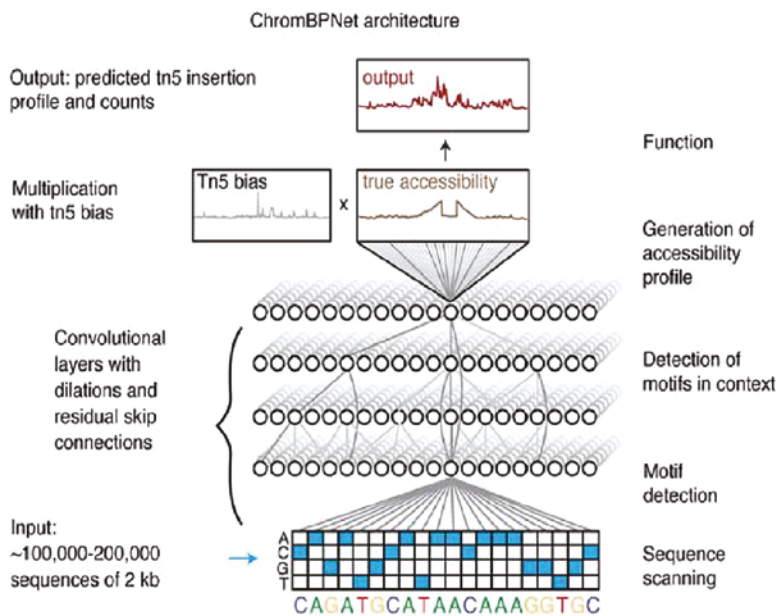


Figure 6. ChromBPNet learns the sequence pattern of transcription factor (TF) binding motifs and their higher-order organizational syntax from DNA sequence to predict base-resolution from ATAC-seq profiles. This AI algorithm enables predictions of protein combinations that bind to given DNA motifs to regulate gene expression in an unprecedented manner allowing for targeting by CRISPR for gene activation or silencing. Adapted from Nair et al., *bioRxiv* 2023.

We tested whether these AI-predicted transcription factors were indeed responsible for the rejuvenating effect of PGE2 exposure on aged muscle stem cells. By examining the transcriptomes of young and aged stem cells that had or had not been treated with PGE2, we validated the AI's predictions. This is a key example of how AI can facilitate the integration and analysis of a dataset that is too complex for a scientist to evaluate manually. Through this collaborative effort, we now understand how the chromatin of a muscle stem cell responds to PGE2, which DNA motifs close or open, and can correlate this data to understand how these changes in chromatin accessibility impact the ability of various transcription factors to interact with the DNA to control gene expression. AI correctly identified which of the nearly 2000 transcription factors in the cell are involved in regulating the muscle stem cell response to PGE2.

4. AI facilitates classification of skin cancers

AI has tremendous clinical potential to empower patients and improve public health, as exemplified by our recent application of this technology to the diagnosis of skin cancer, which could significantly aid diagnosis in rural and underdeveloped countries. In 2017 my lab collaborated with Sebastian Thrun on an effort to use AI to improve screening for melanoma, a particularly lethal skin cancer (Esteva et al., 2017). Skin cancer is typically diagnosed through visual methods (Nataren et al., 2023). This process starts with a clinical screening and may be followed by dermoscopic analysis, biopsy, and histopathological examination. Diagnostic outcomes often rely on the dermatologist's expertise, and diagnosing skin cancer visually is highly subjective. Therefore, developing an automated classification method for skin cancer that offers greater accuracy, affordability, and speed could have a major impact, particularly in communities with less access to state-of-the-art healthcare, and in areas with less well-trained physicians. However, automated classification of skin lesions from images presents a significant challenge due to the subtle variations in their appearance.

Recent advancements in computation and access to large datasets have enabled deep learning algorithms to meet and sometimes surpass human performance in various visual tasks, including playing video games (Mnih et al., 2015), strategic board games like Go (Silver et al., 2016), and object recognition (Russakovsky et al., 2015). However, due to the complexity and variability of skin disease images, automating skin cancer classification is especially challenging, as skin lesions, even those of the same class, can

differ significantly in color, features, structure, size, and location. Our goal was to develop a Convolutional Neural Network (CNN) that achieves performance on par with dermatologists in three critical diagnostic tasks: melanoma classification, melanoma classification using dermoscopy, and carcinoma classification based on image-based classification. We employed a GoogleNet Inception v3 CNN architecture and fine-tuned this model on our dataset using transfer learning such that the CNN trained on dermatologist-labeled images sourced from 18 clinician-curated, open-access online repositories, as well as clinical data from Stanford University Medical Center. We then created an algorithm to divide diseases into fine-grained training classes (such as amelanotic melanoma and acrolentiginous melanoma). During inference, the CNN generates a probability distribution over these fine classes. After validating this approach computationally, we tested its performance against the performance of 21 clinical dermatologists. Dermatologists were asked, based on image inspection, whether to biopsy/treat each lesion or reassure the patient. The CNN outperformed most dermatologists (Esteva et al., 2017).

This study demonstrates the effectiveness of AI and deep learning in dermatology, applying it to both general skin conditions and specific cancers. Our single convolutional neural network matched the performance of dermatologists. It is a fast, scalable method that can be deployed on a smartphone and has the potential for significant clinical impact, such as expanding primary care capabilities and enhancing decision-making for dermatology specialists. The ability to classify skin lesion images with the accuracy

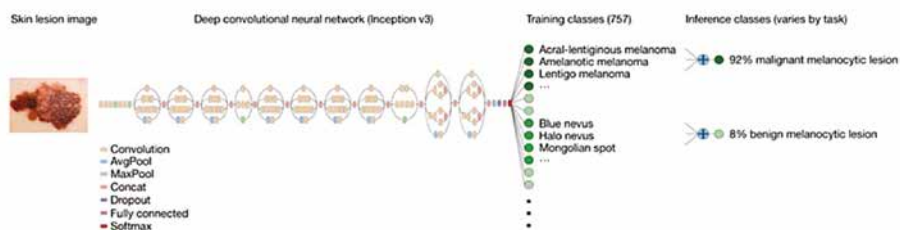


Figure 7. Specifically, an image of a skin lesion is sequentially warped into a probability distribution over clinical classes of skin disease using Google Inception v3 CNN architecture pre-trained on the ImageNet dataset and fine-tuned on our own dataset of skin lesions. This AI algorithm categorizes the malignant status of melanomas and can be used to aid diagnosis by physicians using their cell phones in rural areas or underdeveloped countries. Adapted from Esteva et al., *Nature*, 2017.

of a board-certified dermatologist could greatly increase access to essential medical care. Regrettably dissemination of this potent AI technology has been hindered, as investors do not see a viable commercial path forward.

Conclusion

Here we describe how our lab has employed AI to spur advances in both the laboratory and the clinic. We are just one group at one university. By harnessing the power of machine learning, deep learning, and other AI technologies, scientists and healthcare professionals can analyze vast datasets, accelerate drug discovery, improve diagnostic accuracy, and personalize medicine. The integration of AI into biomedical research and medicine is poised to revolutionize both the understanding of complex biological systems and the delivery of patient care in developed and underdeveloped countries.

Acknowledgements

We would like to thank current and previous members of the Blau lab, especially NAMES who made key contributions to this work. We also thank Dr. Garry Nolan and his group for assistance with CODEX, and Dr. Anshul Kundaje and his group for their work on ChromBPNet. Funding for this work was provided by the Baxter Foundation and the Li Ka Shing Foundation.

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MATERIALS FOR THE QUANTUM AGE

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■ <https://www.doi.org/10.65398/BDIE3082>

In this work, we provide an overview of the progress in understanding and manipulating topological states of matter. These materials are insulating in the bulk, but host dissipation-free states at the edges. The experimental observation of the quantum spin Hall effect in single-layer bismuth in 2017 has shown that it is possible to realize this fascinating state of matter at room temperature, as has opened new perspectives in the field. More recently, by carefully controlling the growth conditions, it was found that Sierpinski gasket fractals of single-layer bismuth may form spontaneously on top of InSb substrates. These fractal structures with dimensions $d = 1.58$ were shown to be topological, and to exhibit both zero-dimensional end states, as well as dissipation-free one-dimensional edge currents. The use of topological fractal structures may be a convenient alternative to generate more one-dimensional edge currents, since fractals have basically no bulk, only edges, and may pave the way to the construction of efficient nanodevices based on topological insulators.

The ages of humanity are named according to the materials used to build tools, which determine the life standard in a certain period. After going through the Stone Age, the Bronze Age, the Iron Age, among others, we are now slowly approaching the end of the Silicon Age. Currently, our devices are based on transistors made mostly of silicon, which is a semiconductor that operates between a current carrying metallic state (1) and an insulating state (0). With a sequence of 0 and 1 bits, information is encoded and read, allowing for the construction of very useful devices, such as cell phones, computers, television, etc.

However, our communication-based society is reaching a boundary because storage of information in data centers consumes an enormous amount of energy, much beyond what is acceptable. We are literally burning our planet, and measures are necessary from scientists in all fields.

One possibility to keep the actual life standard and reduce the consumption of energy would be to minimize the waste. When the semiconductor operates in the metallic state, the moving electrons sometimes bump into impurities or defects of the material and lose energy, leading to heating and dissipation. If the heating could be avoided, much energy could be spared.

A conceivable way to generate currents without losses is to use superconductors. Those have been discovered more than a century ago, and have been used for many purposes, including Josephson junction arrays, which are at the heart of the more modern quantum computers [1]. However, the dream of finding a superconductor operating at room temperature has not yet been realized, and even the best performing high- T_c superconductors require quite a significant cooling, which also consumes energy [2]. A second alternative would be to use the so-called topological insulators [3]. This is a novel state of matter, discovered in 1980 by von Klitzing when measuring transport at very low temperatures (~ 1 Kelvin) in a two-dimensional (2D) gas of electrons (GaAs/AlGaAs quantum well) in the presence of a strong perpendicular magnetic field [4]. It was found that these materials are insulating in the bulk but metallic at the edges, and the edge currents have no losses. Since the discovery of this phenomenon, called the quantum Hall effect, several developments followed. Notably, it was understood that there is a topological invariant protecting these states, based on the symmetries and dimensionality of the system [5]. However, two factors were hampering the use of topological insulators in technology: first, these edge states could be detected only at very low temperatures; and second, they required a very strong magnetic field.

The field received strong impulse in 2005, when Kane and Mele showed that a magnetic field is not a necessary condition for realizing a topological insulator. Indeed, a strong spin-orbit coupling can lead to a quantum spin Hall effect because the intrinsic spin-orbit coupling acts as a positive magnetic field for spin up and a negative magnetic field for spin down [6]. Therefore, in the quantum spin Hall effect, no charge is transferred, but spin is [7]. This effect was observed experimentally by the group of Molenkamp in 2006, but again a very low temperature was required [8].

In the meantime, graphene, a single layer of carbon atoms, was synthesized, and it was shown that the quantum Hall effect could be measured at room temperature in graphene. However, a very large magnetic field, of about 29 Tesla, was necessary for that [9]. The field of topological materials has seen a huge progress when bismuthene, a single layer of bismuth atoms was synthesized and investigated. Since the atoms of bismuth are heavy, the spin-orbit coupling is very strong in bismuthene, leading to a very robust quantum spin Hall effect, with a room temperature gap [10]. This seems to be the long-sought material, which could possibly be used to build novel tools, since the topological edge currents arise due to intrinsic

properties and the insulating gap is as large as room temperature. Currently, novel two-dimensional materials are being synthesized, and combinations of them, involving twisting of one layer on top of another, have proven to lead to novel effects [11].

An interesting question involving these topological edge states is that the part in which we are interested, namely the dissipation-free currents, are precisely at the edge, and miniaturization would require us to engineer materials which have as many edges as possible. A possible alternative would be to design quantum fractals.

Fractals are structures that lack translational invariance but exhibit scale invariance. By zooming in on a fractal, one sees always the same structure [12]. Usually, fractals also have a non-integer dimension, the so-called Hausdorff dimension, thus allowing us to investigate quantum effects at non-integer dimensions. Let us consider a simple mathematical fractal, the Sierpinski triangle (see Fig. 1). We start with a triangle in two dimensions and cut an inverted triangle (white) in the center of the original black triangle. We obtain 3 smaller triangles, identical to the original one. Then, we repeat the procedure and obtain 9 smaller triangles after cutting an inverted triangle in the center of the 3 smaller ones. After repeating this procedure many times, the final structure is no longer a surface, as the original triangle, neither a line, but something in between. Its Hausdorff dimension is $d = \ln 3 / \ln 2 = 1.58$, which is given by the log of the number of copies obtained after scaling.

Fractals are closely related to Nature and humankind. They are found in the shape of rivers, coastlines of countries, roots and branches of trees, ferns, etc. In the human body, the circulatory system, the intestines, the lungs, the neuronal system, and even the heartbeat are fractal. Fractal structures are very convenient when there are exchanges between the system and the en-

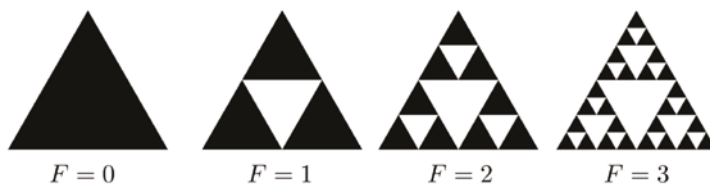


Figure 1. The Sierpinski gasket fractal is constructed by starting with a triangle (generation $F = 0$), and cutting an inverted triangle in its center, such that three rescaled identical triangles remain (generation $F = 1$). Then, inverted triangles are cut in the center of those three smaller triangles to form the next generation $F = 2$). The procedure goes ad infinitum and then, a structure with zero area and infinite perimeter will be realized.

vironment. Since Nature is fractal, our senses perceive fractals as beautiful. Therefore, they have been for long used in decorative arts, much before they were understood and classified by mathematicians. One example are mosaics in Roman Churches, as shown in Fig. 2. In addition, several painters, like Escher and Pollock, used fractals in their artwork. Fractals are also very suitable for technology. Indeed, an antenna made of a fractal can send and receive simultaneously small and large frequencies because of the different length scales in the fractal. In addition, solar cells made of fractals can store more energy upon increasing the complexity of the fractal, in the same 2D area.

In the eighties, fractals were thoroughly investigated. The works of Mandelbrot, De Gennes, Orbach, among others, allowed for much progress in the field [12, 14]. However, those were classical fractals. Now, the time has come to understand quantum fractals. In 2015, the group of Kai Wu has shown how to build fractals using aromatic bromo compounds as the building blocks on a Ag(111) surface [15]. Then, in 2019 the first electronic quantum fractal was realized (see Fig. 3), and it was shown that electrons placed in a fractal can perceive the fractal dimension $d = 1.58$ [16]. Moreover, it was found that diffusion of photons through a fractal leads to a different scaling behavior of the mean-square displacement than in the classical case [17]. Finally, topological properties were investigated in several types of fractals, in a variety of quantum simulator platforms, from photonics [18] to acoustic [19, 20] ones.



Figure 2. Left: Mosaic in the shape of a Sierpinski triangle in the Church of San Clemente, Rome (late 11th century), photo by Carlini. Right: Santa Maria Maggiore, Civita Castellana (12th century), photo by Williams. Figure extracted from Ref. [13].

Recently, it was found that fractals of single-layer bismuth can form spontaneously upon depositing bismuth on the surface of InAs, see Fig. 4 [21]. Moreover, these fractals at dimension 1.58 display topological properties of 2D and 1D materials, then reconciling the best of the two neighboring dimensions. Indeed, the Sierpinski fractals of bismuth were shown to exhibit corner states, which could be used as qubits for quantum computers, as well as 1D propagating edge states, characteristic of 2D materials. In addition, the fractal has internal and external edges, and both types of edge states were detected [22]. The detection of topological properties in these real materials opens the path to their use in novel, more eco-friendly technological devices.

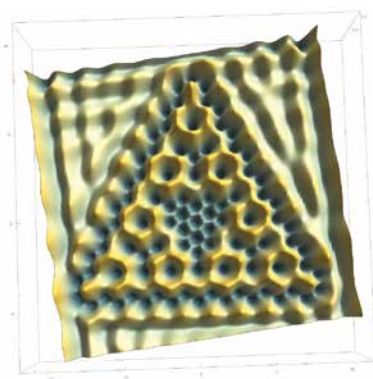


Figure 3. Muffin-tin calculations of the local density of states (LDOS) in a Sierpinski gasket at energy $E = -200$ meV, for electrons trapped in a fractal geometry, engineered by depositing CO adsorbates in a Cu(111) substrate. Courtesy S. Kempkes.

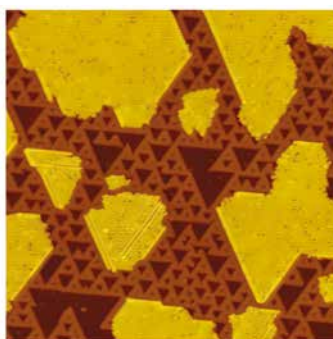


Figure 4. Spontaneously formed fractals of single-layer bismuth on InSb substrate. Courtesy C. Liu and J. Jia [21].

In conclusion, topological insulators have emerged as a possible platform to realize dissipation-free currents, hence preventing energy waste and leading to better performance in quantum nanotechnology. Although the first discovered topological states required high magnetic fields and low temperatures, the field has evolved considerably during the last decades, and it is now possible to realize the topological quantum spin Hall effect, with dissipation-free currents, at room temperature in bismuthene. Moreover, Sierpinski gaskets of single-layer bismuth were spontaneously formed in InSb substrates upon manipulating the growth conditions. Theoretical studies and spectroscopy showed that these fractals, with dimension $d = 1.58$, combine the best topological features of the two-dimensional and one-dimensional topological materials, namely, one-dimensional edge states, as well as zero-dimensional end states, potentially useful for building qubits for quantum computers. The use of topological fractals in nanotechnology would allow us to avoid the energy losses that occur in silicon-based devices, thus leading to a more sustainable life in the Anthropocene. These studies indicate that our search for new materials should not be restricted to integer dimensions. Instead, inspired by Nature and by the human body, new quantum materials will be designed and engineered in a way to increase performance and harmony with the environment. In this realm, quantum topological fractals hold promises to play a prominent role in realizing technological devices with little or no energy loss.

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FUNDAMENTAL CONSIDERATIONS INSPIRED BY QUANTUM PHYSICS

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■ <https://www.doi.org/10.65398/WNME7889>

I'm very grateful to the Pontifical Academy of Sciences for giving me the opportunity to contribute to *Acta*. I hope that I'm not exploiting that opportunity too much by presenting some of my personal views on the foundations of quantum mechanics and on the basic messages which quantum mechanics is conveying to us.

I have been interested in quantum mechanics or, synonymously, quantum physics since the very days when I first learned about them as a student. The initial impression was that of an immense mathematical beauty of the formalism of quantum mechanics. The second impression was the fantastic agreement of the theoretical predictions of quantum physics for experiments, and the third and somewhat surprising impression was that there was widespread disagreement about the interpretation of the new theory.

At that point I would like to emphasize that there are two different levels of interpretation of any formal body in physics. The first level of interpretation is what the symbols one uses correspond to in observations in physical reality. On that level, there is no disagreement about the interpretation of quantum mechanics, particularly since it is commonly accepted that the formalism describes the probabilities of obtaining specific experimental results. The second level of interpretation concerns the meaning of a theory, a theoretical description, for our general view of the world (“Weltanschauung”) that is: What does the theory tell us about the world in general, our position in the world and our relation to the world? At that level, there's a broad spectrum of possible interpretations, which I do not wish to detail here. I want to take the opportunity to present my personal considerations and a few points.

When a physicist observes nature, doing experiments, then one obtains answers, like how fast is a certain body moving, or where is a certain object located, etc. So, from these answers, which we obtain, we construct a reality. In classical physics, this reality concerns all kinds of properties, for example the just mentioned position and momentum, without any inherent

limits. The question which I would now like to raise is: What is this relation between information which we obtain by observing nature and the reality which we construct? What is the relation between the two? What is the relation between material existence and knowledge? What is the relation between reality and information?

Here I would suggest that in physics we should only use concepts which can be operationally verified, that is, concepts where we can do observations of the outside world, at least in principle, which give us an answer about the specific property. Also, any statement about the world is a representation of our knowledge. Therefore, I suggest it is of value to consider what it means to have a representation in terms of information. Any information has to be represented in logical statements. Such logical statements have a structure which is determined by the structure of language. I would like to quote Niels Bohr, who requested that any representation of any experimental results has to be expressed in our classical language, in our everyday language, which concerns classical terms, classical notions. Which classical notions? I suggest that these are merely statements about the properties of the apparatus used in specific experiments, such as whether a particular laser with all its features is turned on or off, whether certain crystals are used, or whether a specific telescope is employed. Additionally, they pertain to the results of observations, such as those observed on camera or recorded by some sort of measurement device, maybe simply just a ruler or a clock, etc. So, if all knowledge is represented in language, in logical statements, the question arises of what this implies at first about knowability of the world. In other words, something which cannot be stated in a logical proposition in the sense just described cannot be a feature of the world, at least not a feature of the world which we can observe, which we can talk meaningfully about. Therefore, I suggest it does not make sense for physics to talk about such in principle unobservable features. So, the question is whether it makes sense to even consider such unobservable features.

I suggest that it is impossible to verify any distinction between reality and knowledge, that is, any distinction between reality and information about reality. So, in other words, we cannot even consider reality without considering the information which can be stated about reality. Therefore, my suggestion would be that language determines what reality can be, that is, statements which we can make about the world determine the possible properties of the world. In quantum mechanics, this knowledge is repre-

sented in the quantum state, which is generally considered to be the state of the system which we observe or which we interrogate. Yet to be precise, what exactly is the quantum state? The quantum state is just a representation of my knowledge about the world, which by necessity is a probabilistic representation.

It is one of the deepest messages of quantum physics that we have an irreducible randomness of individual measurement results, which cannot be explained by a deeper structure. This feature follows from the property that the quantum state only represents possible answers to future experimental questions. Schrödinger called the quantum state an “expectation catalogue” of possible future measurement results. Which specific feature, which specific prediction of the expectation catalogue is then realized in experimental observation is completely random and beyond the possibility of science to explain. Actually, this new randomness in quantum physics is of a new nature, which has not been seen before in science.

As Heisenberg once pointed out, there are two different kinds of randomness. One may be called subjective and the other may be called objective. Subjective randomness is personal ignorance about the details of a situation, like, for example, when we throw a die and we obtain one of the numbers 1 to 6, the result being random. But, in principle, within classical physics, which is the physics before quantum mechanics, the result is determined by how the die is thrown. It's determined by the precise way in which the die falls on the table, in which the die interacts with the surface and so on. Randomness here is due to the personal ignorance of the details of the physical process going on.

The opposite of subjective randomness in classical physics is objective randomness in quantum mechanics. Here we have the situation that the assumption of a deeper underlying mechanism, which might explain each specific experimental result, leads to contradictions with possible experiments. That is, in particular, a consequence of quantum entanglement, and the fact that there, the randomness of individual events plays a crucial role. It is also a consequence of the fact that there are theorems for systems in higher dimensions. Visualize the Kochen-Specker Paradox, where even for an individual system the assumption that the observed result is somehow determined prior to performing the experiment is not possible without the complete context of the specific experiments performed.

The quantum state is thus just the interpretation of our knowledge of the experimental setup and all its features, which allows us to make proba-

bilistic predictions about future measurement results, that is, about future classical properties of the observed system. The quantum state itself, as has nicely been presented, for example, in the Nobel Prize speech of John Clauser, does not exist in real space. It exists in an abstract theoretical space, the configuration space.

I suggest that many of the seeming puzzles and paradoxes with measurement and randomness arise from what is called “reification of the quantum state”, that is, the assumption that the quantum state exists out there in real space. Take, as an example, Schrödinger’s cat paradox, where the unfortunate cat is connected to a quantum device whose outcome is random, and depending on the outcome the cat will be alive or dead. Now, very often, this paradox is represented as the cat actually being both dead and alive before the experiment is finally performed. This is clearly not acceptable if the quantum state does not exist in real space. Rather, the correct way to talk about the situation is the fact that our knowledge of the situation does not allow us to make any statements about the state of the quantum system, therefore about the state of the cat, whether it is alive or dead. So as the quantum state is just a representation of our knowledge, it is more than natural to change that representation of our knowledge, that is, the quantum state, by obtaining new information, like, for example, by observing whether the cat is dead or alive. An interesting feature of quantum mechanics now is that it is not allowed to assume that the cat was either dead or alive, that is, in a well-defined state, before the observation.

So, from that point of view, there is no measurement problem. There is no necessity to see the measurement, namely the way in which a specific result is obtained, as a physical process in the physical world. All there is is just a change of knowledge, just a change of mathematical representation.

We might even go further in an admittedly rather speculative way. I would suggest that the only concept which is unavoidable in all our discussions is the notion of information. Reality independent of information is moot and does not make sense in itself. It suggests itself to assume that, therefore, the structure of information defines the structure of physical states. This also determines the nature of reality. Maybe there is an analog to the way in which in Gödel’s Theorem, statements are countable, and maybe this countability reflects itself in the structure of quantum mechanics. Reality is a secondary concept, not a primary concept which is hidden behind the laws of quantum mechanics. Having thus analyzed the relationship between physical reality and information, one might further speculate

that maybe randomness is a hint beyond what can ever be found in physical observation. Randomness in a very deep sense hints beyond our method.

I would like to conclude in an admittedly very personal way. The gospel according to John starts with “in the beginning was the word”, or maybe even more fundamentally in the Latin version, “in principio erat verbum”.

IV: LIVE SCIENCES INNOVATIONS, HEALTH AND MEDICAL SCIENCES

THE INFLUENCE OF CARBON DIOXIDE LEVELS IN PEROXIDE METABOLISM IN MAMMALIAN CELLS

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■ <https://www.doi.org/10.65398/SGTM9238>

Introduction

Carbon dioxide is a metabolic by-product produced by humans. One person produces approximately 1 kg of carbon dioxide (CO₂) per day (1) much of which is exhaled to the environment through respiration. Physiological levels of CO₂ are associated to the control of pH and are tightly regulated by a series of homeostatic local and systemic mechanisms. Conditions leading to excess production or exposure to CO₂ lead to toxic events and trigger pathological responses. In the context of the “Anthropocene” is important to consider that humans are exposed to higher inner and outdoor CO₂ levels than in any previous time in history and that is becoming evident that increased atmospheric CO₂ creates direct human health risks (2). In this context, I will analyze how CO₂ influences peroxide metabolism in mammalian cells (3); specifically, CO₂ enhances the chemical reactivity of biologically-relevant peroxides such as hydrogen peroxide (H₂O₂) and peroxynitrite (ONOO⁻). Through its reactions with peroxides, CO₂ favors biological oxidations with consequences in redox signaling, inflammation and oxidative damage. Revealing the reactions of CO₂ with peroxides in mammalian systems help to further understand how CO₂ can serve as a biological signaling molecule, stressor, or toxicant.

CO₂: biochemical and physiological aspects of its endogenous production

Mammalian cells continuously produce CO₂ (3-5). This production is mainly connected to the aerobic oxidation of nutrients such as sugars and lipids. Most of the metabolic CO₂ formation in humans occurs in mitochondria, the key organelles responsible of bioenergy generation and cellular respiration (3). Through a series of “oxidative decarboxylation reactions”

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on α - and β -ketoacids including pyruvate, isocitrate and α -ketoglutarate, specific mitochondrial dehydrogenases which enzymatically catalyze the decarboxylation process in metabolic intermediates coupled to the reduction of the electron carrier NAD^+ which evolves to NADH (Figure 1). In turn, NADH fuels electrons to the mitochondrial electron transport chain which, in healthy mitochondria, is coupled to molecular oxygen (O_2) consumption and the generation of ATP, the latter serving as a key bioenergy intermediate in mammalian metabolism. Thus, the formation of CO_2 is a continuous process and is metabolically located at the crossroads of the redox-energy axis.

The metabolic generation of CO_2 can be also achieved by metabolic processes that occur in other cellular compartments such as the cytosol (3). For example, a specific metabolic process known as the pentose phosphate pathway (PPP) carries out an oxidative decarboxylation reaction on the glucose-derived intermediate 6-phosphogluconate and leads to the reduction of NADP^+ to NADPH (Figure 1). This latter compound plays important role on a variety of intracellular redox processes (*e.g.* fatty acid biosynthesis, peroxide catabolism, synthesis of DNA precursors). The metabolic formation of CO_2 also occurs in non-oxidative reactions but their contribution to overall CO_2 formation is minor. Importantly, some metabolic processes also involve the action of carboxylases that use as a substrate CO_2 (usually in the form of bicarbonate, HCO_3^-) to incorporate it into organic molecules (4). Overall, decarboxylation (oxidative and non-oxidative) and carboxylation reactions interconnect mammalian redox and energy metabolism as well as other anabolic and catabolic processes (1, 3, 4). Overall, there is a net (and large) release of CO_2 in mammalian tissues because CO_2 production normally largely exceeds CO_2 consumption (5), with mitochondria usually representing the major source of cellular CO_2 formation (3), in turn coupled to oxygen consumption (Figure 1).

Mitochondrial CO_2 concentrations usually reach values > 2 mM. Then, a concentration gradient is typically established with extramitochondrial sites, with CO_2 normally diffusing out from mitochondria to the cytosol and then, to the extracellular milieu².

² In liver and kidney mitochondria sometimes there is an uptake of CO_2 for carboxylation reactions carried out in mitochondria related to gluconeogenesis and ureogenesis (Ref. 3).

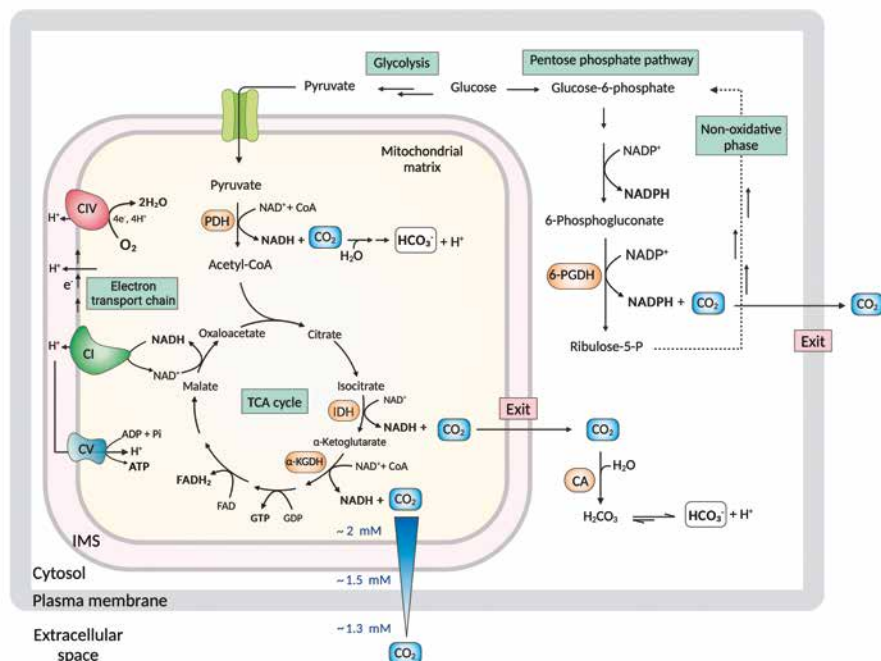


Figure 1. Decarboxylation reactions in mitochondria and cytosol. Oxidative decarboxylation reactions to glucose-derived organic acids lead to the release of CO_2 and reducing equivalents (as NADH) in mitochondria. Then, NADH provides electrons to the mitochondrial electron transport chain in a process that couples O_2 reduction to water with the synthesis of ATP, a bioenergy substrate. In the cytosol, the pentose phosphate pathway catalyzes the oxidative decarboxylation of 6-phosphogluconate which also yields NADPH and CO_2 . The continuous formation of mitochondrial CO_2 typically results on a concentration gradient by which CO_2 diffuses out to the cytosol and then to the extracellular space freely crossing the mitochondrial and plasma membrane, respectively. CO_2 diffusion competes with the hydration reaction to H_2CO_3 (and subsequently HCO_3^-), catalyzed in the cytosol by carbonic anhydrase (CA). Estimated physiological CO_2 concentrations in the different compartments are indicated.

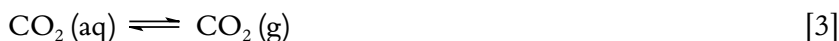
$\text{CO}_2/\text{HCO}_3^-$ dynamic equilibria in human physiology

Metabolically generated CO_2 can be hydrated to carbonic acid (H_2CO_3) and, in turn, H_2CO_3 , a weak acid, is rapidly deprotonated to bicarbonate (HCO_3^-) (3). Both are reversible reactions, so that CO_2 in solution is in equilibrium with HCO_3^- (Eq. 1 and 2):



Reaction 1 is largely accelerated in mammalian tissues by the action of the enzyme carbonic anhydrase which is an extremely efficient enzyme in the catalysis of the hydration reaction and therefore permits to rapidly approach equilibrium *in vivo*.

Importantly, dissolved carbon dioxide is in equilibrium with gaseous CO₂:

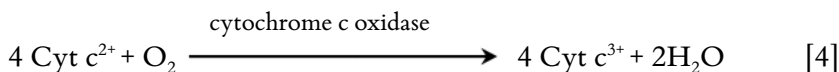


Thus, while the actual pK_a for H₂CO₃ is *ca.* 3.5 (6), the apparent pK_a for this acid-base system applicable to human physiology is *ca.* 6.1–6.4 (7) due to various participating equilibria and physiological systems. Thus, although continuous formation of CO₂ tends to acidify biological milieu (Eqs. 1 and 2) the CO₂/HCO₃[−] pair with the concerted action of physiological processes such as CO₂ exhalation at the lungs and renal management of HCO₃[−], constitutes an important element for the regulation of cellular and extracellular acid-base homeostasis (7).

Normal CO₂ concentrations in tissues is in the order of 1–2 mM. In plasma of healthy individuals, the CO₂ and HCO₃[−] concentrations are *ca.* 1.3 mM and 24 mM at pH 7.4 and 37°C, respectively. Significant deviations from physiological CO₂ and HCO₃[−] levels³ (*e.g.* < 1 mM or > 3 mM for CO₂ and <10 or > 30 mM for HCO₃[−] require medical intervention.

Oxygen metabolism and peroxide formation in mammalian cells

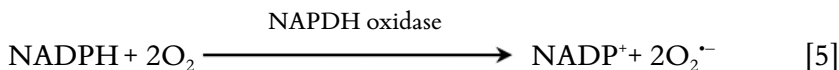
Most O₂ consumed by mammalian cells is utilized as the final electron acceptor of the mitochondrial electron transport chain in the process of cell respiration. In this process, O₂ interacts at the terminal oxidase called cytochrome c oxidase which reduces O₂ in a four-electron process to H₂O at the expense of electrons transferred by cytochrome c, by (Eq. 4).



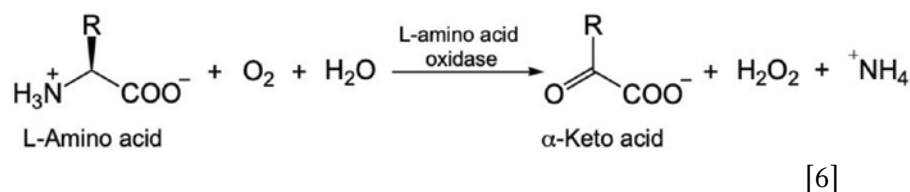
Under physiological conditions more than 99.5% O₂ is consumed via this reaction in human cells.

³ Deviations of CO₂ levels in blood below or above the physiological range are defined as hypocapnia or hypercapnia, respectively.

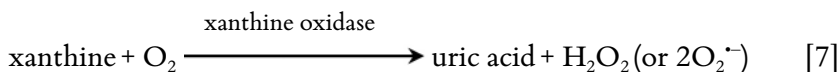
Additionally, O_2 is also utilized as substrate in other redox reactions⁴ where it serves as a one- or two-electron acceptor to yield superoxide radical ($O_2^{\cdot-}$) or hydrogen peroxide (H_2O_2), respectively (8). A prime example of the former is the reaction catalyzed by membrane-bound NADPH oxidase (NOX) that generates $O_2^{\cdot-}$ in macrophages and neutrophils for oxidative killing (Eq. 5).



An example of the second type of O_2 -consuming reaction is the oxidative deamination of L-amino acids to the corresponding α -keto acids and the concomitant formation of ammonia and H_2O_2 (Eq. 6).



Notably, xanthine oxidase, the terminal enzyme of purine metabolism in humans catalyzes the O_2 -dependent oxidation of hypoxanthine and xanthine to uric acid, concomitantly producing both $O_2^{\cdot-}$ and H_2O_2 at variable ratios depending on reaction conditions (Eq. 7) (8).

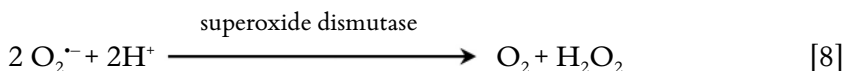


Other non-enzymatic processes may promote the one-electron reduction of O_2 to $O_2^{\cdot-}$, including the autoxidation of quinones, reduced flavins, ascorbate and glutathione, and “electron leakage” at complexes of the mitochondrial electron transport chain, among other sources.

Once formed, both $O_2^{\cdot-}$ and H_2O_2 are unstable and transient intermediates in mammalian cells. For a start, $O_2^{\cdot-}$ readily dismutates to H_2O_2 by the

⁴ Molecular oxygen also participates in oxygenation reactions, namely the incorporation of oxygen to a biomolecule, but these reactions are out of the scope of this manuscript.

near diffusion-controlled reaction catalyzed by (widely distributed) superoxide dismutases:



Alternatively, $\text{O}_2^{\cdot-}$ can react with a limited number of biomolecular targets. In this sense, one of the most important of such reactions is the combination of $\text{O}_2^{\cdot-}$ with nitric oxide ($\bullet\text{NO}$)⁵, a reaction that is at the diffusional limit and the only reported one that can really outcompete $\text{O}_2^{\cdot-}$ dismutation *in vivo* (8). This reaction decreases the bioavailability of $\bullet\text{NO}$ and at the same time leads to the formation of a cytotoxic nucleophile and oxidant, peroxynitrite anion (Eq. 9) (9).



As $\text{O}_2^{\cdot-}$ and $\bullet\text{NO}$ formation are ubiquitous in mammalian cells, their metabolism leads to a continuous biological flow of H_2O_2 and peroxynitrite,⁶ even under relatively low physiological oxygen tensions (*e.g.* 2% O_2) (10). Homeostatic levels of H_2O_2 and peroxynitrite participate in redox signaling pathways (*e.g.* reversible oxidation/inactivation of protein tyrosine phosphatases) while excessive levels promote oxidative stress conditions that may ultimately cause biological oxidative damage (*e.g.* protein overoxidation, lipid peroxidation) (3). Peroxides are largely decomposed by strong peroxidatic systems (*e.g.* peroxiredoxins) (11) and therefore their steady-state concentrations are kept typically low and their toxic actions minimized; however, we now understand that their catabolism is in competition and/or interfered with their reactions with CO_2 .

Reactions of CO_2 with H_2O_2 and ONOO^- and biological oxidations

Despite the mM concentration of CO_2 present in mammalian cells and tissues, it has been normally considered a relatively poor reactant in biolog-

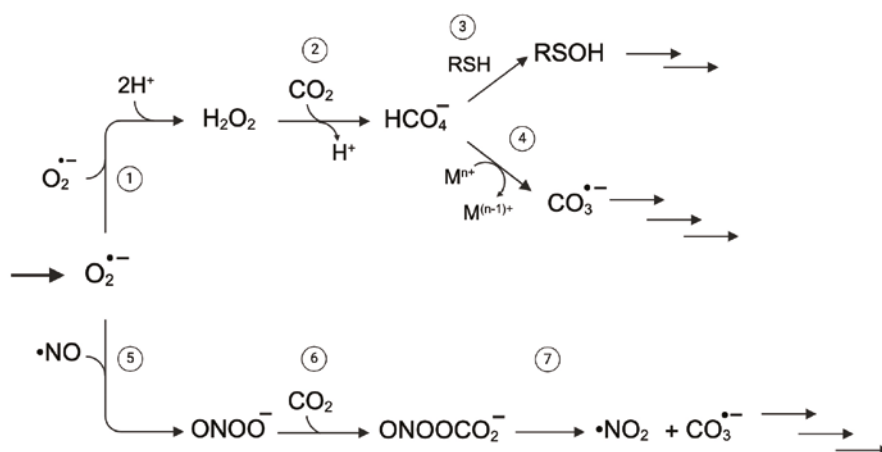
⁵ Nitric oxide is a free radical and signal transducing agent that participates in a variety of physiological processes including vasodilation, neurotransmission, and immune responses. It is mostly generated by the enzymatic action of nitric oxide synthases (NOS) which use as substrates L-arginine, O_2 and NADPH.

⁶ Peroxynitrite refers to the sum of peroxynitrite anion and peroxynitrous acid (ON-OOH , $\text{pK}_a = 6.8$).

ical milieu, except for enzyme-catalyzed carboxylation reactions and the relatively slow reaction with neutral amines in amino acids and proteins. In the latter case, the reaction of CO_2 with *N*-terminal-amino or lysine α -amino groups results in the formation of carbamates (3). This carbamoylation reaction it is well known in the case of hemoglobin (*i.e.* carbamino-Hb); other proteins carrying this reversible posttranslational modification are increasingly revealed (12).

With respect to the role of CO_2 on the chemical biology of redox reactions, there had been several hints in the literature (reviewed in Ref. 3). However, only recently CO_2 has become increasingly appreciated as redox modulator in human biology *via* H_2O_2 and ONOO^- -dependent reactions. The influence of CO_2 ranges from redox signaling to oxidative damage and encompasses both one- and two-electron oxidation processes.

The interplay of CO_2 with H_2O_2 and ONOO^- (3) leads to the formation of CO_2 -derived adducts (*i.e.* peroxydicarbonate, HCO_4^- ; nitrosoperox-



Peroxide formation — CO_2 adduct — Oxidative processes

Figure 2. CO_2 -derived peroxides and oxidation reactions. The upper part of the scheme shows 1) $\text{O}_2^{\bullet -}$ dismutation to H_2O_2 , 2) CO_2 - H_2O_2 adduct formation to HCO_4^- , 3) HCO_4^- mediated two electron oxidation of a thiol and 4) metal-catalyzed formation of $\text{CO}_3^{\bullet -}$ from HCO_4^- . The lower part of the scheme shows 5) $\text{O}_2^{\bullet -}$ reaction with $\cdot\text{NO}$ and peroxynitrite formation, 6) CO_2 - ONOO^- adduct formation to $\text{ONO}_2\text{CO}_2^-$, 7) $\text{ONO}_2\text{CO}_2^-$ homolysis to $\cdot\text{NO}_2$ and $\text{CO}_3^{\bullet -}$. While the sulfenic acid derivative (RSOH) arising from reaction 3 will evolve further to stable products such as disulfides, radical intermediates formed in reactions 4 and 7 will initiate one-electron oxidations and/or promote nitration.

ocarboxylate, ONOOCO_2^- , Figure 2) which efficiently mediate oxidation reactions *in vitro*, *in cellula* and *in vivo*. Due to the transient nature of these reactive species (biological half-life typically in the ms to μs time scale, respectively), their detection is quite challenging, still in evolution, and requires either the use of probes or the detection of molecular footprints.

Current chemical and biological evidence support the idea that CO_2 enhances the oxidative potency of both H_2O_2 and ONOO^- , albeit *via* different molecular mechanisms (3).

For instance, HCO_4^- is a stronger two-electron oxidant than H_2O_2 , typically oxidizing thiol groups at 100–1000 faster reaction rates (3). It is important to consider that the reaction of CO_2 with H_2O_2 is reversible and that under physiological conditions, only *ca.* 1% of total H_2O_2 would be present as HCO_4^- . However, as HCO_4^- is consumed by reacting with target molecules, a re-equilibration process continuously occurs and, under excess CO_2 levels, there will be a continuous flow of HCO_4^- from H_2O_2 . In addition to participate in two-electron oxidations, HCO_4^- can also evolve to carbonate radicals ($\text{CO}_3^{\cdot-}$) in the presence of oxidized transition metal centers (Figure 2), although the relevance of this reaction biology has not been yet demonstrated.

In the case of ONOO^- , the reaction with CO_2 is quite fast and leads to the formation of the rather unstable ONOOCO_2^- which immediately undergoes homolysis to nitrogen dioxide ($\bullet\text{NO}_2$) and $\text{CO}_3^{\cdot-}$. Both $\bullet\text{NO}_2$ and $\text{CO}_3^{\cdot-}$ are strong one-electron oxidants and initiate free radical processes in mammalian systems (13); in addition, $\bullet\text{NO}_2$ mediates nitration reactions in biomolecules, most notably in protein tyrosine residues to yield 3-nitro-tyrosine. Protein tyrosine nitration is a quantifiable oxidative post-translational modification evidenced *in vivo* associated to human disease and aging; CO_2 plays a key role on modulating the extent and site-specificity of peroxynitrite-dependent tyrosine nitration in proteins (13).

In summary, the chemical reactivity of CO_2 with H_2O_2 and ONOO^- can have profound influence on the biology of redox signaling and oxidative stress, much of which still needs to be revealed and characterized.

CO_2 reactions with peroxides *in cellula* and *in vivo*

Recent evidence supports that at least some of the redox signaling actions of H_2O_2 are in fact due to HCO_4^- . These new discoveries tend to reconcile the relatively poor *direct* chemical reactivity of H_2O_2 with H_2O_2 -dependent redox signaling events that depend on protein thiol oxidation are difficult to envision if considering H_2O_2 as the proximal redox mediator.

Indeed, recent elegant work on epidermal growth factor (EGF) stimulation of an adenocarcinoma cell line, a process known to use H_2O_2 as intracellular messenger, showed that increasing intracellular HCO_3^- concentrations enhanced total protein phosphotyrosine levels (14). The actions of EGF are initially mediated through receptor tyrosine kinase (RTK) activation which in turn triggers H_2O_2 production by membrane-bound NADPH oxidase and promotes PTP1B oxidation/inactivation. While it was previously established that the formation of H_2O_2 is a central requisite for protein tyrosine phosphate 1B (PTP1B) inactivation, the new work reveals that this type of H_2O_2 -dependent redox signaling requires the presence of HCO_3^- (and likely through HCO_4^- formation) to mediate EGF-induced cellular oxidation of PTP1B.

Related observations were made in the case of a key glycolytic enzyme, glyceraldehyde-3-phosphate dehydrogenase (GAPDH), that contains an active site Cys and is one of the most sensitive cellular enzymes to oxidative inactivation and redox regulation (15). We have shown H_2O_2 -induced inactivation *in vitro* and *in cellula* was strongly enhanced in the presence of $\text{CO}_2/\text{HCO}_3^-$ and inferred that HCO_4^- was playing a central role on GAPDH oxidation and inactivation. The reversible oxidative inactivation of GAPDH is being recognized as a “redox switch” that can facilitate redirection of glucose to the pentose phosphate pathways.

While the reaction of CO_2 with H_2O_2 to yield HCO_4^- and the oxidative properties of HCO_4^- have been well documented in the chemical and biochemical literature, its detection in biological systems has been mostly inferential. We have just provided the first documented evidence that a type of mammalian cell, activated macrophages, produce HCO_4^- under biologically relevant concentrations of H_2O_2 and $\text{CO}_2/\text{HCO}_3^-$ (16). The detection was possible due to the use of boronate-based probes that react with HCO_4^- and yield a stable (fluorescent) product that can be visualized by a variety of techniques. The comparative cytotoxic capacity of macrophage-derived HCO_4^- vs H_2O_2 to invading pathogens such as bacteria or intracellular parasites remains to be established. Preliminary data support that the presence of CO_2 potentiates H_2O_2 -dependent oxidative killing, consistent with the higher reactivity of HCO_4^- (reviewed in Ref. 3).

The reaction of ONOO^- with CO_2 has been analyzed recently in the context of the mitochondrial metabolism peroxynitrite and the competition with mitochondrial peroxiredoxins *in vitro*, *in cellula* e *in vivo* (9, 17, 18). Mitochondrial peroxiredoxins are key enzymes in the catabolism of ON-

OO^- to NO_2^- (11). However, mitochondrial CO_2 kinetically competes well with peroxiredoxins (17), in which case $\bullet\text{NO}_2$ and $\text{CO}_3\bullet^-$ will be formed. Thus, among other factors, the fate, and actions of mitochondrial ONOO^- depends on the levels of CO_2 , peroxiredoxins and associated reducing systems (e.g. thioredoxin, thioredoxin reductase; Ref. 18). The presence of CO_2 promotes mitochondrial protein nitration, peroxiredoxin inactivation and overoxidation and, depending on metabolic conditions, may lead to mitochondrial oxidative stress and mitochondrial dysfunction (19) in hu-

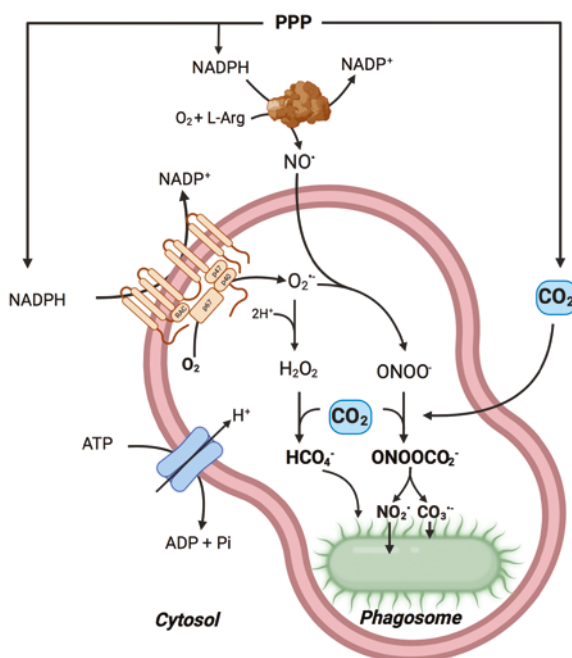


Figure 3. Carbon dioxide-derived oxidants in the macrophage phagosome. The formation of H_2O_2 , ONOO^- and their corresponding CO_2 adducts inside the phagosome is indicated. Engulfment of pathogens leads to metabolic events that yield intermediates that participate in oxidative killing of the invader microbe. The formation of $\text{O}_2\bullet^-$ and H_2O_2 occurs *via* activation of NADPH oxidase that is triggered by phagocytic stimuli; the formation of ONOO^- is secondary to the enzymatic production of $\bullet\text{NO}$ production in macrophages that had been immunostimulated by cytokines. These processes are coupled with the activation of the PPP that generates NADPH for the catalytic action of NOX and NOS and CO_2 that can freely diffuses towards the phagosomal lumen and contribute to the formation of HCO_3^- and $\text{ONOOOCO}_2\bullet^-$. Then, the CO_2 -derived peroxides can promote oxidations and nitration reactions in the pathogen. This Figure was originally published in the Journal of Biological Chemistry. Radi R. (2022). Interplay of carbon dioxide and peroxide metabolism in mammalian cells. *J Biol Chem.* 298(9):102358. doi: 10.1016/j.jbc.2022.102358. © the Author.

man disease and aging (for a recent analysis, see also Refs. 3 and 9). New evidence on the key role of peroxynitrite in mitochondrial dysfunction and disruption of cell physiology *in vivo* has been just reported (20).

Immunostimulated macrophages can yield ONOO⁻ upon activation by invading pathogens. The presence of CO₂ can promote pathogen oxidation and nitration inside the phagosome (reviewed in Ref. 21). The fast reaction of CO₂ with ONOO⁻ and the short half-life of ONOOCO₂⁻ determines that CO₂ focusses the reactivity of peroxynitrite in cellula and *in vivo* to a very narrow region within the mm distance scale. The putative role of CO₂ on HCO₄⁻ and ONOOCO₂⁻ formation and oxidative pathogen killing inside the macrophage phagosome is shown in Figure 3.

Other mechanisms by which CO₂ influences redox biology and inflammation

In addition to the direct actions of CO₂ on peroxide reactivity, oxidative processes may be modulated by CO₂ due to its actions on the regulation of genes related to inflammation (22-24). A complex interaction exists between CO₂ signaling, NF-κB and NOS expression (3). Depending on the CO₂ exposure protocol and the organism, both anti- and pro-inflammatory actions of CO₂ have been observed (including changes on protein levels of target genes for NF-κB such as IL-6 and TNFα), although a definitive and mechanistic-based picture is yet to be provided. CO₂ exposure conditions reportedly leading to inflammation involve activation of the nucleotide-binding domain-like receptor 3 (NLRP3) inflammasome and elevated interleukin (IL)-1β production. Recent reports of the role of CO₂ signaling, transcriptional responses and inflammation have been communicated elsewhere (2, 22-24).

Exogenous CO₂ exposure to human tissues: Perspectives for the Anthropocene

A recent report has analyzed the direct health effects of increasing atmospheric CO₂ levels (2). Environmentally relevant elevations in CO₂ (<5,000 ppm) may pose direct risks for human health. While most of the evolution of humans has been carried out under atmospheric CO₂ levels in the order of 250 ppm, recent increases in the 400-500 ppm range indicates that this could be of toxicological concern. Conditions leading to acute or chronic exposure to high CO₂ levels (extended indoor life and poor ventilation,

populated cities, and excess combustion of fossil fuels, all of which can lead to exposures > 1000 ppm) are increasingly observed and its impact in various organs and physiological systems revealed. Shockingly, reports also indicate that HCO_3^- levels in human serum among the general US population appears be increasing (2, 25, 26) (still within the normal range) which may reflect increased CO_2 exposure to humans. Among other health issues, CO_2 may promote inflammation and oxidative stress pathways, some of which may depend on the reactions of CO_2 with peroxides.

Cities contribute substantially to anthropogenic CO_2 emissions. An aspect that is not particularly appreciated is that even the respiration of humans and livestock can represent a significant CO_2 source in some cities (27). In a context of increased of the world population to *ca.* 11 billion people by 2100, the metabolic-derived formation of CO_2 may not be considered negligible for city carbon budget analysis. This challenging idea must be taken into consideration in the context of the One Health concept.

Thus, from a medical and toxicological perspective, the environmentally relevant elevations in CO_2 may affect human health in common everyday activities: the molecular mechanisms may imply redox processes arising from the reactions of CO_2 with H_2O_2 and peroxynitrite. Importantly, both H_2O_2 and nitrogen oxides (NO_x) are present in urban air and their local concentrations in aerosols can be quite high (28-32). Thus, there is a possibility for corporal surfaces such as skin, mucous membranes, cornea, and respiratory epithelium to be exposed to environmental $\text{CO}_2/\text{H}_2\text{O}_2$ and CO_2 /peroxynitrite mixtures.

Future *in cellula* and *in vivo* experiments under well-controlled CO_2 and O_2 levels in conjunction with additional studies in humans (2) will provide new clues on how the CO_2 /peroxide interplay participates in human physiology and disease.

Acknowledgements

I thank Drs. Lucía Piacenza and Natalia Ríos for their assistance with the artwork.

This work was supported by grants from Universidad de la República (EI_2020), The Richard Lounsbery Foundation and Programa de Alimentos y Salud Humana (PAyS) IDB-R.O.U. (4950/OC-UR). Additional funding was obtained from Programa de Desarrollo de Ciencias Básicas (PEDECIBA).

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DESIGN AND EVOLUTION OF NEW METABOLISM FOR GREENHOUSE GAS ASSIMILATION

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■ <https://www.doi.org/10.65398/LQLH7104>

Introduction

Following the Industrial Revolution in the 18th century, fossil fuels such as coal, petroleum, and natural gas have been heavily exploited and used as primary energy sources. The combustion of these fuels releases significant amounts of CO₂, leading to a rapid increase in atmospheric CO₂ concentration over recent decades. Additionally, the growing world population has led to increased agricultural activities, which emit CO₂ and other greenhouse gases, such as methane.

The accumulation of greenhouse gases has caused global warming and climate change, which could lead to catastrophic consequences if not addressed. Despite efforts to reduce greenhouse gas emissions, progress has been insufficient. Currently, global CO₂ emissions primarily from fossil fuel combustion, agriculture, and land use changes, total approximately 40 billion tons per year and are still increasing. The CO₂ level in the atmosphere is greater than 420 parts per million (ppm), which is 100 ppm more than the level in 1960.

Biology offers a potential solution for absorbing greenhouse gases. Plants, algae, and cyanobacteria have evolved to utilize carbon dioxide, and certain microorganisms, such as methanotrophs, can use methane for growth. Biological organisms naturally assimilate approximately 440 billion tons of CO₂ from the atmosphere each year, which is more than ten times the amount of CO₂ produced by human activities. However, about half of this assimilated CO₂ is rapidly respired back into the atmosphere, and the remaining portion is slowly released as CO₂ or methane.

Before the Industrial Revolution, Earth's natural biological systems effectively balanced the carbon cycle, keeping atmospheric CO₂ levels in check. However, the rapid increase in human-caused CO₂ emissions, driven by fossil fuel combustion, agricultural expansion, and land-use changes, has overwhelmed this natural balance.

Despite this challenge, biological systems still offer one of the few scalable solutions for mitigating atmospheric greenhouse gases. By boosting the rate at which plants and microorganisms capture carbon dioxide, we could convert it into forms that benefit agriculture or replace fossil fuels. Such enhanced carbon assimilation could significantly reduce human-caused greenhouse gas emissions by improving agricultural efficiency and reducing reliance on fossil fuels. To achieve this vision, the first step is to enhance CO₂ fixation by plants and cyanobacteria, as well as increase methane or methanol assimilation by microorganisms.

Nature has evolved several molecular systems to fix one-carbon (C1) compounds such as CO₂, methane, and methanol. However, such systems are insufficient to deal with the increased challenge posed by the increased carbon emission due to human activities. Thus, new mechanisms to boost C1 fixation need to be designed and evolved. Here we discuss a few examples of how biological systems are re-designed to boost C1 fixation using plants and microorganisms as examples.

I. Recycling the photorespiration product

The majority of CO₂ on earth is fixed by an enzyme called RuBisCO, the most abundant protein on earth. Through billions of years' evolution, an equilibrium between activity and specificity has been reached. Consequently, RuBisCO cannot distinguish between CO₂ and O₂, and possesses both a carboxylase and an oxygenase activity. The oxygenase activity typically accounts for 20–30 percent of RuBisCO's activity in C3 plants. This activity produces glycolate, which is converted into glycerate in peroxisomes and CO₂ in mitochondria (Maier et al., 2012) accompanied by ammonia release. This process, called photorespiration, is thought to be one of the factors limiting agricultural productivity and CO₂ fixation on earth. In the past decade or so, several novel pathways have been devised to recycle the photorespiration product to a productive pathway.

The first approach is through complete oxidation of the photorespiration product, glycolate, to CO₂ in chloroplasts, followed by re-assimilation of CO₂. Native plants degrade glycolate in peroxisome and mitochondria. If glycolate can be degraded completely to CO₂ in chloroplasts, CO₂ can be re-assimilated by RuBisCO directly without ammonia release.

This concept was implemented (Maier et al., 2012) by introducing two heterologous enzymes, a malate synthase (MS) from pumpkin and a catalase (CAT) from *E. coli*, and overexpressing an endogenous enzyme, peroxisomal glycolate oxidase (GO) in *Arabidopsis* chloroplasts (Fig. 1a). With these modifications, glycolate is

converted to CO₂ in chloroplasts and re-assimilated by RuBisCo. The resulting transgenic *Arabidopsis* showed an increase in rosette size and quantity, as well as greater biomass. Nevertheless, incorporating the three aforementioned genes into tobacco plants did not enhance their biomass in greenhouse experiments (South

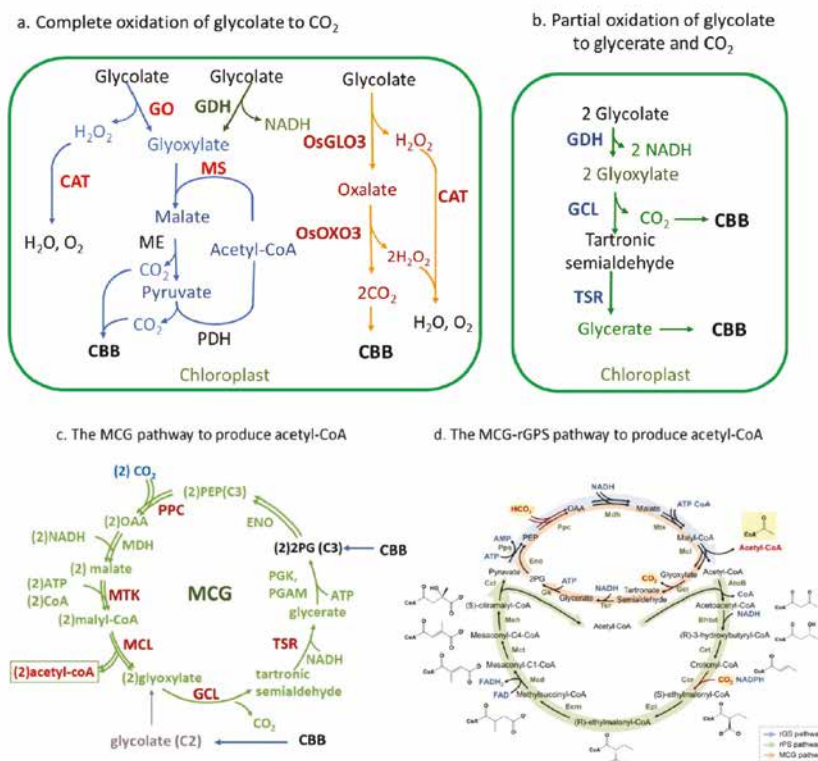


Figure 1. Recycling of photorespiration product glycolate. a) Glycolate is completely oxidized to CO₂ and re-assimilated the CBB cycle. b) Glycolate is partially oxidized to glycerate and CO₂, both of which are re-assimilated in the CBB cycle. c) The MCG pathway that fixes one more carbon by PPC and produces acetyl-CoA from CBB products 2-phosphoglycerate (2PG) or glycolate. d) The MCG-rGPS pathway that is independent of Rubisco can fix CO₂. Enzyme abbreviations are: malate synthase (MS), catalase (CAT), glycolate oxidase (GO), glycolate dehydrogenase (GDH), rice glycolate oxidase (OsGLO3), oxalate oxidase (OsOXO3), and a catalase glyoxylate carboligase (GCL), tartronic semialdehyde reductase (TSR), acetyl-CoA acetyltransferase (AtoB), 3-hydroxybutyryl-CoA dehydrogenase (Bhbd), crotonase (Crt), crotonyl-CoA carboxylase/reductase (Ccr), ethylmalonyl-CoA/methylmalonyl-CoA epimerase (Epi), (2R)-ethylmalonyl-CoA mutase (Ecm), (2S)-methylsuccinyl-CoA dehydrogenase (Mcd), mesaconyl-C1-CoA-C4-CoA transferase (Mct), mesaconyl-C4-CoA hydratase (Meh), (S)-citramalyl-CoA lyase (Ccl), malyl coenzyme A lyase (Mcl), phosphoenolpyruvate synthetase (Pps), phosphoenolpyruvate carboxylase (Ppc), malate dehydrogenase (Mdh), malate thiokinase (Mtk), malyl coenzyme A lyase (Mcl).

et al., 2019). Interestingly, when glycolate oxidase (GO), which produces H_2O_2 , is substituted with glycolate dehydrogenase (GDH) from *Chlamydomonas* (Fig. 1a), which produces NADH, the transgenic tobacco demonstrated higher carbon assimilation rates, enhanced resistance to photorespiration stress, and a significant increase in biomass during field tests (South et al., 2019). This approach also prevented yield loss at high temperatures (Cavanagh et al., 2022).

Another implementation of this concept is a pathway called GOC (Shen et al., 2019), which consists of a rice glycolate oxidase (OsGLO3), an oxalate oxidase (OsOXO3), and a catalase (OsCATC) (Fig. 1a). These enzymes were expressed in rice chloroplasts, and completely converted glycolate to CO_2 via oxalate. The GOC pathway in rice led to as much as 22% improvement in photosynthesis; however, field tests showed that the yields fluctuated with the season (Shen et al., 2019).

Instead of fully oxidizing glycolate, a synthetic pathway derived from *E. coli* can partially oxidize two glycolate molecules into one CO_2 and one glycerate (Fig. 1b). Both of these products can be assimilated in the chloroplast through the Calvin-Benson-Bassham (CBB) pathway. This synthetic pathway retains 75% of the carbon from two glyoxylate molecules to produce glycerate, which is then recycled back into the CBB cycle. The remaining carbon is released as CO_2 , which can theoretically be reassimilated by RuBisCO. Expression of these genes in *Arabidopsis* chloroplasts (Kebeish et al., 2007) led to increased growth rates and biomass yields. This pathway also proved beneficial for some crop plants such as *Camelina sativa* (Dalal et al., 2015) and potato (Nölke et al., 2014) under greenhouse and growth chamber conditions.

II. Synthetic CO_2 fixing pathways

In addition to recycling photorespiration products from RuBisCO, other efforts aim to increase CO_2 fixation by devising synthetic CO_2 fixation pathways. These include the Malyl-CoA glycerate (MCG) cycle (Yu et al., 2018), and the tartronyl-CoA (TaCo) pathway (Trudeau et al., 2018), the CETCH pathway (Schwander et al., 2016) and the rPS-MCG cycle (Luo et al., 2022). Except for the first one, others have not been implemented in organisms, and still in the stage of in vitro development.

The MCG cycle (Yu et al., 2018) utilizes an abundant oxygen-insensitive carboxylase, phosphoenolpyruvate carboxylase (PPC), and forms a cycle with 3-, 4-, and 2- carbon intermediates (Fig. 1c). The additional carboxylase can increase CO_2 fixation rate, and the product, acetyl-coA is a key metabolite in all cells. Thus, the advantage of this cycle is that it is compat-

ible with existing organisms. This cycle was implemented in cyanobacteria *Synechococcus elongatus* PCC7942 (Yu et al., 2018) and showed increased CO₂ fixation and acetyl-CoA production.

Since RuBisCO exhibits a limitation in distinguishing between oxygen and CO₂, other carboxylases have been used, including PPC mentioned above, crotonyl-CoA carboxylase/reductase (CCR) (Schwander et al., 2016) and a new-to-nature glycolyl-CoA carboxylase (GCC) (Scheffen et al., 2021). To utilize CCR as the carbon-fixing enzyme, a synthetic cycle, CETCH (Schwander et al., 2016), has been designed and tested in vitro. Another synthetic cycle rPS-MCG (Luo et al., 2022), which utilizes both CCR and PEPC has also been demonstrated in vitro with optical controls for cofactor regeneration. Both cycles have shown in vitro CO₂ fixation activities comparable to plants. Another synthetic pathway, the TaCO pathway, utilized a rationally designed and then evolved GCC to carboxylate glycolyl-CoA to make glycerate, which is then assimilated in the CBB pathway (Scheffen et al., 2021).

III. Deleting a cyanobacterial CBB brake to boost carbon fixation

Similar to plants, cyanobacteria utilize solar energy to split water and produce NADPH and ATP to support carbon fixation via the CBB cycle. Nevertheless, the cellular energy status is dynamic because of light fluctuation and various stress conditions. Controlling utilization of energy and reducing equivalents by carbon fixation is pivotal for cell growth and survival. Sophisticated regulatory mechanisms have been reported to control the CBB cycle in cyanobacteria. The post-translational oscillator KaiABC modulate circadian gene expressions, based on phosphorylation states of the core clock regulators, to control various processes including photosynthesis and nitrogen fixation (Ishiura et al., 1998). Additionally, the thioredoxin-modulated protein CP12 regulates some CBB enzyme activities based on the redox state through protein complex formation (Lucius et al., 2022). In contrast, regulation of carbon fixation in response to energy fluctuations remains unclear. We recently discovered that *S. elongatus* phosphoketolases (SeXPK) plays an important role in dynamic regulation of carbon fixation flux (Fig. 2a) (Lu et al., 2023).

We found that under light conditions, *S. elongatus* PCC7942 contains high levels of ATP, which inhibits SeXPK through a unique ATP binding domain (Fig. 2a), which exists between two SeXPK subunits in the dodecamer (Lu et al., 2023). However, during the transition from light to dark

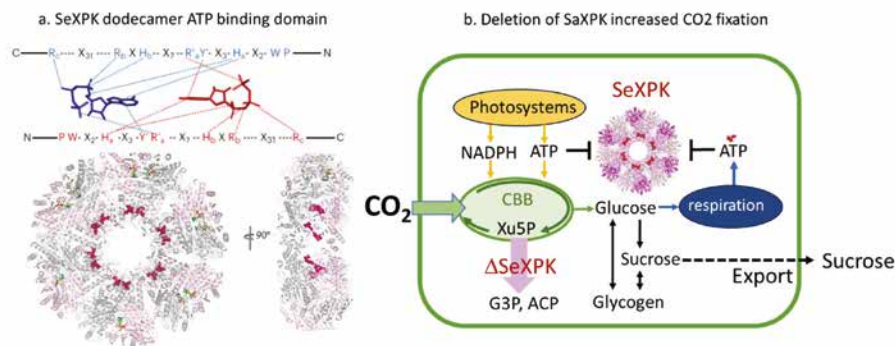


Figure 2. Discovery and Deconstruction of a cyanobacteria CBB brake. a) *Synechococcus elongatus* phosphoketolase (SeXPK) possesses a unique ATP binding site. Upon binding, ATP inhibits its activity of converting the CBB cycle intermediate, xylulose 5-phosphate (Xu5P) to glyceraldehyde 3-phosphate (G3P) and acetyl-phosphate (Acp). b) When SeXPK is deleted, *S. elongatus* increases its CO₂ fixation rate under fluctuating light conditions, and exports sucrose.

conditions, the ATP level drops within a minute and XPK is released from ATP-inhibition. During this time, SeXPK becomes active and divert the CBB cycle intermediate Xu5P to C2 and C3 compounds (Fig. 2b). This action drains the CBB cycle intermediates and shuts down carbon fixation immediately. When the cell is exposed to light again, its ATP level rapidly returns to normal, and inhibits XPK activity to allow carbon fixation. Therefore, XPK serves as a metabolic “brake” to control carbon fixation under fluctuating light conditions (Fig. 2b).

Interestingly, when XPK is deleted, *S. elongatus* exhibited higher CO₂ fixation under fluctuating light conditions. This fluctuating light condition can also be created in high density cultures by self-shading. The DSeXPK mutant showed 60% higher CO₂ fixation in high density shaking culture (OD730=4-7). Unexpectedly, the additional carbon fixation all resulted in sucrose and secreted into the medium (Fig. 2b) (Lu et al., 2023). This result creates a possibility to use *S. elongatus* for sucrose production after optimizing productivity. Since cyanobacteria grows faster than plants, the system may provide an additional avenue for agricultural production.

IV. Evolution engineering for methanol assimilation

Methanol is the only C1 compound that exists in the liquid form under ambient conditions. It can be derived from either CO₂ or methane, both of which are potent greenhouse gases. Therefore, effective methanol

utilization may open the door for recycling C1 greenhouse gases to useful products. Thus, developing an industrial organism that can assimilate methanol as the sole carbon source for growth is essential for such an application. Compared to glucose utilization, methanol utilization requires only three additional enzymes (methanol dehydrogenase, Hps, Psi) to complete the pathway. Thus, it was deceptively straightforward to engineer *E. coli*, a glucose-utilizing industrial microorganism, to grow on methanol as the sole carbon source. However, several groups have attempted to achieve this goal, but have met with surprising difficulties. We have developed a strategy to evolve an *E. coli* strain to grow on methanol as a carbon source, and identified the mechanistic difficulties involved.

The first step was to create an *E. coli* strain whose growth on xylose was dependent on methanol (Fig. 3a) (Chen et al., 2018). This is done by deleting two essential genes *rpiAB*, such that the xylose metabolic product ribulose 5-phosphate (Ru5P) cannot be further metabolized. This strain was then rescued by introducing three heterologous genes, *mdh*, *hps*, *psi* which can convert methanol and Ru5P to fructose 6-phosphate, which then enters the normal glycolytic pathway. This strain can grow on xylose only in the presence of methanol, and is called a methanol auxotroph.

The second step was to evolve this methanol auxotroph to wane down its dependence on xylose by expressing *rpiAB*. This step turns out to be the most challenging. After several trials, we discovered that the first step of methanol metabolism produces formaldehyde, which is highly toxic because it causes DNA-protein cross-linking (DPC) (Chen et al., 2020). During cell growth, formaldehyde accumulates and diffuses out of the cell to affect neighboring cells. So even if some beneficial mutations emerge to allow cell growth, formaldehyde accumulation at the stationary phase eventually killed the cell. Thus, this cell is not evolvable. Native methylotrophs have evolved a formaldehyde detoxification process that oxidizes this compound to CO_2 , but it is counter productive if we try to utilize this compound for growth. Furthermore, since this compound can freely diffuse through the cell membrane to poison the neighboring cells, beneficial mutations are difficult to be selected or enriched in a culture. We used both rational design and evolution techniques and successfully developed a synthetic methylotrophic *E. coli* strain (Chen et al., 2020).

To further improve the synthetic methylotrophic *E. coli*, we developed a copy number tuning technique. This technique is based on an unexpected finding that a particular sequence on the *ddp* operon was able to intervene

the replication of Bacterial Artificial Chromosome (BAC) and cause it to form tandem repeats of concatemers with a wide-range of copy number distribution. We used this technique to dynamically tune the expression level of enzymes that are involved in formaldehyde consumption. The introduction of this *ddp*-BAC containing the formaldehyde consumption genes (RHTTP) was able to facilitate the cell to overcome the evolutionary block of DPC, even though at the cost of higher protein burden. After the cell continue to evolve, the cell was able to accumulate beneficial mutations that were able to avoid DPC more effectively, and tuned down the copy number of *ddp*-BAC::RHTTP by an IS insertion of the *recA* gene. Thus, this dynamic copy number tuning technique provides an expediency to overcome an evolutionary block and allow the accumulation of other beneficial mutations to occur at a much lower frequency.

After several rounds of evolution, we have developed a synthetic methylotrophic *E. coli* strain with a doubling time of 3.5 hours, faster than native model methylotrophs, *Methylobacterium extorquens* AM1 ($T_d \sim 4\text{hr}$) and *Bacillus methanolicus* at 37°C ($T_d \sim 5\text{hr}$).

Conclusion

Biology has provided one of the best approaches at scales to assimilate C1 greenhouse gases. However, native organisms did not evolve to solve the problems caused by the anthropogenic release of C1 greenhouse gases. Artificial design and evolution must be used to accelerate this process. Here we showed a few examples to increase C1 assimilation by redesigning the carbon fixation cycle in plants and microorganisms. In many cases, human design can only provide the biochemical capability to enable new biochemical pathways. It must be followed by laboratory evolution for fine-tuning to fit organismal growth demand. The examples discussed here provide some enabling tools for further investigations. These tools can be pivotal in developing sustainable solutions for reducing greenhouse gas concentrations and mitigating climate change.

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A SOLUTION TO ANTIMICROBIAL RESISTANCE: ANTIMICROBIAL PHOTODYNAMIC THERAPY

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■ <https://www.doi.org/10.65398/UJME2698>

Abstract

Modern medicine is exploring new approaches to combat infections associated with antimicrobial resistance. Among these, antimicrobial photodynamic therapy (aPDT) stands out for its ability to target pathogenic microbes effectively. This review focuses on methods to enhance aPDT on planktonic cells and biofilms. The combination of nanoparticles and antibiotics with the photosensitizers results in improved aPDT.

1. Introduction

Antimicrobial resistance (AMR) occurs when microorganisms no longer respond to antimicrobial medicines. Because of AMR, antimicrobial medicines become ineffective, increasing the risk of severe illness. Thus, preventing resistance is crucial in microbial treatment. AMR is a problem for all countries at all income levels. The World Health Organization (WHO) has listed the following as some of the high-priority pathogens in urgent need of drug development [1]: Methicillin-resistant *Staphylococcus aureus* [2], vancomycin-resistant *Enterococcus faecium* (VREF) [3], and multidrug resistant *Klebsiella pneumoniae* [4]. The emergence of multidrug resistant fungus *Candida auris* is of particular concern [5].

In addition, biofilms, linked to over 60% of antibiotic-resistant infections, present significant challenges in biomedicine [6]. Biofilms strongly resist antimicrobial agents [7]. The concentration of antimicrobials needed to eradicate biofilms is about 1,000 times higher than that for planktonic bacteria, partly due to the biofilm matrix acting as a physical barrier to antibiotics [8]. A biofilm is a well-organized community of bacteria embedded in an exopolymeric substance (EPS) that is attached to a biotic or abiotic surface [9]. EPS plays a key role in the development, maintenance as well as protection of biofilms against dehydration and the effects of antimicrobials [10]. Compared to planktonic cells, biofilm cells exhibit different physiological and metabolic states. They account for up to 80% of all bacterial chronic infections in humans and the formation of bacterial biofilms is one

of the major causes of bacterial resistance [11]. Antimicrobial photodynamic therapy (aPDT) has been proposed for the elimination of drug resistance.

2. Antimicrobial photodynamic therapy (aPDT)

The concept of cell death induced by the interaction of light and chemicals was first reported by Osar Raab, a medical student working with Professor Herman von Tappeiner in Munich [12]. Subsequent work in the laboratory of von Tappeiner coined the term “Photodynamic action” and they showed that oxygen was essential for cell death.

aPDT is an antimicrobial treatment modality based on using light of a specific wavelength in combination with a photosensitizer, leading to a phototoxic reaction that induces micro-organism destruction, known as the photodynamic effect [13]. aPDT is expected to eradicate micro-organisms through the photosensitized production of toxic reactive oxygen species (ROS) including singlet oxygen in the presence of molecular oxygen [14], as shown in Fig. 1. This approach causes irreversible cell membrane damage preventing resistance against aPDT [15]. aPDT is particularly good for dental [16] and dermatological [17] applications, where there is light irradiation of a tissue containing microorganisms that were previously exposed to a photosensitizing (PS) dye.

In dentistry, aPDT can be considered as an adjunctive to conventional mechanical therapy. The liquid photosensitizer placed directly in the periodontal pocket can easily access the whole root surface before activation by the laser light through an optical fiber placed directly in the pocket [18].

In aPDT, the molecules absorb light to the first excited state (S_1) and can further undergo a spin conversion through intersystem crossing (ISC) from S_1 to long-lived triplet state (T_1), where they either emit photons through phosphorescence or can undertake other chemical reactions known as either type I or type II pathways. In type I, a photosensitizer reacts directly with the biological substrates or oxygen to generate ROS such as hydroxyl radical, peroxide and superoxide anion radicals through electron transfer. In the type II reaction, the activated PS transfers energy to the $3O_2$ forming $1O_2$, Fig. 1. Both pathways can occur simultaneously and are responsible for the inactivation of multiple pathogens, with the most dominant pathway being largely dependent on the photosensitizer used [19].

An ideal photosensitizer should exhibit high photochemical reactivity, which is essential in producing ROS. The PS should have a high absorption coefficient, be photostable, have thermal and chemical stability.

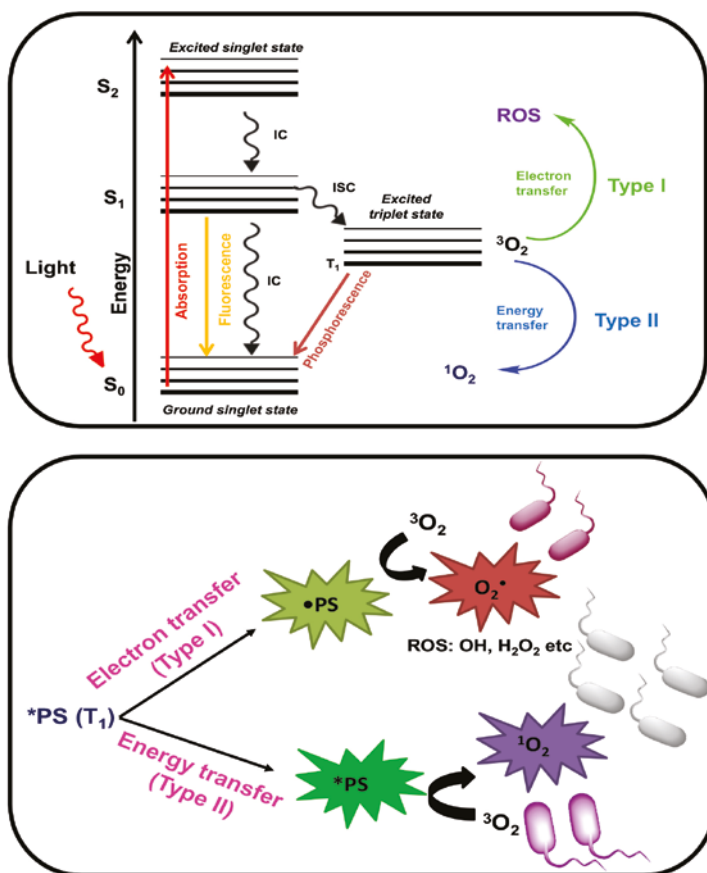


Figure 1. a) The Jablonski diagram illustrating the photochemical process of photosensitizers (PS) upon activation and b) typical reactive oxygen species generation in aPDT. ISC = intersystem crossing. ROS = reactive oxygen species.

The PS should be able to produce high triplet quantum yields and have a long triplet lifetime to allow for efficient energy transfer to ground-state oxygen [20]. PSs can be classified into two categories, porphyrinoids and non-porphyrinoids, Fig. 2. Porphyrinoids are aromatic tetrapyrrole macrocycles derived from natural pigments such as chlorophyll. Porphyrinoids include porphyrin, chlorin, phthalocyanine, bacteriochlorin, porphycene, texaphyrins, and sapphyrins [21,22]. The non-porphyrinoids refer to aromatic dyes that can generate singlet oxygen, including methylene blue, rose

bengal, 4,4-difluoro-4-bora-3a,4a-diaza-s-indacene (BODIPY), eosin blue and erythrosine B [22,23], Fig. 2. aPDT can be used on various microorganisms such as fungi, parasites, bacteria, and viruses.

aPDT is effective against fungal infections since it can be combined with other therapies and is applicable to patients who are unresponsive to oral antifungal agents [24]. Currently, aPDT is widely used to treat many cutaneous fungal infections [24].

The emergence of drug resistance in parasites has been a major concern [25]. Human pathogenic parasites have been killed by combinations of PS and light, thus aPDT has successfully been employed against parasites [25]. In a similar fashion to viruses, there have been several reports on the use of aPDT to kill yeasts [26]. Membrane damage and the consequent increased permeability was reported to be the cause of cell death using aPDT for yeasts [26].

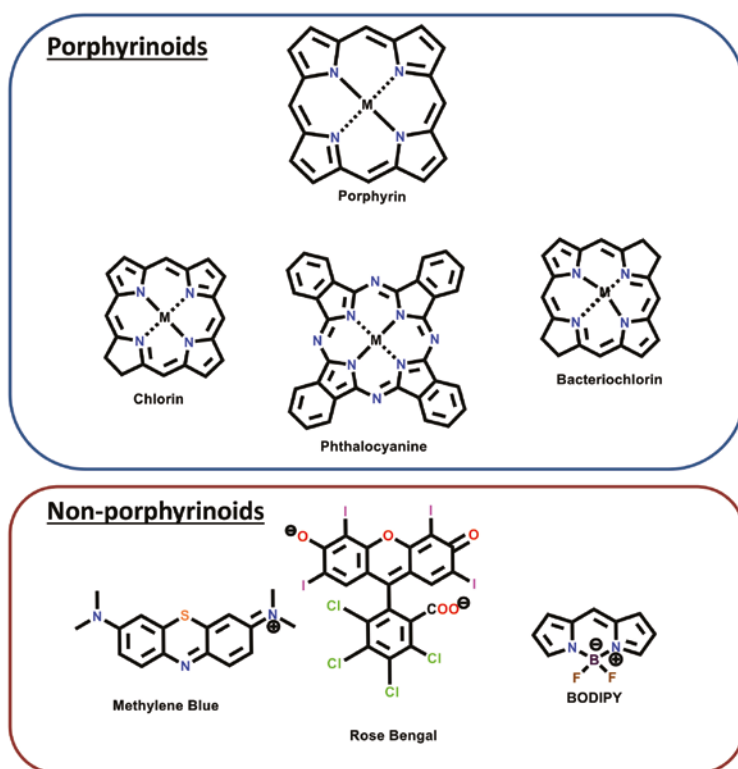


Figure 2. Chemical structures of common photosensitizers.

Antimicrobial PS should be able to kill multiple classes of microbial cells at relatively low concentrations and low fluences of light. The PS should also be reasonably nontoxic in the dark and should show selectivity for microbial cells over host mammalian cells.

2.1. Focus on Bacteria

The activity of photosensitizers on bacteria can be determined using Log reductions, equation 1

$$\log \text{ reduction} = \log (A) - \log (B) \quad (1)$$

A and B are the number of viable colonies (in colony forming units/mL) of bacteria for the untreated and treated samples. A log reduction > 3.0 and a 99.9% reduction in viability is classified as an efficient antimicrobial agent [27].

Gram-negative bacteria are responsible for many life-threatening infections, and they are often resistant to the most commonly used antibiotics, making the search for new antibacterial drugs and alternative therapies, such as aPDT, very important [28]. Neutral PSs have been efficiently applied in the aPDT of gram-positive bacteria while cationic PSs are effective for both gram-positive and gram-negative bacteria [29,30]. In aPDT, the PS employed needs to penetrate the cell wall. Cationic molecules can more easily bind to the cell wall of Gram-negative bacteria, which is negatively charged. Gram-negative bacteria have a double lipid bilayer sandwiching the peptidoglycan layer plus an outer layer of lipopolysaccharide, resulting in a low degree of permeability, while gram-positive bacteria possess a porous peptidoglycan layer and a single lipid bilayer [31]. The outer membrane of Gram-negative bacteria plays an important role that is related to resistance to many antibiotics that are highly effective against Gram-positive bacteria. This explains the higher prevalence of Gram-negative infections in the modern hospital environment [32]. Therefore, aPDT killing of Gram-positive bacteria is definitely much easier to accomplish than that of Gram-negative bacteria. Thus, it is more difficult to obtain highly potent PS to mediate PDT of Gram-negative bacteria since their membrane barrier prevents the uptake of anionic and neutral PS [33,34]. Nevertheless, different approaches have been documented aimed at efficiently killing Gram-negative bacteria via aPDT. Several of these approaches involve the optimization of the chemical structure of the PS.

2.2. *The role of nanoparticles in aPDT*

Nanoparticles (NPs) are particulates with one or more nanoscale dimensions (1–100 nm). Their superior physicochemical, optical, and thermal properties make them valuable functional materials for various technologies [35,36]. There are numerous varieties of NPs, including metallic and non-metallic NPs [37]. Nanoparticles based on metals and silica offer advantages over organic nanoparticles, such as having easy-to-control particle sizes, shape, porosity, and monodispersibility; however, these inorganic nanoparticles do not readily degrade in the biological system [38]. Some of the main advantages of using NPs include their ability to target drugs and enhance aqueous solubility of other materials; they have tuneable properties and large surface areas, which allow for multiple functional groups to be added to their surfaces [39]. In addition, NPs can influence the photophysicochemical properties of a photosensitizer and they tend to exhibit size-related properties that differ significantly from those observed in fine particles or bulk materials [40,41]. To enhance the efficacy of aPDT, nanoparticles can be conjugated with photosensitizers. NPs can act as a drug-delivery system and consequently facilitate the internalization of photosensitizers; this approach allows for the use of low concentrations of photosensitizers and the shortest light exposure time [42]. The loading of the PSs onto carbon nanomaterials can be achieved by π - π stacking noncovalent functionalization, since both have benzene rings in their structure. The covalent chemical functionalization with the PS molecule can be done through formation of amide or ester bonds. This surface functionalization helps to improve the photophysicochemical properties and the targeting and therapeutic efficiency of the PSs for aPDT. PSs are often ineffective when using lower concentrations and light doses, especially in the case of Gram-negative bacteria biofilms, due to the complexity of their envelope. aPDT activity improves (log reduction increase) in the presence of NPs.

2.3. *aPDT-antibiotic dual therapy*

aPDT-antibiotic dual therapy combines two therapies, photodynamic and chemotherapy, that act in two quite different therapeutic mechanisms resulting for reductions in treatment time, drug doses, side effects, and drug-resistance problem [43]. In dual photo-chemotherapy, three approaches can be considered: sequential administration of a PS and an antibiotic drug, the use of PS and antibiotic conjugates, and co-encapsulation of the two in a nanocarrier. As an example, ciprofloxacin (CIP), a quinolone-

type antibiotic that is commonly used to treat infections in humans, [44] was employed together with a phthalocyanine for aPDT [45]. The data show that greater antibacterial activities are obtained in the dual therapy of aPDT and chemotherapy when the biofilms were sequentially photoinactivated with PSs, then incubated with ciprofloxacin. Coupling aPDT with CIP offers several advantages, preferably when aPDT precedes the antibiotic. This is because aPDT can disrupt the EPS layer, lower the expression of the antibiotic resistance-conferring genes and inactivate the drug modifying enzymes beforehand. Subsequently, this will result in an increased uptake of the antibiotic and potentiate a localized photo-destructive effect, making the cells inside the biofilm more susceptible to the antibiotic. It is

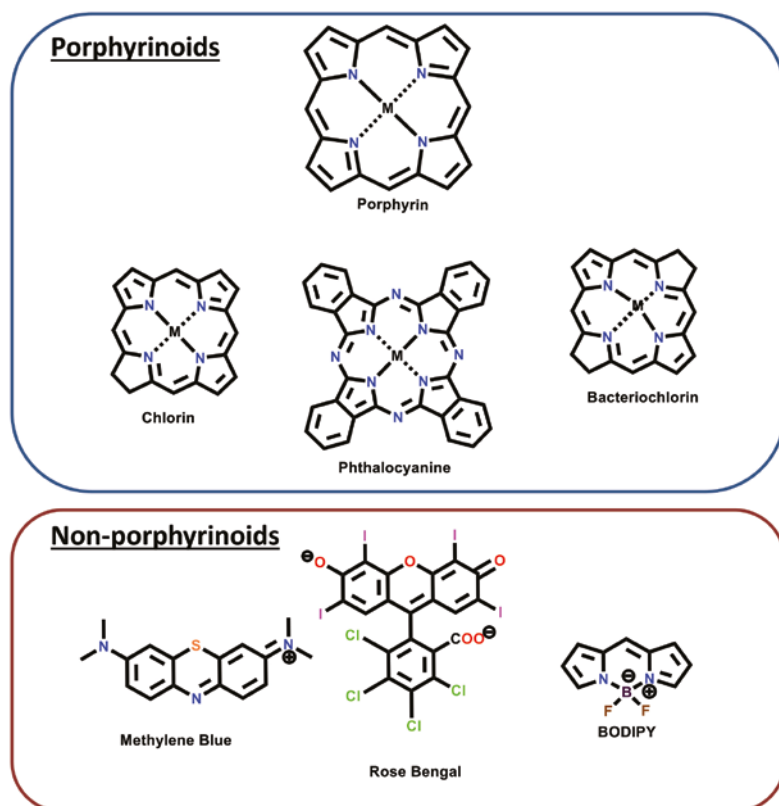


Figure 3. Synergistic effect of 15 min aPDT mediated by a porphyrin and ciprofloxacin on bacterial biofilms of (A) *S. aureus* and (B) *E. coli* with irradiation at 415 nm.

worth emphasizing that the complete inhibition of biofilms only occurred under the influence of simultaneous treatment with aPDT and ciprofloxacin [45]. This combination totally eradicated the biofilm, regardless of the incubation time, Fig. 3. The presence of two modes of action enables the killing of bacteria in their stationary growth phase (inside biofilms) and to lower the toxic effects of antimicrobial chemotherapy on normal host tissues. The synergistic effect of aPDT combined with antibiotic treatment could be a promising strategy to overcome the multidrug-resistant bacterial infections caused by biofilms.

Other molecules such as ampicillin (AMP) and gallic acid have been used together with PS for aPDT [46,47]. AMP has antimicrobial activity [48]. According to reports, gallic acid (GA) has a potent antibacterial effect that induces cell death by disrupting the membrane integrity of some gram-negative and gram-positive bacteria [49–51]. Thus, combining AMP or GA with PS for aPDT resulted in enhanced antibacterial activity.

3. Conclusion

Antimicrobial photodynamic therapy (aPDT) of various microorganisms is effective against planktonic and biofilm forms, with cationic photosensitizers showing high log reductions values against bacteria. Combining photosensitizers with antibiotics or other antimicrobial agents enhances aPDT. Thus, aPDT is the solution to drug resistance. Conjugating photosensitizers to nanoparticles further improves aPDT.

Acknowledgments

This work was supported by the Department of Science and Innovation (DST), Innovation and National Research Foundation (NRF), South Africa through DSI/NRF South African Research Chairs Initiative for Professors of Medicinal Chemistry and Nanotechnology (UID 62620), Rhodes University, CSIR National Laser Centre Rental Pool Program and by DSI/Mintek Nanotechnology Innovation Centre-Sensors.

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BIOLOGICAL CLOCKS, THERMOTOLERANCE, AND FITNESS: SEEING THROUGH THE EYES OF A FUNGUS

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■ <https://www.doi.org/10.65398/ZPIT9966>

*“God saw that the light was good;
and God separated the light from the darkness”
(Genesis 1:4).*

Undeniably, the history of life on this planet has been shaped by the unceasing cycles of days and nights. While the Bible recounts that “*God separated the light from the darkness*”, the study of biological systems reveals that evolution has indeed partitioned processes in a daily fashion, with some occurring during the day and others at night. Likewise, Ecclesiastes 3:1-22 verses that “*To everything, there is a season, a time for every purpose under heaven*” and, certainly, cellular and organismal activities are governed by the same principle: diverse processes are temporally compartmentalized peaking, for example, at defined times each day, or even exhibiting seasonal rhythms [1]. And importantly, while biological rhythms can be observed at various scales (i.e. from milliseconds to seasons), I will focus on those with a periodicity of 24 hours: the so-called circadian rhythms, from the Latin *circa diem* (close to a day). These rhythms have a period close to, but not exactly, 24 hours under constant conditions. However, when exposed to environmental cycles of temperature or light, they synchronize precisely to a 24-hour period, akin to the precision of a wristwatch.

While the study of circadian clocks spans the entire tree of life, including prokaryotes, my focus here will be on fungi. These organisms serve as powerful model systems for exploring and unraveling the complexities of circadian rhythms. By studying these phenomena in fungi, we can also gain unique insights into the evolution of clocks and the nuanced mechanisms of light-sensing systems

Circadian clocks allow individuals to synchronize different aspects of their biology with earth’s day-night rhythms. *Bona fide* circadian rhythms *i)* persist in the absence of external cues with a free running period of *circa*

24 h, *ii*) maintain this period in a range of physiological temperatures (temperature compensation) and *iii*) “entrain” to the environment [2–4]. Clocks are not only fascinating from an evolutionary and molecular perspective, but are also relevant for cellular and organismal function: they temporarily compartmentalize diverse and even antagonizing cellular processes, such as catabolic and anabolic ones. This allows the optimization of organismal physiology, synchronizing it with the environment and permitting individuals to anticipate daily rhythmic changes [5–7]. Not surprisingly, genetic or environmental perturbations of clocks can compromise fitness [8], alter organismal interactions [9,10], and have physiological severe consequences, including significant health problems [11,12].

The evidence suggests that circadian clocks have appeared – independently – at least three different times throughout evolution, and consequently, the analysis of the core-clock elements across the tree of life shows that they do not share a common evolutionary origin [13,14]. Nevertheless, despite the lack of sequence conservation, the architecture of the central clock circuit (oscillator), which is based on a transcription-translation negative feedback loop (TTFL), is highly conserved across eukaryotes from fungi to mammals: a compelling example of convergent evolution, permitting to translate mechanistic details learned in, for example, a fungus, to humans and *vice versa* [15,16]. Indeed, from fungi to animals, circadian oscillators are based on a one-step transcription-translation negative feedback loop (TTFL) where positive elements (the transcription factors WC-1/WC-2 in *Neurospora*; CYC/CLK in *Drosophila*; BMAL1/CLOCK in mammals) directly drive the expression of a negative element (FRQ; TIM/PER; CRY/PER, respectively). The negative elements form multiprotein complexes – that always include the enzyme Casein Kinase 1 (CK1) – and feedback to inhibit the activity of the positive elements [3,17]. As a result, the expression of new negative elements is shut down, whereas the existing negative components are progressively modified (mainly by CK1) until inactivated and degraded, time at which a new cycle of expression starts. The entire process takes about 24 hours [4]. Notably, most of the molecular details of eukaryotic core-clocks have been elucidated in a handful of model species: the fruit fly *Drosophila melanogaster*, the fungus *Neurospora crassa*, mice, and humans [3,4,12]. However, as more genomes have been sequenced, it has become increasingly clear that numerous examples exist in various taxa across the Tree of Life where, despite the presence of circadian phenomena, genes encoding canonical clock components are not identifiable. These

findings suggest the possible existence of other, so far uncharacterized, pervasive (yet evasive) clock mechanisms [18,19]. Together with others in the field, we have considered this possibility, and in the following pages, I will outline how we are tackling this and other problems in fungi.

For almost half a century, the filamentous fungus *N. crassa* has played, along with the fruit fly *D. melanogaster*, a key role in the molecular dissection of the circadian clockworks [20]. In *Neurospora*, the TTFL is composed of a positive element, the White-Collar Complex (WCC), comprised of the transcription factors White Collar-1 (WC-1) and White Collar-2 (WC-2), which promotes the expression of the negative element *frq*, encoding for the protein FREQUENCY (FRQ). One full cycle takes about 22.5 hours under constant darkness and can be tracked by monitoring rhythms in *frq* mRNA and protein levels [21,22]. Under daily Light: Dark or temperature cycles these rhythms entrain to exactly 24 hours, yet *Neurospora* is arrhythmic under constant light. One feature that has made *Neurospora* a great circadian system is the ease with which circadian rhythms can be tracked by monitoring the daily appearance of “conidial bands” representing the synchronous formation of asexual spores before dawn. The clock controls sporulation and a large extent of *Neurospora* biology, including daily rhythms in ~40% of its transcriptome [21,22]. In addition, the use of luciferase as a real-time reporter has allowed us to promptly track the inner workings of the core clock by monitoring changes in bioluminescence, which has dramatically expedited the analyses of circadian mechanisms in this fungus [22]. Despite significant advances in this model system, our understanding of clocks in fungi other than *Neurospora* remains limited [18]. This is striking when we consider that the fungal kingdom encompasses between 2–5 million species, of which ~5% have been formally described. Fungi have played a crucial role in shaping life on Earth by, among other things, driving nutrient cycles, supporting plant evolution through symbiosis, and continuing to play key roles in both terrestrial and aquatic ecosystems [23]. Thus, considering the mesmerizing fungal diversity and the relevance of these organisms, it is surprising that when it comes to molecular circadian mechanisms, of the dozens of thousands of known fungal species, most of the knowledge is circumscribed to only one, the ascomycete *N. crassa*.

From an evolutionary perspective, the scenario is even more intriguing when considering that of the ~1090 fungal genomes currently available, FRQ homologs are restricted to a limited number of clades [5]. Moreover, in fungi whose genome exhibit all putative core-clock elements, the charac-

terization of molecular rhythms has often been hard to achieve, which contrasts with the robust phenotypic and molecular circadian rhythms seen in *Neurospora* [18]. This raises fundamental questions about the evolutionary origins of FRQ and how ecological niches may have influenced the loss or retention of FRQ-based clocks across diverse fungal taxa.

We and others have sought to close this knowledge gap by exploring the extent and impact of circadian clocks in various fungi. So far, some of the findings highlight the importance of circadian rhythms in multiple aspects of the fungal daily life, modulating metabolism, interactions with other organisms, and even virulence. However, evidence of a functional clock has been elusive in some species. Moreover, some of these studies have uncovered numerous peculiarities, such as unexpected extra-circadian roles for FRQ and robust rhythms (of ecological relevance) in species without any identifiable conventional clock components [18,24]. Notably, while the absence of known core-circadian components appears widespread among major fungal taxa, this phenomenon is less common within animals or the green lineage. Indeed, in taxa outside the fungal kingdom, the occurrence of rhythms in organisms lacking obvious eukaryotic clock components is more of an exception than the rule [18].

Yet, work in *Neurospora* not only continues to inform us about mechanistic details of the clockworks but also facilitates adopting strategies to tackle fundamental aspects of the evolution of eukaryotic clocks. Thus, we adopted a Synthetic Biology approach by challenging the known evolutionarily conserved circadian TTFL architecture, creating a semi-synthetic clock in *Neurospora*, for which we combined (by transcriptional rewiring) canonical clock components and elements naturally restricted to the circadian output pathways [25]. The resulting semi-synthetic clock not only was functional, but it also exhibited new unexpected properties, regarding how light cues are processed. But, even more relevant in the context of this discussion is that we were able to show that the evolutionarily conserved clock circuitry (one-step TTFL) is only one of the possible topologies that a circadian oscillator could assume. Yet, the existing conventional TTFL is the simplest design and, by parsimony, is what nature has always chosen.

In addition, fungi offer several advantages for reexamining the adaptive role of circadian clocks. Over the past years, several colleagues have critically revisited the general concept of the “adaptive advantage of clocks” and the pressures behind the evolution of circadian systems [8,26]. Inspired by these ideas, we have begun applying circadian paradigms to investigate the

importance of a functional clock in *Neurospora*, evaluating its impact on fitness under stressful rhythmic environments. Thus, we have been examining whether the presence of a circadian clock can facilitate the appearance of increased thermotolerance. To do so, we expose *Neurospora* to rhythmic experimental evolution protocols, mimicking progressively increasingly hot environments. Currently, we are trying to interpret the preliminary results from ecological and evolutionary angles.

The proverb “*seeing is believing*” may have modern origins, but it is often associated with the skepticism of Saint Thomas the Apostle, as depicted in the Gospel of John (John 20:24-29). This proverb suggests that visual evidence facilitates understanding, a concept that helps to introduce some of our molecular studies on how *Neurospora* senses light—a critical process for synchronizing its circadian clock with day-night cycles. In gene expression analyses, we frequently rely on limited datasets to draw conclusions, oftentimes without the possibility of observing the complete expression patterns of our gene of interest, especially across a range of stimuli. In light of this, I would like to discuss some of our recent work in the laboratory, where we aim to map the dynamic range of gene expression triggered by light. In doing so, I hope to captivate (or provoke?) readers with the idea that the sensitivity offered by such a molecular system enables *Neurospora* to “see” the intricate details of its surroundings and that, moreover, we can get to “see” what *Neurospora* has perceived.

Neurospora and many other fungi can sense blue light via a LOV (Light Oxygen Voltage) domain in proteins such as WC-1 (part of the White-Collar Complex). *Neurospora* senses light and quickly elicits transcriptional responses, spanning the activation of hundreds of genes [27]. One of these genes is *frq*: therefore, upon light, FRQ levels go up, changing the internal “time” and, therefore, adjusting the phase of the clock. Thus, WC-1 stimulation by light is key in synchronizing and entraining the clock to environmental Light: Dark cycles [22]. But how sensitive is WC-1 to light, and how well can it tell apart lights of various intensities? Actually, most of what we know about WC-1 responses are snapshots of *Neurospora*’s full ability to respond to light: they correspond to data points gathered under a handful of intensities and after a fixed number of minutes. Yet, we were interested in obtaining (literally) an accurate picture of the response of *Neurospora* to a broad range of radiance levels.

Using luciferase under the control of a *light-responsive* promoter, we can stimulate *Neurospora* with light and measure its response in real-time, mon-

itoring changes in luciferase levels (bioluminescence). It is worth mentioning that we can grow *Neurospora* on large agar plates, yielding a high-density mycelial mat resembling a “cottony canvas”. On top of this mycelial mat, we can focus light of different intensities, inquiring whether the genetic response (measured as bioluminescence output) yields a result resembling the original stimulus. Therefore, we have called this approach “*Live Canvas*,” as it represents a living surface (fungal mat) where light images can be perceived (seen), genetically processed, and emitted back as bioluminescence (*manuscript in preparation*). Relevantly, an image emitted by a projector is in itself a map of light intensities. Thus, our layman’s question is whether an image, projected for one second onto a fungal mat, can elicit a bioluminescence response that accurately replicates the projected image. If so, it would indicate that WC-1 can effectively capture the detailed information encoded in a full array of light intensities. Remarkably, the results surpassed our expectations, demonstrating a broad dynamic range of responses to a wide spectrum of radiance levels. This suggests that WC-1 activity yields an analog response rather than a digital one. Notably, in the field of optogenetics (where light is used to control biological processes), there are several examples of using a projected image to induce a genetic response that mirrors the original picture. However, these experiments typically require at least 20 hours of light stimulation to produce the desired effect [28,29]. This radically differs from the situation in *Neurospora*, where we can trigger a robust response with one second of stimulation, evidenced by the appearance of a clear image within minutes. Fig. 1 contains an example of a *Live Canvas* image generated with the picture of an artistic representation of the Shroud of Turin: projecting this picture on top of a *Neurospora* fungal mat (of 30x18 cm) yielded, within minutes, a response that recreated with exquisite resolution the original projected picture. While the aesthetic appeal of the *Live Canvas* (essentially a gene expression response) is undeniable, it is equally important to emphasize the rich biological and molecular insights that can be gleaned from such a “simple” bioluminescent image. Indeed, the *Live Canvas* prompts us to reexamine crucial aspects of *Neurospora* fungal biology, such as inconsistencies in the current understanding of photoadaptation or the syncytial state of *Neurospora* in solid culture. In addition, such images provide dynamic series of gene expression of unprecedented resolution, establishing a biological platform where we can analyze with great detail the consequences and effects of distinct mutations affecting key aspects of light-triggered transcription (i.e., chromatin remodeling, nuclear export, etc.).

Consequently, we have extended this approach into the circadian field, exploring additional scientific aspects underlying the *Live Canvas*. As explained earlier, light can shift the *Neurospora* circadian clock; thus, if this fungus is exposed to light, the “phase” of the clock will be shifted depending on the strength of the light perturbation [22]. Thus, if we have a reporter strain, where luciferase is under the control of a promoter that is both light-induced and clock-regulated, in constant darkness one would



Figure 1. Live Canvas image of the Shroud of Turin. The photograph corresponds to a 1 Megapixel CCD-acquired image of a bioluminescent response generated by *Neurospora* after being stimulated with a map of light intensities, encoded in a projected image. An artistic depiction of the Shroud of Turin was projected for 1 second on top of a fungal mat of a *Neurospora* strain containing a luciferase reporter, under the control of a light-inducible promoter. The strain was cultivated on agar media in a glass tray (30 x 18 cm) that was kept in darkness for 1 day, after which the image was projected on top of the fungal mat for 1 second. Afterwards, it was monitored under a sensitive CCD camera, and luciferase activity (bioluminescence) was captured within the first 30 mins (exposure time 1 min). In the picture it is possible to see the edges of the glass recipient, and some of the imperfections of the agar. Special thanks to Dr. Consuelo Olivares-Yañez for her assistance and expertise in obtaining this image.

see synchronous levels of luciferase all over the fungal mat and, once every ~22.5 hours, the entire culture would show a coordinated peak of bioluminescence. However, suppose parts of the fungal mat (canvas) are shortly exposed to light. In that case, locally the phase of the clock will be altered: the clock will continue oscillating with the same periodicity but at a different phase, similar to having a different “local time”. The latter is akin to shifting from Eastern Standard Time to Pacific Time with a strong light exposure or to Central Standard Time with a weaker one. Thus, light can shift the phase of the biological clock, similar to moving to a new time zone. Therefore, we sought to explore whether a map of light intensities (delivered as a 1 second image projection) could be converted into a map of phase changes. The results prove that; indeed, it was possible to locally alter the phase of the clock such that the resulting map of phase alterations (throughout the fungal mat) creates an emergent property, allowing the visualization of the image appearing and disappearing over many days (*unpublished*). Indeed, it was possible to observe the picture as a bioluminescent image, appearing, fading away, and then reappearing the next day and for many days. While the visual effect is mesmerizing, it is also humbling to appreciate the precision of the *Neurospora* circadian system, witnessing how phase information can be faithfully maintained at the cellular level over multiple days.

Thus, if readers are willing to entertain the initial idea that *Neurospora* can “see” an image, I would like to push this concept even further by suggesting that *Neurospora* can “remember” what it has seen – possessing a form of photographic or eidetic memory, so to speak. While I leave that idea open for thought, I would like to conclude with a more fundamental – yet basic – question: why has a fungus like *Neurospora* evolved such a precise, accurate and sensitive light-measuring system? Another way to approach this question is to ask whether such sensitivity is a peculiarity of *Neurospora*’s ecological niche or a common characteristic among filamentous fungi possessing WC-1 homologs. Rather than attempting to elucidate an answer, I will conclude by pondering why *Neurospora* possesses such a clear and robust circadian clock, while other fungi either *i*) have FRQ-based clocks that seem less robust or *ii*) rely on clock mechanisms that do not depend on FRQ. Personally, I see all these questions and challenges as excellent opportunities to explore the diversity of the fungal world and deepen our understanding of how these biological agencies have evolved to respond to their environment, day after day, since the dawn of time, ultimately learning to measure time itself. I think we are finally beginning to obtain a true “picture” of these intricate mechanisms.

Acknowledgments

I want to express my deep appreciation for the dedication and enthusiasm of a remarkable team of individuals who, over the years, have contributed to shape our lab into what it is today. I would also like to acknowledge funding sources, in particular ANID-Millennium Science Initiative Program-Millennium Institute for Integrative Biology (iBio ICN17_022), the international Research Scholar program of the Howard Hughes Medical Institute, and the Richard Lounsbery Foundation.

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■ V: ASTRONOMY AND CHANGING WORLD VIEWS

ASTROBIOLOGY AND THE ANTHROPOCENE: HOW SEARCHING FOR LIFE ELSEWHERE CAN HELP US SUSTAIN LIFE ON EARTH

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■ <https://www.doi.org/10.65398/YQQL8034>

Tracing life's history through an astrobiological lens can provide valuable perspective on the global changes and challenges facing us today. Many of the same technological developments which have allowed humans to thrive globally, and to dangerously alter our planet, have also allowed us to launch satellites into space, and thus to observe and monitor these changes. Without this new power of self-observation, we would not have a fighting chance of making the corrections necessary to make wiser choices about how we live on this planet. Beyond Earth observations, exploration of other planets has delivered vital new knowledge applicable on our home planet. For example, studying the atmospheres of Venus and Mars has provided crucial insights into climate change. There are many concrete examples of space technology advancing sustainability, but I will focus more here on the gift of perspective provided by my field of Astrobiology, which seeks to understand the prevalence and distribution of life in the universe.

The perspective of Astrobiology is one of deep space and deep time. The *deep space perspective* is one of plenitude, humility and wholeness. We have learned that our location in the universe, at least in terms of physical position, is nothing special, and that planets are more abundant than we can comprehend.

Carl Sagan spoke of the “great demotions” through which science has put humanity in its place, by successively undermining the ways in which we had once seen ourselves as central and important in the story of the universe (Sagan, 1994). Arguably, the realization that we are now in the “Anthropocene,” that our agency, or lack thereof, has allowed us to become unwitting planet changers, has recast this narrative. Perhaps we are, after all, significant players in the story of the Earth. The Anthropocene is the proposed name for the epoch of geologic time we have now entered, characterized by human-driven planetary-scale changes. By recognizing and naming the Anthropocene are we in effect reversing things and giving ourselves a “great promotion”?

Perhaps. But it is questionable whether this is really such a great honor to bestow upon ourselves, for we don't know whether ultimately we are to be planet wreckers or planet savers. Strangely, we may have to choose between these two. By becoming agents of planetary change we may have lost the option of remaining merely innocent bystanders or bit players in evolution.

Yet how much agency do we really have if we can't obviously choose our role in Earth's story? We seem to have agency on certain small scales of organization. We are obviously very skilled at building machines and organizing activities that cumulatively act to change our world. So, we are *acting* at a global scale. Yet have we shown *agency* or *intentionality* on that planetary scale? Arguably, yes, we have. There are examples of global-scale efforts to fix environmental problems, such as the Montreal Protocol, which is more or less on track to successfully repair the damage we've done to Earth's protective stratospheric ozone layer. Other examples from the realm of global health show that planet-wide efforts can eradicate deadly diseases. Yet the most concerning planetary changes being caused by humans do not result from globally coordinated efforts or plans but rather from accidental concatenations of more localized and short-term decisions. If we, global humanity, have agency over our planetary-scale impact it is – so far at least – limited and tentative. Thus, perhaps that “great promotion” toward recognizing our importance in the current chapter of Earth history should be felt not as a pat on the back but more of a kick in the rear. If we want to translate our significance into something to be proud of then we have some work to do.

The search for identifiable biosignatures on other planets is requiring us to understand life as a component of a larger physical system. In the 1970s scientists working on the first life detection spacecraft mission to Mars realized that we might recognize life on a planet simply by observing its perturbing effects on the planet's atmosphere. After all, Earth's atmosphere, heavily oxygenated by life, is drastically different from what we would expect on a lifeless Earth. This insight was also the origin of the Gaia hypothesis, the idea that life should be understood as a planetary-scale phenomenon, so deeply embedded in the cyclic behavior of our Earth that the distinction between the living and nonliving components is difficult to discern and perhaps illusory (Margulis and Lovelock, 1974). Today we have learned that planets are abundant throughout our galaxy. As we are building new telescopes to search for the signs of life on exoplanets, the notion of planetary-scale life is essential to this quest. It is in finding biological

perturbations breathed into the atmospheres of these worlds by our cosmic brethren that we invest our hopes of finding them.

Astrobiology has allowed us to see ourselves, and our biosphere, as fundamentally and deeply entwined with other planetary systems. The contrast between living and lifeless planets drives home to us that we are not discrete organisms living on an otherwise dead world, but parts of a grand cyclic planetary scale biosphere, exchanging matter and energy with our environment and with other living systems. This perspective can help us to see our current global environmental challenges as more than just momentary technical puzzles to be solved. Rather the challenge is to fundamentally reimagine our role in Earth systems. In order to build a healthy technosphere we will need a deepened understanding of the relationship between planet and life – between Earth’s biosphere and its other physical systems – so that we can learn to work with the Earth instead of against it, to gracefully integrate our global scale activities within these systems.

The *deep time perspective* also promotes humility, and identification with a larger whole. As an astrobiologist I am fascinated by the major historical transitions in planetary evolution and how they reflect the evolving relationship between planet and life. This informs my view of recent debates over the Anthropocene. How does our time fit into the larger narrative of planetary evolution?

In our quest to understand how life fits into the story of the universe, we’ve traced our existence back to the earliest signs of life on Earth, 3.5 to 3.8 billion years ago, and life’s inferred origin perhaps 4 billion years ago. We’ve followed the story back to the origin of our planet itself in a flurry of energetic collisions 4.5 billion years ago and all the way to the birth of our universe, which exploded into being from a singularity of nothingness about 13.8 billion years ago.

In a certain sense our appearance here is astonishingly ephemeral compared with the timescale of cosmic evolution. As individuals our existence is fleeting, and even our tenure as a genus or a species, hundreds of thousands to millions of years, is incredibly brief measured against geological or cosmic time. However, if we choose to identify with our biosphere, with “Gaia”, then this can radically change our temporal perspective. We, Gaia, have been here for about 4 billion years. We have been here for nearly one third of all time. That is something. Yet we have quite recently begun behaving, and altering our planet, in wholly unprecedented ways.

Many scientific discussions of the Anthropocene have focused on the debate over when it began. However, that obscures perhaps the most interest-

ing and crucial question raised by the transition to a largely human-altered planet: When and how will it end? What will the Anthropocene ultimately be in Earth history? Viewed from some future deep-time perspective will it have been a momentary event (like the Cretaceous/Paleogene boundary 65 million years ago, marked by the centimeter thick layer of fallout from the dinosaur-killing asteroid), a prolonged interval (like the Paleocene Epoch that lasted from 66 to 56 million years ago), or could it actually become something even more significant?

I suggest that this transition may not be, as proposed, merely an Epoch boundary, but something much rarer. Epoch boundaries are a frequent occurrence throughout Earth history. Epochs are the relatively thin and numerous layers usually drawn toward the right side of the geological time scale. Their boundaries are often characterized by episodes of global change and extinction events. Much more consequential are the boundaries separating the very long phases, called Eons, usually shown on the far-left side of this chart. Each of these represents a fundamental branching point in our planet's history. Our dynamic Earth has gone through many fluctuating changes, but geologists separate our planet's long history into only four Eons, during which our planet's character was fundamentally different from the others. I suspect we may now be at another of these pivotal moments, and our planet may be at the beginning of its 5th Eon, which I have proposed we call the "Sapiezoic" (Grinspoon, 2016).

The first Eon was pure hell. All the planets started with conditions hostile to any kind of life, with leftover debris from planet formation crashing down from space, erratically smashing, churning and heating their surfaces, making red-hot atmospheres first of vaporized rock and then of boiling steam. In recognition of these conditions, Earth's first Eon is named the Hadean. All that we've learned about the violent, collisional nature of planetary origins suggests that each rocky planet started off with its own private Hadean. Eventually, the cosmic pounding subsided and the steam turned to rain which filled the oceans.

The transition to Earth's second Eon, the Archean, came around 4 billion years ago, and corresponds roughly to the arrival of stable habitable conditions and the origin of life. Although we are still testing our hypotheses with ongoing and planned missions of exploration, our nearest neighbors, Venus and Mars seem to have both experienced transitions to conditions similar to those which enabled an origin of life on Earth, including geologically active surfaces and warm, organic-rich seas. Such a phase may be com-

mon for rocky planets at the right distance from their stars, and life might possibly have begun on all three of these planets. Apparently only on Earth did a robust, long-lived, global biosphere develop and become a permanent, planet-altering feature. The transition to the Archean Eon was when Earth diverged from the path of a lifeless planet. Since then, biology has been a major driver of geologic change.

The extent of biological influence on our planet is still being discovered. Beyond obvious anomalies such as an oxygenated atmosphere, ozone layer, and continents whose reflective properties and cloud cover are greatly altered by forests, Earth's topography, mineral diversity, and perhaps the material properties of its interior, have been altered by life's infiltration into its physical and biogeochemical cycles. As astrobiologist Colin Goldblatt has said: "The distinguishing characteristic of Earth is planetary-scale life."

We don't know exactly how or when Earth went from being a dead planet graced by some organisms to a planet thoroughly permeated with life, but certainly by Earth's third Eon, the Proterozoic, Earth could be described as a living world. The beginning of the Proterozoic, 2.5 billion years ago, corresponds roughly to the Great Oxygenation Event when, chemically, life took over. In discovering solar energy, photosynthetic bacteria began to flood the atmosphere with oxygen, a poisonous gas that caused mass extinction, but also created the chemical conditions for animal respiration and the protective ozone layer that allowed life to leave the oceans and colonize the land.

Then, 540 million years ago came the "Cambrian Explosion" – the sudden appearance of a myriad of complex, multicellular animal and plant life forms, including the body plans of basically all modern animals. This enabled, among many other things, the evolution of intricate nervous systems, elaborate behavior and learning. This burst of biological innovation is recognized as the beginning of the fourth and (so far) final Eon of Earth history – the Phanerozoic Eon, which continues to this day.

These four Eons of Earth history are each distinguished by a different role for life on the planet, and each Eon boundary represents a major shift in the relationship between life and the planet. The origin of life, the "oxygen catastrophe" and the origin of complex multicellular life each resulted in a permanently changed planet.

Now, this saga has reached the pivotal moment when humans have become a dominant force of planetary change, and geological and human history are becoming – perhaps irreversibly – conjoined. As a result, we are witness to, and party to, the advent of a radically new type of global

change: Self-aware cognitive/geological processes (Grinspoon, 2016; Frank et al., 2022).

Now that cognitive systems have gained a powerful influence on the planet, we are observing the effects of not only a new geologic force, but a new type of geologic force – one becoming aware of its own influence. I believe that the beginning of a time when self-aware cognitive processes become a key part of the way the planet functions is potentially as significant as the origin of life and the pivotal changes marking the other Eon boundaries in Earth history.

Yet, in order to qualify as the start of a new Eon, such a transition would also require extreme staying power. Eons typically last for at least hundreds of millions of years. Even if we accept that this new force represents a sufficiently radical break from the past – a fundamentally new phase in the planet/life relationship – can it possibly persist for such an interval?

Questions of civilization persistence over geological or cosmological timescales are familiar to theorists in the field of SETI (the Search for Extraterrestrial Intelligence), who have long recognized that the number of technological civilizations in the universe must be proportional to their average longevity (Bracewell, 1974). The literature of this field contains discussion of the potential longevity not just of human civilization, but of human-like civilizations elsewhere in the galaxy. What do we mean by “human-like?” That is a wonderful question which connects our essential nature, our exceptionalism compared to the rest of life, and our role on the planet. Can we, or can any technological civilization, persist for geologically meaningful timescales? Can a civilization become integrated into the cyclic functioning of its planet in a robust way, as life did on Earth (but apparently not on Venus or Mars) long ago?

For the Anthropocene to become the first epoch of a new Sapiezoic Eon would require a permanently changed planet in which cognitive processes become, as life did by the end of the Archean, a long-term stabilizing component of a functioning planet. This implies a radically different mode of interaction with the planet than is currently being exhibited by “intelligent” technological life.

The success of technological societies in increasing their populations and expanding their habitats and environmental reach can produce positive feedbacks which create instabilities and threaten catastrophe. The most basic imperatives of biological evolution (reproduction and survival) are likely to replicate this pattern on other planets with global biospheres which

develop complex, cognitively capable life. From a systems perspective, the early stages of a cognitive planetary transition are arguably highly unstable because global influence will likely always precede global awareness and self-control. Hence the dangers of our current “Anthropocene dilemma” (Grinspoon, 2016) where, like mindless automatons at the controls of a complex vehicle, we are a danger to ourselves because the scale and scope of our power exceeds that of our awareness.

However, conscious awareness of self-induced threats can initiate stabilizing negative feedbacks. Consider the stratospheric ozone depletion which arose as an unintended consequence of new technology. This threat to terrestrial habitability was recognized, studied and deliberated. Now, through global agreements it is being successfully mitigated, and serves as an illustrative example of the stabilizing negative feedback that can arise from self-recognition by global technological actors. Such examples suggest there are pathways by which cognitive geological processes could become a very long-lived and even permanent part of the Earth system.

Global technological influence clearly contains both peril and promise. Several scholars have described our near future as a bottleneck of technological adolescence and self-ignorance (Rees, 2003; Wilson, 2002). This implies that although we may not survive, we could also potentially get a handle on ourselves and learn to use our technology in ways that enhance, rather than threaten our survival. Our increasing powers of global influence are fundamentally unpredictable, but contain the potential for ruin & triumph, for existential threat as well as for circumventing natural and artificial disasters. The latter would require that we achieve a deep understanding of, and mastery over, both self and nature. In other words, it would require both technical and spiritual progress.

Are similar challenges likely to be faced by complex life elsewhere reaching a stage where cognitive processes become planetary processes? If so, then the technical, ethical and even spiritual choices and dilemmas facing extraterrestrial civilizations may resemble our own in some respects.

One does not have to be optimistic about humanity’s chances to see that the likelihood of such technological bottlenecks, if they can ever – even very rarely – be navigated – implies the possibility of a very different kind of planetary entity: An extremely long-lived technologically enhanced biosphere.

How might this vision affect the way we view our own future? It re-frames our task. And it puts our immediate challenges over the next century (devising agricultural and energy systems that can provide for the needs of

our population without wrecking the natural systems upon which we depend) against the backdrop of a much longer term challenge: Once we get over the short term (century scale) threat of destabilizing fossil-fuel induced climate change, we need to learn how to become a long-term stabilizing component of the planet. This will include: Over the next several hundred to thousand years, devising an effective asteroid and comet defense; Over the next several tens of thousands of years, learning how to prevent catastrophic natural climate changes, such as ice ages and intervening episodes of dangerous global warming; Over several billions of years we'll have to find a way to compensate for the warming sun and prevent the otherwise inevitable runaway global warming that will result from the sun's bright senescence. Or we'll need to move.

The origin of life represented a fundamental branching point, setting our planet on a path distinct from those of our neighbors. The origin of self-aware intelligent geology may represent another. If a Sapiezotic transition is something that can happen to some planets then, as we explore the universe and begin to decipher the nature of exoplanets, we may find there are 3 kinds of worlds: dead, living and *sapient*.

How rare are sapient worlds? This depends on whether a species that develops world-changing technology can evolve culturally to a state where it can apply this power sustainably, in the service of its biosphere. The answer to this question will determine both our own future chance of survival and the likelihood of finding a long-lived technological phase on other planets. Thus, the central question of SETI is also the central question that confronts humanity about our own future. Can technological intelligence become something built to last?

Can humanity make it through the technological bottleneck? To do so would require us to re-invent ourselves, to find a way to operate cooperatively on a larger scale than we have done previously. A look at our deep history shows that we have found such capacities when the need arose. *Homo Sapiens Sapiens* arose in Africa between 200,000 and 160,000 years ago after our predecessors were nearly wiped out by devastating climate change. We survived by using sophisticated new technology that required language and new modes of cooperation to meet what would otherwise have been existential threats (Marean, 2010). It is our nature to invent, to cooperate in new ways, to survive. Our current dilemmas require the same skills applied on new temporal and spatial scales. *We have done this before*. Although right now we are in danger of initiating a mass extinction, if we

get a handle on ourselves we could not only save our own civilization and call off the gathering extinction event but learn to prevent future asteroid impacts and ice ages. In the long run, by forestalling future mass extinctions and prolonging the life of the biosphere, we could be the best thing that ever happened to planet Earth.

When Carl Linnaeus, the Swedish botanist who invented modern biological taxonomy and nomenclature was looking for a name for the human species he chose *Homo Sapiens*, differentiating us from other primates by our quality of sapience, or wisdom. Perhaps this was overly optimistic. Or perhaps it was prescient. Whether or not we can live up to this name may depend on whether we can learn to gracefully integrate our technological prowess with the functioning of our planet, creating a *Terra Sapiens*. Nobody alive today will know whether we were able to begin this new Eon. We may not know for many millennia. But it gives us something to strive for.

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ADVANCING SUSTAINABILITY WITH SPACE TECHNOLOGY

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■ <https://www.doi.org/10.65398/ARNC1278>

Introduction

As humanity confronts the escalating challenges of climate change, resource depletion, food and freshwater availability and environmental degradation (cf. Steffen et al., 2015), space technology will play an increasingly central role in constructing solutions to maintain a sustainable planet. From monitoring Earth's weather and climate, to optimizing agriculture, to making more efficient use of resources, to communicating environmental conditions and threats, space-based technologies offer opportunities to foster a more sustainable future. By leveraging capabilities of satellites, sensors, communications, precise positioning systems, radiation-resistant semiconductors and computation, it is possible to observe, collect, analyze and disseminate information regarding the state of the planet. Such information can be used to develop informed strategies to protect and preserve the Earth for current and future generations. This contribution provides a sampling of applications based on past and current Earth-orbiting spacecraft and concludes with discussion of emerging technologies that are accelerating progress.

Earth Observation and Monitoring

Weather: One of the longest-standing contributions of space technology to sustainability is weather monitoring. From the 1960 launch of the first weather satellite, NASA TIROS-1 (Television Infrared Observation Satellite) (Stroud, 1961), satellites equipped with advanced sensors have continuously orbited our planet, collecting data that is used to understand and manage environmental changes. Satellites like the National Oceanic and Atmospheric Administration GOES (Geostationary Operational Environmental Satellites) (Schmit et al., 2017) and Japanese Himawari (Bessho et al., 2016) series provide real-time data on atmospheric conditions including cloud cover, water vapor, smoke, dust and aerosols, land and sea surface temperature and space weather. These satellites help to forecast weather

patterns, detect and monitor storms, and provide data for aviation route planning.

Space-based monitoring also provides continuous observations of incoming (solar) and outgoing (thermal) radiation. Satellites like NASA's Clouds and the Earth's Radiant Energy System (CERES) (Wielicki et al., 1996) measure these energy fluxes at the top of the atmosphere, allowing scientists to quantify changes in Earth's energy budget over time. These measurements have revealed an increasing imbalance, with more energy being trapped in the Earth system than escaping to space, primarily due to increasing greenhouse gas concentrations (Loeb et al., 2021).

Soil Moisture: The Soil Moisture Active Passive (SMAP) satellite (Entekhabi et al., 2010; Chan et al., 2018) plays a critical role in monitoring soil moisture levels worldwide. This data is essential for understanding drought conditions, improving agricultural productivity, and managing water resources more effectively. By providing detailed maps of soil moisture, SMAP helps farmers optimize irrigation, reducing water waste and promoting more sustainable agricultural practices.

Water and Ice Mass Transport: The Gravity Recovery and Climate Experiment (GRACE) (Tapley et al., 2004; Famiglietti & Rodell, 2013) and GRACE-FO (Follow-On) (Kornfeld et al., 2019) missions minute temporal changes in Earth's gravity from which changes in water reservoirs, including ice sheets, glaciers, and underground aquifers can be inferred. GRACE data have been instrumental in tracking the loss of ice mass in Greenland and Antarctica, as well as the depletion of groundwater in major aquifers, both of which have critical implications for sea-level rise and water security.

Sea Level Rise: Space geodetic observations provide validation of climate models that make predictions of phenomena such as sea level rise (cf. Nerem et al., 2016). Moreover, gravity, combined with sea surface altimetry, permits assessment of how much sea level rise is due to continental runoff vs. thermal expansion of the oceans associated with rising global temperatures. This is essentially an exercise in isolating mass vs. volume change of seawater. GRACE/GRACE-FO, for example, measure mass transport from continental ice sheets to the oceans (Rignot et al., 2011), while satellite altimeters, such as the TOPEX/Poseidon (Fu et al., 1984) or Jason (e.g., Pujol et al., 2016) satellites, provide information on volume change associated with thermal expansion and land runoff (Cazenave et al., 2018).

Greenhouse Gas Monitoring from Space: CO₂ and Methane

Greenhouse gas monitoring from space has become an essential tool in the global effort to understand and mitigate global warming. Among greenhouse gases, carbon dioxide (CO₂) and methane (CH₄) are of particular concern due to their abundance and warming potential. Space-based monitoring provides a comprehensive and continuous means to track these gases, providing information on sources, distribution and trends.

Carbon Dioxide (CO₂) Monitoring: Carbon dioxide is the primary greenhouse gas responsible for the anthropogenic greenhouse effect. Monitoring CO₂ from space enables scientists to quantify emissions, understand natural carbon sinks, and assess the effectiveness of climate policies. NASA's Orbiting Carbon Observatory-2 (OCO-2) (Crisp et al., 2017; Eldering et al., 2017), launched in 2014, provides information on the spatial and temporal variability of CO₂, particularly in regions where ground-based observations are sparse. The satellite's ability to detect small variations in CO₂ levels allows identification of specific emission sources, such as urban areas and power plants. Additionally, data from OCO-2 supports climate models that predict impact on global temperatures of future atmospheric CO₂ levels.

Methane (CH₄) Monitoring: Methane, although present in smaller quantities than CO₂, is a more potent greenhouse gas, with a global warming potential approximately 28 times that of CO₂ over a 100-year period. Methane emissions come from both natural sources, such as wetlands, and anthropogenic sources, including agriculture; fossil fuel extraction, production, transportation; and waste management.

The European Space Agency's Sentinel-5P satellite, equipped with the Tropospheric Monitoring Instrument (TROPOMI) (Veefkind et al., 2012; Hu et al., 2018), provides high-resolution measurements of atmospheric methane that permit detection of emissions from specific sources such as oil and gas facilities, coal mines, and landfills. This capability is essential for implementing and verifying mitigation strategies aimed at reducing such emissions.

Other satellites, such as the Japanese Greenhouse gases Observing Satellite (GOSAT) (Yokota et al., 2009) and the ongoing MethaneSAT mission (Jacob et al., 2016; Hamburg et al., 2021) by the Environmental Defense Fund (EDF), contribute to the global effort to monitor methane. These missions complement each other by providing data at different spatial resolutions and temporal coverage, ensuring a comprehensive understanding of global methane dynamics.

Resource/Land Management and Optimization

Space technology plays a crucial role in optimizing the use of Earth's resources. Precision agriculture (Mulla, 2013), for example, relies on satellite data to guide farmers in making informed decisions about planting and fertilization. By analyzing data from satellites like Landsat, which provides detailed imagery of the Earth's surface, farmers can monitor crop health, assess soil conditions, and identify areas that require intervention (Gitelson et al., 2012). This approach not only contributes to improving crop yields but also reduces the environmental impact of farming by minimizing the use of water, fertilizers, and pesticides.

Similarly, space-based systems are essential for sustainable fisheries management (Kourti et al., 2005). Satellites such as the European Space Agency's Sentinel-1 use synthetic aperture radar (SAR) to monitor illegal fishing activities, track fishing vessels, and assess fish stocks (Mazzarella et al., 2017). By providing real-time data on the location and behavior of fishing vessels, these systems help enforce regulations, protect marine ecosystems, and ensure the long-term viability of fish populations.

International Collaboration and Global Sustainability

Space technology facilitates international collaboration, which is vital for global sustainability efforts. Initiatives such as the United Nations' Sustainable Development Goals (SDGs) increasingly rely on space-based solutions to monitor progress and achieve targets (Bensi et al., 2021). For example, satellite data is used to track deforestation rates, monitor global water quality, and improve disaster response efforts (Tralli et al., 2005). Collaborative projects like the International Space Station (ISS) also serve as platforms for researching and developing sustainable technologies.

The Future

Sustainability solutions will increasingly be informed and aided by space-based technology due to ongoing advances that are driving down the cost of orbital assets, providing a more ubiquitous presence, and facilitating communication and analysis.

Launch costs: The emergence of innovative companies in the rocket business such as SpaceX, Blue Origin, and Rocket Lab has contributed to substantial decreases in launch costs (Jones, 2018) that are opening the space frontier, at least in Low Earth orbit (LEO).

SmallSats and CubeSats: Miniaturization of satellite technology including thrusters, altitude control, computing and communication systems are ena-

bling more frequent and inexpensive launches and result in improved temporal and spatial coverage. For example, the NASA TROPICS (Time-Resolved Observations of Precipitation structure and storm Intensity with a constellation of SmallSats) (St. Germain et al., 2021) was the first agency science mission implemented with CubeSats and provided high-resolution microwave observations of storm intensity, precipitation, and thermal structure relevant to improving storm forecasts.

Sensors: Advances in sensor technology, for example, in optical, hyperspectral and thermal infrared imaging, Synthetic Aperture Radar (SAR), Global Navigation Satellite System (GNSS) reflectometry, laser altimetry and LIDAR sensing, provide higher resolution and higher sensitivity observations of water quality, vegetation health, deforestation, land deformation, soil moisture, sea level, snow depth and weather and climate monitoring.

Communications: Space communications will play an expanding role in the global exchange of sustainability information, enabling the monitoring, analysis, and dissemination of data related to environmental and social sustainability. By facilitating real-time data transmission across vast distances, space-based communication systems such as Starlink (Shotwell & Venkatesh, 2020) support a wide array of sustainability initiatives, from climate monitoring to disaster response and agricultural management.

The role of space communication in providing information to remote and under-served communities, where access to traditional communication infrastructure may be limited (Loboguerrero et al., 2018) is worthy of special mention. Satellite-based communication systems can deliver vital information on, for example, weather forecasts, agricultural best practices, health and education, and disaster preparedness to these communities.

Advances in laser communications hold the promise of greatly increasing bandwidth over current radio systems. NASA's Lunar Laser Communication Demonstration (LLCD) (Borson et al., 2009) was NASA's first system for two-way communication using a laser instead of radio waves. LLCD featured a pulsed laser beam that transmitted data over the 239,000 miles between lunar orbit and Earth with a downlink rate of 622 megabits per second (Mbps).

Data Integration and Cloud Computing: Combining data from multiple sensors and satellites with ground-based data provides an increasingly holistic picture of environmental changes, allowing for better decision-making and predictive modeling. Advances in cloud computing enable the storage,

processing, and sharing of large datasets from satellite observations that facilitates real-time data analysis and broader access to satellite data.

Artificial Intelligence and Machine Learning: AI and ML algorithms are increasingly being used to process and analyze enormous volumes of satellite data. AI enhances the ability to detect patterns, predict environmental changes, automate the monitoring process and sort through vast data sets.

Space Resources: In the distant future, solar system objects may provide resources needed on Earth (Anand et al., 2012; O'Rourke & Jansen, 2020). For example, the potential for off-world mining of asteroids, some of which are rich in minerals and metals, presents the possibility of reducing the strain on Earth's finite resources. While still in the conceptual stage, such efforts could in principle revolutionize resource management, though such solutions are high risk due to technical complexity and prohibitive costs.

In the near term, space exploration will drive innovation in sustainable technologies, for example in improved components such as radiation-tolerant chips. And efficiency, resource recycling and waste reduction in space can lead to breakthroughs that can be applied on Earth.

Conclusion

Space technology offers powerful tools that contribute to advancing sustainability on our planet. By harnessing the capabilities of satellites and space exploration, we can monitor environmental changes, optimize resource use, and develop innovative solutions to the climate change and other challenges to the human condition. As civilization continues to explore space, it is essential to ensure that technological advancements contribute not only to our knowledge of the universe but also to the protection and preservation of our home planet.

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CHANGING ASTRONOMY AND AI: THE CASE OF RUBIN OBSERVATORY AND ITS LEGACY SURVEY OF SPACE AND TIME

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■ <https://www.doi.org/10.65398/WWUM1964>

1. Changing Astronomy and Astrophysics

Major advances in our understanding of the universe have historically arisen from dramatic improvements in our ability to “see”. With the development of advanced instrumentation we have been able to parse radiation detected from distant sources over the full electromagnetic spectrum in increasingly subtle ways. These data have provided the detailed information needed to construct physical models of planets, stars, galaxies, quasars, and larger structures and to probe the new physics of dark matter and dark energy.

Over the past few decades, advances in technology have made it possible to move beyond the traditional observational paradigm, focused on small samples of cosmic sources or individual objects, and to undertake large-scale sky surveys. During the last decade, sky surveys across the electromagnetic spectrum have collected petabytes of astronomical data for billions of sources. These survey projects, based on a synergy of advances in telescope construction, detectors, and, above all, information technology, have dramatically impacted nearly all fields of astronomy and astrophysics.

With the increase of data volume and data complexity, modern computational technologies, such as machine learning and AI methods, are necessary tools to reduce, analyze, and comprehend these data. Modern algorithms are able to classify and predict the paths of comets and asteroids, uncover subtle patterns in galaxy large-scale sky distribution, as well as to help with mundane tasks that would require prohibitively large or expensive human effort. As an example, a recently created large language model called *astroBERT* can help researchers search and navigate a sample of 15 million scientific papers on astronomy (Grezes et al. 2022).

Astronomers have been successively using such algorithms for over three decades (for a compendium of the most popular machine algorithms in astronomy, see Ivezić et al. 2019a). The rapid recent development of machine learning and AI methods goes hand in hand with the rapid development of

astronomical surveys. I will illustrate this synergy here by focusing on the NSF-DOE Vera C. Rubin Observatory that is being constructed in Chile.

The Rubin Observatory will revolutionize the way we explore the cosmos. Its first 10-year project, the Legacy Survey of Space and Time (LSST), will collect about 60 petabytes of raw image data and produce *the largest catalog of celestial objects in history* – it will include about 20 billion galaxies and a similar number of stars: for the first time, astronomers will have cataloged more objects than there are living people on Earth!

2. The Case of Rubin Observatory

The primary goal of Rubin Observatory is to conduct LSST and deliver a 500-petabyte set of data products that will address some of the most pressing questions about the structure and evolution of the universe and the objects in it. The Rubin Observatory's LSST is designed to address four science areas (for more details, see Ivezić et al. 2019b):

- Probing dark energy and dark matter.
- Taking an inventory of the solar system.
- Exploring the transient optical sky.
- Mapping the Milky Way.

The scientific questions that the Rubin Observatory will address are profound, and yet the concept behind the design of the Rubin Observatory is remarkably simple: conduct a deep survey over an enormous area of sky; do it with a frequency that enables images of every part of the visible sky to be obtained every few nights; and continue in this mode for ten years. The working paradigm is that all scientific investigations will utilize a common database constructed from an optimized observing program.

The Rubin Observatory Summit Facility is located on the Cerro Pachón ridge in north-central Chile, and its construction will be completed in 2025.

2.1 The Simonyi Survey Telescope and LSST Camera

The Rubin Observatory takes advantage of new technologies to provide a qualitatively new capability for astronomy. The Rubin Observatory houses the Simonyi Survey Telescope, an 8.4-meter telescope with a novel, three-mirror design. The telescope's compact shape allows it to move quickly from one point in the sky to the next. It will image the sky continuously each night, on an automated cadence, and over the course of the ten-year survey will collect about 800 images of each location over half the sky.

The Rubin Observatory LSST Camera is the largest digital camera ever constructed for the field of astronomy. The size of a small car and weighing more than 3 tons, the 3200-megapixel camera has a field of view of about 10 square degrees.

In addition, Rubin Observatory will include a complex data management system, described below.

2.2 Rubin Observatory Software Tools

As with all large modern surveys, the large data volume, the real-time aspects, and the complexity of processing involved require that the survey itself take on the task of fully reducing the data. The data collected by Rubin Observatory will be automatically reduced to scientifically useful catalogs and calibrated images, and delivered to users using a custom access platform and tools.

The entire software framework developed for the needs of the Rubin Observatory includes several million lines of code and is mainly written using the programming languages python and C++. The required software can be divided into three main groups: i) management of the Observatory, i.e. telescope, camera, dome, etc. ii) correction of imperfections in images, calibration of images, and finding and measuring astronomical objects in images, iii) tools to access data via the Internet. I will briefly illustrate their main features.



Figure 1. part of the Rubin Observatory control interface in the control room during observation preparations.

Practically all processes at the Rubin Observatory are controlled by software. The telescope and dome are large, complex and very sensitive mechanical systems (each has a mass of about 300 tons). For example, deformations of the surface of the primary mirror caused by gravity and thermal stresses are corrected about 10 times per second using 156 cylinders that from the underside of the mirror (gently!) push or pull the mirror with an accuracy of a few nanometers. The positions and orientation of the secondary mirror and camera are managed with similar accuracy. Figure 1 shows part of the control interface in the control room during the preparations for the observation. The Rubin control room is very similar to the control room of large industrial systems, for example, nuclear power plants.

Each observing night, Rubin will capture about a thousand 3,200-megapixel LSST images. Deciding exactly where to point the telescope and with which filter the camera should optimally capture the next image is a complex optimization step and includes a detailed consideration of the observing conditions (what time of night is it, where is the Moon and in what phase, is the atmosphere stable, how many images have already been collected, etc.). Such a decision needs to be made every forty seconds, so due to speed and complexity it is necessary to use a computer program (called “LSST Scheduler”). In other words, Rubin’s observing system, telescope

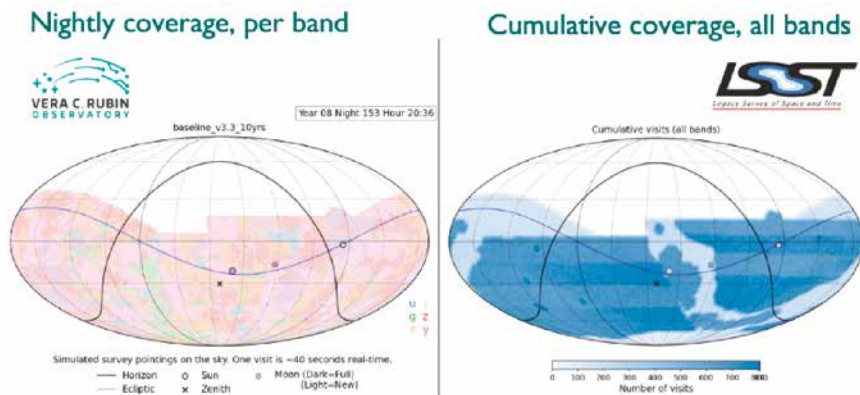


Figure 2. the distribution of LSST pointings in the sky during one (simulated) observation night (left), and the total number of observations up to that night (right). Astronomers on observation duty will use such an interface to monitor the decisions of an autonomous AI program that will “decide” about 1,000 times in one night where exactly to point the telescope and with which filter the camera should take the next image. Over 10 years, Rubin will capture over two million LSST images.

and camera, is essentially an AI-powered robot that will observe all night on its own with minimal supervision from astronomers (see Figure 2).

The software pipelines for processing LSST images are the most complex part of Rubin's software due to the large amount of data (about 20 TB each observing night) and the need for fast data processing (data on objects that have changed brightness or position compared to previous observations will be available to everyone via the Internet within just 60 seconds after taking a new image). The reason for the large amount of data is Rubin's huge field of view and 3,200-megapixel camera (Figure 3 left). In the past, astronomers used to visually study images of the sky (Figure 3 right), but that way of working with LSST data is no longer possible. Additionally, sensitive LSST images look very complex due to the large number of partially overlapping objects (see Figure 4, right). Through the work of about a hundred Rubin programmers specialized in astronomical algorithms, computer programs have been developed over ten years that "know" how to "recognize" objects in images and measure their features such as position, brightness, angular size and shape (Bosch et al. 2018). Figure 5 shows a small part of the sky where the computer recognized six objects and calculated an excellent image model that is almost identical to the observed scene.

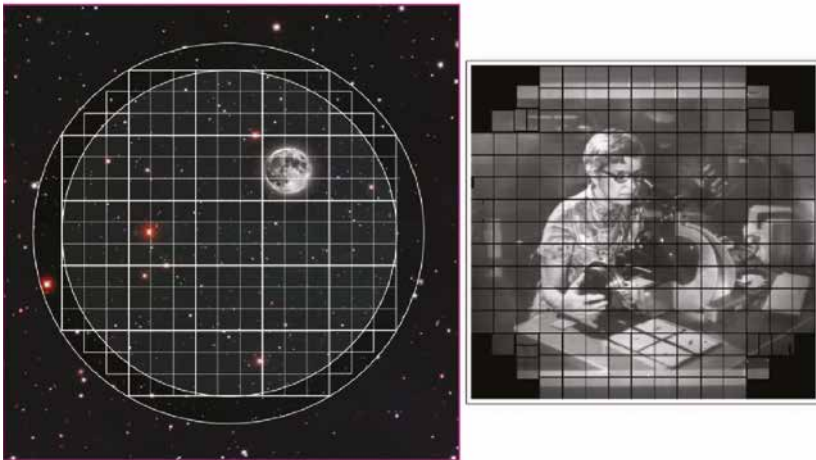


Figure 3. Rubin's field of view is about 100 times larger than the typical field of view for large telescopes, and about 45 times larger than the full Moon. In the picture on the left, each of the 201 small squares is one sensor (CCD) with 16 megapixels. The image on the right was taken with the LSST camera; it shows a photo of Vera Rubin in the lab studying photographs of galaxies.

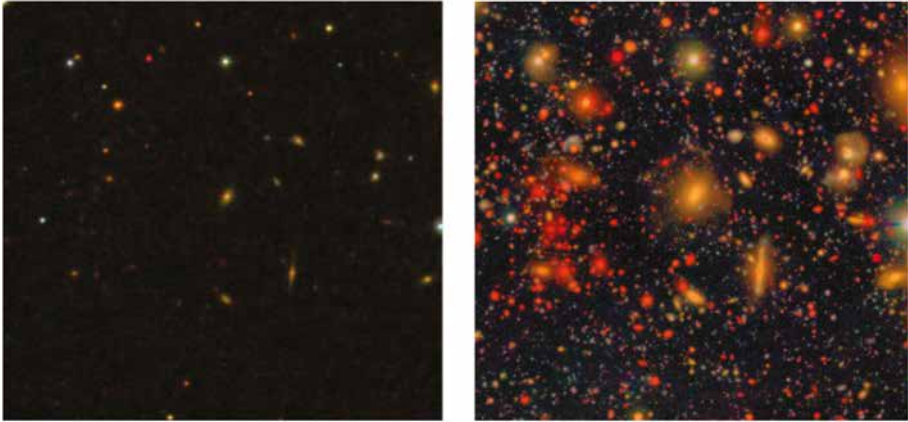


Figure 4. a comparison of an image of a patch of sky (the side of the square is about one-tenth the diameter of the full Moon) from the Sloan Digital Sky Survey (left) with an image of the same patch of sky from the Subaru Telescope (right) that has similar sensitivity to what the LSST images will have. Due to better sensitivity, many more objects (mainly galaxies) are visible in the right image. The half of the sky that the LSST will cover is about 8 million times larger than this image.

Without the help of these advanced algorithms, it would be impossible for astronomers to figure out what the expected tens of billions of objects in LSST images will teach us about the Universe!

It is anticipated that several thousand astronomers and physicists will regularly use Rubin’s LSST data, while the interface for popularization and work with the public, available to everyone in the world, expects millions of visitors. The software for accessing scientific data is organized in the Rubin Science Platform (RSP; O’Mullane et al. 2021). Figure 6 shows the RSP interface with three main data modes. The portal is a web interface for interactive analysis of a relatively small number of objects. Jupyter notebooks option enables the search of the entire database and the analysis of selected data using programs that the user can develop and use without the need to “download” the data to the local computer (see Figure 7). This method of data access and analysis enables working with LSST data from any part of the world, from Chile to Rome.

3. Discussion and Conclusions

The LSST survey will open a movie-like window on objects that change brightness, or move, on timescales ranging from 10 sec to 10 yr. The survey

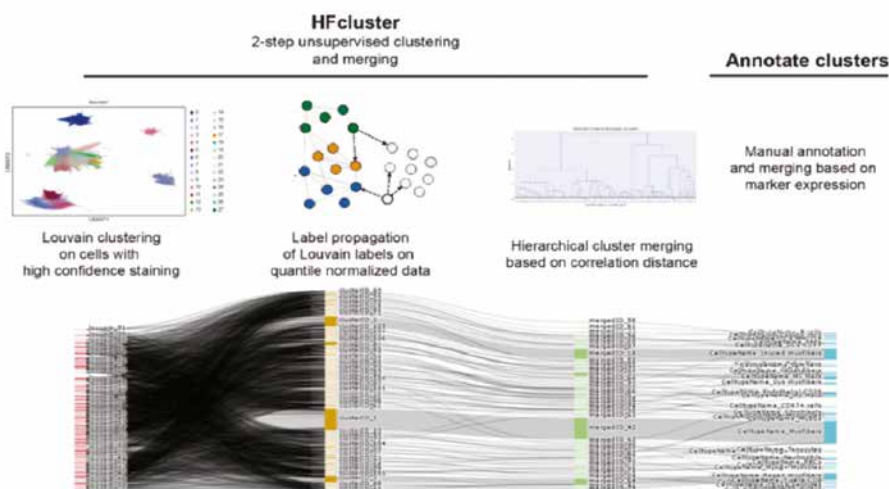


Figure 5. an example of how Rubin software will analyze LSST images. The image in the middle is an observed image of the sky, and the image on the left is a computer model (Bosch et al. 2018). The image on the right is the difference between the two images and shows that the computer explained the observed image almost perfectly, including the recognition of six objects.

will have a raw data rate of about 20 TB per night and will collect about 60 PB of data over its lifetime, resulting in an incredibly rich and extensive public archive that will be a treasure trove for breakthroughs in many areas of astronomy and physics. This archive will represent the largest catalog of celestial objects in history – it will include about 20 billion galaxies and a similar number of stars, with a total of about 32 trillion observations. With Rubin data we will all understand our Universe better, chronicle its evolution, delve into the mysteries of dark energy and dark matter, and reveal answers to questions we have yet to imagine.

Modern computational technologies, such as machine learning and AI methods, are necessary tools to reduce, analyze and comprehend these data. The LSST archive, available through Rubin Science Platform, will be mined for the unexpected and used for precision experiments in astrophysics. Rubin Observatory’s LSST will be in some sense an internet telescope: “the ultimate network peripheral device to explore the universe, and a shared resource for all humanity” (B. Gates, priv. comm.).

In summary, modern astronomy is critically dependent on modern computational technologies. By and large, it is a positive development that helps us improve our knowledge of origin and development of the universe.

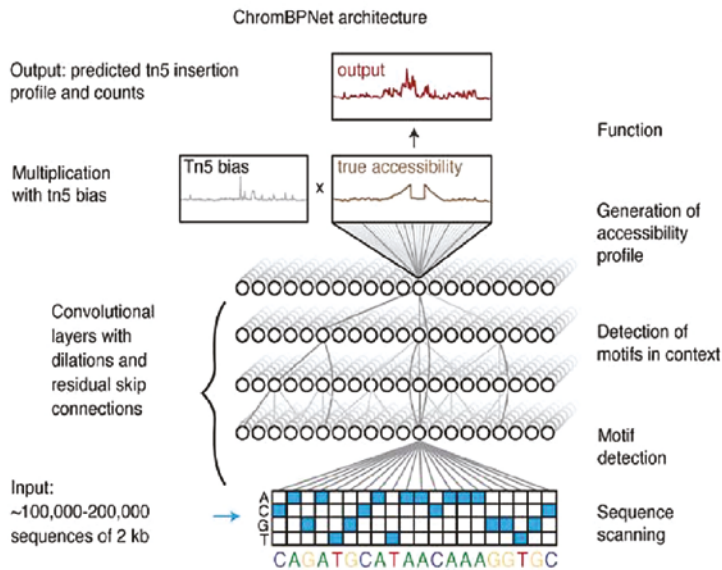


Figure 6. interface to Rubin Science Platform with three different ways to remotely access Rubin’s LSST data.

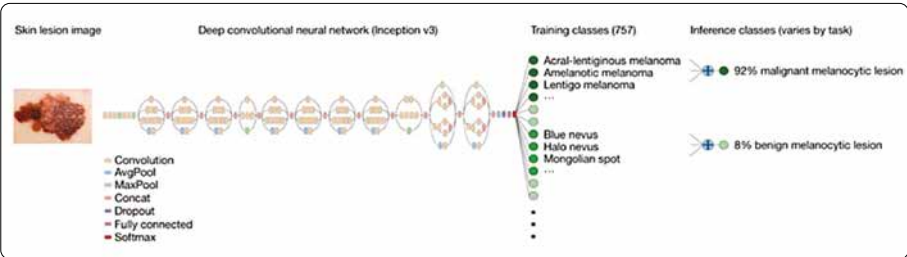


Figure 7. illustration of future work with LSST data using the Notebooks option from the Rubin Science Platform with simulated data and the python programming language.

Nevertheless, it is not without shortcomings. I will conclude by referring to Hogg and Villar who in their position paper “Is machine learning good or bad for the natural sciences?” (Hogg & Villar, 2024) answer this question with “Both!”.

Acknowledgments

This material is based on work supported in part by the National Science Foundation through Cooperative Agreement 1258333 managed by the As-

sociation of Universities for Research in Astronomy (AURA), and the Department of Energy under Contract No. DE-AC02-76SF00515 with the SLAC National Accelerator Laboratory. Additional LSST funding comes from private donations, grants to universities, and in-kind support from LSSTC Institutional Members.

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NEW ADVANCES IN EXOPLANET SCIENCE WITH JWST – THE HYCEAN PARADIGM

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■ <https://www.doi.org/10.65398/BXPR8704>

Abstract

The discoveries of thousands of extrasolar planets over the last three decades have revealed their ubiquity and diversity in physical characteristics. Exoplanets known today range from giant planets larger than Jupiter to rocky planets smaller than Earth over a wide range of temperatures, orbital parameters and host stars, including several in the habitable zone. The advent of JWST is revolutionising atmospheric spectroscopy of exoplanets with unprecedented constraints on their atmospheric compositions and physical processes, internal structures and potential habitability. Recently, a new class of temperate sub-Neptune exoplanets, called Hycean worlds, has been theorized as a promising avenue in the search for life beyond the solar system with JWST. Hycean worlds are planets with H₂-rich atmospheres and planet-wide oceans with thermodynamic conditions similar to those in the Earth's oceans. Their large sizes and extended atmospheres, compared to rocky planets of similar mass, make Hycean worlds significantly more accessible to atmospheric observations. These planets open a new avenue in the search for planetary habitability and life elsewhere using spectroscopic observations. JWST observations of a candidate Hycean world, K2-18 b, led to the first detections of carbon bearing molecules CH₄ and CO₂ in its atmosphere, and an overall atmospheric composition consistent with prior predictions for a Hycean world. We discuss inferences of the atmospheric chemical composition and its implications for the atmospheric, interior and surface conditions on the planet, along with the possibility of a habitable ocean underneath the atmosphere. We discuss new observational and theoretical developments in this emerging frontier and their implications for exoplanetary habitability and search for life elsewhere.

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1. Introduction

The Anthropocene marks a transformative change on Earth from a cosmic perspective. Besides the major geophysical and environmental consequences of human activities, the resulting change in the atmospheric composition of the Earth can be viewed as an observable phenomenon from outside the solar system – a fingerprint of planetary scale. Conversely, it serves as a demonstration that signatures of atmospheric pollution can be used to search for advanced life on habitable exoplanets, i.e., planets outside the solar system. More generally, life on Earth is known to have modulated the atmospheric composition over billions of years, starting with microbial life in the Earth's early oceans. A central challenge in the search for life elsewhere is to use the observed atmospheric composition of a habitable planet to decipher the possible biosignatures and biota that may be prevalent on such a planet. Therefore, the biological and atmospheric evolution on Earth serves as a guide in the search for life elsewhere.

The observational capabilities of state-of-the-art facilities, such as the James Webb Space Telescope (JWST), and other upcoming large telescopes on ground and in space make it feasible to detect atmospheric signatures of a wide range of exoplanets. At the same time theoretical developments are expanding the limits of planetary properties which could be considered conducive for life, beyond Earth-like planets orbiting sun-like stars. All these developments together mean that there is a realistic chance that we may detect the first signs of life on an exoplanet within the next one or two decades, if not much sooner.

Looking up in the night sky it is easy to wonder if this cosmic sphere that we inhabit is alone in the universe, as a planet hosting life. Until about 30 years ago, we did not know of any planet orbiting a sun-like star outside the solar system. Today we know that extrasolar planets, or 'exoplanets', are extremely common and extremely diverse. We know of over 5800 exoplanets today, spanning a wide range of masses, radii, and orbital architectures. These planets span a wide range, from planets larger than Jupiter to those smaller than Earth, over a wide range of temperatures, orbital parameters and stellar hosts. Furthermore, exoplanet demographics reveal that small planets are the most common, especially planets with sizes between those of Earth and Neptune (1-4 Earth radii), also known as the sub-Neptune regime. It is an open question as to which of these planets are larger versions of Earth ('super-Earths') versus smaller versions of Neptune ('mini-Neptunes'). This is just one of many open questions on the internal structures,

atmospheric processes, formation and evolution history, and habitability of exoplanets. The sub-Neptune regime, in particular, opens a new frontier in the understanding of planetary processes in low-mass exoplanets and the search for habitable conditions beyond the solar system.

Exoplanet observations are increasingly focused on detecting nearby sub-Neptune exoplanets and characterising their atmospheres using spectroscopy. The atmospheric spectrum of an exoplanet acts as a Rosetta Stone for its atmospheric, interior and surface processes. The bulk parameters of a planet, such as its mass, radius and orbital parameters, can provide initial estimates of the planet type based on the density, gravity, and/or equilibrium temperature. However, spectroscopic observations are essential to understand in detail the atmospheric composition and the chemical, radiative and dynamical processes in the atmosphere, possible surface-atmosphere interactions, and constraints on the internal structures. All these aspects are interlinked and influence the observed spectrum. The most successful technique for atmospheric observations of low-mass exoplanets has been transmission spectroscopy. This technique relies on the transit method of exoplanet detection, whereby the orbital inclination of the system is such that the observer can infer the planet in transit, i.e., passing in front of the star, by measuring a small decrease in the star light during transit. The transit depth is the ratio of the projected area of the planet over that of the star, i.e., square of the ratio of the radii. A transmission spectrum is the transit depth as a function of wavelength. A survey of observational and theoretical methods for studying exoplanetary atmospheres can be found in recent reviews (e.g., Madhusudhan 2019, Fortney et al. 2021).

The JWST is revolutionising atmospheric spectroscopy of exoplanets. In the pre-JWST era, atmospheric spectroscopy of exoplanets was largely limited to UV-optical and near-infrared wavelengths (typically below 1.8 μm) with limited constraints on molecular species, which tend to have stronger features in the infrared. While H_2O was detected in numerous giant exoplanets, and CO in some, especially in hot Jupiters orbiting close to their host stars, few constraints were possible on other molecules (Madhusudhan 2019). Atmospheric characterisation of low-mass exoplanets was even more difficult. The advent of JWST observations in the last three years is transforming this area. The unprecedented sensitivity and wide spectral range of JWST, from 0.6 to over 20 μm , is allowing numerous chemical detections and precise measurements of atmospheric properties for a wide range of exoplanets, including sub-Neptune exoplanets. These include de-

tections of important molecules such as H_2O , CO , CH_4 , CO_2 , H_2S , and/or SO_2 in diverse planets, from hot giant exoplanets (e.g., Bell et al. 2023, Constantinou et al. 2023, Rustamkulov et al. 2023, Dyrek et al. 2024) to temperate sub-Neptunes (Madhusudhan et al. 2023, Benneke et al. 2024, Holmberg & Madhusudhan 2024). Besides transiting exoplanets, JWST observations are also enabling high-precision spectroscopy and chemical detections in directly-imaged giant exoplanets at large orbital separations around young stars (Gandhi et al. 2023, Miles et al. 2023). Overall, exoplanet spectroscopy with the JWST is providing unprecedented insights into their atmospheric compositions and physical processes, which paves the way to answering three fundamental questions in the field: (1) How do planets form and evolve? (2) How diverse are planetary processes? (3) Are we alone? In this article, we discuss recent developments towards answering the third question: Are we alone? We focus on new prospects in the search for life on exoplanets with JWST made possible by the Hycean paradigm.

Traditionally, the search for life on exoplanets has been primarily directed towards habitable planets similar to the Earth orbiting other stars. The concept of planetary habitability originated primarily with Earth-like planets in view. The terrestrial habitable zone around a star is defined as the range in orbital separation over which an Earth-like planet can host liquid water on its surface (e.g. Kasting et al. 1993). The habitable zone is closer-in for stars that are smaller and cooler than the sun and is farther out for stars that are larger and hotter, as shown in Figure 1. Extensive efforts are underway to detect Earth-like exoplanets orbiting nearby stars and to characterise their atmospheres using transit spectroscopy in search of chemical signatures of habitable conditions and/or biological processes. By Earth-like, it is customary to assume planets with sizes, densities and temperatures comparable to those of Earth.

The search for biosignatures on Earth-like planets is hindered by two key limitations. Firstly, there is currently no exact Earth-like planet known to orbit a sun-like star beyond the solar system. Nevertheless, efforts are underway to detect and characterise such planets around smaller stars, M dwarfs, which are more accessible to observations. Even then, there is a dearth of such planets known to be transiting nearby stars, with only about five planets that are conducive for detailed atmospheric observations with current facilities and several of which are in the same system – the TRAPPIST-1 system (Gillon et al. 2017). Secondly, even for the few such planets known, atmospheric observations are challenging. Theoretical studies

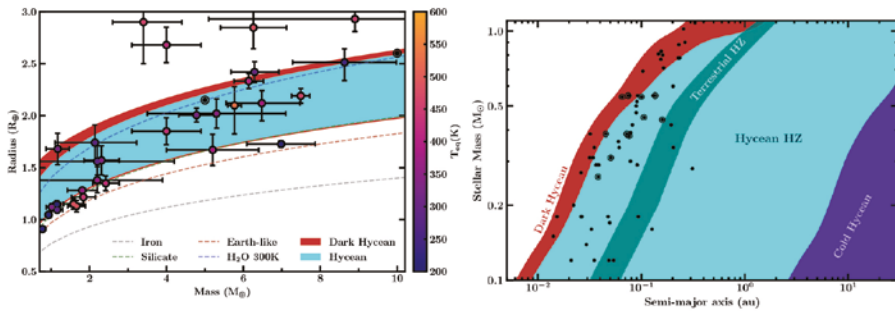


Figure 1. The Hycean mass-radius (M-R) plane and Habitable Zone (from Madhusudhan et al. 2021). The left panel shows the range of masses and radii possible for Hycean worlds. The dashed lines show M-R curves for planets with uniform compositions as noted in the legend. The circles with error bars denote several known exoplanets. The right panel shows the Hycean habitable zone. The cyan, dark-red, and purple regions show the habitable zones for regular, Dark (nightside), and Cold (non-irradiated) Hycean planets, respectively. The terrestrial habitable zone is shown in teal (Kopparapu et al. 2013). Black circles denote several known sub-Neptune exoplanets. The planets with concentric circles indicate promising Hycean candidates.

show that a substantial amount of JWST time may be required to robustly detect prominent biosignatures if present in such atmospheres (Barstow & Irwin 2016, Lustig-Yaeger et al. 2019).

The sub-Neptune regime has emerged as a new frontier in the study of exoplanetary habitability and search for life (e.g. Madhusudhan et al. 2021). As discussed above, the sub-Neptune regime refers to planets with sizes between those of Earth and Neptune, which have no analogue in the solar system but dominate the exoplanet population (Fulton & Petigura 2018). These planets span a wide range in possible atmospheric and internal structures, from predominantly rocky interiors with heavy secondary atmospheres to volatile-rich interiors with light hydrogen-rich atmospheres (Rogers & Seager 2010, Valencia et al. 2013, Zeng et al. 2019, Madhusudhan et al. 2020). It is unknown which of these planets could host conditions that are conducive for life. Nevertheless, the large numbers of such planets known in the exoplanet population, including a significant number of temperate sub-Neptunes, raise important questions in the search for exoplanet habitability. Which currently-known exoplanets in the sub-Neptune regime are potentially habitable? Which of them are conducive for atmospheric observations? What are the possible biosignatures that may be detectable?

In essence, the large population and diversity of the sub-Neptune regime motivate us to revisit the primary conditions of planetary habitability. While a wide range of planetary properties contribute to planetary habitability (Meadows & Barnes 2018), the following question serves as an essential starting point. What are the limits on planet mass, radius and temperature for habitability in the sub-Neptune regime? A recent attempt to answer this question has opened the possibility that a wide range of planets with markedly different interiors and atmospheres to Earth may also be habitable, and observable with JWST (Madhusudhan et al. 2021). This Hycean paradigm has the potential to significantly expand and accelerate the search for habitable environments and life elsewhere and to place important constraints on the conditions conducive for the origins of life.

2. The Hycean Paradigm

Hycean worlds are planets with habitable ocean covered surfaces underlying hydrogen-rich atmospheres (Madhusudhan et al. 2021). The word Hycean is a portmanteau of “**H**ydrogen” and “**O**cean”. The motivation for this new class of planets originated with the habitable-zone sub-Neptune K2-18 b (Montet et al. 2015). The planet has a mass of $8.63 \pm 1.35 M_{\oplus}$ and a radius of $2.61 \pm 0.09 R_{\oplus}$ (Cloutier et al. 2019, Benneke et al. 2019), and orbits an M3 dwarf star with an orbital period of 33 days. The planet receives a net stellar irradiation comparable to that received by the Earth from the sun, giving it a zero-albedo equilibrium temperature of 297 K. However, the large mass and radius of the planet, with nearly half the density and 27% higher gravity compared to the Earth, are incompatible with a rocky Earth-like interior. The lower density requires the presence of a substantial volatile layer in the interior. Initial atmospheric observations of the planet with the Hubble Space Telescope (HST) revealed the presence of a H₂-rich atmosphere in the planet (Benneke et al. 2019, Tsiaras et al. 2019, Madhusudhan et al. 2020).

The combination of atmospheric observations and the bulk properties of the planet allowed for three possible scenarios for the interior composition (Madhusudhan et al. 2020): 1. A mini-Neptune with a rocky core, icy mantle and a thick H₂-rich atmosphere, 2. A gas dwarf with a rocky core and mantle and a thick H₂-rich atmosphere, and 3. A water world with a thin H₂-rich atmosphere. Based on coupled modelling of the atmosphere and interior, we were able to explore the range of possible conditions at the interface between the H₂-rich atmosphere and the interior (Madhusudhan

et al. 2020). In particular, for the water world scenario we found that for most of the model solutions the water at the surface was in supercritical phase, too hot to be habitable. However, a small subset of solutions allowed for liquid water at pressures and temperatures comparable to those in the Earth's oceans. This later scenario implied the possibility of a habitable ocean-covered surface and a thin H_2 -rich atmosphere in K2-18 b. The possibility of liquid water also depends on the right atmospheric conditions such as an adequate Bond albedo, atmospheric thickness and internal flux (Madhusudhan et al. 2020, Piette & Madhusudhan 2020, Leconte et al. 2024). For example, models without an adequate albedo due to clouds/hazes predict surface temperatures too high to allow liquid water (Schecher et al. 2020, Piette & Madhusudhan 2020, Innes et al. 2023).

Motivated by the above finding, we conducted a detailed exploration of the full range of possible planetary masses, radii, equilibrium temperatures and host stars which could allow habitable conditions similar to those possible on K2-18 b, i.e. with habitable ocean-covered surfaces underneath H_2 -rich atmospheres, referred to as Hycean planets (Madhusudhan et al. 2021). We found that Hycean planets can occupy a wide region in the mass-radius plane, with radii up to $2.6 R_E$ for a $10 M_E$ planet. Similarly, such planets also significantly expand the habitable zone for all stellar types, as shown in Fig. 1. Besides the regular Hycean worlds with planet-wide habitability, we also identified dark Hycean worlds that are habitable only on the night side and cold Hycean worlds that receive little stellar irradiation but can still be habitable thanks to the strong greenhouse effect due to H_2 . Overall, the wider habitable zone for Hycean planets significantly increases the number of potentially habitable planets in the search for life elsewhere. Their large radii and light (H_2 -rich) atmospheres give rise to significantly larger spectral features compared to rocky planets of similar mass, making Hycean worlds significantly more accessible to atmospheric observations.

Based on these limits, we identified a dozen known temperate sub-Nepunes as candidate Hycean worlds which would be conducive for atmospheric spectroscopy with JWST. We also explored the feasibility of detecting biomarker molecules in such atmospheres. For Earth-like planets the prominent biomarker molecules are expected to be O_2 , O_3 and/or CH_4 (e.g. Catling et al. 2018). However, the same molecules could either be under-abundant or have abiotic sources in H_2 -rich atmospheres of Hycean worlds. We therefore consider several secondary biomarkers (e.g. Domagal-Goldman et al. 2011, Seager et al. 2013, 2016) as more robust biomarkers on Hy-

cean worlds. These include molecules such as dimethyl sulphide (DMS) and methyl chloride (CH_3Cl) which are expected to be present in small quantities but are not known to have significant abiotic sources and are detectable in the atmospheres of Hycean worlds. Based on simulated JWST observations, we demonstrated that these molecules can be detected robustly in several Hycean worlds with only a few tens of hours of JWST time per planet.

3. First JWST Spectrum of a Possible Hycean World

The advent of JWST is revolutionising the characterisation of sub-Neptune atmospheres, thanks to the generational leap in sensitivity and spectral coverage. We observed a transmission spectrum of K2-18 b as part of the JWST Cycle 1 GO program 2722, to characterise the chemical and physical conditions in the atmosphere and their implications for the interior. The program involves observations with three JWST instruments (NIRISS, NIRSpec G395H and MIRI) spanning a spectral range of $\sim 1\text{--}10\text{ }\mu\text{m}$, of which two observations have been conducted to date with NIRISS and NIRSpec in the $\sim 1\text{--}5\text{ }\mu\text{m}$ range. A transmission spectrum is observed when the planet passes in front of its host star as seen by the telescope. During the transit the planet blocks part of the stellar disk causing a reduction in the star light observed. Some of the starlight passes through the atmosphere of the planet at the day-night boundary ('terminator') region before reaching the telescope. The reduction, or 'absorption', of the star light observed varies with wavelength of light as the planetary atmosphere absorbs different amounts of light at different wavelengths depending on the atmospheric composition. This absorption as a function of wavelength is referred to as a transmission spectrum. The transmission spectrum of K2-18 b observed with JWST is shown in Figure 2 (Madhusudhan et al. 2023).

The spectrum led to robust detections of multiple carbon-bearing molecules and unprecedented constraints on a range of atmospheric properties of K2-18 b, the first for a sub-Neptune. The spectrum revealed strong features of methane (CH_4) and carbon dioxide (CO_2), detected at 5σ and 3σ confidence, respectively. The atmospheric chemical abundances retrieved using the spectrum revealed substantial quantities of both molecules, at $\sim 1\%$ each, in a H_2 -rich atmosphere. CH_4 is abundant in all giant planet atmospheres of the solar system, which are H_2 -rich, and is similarly expected in temperate H_2 -rich exoplanetary atmospheres but had not been detected in a temperate exoplanet before (Stevenson et al. 2010, Madhusudhan & Seager 2011). Therefore, the detection of CH_4 in K2-18 b addresses this long-standing

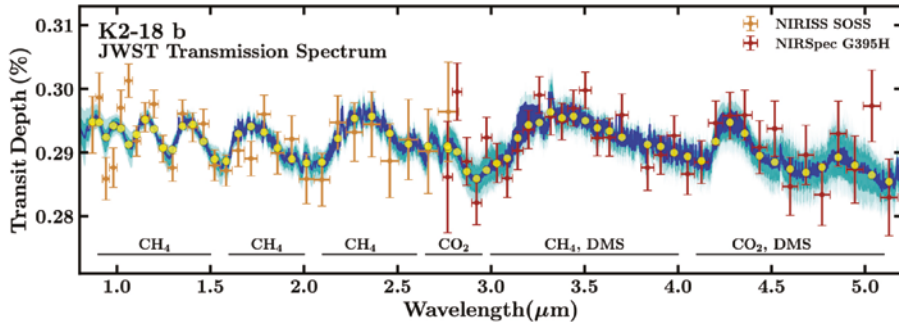


Figure 2. The transmission spectrum of the sub-Neptune K2-18 b, a candidate Hycean world (from Madhusudhan et al. 2023). The observed JWST spectrum is shown in the orange and red data obtained with the NIRISS and NIRSpec instruments on JWST as noted in the legend. The dark blue line denotes the median-fit model spectrum while medium and lighter blue regions denote the 1σ and 2σ contours, respectively. CH_4 and CO_2 are detected robustly at 5σ and 3σ confidence, respectively, as evident from their strong spectral features labelled in the figure. Only marginal evidence for DMS is found in regions of the spectrum overlapping with the strong CH_4 and CO_2 features as shown. The yellow circles show the median-fit model binned to the same resolution as the data.

‘missing methane’ problem. On the other hand, the spectrum did not show significant evidence for other prominent molecules, including water vapour (H_2O), ammonia (NH_3), or carbon monoxide (CO) which are typically expected in H_2 -rich atmospheres. Finally, the spectrum revealed tentative evidence (2σ or less) for dimethyl sulphide (DMS) which has been predicted to be a potential biomarker, both in Earth-like and Hycean atmospheres (Catling et al. 2018, Domagal-Goldman et al. 2011, Seager et al. 2013, Madhusudhan et al. 2021). The spectrum also provided 3σ evidence for the presence of clouds/hazes in the atmosphere at the day-night terminator.

The chemical detections provide important insights into possible atmospheric and surface conditions on the planet. The detections of CH_4 and CO_2 and the non-detections of NH_3 and CO are consistent with predictions for a thin H_2 -rich atmosphere in contact with an ocean surface (Hu et al. 2021, Madhusudhan et al. 2023b). The lack of NH_3 in this scenario is explained by its high solubility in the underlying ocean. On the contrary, a deep H_2 -rich atmosphere that would be required in the case of a mini-Neptune or rocky planet scenario is unable to explain the observed atmospheric composition as that would predict a higher NH_3 and CO compared to what is observed (Yu et al. 2021, Hu et al. 2021, Tsai et al. 2021, Madhusudhan et al. 2023b). The non-detection of H_2O is also consistent with expectations

for a cold trap in the stratosphere whereby the temperature is low enough for H₂O to condense out of the observable atmosphere (Madhusudhan et al. 2023b). The observed constraint on the atmospheric temperature and the 3σ evidence for clouds/hazes are also consistent with this picture. Finally, the marginal evidence for DMS is of significant interest given its promise as a potential biomarker. Given the low evidence, 2σ or less, more observations are required to robustly establish or rule out its presence in the atmosphere, which could have important implications for the possibility of biological activity on the planet.

A key question in the Hycean scenario is what atmospheric properties are required to sustain a liquid water ocean under the H₂-rich atmosphere of K2-18 b. As discussed above, some theoretical studies have shown that a significant albedo, up to ~ 0.5 - 0.6 , due to clouds/hazes may be required to maintain a low temperature and a liquid water ocean in K2-18 b (Madhusudhan et al. 2020, Piette & Madhusudhan 2020, Madhusudhan et al. 2021, Leconte et al. 2024). On the other hand, a cloud/haze-free atmosphere could lead to a supercritical water layer that would not be conducive for habitability (Piette & Madhusudhan 2020, Scheucher et al. 2020, Innes et al. 2023). The evidence for clouds/hazes at the day-night terminator provided by the present data may contribute towards the required albedo. However, more observations are required to both improve upon the present constraints on the cloud/haze properties at the terminator as well as more directly measure the albedo on the dayside atmosphere using emission spectroscopy. Recent studies have also explored alternate mechanisms to explain the observed atmospheric composition of K2-18 b (Wogan et al. 2024, Shorttle et al. 2024). However, none of those mechanisms are able to simultaneously explain the non-detections of NH₃ and CO and the high CO₂ and CH₄ abundances in the planetary atmosphere (e.g. Glein 2024, Cooke & Madhusudhan 2024, Rigby et al. 2024). Therefore, currently, the Hycean explanation remains the most favoured by the data. More observations and theoretical work in the future could enable more stringent constraints on the different possible interpretations.

4. Summary and Emerging Directions

The JWST observations of K2-18 b represent a paradigm shift in the study of exoplanet habitability and search for life. Firstly, they have led to the first detections of carbon-bearing molecules in a potentially habitable exoplanet. Besides resolving the long-standing missing- methane problem,

this is a major technical demonstration of the ability of JWST to characterise candidate Hycean worlds and temperate sub-Neptunes in general. This opens a new avenue to study a wide range of planetary processes in such planets, including atmospheric, surface and interior conditions as well as formation pathways. Secondly, and more specifically to K2-18 b, the detected atmospheric chemical composition is consistent with predictions for a Hycean world. Furthermore, the potential inference of DMS, if confirmed, raises the possibility of potential biological activity on the planet. Overall, these observations have opened a promising pathway to explore exoplanet habitability with JWST and to understand potential conditions for life in environments very different from Earth.

It is natural to wonder whether, theoretically, the conditions on Hycean worlds would be conducive for the origin and sustenance of life as we know it on Earth. The origin and evolution of life on a planet depends on a complex interplay of astrophysical, geological, geochemical and biological factors. As a first step in answering this broad question, we investigated whether Hycean worlds would allow the chemical conditions required for primordial life similar to that originated in Earth's oceans (Madhusudhan et al. 2023b). We find that the temperate H_2 -rich atmospheres of Hycean worlds provide a rich source of organic prebiotic molecules in the early stages of the planets history that could be conducive for seeding life. The planet-wide oceans in Hycean worlds could also contain adequate bio-essential elements (CHNOPS) at concentrations comparable to those in the early Earth's oceans. This is particularly important considering that the oceans on such planets are expected to be up to hundreds of km deep with a sea floor of high-pressure ice which precludes direct interaction of the water with the mineral-rich rock (Nixon & Madhusudhan 2021, Rigby & Madhusudhan 2024). Overall, Hycean worlds provide promising prospects and a rich testbed for investigating the origin and evolution of life in planetary environments.

Is K2-18 b unique? From an observational perspective, it is natural to ask whether K2-18 b is a unique, and perhaps fortuitous, case, or whether it belongs to a more general class of planets with similar characteristics. Most recently, JWST observed the transmission spectrum for a second candidate Hycean world TOI-270 d (Holmberg & Madhusudhan 2024, Benneke et al. 2024), as shown in Figure 3. The planet has a mass of 4.8 Earth masses and a radius of 2.1 Earth radii (Günther et al. 2019, van Eylen et al. 2021). Quite remarkably, the spectrum shows very similar spectral features as K2-18 b of CH_4 and CO_2 in a H_2 -rich atmosphere and no strong evidence for

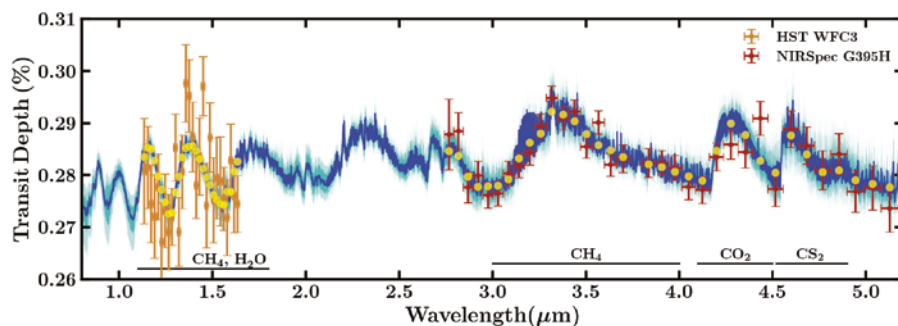


Figure 3. The transmission spectrum of the sub-Neptune TOI-270 d, a candidate Hycean world (from Holmberg & Madhusudhan 2024). The observed JWST spectrum is shown in the red data, along with a previously observed HST spectrum (Mikal-Evans et al. 2023) shown in orange, as noted in the legend. The dark blue line denotes the median-fit model spectrum while medium and lighter blue regions denote the 1σ and 2σ contours, respectively. The yellow circles show the median-fit model binned to the same resolution as the data.

NH_3 or CO . In addition, the spectrum also revealed additional signatures of H_2O , confirming previous detection with HST (Mikal-Evans et al. 2023) and consistent with the equilibrium temperature of the planet being ~ 80 K hotter than K2-18 b, and carbon disulphide (CS_2). The hotter temperature means that H_2O is unlikely to be condensed out over the whole atmosphere, and the surface temperature may also be significantly hotter compared to K2-18 b. Therefore, while a Hycean scenario cannot be ruled out (Holmberg & Madhusudhan 2024), it is also possible that TOI-270 d may instead be too hot to be habitable (e.g. Benneke et al. 2024). More observations and theoretical work are needed to robustly constrain the atmospheric and interior properties and the possibility of habitable conditions on TOI-270 d.

Irrespective of their habitability, the remarkable similarity in the spectra between K2-18 b and TOI-270 d point to a new class of temperate sub-Neptunes with some commonality in the underlying physical and chemical conditions. Over the next few years, initial reconnaissance observations with JWST will be available for several more such candidate Hycean worlds. These developments provide impetus to a new era in exoplanetary science and astrobiology, with the potential for transformational insights into the sub-Neptune regime. It may be expected that these observations will provide unprecedented insights into three fundamental questions: How do planets form and evolve? How diverse are planetary processes? And, are we alone?

Overall, the phenomenal capability of JWST and other upcoming facilities promise a golden age in exoplanet science. The confluence of powerful observational facilities, diverse exoplanet population and transformational science questions provides the perfect storm for major scientific breakthroughs. In this backdrop, the Hycean paradigm provides an unprecedented opportunity in the search for habitable environments beyond the solar system. Theoretical and observational studies have already demonstrated the capability of JWST to detect potential biomarkers in Hycean worlds. The central question at present is not whether we would be able to detect presence of life on a Hycean world but whether we are prepared to identify a signature of life on a planet so unlike Earth. Are we prepared to find life as we don't know it?

Acknowledgements

This article is an expanded version of the article presented for the Vatican Workshop on *Astrophysics: The James Webb Space Telescope: From First Light to New Worldviews*. The author thanks the organisers, participants and the Pontifical Academy of Sciences for the hospitality during the meeting at the Vatican.

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**VI: SCIENCES AND AI LINKING WITH TRADITIONAL
& INDIGENOUS KNOWLEDGE FOR ADDRESSING
ANTHROPOCENE ISSUES**

ARTIFICIAL INTELLIGENCE, TRADITIONAL ECOLOGICAL KNOWLEDGE AND INDIGENOUS PEOPLES

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■ <https://www.doi.org/10.65398/BIQM6939>

The world is changing rapidly, but it is seemingly not as fast as the advancements in artificial technology and artificial intelligence (AI). AI's proliferation has material impacts on nearly all aspects of society, both positive and negative. On the one hand, AI has the potential to improve monitoring and predicting climate change impacts, such as wildfires, droughts and floods. However, it is also increasingly used to automate decision-making, including environmental activities and decisions. On March 14 of this year, the United States led a motion called "Seizing the opportunities of safe, secure and trustworthy artificial intelligence systems for sustainable development" that was backed by 120 other Member States, that calls upon member states to work with various stakeholders to develop "safe, secure and trustworthy" artificial intelligence (AI) systems. Although Indigenous communities were not explicitly mentioned in that call to action, my message here today is that Indigenous Traditional Ecological Knowledge and stewardship are unique, critical, and indeed crucial perspectives to bring to these issues. As AI continues to advance, there is a need to ensure Indigenous Knowledge Systems, including TEK, are incorporated into AI's design and use processes in ways that respect Indigenous peoples' rights to self-determination, knowledge protection and data sovereignty. Building off the themes discussed in the Pontifical Academy of Sciences' Workshop on *Indigenous Peoples' Knowledge and the Sciences* that also took place on March 14th this year, I will share some of the current challenges and opportunities presented by AI for TEK and Indigenous peoples.

Before meeting with you today, I explored past published research studies in Scopus, the largest repository of peer-reviewed research. The first paper published connecting indigenous knowledge was from a 2012 conference included the Nganyi clan of Western Kenya's perspectives on developing a seasonal climate forecast with artificial intelligence. To date 133

papers have been published, with papers published in 2023 doubling that of 2024, and 2024 on track to double that of 2023. Conferences and conversations like those of today are vital to ensuring Indigenous voices are included in scientific discussions. A key theme of our conversation in March was that of “braiding.” This is a unique form of cooperation where the knowledge of Indigenous Peoples and scientific insights intertwine, each preserving its distinct identity. AI systems are changing the way science and Indigenous Peoples interact, and other actors like governments inform their policies and decisions that impact all of us. Of the existing Scopus indexed academic literature connecting Indigenous communities and AI, many focused on important issues like native language preservation, access to government services, and data sovereignty. However, there is potential to expand the focus to grand issues like developing nature-based solutions for climate change impact and resilience discussed today. Next, I will highlight how this conversation around AI and ITEK can relate to the conference themes of Recognition and Dialogue, Collaborative Policy and Decision-Making Involving Indigenous Peoples and Scientific Communities, and Critical Action Areas for Collaboration in Biodiversity, Food, Climate and Health from a North American context.

Recognition and Dialogue

The relationship between colonialism and Indigenous knowledge systems has long been fraught with tension and marginalization. Colonial powers systematically suppressed Indigenous cultures, languages, and knowledge, often deeming them inferior to Western scientific paradigms. This historical context casts a long shadow over contemporary efforts to integrate Indigenous Traditional Ecological Knowledge (TEK) into modern technologies like Artificial Intelligence (AI). As AI rapidly evolves, it presents both risks and opportunities for Indigenous communities. AI’s reliance on data-driven models, algorithms, and automated decision-making processes could inadvertently perpetuate the same colonial patterns that have long excluded Indigenous voices. However, with deliberate and thoughtful engagement, AI could also serve as a tool to challenge these patterns, amplifying and respecting the distinctiveness of TEK.

Indigenous Traditional Ecological Knowledge (TEK) should not be viewed as a static set of practices but a dynamic, complex system deeply rooted in the relationships between Indigenous peoples and their environments with a highly local context. TEK encompasses a holistic understand-

ing of ecosystems, developed over millennia through direct interaction with the land. This knowledge is inherently place-based, contextual, and often transmitted orally across generations. The challenge with AI is that it tends to abstract and generalize, potentially overlooking the nuances and specificities that are central to TEK. AI models, by their nature, are designed to find patterns in large datasets, which can lead to the oversimplification of the rich, contextual knowledge that TEK embodies. As such, there is a real concern that AI could inadvertently reduce TEK to mere data points that are generalizable across contexts, stripping away its cultural and spiritual significance.

Despite these challenges, there are emerging platforms and initiatives aimed at fostering continuous, respectful dialogue between Indigenous communities and AI developers or other stakeholders. One such initiative is a series of roundtable discussions soon to be launched by the Commission for Environmental Cooperation (CEC). These roundtables bring together Indigenous leaders, AI experts, policymakers, and environmentalists to explore how AI can be harnessed in ways that respect and incorporate TEK. The CEC roundtable initiative is a promising step towards ensuring that AI development is not just inclusive but also genuinely collaborative. These discussions emphasize the need for Indigenous communities to have a seat at the table, not just as participants but as equal partners in the decision-making process.

From an environmental perspective, AI presents both significant opportunities and pressing concerns for Indigenous peoples and TEK. For example, the increased reliance on AI-driven modeling, drones, and sensors for monitoring wildlife, environmental conditions, and pollution could have profound implications. On the one hand, these technologies offer unprecedented capabilities for tracking and predicting environmental changes, which could enhance conservation efforts. On the other hand, there is a risk that these technologies could marginalize Indigenous peoples' traditional roles in environmental stewardship. The data-driven nature of these technologies could lead to a decrease in direct engagement with Indigenous communities, as decision-makers might rely more on AI models than on the lived experiences and insights of Indigenous peoples. This shift could undermine the participatory approaches that are crucial for effective and equitable environmental governance.

One of the key opportunities for Indigenous communities lies in the potential for AI to support the preservation and revitalization of TEK. AI can be used to document and archive TEK, ensuring that this knowledge is not

lost to future generations. Moreover, AI-driven tools can help Indigenous communities manage and protect their lands more effectively, by providing real-time data on environmental changes and threats. However, for these tools to be truly effective, they must be developed in close collaboration with Indigenous communities, ensuring that they align with the values and priorities of those they are intended to serve.

In this context, it is important to highlight the role of Canada and Mexico as members of the Digital Nations group. This coalition of countries is committed to using digital technology to improve public services, and it has established guidelines for the ethical use of AI in decision-making. Both Canada and Mexico require that federal governments clearly communicate how AI tools are used in decision-making contexts, setting a standard for transparency and accountability. However, these requirements should not be limited to federal governments alone. There is a pressing need for other levels of government, as well as private organizations, to adopt similar practices. This would help ensure that the use of AI in environmental management is transparent and that Indigenous communities are fully informed and involved in the processes that affect their lands and livelihoods.

While there are legitimate concerns about the potential for AI to perpetuate colonial patterns, there are also significant opportunities to use AI as a tool for preserving and revitalizing TEK. To realize these opportunities, it is essential to foster continuous, respectful dialogue between Indigenous communities and AI developers, ensuring that AI is developed and deployed in ways that respect Indigenous rights and knowledge systems. The initiatives like the CEC roundtables are a promising start, but much work remains to be done to ensure that AI serves as a force for good in the ongoing relationship between Indigenous peoples and the environment.

Collaborative Policy and Decision-Making Involving Indigenous Peoples and Scientific Communities

Indigenous data sovereignty is increasingly crucial in discussions surrounding the ethical use of AI and the inclusion of Indigenous peoples in policy and decision-making processes. Indigenous data sovereignty asserts the rights of Indigenous communities to govern the collection, management, and use of data concerning their people, lands, and knowledge systems. This principle is particularly important in the context of AI, where data is often the foundation upon which technologies are built. Despite its significance, current AI policies often fall short in addressing the unique needs and rights of Indigenous communities.

One of the most pressing concerns is that many AI policies and initiatives have been developed without meaningful input from Indigenous communities, leading to ethical concerns about how Indigenous data is used and protected. For instance, a review of AI-related initiatives in Canada shows that while there are efforts to incorporate Indigenous perspectives, these efforts are not always consistent or sufficient. Some projects have inadvertently or deliberately bypassed Indigenous data sovereignty principles, resulting in tensions and mistrust between Indigenous communities and AI developers. In response advocacy groups like the First Nations Information Governance Centre (FNIGC) has been instrumental in advocating for the principles of Ownership, Control, Access, and Possession (OCAP) in the context of data sovereignty. As described by their founder, there is a need for advocacy on far pressing issues like AI to move beyond project-based advocacy, toward a broader vision. A major concern of Canadian indigenous scholars like Dr. David Gaertner of University of British Columbia, is classifying contemporary AI data collection as extractivist AI. Extractivism has strong environmental and colonialist connotations for indigenous communities. Vital resources were not valued the same way between settlers and first nations people resulting in the pillaging of environments, rather than co-creating through a systems thinking approach. If data is collected and harvested without clear OCAP principles, this cycle can continue into the digital space.

Similarly, in the United States, the Native American Rights Fund (NARF) has been involved in shaping AI policies that respect Indigenous data sovereignty. NARF has collaborated with various stakeholders to develop guidelines that ensure AI technologies do not infringe upon the rights of Indigenous communities. These guidelines emphasize the importance of free, prior, and informed consent (FPIC) and the protection of Indigenous intellectual property rights. The collaboration between NARF and AI developers has led to more ethical AI applications, particularly in areas such as environmental monitoring and natural resource management (NARF, 2021). It essential to state that consulting AI tools for Indigenous perspectives on environmental issues, or any issues, does not and cannot replace true consultations with real communities.

Despite these positive examples, challenges remain. In Mexico, for example, the use of AI in environmental management has sometimes overlooked the rights of Indigenous communities. With the support of Google.org charity, the World Wild Life Fund launched the ManglarIA, “AI for

Mangroves” in Spanish, project. This project involves installing multiple cameras, remote sensors, and autonomous drones to help set up and monitor the AI-powered equipment. Historically, WWF worked directly with local Mexican indigenous communities for this effort, and this current project continues to work with the same communities who help install, maintain, and collect data from the project sensors. Fortunately, this project was developed with guidance from the Global Indigenous Data Alliance to ensure data sovereignty best practices for local communities. As these AI projects continue to scale in scope and complexity, it is vital to recognize that AI cannot and should not replace the ongoing input and inclusion of Indigenous communities in environmental stewardship and consultations.

These examples highlight the importance of co-creation in AI policy and development. Co-creation involves Indigenous communities working alongside AI developers, scientists, and policymakers from the outset to ensure that their knowledge, values, and rights are integral to the development process. However, co-creation is not without its challenges. One of the primary obstacles is the need for capacity building within Indigenous communities to engage with AI technologies. This includes providing education and training on AI, as well as ensuring that Indigenous communities have access to the necessary resources and infrastructure. Additionally, there is a need for greater awareness and understanding among AI developers and policymakers of the unique needs and rights of Indigenous peoples. Without this understanding, there is a risk that AI initiatives will continue to perpetuate the exclusion and marginalization of Indigenous communities.

The ongoing discussions and actions around Indigenous data sovereignty and AI highlight the importance of collaborative policy and decision-making involving Indigenous peoples and scientific communities. While there are promising examples of successful collaborations in North America, much work remains to be done to ensure that AI policies are developed in ways that respect and uphold Indigenous rights. By continuing to foster dialogue and co-creation, we can work towards a future where AI can be used to support and empower Indigenous communities in the spirit of braiding.

COUPLING TECHNOLOGY WITH TRADITIONAL KNOWLEDGE FOR HEALTH AND WELLBEING: HARNESSING AI

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Introduction

Artificial intelligence (AI) has emerged as a transformative force across various fields, including healthcare, in recent times. The scope for AI applications lies in its ability to augment traditional knowledge systems, specifically in health and well-being (Chu et al., 2022). Having a rich history and a wide range of repositories of herbal remedies, holistic practices, and Indigenous knowledge, traditional medicine has provided many effective health solutions across diverse cultures (Saini & Parashar, 2024). Integrating traditional knowledge with modern healthcare practices is highly challenging due to the immense complexity of the data involved. AI offers a unique opportunity that bridges the gap and enables the systematic analysis, preservation, and application of traditional medicinal knowledge (Al Kuwaiti et al., 2023). Using natural language processing (NLP), Deep learning, Predictive Analytics and Machine learning (ML), AI can sift through extensive historical texts, folk remedies, and anecdotal evidence to identify patterns, validate efficacy, and suggest novel applications (Arowosegbe & Oyelade, 2023). AI-based databases can collate and analyse the available ethnobotanical resources, mining bioactive compounds in traditional remedies that have therapeutic potential (E. Zhou et al., 2024).

AI can assist in formalising treatments using traditional methods for individual needs by integrating data generated from genomics, metabolic, and environmental factors, which help create personalised health solutions. This personalised approach, or precision medicine, is increasingly gaining traction as AI facilitates the integration of traditional medicinal practices with cutting-edge genomic research (Johnson et al., 2021). By mapping

genetic markers to the efficacy of traditional remedies, AI can guide the development of treatments more aligned with an individual's genetic makeup, enhancing their effectiveness while minimising adverse effects. AI technologies like deep learning can support digitising and preserving traditional knowledge, ensuring that ancient wisdom is not lost to time but adapted to modern contexts. For example, AI algorithms can transcribe and translate ancient manuscripts, making them accessible to researchers and practitioners worldwide (Münster et al., 2024). Additionally, AI can enable the creation of knowledge graphs that connect traditional medical practices with contemporary scientific findings, facilitating a more integrated approach to health and well-being. By leveraging AI, the potential of traditional medicine can be unlocked, making it more accessible, adaptable, and effective in addressing contemporary health challenges (E. Zhou et al., 2024). The connection between AI and traditional medicine has great potential to transform healthcare globally and in knowledge-rich countries like India, providing culturally relevant and scientifically validated solutions that are sustainable and scalable (Das et al., 2024).

Understanding Traditional Knowledge

Traditional knowledge is a vast repository of wisdom, beliefs, and practices accumulated and passed down through generations within indigenous and local communities. The knowledge is deeply rooted in the communities with cultural heritage and empirical knowledge, which offers a holistic approach to health and well-being, often overlooked by modern medicine. Traditional knowledge is not static; it evolves over time as communities adapt to changing environments and societal conditions.

Herbal Medicine

One of the most well-known aspects of traditional knowledge is its extensive use of herbal medicine. Indigenous communities have long relied on the medicinal properties of plants to treat various ailments, ranging from common colds to chronic diseases. This knowledge is often based on centuries of trial and error, observation, and a deep understanding of local biodiversity (Pan et al., 2014). For example, using the *Artemisia annua* plant in traditional Chinese medicine to treat malaria led to the discovery of the artemisinin drug. This compound is now a cornerstone of modern antimalarial therapy (Tu, 2011).

Herbal medicine, in traditional knowledge, is not just about using plants for healing but also understanding how they should be prepared and administered to achieve optimal results. The knowledge of when to harvest, how to process, and how to combine various herbs is intricately tied to the cultural practices of these communities. Such practices often emphasise sustainability and respect for nature, ensuring that the natural resources used in healing are not depleted (Chaachouay & Zidane, 2024).

Spiritual Healing

Traditional knowledge also encompasses spiritual healing practices that are integral to the well-being of individuals and communities. Spiritual healing in traditional medicine is based on the belief that health is a state of harmony between an individual's physical, mental, and spiritual aspects. Illness is often viewed as a disruption of this balance, which can be restored through rituals, prayers, and the involvement of spiritual healers or shamans (Dein, 2020).

The following traditional practices show the connection between health and spirituality, in which healing is seen as a process that addresses physical symptoms and nurtures the soul and mind. For example, in many Native American cultures, the “medicine wheel” symbolises the holistic approach to healing, where physical, emotional, mental, and spiritual well-being are all interconnected and must be balanced for proper health (Gall et al., 2021; Montour, 2000).

Lifestyle Practices

Lifestyle practices are another critical component of traditional knowledge. These include dietary guidelines, exercise routines, and daily habits that promote long-term health and prevent illness. Traditional diets, for instance, are often based on locally available foods that are seasonally consumed and prepared in ways that enhance their nutritional value (Singh et al., 2020). The diet in the Mediterranean region is full of fresh greens, fruits, vegetables, whole grains, and olive oil, a prime example of traditional dietary knowledge that has gained recognition for its health benefits (Bach-Faig et al., 2011).

In addition to diet, traditional knowledge includes long-term physical activities like Yoga, Tai Chi, and various other forms of physical activity that are deeply embedded in cultural rituals and daily routines (Varambally & Gangadhar, 2020). The cultural physical practices are not just limited

to physical exercises but are also meant to cultivate mental clarity, emotional balance, and spiritual growth, contributing to overall well-being (Ramos-Jiménez et al., 2015).

Community-Based Healthcare Systems

Community-based healthcare systems are central to traditional knowledge, where healthcare is a collective responsibility. In these systems, the knowledge of healing practices is often shared within the community, and healthcare providers such as midwives, herbalists, and spiritual healers play essential roles. These systems emphasise the importance of community solidarity and mutual aid, where the well-being of one individual is seen as interconnected with the entire community's well-being (Krah et al., 2018).

For example, in many African societies, community-based approaches to healthcare are prevalent, where traditional birth attendants and herbalists are highly respected for their roles in maintaining the community's health. These systems are often more accessible and culturally relevant than formal healthcare services, especially in remote or underserved areas (Abrahams et al., 2001).

Interconnectedness with the Environment

A fundamental aspect of traditional knowledge is that it emphasises the interconnectedness between individuals and their environment. Indigenous communities often profoundly understand their ecosystems, recognising that human health is closely linked to environmental health. This understanding is reflected in practices such as sustainable agriculture, the conservation of medicinal plants, and rituals that honour natural cycles (Jakes, 2024).

For example, agroforestry in many indigenous communities involves cultivating trees alongside crops, supporting biodiversity, enhancing soil fertility, and providing medicinal resources. This practice is a testament to the profound ecological knowledge embedded in traditional systems, where maintaining environmental balance is essential for human health (González & Kröger, 2020; Pan et al., 2014).

Traditional knowledge, therefore, offers valuable insights into how health and healthy well-being can be achieved through a holistic approach that integrates physical, mental, spiritual, and environmental dimensions. Modern healthcare systems can benefit from a more comprehensive and culturally inclusive approach to health by understanding and respecting traditional knowledge (Nanda, 2023; Payyappallimana, 2013).

The Role of AI in Health

Artificial Intelligence (AI) has revolutionised the integration of traditional medicine by analysing vast datasets, identifying patterns, and providing insights for decision-making. Traditional medicine encompasses a wealth of knowledge and practices passed down through generations. However, this knowledge is often fragmented, localised, and encoded in various languages and formats, making it challenging to analyse and integrate with modern healthcare systematically. The ability of AI to process and analyse vast datasets can bridge this gap by organising and interpreting traditional medical knowledge in ways that are accessible and useful to healthcare providers and researchers (Al Kuwaiti et al., 2023; Alowais et al., 2023; Bajwa et al., 2021).

AI can analyse extensive collections of ethnobotanical data, ancient medical texts, and clinical records of traditional medicine practices to identify patterns and correlations. For example, AI algorithms can map the therapeutic uses of specific herbs across different cultures, enabling a deeper understanding of their potential applications. Additionally, AI can integrate traditional knowledge with modern clinical data to validate traditional remedies, identify possible drug interactions, and optimise treatment protocols. By creating databases that combine traditional medicine with modern clinical data, AI can support evidence-based integration of traditional practices into mainstream healthcare, ensuring that valuable traditional knowledge is preserved and utilised effectively (Chu et al., 2022; Saini & Parashar, 2024).

AI applications in traditional medicine include discovering new herbal treatments, personalised traditional medicine plans, and predictive analytics for wellness and prevention.

Discovery of New Herbal Treatments

AI has the potential to revolutionise the discovery of new herbal treatments by mining traditional medicine databases and identifying compounds that can be repurposed for modern therapeutic uses (Ma et al., 2023; Patwardhan & Vaidya, 2010). Traditional medicine systems, such as Ayurveda, Traditional Chinese Medicine (TCM), and African traditional medicine, have documented the use of thousands of plants and herbs for various ailments (Ranade, 2024; H. Zhang et al., 2020). AI can sift through this vast knowledge base, identifying active compounds that may be effective against modern diseases.

For example, AI can analyse the chemical composition of herbs used in traditional medicine and predict their biological activities using machine

learning models (Y. Zhang & Wang, 2023). This approach can lead to identifying new drug candidates, which can be tested in laboratory settings. AI has already been used to discover potential antiviral compounds from traditional medicinal plants, accelerating drug discovery and validating traditional remedies (Wu et al., 2022).

Personalised Traditional Medicine Plans

Personalised medicine, which tailors treatments to individual characteristics, can also be applied to traditional medicine with the help of AI. Traditional medicine often emphasises individualised treatment approaches, considering a person's unique constitution, lifestyle, and environment. AI can enhance this personalisation by integrating traditional diagnostic methods with modern data, such as genetic information, to create customised treatment plans (Ng et al., 2024).

For example, AI can help analyse a patient's genetic signatures, health history, and lifestyle with the diagnostic tools used in traditional medicine, like pulse diagnosis in Ayurveda or tongue diagnosis in Traditional Chinese Medicine. The combination of the latest and traditional approaches with integration can help provide accurate diagnoses and person-specific treatment strategies rooted in traditional medicine but enhanced by modern science (Nashwan & Rao, 2024; H. Zhang et al., 2020).

Predictive Analytics for Wellness and Prevention

AI's predictive analytics capabilities can be applied to traditional medicine to promote wellness and disease prevention. Traditional medicine strongly emphasises preventive care, with practices designed to maintain balance and harmony within the body (Jansen et al., 2021). AI can analyse data from traditional health practices, such as dietary habits, herbal use, and lifestyle routines, to identify patterns that contribute to long-term health (Amabie et al., 2024).

For instance, AI can predict the onset of chronic conditions based on traditional medicine principles, allowing for early interventions that align with conventional practices. AI-driven wellness apps can also incorporate traditional knowledge, offering personalised recommendations for diet, exercise, and herbal supplements based on an individual's constitution and health goals (Williamson, 2001).

Integration of AI with Traditional Knowledge

AI technologies like natural language processing (NLP) and Machine learning (ML) can serve as crucial tools in preserving and utilising traditional medicine knowledge by analysing unstructured data. Much of traditional medicine knowledge is embedded in ancient texts, oral traditions, and environmental observations, which are often not digitised or structured in a way that is easily accessible to modern science. Integrating AI technologies with traditional knowledge presents a unique opportunity to bridge the gap between ancient wisdom and modern healthcare. Traditional medicine, rich with centuries of empirical knowledge, often faces documentation, preservation, and validation challenges. AI offers powerful tools to address these challenges, ensuring that valuable traditional practices are preserved and systematically integrated with contemporary healthcare approaches.

Analysing Ancient Texts with NLP

Natural language processing (NLP) can be used to digitise and analyse ancient medical texts, often written in classical languages and containing valuable insights into traditional medical practices. NLP allows researchers to uncover patterns, correlations, and treatment protocols used for centuries by converting these texts into structured data (Gayathri & Kannan, 2020; Tonja et al., 2024).

For instance, NLP can be applied to ancient Ayurvedic texts to extract information about herbal formulations and their uses. This information can be cross-referenced with modern scientific research to validate traditional treatments' efficacy or identify potential new therapies. Similarly, NLP can be used to analyse Traditional Chinese Medicine texts to identify the therapeutic properties of herbs and their interactions (Wijaya et al., 2023; L. Zhou et al., 2021).

Machine Learning for Environmental Data Analysis

Traditional medicine is deeply connected to the environment, with many practices based on locally available plants, animals, and minerals (Alves & Rosa, 2007; Kala, 2022). Machine learning can analyse environmental data, such as climate patterns, soil composition, and biodiversity, to support the sustainable use of traditional medicine resources (Roopashree et al., 2024).

For example, ML can predict the availability of medicinal plants based on environmental conditions, helping to ensure their sustainable harvest and use. ML can also assist in identifying regions where traditional med-

icine practices are at risk due to the degradation of the environment by guiding conservation efforts that help preserve both the natural resources and the traditional knowledge associated with them (Kavitha et al., 2023).

Sensor Data Analysis for Traditional Health Practices

AI can also be applied to analyse sensor data from traditional health practices, such as pulse diagnosis in Ayurveda or acupuncture in TCM. By collecting data from sensors that measure physiological parameters, AI can help validate and refine traditional diagnostic methods, making them more consistent and reliable (Fatangare & Bhingarkar, 2024).

For example, AI-powered devices can analyse pulse data to provide more accurate and reproducible diagnoses, enhancing the precision of traditional medicine practices. Integrating AI with traditional diagnostic tools can help to bridge the gap between traditional and modern medicine, providing a more holistic approach to healthcare (Amabie et al., 2024; Lu et al., 2020).

Documenting and Conserving Traditional Knowledge

Traditional healing practices are primarily transmitted from generation to generation within communities without formal documentation, which may lead to the risk of knowledge being lost with time. AI can play a critical role in documenting and preserving these practices by creating digital repositories of traditional medical knowledge. Through AI-driven data collection and storage, recording of oral traditions, categorisation, and stored in formats that are easily accessible and analysable (Marques et al., 2021; E. Zhou et al., 2024).

Moreover, AI can facilitate the digitisation of traditional medicine practices, transforming them into structured databases that can be used as a reference for future research and clinical applications. This may help preserve the cultural heritage associated with traditional medicine and make knowledge more accessible to a broader audience, including healthcare professionals and researchers (Lauricella & Pêgo-Fernandes, 2022).

Validating and Enhancing Traditional Healing Practices

One of the significant challenges of integrating traditional medicine into modern healthcare is the validation of its efficacy. AI can assist in analysing patterns in the usage and outcomes of traditional remedies, helping to identify which practices are most effective. By leveraging large datasets, AI can uncover correlations and causal relationships that may not be immediately

apparent, thereby validating traditional treatments scientifically (Alowais et al., 2023).

For instance, machine learning algorithms can analyse patient outcomes associated with traditional medicine practices, helping to identify treatments that are particularly effective for specific conditions. This validation can enhance the credibility of traditional medicine and facilitate its integration into mainstream healthcare systems, ensuring that patients benefit from a holistic approach to health and well-being (Ng et al., 2024).

Translating and Digitising Traditional Texts

Natural Language Processing (NLP) algorithms offer a powerful tool for translating and digitising traditional medical texts, many written in ancient or indigenous languages. These texts often contain a wealth of knowledge about traditional healing practices, but language barriers and the lack of digital versions limit their accessibility (Piotrowski, 2012).

AI-driven NLP can automatically translate these texts into modern languages and convert them into digital formats, making them available for analysis and application in healthcare settings. It preserves the knowledge in these texts and makes it easier for researchers and practitioners to study and apply traditional medicine principles in their work (Névéol et al., 2018).

AI-Driven Decision Support for Traditional Healers

AI-driven decision support systems can empower traditional healers by providing evidence-based recommendations that enhance their practices. These systems can integrate traditional knowledge with the latest scientific research, offering traditional healers insights grounded in their cultural practices and informed by modern medical science. The application of AI to facilitate the connection between traditional healers and modern healthcare practitioners can benefit both contrasting worlds of traditional medicine and modern medicine (Zeng & Jia, 2024). For example, AI can supply traditional healers with details of potential interactions between traditional therapies and modern remedies, helping to ensure patient safety and improve therapeutic outcomes with safety. The collaborative approach can lead to a more integrative healthcare system that appreciates and leverages the strengths of both traditional and modern medicine (Münster et al., 2024).

Examples of AI-Traditional Knowledge Integration

AI offers significant potential to enhance and complement traditional knowledge systems in healthcare, creating opportunities to innovate in ar-

eas like herbal medicine discovery, community health monitoring, and culturally sensitive healthcare delivery.

1. Herbal Medicine Discovery

Traditional knowledge often includes the use of medicinal plants to treat various ailments. These remedies, passed down through generations, provide valuable insights into the therapeutic properties of plants. AI can revolutionise the discovery and validation of herbal medicines by analysing both traditional knowledge and modern scientific data to predict the therapeutic potential of medicinal plants (Rustandi et al., 2023).

AI algorithms, particularly machine learning models, can analyse large datasets containing information about the chemical composition of plants and their historical usage in traditional medicine. Established on the grounds of cross-referencing this data with scientific evidence from biomedical research, AI can predict which plant compounds will likely have specific therapeutic properties, such as anti-inflammatory, antioxidant, or antimicrobial effects. This approach accelerates the discovery of new medicinal uses for traditional plants and helps validate their efficacy (Paul et al., 2021).

For example, AI can predict plant-derived compounds' bioactivity by mining data from traditional medical systems like Ayurveda, Traditional Chinese Medicine (TCM), or African herbal medicine. By applying AI algorithms to vast databases of phytochemicals, researchers can identify plants with potential for new drug development based on patterns and correlations observed in traditional usage. It reduces the need for costly and time-consuming laboratory experiments by prioritising plants more likely to show promising results (Azadnia et al., 2022).

Moreover, AI can assist in identifying synergistic combinations of plant-based compounds that work together to enhance therapeutic effects, a concept widely recognised in traditional medicine. By analysing the interactions between multiple compounds, AI can suggest optimised herbal formulations that may provide more effective treatments than isolated compounds (Ma et al., 2023).

2. Community Health Monitoring

For communities practicing traditional medicine, AI-driven health monitoring can align with existing practices of holistic health assessment. In the Traditional Chinese medicine (TCM) technique, the balance of Yin and Yang is considered crucial for maintaining health. AI-based tools can

monitor lifestyle habits that may influence this balance. This way, wearable technology and AI can track physiological and environmental factors, providing personalised feedback based on traditional healing concepts (Lu et al., 2024; Nahavandi et al., 2022).

AI-based platforms can also facilitate community health initiatives by aggregating individual data and identifying trends that may suggest emerging health risks. In remote or underserved communities where traditional healthcare is the primary or the only source of medical treatment, introducing AI-driven systems can alert traditional healers and community leaders about potential health concerns, enabling early interventions that align with their cultural approaches to disease prevention and treatment.

For example, an AI-based app can monitor the health outcomes of individuals taking herbal remedies, correlating those outcomes with lifestyle factors and traditional healing practices, thus providing evidence-based insights that can be shared with traditional healers and modern healthcare providers (Alowais et al., 2023).

3. Cultural Sensitivity in Healthcare

Traditional knowledge systems are deeply embedded in the Indigenous communities' cultures and belief systems, and effective healthcare delivery must be sensitive to these cultural contexts. AI-driven language translation tools can facilitate communication between healthcare providers and patients from diverse cultural backgrounds, ensuring that traditional beliefs and practices are followed during diagnosis and treatment (Marques et al., 2021).

Natural language processing (NLP) tools can be developed and implemented to translate indigenous languages or culturally specific medical terminologies into the language used by healthcare providers, allowing for more accurate communication and fostering a better understanding of patient needs, which can be particularly valuable in regions where patients primarily rely on traditional healers or community-based healthcare systems. By translating the terminology used in traditional medicine into modern medical language, healthcare providers can better understand the cultural context of a patient's symptoms and treatment preferences.

For instance, in many traditional medicine systems, health may be associated with balance, spirituality, or harmony with nature – concepts that may not easily translate into Western medical terminology. AI-driven translation tools can help bridge this gap, ensuring that healthcare providers are

aware of these cultural nuances and can tailor their treatments accordingly (Mohamed et al., 2024).

Additionally, AI can assist healthcare providers in learning about cultural practices that influence patient care. Machine learning algorithms can analyse cultural practices and preferences from patient records, enabling healthcare providers to offer treatment options that align with a patient's traditional beliefs. This cultural sensitivity improves patient satisfaction and trust. It can improve health outcomes by ensuring patients are more likely to adhere to treatments that respect their cultural norms.

Challenges and Considerations

While integrating Artificial Intelligence (AI) with traditional knowledge presents exciting opportunities for healthcare, it also brings forth several challenges and ethical considerations. These include respecting the intellectual property rights of indigenous communities, cultural sensitivity, and ensuring data privacy and security. Addressing these concerns is essential for building equitable, respectful, and effective AI-traditional knowledge collaborations.

Ethical Considerations: Intellectual Property Rights and Equitable Partnerships

One of the primary ethical challenges in using AI to harness traditional knowledge is the protection of intellectual property rights (IPR) for indigenous communities. Traditional knowledge is often maintained or practised collectively and passed down through generations within communities. Many communities have not historically participated in formalised intellectual property regimes and agree with government policies, making it challenging to ensure their knowledge is recognised, respected, and fairly compensated in the modern world (Wagner & de Clippele, 2023). In AI-traditional knowledge collaborations, it is crucial to develop frameworks that protect the rights of indigenous communities. This involves creating equitable partnerships where these communities retain control over their knowledge and benefit from commercialising or using their traditional remedies and practices (Timmermans, 2003). Misappropriation or exploitation of traditional knowledge for profit, without proper consent or benefit-sharing, has been a persistent issue, and AI applications must not exacerbate this.

A solution to this challenge lies in adopting frameworks like the Nagoya Protocol, which emphasises access to genetic resources and traditional

knowledge with prior informed consent and equitable sharing of benefits (Heinrich et al., 2020). AI developers and healthcare organisations must engage in ethical agreements with indigenous communities, ensuring they actively participate in decision-making. This will ensure that their knowledge is not exploited but is leveraged in a way that honours their cultural heritage.

Cultural Sensitivity: Avoiding Western-Centric Perspectives in AI Applications

Traditional knowledge systems are practiced mainly by indigenous people from different cultures, races, traditions, and locations. However, AI technologies are often developed based on Western-centric models of knowledge and healthcare, which may need to align with traditional medicine's holistic and community-based approaches (Mazzocchi, 2006).

AI applications designed to work with traditional knowledge must be culturally sensitive and avoid imposing any particular scientific frameworks that may not be relevant to the context. For instance, traditional medicine often emphasises the balance between the body, mind, spirit, and environment, a concept that may only sometimes be easily quantifiable through AI models. To respect diversity and traditions, AI systems should be adaptable and able to integrate traditional knowledge on its terms rather than forcing it to fit into a pre-defined mould.

Moreover, developers of AI systems must engage directly with Indigenous communities to ensure that their cultural values and healing practices are accurately represented. This collaboration should involve Indigenous healers and practitioners in the design and development, ensuring that AI systems reflect traditional medicine systems' cultural richness and nuances (Silano, 2024).

Data Privacy and Security: Safeguarding Sensitive Information

Incorporating AI into traditional medicine often involves collecting, storing, and analysing sensitive health and cultural data from indigenous populations. This raises significant concerns about data privacy and security, particularly in light of past abuses where Indigenous communities were exploited for research without their consent or knowledge (Murdoch, 2021).

AI-driven healthcare technologies must ensure that Indigenous communities retain control over their data and that data collection is conducted with complete transparency and informed consent. This is especially im-

portant as traditional knowledge is often viewed as sacred or proprietary, and sharing this knowledge outside the community without proper safeguards can lead to exploitation or misrepresentation.

In addition, AI systems must be mandated to implement robust security measures that not only protect the interest of the people using it but also protect the collected data from unauthorised access, breaches, or misuse (Kaur et al., 2023). Given that healthcare data is susceptible, AI systems should comply with global privacy regulations, such as the General Data Protection Regulation (GDPR) and country-specific rules, while ensuring that community-specific ethical considerations are considered. Indigenous communities should be fully informed about how their data will be used and be able to withdraw consent or access their data at any point (Reddy, 2023).

AI developers must also build trust by ensuring transparency in how AI models are trained, their data sources, and the outcomes they generate. This transparency is critical in avoiding the misuse of sensitive cultural or health-related data and ensuring that AI tools are accepted and trusted by the communities they aim to serve (Balasubramaniam et al., 2023).

Conclusion

Integrating Artificial Intelligence (AI) with traditional knowledge offers a promising pathway to enhance health and well-being in diverse communities. Combining the deep-rooted wisdom of traditional healing systems with the analytical power of AI, we can create more inclusive and culturally sensitive healthcare solutions. AI can be a great tool that will be used to document, preserve, and validate traditional practices followed over centuries while identifying new insight that bridges the gap between ancient remedies and modern scientific methods. By honoring and respecting the traditional knowledge passed down through generations, the integration of AI with traditional medicine will be a game changer that will pave the way for innovative approaches to global healthcare.

To fully realise the potential, fostering collaboration between scientists, technologists, and traditional healers is crucial, ensuring each plays an active role in shaping AI applications. Such partnerships can help navigate ethical considerations, respect cultural sensitivities, and safeguard indigenous knowledge. Together, we can develop healthcare systems that embrace the wisdom of the past while harnessing the possibilities of the future, leading to more holistic, equitable, and effective health solutions for all.

Acknowledgement

SR is thankful to the Indian Council of Medical Research, Department of Health Research and the Government of India for permission to deliver an invited lecture on this paper at the Plenary Session of the Pontifical Academy of Sciences, 23-26 September 2024, Casina Pio IV, Vatican City.

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**■ VII: SCIENCE-POLICY PERSPECTIVES – A HIGH-LEVEL
PANEL SESSION WITH BRIEF INTRODUCTORY
STATEMENTS BY PANELLISTS RELATED TO ASPECTS
OF THE THEMES OF ANTHROPOCENE AND AI**

THE SCIENCE-POLICY INTERFACE: CLOSING KNOWLEDGE GENERATION GAPS BETWEEN THE GLOBAL NORTH AND THE GLOBAL SOUTH FOR SUSTAINABLE DEVELOPMENT

QUARRAISHA ABDOOL KARIM

President of The World Academy of Sciences

■ <https://www.doi.org/10.65398/JXBE7818>

Let me start by thanking the organisers of this meeting for the honour and privilege to be part of this bi-annual plenary focused on *Science for sustainability and wellbeing in the Anthropocene: Opportunities, challenges and AI*, and specifically to share some thoughts from the science-policy perspective on behalf of The World Academy of Sciences.

This gathering is a powerful reminder of the transformative role of science in shaping a more inclusive and just world. In this tumultuous time, the ubiquity of science gives us hope, in transcending political and cultural barriers as the universal language to build bridges between the peoples of this world. The intersection of the Anthropocene and AI represents both challenges and opportunities. The presentations and knowledge garnered to date on the Anthropocene and AI has been breathtaking in breadth and depth and epitomises how much human beings have evolved during this era/epoch.

We are living in a tumultuous and dynamic time of converging and multiple threats of climate change; pandemics; natural disasters, wars and conflicts and widening inequalities within and between countries. Our ability to mitigate and adapt to ensure sustainable planetary health and human security has to premised on our interconnectedness and shared vulnerability and that given the range of challenges in diverse contexts, it will not be a 'one size fits all' approach. Our success in harnessing the power of science for our survival will depend on closing the gaps on existing inequalities in knowledge generation including who has access to knowledge and who benefits from new knowledge generated.

Solutions to the challenges for sustainable development will require partnerships and collaborations across scientific disciplines, across all sectors and has to include all stakeholders – an all of society approach! To be effective these partnerships have to be built on mutual respect and trust and a shared

vision and unity of purpose. Partnerships have to be synergistic – in several instances particularly in North-South collaborations or across subject disciplines, while one partner may initially contribute more than the other, by coming together each partner has something to contribute that by coming together the partnership enables more to be achieved than what each could accomplish on their own. These are important foundations to take the process to the next level viz achieving the transformational and transcendental science needed to tackle the complex challenges facing us and achieve successful interventions to mitigate and/or adapt to these challenges.

What is the role of AI in this tumultuous time? Will AI be the great equalizer or will it accelerate the widening of inequalities? For AI to be an positive and impactful tool a pre-requisite is access to stable supplies of electricity, data, devices, water and a skilled workforce. Yet, the majority of low and middle income countries (LMICS) don't have access to these essential AI enablers. Further, these gaps are widening with advanced AI tools due to the lack of access to the required computational power, data access, and skilled professionals. Currently, wealthier nations dominate in AI research, often applying these technologies to issues that may not be immediately relevant to LMICs, where the focus is on meeting basic needs such as primary and high school education, healthcare, and food security. Without proper inclusion policies, AI will continue its current trajectory of development reflecting the priorities of high-income countries. There is a real risk of putting a higher value on some lives than others as solutions are likely to be misaligned with the needs of vulnerable populations in LMICs. If AI tools are not designed to address localized issues – such as sustainable agriculture, health systems, or education. While AI holds promise for bridging inequalities, the current trend shows that it is often widening the gap. Countries with well-established scientific infrastructure and advanced AI capabilities are benefiting disproportionately from AI's potential, while LMICs face obstacles in accessing these technologies.

Addressing the complexities of the Anthropocene through the lens of AI requires thoughtful, interdisciplinary approaches that integrate scientific understanding with effective policy frameworks. The interplay between human impact and technological advancement presents both challenges and opportunities for creating a sustainable future. As such, dialogue among diverse stakeholders is essential to navigate this evolving landscape, ensuring that technological innovation contributes positively to both the environment and society at large.

How do we work together at this juncture? Science academies already play a pivotal role in fostering research, informing policy, promoting ethical considerations, and engaging with the public. By leveraging their resources and expertise, these institutions could lead the way toward a sustainable future, ensuring that both science and technology work hand in hand to address the pressing issues of our time for everyone everywhere...

The World Academy of Sciences (TWAS) is one such science academy playing its role for building sustainable futures for all with a priority on LMICs and Science and Technology Lagging Countries (STLCs). Established 40 years ago by Nobel Laureate Abdus Salam with the vision of use of science, technology for addressing the challenges facing developing countries. Today TWAS has over 1400 Fellows across 10 subject categories through a peer-election process it recognises the best scientists in the Global South and who are actively engaged in generating knowledge for sustainable development. Recognising the need for a critical mass of scientists across disciplines and within similar regions, TWAS has additionally trained several thousand Masters and doctoral students further expanding the number of highly training scientists addressing critical challenges facing their countries. The training and capacity building efforts have fostered S-S, S-N and N-S partnerships between institutions and scientists and this bilateral training opportunities are shaping a new form of diplomacy through science. The science-policy interface is intentionally addressed through formal workshops on science diplomacy in partnership with the American Academy for the Advancement of Science. In its current iteration it is unique in bringing together scientists with policy makers. This is contributing to strengthening government investments in evidence based policies; investments in science and science infrastructure and support countries to utilize science and science advisors for decision-making. While much has been accomplished, much remains to be done particularly in AI that remains at a nascent stage even though it has changed everyday life and living significantly.

Notwithstanding this progress, efforts are being undermined with the escalation of displaced populations resulting from wars and conflicts that are disproportionately negatively impacting already vulnerable populations and communities in LMICs. It is estimated that there are over 140 million displaced people including highly trained scientists. The destruction of educational and research infrastructure; lives lost and its inter-generational impacts are immeasurable.

Globally, forced displacement and conflict are at historic highs, driven by ongoing wars and crises. By mid-2024, the number of forcibly displaced people surpassed 130 million, marking the 12th consecutive year of rising displacement. Key contributors to this surge include conflicts in Sudan, the Democratic Republic of Congo, Myanmar, and the State of Palestine. Syria remains the largest source of displaced persons, with 13.8 million forced to flee both internally and internationally.

Conflicts are widespread across Africa, the Middle East, and parts of Europe and Latin America. The Ukraine war, Sudan's civil conflict, and Israel-Palestine violence were among the deadliest in 2023. Africa experienced the most wars, while non-state conflicts, often involving gangs and cartels, are highly prevalent in Latin America.

Displacement due to war not only affects the immediate regions but often spills over to neighboring countries, with 75% of refugees hosted in low- and middle-income nations and eroding an a unique global asset, viz youth.

Displaced scientists and researchers frequently migrate to safer regions, stripping their home countries of valuable intellectual capital. In places like Syria, Sudan, and Venezuela, this erosion of the academic workforce is profound, affecting local research capabilities and further deepening economic and social disparities.

Internally displaced persons (IDPs) and refugees often lack access to quality education. This disruption affects the next generation of scientists, engineers, and technologists who could otherwise contribute to their countries' development. Many children in conflict zones, such as in parts of Africa and the Middle East, miss years of education, limiting the talent pool from which future scientists can emerge.

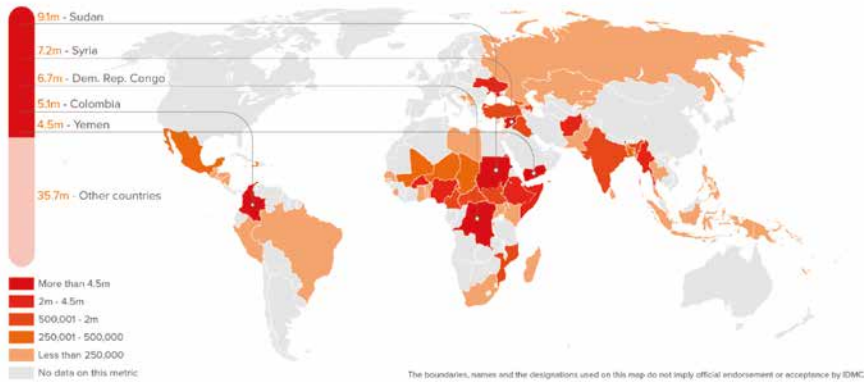
In conflict-ridden regions, infrastructure vital to scientific research – universities, laboratories, and libraries – is often damaged or rendered inaccessible. This lack of resources prevents scientific progress and innovation. The divide between countries with strong, resilient research systems and those affected by conflict grows wider.

The importance of peace cannot be over stated. Pope Francis captured this eloquently and concisely in the foreword to this: *'...peace is a prerequisite for sustainable development.'* Without stability, countries cannot build the foundations necessary for growth, innovation, or the proper use of scientific and technological advancements. Peaceful conditions foster collaboration, the strengthening of institutions, and the development of societies. This vision aligns with global frameworks like the UN's 2030 Agenda for

Sustainable Development, which places peace and justice as core goals for long-term prosperity in LMICs and indeed the world.

As we move forward, I leave you with three lessons to reflect on:

Forty years ago the world faced a major crisis resulting from HIV that again disproportionately impacted LMICs with Africa being home to 70% of people living with HIV. Life expectancy dropped by about 20 years in sub-Saharan Africa and hundreds of thousands of children were orphaned due to limited access to anti-retroviral therapy. But in the early 2000s there was a major shift in the global response – UN member states came together



Below is an image of conflict and violence displacement:

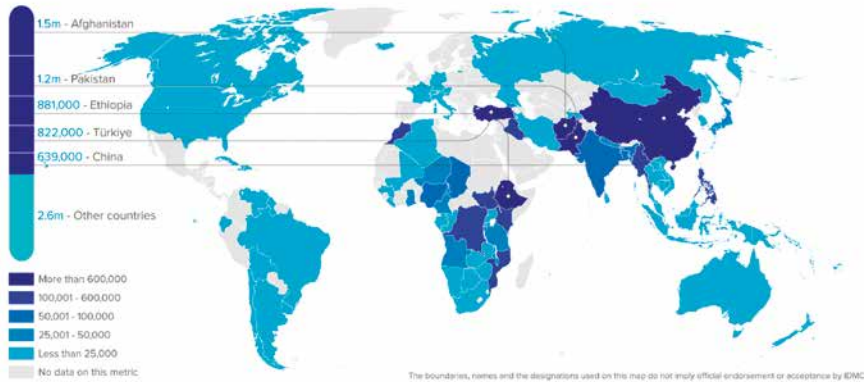


Figure 1. Temporal trends in global patterns of displacement due to conflict and violence.

with activists and advocates, and pharmaceutical companies to commit to ensuring that everyone ever where could have access to these life-saving medication. This unprecedented act of global solidarity will go down in history as an important turning point and serves as an important lesson in challenges facing humanity. Today, about 30 million people are on triple anti-retroviral therapy and AIDS has shifted from an inevitably fatal condition to one that is chronic and manageable.

In 2020 the world faced another challenge, Covid-19. Many of us can vividly recall the fear, uncertainty and anxiety that engulfed us. We were reminded again of our interconnectedness and shared vulnerability. Science through the development of diagnostics; therapeutics and vaccines brought us hope but our failure to act with solidarity saw inequities in access to life saving medicines and vaccines and wealth defined who would benefit or not.

In the words of an iconic leader Nelson Mandela: *'Addressing inequalities is not an act of charity or generosity, it is a basic human right!'*

In conclusion, science for humanity has to be for all of humanity and a sustainable future for all cannot afford a situation where some lives are viewed as more valuable than others. Our interconnectedness and shared vulnerabilities underscore the importance of working together as scientists to generate knowledge and innovations to make the world a better place for everyone.

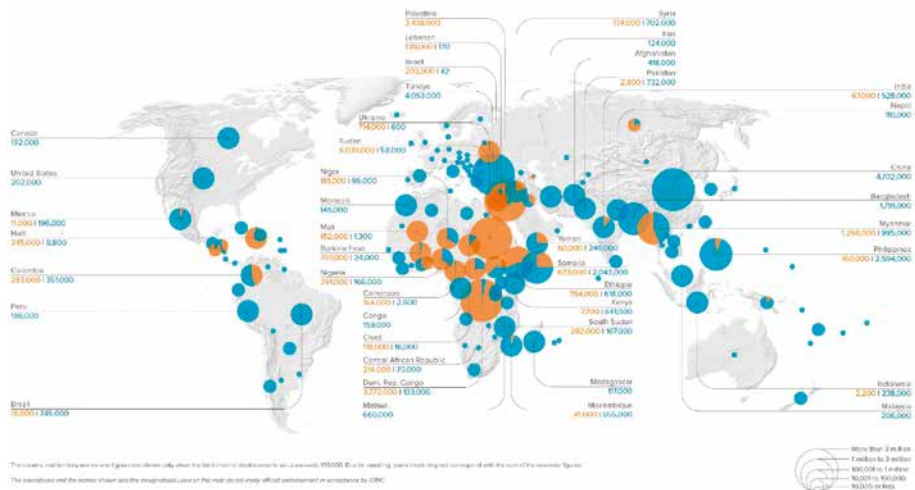


Figure 2. Displaced populations in 2023. There were 46.9 million internal displacements, or movements, recorded during 2023, across 151 countries and territories. All but three of the 45 countries and territories are in LMICs.

SCIENCE-POLICY PERSPECTIVES

CARLOS GILBERTO CARLOTTI JR

Rector of Universidade de São Paulo, Brazil and Professor Faculty of Medicine, Neurosurgery

■ <https://www.doi.org/10.65398/TSGC5460>

Good afternoon, everyone. It is a pleasure to participate in a meeting of the Vatican Academy of Sciences representing a university from Latin America, showcasing what we are doing to make the Anthropocene sustainable.

The University of São Paulo (USP) is a Brazilian university located in the State of São Paulo, which funds its operations. The State of São Paulo is the most developed state in Brazil and is responsible for one-third of the country's GDP. In addition to the state capital, the university has campuses in several cities throughout the interior.

USP is the largest university in Brazil, with around 90 thousand students, and is responsible for training a significant portion of the country's qualified human resources as well as contributing to 20% of Brazil's scientific production.

Brazil is currently facing challenging times regarding climate change. In southern Brazil, we experienced unprecedented flooding at the beginning of the year. Meanwhile, the rest of the country is enduring an intense dry season, leading to wildfires across all Brazilian states, including the Amazon region, where rivers have reached alarmingly low levels for this time of the year.

To collaborate with society, we are undertaking two main initiatives: making our campuses more sustainable by generating renewable energy and reducing overall energy consumption, managing solid waste, and improving water usage. We aim to set an example for our cities. Additionally, we have created interdisciplinary thematic centers to develop sustainable solutions for both companies and the public sector.

I would like to mention six of these centers: one for sustainable technologies in offshore oil exploration (OTIC), one for sustainable tropical agriculture (STAC), one for carbon research in agriculture (Ccarbon), one research center for greenhouse gas innovation (RCGI), one center for artificial intelligence (C4AI) and one center for Studies on Amazon Sustainability.

The offshore center has five major research areas, some of which connect sustainability with artificial intelligence, analyzing data for ocean engineering, and creating simulations and virtual realities for platform operations.

One project involves developing vertical turbines for operation in deep waters to generate renewable energy for platform operations. Another project focuses on floating nuclear micro-reactors for energy generation in deep waters.

Digital monitoring systems are being developed to track platform activities, identify risks, and prevent accidents while optimizing operations.

STAC focuses on four major areas to improve tropical agriculture.

1. The first area is the domestication of macaúba, a native plant in Central and South America. Studies are underway to understand the plant's biology and needs, with plans for a huge commercial planting in southern Bahia, Brazil. The fruit of this palm has oil that could potentially be converted into sustainable aviation fuel due to its high energy content.
2. Another project aims to expand irrigable agriculture in Brazil, increasing productivity and reducing the need for new agricultural land by studying water potential, soil types, crops, and the best agricultural models for each situation.
3. Another initiative proposes increasing connectivity in rural areas to enable digital inclusion. Digital inclusion and artificial intelligence will allow enhance agricultural productivity, real-time monitoring of agricultural machinery, and environmental protection.
4. The final initiative involves providing technical support for a “Green Seal Brazil” that assures consumers that these products adhere to sustainable agricultural principles, thus reducing the commercialization of products that result from deforestation or improper practices. If deforestation-related products are not marketed, this practice will likely be phased out.

Ccarbon aims to reduce emissions and increase carbon capture. Its strategy is based on climate change mitigation, food security, a low-carbon economy, and social development.

The first initiative focuses on developing a project to establish a baseline for carbon in Brazil – whether in the soil, plants, or air – by analyzing approximately 250 thousand samples across all Brazilian biomes.

A second project aims to accelerate the recovery of degraded coastal areas using new technologies to promote root growth.

Evaluation kits have been developed to assess the physical, chemical, and biological properties of soil in field assessments.

Now, I will present RCGI. The first project involves converting ethanol into green hydrogen. Ethanol derived from sugarcane is widely used in Brazil, and its energy utilization can be enhanced by using hydrogen in more efficient engines. A pilot plant will produce 100 kg of hydrogen per day, which will be utilized in buses and cars on the USP campus to assess the efficiency of this proposal.

Another pilot project studies the production of methanol from CO₂ emitted by ethanol plants. Since methanol has a higher energy content than ethanol, it can be used in larger vehicles than those using ethanol.

A prototype for hydrogen production through water catalysis using solar energy is being developed. This is a well-known reaction, but further studies are needed to make it economically viable.

Another possibility is the development of solid oxide fuel cells capable of converting ethanol into hydrogen, which can subsequently be converted into electricity. The vehicle would be fueled by ethanol at conventional stations, with the transformations occurring internally.

Now I will present the artificial intelligence center. At least three of its areas of study are strongly related to sustainability: the study of oceans, climate studies to predict extreme events, and decision-making related to food production and food security.

Finally, I will present the Center for Amazon region, the goal is to promote production and dissemination of science related to education, research, culture for the sustainable development of the Amazon region, taking into account its biodiversity, the complexity of socio-physical-chemical-biological processes, ethnic and population diversity, as well as socioeconomic issues.

Thank you for the opportunity to present our initiatives for making the Anthropocene sustainable.

STATEMENT ON SCIENCE-POLICY PERSPECTIVES

GEORG SCHÜTTE

Volkswagen Foundation, Germany

■ <https://www.doi.org/10.65398/IKIE1473>

1. AI, the anthropocene, and science policy

In this new era of technological disruptions and global transformations, we have to deal with the ambiguous nature of AI – and it will depend on us, as His Holiness Pope Francis states, to decide the degree to which it will bring “benefits or harm.” More than ever before, science and modern technologies that advanced research brings about shape the way we live, we work, and we relate to each other. For good reasons, therefore, science and research have become an object of public interest and public debate. At the same time, they have become an instrument of public policy making.

How do we define this political arena that we might call science policy? What are the global megatrends that currently shape the global scientific sphere? How do they affect international collaboration in science and research? And what does this mean for academies of science?

I will answer these questions from the perspective of a funding agency, the Volkswagen Foundation. This is one of Germany’s largest private funders of research and innovation. The foundation operates for the benefit of the public. It is an independent foundation which was established by the Federal Republic of Germany and the State of Lower Saxony when the state-owned company Volkswagen went public. The two former owners put all the revenues into an endowment which is the foundation’s source of income.

I myself have worked in research management for 30 years. I have spent ten out of these 30 years in public administration as state – or permanent – secretary in the German Federal Ministry of Education and Research. At the time of the 2024 Biennial Plenary, I was part of an Expert Group of the European Commission on the “Interim Evaluation of Horizon Europe” and the future of the 10th Framework Program. My presentation refers to the work of this group in multiple ways.¹

¹ European Commission (2024), *Align, Act, Accelerate. Research, Technology and Innovation to boost European competitiveness*. Report of the Commission Expert Group on the Interim Evaluation of Horizon Europe. Brussels.

2. Science Policy

Science policy addresses the organizational context to generate new ideas and the distribution of expertise. It focuses on the production of scientific and scholarly knowledge and the role of knowledge networks and collaborations. Thus, science policy influences the organization and the conduct of science within society and its intermediating agencies and consortia. It is concerned with the allocation of resources to conduct science in the public interest. Science policy strives to strike a balance between the perceived public or general interests and the perceived self-interest within the science system.²

Science policy unfolds on the national as well as the international level. It usually is an instrument of soft power: it builds up reputation to attract interest, knowledge, talents and collaborators.³

While science and research per se strive for truth, even though it might only be a “temporary truth”, the political sphere is dominated by the functional logic of power execution. Therefore, whenever science enters the political sphere, these different functional logics lead to tensions and conflicts of interest.

3. Megatrends in the global scientific sphere

3.1. *The end of the end of history or the return of great-power competition*

More than 30 years ago, Francis Fukuyama proclaimed the end of history. At the end of the Cold War, he expected that there would be only one remaining superpower and a ‘pax americana’. However, power politics have come back into international relations. The Russian war of aggression against Ukraine, the war in the Middle East, violent conflicts in Darfur, in East Congo, and other regions in Africa, military tensions in the South China Sea – they all provide evidence that nations and violent groups consider war and aggression as means to resolve conflicts. The 1980s and 1990s seemed to support the idealistic notion that international relations in science and research can lead and can contribute to international understanding. The 2020s challenge this notion. The hard power of military conflicts overrides the soft power of international collaboration in science and re-

² Simon, Dagmar; Knie, Andreas, Hornbostel, Stefan; Zimmermann, Karin, Eds. (2016), *Handbuch Wissenschaftspolitik*, 2. Edition. Wiesbaden: Springer VS.

³ Schütte, Georg (2008): “Wettlauf ums Wissen: Außenwissenschaftspolitik als Herausforderung moderner Wissensgesellschaften“ in: *Wettlauf ums Wissen. Außenwissenschaftspolitik im Zeitalter der Wissensrevolution*. Berlin: Berlin University Press, p. 12-26.

search. We currently observe new frictions in research collaborations across borders and new restrictions on global academic mobility. No longer does the European Commission, for example, follow its former call for radical openness: open data, open science, open to the world. It rather calls for the new guideline: as open as possible, as closed as necessary.⁴ Distrust in the political realm seems to challenge established relationships based on trust in science and research.

3.2. *The Worsening Climate Crisis*

While science and research continue to provide evidence of the detrimental effects of accumulated greenhouse gas emissions, international political mitigation and adaptation mechanisms are rather slow to react. The International Panel on Climate Change, for example, has developed a process to translate this increasing evidence into political recommendations. These recommendations are the basis for Conferences of Parties on Climate Change. And yet, major emitting nations have so far not agreed upon a coherent approach to reverse the current trends. Rather, wars and violent conflicts contribute to the worsening of the climate crisis. In addition, the loss of biodiversity resumes speed, and infectious diseases reappear and reach a hitherto unknown level. They are, amongst others, also the root causes of international migration.

3.3. *Rise of disruptive and generative technologies*

Science and research continue to explore hitherto unknown territory. The rapid development of COVID vaccines is but one example of the power of long-term, curiosity-driven research turned into application for the benefit of humankind. The staggered provision of the vaccines, however, indicates that uneven international power relations continue to exist in the world of high-tech goods. While synthetic biology continues to revolutionize the life sciences and will bring about new drugs and new organisms that will shape and change our lives – for good and for bad, AI technologies will, to some extent, revolutionize knowledge production across all fields and disciplines and challenge the established mode of enlightened thinking and reasoning. A new knowledge order is taking shape on the horizon. AI technologies are now “reaching the point where their broad transformative potential – for

⁴ Schütte, Georg (2022), „Eiszeit für die Wissenschaft“ in: *Frankfurter Allgemeine Zeitung*, 31. March 2022, p. 6.

business, science, humanity and the planet – is becoming more widely understood unleashing hopes and fears of utopias and dystopias”.⁵

3.4. The Rise of U.S. and Chinese companies conducting research

Publicly funded research is no longer the sole driver of this development. Rather a small number of international high-tech companies, mainly from the United States and China, develop these new technologies and shape the general modes of their applications. In addition, they re-invest revenues from the high-tech enterprise in research and innovation. Thus, in the United States the share of federally funded research decreased from 30 percent in 2011 to 19 percent in 2021. Today, the business sector in the U.S. funds 36 percent of basic research which is close to the 40 percent share of the U.S. federal government.⁶ This leads to new questions of ownership of knowledge and legitimization of research and innovation activities.

3.5. Geopolitics of science and research

It is this context which leads to fundamental changes in the international scientific sphere. During the past ten years, China has emerged as a scientific and technological superpower. The European Union now considers China as partner, competitor, and systemic rival. As the EU Expert Panel observes: “The geopolitical frictions between China and the US can partially be explained by two factors: Firstly, the rise of disruptive technologies mentioned above and their growing importance for power (military, economic, political), and secondly, a rather dramatic shift in the global distribution of scientific resources from democracies to authoritarian regimes and from the West to the East. Regarding the latter factor, China is the dominant force in both phenomena. While China’s scientific rise has added tremendous resources to the global research enterprise of science, it is also challenging established systems, institutions and norms, due to its sheer size and the government’s ambitions, but also its view of the relationship between science and the state”.⁷

Academic mobility unfolds today in this new world of great power competition. While negative demographic developments in high-income countries propel the need to attract further talent, physical and social insecurity

⁵ European Commission, p. 18.

⁶ European Commission, p. 20.

⁷ European Commission, p. 19.

is a major driver of migration, including academic talent from low-income countries, leading to an uneven distribution of talents and intellectual progress around the globe.

In addition, research security has become a new field of concern. Nations and academic institutions deny access to certain fields of knowledge out of fear of espionage and illegal exploitation.

New restrictions on open academic discourse appear as international conflicts are being debated on national campuses. Faked news, distributed through online networks pose challenges to open societies and democracies.

3.6. Speed of transitions

The speed of technological change and its adoption, the speed of transformation of the international order and of national societies, and the speed of ecological changes currently collides with the “embedded inertia in science systems” (OECD, 2023) and the slow decision-making processes in mature democracies. It increases both a sense of urgency and a sense of uncertainty, leading to friction within open democratic societies.

4. The search for answers

How can science policy makers address these challenges? How can intermediating agencies like academies of science live up to this challenge? A number of pragmatic approaches seem conducive to coping with the megatrends mentioned above:

When geopolitical tensions contribute to a ‘securization’ of research collaboration, the OECD proposes to its members a three-fold approach: (1) protect and restrict flows of knowledge and technology which are of critical importance to individual countries, (2) promote and improve the domestic performance of the respective research and innovation systems, and (3) project the need to address global challenges to the international level and form international alliances.⁸

In order to adequately control knowledge flows and the respective risks involved, several countries have started to set up expert groups and monitoring agencies to observe science, research, innovation, foreign and security policies of other countries.

⁸ OECD (2023), *OECD Science, Technology and Innovation Outlook 2023: Enabling Transitions in Times of Disruption*, OECD Publishing, Paris, <https://doi.org/10.1787/0b55736e-en>.

Transnational agencies like the International Panel on Climate Change (IPCC) play an important role to further facilitate research collaboration on planetary challenges across geopolitical blocks. While there is an in-built inertia in the process, it is nevertheless worthwhile to continue the efforts to translate research results into political action. Collaboration with and among diaspora researchers may further contribute to an ongoing international cooperation in these fields beyond national restrictions.

The rise of disruptive technologies like AI will lead to the creation of new architectures of knowledge. Given the ambivalent potential of AI, we need a smart and open regulation of these new technologies to unleash their potential for scientific breakthroughs. At the same time, we need to control the divisive power inherent in it. The adequate representation of indigenous knowledge seems to be just one indicator of the challenge of fair representation and just acknowledgement of ownership within these new architectures.

Deep tech innovations like AI advance the economic competitiveness of nations. Science policy makers need to make sure that researchers continue to be able to take advantage of these new technologies in the global public interest. Therefore, the Scientific Advice Mechanism to the European Commission recently issued a set of recommendations which addresses both the opportunities and the challenges of using Artificial Intelligence in science. The expert panel calls for the establishment of a European institute for AI in science to counter the dominance of a limited number of corporations over AI infrastructure and to empower public research across diverse disciplines. AI-powered scientific research requires a vast amount of data. Data should be of high quality, responsibly collected and meticulously curated, ensuring fair access for European researchers and innovators. The panel calls for transparent public AI models which help, among others, to increase the trustworthiness of AI and reinforce the reproducibility of research results. To help scientists enhance their overall efficiency, the panel advises the EU to support the development of AI tools and technologies specialized on scientific work (e.g., foundation models for science, scientific large language models, AI research assistants and other ways to use AI technologies). According to the group, prioritizing AI-powered research in areas like personalized healthcare and social cohesion, where data is abundant but difficult to interpret, would maximize benefits for EU citizens.⁹

⁹ Group of Chief Scientific Advisors (2024), *Successful and timely uptake of Artificial Intelligence in science in the EU*, European Commission, Brussels. The SAM opinion was requested by Executive

Academies of science are, among others, important intermediaries at the interface of science and science policy. They can help scientists, policy makers, and the general public to understand and interpret the current state of scientific discoveries and scholarly knowledge. Academies are well-positioned to describe and analyze long-term trends in nature and society. They can reflect upon the ongoing challenges and introduce issues of concern. In this capacity, they can also serve as intermediary among generations. Mental health challenges among the younger generation today are but one indicator of generation-specific concerns about the future. They point to intergenerational challenges and the question of being *good ancestors*. Last, but not least, academies of science can open up arenas to deliberate about potential answers to the planetary challenges we face. They can help them to evaluate the challenges and opportunities of concrete political actions. Answers will not always be easy. But they are in high demand at a time when global challenges are larger than ever before.

Vice-President Vestager in July 2023. It complements a range of material that the Commission has developed on the use of AI in research and innovation.

EARTH'S CHANGING CLIMATE: STEWARDED TECHNOLOGY TO BENEFIT PEOPLE AND OUR PLAN

WILLIE E. MAY

Vice President for Research and Economic Development, Morgan State University;
President, American Association for the Advancement of Science

■ <https://www.doi.org/10.65398/PBXR7527>

The pace of scientific progress is accelerating, bringing the potential of artificial intelligence (AI) and other emerging technologies to both sustain and enhance our planet's health. However, these advancements also pose significant environmental challenges. The need for innovative technologies that can address the pressing issue of climate change while benefitting both people and the planet is essential. How these technologies are developed and by whom really matters. Rapid advancements in technology present both opportunities and challenges. It is crucial to balance the drive for innovation with careful consideration of its long-term environmental and social impacts. How we craft policies to ensure these technologies are being developed sustainably, equitably, and responsibly will be the focus of my discussions.

AI and other emerging technologies have the potential to play a pivotal role in addressing climate change and promoting sustainability. These technologies can be leveraged to develop more efficient energy systems, optimize resource utilization, and enhance our understanding of complex environmental processes. Additionally, AI can support interdisciplinary research to create technologies that are both sustainable and equitable – this collaboration is vital in finding comprehensive solutions that can be adopted with efficacy. At the same time, it is critical that we develop models that utilize small-data techniques, such as few-shot learning and transfer learning, because training and running AI models on large datasets require vast amounts of electricity, leading to increased environmental impacts. Sustainable AI is essential in reducing the environmental impact of AI systems themselves.

But there are challenges:

- Reducing AI's carbon footprint (renewable energy sources for data centers).

- Ensuring equity – AI systems need to be environmentally sustainable and socially equitable.
- Regulatory frameworks – there need to be robust policies and frameworks that encourage the development and use of sustainable AI tech (this should include standards for energy use, resource conservation, and ethical considerations).
- Global collaboration – global buy-in on shared standards and practices for achieving sustainable AI.

How Do We Get There?

- Hardware and software innovations – continued research and development is required.
- Community engagement and collaboration – promote educational initiatives around the development of sustainable AI for users and developers.
- Accomplishing these goals requires a sustainable AI vision and an unwavering resolve to get there.
- Every nation must answer the call to action.

ANNEX

PLENARY SESSION PROGRAM

DAY 1 | MONDAY 23 SEPTEMBER, 2024

09.00-10.30	Audience with Pope Francis (including welcoming new PAS Academicians)
10.30-11.00	Coffee Break at Casina Pio IV
11.00-13.00	Guided tours in Vatican (options such as Library, or Museum, or St. Peter's Dome)
13.00-14.30	Lunch at Casina Pio IV
17.00-19.00	Ethics and AI - Challenges and Regulations in Europe and beyond A Panel session followed by a reception organized by the French and German Embassies to the Holy See, in collaboration with the Pontifical Academy of Sciences, the Decastery for Culture and Education, and with the support of the Delegation of the European Union to the Holy See, held at Curia Generalizia della Compagnia di Gesù, Borgo S. Spirito, 4. Moderator: Archbishop Paul Desmond Tighe Speakers and Panelists: <ul style="list-style-type: none">• Prof. Frances Hamilton Arnold ■ PAS Academician Professor of Chemical Engineering, Bioengineering and Biochemistry at the California Institute of Technology (Caltech), External co-chair of President Biden's Council of Advisors on Science and Technology• Sir Demis Hassabis ■ PAS Academician Co-Founder & CEO, Google DeepMind• Prof. Paul F. Nemitz Principal Advisor for Digital Transformation in the Directorate-General for Justice and Consumers of the European Commission• Rev. Fr. Eric Salobir President, Human Technology Foundation, Paris, France• Prof. Bernhard Schölkopf Director at Max Planck Institute for Intelligent Systems & ELLIS Institute Tübingen and Professor, ETH Zürich

DAY 2 | TUESDAY 24 SEPTEMBER, 2024

09.00-09.10	OPENING SESSION <i>Chair: President Prof. Joachim von Braun: Words of Welcome and Concept of the Plenary</i> Cardinal Peter K.A. Turkson: Words of welcome
09.10	Session I – The Anthropocene – concept, measurement, human adaptation, and role of the sciences as cause and cure
09.10-09.30	<i>Science for the Anthropocene – An Introduction</i> Prof. Jürgen Renn Max Planck Institute for Geanthropology, Jena, Germany

09.30-9.50	<i>Anthropocene Stratigraphy</i> Prof. Francine M.G. McCarthy Professor, Earth Sciences. Brock University, Canada, and Anthropocene Working Group, International Commission on Stratigraphy
9.50-10.10	<i>On Human Anthropology – Looking Back Into Human Adaptation and Evolution</i> Prof. Tekklu Zeresenay Alemseged ■ PAS Academician Donald N. Pritzker Professor in the Department of Organismal Biology and Anatomy at the University of Chicago, USA
10.10-10.30	<i>Religion, the Sciences and the Anthropocene</i> Cardinal Peter K.A. Turkson PAS Chancellor
10.30-10.40	Discussion
10.30-11.00	Coffee Break
11.00	Session II – Climate crisis, biodiversity loss, and human contexts – outlook and needed actions for a habitable earth <i>Co-Chairs: Prof. Hans J. Schellnhuber</i> ■ PAS Academician and Prof. Veerabhadran Ramanathan ■ PAS Academician
11.00-11.20	<i>An Historic Down Payment of Actions to Tackle the Interacting Triple Crises of Climate Change, Loss of Biodiversity, and Inequity</i> The Honorable Jane Lubchenco, PhD ■ PAS Academician Deputy Director for Climate and Environment, White House Office of Science and Technology Policy; and University Distinguished Professor and Valley Professor of Marie Biology, Oregon State University
11.20-11.40	<i>Building a Strong Inclusive AI Driven Global Commons for Development Impact at the Nexus of Climate, People, Landscape Health and Food Security</i> Dr. Éliane Ubalijoro Chief Executive Officer, CIFOR-ICRAF, Kenya
11.40-12.00	<i>Challenges in Climate Change Research and Bending the Curves Towards a Sustainable Stewardship</i> Prof. Örjan M. Gustafsson ■ PAS Academician Professor Stockholm University, Department of Environmental Science, Bolin Centre for Climate Research
12.00-12.20	<i>Air Quality, Health, and Climate in the Anthropocene</i> Prof. Ulrich Pöschl Director at the Max Planck Institute for Chemistry and professor at the Johannes Gutenberg University (JGU) in Mainz, Germany
12.20-12.40	<i>Challenges to Habitability and Multi-Level Responses</i> Dr. Kira Vinke Head of the Center for Climate and Foreign Policy at the German Council on Foreign Relations (DGAP)
12.40-13.00	Discussion
13.00-14.30	Lunch

14.30	SESSION III – Quantum physics, and -computing – science perspectives, emerging applications and implications for AI <i>Co-Chairs: Prof. Vanderlei Bagnato ■ PAS Academician and Prof. William D. Phillips ■ PAS Academician</i>
14.30-14.50	<i>The Fundamental Message of the Quantum</i> Prof. Anton Zeilinger University of Vienna, Institute for Quantum Optics and Quantum Information, Austria
14.50-15.10	<i>Exploring the Quantum World using Quantum Simulations</i> Prof. Immanuel Bloch Scientific Director, Max Planck Institute of Quantum Optics, Germany
15.10-15.30	<i>Global Environmental Measurement and Monitoring (GEMM)</i> Prof. Donna T. Strickland ■ PAS Academician Professor at the University of Waterloo in Ontario, Canada, Chair of Optica's Presidential Advisory Committee
15.30-15.50	<i>Quantum Simulation and New Quantum Phases with Long-Range-Interacting Ultra-Cold Atoms</i> Prof. Dr. Francesca Ferlaino Professor of Physics, University of Innsbruck (Austria); Research Director of the Institute for Quantum Optics and Quantum Information (IQOQI), Austria
15.50-16.10	<i>Quantum Systems Open to the World</i> Prof. Ana Asenjo-Garcia Associate Professor of Physics, Columbia University, USA
16.10-16.30	Discussion
16.30-17.00	Coffee Break
17.00	SESSION IV – Artificial Intelligence for sciences, innovations and sustainability – opportunities and risks <i>Co-Chairs: Prof. Klaus von Klitzing ■ PAS Academician and Prof. Vanderlei S. Bagnato ■ PAS Academician</i>
17.00-17.20	<i>Accelerating Scientific Discovery with AI</i> Sir Demis Hassabis ■ PAS Academician Co-Founder & CEO, Google DeepMind, UK
17.20-17.40	<i>AI and the Forces Changing Science in the 21st Century</i> Prof. Frances Hamilton Arnold ■ PAS Academician Professor of Chemical Engineering, Bioengineering and Biochemistry at the California Institute of Technology (Caltech), External co-chair of President Joe Biden's Council of Advisors on Science and Technology
17.40-18.00	<i>Beyond the AI hype: Balancing Innovation and Social Responsibility</i> Prof. Virginia Dignum Professor of Responsible Artificial Intelligence at Umeå University (Dept of Computing Science) and director of the AI Policy Lab. Member of United Nations High Level Advisory Body in AI
18.00-18.20	<i>Materials for the Quantum Age</i> Prof. Cristiane Morais Smith Chair Condensed-Matter Physics, Utrecht University, ITP
18.40-18.45	Discussion
19.00-21.00	Dinner at Casina Pio IV

DAY 3 | WEDNESDAY 25 SEPTEMBER, 2024

9.00	SESSION V – Live sciences innovations, and new approaches <i>Co-Chairs: Edward M. De Robertis ■ PAS Academician and Frances Hamilton Arnold ■ PAS Academician</i>
09.00-09.20	<i>The Future of Genomic Medicine</i> Prof. Eric Lander ■ PAS Academician Professor of biology at the Massachusetts Institute of Technology (MIT), and professor of systems biology at Harvard Medical School
09.20-09.40	<i>Interplay of Oxygen, Carbon Dioxide and Peroxide Metabolism in Mammalian Cells</i> Prof. Rafael Radi ■ PAS Academician Professor Departamento de Bioquímica, Facultad de Medicina and Director of Centro de Investigaciones Biomédicas (CEINBIO), Universidad de la República, Montevideo, Uruguay
09.40-10.00	<i>Design of New Metabolism for Increasing Carbon Fixation</i> Prof. James C. Liao President of Academia Sinica, Taiwan, Professor and Chair of the Department of Chemical and Biomolecular Engineering at the University of California, Los Angeles
10.00-10.20	<i>Marine Science with AI for Sustainability and Wellbeing</i> Prof. Takashi Gojobori ■ PAS Academician Vice-Director of the National Institute of Genetics (NIG) in Mishima, Japan and Distinguished Professor at King Abdullah University of Science and Technology (KAUST), Saudi Arabia
10.20-10.30	Discussion
10.30-11.00	Coffee Break
11.00	SESSION VI – Health and Medical Sciences – emerging science incl. AI to address pandemics and chronic diseases <i>Co-Chairs: Prof. Chien-Jen Chen ■ PAS Academician and Prof. Edith Heard ■ PAS Academician</i>
11.00-11.20	<i>Development of Drugs for Multidrug Resistance Bacteria: The Role of Artificial Intelligence</i> Prof. Tebello Nyokong ■ PAS Academician Distinguished Professor of Chemistry and the Director of Institute for Nanotechnology Innovation at Rhodes University, South Africa
11.20-11.40	<i>Biological Clocks, Thermotolerance, and Fitness: Seeing Through the Eyes of a Fungus</i> Prof. Luis F. Larrondo C. Full Professor, Fac. Biological Sciences, Pontificia Universidad Católica de Chile, Chile
11.40-12.00	<i>AI Research and Infrastructure for the Life Sciences – The EMBL Perspective</i> Dr. Rolf Apweiler Joint Director of European Molecular Biology Laboratory (EMBL) European Bioinformatics Institute (EBI), UK
12.00-12.30	Discussion
12.30-14.00	Lunch

14.00	SESSION VII – Astronomy and changing world views <i>Co-Chairs: Prof. Ewine van Dishoeck ■ PAS Academician and Brother Guy Joseph Consolmagno, SJ ■ PAS Academician Perdurante Munere</i>
14.00-14.20	<i>Astrobiology and the Anthropocene: How Searching for Life Elsewhere Can Help Us Sustain Life on Earth</i> Prof. David Grinspoon NASA
14.20-14.40	<i>Vera C. Rubin's Legacy Survey of Space and Time: The Greatest Movie of All Time</i> Prof. Zeljko Ivezic Professor of Astronomy University of Washington, Director of the Vera C. Rubin Observatory Construction Project
14.40-15.00	<i>Advancing Sustainability with Space Technology</i> Prof. Maria T. Zuber Presidential Advisor for Science and Technology Policy and E. A. Griswold Professor of Geophysics at MIT; Co-chair of President Biden's Council of Advisors on Science and Technology
15.00-15.20	<i>"Life in the Universe", Astrophysics Perspectives</i> Prof. Didier Patrick Queloz ■ PAS Academician Director of the Center for the Origin and Prevalence of Life at ETH Zurich and Professor of Natural Philosophy at the University of Cambridge
15.20-15.40	<i>New Advances in Exoplanet Science with JWST</i> Prof. Nikku Madhusudhan Professor of Astrophysics and Exoplanetary Science, University of Cambridge, UK
15.40-16.00	Discussion of the presentations
16.00-16.30	Coffee Break
16.30	SESSION VIII – Sciences and AI linking with traditional & indigenous knowledge for addressing Anthropocene issues <i>Co-Chairs: Prof. Mohamed Hassan ■ PAS Academician and Prof. Joachim von Braun ■ PAS President</i>
16.30-16.50	<i>Developing Country Problems, Reducing the Environmental Impact of Crops, Equitable Use of New Technology as Part of Holistic Innovation of Agriculture and Food Production Systems</i> Prof. David Baulcombe ■ PAS Academician Emeritus Regius Professor of Botany, Cambridge University
16.50-17.10	<i>Ancestral Wisdom and Artificial Intelligence: Pathways for a Sustainable Planet and Well-Being of Humanity</i> Prof. Octaviana Trujillo Professor Emerita, Northern Arizona University; JPAC, Commission for Environmental Cooperation, USA
17.10-17.30	<i>Coupling Technology with Traditional Knowledge for Health and Wellness</i> Dr. Subarna Roy Director, ICMR National Institute of Traditional Medicine, Belagavi, India
17.30-17.45	Discussion

18.00	SESSION IX – IX Science-Policy perspectives – a high level panel session with brief introductory statements by panellists related to aspects of the themes of Anthropocene and AI <i>Chair: Prof. Joachim von Braun ■ PAS President</i>
	Prof. Quarraisha Abdool Karim President of The World Academy of Sciences for the advancement of science in developing countries (UNESCO-TWAS), South Africa
	Prof. Carlos Gilberto Carlotti Jr Rector of Universidade de São Paulo, Brazil and Professor Faculty of Medicine, Neurosurgery
	Georg Schütte Secretary General of Volkswagen Foundation, Germany
	Francesca Cesari Chief Editor with Journal Nature (Biological, Clinical and Social Sciences), United Kingdom
	Prof. Willie E. May Vice President for Research and Economic Development & Professor of Chemistry. Morgan State University and President, American Association for the Advancement of Science (AAAS)
19.00-19.30	Open discussion of panellists with participants
19.30	SESSION X – Commemorations and Self-Introductions of PAS Academicians <i>Co-Chairs: President Joachim von Braun and Chancellor Cardinal Peter K.A. Turkson</i>
19.30-19.45	Commemorations of Academicians that passed since Plenary 2022 Ignacio Rodríguez-Iturbe (Edward de Robertis, PAS) Yuri Ivanovich Manin (Daya Reddy, PAS) Paul Berg (Eric Lander, PAS) Albert Eschenmoser (Rafael Radi, PAS) Hans Tuppy (Stefano Piccolo, PAS) Sergey Petrovich Novikov (Mohamed Hassan, PAS) Maxine F. Singer (CJ Chen, PAS)
19.45-20.00	Self-introductions of new Academicians Örjan Gustafsson Stockholm University, Sweden Demis Hassabis Google DeepMind, UK Mauro Mantovani Vatican Apostolic Library, Vatican City Masashi Mizokami National Center for Global Health and Medicine, Japan Tebello Nyokong Rhodes University, South Africa Didier P. Queloz ETH Zurich, Switzerland Rafael Radi Universidad de la República, Montevideo, Uruguay Daya Reddy University of Cape Town, South Africa Rocco Ronzani Pontifical Archive, The Vatican City
20:00-21.30	Dinner at Casina Pio IV


PRESENTATIONS

YOUTUBE LINKS

On Human Anthropology: Human Adaptation and Evolution

Tekklu Zeresenay Alemseged


(PAS), University of Chicago, USA

 https://youtu.be/wbTdObbcqus?si=vEOoMbdw__sLOips

AI Research and Infrastructure for the Life Sciences. The EMBL Perspective

Rolf Apweiler


Joint Director of European Molecular Biology Laboratory (EMBL), European Bioinformatics Institute (EBI), UK

 <https://youtu.be/wb1cIbM5doQ?si=40hAI2Z1Ozt9uqRN>

Balancing Food Security, the Environmental Impact of Crops, and Equitable Use Of New Technology

David Baulcombe


(PAS), Regius Professor of Botany Emeritus, Cambridge University, UK

 <https://youtu.be/2NDd4tSJJlE?si=y11c0mk7aMDYkAXf>

Exploring the Quantum World through Quantum Simulations

Immanuel Bloch


Scientific Director, Max Planck Institute of Quantum Optics, Germany

 <https://youtu.be/vQQVhO3PFT4?si=x6xy0BjIBNyIRtwZ>

Science Policy Perspectives

Francesca Cesari


Chief Editor, Nature, Biological, Clinical and Social Sciences, United Kingdom

 https://youtu.be/V9JVs0hXFhY?si=l8yOLcDccZfgB_qQ

Quantum Simulation and New Quantum Phases with Long-Range-Interacting Ultra-Cold Atoms

Francesca Ferlaino

Institute Scientific Director, University of Innsbruck, and Austrian Academy of Sciences, IQOQI, Austria

 <https://youtu.be/mRvtVLxoKiY?si=BqhhvFETr6ZGWg5w>

Quantum Systems Open to the World

Ana Asenjo-Garcia

Associate Professor of Physics, Columbia University, USA

 https://youtu.be/FZnBbxrIpnA?si=HJKNv37V_Khl8rF6

Marine Science with AI for Sustainability and Wellbeing. Geomic Big Bang

Takashi Gojobori

(PAS), Distinguished Professor King Abdullah University of Science and Technology

 <https://youtu.be/XccC6ZR7044?si=dSLdBzoSUuJkjoj>

Challenges and Advances in Climate Change Research and in Bending the Curves towards a Sustainable Stewardship

Örjan M. Gustafsson


(PAS), Stockholm University, Sweden

 https://youtu.be/XEpv7wPzCaM?si=bUSoiPMbL_GRw-0O

Accelerating Scientific Discovery with AI

Demis Hassabis

(PAS), Google DeepMind, UK

 <https://youtu.be/UX8uIW9oIZk?si=HCTfz8dTZdi4zDVj>

Summary of the PAS Workshop on Indigenous Knowledge and the Sciences

Mohamed Hassan


(PAS)

 <https://youtu.be/nPjaxg90nME?si=xNOZIOH7OXzWzCGc>

The Future of Genomic Medicine

Eric Lander


(PAS), Broad Institute, MIT, and Harvard, USA

 <https://youtu.be/dM3VeUaqqqU?si=BnFG-Zho2ON7NdEh>

Life in the Universe: Astrophysics Perspectives

Didier Patrick Queloz


(PAS), Professor ETH Zurich, Switzerland

 <https://youtu.be/Cry41d07Eew?si=Y1uYEbCOftkLfOU>

Climate Crisis, Biodiversity Loss and Human Contexts

Veerabhadran Ramanathan


(PAS), Professor Emeritus, Scripps Institution of Oceanography, University of California, San Diego, USA

 https://youtu.be/0_Ny48ssrVs?si=Ia_NehMaEjwdVER

Climate Crisis, Biodiversity Loss and Human Contexts

Hans Schellnhuber

(PAS), Director General IIASA, Austria

 <https://youtu.be/vHifF4n8W30?si=pSsFesGlTLWWZLMH>

Global Environmental Measurement and Monitoring (GEMM)

Donna T. Strickland


(PAS), Professor, University of Waterloo, Canada

 https://youtu.be/_XjFIgJNVk?si=pFKJUQBh6Dedwml

Astronomy and Changing World Views

Ewine van Dishoeck

(PAS), Leiden University, The Netherlands


 https://youtu.be/LJ441YU49y8?si=4x37BZxm0jFKYN_E

COMMEMORATION OF DECEASED ACADEMICIANS

YOUTUBE LINKS

Commemoration of Ignacio Rodriguez Iturbe

Edward De Robertis
(PAS)

 <https://youtu.be/UKEVJTsu8fs?si=YxuHI52n687pD1Lm>


Commemoration of Yuri Ivanovich Manin

Daya Reddy
(PAS)

 https://youtu.be/-pBr9BUaO8g?si=45H6xtlxqrqrt_9n


Commemoration of Albert Eschenmoser

Rafael Radi
(PAS)

 <https://youtu.be/uFtMFMLpzpI?si=KHnVOOh4nO5WJtAe>


Commemoration of Hans Tuppy

Stefano Piccolo
(PAS)

 <https://youtu.be/EWCyjS1yi9k?si=fCbey0eYQ0Mmgc0E>


Commemoration of Sergey Petrovich Novikov

Mohamed Hassan
(PAS)

 <https://youtu.be/YXpey2yxOm4?si=xlz-xWb4mKYsG65>

Commemoration of Maxine F. Singer

Chien-Jen Chen
(PAS)


 https://youtu.be/xkka_PH-0aM?si=djoi22OK96qneL4K

SELF-PRESENTATIONS

YOUTUBE LINKS


Örjan Gustafsson

Stockholm University, Sweden

 <https://youtu.be/hO2Jj794wS0?si=ImqGyL4RQavz9AFC>


Demis Hassabis

Google DeepMind, UK

 <https://youtu.be/bJdOybjcyP4?si=5S4M0jp37Xgn5gZz>


Masashi Mizokami

National Center for Global Health and Medicine, Japan

 <https://youtu.be/SO9ScdFwLrk?si=fh1yzTEsWd3oKN6P>

Tebello Nyokong

Rhodes University, South Africa

 Rhodes University, South Africa


Didier P. Queloz

ETH Zurich, Switzerland

 <https://youtu.be/arLLDCCWiAo?si=Nmi2f-SoIqiaKV0z>

Rafael Radi

Universidad de la República, Montevideo, Uruguay

 https://youtu.be/COtCQjy_HJc?si=4pvlSdRx9UKS8z5R

Daya Reddy

University of Cape Town, South Africa

 https://youtu.be/oNPs_SQps0o?si=GmJWJ7A7er0cC1uA

Mauro Mantovani

Good morning / afternoon,

I'm very pleased and honoured to join this Plenary of our Pontifical Academy of Sciences and to briefly introduce myself.

I'm father Mauro Mantovani, member of the Congregation of Salesians of Don Bosco, Italian. Since February 2023 I am the Prefect of the Vatican Apostolic Library.

I studied in Turin (my hometown), in Rome and in Salamanca (Spain), achieving a Doctorate in Philosophy at the Pontifical University of Salamanca, and a Doctorate in Theology at the Pontifical University Saint Thomas Aquinas "Angelicum" in Rome.

I'm still teaching Theoretical Philosophy – even though now in a very reduced way – at the Pontifical Salesian University, Rome, where I was the Dean of the Faculties of Philosophy and Sciences of Social Communication, and the President, in the period 2015-2021. During those same years I also directed the Conference of Rectors of the Roman Pontifical Universities (CRUIPRO).

My principal fields of research and publication are various questions at the border between philosophy and theology, often also in dialogue with natural and human sciences, considering the works and tradition of thought connected with Thomas Aquinas, like the notions of creation, eternity and time, nature and grace, freedom, human person, integral ecology, and the meaning of history. I have worked in particular on the commentaries to the *Summa Theologiae* by the Dominican and Jesuit Masters in Theology of the 16th and 17th centuries, the so-called "Second Scholasticism".

Among other things, I am a member of the Pontifical Academy of Saint Thomas Aquinas, of the Scientific Committee of AVEPRO – the Agency of the Holy See for promoting Quality and Evaluation in the Universities – and consultant of the Dicastery of Education and Culture.

In the last few years a particular object of reflection has been the Foreword (*Proemium*) of the Apostolic Constitution *Veritatis gaudium* by Pope Francis, with the invitation to deepen and to practice inter- and cross-disciplinarity in relation to and in dialogue among the sciences: this is a very fruitful epistemological perspective and concrete indication of work.

The idea of interdisciplinarity and dialogue is also represented on the entrance door of the Vatican Library, with the presence of theology, canon law, philosophy, mathematics, natural sciences, astronomy, literature, arts and education; it is a place where PAS Academicians will always be welcome.

Thank you.

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White House Office of Science and Technology Policy, and Professor at Oregon State University

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Pontificia Universidad Católica de Chile
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Head of Center for Climate and Foreign Policy
German Council on Foreign Relations
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Prof. Klaus von Klitzig 🕉 PAS Academician
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Professor Emeritus
University of Vienna
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Prof. Maria T. Zuber
Presidential Advisor for Science and Technology Policy and E. A. Griswold
Professor of Geophysics at MIT; Co-chair of President Biden's Council of Advisors
on Science and Technology
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