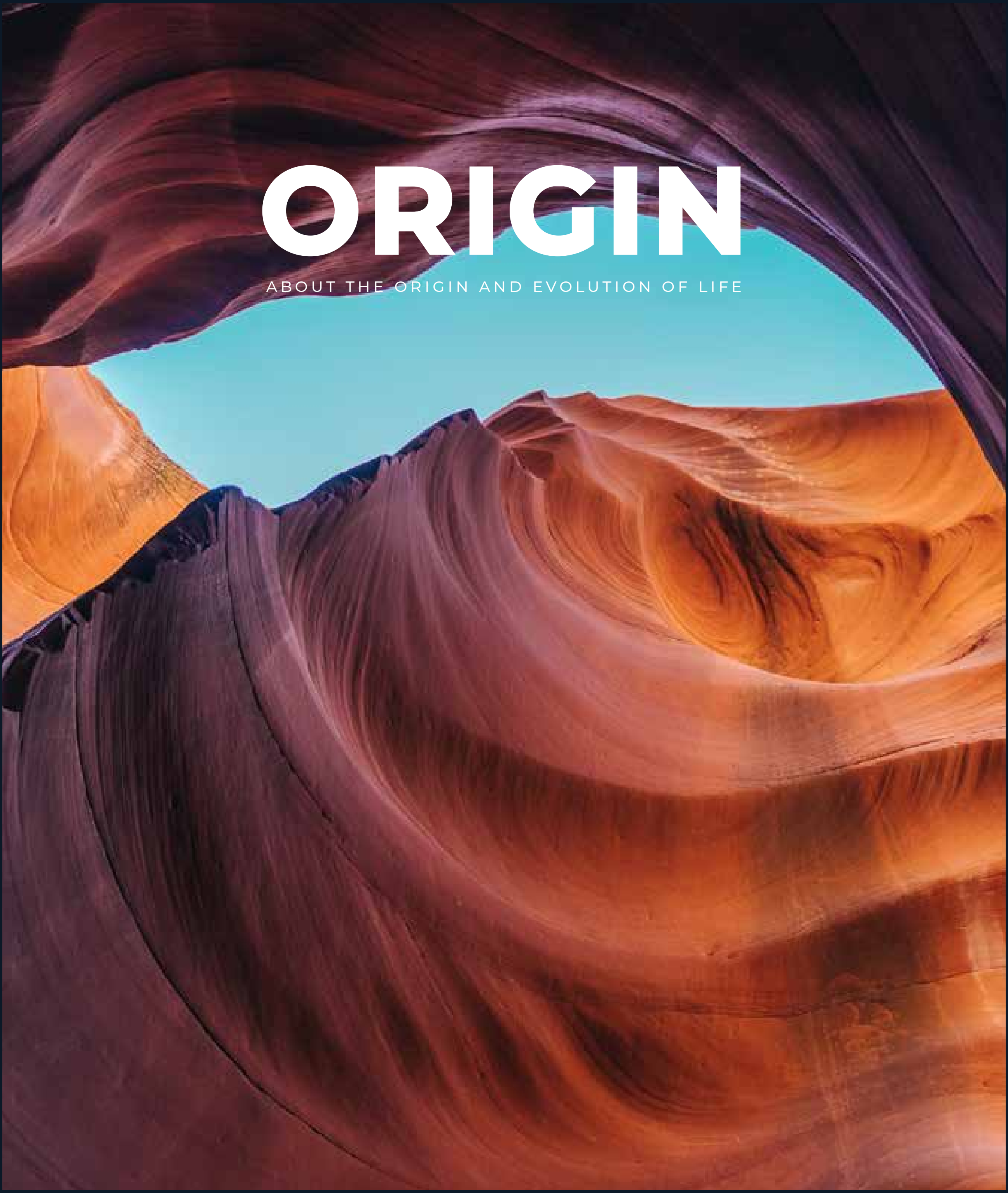


ORIGIN

ABOUT THE ORIGIN AND EVOLUTION OF LIFE

Origins Center

2022 / Special issue

Index.

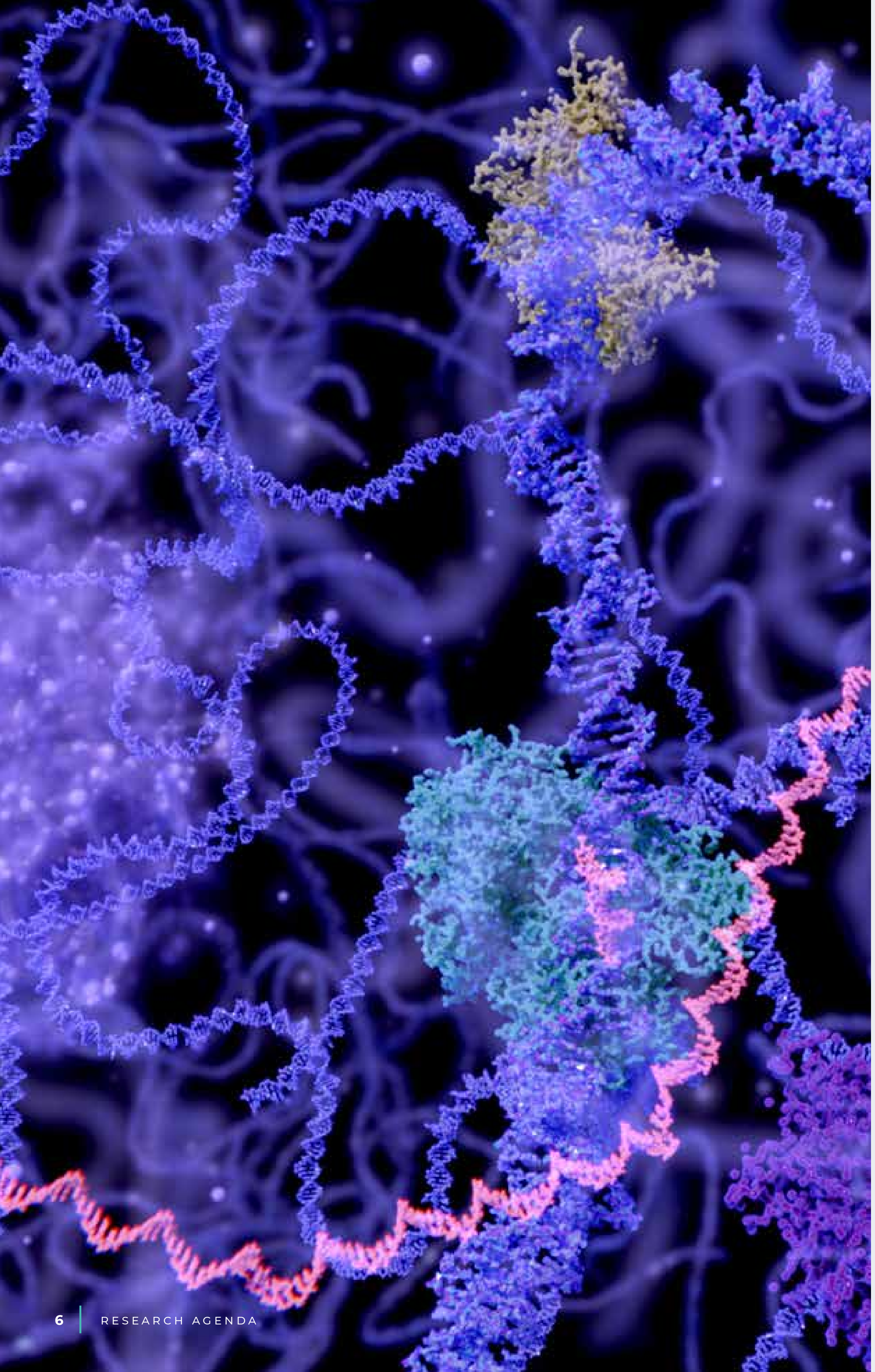
FOREWORD

Origins: an ancient fascination

The Origins Center focuses on some of the most profound unanswered questions in contemporary science: how can life emerge from inanimate matter, how does life evolve from simple beginnings to a complex global ecosystem, and can we bring lifeless matter into the state of being alive?

The question of the origin of life has fascinated mankind for thousands of years. For example, the important place of scarab beetles in Egyptian mythology relates to observation that scarabs were believed to emerge fully-formed from a ball of dung. The Greek philosopher Aristotle also advocated the notion of spontaneous generation, where living creatures emerge from inanimate matter all the time. It took until the work of Pasteur in 1861 to realize that life does not emerge de-novo, but that it derives from pre-existing forms of life. This insight shifted the problem of the origins of life billions of years back in time and also meant it remained an intractable problem for another one and a half centuries. Yet with the advances in multiple different fields of science this situation has now changed. Life-like properties are increasingly being engineered in artificial systems in chemistry, materials sciences, robotics and, due to the intimate linkage of life and information, also informatics.

The question how life may emerge may be resolved in the near future. Also the question of the distribution of life across the universe is becoming increasingly tractable, now that several new observatories (have) become operational.



FOREWORD

ABOUT THE ORIGINS CENTER

The Origins Center owes its existence to the continuous fascination for the origins questions. In 2015 the general public in the Netherlands was asked to identify the most important current scientific questions. This consultation resulted in the identification of 25 main themes, including "The Origin of Life on Earth and in the Universe". In 2016 Dutch scientists from a diverse range of backgrounds came together in a series of bottom-up meetings. The momentum and enthusiasm that arose there culminated in the 2016 founding of the Origins Center, celebrated with a two-day international conference "Fundamentals of Life in the Universe" at the University of Groningen in the summer of 2017.

ACTIVITIES OF THE ORIGINS CENTER

Within the Origins Center, Netherlands-based scientists address questions about the origins and evolution of life as we know it (assuming it originated on Earth). Research on these questions also supports the search for life beyond the confines of our planet. The current goals of the Origins Center are (i) to bring together scientists involved in the disciplines needed to address origins questions, (ii) to identify open questions on crossroads within the Dutch scientific community that study Origins Center related questions, (iii) to enable and support networks and consortia focused on central questions within the origins landscape, (iv) to foster national and international collaboration, through workshops and conferences, (v) to keep the community informed about Origins Center activities, funding opportunities, other relevant scientific news and opportunities, and (vi) to provide a visible platform for scientists, societal partners, and the public to connect.

ORIGINS RESEARCH LANDSCAPE AND RESEARCH AGENDA

This Research Agenda outlines the landscape of scientific questions in which the Origins Center operates (Page 10). It maps the scientific strengths of research in the Netherlands in areas relevant to these questions (Page 30) and surveys other initiatives that have sprung up in this area outside the Netherlands (Page 34). Finally, it describes an agenda for future research (Page 38).

ON THE TRAIL OF EARLY LIFE AND EVOLUTION

Discovering Origins.

Perseverance explores Mars, the James Webb telescope promises new discoveries, and space tourism from Blue Origin and SpaceX brings the world beyond the atmosphere live on everyone's screen. But the search for the origin of life and the understanding of evolution goes much further than that. Ground-breaking discoveries about life often begin as a small observation. The Origins Center supports researchers to develop initial, hopeful, results into new insights.

The Origins Research Landscape.

Life originated as a result of the confluence of many factors spread over space and time. Unravelling its origin requires an effort from many different disciplines and approaches from many different angles, involving processes that occur on vastly different length and timescales.

To provide the appropriate context to the research addressed within the Origins Center, we identified a series of key events in the emergence and development of life. The chronology of these events is not precisely known and some events are interdependent, so treating them separately may not be justified.

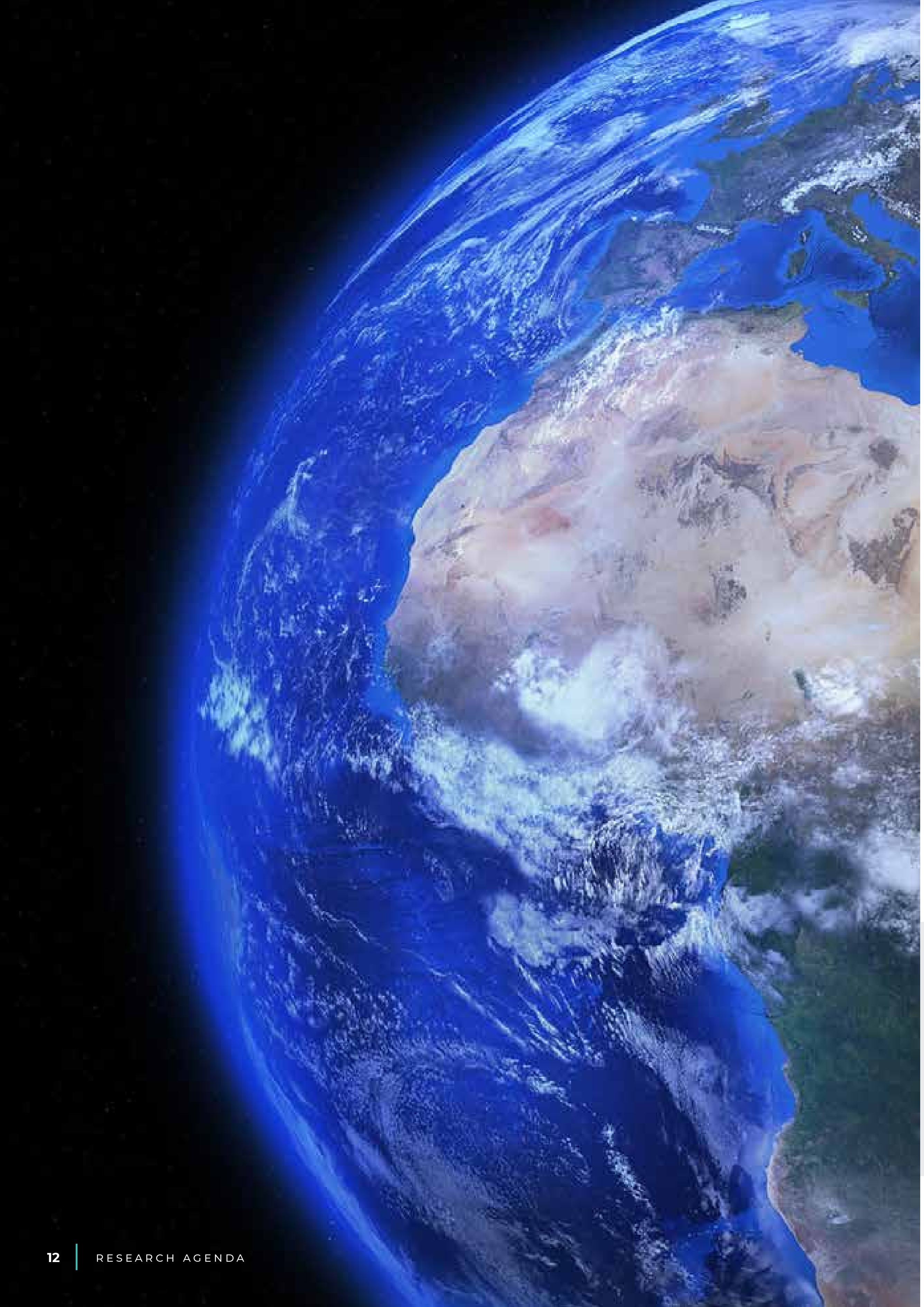
TWELVE KEY EMERGENCE EVENTS

In our bottom-up meetings the following key emergence events have been identified that could have resulted in the origin of life and the evolution towards contemporary complex life.

- **1 -** The formation and early evolution of Earth-like planets and moons
- **2 -** The emergence of conditions allowing for the origin of life
- **3 -** The emergence of molecules relevant to life
- **4 -** The emergence of life-like functions in prebiotic systems
- **5 -** The emergence of Darwinian evolution
- **6 -** The emergence of life
- **7 -** The interaction between local and planetary scale environments and life
- **8 -** The emergence of genotype-phenotype separation
- **9 -** The emergence of contemporary biochemistry
- **10 -** The emergence of a contemporary-like prokaryotic cell
- **11 -** The emergence of eukaryotes
- **12 -** The emergence of multicellularity

These research themes encompass processes starting from planet formation all the way to the emergence of multicellularity, and require input from scientists from astronomy, Earth science, chemistry, (bio)physics, biology, ecology, and mathematics. While perhaps not explicit, the ability to model complex systems and processes and to bridge temporal and spatial scales is essential for a complete understanding of many of the topics addressed below. Developing the relevant computational tools is thus also an integral and recurrent part of the approach to these topics.

Our vision is that, building on the continuously extending knowledge of the origin and evolution of life, the prediction of the (co-)evolution of life and planets, and finding extraterrestrial life may eventually become feasible.

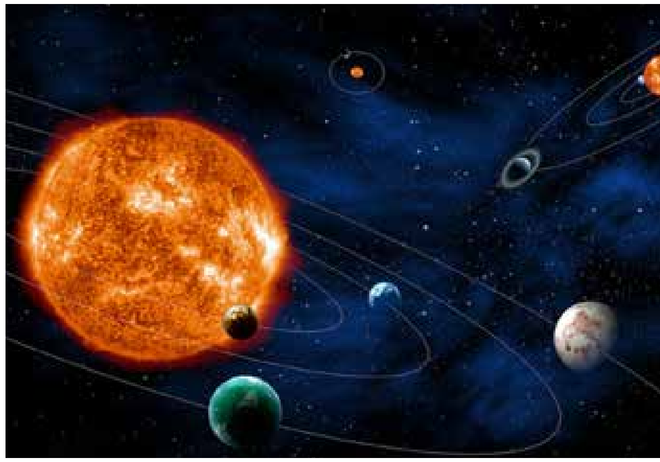


Theme 1

The formation and early evolution of Earth-like planets and moons.

In this Research Agenda it is assumed that life as we know it originated on Earth, and that the same might have occurred on other rocky or icy (but not gaseous) planets or moons. The potential for planets or moons to become solid bodies thus depends on the earlier stages of their physical development. Planet formation is driven by the astrophysical environment of the formation. This is in turn determined by the composition of the galaxy, the location and the composition of the dust and gas cloud from which a planetary system evolves, the composition of the host star, and the physical and chemical conditions in protoplanetary disks. Processes such as dust coagulation, run-away accretion (the accelerated growth of planetary mass from the protoplanetary disk), grain surface chemistry, reshuffling of orbits, and bombardments are all relevant.

> *Whether an Earth-like planet can potentially harbor life depends crucially on the location of the planet in its planetary system.*

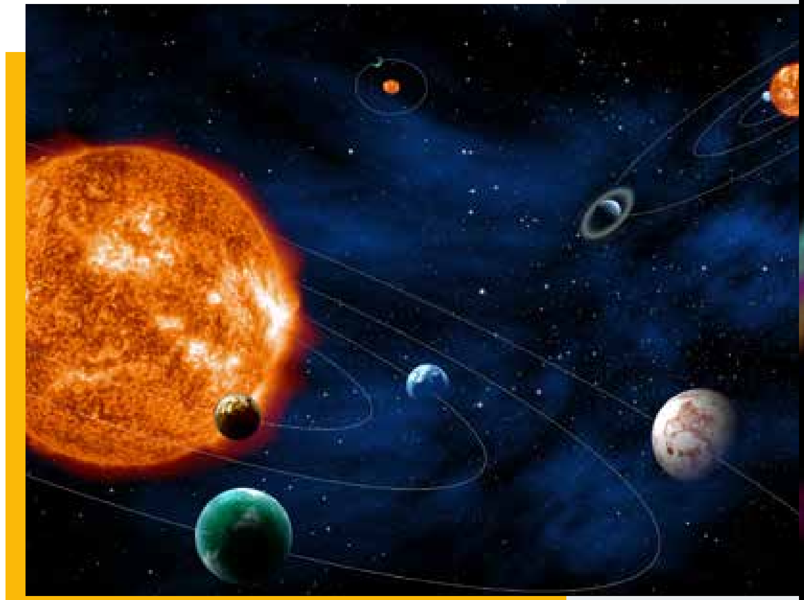


Especially important to this Research Agenda are the physical and chemical processes by which a gas and dust protoplanetary disk develops into fully-fledged planets. Whether an Earth-like planet can potentially harbor life depends crucially on the location of the planet in its planetary system. Research objectives therefore include identifying growth mechanisms from pebble to protoplanet and unravelling migration processes in our own early Solar System that have led to the current planet distribution.

Theme 2

The emergence of conditions allowing for the origin of life.

After their formation planets and moons continue to change. The first 1-1.5 billion years of the Earth's evolution were crucial for the development of processes that allowed for the emergence of life. In this early stage the Earth shared many properties and phases in its evolution with other solid bodies. These properties included a certain degree of interior differentiation, a surface magma ocean phase, and degassing of volatiles into an atmosphere. Like the Earth, some other solid solar system bodies have experienced prolonged episodes of volcanism and liquid water on their surface, indicating the presence of an atmosphere, and some once had, or still have, an active magnetic field. In addition to these shared characteristics, the current-day Earth has a range of unique features. These features include an active dynamo in the core leading to a strong magnetic field, plate tectonics leading to recycling of the crust, and liquid surface oceans. On Earth these features have led to global cycles of, for example, water and carbon through ocean-atmosphere interaction and sedimentation processes, and the formation of new minerals.



Research objectives include identifying which geochemical and geophysical features of the Earth facilitated the origin and early evolution of life, how these features constrained the possible locations for life to originate, and how Earth-specific these features are.

Theme 3

The emergence of molecules relevant to life.

Life originated around certain molecules, yet we do not know exactly which ones and why. To be able to identify which molecules gave rise to life we need to know (i) the geochemical processes that occurred on the prebiotic Earth, (ii) the chemical and physical composition of the prebiotic environment, and (iii) the energetic drivers behind the formation of complex molecules that were utilized by primitive life. Additional objectives are identifying plausible prebiotic syntheses of the small molecule building blocks of contemporary life, prebiotically plausible syntheses of (functional) biopolymers, and prebiotic catalysts and energetic couplers and their emergence. General chemical properties of life, such as homochirality, should also be explained. It is, however, unclear where and when the chiral symmetry-breaking emerged that led to homochirality in life. Did the prebiotic environment provide a small deviation from chiral symmetry that was amplified to yield homochiral molecules?

Theme 4

The emergence of life-like functions in prebiotic systems.

Even though no consensus exists on the definition of life, there is widespread agreement that living systems require the functional integration of the following elements:

> (i) - Self-replication: the ability to generate copies of oneself, accompanied by transfer of information stored in (and acquired by) the system. When this information is stored at the level of its constituent molecules such systems are self-replicating. Alternatively (or additionally) information can be stored and copied at the level of a molecular network. Such systems may be able to undergo Darwinian evolution if specific conditions are met (see below).

> (ii) - Metabolism: the ability to utilize energy and building blocks from the environment to sustain processes that require material and energy, such as growth and replication.

> (iii) - Compartmentalization: the ability to separate oneself from the environment, as well as to communicate with the environment and exchange matter and energy.

Another aspect that might have occurred early in the evolution of life is motility, as active motion promotes the spreading of material and allows systems to access resources more efficiently than their non-motile counterparts.

Research objectives are to identify new routes through which these functions can emerge from inanimate matter and, where routes already have been identified, to better understand the process of their emergence. Since life relies on the intimate functional integration of replication, metabolism, and compartmentalization, another important goal is to establish pathways that result in such integration. Initially pairwise combinations of the three important functions can be targeted, which may ultimately lead to insight into how all three functions may be combined. These questions may be addressed within the constraints of prebiotic chemistry or, alternatively, be addressed at a more general conceptual level and making use of systems of completely synthetic components, unconstrained by prebiotic relevance or current biochemistry.

Theme 5

The emergence of Darwinian evolution.

Darwinian evolution requires a continuous cycle of replication, mutation, and selection. It can lead to open-endedness, meaning the processes continue endlessly and new traits and functions can emerge that may enhance fitness of the individuals that possess these. Three essential elements can be identified within Darwinian evolution:

(i) - Individuality, giving rise to units of selection;

(ii) - Inheritance, relying on the existence of information (in the form of chemical structure/sequence or composition) that is replicated and subject to variation (mutation);

(iii) - Selection, resulting in a consistent bias in the outcome of the competition between different variants within a certain environment.

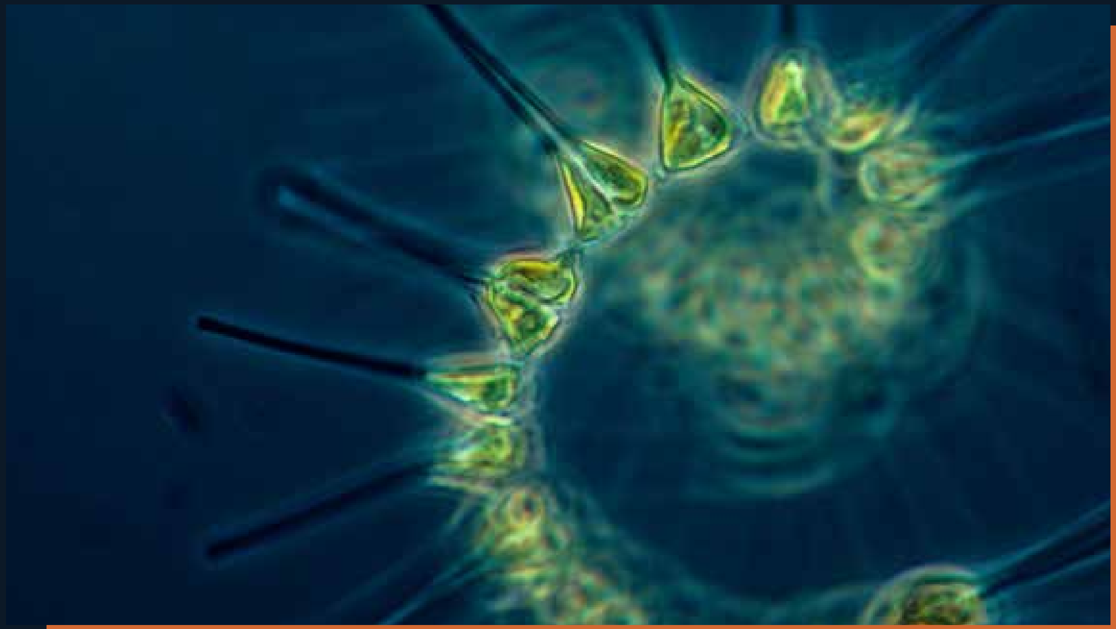
One objective is to identify routes through which chemical systems (populations of molecules) can emerge that can undergo Darwinian evolution. Another objective is to identify what makes evolution open-ended. Open-ended evolution would require the existence of a vast landscape of (realized and unrealized) possibilities of which the population, at any given timepoint, only occupies a very small subset, so that new (unrealized) possibilities are always available. This notion conflicts with the inherently divergent nature of chemistry, where the extensive cross-reactivity between molecules rapidly leads to a combinatorial explosion of new molecules, causing a chemical system to rapidly occupy a comparatively large fraction of all possibilities. An important element of this objective is to discover mechanisms that restrain the divergent nature of chemistry and channel it into specific populations of evolving entities.

Evolving systems are likely to cause changes in their environment or ecosystem, which in turn are likely to influence the evolving system itself. Understanding the mechanisms and role of such eco-evolutionary dynamics and feedback are further objectives.

Theme 6

The emergence of life.

At some point and by some means chemistry transitioned into biology. It remains unclear which exact features are most relevant to make a distinction between inanimate chemistry and biology.

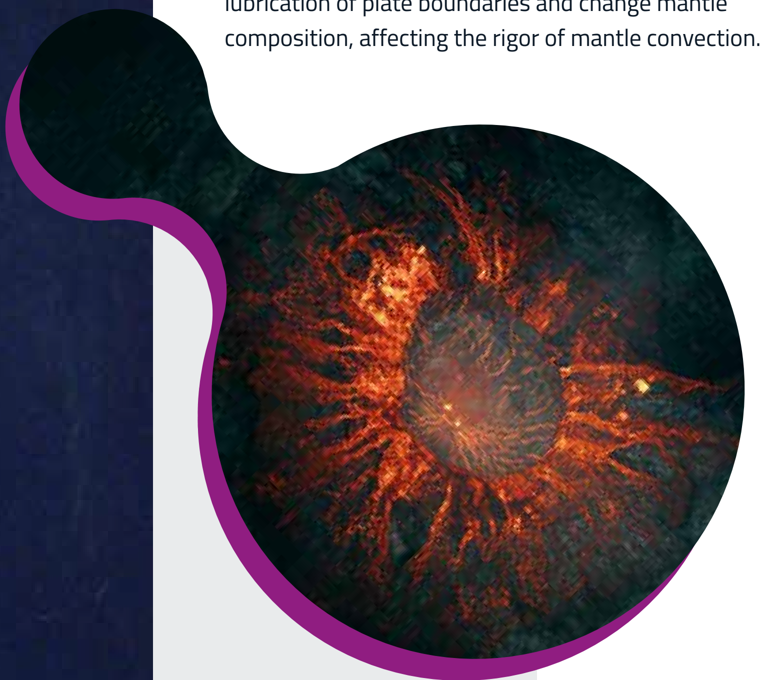


To complicate matters further, we do not know whether this transition was discontinuous, similar to a phase-change, or whether it was a gradual process. Apart from the nature of the transition being unclear, also defining life is fraught with difficulty.

These considerations provide a strong incentive to create and investigate minimal forms of life and experimentally probe the transition from chemistry to biology. While highly challenging, such approaches may inform us on what constitutes the essence of life. It will also stimulate work towards engineering life's characteristics in artificial systems and technologies.

Theme 7

The interaction between local and planetary scale environments and life.



Classically, planet-life interaction has been viewed as a one-way street, with planetary processes and properties determining the boundary conditions for life that then adapts to these conditions through evolution. However, it is now becoming increasingly clear that planetary evolution may be strongly affected by the evolving life it sustains on all geological timescales.

The effects of life on the environment can be profound at the local scale, but when will these effects exceed the local environment and alter the environment globally? For example, sedimentation and subduction of water-bearing clay minerals driven by organic compounds enhances the lubrication of plate boundaries and change mantle composition, affecting the rigor of mantle convection.

The existence, abundance, and diversity of life can change Earth's environment, for example through its role in the carbon and oxygen cycles. Planetary carbon cycles depend in part on surface weathering, which is linked directly to life activity. How, in turn, will life adapt to this altered environment? Not only gradual change but also catastrophic events, such as meteor impacts, volcanism, and large igneous provinces (remnants of ancient eruptions of extremely large volumes of magma from deep in the Earth) can influence the environment on scales from local to global and cause mass extinctions. Will the planetary boundaries under which life was formed be maintained through biotic and abiotic feedback processes?

Objectives are to determine how life affects planetary evolution and how life is influenced by catastrophic events and gradual environmental change, including human induced change, and how these changing ecological drivers of selection lead to evolution.

Theme 8

The emergence of genotype-phenotype separation.

The separation between genotype and phenotype marks an important stage in the development of life, as it boosts the ability of evolution to invent. The high complexity of the current biological machinery of transcription and translation that connects phenotype to genotype suggests that this system is itself a product of evolution. This notion raises the questions whether there are other conceivable molecular implementations of phenotype-genotype separations that could have preceded the genetic code and how these then transitioned into the transcription-translation mechanism of extant life. Another objective is to develop synthetic systems capable of self-replication achieving a separation between phenotype and genotype that are altogether different from that found in current life.

It is also important to improve our understanding of genotype-phenotype interactions in evolution. Specific objectives include:

> (i) Establishing how genetic information specifies the structure and the function of a level of biological organization: the genotype-phenotype map;

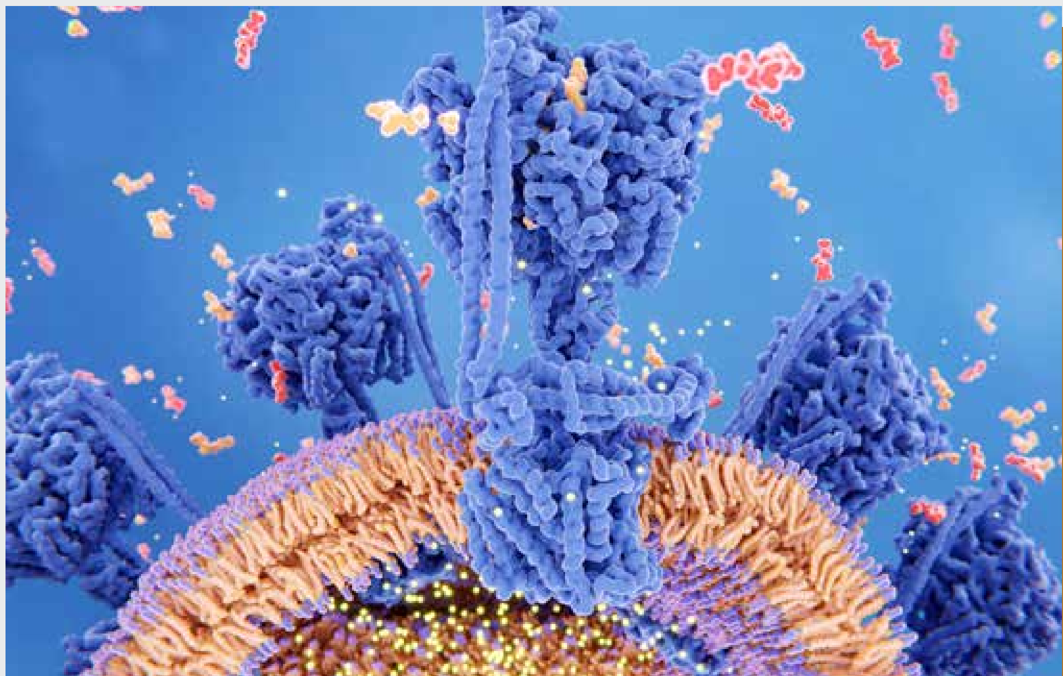
> (ii) Understanding how the genotype-phenotype map is shaped by evolution.

Theme 9

The emergence of contemporary biochemistry.

All life forms we currently know share essentially the same biochemistry, based on DNA, RNA, and proteins, connected through a common genetic code and a universally conserved core of metabolites. But why does life use the specific set of nucleobases and amino acids where many others are conceivable and accessible?

At present it is unclear whether this current biochemistry is an inevitable outcome (a consequence of characteristics embedded in the underlying chemistry) or a chance result arrived at by the stochastic nature of evolution. Regardless, it is relevant to identify evolutionary routes through which contemporary biochemistry could have come about. Phylogenetic analysis is an important tool to approach this objective. An alternative approach to this question is to develop completely synthetic forms of life, allow these to evolve, and observe whether they converge on extant biochemistry. As an intermediate approach also synthetically modified biological systems may be studied (xenobiology) and their performance compared to current life.



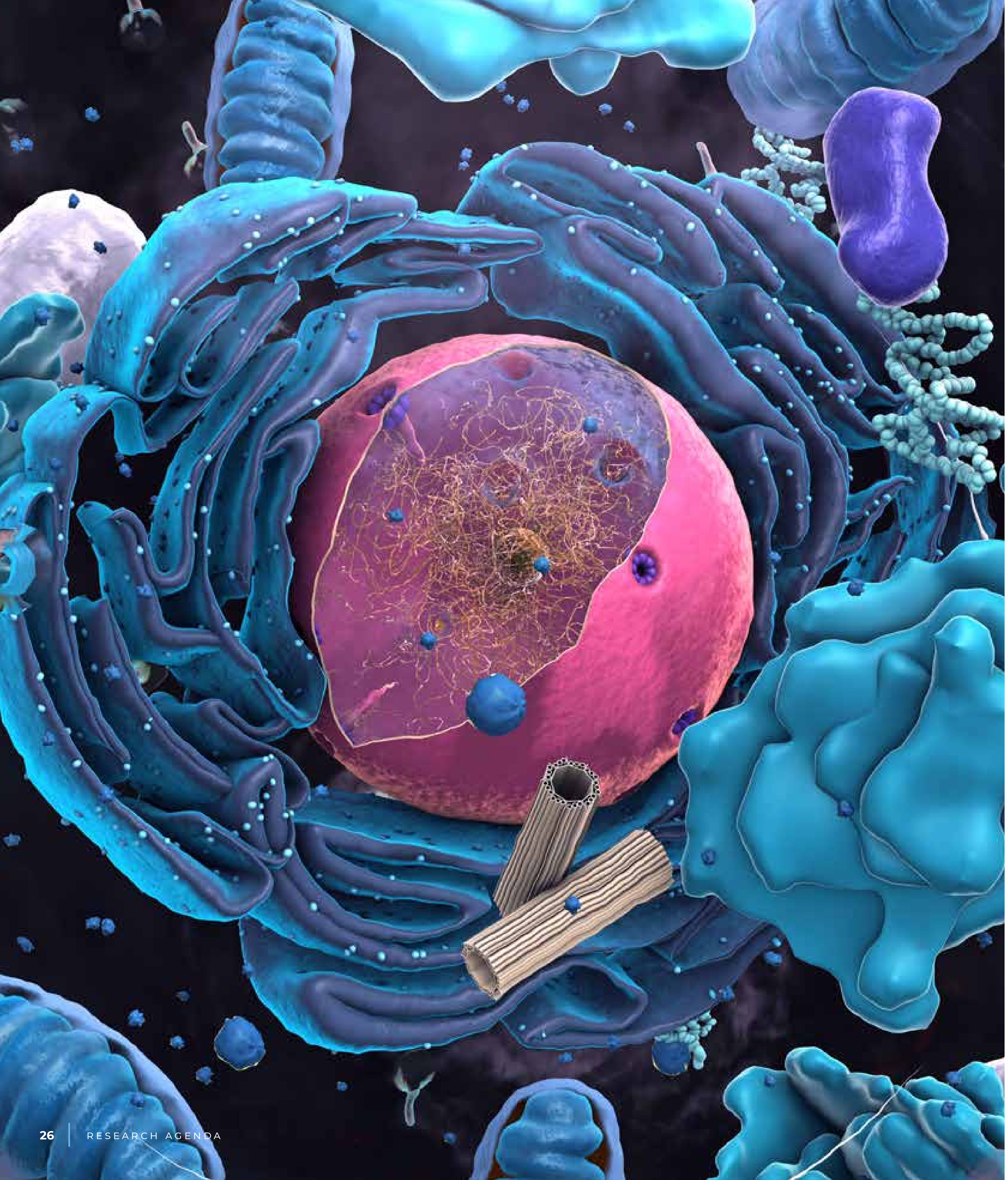
Theme 10

The emergence of a contemporary-like prokaryotic cell.

The question of how the first cells emerged that closely resembled contemporary prokaryotes can be approached bottom up. This approach is essentially an extension of several of the research questions listed above, aimed at the integration of the important functions of life, but addressed through making use of the canonical classes of biomolecules (carbohydrates, proteins, and lipids). It may also be informed by an improved conceptual understanding of the most important functional characteristics of cells:

- (i) - Replication;
- (ii) - Metabolism;
- (iii) - Spatial patterning, compartmentalization.

How these functional characteristics can become integrated and act collectively may be revealed through systems biology approaches and efforts aimed at the construction of a synthetic cell.



Theme 11

The emergence of eukaryotes.

Compared to prokaryotes, eukaryotic cells are tremendously complex. Eukaryotic cells tend to be larger, tend to contain more genetic material, have multiple membrane-bound compartments, and operate a dynamic cytoskeleton. The last eukaryotic common ancestor already had an intracellular organization and gene repertoire characteristic of present-day eukaryotes. These features make the transition from prokaryotes to the first eukaryotes, eukaryogenesis, the evolutionary transition with the largest increase in cellular complexity (after the origin of life) and one of the main unresolved puzzles in evolutionary biology.

Most eukaryogenesis models involve a host, related to the recently discovered Asgard archaea, which took up an Alphaproteobacteria-related endosymbiont that gave rise to the mitochondrion. However, the timing and impact of this endosymbiosis event in the evolution of eukaryotic complexity are hotly debated and at the heart of different scenarios on eukaryogenesis. Besides the acquisition of genes via the endosymbiont, the proto-eukaryotic genome expanded through gene inventions, duplications, and horizontal gene transfers during eukaryogenesis. Previous work suggested that gene duplications nearly doubled the ancestral proto-eukaryotic genome. Gene families such as small GTPases, kinesins, and vesicle coat proteins greatly expanded, which enabled proto-eukaryotes to employ an elaborate intracellular signaling network, a vesicular trafficking system, and a dynamic cytoskeleton.

The study of eukaryogenesis is complicated by the absence of evolutionary intermediates. Massive amounts of novel sequencing data and development of novel phylogenomic methods promise to bring us closer to describing the events during one of the long-standing unresolved puzzles in biology. To explore mechanisms that can explain the observations in these data, computational models are needed. These models may, for example, reveal whether eukaryogenesis was a one-time historical accident or whether some mechanisms during this transition happened more often.

Theme 12

The emergence of multicellularity.

Multicellularity is a new level of biological organization, in which cells have partly or entirely given up their autonomy by being part of a larger organism. This organism forms a new unit of selection and evolution. Multicellularity evolved several times independently: in plants, fungi, and animals, and - in simpler form - in other eukaryotes and some bacteria.

While many of the interactions between cells in a (developing) multicellular organism are driven by self-organization principles, the new level of organization also entails a considerable extension of the genotype-phenotype map.

Objectives therefore are:

> (i) Identifying what physico-chemical principles drive the self-organization of cells to form aggregative clusters;

> (ii) Identifying what are the selective pressures that facilitated the transition to multicellularity, and the evolutionary consequences of self-organization into a higher-level biological entity for the constituting cells;

> (iii) Identifying how these processes are cemented into, and enabled by, an evolving genotype-phenotype map, ultimately giving rise to (embryonic) development.

Several approaches are needed to achieve these objectives. Bioinformatic analysis is instrumental in reconstructing the evolutionary history of ancient pre-multicellular life and the genetic toolkit that enabled self-organization in cell clusters. Computational models are needed to understand the mechanistic basis and the long time-scale evolutionary consequences of such self-organization. The principles found with such models should be tested in vivo in experimental evolution model organisms.

AN ANALYSIS OF ORIGINS-RELATED RESEARCH STRENGTHS IN THE NETHERLANDS

The Origins Strengths in the Netherlands.

All the research areas needed for a consolidated research program in Origins-related science are present in the Netherlands. Within the different disciplines several key areas are recognized as internationally leading. The Origins Center is committed to support, unify, and enable advancements in these academic areas of expertise.

Strong Scientific Roots Empower Origins NL.

- Caroline Bleeker & Frits Zernike, inventors of the phase contrast microscope
- Henry van 't Hoff, founder of stereochemistry, osmosis, and physical chemistry
- Christiaan Huygens, inventor of telescopes
- Jacobus Kapteyn, fundament of astronomy in the Netherlands, discoverer of galactic rotation
- Albert Jan Kluyver, discoverer of the unity of biochemistry
- Antoni van Leeuwenhoek, inventor of microscopes, founder of microbiology
- Carolina MacGillavry, crystallographer, co-founder of the direct methods of crystallography
- Jan Oort, fundament of Dutch astronomy, postulated the Oort cloud and dark matter
- Niko Tinbergen, founder of ethology
- Hugo de Vries, founder of genetics
- Johanna Westerdijk, plant pathologist and founder of the Central Bureau for Fungal Cultures

The Origins Strengths.

ASTRONOMY

The historically strong role of the Netherlands in astronomical research, with famous figures such as Oort and Kapteyn, continues to the present day. Dutch astronomy is coordinated by the Netherlands Research School for Astronomy (NOVA), which is consistently described as world-leading by international review boards. The Netherlands is a major partner in European organizations such as ESO and ESA, and Dutch astronomers have won many international prizes for their research *(such as the recent 2018 Kavli prize for Ewine van Dishoeck).*

ASTROBIOLOGY

Astrobiology, formerly known as exobiology, is an interdisciplinary scientific field concerned with the origins, early evolution, distribution, and future of life in the universe. The Netherlands hosts world-leading researchers who operate both in their discipline and in the interdisciplinary field of astrobiology. This research includes the definition and study of planetary habitability, indicators of habitability, identify signatures of extinct and extant life (biosignatures), and instrument development to detect these biosignatures.

The Origins Strengths.

GEO- AND PLANETARY SCIENCES

All aspects of geosciences, from the Earth's core via the surface to its atmosphere and climate, are represented in the Netherlands at an internationally leading level. The NWO gravition program funded The Netherlands Earth System Science Center, the large-scale research facility European Plate Observing System – Netherlands (EPOS-NL), and their predecessors the Netherlands Research Centre for Integrated Solid Earth Science (ISES) and the Darwin Center for Biogeoscience, are exemplary for the state of the art of geosciences in the Netherlands. In addition, the Netherlands has a long-standing, strong involvement in the development of space-based instrumentation for atmosphere, vegetation, and climate monitoring. Geodynamics, the geophysics and geochemistry of interior evolution of planets and rocky and icy moons, paleoclimate, and Early Earth research are among the current world-leading research fields that are directly related to the Origins Center.

CHEMISTRY

Supramolecular chemistry in the Netherlands is world-leading (spearheaded by the Functional Molecular Systems NWO gravitation program; *2016 Nobel prize in chemistry for Ben Feringa*), as is research in catalysis. Recent focus on out-of-equilibrium systems is at the forefront of international developments. Systems chemistry and colloid chemistry are both themes that are strongly rooted in the Netherlands.

PHYLOGENETICS

The Netherlands is internationally recognized for its phyloinformatics expertise, uncovering the evolution of genes, taxa, and populations up to eco-regions. The recently funded large-scale research facility for the Netherlands Infrastructure for Ecosystem and Biodiversity Analysis (NIEBA-ARISE) will develop a globally unique authoritative and rapid identification system for essential biodiversity information. This initiative, which combines DNA sequencing and machine learning techniques, enables the research community to improve our understanding of the patterns and trends in biodiversity and the interactions between species. The NIEBA-ARISE infrastructure, under the responsibility of the Naturalis Biodiversity Center, will help current studies focusing on smaller regions to further expand and uncover global cross-taxonomic and pan-biomic patterns.

MOLECULAR BIOSCIENCES

The Netherlands is world leading in synthetic systems that reconstitute cellular functions, in single cell sequencing and genomics, and in organoids and organs-on-a-chip, exemplified by the NWO gravitation program Building a Synthetic Cell (BaSyC). Another strength is cellular/molecular metabolism, where a number of Dutch research groups use systems biology approaches to uncover the principles of the complex cellular chemical reaction network. Quantitative life cell microscopy is also at the forefront of international development, as is systems biophysics, and theoretical and computational biophysics. There is a world leading tradition of single molecule biophysics both in vitro and in vivo.

EVOLUTIONARY BIOLOGY AND ECOLOGY

The Netherlands is internationally leading in the field of community and evolutionary ecology (unravelling species interactions and adaptation of species to a changing environment and eco-evolutionary interactions), especially with respect to soil ecology, above-belowground interactions, trait-based ecology and ecosystem engineering by organisms. Another strength is theoretical biology with an emphasis on the adaptive dynamics of ecology and evolution including evolution of gene regulatory networks. Other themes with global impact are quantitative genetics, including plant and animal breeding, and molecular evolution and phylogeny.

MULTISCALE MODELLING

Mathematical and theoretical approaches in the biological sciences have a strong tradition in the Netherlands and they are internationally at the forefront. Examples include multilevel and multiscale theories of prebiotic and biotic evolution, mathematical and biophysical modeling of biological development and morphological evolution. Systems approaches to metabolic network dynamics, e.g., to analyze bacterial and human cellular metabolism are internationally leading. On top of that, there exists a much larger community of mathematicians working on nonlinear dynamics arising in contexts ranging from interacting particle systems, population dynamics and ecology to climate modelling.

COMPLEMENTARY INITIATIVES

Pars pro Origin

Research into the origin and evolution of life has a tremendous appeal and the Origins Center is not alone in its quest for new knowledge. Several similar scientific initiatives have appeared in recent years elsewhere in the world.

Research Coordination Network (RCN) for Exploration of Life's Origins, Santa Fé Institute, USA

Aims at the convergence of biological, chemical, and geophysical sciences in which many high-throughput methods, massive computational power, and exceptional instrument sensitivity may yield new insights. Signals a need to convince scientists from many fields that origins of life constitutes one of the main scientific challenges. Extensive outreach policy including a MOOC on the origins of life.

International Society for the Study of the Origins of Life (ISSOL) - the Astrobiology Society, USA

Aims to provide a forum for dialogue, support and education for all researchers worldwide who are interested in astrobiological questions.

Origins of Life Initiative Munich, Germany (OLIM)

Local center at Ludwig Maximilians Universität München with a strong focus on experimental work ('the nanoscience of the origins of life') that should indicate conditions and processes allowing molecules to evolve autonomously into living systems. Aims to convince scientists from many fields that origins of life, or rather the living state of matter, constitutes one of the main scientific challenges.

Origins of Life Initiative Heidelberg, Germany (HIFOL)

Initiative linked to the Max Planck Institute for Astronomy. Aims to facilitate a wide range of interdisciplinary - theoretical, experimental, and observational - research covering the fields of astronomy, physics, geosciences, chemistry, biology and life sciences from a range of research institutes based in Heidelberg.

Earth-Life Science Institute, Japan (ELSI)

Independent institute. Aims to integrate scientific disciplines to study the Origin of Life within the context of the Origins of the Earth and other planets.

Origins of Life Initiative, Harvard University, USA

Aims to understand how the initial conditions on planets, including our own Earth and planets around other stars, dictated the origins of life and its subsequent evolution. Using this knowledge, it will eventually be possible to study the atmospheres of far distant planets for signs of life, including planets that might be Earth twins.

Origins Institute, McMasters University, Canada

General 'Origins' institute that includes the origin of the universe, the origins of structures and processes in the universe, the origin of consciousness, and the origin of language and other social phenomena in its scope. The origin of life is a central theme and the institute runs a long-term program in astrobiology.

Center for Chemical Evolution, Georgia Tech University, USA

The Center is searching for molecules and reactions responsible for the initial synthesis and evolution of the polymers associated with life. It hypothesizes that while the first biopolymers may have resembled those known in life today, they would need unique properties to survive, flourish, and evolve on the early Earth.

Simons Collaboration on the Origins of Life, USA

Provided financial support for research that targets questions ranging from the astrophysical and planetary context of the origin of life, to the development of ever more complex aspects of prebiotic chemistry, to the assembly of the first cells and the advent of Darwinian evolution and the subsequent evolution of increasingly complex forms of life.

Origines et Conditions d'Apparition de la Vie (OCAV), Université de Paris, France

Furthers multidisciplinary research along three main directions: i) conditions for the emergence of life in the solar system and beyond: exploration of the solar system and exoplanets, ii) emergence of living matter: prebiotic chemistry, transitions toward complexity, biological feedbacks on planetary environment, and iii) cultural variations and artistic representations.

European Astrobiology Institute

Association of institutes across Europe. Aims to provide a forum for Europe-based scientists in astrobiology, through the organization of conferences, webinars, working groups, and summer schools.

Carl Sagan Center for Research at the SETI Institute, USA

The mission of the SETI Institute is to explore, understand and explain the origin and nature of life in the universe and how we might find it and the evolution of intelligence. Its six core divisions include: astronomy and astrophysics, astrobiology, climate and biogeoscience, planetary exploration, exoplanets, and the search for extraterrestrial intelligence.

CATEGORIZING THE LEADING INTERNATIONAL RESEARCH THEMES

Research Agenda.

Upon overlaying the recognized research strengths in the Netherlands on the Origins Center research themes, the following key research areas have been identified, in which the Netherlands has the potential to play a leading role.

FINDING EXTRATERRESTRIAL LIFE

Exoplanets with varying compositions have been detected around a wide range of stars. The first step in gauging the potential for life to originate and sustain itself on these planets is to understand how life originated on Earth. With this knowledge we can extend our focus to exoplanets. Three fundamental questions need to be answered when searching for extraterrestrial life: (i) where to search for life, (ii) how to define what to search for, and (iii) how to correctly interpret the findings. We need to determine which stars host planetary systems with habitable planets, we need to determine what useful biomarkers/biosignatures are, and we need to define technology that will enable detection of extraterrestrial life. To answer these questions we need strong collaborations between astronomy, astrobiology, geosciences, biology, ecology, chemistry, and physics. Key in these collaborations is to avoid misconceptions due to the multitude of scientific languages and data interpretations.

> *How unique is life on Earth and how important are the (unique?) conditions on Earth for life's emergence?*

GEOCHEMICALLY GUIDED PREBIOTIC CHEMISTRY

The physical and geochemical conditions of the early Earth are still only roughly understood and need to be further investigated to constrain potential environments suitable for life to emerge. Furthermore, prebiotic chemistry research is needed to reveal the chemical space that was populated prior to the onset of life. Pertinent questions include: what were the dominant molecules present at different environments on early Earth (including, but not limited to, hydrothermal vents, tidal pools, lakes, and oceans). What chemical networks arise from the reaction of these molecules? And what are the properties relevant to life that may emerge from these networks (see below)? In order to address these questions input is needed from astronomy, geo-, synthetic-, analytical-, and systems chemistry, and astrobiology.

EMERGENCE OF CHIRALITY

Prior to the emergence of life, chemistry likely produced both left and right-handed versions (enantiomers) of molecules in essentially equal proportions. Life, however, mostly uses a single enantiomer, only left or only right, of these chiral molecules. The mechanisms by which the racemic, 50% left - 50% right, state transitioned to a homochiral one, 100% left or right, remains a mystery. At what stage during the emergence of life did this transition occur? Was there an excess of one enantiomer that led to its incorporation in contemporary biochemistry? Or was it the (geo)chemistry leading to biochemistry that displayed the need for homochirality? Physics, chemistry, geosciences, astronomy, and biochemistry all contribute to addressing the question of the origin of homochirality. Homochirality is such a life-specific trait that it is considered an excellent characteristic for life detection missions, extending the question from how did homochirality originate to how we can detect it remotely.

PLANETARY HABITABILITY

Planetary habitability, the potential for a planet to develop and sustain life is constrained as well as driven by a range of factors. These factors include the mass and composition of the host star, the location of the host star and its planetary system in a galaxy, the presence of additional planets, the location of a planet in a planetary system and its orbital parameters, the composition and geological activity of a planet, and potentially even the presence of a moon. Many open questions exist related to habitability. Does a planet need a magnetic field? What is the influence of a moon on habitability and the evolution of life? What are typical geological and geochemical processes on Earth that are linked to the origin of life? Could alternative processes lead to the same favorable geochemical environment?

EMERGENT PHENOMENA IN OUT-OF-EQUILIBRIUM SYSTEMS

Life is an emergent property that arose from an out-of-equilibrium chemical "soup". This process of emergence may have occurred through different smaller steps. What these steps were, is still largely unclear. Efforts are needed to investigate the properties that emerge out of chemical systems when these are kept away from equilibrium, by supplying them with a continuous input of energy and/or materials. Among the many emergent properties, the dissipative formation of compartments, metabolic networks, and self-replication as well as motility are of particular interest. The theory of such systems, i.e. non-equilibrium thermodynamics, also needs to be further developed to pave the way for synthetic life-like systems.

LIFE 2.0

The creation of synthetic life is one of the grand challenges in this Research Agenda and in science at large. Can a fundamentally new form of life exist, a form of life based on a chemistry that differs from life-on-Earth's biochemistry that is based on carbon, proteins, RNA, and DNA? Reaching this highly challenging objective requires the integration of self-replication with compartmentalization and metabolism into a system that is able to maintain itself out-of-equilibrium, and can undergo open-ended Darwinian evolution. Success will rely on input from (supramolecular) chemists, and will be guided by principles and concepts from evolutionary biology, ecology, and systems biology.

TOWARDS A SYNTHETIC CELL

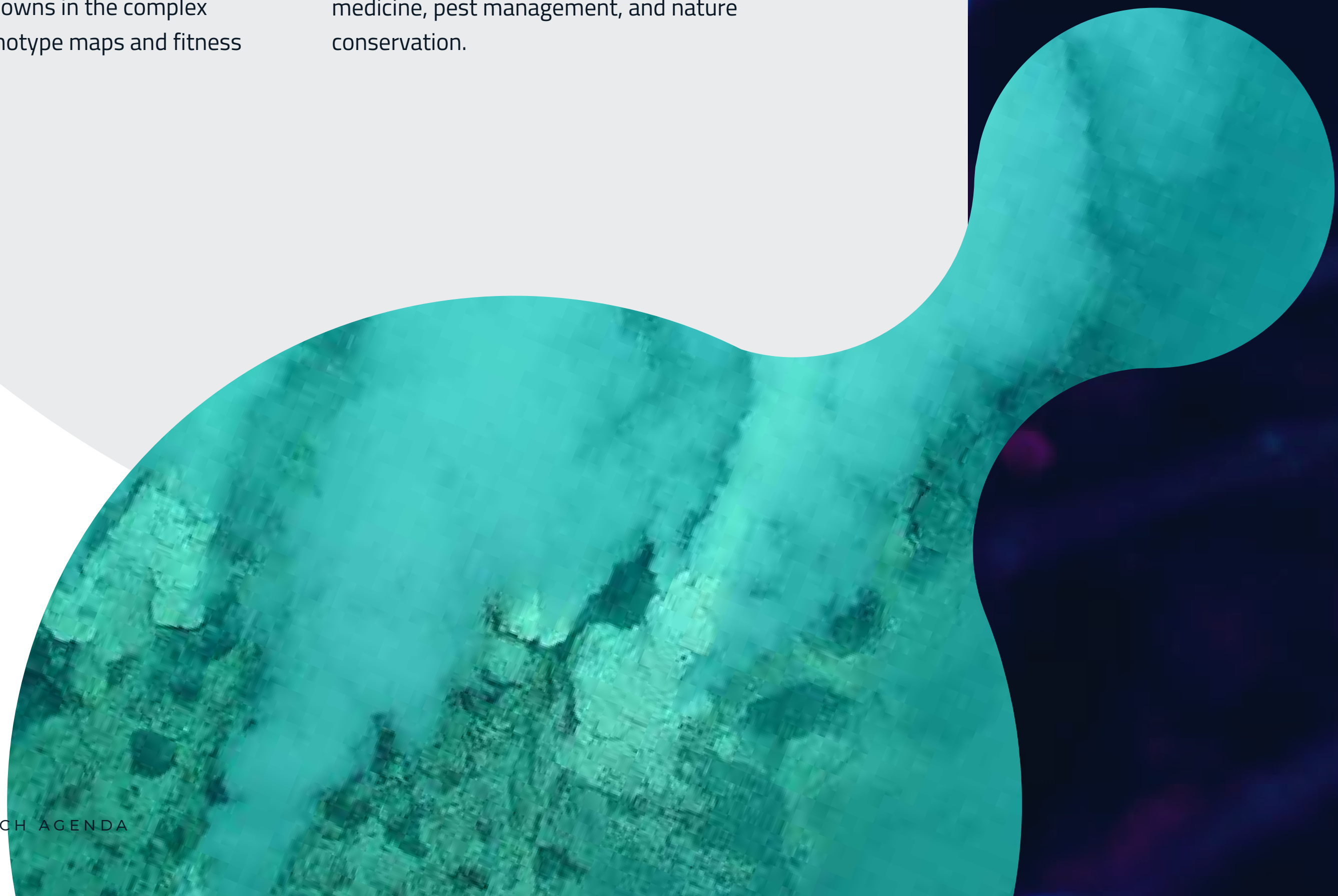
With the massive amount of knowledge that has been gathered about the structure of cells and the processes within, based on canonical biochemistry, research is now at a stage where the prospect of building a cell from its separate components is becoming realistic. This requires the integration of expertise from cell biology with biophysics and modelling. Minimal subsystems need to be identified that fulfil critical roles in the cell cycle and these need to be integrated into a genome that codes for a functional entity that can maintain its internal organization, grow, and divide.

PREDICTING THE EVOLUTION OF LIFE

The ability to predict the outcome of evolutionary processes can be of huge significance when it comes to fighting disease (such as cancer and viral and bacterial infections that evolve resistance to existing treatments), in developing sustainable agricultural practices (domestication of crops and livestock, the spread of invasive species, the evolution of pesticide resistance), and in nature management (which species are most vulnerable to climate change or habitat loss, and which keystone species or traits are crucial for the persistence of entire ecosystems). The ability to predict evolution may be used to prepare for the future, or to try and adjust the course of evolution, or simply to assess how well we understand an evolving system.

Predicting the evolution of organisms has long been considered impossible, due to the inherent stochasticity of mutations, reproduction, and environment, and the many unknowns in the complex genotype-phenotype maps and fitness landscapes. However, based on our current knowledge, theories, careful observations, and experimental methods, we can make meaningful predictions on the future state of an evolving population. For example, we can predict the dominant influenza variants in the next influenza season, or how phenotypic traits will evolve under various environmental stressors, or forecast biodiversity under different climate change scenarios.

Key challenges for this field are to better connect theory and application, and to improve the knowledge of the many unknowns. We are developing mechanistic models of evolution across different levels of organization, and integrating new methods and multiple disciplines. A better understanding into what determines the evolvability of species, and an enhanced prospect to predict evolution, may support and aid the development of effective strategies and policies in evolutionary medicine, pest management, and nature conservation.



THE PROKARYOTE TO EUKARYOTE TRANSITION

Combining phylogenetic analyses with studies of cellular processes at the molecular level have revealed that the majority of these processes arose during the origin of the eukaryotic cell. As a consequence, to understand the evolutionary origin and current diversity of cellular complexity it is necessary to study eukaryogenesis and the fate of resulting systems in present day biodiversity. The interaction and integration of two prokaryotic organisms (archaeal host and bacterial symbiont) enabled the origin of a new life form with unprecedented emergent properties including an extreme increase in intracellular and genomic complexity. Although genome sequencing data is revealing the blueprints of organisms close to this transition, a mechanistic, environmental, and theoretical framework for the origin and evolution of intracellular complexity is lacking. We not only need more genomic data and improvements in bioinformatic data analysis but also a stronger focus on cell biology and physiology of extant archaea related to the host and of a wider diversity of eukaryotic representatives. Biochemical testing of hypotheses can be achieved by studying metabolic interactions between archaea and bacteria and through resurrecting ancestral protein machines (synthetic biology).

SINGLE CELL TO MULTICELLULARITY TRANSITION

Multicellularity has arisen over 40 times in the history of life in both eukaryotes and bacteria. Genomes of closely related unicellular or colonial relatives of multicellular organisms show the many pre-adaptations and alternative routes to achieve this higher level of cellular organization. Systems biology and biophysical investigations on self-organization and division of labour, as well as evolutionary developmental biology approaches addressing the emergence of complex regulatory circuits are needed to elucidate the deep evolutionary and genomic constraints that determine the ultimately complex body plans of for example animals and flowering plants.

Impacts and Spin Offs.

The Origins Center brings expertise from very different disciplines to bear on problems involving complex systems that present difficult multidisciplinary challenges across large time and spatial scales. Approaches to these problems bring together theory and experiment. This mode of operation creates a research environment that is likely to yield new dynamics with the potential to branch off into directions beyond the origins-related topics sketched above. New insights into a diverse range of topics can be expected as spin-off of origins-focused research in a number of areas of high societal relevance.

In the area of health examples include: insight into the emergence and evolution of pathogens (viruses and bacteria); the evolution of immune defenses against pathogens, the resistance to antibiotics, the evolution of cancer cells, and the ecology of bacterial communities that inhabit the intestines. In the area of food, agriculture, and sustainability, this includes insight into the interactions and evolutionary dynamics between crops and bacterial communities and pests.

When it comes to protecting and preserving our natural environment, insights into ecosystem evolution will enable ecosystem engineering for the benefit of preserving biodiversity. Also addressing the global problem of climate change will benefit from the insights obtained by bringing together the expertise from geoscience, ecology, chemistry and multiscale modelling.

In the area of security, the technology developed for detecting signs of extraterrestrial life may find use in new or improved equipment for detecting hazardous substances (toxins, explosives) at airports, railway stations, borders etc. The principles of evolution may also be applied beyond (bio)chemically based systems and may inform the evolution of things, leading to applications in robotics, and in computer code. This can lead to adaptive artificial systems and even ecosystems of artificial systems.

Executive summary.

The Origins Center is the Dutch national knowledge center for research, education, and knowledge exchange that focuses on the origin and evolution of life. We support researchers in setting up innovative partnerships, organizing conferences, webinars, networking events, and in making their scientific results visible to everyone. This Research Agenda details the twelve research themes that form the scientific landscape in which the Origins Center has positioned itself. Research strengths of the Dutch scientific fields that are combined to form the Origins Center are described. Ten key research areas have been identified by overlaying the research themes on scientific disciplines where the Dutch research community is strong, and thus where the Origins Center foresees to make significant progress in the next five to ten years.

Key Origins Center Activities 2017-2021.

- 11 online webinars with internationally known speakers
- 10 postdoctoral fellows
- 6 large research projects
- 18 small research projects
- Fundamentals of Life 2017, Groningen: 180 participants, 21 speakers
- Origins2021 online conference: 140 participants, 29 speakers
- 627 subscribers to the monthly newsletter for scientists

THE ORIGINS CENTER FUSES SCIENTIFIC WORLDS

Coordinating, connecting, facilitating.

The 2017 2.5 M€ Startimpuls from the Dutch National Science Agenda and the efforts of a committed Steering Committee, active partners, and members, have allowed the Origins Center to build a valuable position in the scientific field in just over four years. The connecting work has yielded promising, strong networks and a new generation of researchers: the Origin Center Fellows.

As a national expertise center for research into the origin and evolution of life, we connect the work of researchers to existential questions that exist in society, show policymakers and the public what and how researchers in the Netherlands contribute to unravel mysteries surrounding life and evolution, and empower interdisciplinary collaboration in our scientific field. This is the Origins Center, born from a unique mission to serve the progress of scientists, while improving the public understanding of the origin and evolution of life on Earth and in the universe.

CREATING A BETTER UNDERSTANDING

We want to continue our mission and keep energizing the ambitious research Dutch scientists perform every day. We take an integral perspective in which different scientific disciplines give each other momentum, that is durable, forward-looking, and game-changing.

ORIGINS CENTER FUTURE

The Netherlands is fully involved internationally in the vanguard of evolution science, (geo)chemistry, climate research, ocean research, astronomy, and planetary and exoplanetary science. Our role in, and the significance of interdisciplinary research into life and evolution is growing. Further internationalization of funding and research projects requires central coordination of affiliated scientists. This is where the future of the Origins Center lays: contribute to valuable knowledge development about life and evolution by connecting scientists and making their work visible.

COLLABORATION PAYS OFF

Partners of the Origins Center.

The Origins Center stands for new, interdisciplinary forms of collaboration. Dutch science is a global leader in research into the origin and evolution of life. We show that collaboration pays off.

Colophon.

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The Origins Center is the Dutch national, inter-university knowledge center for research, education, knowledge exchange and networks that focuses on the origin and evolution of life. We support researchers in setting up innovative partnerships, organize conferences, webinars and networking events and make their scientific results visible to everyone. Because the progress we make together concerns us all.