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CRC 392
Molecular Evolution in
Prebiotic Environments
ABSTRACT BOOK
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Molecular Evolution in
Prebiotic Environments

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WELCOME NOTE

by Dieter Braun

Dear Origins of Life researchers!

A very warm welcome to Molecular Origins of Life, Munich (MOM) 2024 from Friday, July 19th to Saturday, July 20th. We are back on track (see our CRC 392 website www.molecular-evolution.de) and invite you to our upcoming event, which will follow our established rhythm of on-site MOM conferences in even years and online MOM conferences in odd years. This means that MOM 2025 will be broadcast virtually from July 16-18, 2025.

But we are jumping ahead a bit. The PIs of CRC 392 are really excited to welcome speakers and attendees at LMU Downtown! Just exit the U3/U6 at the metro station "Universität" either north or south, walk south or north, and enter the LMU behind the western fountain. Follow the signs into the shiny big "grosse Aula" with some fancy historical touches.

Apologies for the odd timing of Friday and Saturday this year – it helps us keep costs down and the registration fee at the traditional €0.

The conference will feature short talks with discussion, followed by a combined discussion session to maximize interaction – complemented by two on-site poster sessions. All participants are invited to a barbecue on Friday, July 19th, under the beautiful trees of the Salinenhof, south of the conference venue.

The field of Origins of Life is home to a small number of highly specialized experts scattered around the world. Our goal is to bring these experts together each year, not only to share knowledge and expertise, but also to initiate productive collaborations.

Thank you for joining us in this endeavor and becoming part of the global Origins of Life team!

We look forward to a fruitful and fun event.

CODE OF CONDUCT

Inappropriate/illegal behavior and/or harassment of any kind will not be tolerated at Molecular Origins of Life, Munich conference.

This includes, but not limited to,

- comments and content that are offensive or inflammatory due to gender, gender identity or expression, race, religion, ethnicity, lifestyle, age, physical appearance or disability
- inappropriate contact, sexual attention or innuendo, deliberate intimidation, stalking, and screenshots and/or recordings of individuals without consent
- screenshots and/or recordings of scientific content without consent

Participants who refuse to follow this code can face temporary/permanent ban from the Molecular Origins of Life, Munich conferences and other CRC 392 - Molecular Evolution events.

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8:55 **Kerstin Göpfrich**
Engineering a synthetic protocell with RNA origami

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9:45 **Discussion**

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10:55 **Andres Jäschke**
Probing the Origin of the Genetic Code by High-Throughput Sequencing

11:20 **Christoph Weber**
Phase separation directs polymerization and selects sequences

11:45 **Discussion**

12:05 **Poster Session I (onsite with lunch)**

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Cyclicphospholipids in the emergence of primitive (functional) protocells

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The role of crystallization in prebiotic polymerization processes

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Atmospheric HCN production and the emergence of the RNA world on early Earth

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Is the Enantiomeric Excess in Meteorites *(truly)* the Missing Link to Understanding Biomolecular Homochirality?

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Possible roles of peptides in early life

16:20 **Elisa Biondi**
Empowering Nucleic Acid Evolution with Expanded Genetic Alphabets

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Role of helicity in the nonenzymatic template-directed primer extension of DNA

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HADEAN EARTH RECIPES

9:20 **Martina Preiner**
Organic cofactors as connection between minerals and protometabolism?

9:45 **Discussion**

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15:55 **Job Boekhoven**
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16:45 **Discussion**

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TALK ABSTRACTS

SESSION A

Friday, July 19, 08:30 CEST

Spatial and temporal dynamics of fluid-rock interactions promoting organic synthesis in the terrestrial lithosphere

Bénédicte Menez et al.
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Abiotic production of molecular hydrogen (H2) through water/rock reactions is now acknowledged to represent a long-lasting and widespread process in the Earth's lithosphere. In the presence of gaseous, dissolved or solid inorganic carbon, this efficient reductant can promote the formation of organic compounds through the concomitant oxidation and reduction of H2 and carbon compounds, respectively. While water thus plays an obvious role in H2 production, the multi-faceted role played by rock-forming minerals on reaction yields and pathways and how they further coevolve with organics and contribute to their diversification during the multiple geodynamic events that affect a rock over the course of its history remain to be elucidated. While analogical experiments have advanced our understanding of the role of minerals as suppliers of reduced iron or catalysts in the generation of H2 and the subsequent formation of organic compounds, we lack supporting evidence in natural rocks. Through a series of results obtained by multimodal examination at the micrometer scale of drilled oceanic rocks, we will show (i) how minerals exert a local control on H2 formation and on the type of produced carbon compounds and (ii) how minerals and organics can co-evolve and diversify through metamorphic reactions to compounds of prebiotic interest or potentially key to support the development of life. These may indeed represent outstanding resources for hydrogenotrophs and heterotrophs inhabiting the rocky subsurface which could then be able to sustainably thrive in the depths of the Earth crust without any supply of organic carbon of photosynthetic origin and in turn participate to these complex but still poorly understood dark H2 and carbon cycles.

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Engineering a synthetic protocell with RNA origami

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The emergence of life on earth proves that living matter can arise from inanimate building blocks. But is it possible to reproduce this process in the laboratory? Can individual molecules be assembled to engineer a system capable of self-replication and evolution? Our vision is to create a simpler model of a cell that consists of a lipid vesicle and operates based on our own custom-engineered molecular hardware made from highly functional and folded RNA origami, as an alternative to today's protein-based machinery, with only a single copying step between genetic information and function. We report the genetic encoding and expression of an RNA origami cytoskeleton-mimic within giant unilamellar lipid vesicles (GUVs). We design the first RNA origami tiles which fold co-transcriptionally from a DNA template and self-assemble into higher-order 3D RNA origami nanotubes at constant 37°C in GUVs, where they reach several micrometers in length. Unlike pre-formed and encapsulated DNA cytoskeletons, these GUVs produce their own molecular hardware in an out-of-equilibrium process fueled by nucleotide feeding. To establish genotype-phenotype correlations, we investigate how sequence mutations govern the contour and persistence length of the RNA origami nanotubes with experiments and coarse-grained molecular-dynamics simulations, realizing a phenotypic transition to closed rings. Finally, we achieve RNA origami cortex formation and GUV deformation without chemical functionalization by introducing RNA aptamers into the tile design. Altogether, this work pioneers the expression of RNA origami-based hardware in vesicles as a new approach towards active, evolvable and RNA-based synthetic cells.

Reference:
Tran, M. P., Chakraborty, T., Poppleton, E., Monari, L., Giessler, F., & Göpfrich, K. (2024). Genetic encoding and expression of RNA origami cytoskeletons in synthetic cells. *bioRxiv*, 2024-06.

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Before cells: Prebiotic compartments based on phase separation and molecular self-assembly

Christine Keating

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An important step towards the first cells at the origin of life is thought to have been the collection of certain molecules together to form compartments, and ultimately protocells. These structures would provide distinct microenvironments able to facilitate lifelike functions such as catalytic activity and define individuals that can be acted on by selection. Important classes of prebiotically-plausible precellular compartments include lipid vesicles, which can be thought of as a primitive version of the cell membrane of today's cells, and polymer-rich coacervate droplets that are similar today's membraneless organelles.
Both types of compartment form by molecular self-assembly and offer different benefits as precellular compartments. This presentation will consider the possibility of a "cytoplasm-first" mechanism of protocell formation, with coacervates serving as compartments for RNAs and as templates for lipid membrane formation such that each coacervate droplet becomes the cytoplasm of a resulting protocell.

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Toward an autonomous “artificial cell” in 2D

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We study cell-free gene expression in miniaturized 2D compartments across the scales, observing single-molecule fluctuations at the nanoscale up to the collective modes of coupled compartments on the millimeter scale. We will describe progress toward assembly of a minimal self-regenerating protein synthesis system.

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Probing the Origin of the Genetic Code by High-Throughput Sequencing

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The genetic code is a fundamental mechanism of life, linking a three-letter nucleotide sequence with corresponding amino acids to encode proteins from genetic information. Despite its critical role, the evolutionary origin of the genetic code remains poorly understood. Our lab has developed a novel high-throughput method for determining rate constants to test various theories about the origin of coded peptide synthesis.
Our approach involves reacting complex pools of RNA sequences with activated amino acids, separating reacted from unreacted RNA species, and analyzing the fractions using Illumina sequencing. The abundance of sequencing reads in the reacted RNA fraction serves as a proxy for reactivity towards a particular amino acid. We applied this method to investigate whether certain RNA sequences are more rapidly aminoacylated than others, to determine the (stereo)specificity of the reaction, and to assess the influence of different environmental conditions on rate and specificity.
Specifically, we tested a hypothesis postulated in 1978 by John Hopfield, involving refolded tRNA precursors and different aminoacyl adenylates. Our high-throughput screen of 16,384 sequence variants revealed substantial differences in rate and specificity, which we confirmed through bio-chemical assays.
Our findings provide new insights into the potential evolutionary pathways of the genetic code and highlight the power of high-throughput sequencing in probing the origins of fundamental biological processes.

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On the origin of cells, genomes and viruses

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Origin of Life is the hardest problem in biology if not in all of science. We might never know what actually happened on Earth some 4 billion years ago that resulted in the emergence of the first cells.

Nevertheless, the only hope to arrive at plausible scenarios of those pivotal events is to seek consilience of (at least) four complementary approaches: 1) theoretical modeling of the first stages of life's evolution, 2) bottom up approach, that is, attempts to recapitulate the events at the origin of life through physico-chemical experimentation, 3) top down approach, that is, attempting to back extrapolate from comparative analysis of extant genomes as well as protein and RNA structures, 4) astrobiology, that is, harnessing data on exoplanets and meteorites for potential insights into the origin of the earthly life, the only one known to us. I will present a mathematical model of the origin of cells via symbiosis between primordial reproducers (protocells) and primordial replicators that gave rise to genomes. I will further resent theoretical arguments for the inevitability of the emergence of parasites in the evolution of replicators and the essential role of host-parasite coevolution in the origin of biological complexity. I will then discuss several attempts on top down reconstruction of the earliest events in biological evolution, in particular, the origin of the translation systems within the primordial RNA-peptide world, the origin of viruses, and the concomitant origin of replication and transcription.

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Cyclicphospholipids in the emergence of primitive (functional) protocells

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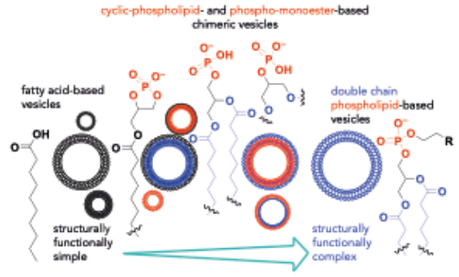
The origin of prebiotic protocells has primarily focused on fatty acid-based vesicles with phospholipid-based vesicles emerging as a later evolutionary development. However, introducing phosphorylation steps early in the prebiotic scenario enables phospholipids to co-emerge with fatty acid-based systems. Specifically, cyclic-phospholipids formed from fatty acids and glycerol give rise to a heterogeneous library of vesicles with diverse morphologies and tolerance to a range of metal ions, temperature, and pH. Furthermore, cyclicphospholipid-based vesicles have been shown to retain encapsulated nucleic acids during growth and division, acquire nucleotides from their surroundings, and be compatible with the nonenzymatic extension of an RNA oligonucleotide.

We are currently exploring the properties of cyclicphospholipid-based vesicles as part of a continuous spectrum of hybrid composomes of (functional) vesicles – as an amalgam of starting materials, intermediates, and products. Such an approach to protocell evolution may provide a basis for understanding the chemical etiology of phospholipids in the context of chemical evolution.



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The role of crystallization in prebiotic polymerization processes

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Crystallization is a very efficient way for accumulating molecules in a highly ordered solid-phase form. Our earlier studies [1, 2] suggest that the process could play a pivotal role also at the prebiotic production of the first oligonucleotide sequences. In the first part of the talk I will show an example how crystallization could assist the sequestration and polymerization of cyclic nucleotides from an acidic prebiotic brine containing all four canonical nucleobases present in RNA.[3]
In the second part of my talk I will illustrate that a phosphate containing acidic prebiotic pool could also host co-crystallization of amino acids with phosphoric acid. The crystalline salts produced in this way enable a polymerization chemistry that proceeds under much milder conditions than any other phosphoric acid catalyzed polymerization reactions studied in the past [4, 5, 6]. We will also discuss the efficiency of polymerization processes in crystalline salts formed by amino acids with other strong inorganic acids in light of crystal data available from the crystallographic literature.

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Atmospheric HCN production and the emergence of the RNA world on early Earth

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The origin of life on Earth is thought to involve the early emergence of the RNA world. The basic building blocks of RNA could have arisen in situ through non-equilibrium chemical processes in the reducing, early Earth atmosphere - specifically through the synthesis of the feedstock molecule, hydrogen cyanide (HCN). We have developed a comprehensive model of early Earth involving photochemical processes in a reducing atmosphere that is coupled to the effects of late meteoritic bombardment, and geophysical processes such as methane release from deep ocean vents. We use non-equilibrium atmospheric photo-chemistry networks driven by ultraviolet radiation to compute HCN production. We then derive the abundances of nucleobases, ribose, and nucleotide percursors that are produced as a consequence of HCN rain out into surface ponds. Our results show that the evolution of biomolecule production is dictated by the decrease of hydrogen over time as the impact rates fall, as well as the increasing oxidation of the atmosphere arising from the photolysis of water. We conclude that the RNA world on Earth had an early origin, within 200 Myr of the Moon-forming impact.

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Is the Enantiomeric Excess in Meteorites *(truly)* the Missing Link to Understanding Biomolecular Homochirality?

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The exclusive preference for L-amino acids in proteins and D-sugars in nucleic acids is a key feature of life. The origin and evolution of biological homochirality still remains unresolved. The detection of L enriched amino acids in meteorites[1] often supports asymmetric photochemistry induced by stellar UV circularly polarized light (CPL) as the most likely cause of symmetry breaking.[2] Nevertheless, such detections are often questioned based on potential terrestrial contamination or rather large detection uncertainties. Moreover, recent findings concerning the enantioselective analyses of amino acids from asteroids Ryugu[3] and Bennu[4] seem to contradict the CPL scenario, as all amino acids found in these pristine samples—for which terrestrial contamination can be in principle neglected—have been claimed to be racemic. Here we aim to challenge these findings by comparing them with the results of our reliable enantioselective analyses[5] of extra-terrestrial chiral amino acids in samples returned from Ryugu. To support our analyses, we re-examined the distribution of enantiomeric excess (ee) in amino acids extracted from the Orgueil meteorite—a CI chondrite renowned for its similarities in mineralogy and amino acid composition with asteroid Ryugu. Moreover, our recent results on the asymmetric photolysis of isovaline[6]—an extraterrestrial amino acid of interest due to its absence in the biosphere and low racemization rate—offer a sound explanation for the relatively low ee in carbonaceous chondrites and returned samples, assuming they originated from stellar CPL. We will conclude by highlighting alternative chiral biomarkers, such as lipids and their chiral backbones, which our team has investigated for their chiroptical properties[7] to assess potential chirality transfer from light to matter. Due to their high resistance to degradation, lipids are among the most promising biomarkers in exobiology.[8] These results provide guidelines for future enantioselective analyses of meteorites and return samples, especially from missions like Hayabusa2, OSIRIS-REx, and Martian Moons eXploration, as well as for the in situ exploration for traces of life in space as part of the ExoMars 2028 mission.

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Possible roles of peptides in early life

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Cellular metabolism of all life relies on proteins composed of the universal alphabet of 20 canonical amino acids and assisted by organic or inorganic cofactors. These proteins have been tuned by eons of evolutionary optimization and it is unclear how early life functioned without them.
Before the onset of templated ribosomal synthesis, short peptides of random sequences were plausible on early Earth by condensation of amino acids under a variety of conditions. Early peptides and proteins probably exhibited distinct compositions, enriched in small aliphatic and acidic residues that were prebiotically more abundant. To what extent could such polymers contribute to early metabolism and could they possibly precede the role of extant enzymes?
Recent research from our group shows that highly acidic peptides/proteins comprising only the presumably "early" amino acids are competent at secondary structure formation. In fact, peptides of such composition stand out in their capacity to promote higher order soluble assembly via formation of beta-sheets. Moreover, we observed that highly acidic proteins of presumable "early" composition can bind (i) RNA by utilizing metal ions as cofactors to bridge carboxylate and phosphoester functional groups, and (ii) organic cofactors, supporting their folding properties and providing sophisticated functional groups.
All the above listed properties of peptides/proteins based on prebiotically plausible composition would nominate them as possible catalytic hubs of prebiotic relevance although more experimental evidence is needed to test their capacity to bridge the prebiotic and biotic catalytic powers.

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Empowering Nucleic Acid Evolution with Expanded Genetic Alphabets

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It is believed that the first organic molecular systems most likely gained access to Darwinism through the prebiotic formation of RNA-like evolvable macromolecules.
Unfortunately, decades of research have shown that it is extremely difficult to reproduce RNA species that should be central to this "RNA first" hypothesis, such as RNA replicases. This suggests that we might be missing something. Thus, many laboratories have sought alternative biopolymers that are both prebiotically accessible, and also support Darwinism better than standard nucleic acids, managing the limited catalytic ability of RNA and DNA.
Further, when we investigate how life might have originated on our planet, or look for alien life on other planets, we must recognize the possibility that before, or instead of, adding a second biopolymer to the informational molecules (such as proteins), primeval life might instead have taken a different route.
On Earth, starting with what was likely a RNA-like polymer, life decided to expand the catalytic activity of the polymer itself. We can see evidence that this path was at least one of the options on Earth in many contemporary examples that are regarded as relics of an "RNA Word". From these, the question arise of what kind of polymer was really the first that started molecular evolution, and what kind of building blocks was it composed of. Can we experimentally evaluate what the basic information requirements might have been for this polymer to achieve optimal and effective evolution through the most possible straightforward, resource-saving pathway?
This work reports on experimental results with such nucleic-acid-like biopolymers enriched in building blocks by components of an Artificially Expanded Genetic Information System (AEGIS). These additional nucleotides carry functionality that chemical theory suggests might assist in binding and catalysis.
This work describes molecular biology for this genetic system, including procedures that place the expanded, richer system under Darwinian selection pressure.
These have led to several discoveries. For example, AEGIS appears to allow the system to access specific binding conformations. The added functionality allows the system to get tighter and more specific interactions with a target as it serves both genetic and phenotypic roles. Further, results from parallel in-vitro selections of standard and AEGIS libraries indicate that added functionality does indeed allow for more efficient and faster evolvability of shorter biopolymers. Finally, specific chemical groups on the alien nucleobases provide catalytic and binding properties unseen in standard nucleic acids.
These results show not only that expanded libraries are better reservoirs of functional molecules than extant four-letters libraries, but also that specific alternative chemical groups, perhaps lost later in time as nucleic acids specialized for their informational roles, might have been present and pivotal for some steps of prebiotic evolution.

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Role of helicity in the nonenzymatic template-directed primer extension of DNA

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The nonenzymatic copying of RNA is thought to have been necessary for the transition between prebiotic chemistry and ribozyme-catalyzed ribonucleic acid (RNA) replication. Nonenzymatic template-directed primer extension offers an alternate method of synthetic RNA or deoxyribonucleic acid (DNA) synthesis, in a one-pot reaction. To date, these reactions have mainly been conducted using RNA-based systems rather than DNA-based systems due to DNA primers being significantly slower to extend than RNA primers. This talk discusses the significance of having a C3'-endo conformation of both the primer and the incoming nucleotide to facilitate enhanced DNA primer extension. This can be achieved by using an RNA template to promote an A-type helicity in the DNA primer and nucleotide. Further, the use of reaction confinement inside liposomes was investigated in order to accelerate the reaction rate. Studies have also been performed to regulate activated nucleotides into the liposomes using surface acoustic waves.

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Hadean Earth Recipes

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Silicate + metal worlds like Earth form hot owing to gravitational heating from accretion and differentiation, and intrinsic radioactive decay. Concurrent cooling sets off a chemical and mechanical cascade wherein siderophile elements (Fe+Ni) form a metallic core, and lithophile elements (Mg, Si, Al, Ca, Na, etc.) partition into mantle and siliceous crust. The outcome is a rocky surface beneath an outgassed fluid envelope composed of atmophile elements and compounds (CO_2, H_2O, H_2, etc.). In its first 500 Myr (q.v. Hadean eon), Earth's crust co-existed with liquid water; it was molded by volcanism, affected by late accretion bombardments and harbored diverse hydrothermal systems. Volcanism and differential buoyancy of the crust mandates the presence of scattered emergent landmasses. Such Hadean surfaces could host diverse (sub-)aqueous where organic chemical ingredients became concentrated to reactivity beneath a dense atmosphere bathed by the active young Sun. Soon after planet formation, it seems proto-biochemical reactions led to full-fledged living biochemistry. We do not know whether the earliest environments for life were ideally suited for its origin, or merely just good enough to accomplish the task. The inferred complexity for even the minimum biological entity means that operative and persistent biochemistry are the most difficult developmental stages to reach.

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Organic cofactors as connection between minerals and protometabolism?

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We can connect the metabolism of the first cells on Earth (Last Universal Common Ancestor, LUCA) to its geochemical roots through top-down comparative bioinformatics [1] and through bottom up geochemical laboratory studies, using minerals and inorganic redox partners (H_2, metal ions) as predecessors of enzymes [2]. Our aim is to connect central metabolic cofactors and enzymatic reactions that were present in LUCA to early Earth geochemical reaction partners in order to better understand the transition from environmental reactions to genetically encoded metabolic functions. The hypothesis: cofactors are the missing link between abiotic and biotic (enzymatic) catalysis.
In the presented studies, we focus on bridging abiotic and biotic hydrogen/electron transfer. Hydrogen gas, H_2, is generated in various geochemical settings, among them serpentinization, a water-rock interaction process during which iron-containing minerals transfer electrons to the protons of water. H_2 is also the electron donor for the most ancient route of biological CO_2 fixation, the acetyl-CoA pathway. In metabolism itself, H_2 is being transformed into biochemical electron donors, cofactors such as the dinucleotide NADH which can be seen – simply put – as hydride (H^-) donors. We successfully activated hydrogen on minerals found in serpentinizing systems to reduce NAD+ to NADH under aqueous conditions [3]. We transferred these principles onto other biochemical electron acceptors such as flavins and have furthermore discovered unexpected mechanistic differences between the reduction of di- and mononucleotides.
Our results establish a connection between central reactions in metabolism and abiotic, geochemical catalysis with hydrogen as a common denominator.

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Keywords: hydrogen • cofactors • minerals • catalysis • serpentinization

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Nucleic Acid Replication Enabled by Wet-Dry Cycles: A Robust Solution to the Product Inhibition Problem

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Most models for the origins of life consider nucleic acid replication essential for chemical evolution before the emergence of polymerase enzymes. While single-stranded nucleic acids can assemble substrate oligomers for non-enzymatic template-directed synthesis, the stability of the resulting template-product duplex inhibits substrates from binding to either strand in subsequent reactions. This product inhibition problem is widely recognized as one of the key limitations to achieving multiple rounds of polymerase-free nucleic acid replication. Using DNA as a model system, we demonstrate that wet-dry cycles circumvent product inhibition by facilitating duplex strand separation and by providing substrate oligonucleotides a kinetic advantage for association with the strands of the denatured duplex. The simplicity of this process, and the wide range of conditions that allow replication (e.g., variable temperature, cycle rate, solvent composition) suggest that a similar process could have facilitated nucleic acid replication on the prebiotic Earth.

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Exploring the habitability of ocean moons by in situ analysis of emitted ice grains

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Saturn's icy moon Enceladus harbours a global ocean, which lies under an ice crust but has a rocky sea floor. Through warm cracks in the crust a cryo-volcanic plume ejects ice grains and vapour into space providing access to materials originating from the ocean. Hydrothermal activity is suspected to be occurring deep inside the water-percolated porous rocky core and powered by tidal dissipation. Two mass spectrometers aboard the Cassini spacecraft, frequently carried out compositional in situ measurements of vapor and ice grains emerging from the subsurface of Enceladus.
In the first part of the presentation, we summarize the current knowledge about the habitability of Enceladus' ocean - including the latest finding of abundant phosphate dissolved in it. In the second part we look forward to the future exploration of ocean worlds by space missions using mass spectrometry. In particular NASA's Europa Clipper Mission scheduled for launch in October 2024 and ESA's future flagship mission (L4) with the main goal to search for extant life on Enceladus.

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Impacts of Environmental Parameters on Prebiotic Organic Reactions in Hydrothermal Systems

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Hydrothermal vents, where seawater is chemically altered and heated by reactions with ocean crust, generates energy from redox / pH / chemical gradients and leads to precipitation of reactive minerals. Understanding mechanisms that can drive prebiotic chemistry in hydrothermal contexts is important for Earth and also for astrobiology of ocean worlds such as Enceladus and Europa. However, understanding prebiotic reactions in hydrothermal systems is complex, since the products and yields of organic reactions are highly sensitive to experimental parameters and vents are gradient systems that contain a wide variety of chemical conditions within the same localized environment. Studies of an example reaction (reduction and reductive amination of keto-acids) demonstrate the reaction sensitivity to permutations of experimental conditions such as pH, temperature, and iron redox state. Reactions like this could have occurred on ocean worlds; therefore, a comprehensive understanding of environmental conditions will be necessary in order to interpret organic detection data from future missions.

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Towards Recreating a Metabolic Origin of Life

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Recreating an origin of life in the lab is essential for a deep understanding of biology. In several areas of science, systems are found to organize themselves in a dynamic way when an energetic stress is applied under specific constraints; the emergence of life in the form of self-organized chemistry should also have satisfied this criteria. Our lab is therefore searching for conditions under which geochemistry might organize itself into dynamic reaction networks that embody features of metabolism and its bioenergetics.
In the first phase of our work, we found experimental conditions that enable many of the individual reactions in the core of anabolism without enzymes, strengthening the case that the core anabolic network might have initiated nonenzymatically.
In a second phase, we experimentally found that products of the metabolic network, today known as coenzymes, could act to nonenzymatically promote the reactions that produced them or to enable new reactions that were not possible until their emergence. These observations show how a primitive nonenzymatic metabolic network could have been pruned and expanded through catalytic feedback effects, leading to self-complexification and increased catalytic autonomy from the environment.
In the third ongoing phase of our work, we integrate knowledge from the first two phases to propose and test environments that might allow self-organized reaction networks to emerge. The talk will conclude with a discussion of the specific features this environment likely embodied.

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A Mechanistic Approach to Prebiotic Chemistry: Coenzymes, Chirality, and Catalysis

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Reduction reactions are essential within biochemical metabolism, but it remains unclear how they emerged before the availability of enzymes at the origins of life. Within early metabolism, NADH is considered to be the most important cofactor, where it takes a central role in reduction reactions. As NADH can be obtained under prebiotic conditions using hydrogen as a reducing agent, NADH takes a central role in theories on the emergence of life by allowing the transition from abiotic to organic reducing agents. However, experimental verification of such models is still missing, as previous studies have shown that NADH is unable to act as a reducing agent in water outside of enzymes.
By combining high-throughput screening and statistical reaction optimization, we have now identified conditions under which catalytic amounts of metal ions drastically enhance the reactivity of keto acids, enabling their reduction by NADH and NADH analogs in neutral unbuffered water at 40 °C. Under the identified reaction conditions, NADH acts as a chiral hydride donor, yielding enantioenriched hydroxy acids with 16-60 %ee. DFT computations were used to elucidate the detailed reaction mechanism and to identify an intramolecular hydride transfer within a highly organized adduct to be responsible for the observed chirality transfer. The identified reaction conditions provide a link between genetic molecules and metabolism and are the first example where a metal ion mimicking enzyme function enables chirality transfer of a biochemical reaction.

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Shaping early life: the chemistry of primitive compartments

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The complexity of modern biochemistry suggests that a systems biochemistry approach is required to understand and potentially recapitulate the network of prebiotic reactions that led to the emergence of life. Early cells probably relied upon interconnected chemistries to link nucleic acids, peptide-based catalysts and membranes. In this context, I will discuss our recent advancements about:

- what, how and when membrane-based and membrane-less compartments appeared on early Earth;
  and
- what functions these primitive compartments could exhibit.

Addressing all these points can help us to elucidate the prebiotic pathways that led to the emergence of functional primitive cells and, from there, the rise of life as we know it.

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Phase separation directs polymerization and selects sequences

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Sequence distributions of hetero-polymers, such as RNA and DNA, are essential for information storage, catalyzing chemical reactions, and regulating functions in living cells and at the molecular origin of life.

Since most possible hetero-polymer sequences are dysfunctional, a key question is which physicochemical mechanism can direct polymerization and the selection of specific sequences. Interestingly, phase-separated condensates were shown to direct various chemical processes, including polymerization of homopolymers, raising the question of whether condensed phases can provide mechanisms for sequence selection.

To answer this question, we use non-equilibrium thermodynamics and describe the reversible polymerization of different monomers to sequences at non-dilute conditions prone to phase separation.

We find that when sequences nucleate and polymerize, their interactions give rise to phase separation, boosting the enrichment and depletion of specific sequences. Strikingly, various pathways for sequence selection exist when maintaining the system away from equilibrium. These results suggest condensed phases acting as hubs for Darwinian-like evolution toward functional sequences.

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Challenging the Discontinuous Synthesis Model to Make Prebiotic Polyribonucleic Acid

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One line of work hoping to understand the origin of life on Earth seeks chemical reaction paths that generate polyribonucleic acid (RNA) from molecular species that were undoubtedly present at the relevant time. Here, it is insufficient to present a path that is "plausible". Rather, to be persuasive to those who are not inclined to be persuaded, that path must be "privileged". Its reactions could not *not* have occurred in a Hadean geological context.
Each of these steps in the Discontinuous Synthesis Model (DSM) to make RNA is privileged. They could not *not* have occurred:

(1) Photochemical formation of formaldehyde (HCHO) and parts per million glycolaldehyde ($HOCH_2CHO$) undoubtedly occurred in Hadean redox neutral atmospheres (CO_2, N_2, H_2O), ~10^{21} molecules/m^2•year.
(2) These were undoubtedly captured by volcanic SO_2 emerging in similar amounts from the mantle with a quartz-fayalite-magnetite redox potential, raining metastable bisulfite organic minerals into constrained aquifers at rates of ~10^3 moles/year/km^2.
(3) These carbohydrates could not *not* have matured, hopefully with borate leaching from residual basaltic melts (as on Mars) to prevent their forming "tar".
(4) Nucleotides could not have avoided being formed with ribose 1,2-cyclic phosphate, if it were available from ribose-borate and phosphoramides made from ammonia and polyphosphates.
(5) The Hadean atmosphere was certainly transiently reduced by shattered Fe cores of a few (not many) Vesta-to-Ceres sized impactors, giving NH_3, HCN, HCCCN, and other reduced nitrogen compounds. These give RNA nucleobases by known paths.
(6) Nucleoside triphosphates could not *not* have been formed from cyclic triphosphate and borate-coordinated nucleosides, catalyzed by Ni^{2+} from impactor cores.
(7) Polyribonucleic acid 100-200 nucleotides long could not *not* have been formed from nucleoside triphosphates on basaltic glass.

Laying the DSM out in this format identifies its weaknesses, which lie between Steps (3) and (4). Reactions connecting the end products of borate-moderated carbohydrate maturation, 5-carbon species, and ribose-1,2-cyclic phosphate are *not* obviously privileged. For example, borate is needed to control tar formation during carbohydrate maturation and to control regiochemistry in downstream triphosphate formation. However, borate may *inhibit* reaction of ribose with diamidophosphate (DAP) to yield nucleosides.

We will report results from efforts understand the middle of the DSM to complete the path from formaldehyde and reduced species coming from a post-impact atmosphere to polyribonucleic acid.

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Template-based copying in dynamic combinatorial libraries out of equilibrium

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One of science's greatest challenges is how life can spontaneously emerge from a mixture of molecules. A complicating factor is that life and its molecules are inherently unstable—RNA and proteins are prone to hydrolysis and denaturation. For the de novo synthesis of life or to better understand its emergence at its origin, selection mechanisms are needed for unstable molecules. Here, we present a chemically fueled dynamic combinatorial library to model RNA oligomerization and deoligomerization and shine new light on selection and purification mechanisms under kinetic control. In the experiments, oligomers can only be sustained by continuous production. Hybridization is a powerful tool for selecting unstable molecules, offering feedback on oligomerization and deoligomerization rates. Moreover, we find that templation can also be used to purify libraries of oligomers. Further, template-assisted formation of oligomers within coacervate-based protocells changes its compartment's physical properties, like their ability to fuse. Such reciprocal coupling between oligomer production and physical properties is a key step toward synthetic life.

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Self-Assembly and Non-Enzymatic Polymerization of Plausible Proto-Nucleotides: A Model for Monomers and Polymers that Preceded RNA

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The possibility that RNA was the first genetic polymer of life has motivated the search for a prebiotic synthesis of RNA. However, it is well documented that the nucleobases of extant RNA do not assemble in water as free bases or as nucleosides or nucleotides, presenting a challenge to the spontaneous formation of RNA polymers from the complex pool of molecules likely present on the early Earth. As an alternative hypothesis, we are investigating the possibility that RNA evolved from a proto-RNA polymer with subunits that were capable of forming supramolecular assemblies at the monomer level. Our studies have identified plausible prebiotic nitrogenous heterocycles as candidate proto-nucleobases that are similar in structure to the extant nucleobases of RNA, but pair in aqueous solution at the monomer level. Results from experimental and computational investigations show that these heterocycles, and some of their modified derivatives, spontaneously assemble into linear supramolecular polymers consisting of stacked, hydrogen-bonded hexads that contain Watson-Crick-like base pairs. Recently, we have found that di-peptides composed of an amino acid conjugated with one of these putative proto-nucleobases and a negatively charged amino acid (model proto-nucleotides) also form supramolecular assemblies and polymerize upon the addition of a condensing agent, while no polymerization is observed in the absence of assembly. Oligomers of these proto-nucleotides with complementary nucleobase sequences associate with thermal stabilities that are greater than what is observed for duplexes of RNA oligomers of the same length. These results, and those of our collaborators, support the hypothesis that proto- and pre-RNA polymers existed on the prebiotic Earth; polymers which could have gradually been replaced by RNA during an early stage of life.

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POSTER INDEX

POSTER ABSTRACTS

Physical selection pressures to drive early molecular evolution

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A crucial step during the origins of life is the emergence of biopolymer building blocks. However, the optimal reaction pathways for their formation usually require feedstocks of pure reactants and defined purification and mixing steps to suppress unwanted side reactions and allow for high product yields. We show that heat flows through thin crack-like compartments purify complex mixtures of prebiotically relevant building blocks and drive prebiotically relevant reactions such as the dimerization of glycine. In these same compartments, we furthermore study how we can control RNA hydrolysis in thermally induced pH gradients. RNA is less stable than RNA and more readily hydrolyzed at alkaline pH, while hydrolysis is slower at acidic pH. In thermal nonequilibrium, we study how heat-flow driven pH gradients and hydrolysis of RNA can interact to provide long-term protection allowing nucleic acids to undergo further reactions. Another prominent physical selection pressure is UV light. UV light induces damages into our DNA, namely by forming cyclobutane pyrimidine dimers (CPD). We study how the combination of damaged an undamaged nucleic acids behave in a thermal gradient and whether the damaged or undamaged nucleic acids are accumulated in our crack-like compartments. Combining these effects we aim to understand how different physical selection pressures can act upon prebiotic building blocks to drive early molecular evolution during the origins of life.

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The Role of Sequence-Dependent Kinetics in DNA Unzipping

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The comprehension of the dsDNA unzipping process surpasses the scope of thermodynamics and chooses kinetics. During the DNA unzipping process, distinct dissociation rates for sequences like 5′-CCCCGG-3′/3′-GGGGCC-5′ and 5′-GGGGGCC-3′/3′-CCCCCGG-5′ are observed. While thermodynamics would suggest they should exhibit similar behavior, this is not the case. So, it is evident that the sequence itself conceals certain kinetics that impact the overall dissociation rates of inter-strand hydrogen bonds. Our previously proposed kinetic model, the sequence-dependent asymmetric cooperativity model enables a comprehensive understanding of dsDNA unzipping. The model elucidates the asymmetric influence of a formed base pair on the kinetic barrier heights of its nearest right and left neighbor base pairs. This model successfully explains the sequence-dependent unzipping phenomenon and highlights the predominance of kinetics over thermodynamics in the dynamics of unzipping.

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Efficiency of Replication in Oligomer Pools Encoding Prebiotic Circular Genomes

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Adopting an "information first" point of view on the emergence of life, the transition from prebiotic chemistry to living systems requires the existence of a reliable enzyme-free replication mechanism. Despite recent advances in template-directed primer extension, challenges like the short length of copied products and high error rates persist. In this work, we investigate an alternative replication mechanism proposed by the Szostak lab, the so-called Virtual Circular Genome (VCG) [Zhou et al., RNA 2021, 27, 1-11]: Replication takes place in a pool of oligomers, where each oligomer contains a sub-motif of a predefined circular genome, such that the oligomers encode the full genome collectively. While long oligomers contain long-range information on the sequence of the genome, short oligomers merely act as replication feedstock. We observe a competition between the predominantly error-free ligation of a short oligomer to a long oligomer and the predominantly erroneous
ligation of two long oligomers. Increasing the length of long oligomers and reducing their concentration decreases the fraction of erroneous ligations, enabling high-fidelity replication in the VCG. Alternatively, the problem of erroneous products can be mitigated if only monomers are activated, meaning each ligation involves at least one monomer. Surprisingly, in such systems, shorter oligomers are extended by monomers more quickly than long oligomers, a phenomenon which had already been observed experimentally [Ding et al., JACS 2023, 145, 7504-7515]. Our work provides a theoretical explanation for this behavior, and predicts its dependence on system parameters such as the concentration of long oligomers.

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Accelerating non-enzymatic template directed primer extension for the production of DNA and RNA

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Non-enzymatic primer extension is a chemically driven method of replicating DNA or RNA using activated nucleotides rather than enzymes. Whilst predominantly studied as a method for the production of genetic material in a primordial world, non-enzymatic primer extension offers a promising method for simple and modifiable DNA or RNA production for a wide range of biomedical, material, or therapeutic applications. However, the rate of reaction is prohibitively slow, especially for DNA. Though techniques have been explored to improve the reaction rate including alternate activating groups or manipulating the helicity of DNA, non-enzymatic primer extension still remains too slow for practical applications. As such, this work has focused on further accelerating the rate of primer extension through the use of confinement within liposomes, showing promise of a more efficient method of DNA production.

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Exploring the Interplay between Random Peptide Libraries and Decanoic Acid/Decanol Vesicles

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Prebiotic protein chemistry relied on a set of amino acids different from today's. Decanoic acid/decanol vesicles serve as a model for prebiotic membranes and have been extensively studied. Understanding how these vesicles interact with prebiotically plausible peptides can provide crucial insights into the mechanisms that drove early proto-cell evolution. However, the interaction between decanoic acid/decanol vesicles and peptides of various amino acid compositions remains unknown.

We conducted preliminary experiments to explore interactions between random peptide libraries and decanoic acid/decanol vesicles. For this purpose, we synthesized several 8-mer peptide libraries with different amino acid compositions, including some of the most abundant non-canonical, prebiotically plausible amino acids. We have thus synthesized libraries comprised of both contemporary and prebiotically available amino acid alphabets, further enriched by non-canonical amino acids, 5 libraries in total.

Using fluorescent spinning-disc microscopy of decanoic acid/decanol vesicles with peptide libraries in the solution, we discovered that certain peptide libraries might interact with the vesicles, impacting their morphology and stability. This data is further supplemented by direct-light scattering measurements. Interestingly, the peptide-vesicle interaction was also pronounced upon addition of 363 mM NaCl to the solution, impacting decanoic acid/decanol vesicle flocculation.

Our findings suggest the possibility of interactions between specific peptide libraries, featuring diverse amino acid compositions, and prebiotically plausible lipids. Notably, these interactions may not be solely based on binding or dissolution, opening new avenues for understanding the complex interplay between molecules crucial for early life emergence.

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2‘,3‘-cP RNA Replication by Ligation

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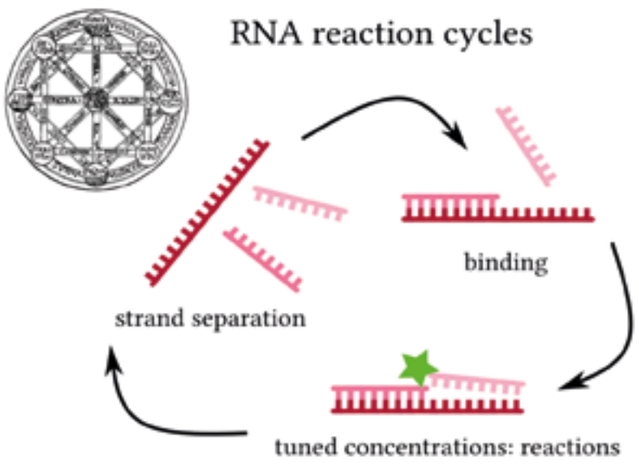
To replicate long RNA strands, templated ligation from 2′,3′-cyclic phosphate RNA is a promising pathway (https://doi.org/10.1021/jacs.3c10813). Preliminary screenings suggest that through tuning of monovalent salt content and through adding Lysine or other amino acids to the solution, no additional catalysts are required to attain yields of 50% ligation product in one day. Varying physical conditions such as pH and salt/RNA concentration likely solves the strand separation problem. This opens the possibility of prebiotic ligation chain reactions and thus open-ended evolution from short RNA strands.



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New approach for fast meteorite identification and prediction of astrobiologically interesting samples through portable X-ray fluorescence spectrometry (XRF)

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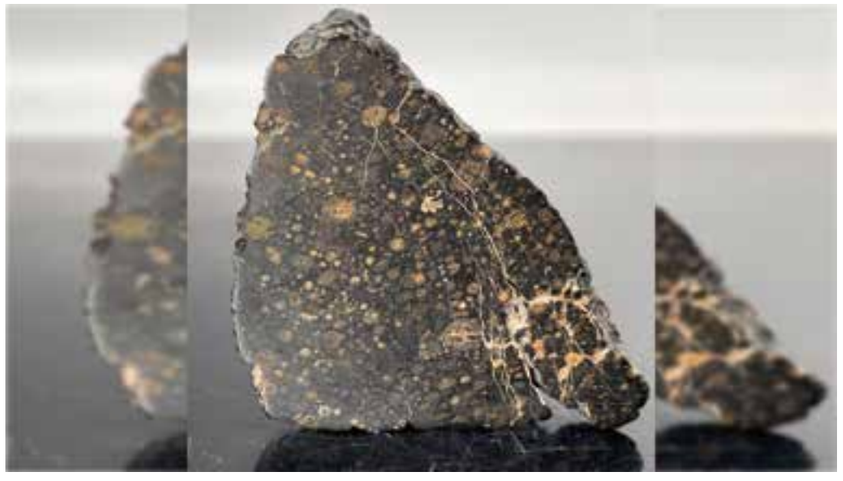
This study presents a novel methodology for rapid meteorite identification and prediction of astrobiologically significant samples utilizing portable X-ray fluorescence spectrometry (XRF). The research introduces a fast and reliable approach that leverages the Skyray Instruments Explorer 7000 capabilities to analyze meteoritic samples efficiently and predict their classification and significance for further research. By employing this advanced XRF technique, the study aims to enhance the speed and precision of meteorites identification, particularly in identifying samples of interest for astrobiology investigations. The results of this research offer a promising avenue for expedited meteorite characterization and selection of samples with potential astrobiological relevance.



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Dynamical interactions among coexisting protocellular populations result in emergent properties with selective advantages

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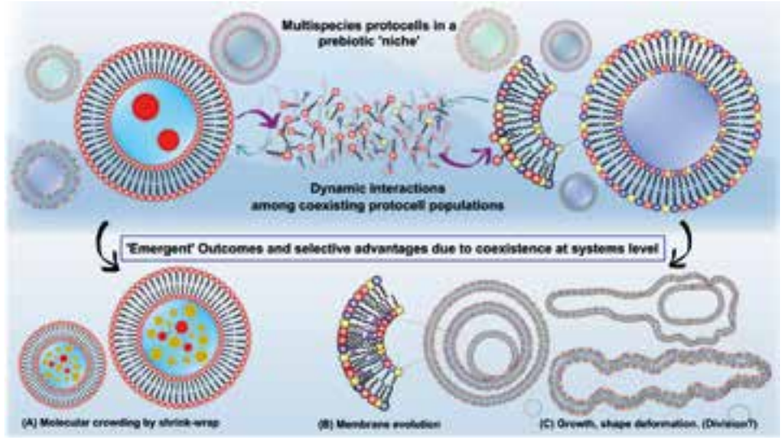
Primordial membranes are thought to have been composed of single-chain amphiphiles (SCA). The prebiotic soup was presumably a host for a variety of such membrane forming components that demonstrate the propensity to spontaneously self-assemble into vesicles, resulting in 'protocells'. Taken together with the heterogeneity of the prebiotic amphiphile library, the aforesaid spontaneity could have resulted in a random variety of 'protocellular species' in an early-Earth 'niche', akin to biodiversity found in an ecological niche. Inspired by this, we explored a multispecies approach to studying physicochemically distinct protocell populations to test whether their interaction dynamics could facilitate 'emergent' properties at the systems level. We used an SCA-based model system to generate a library of distinct protocell species to characterize the aforementioned proposition. Our study shows that the implications are multipronged and the outcomes vary, all of which mainly depend on the membrane properties of the different protocells in the system. We show how one of the protocell populations acts as the 'predator' while the other acts as a 'prey' in a two-candidate model. The predator showed resultant growth and morphology changes at the expense of the prey. Further, we also show that this 'fitter' membrane achieves more robustness due to this process. Interestingly, the prey population also accrued emergent properties resulting in molecular crowding in the lumen. We further extrapolated this to a three-candidate population and found that the outcomes were even more varied. These findings strongly hint towards a possible route for protocell membrane evolution that could have benefitted coexisting populations, while indicating how a 'fitter' membrane might have come about.



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Metal-Pyridoxal Cooperativity in Nonenzymatic Transamination

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Coenzymes, life's organocatalysts, are involved in ≥30% of enzymatic reactions and likely predate enzymes, going back to prebiotic chemistry. However, they are considered poor catalysts on their own, and thus their pre-enzymatic function remains unclear. Since metal ions are known to catalyze metabolic reactions in the absence of enzymes, here we explore the influence of metal ions on the mechanism of catalysis by pyridoxal (PL) coenzymes. Specifically, Fe or Al, the two most abundant metals in the Earth's crust, were found to exhibit substantial cooperative effects in transamination reactions catalyzed by pyridoxal (PL), a scaffold used by roughly 4% of all enzymes. Initial screening showed that Fe3+-PL was 90-fold faster at catalyzing transamination than PL alone and 174-fold faster than Fe3+ alone, whereas Al3+-PL was 85-fold faster than PL alone and 38-fold faster than Al3+ alone. Under conditions more relevant to the origins of life, reactions catalyzed by Al3+-PL were >1000 times faster than those catalyzed by PL alone. Pyridoxal-5'-phosphate (PLP) exhibited similar behavior to PL. Experimental and theoretical mechanistic studies uncovered the catalyst resting-state and indicate that the rate-determining step in the PL-metal-catalyzed transamination is different from metal-free and biological PL-based catalysis. Metal coordination to PL lowers the pKa of the PL-metal-imine complex by several units and slows the hydrolysis of the imine intermediate by up to 259-fold, allowing catalysis to proceed in an aqueous environment. Coenzymes, specifically pyridoxal derivatives, could have exhibited useful catalytic function even before enzymes.

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Self-assembly of Prebiotic Peptides into Catalytically Active Amyloids

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A diverse array of macromolecules has been proposed as prebiotic candidates for their role in the chemistry preceding living organisms. Ribonucleotides can encode both hereditary and catalytic characteristics but are highly unstable, difficult to polymerize and need large sizes for function. Prebiotic routes for synthesis of peptides are diverse and more feasible but the products are still unstable and poorly functional. Recently, the assembly of peptides into highly stable intermolecular assemblies such as amyloids has emerged as an alternative scenario. Here, we show that peptides composed of prebiotic amino acids and with their N- and C-terminals free can spontaneously self-assemble into active supramolecular scaffolds. Fluorescence and transmission electron microscopy studies showed that these assemblies are amyloids. Their formation can be induced by diverse experimental conditions of prebiotic relevance including different pH extremes and high salt concentrations. Moreover, these prebiotic amyloids exhibited enzyme-like behavior, catalyzing the hydrolysis of biologically relevant molecules such as adenosine triphosphate. Once formed, the amyloids remained functionally active even after treatment under harsh conditions. These results demonstrate that peptides with prebiotic composition can effectively self-assemble into catalytically active conformations that can withstand prebiotically plausible conditions.

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Enantiomer excess differences in carbonaceous chondrites organic content. A systematic review of the literature data.

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The presence of asymmetry in organic enantiomers in carbonaceous chondrites has been a topic of significant interest in astrochemistry. Our research aims to compile the literature data on enantiomer excess differences in the organic content of these meteorites and provide useful insights into enantiomer distribution in various classes of meteorites. Several studies have reported differences in the distribution of enantiomers, suggesting the possibility of asymmetric synthesis or processing in the early solar system. The observed discrepancies in enantiomeric excess between different chondrites and within the same meteorite class highlight the complexity of organic chemistry in extraterrestrial environments. Further investigations into the origins of these enantiomeric variations are essential for understanding the formation of complex organic molecules in space and for the origin of life.

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Cell-free expression localized and activated at heated air-water interfaces

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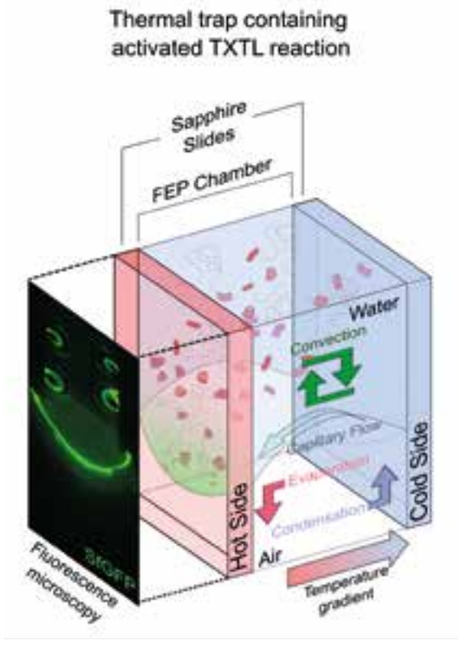
The reaction networks that define modern cells and maintain their living functions have been finely optimized throughout their evolutionary history. Their components are kept at the working concentrations either by metabolic synthesis or uptake from the surrounding environment through a complex transmembrane transport machinery. But how could such a wide array of molecules come together in the first place to kick start the first cell-like reactions? Moreover, how could the concentrations required for them to interact be maintained without active transport and production by the cell itself? We propose a simple physical mechanism that is able to accumulate all the molecular pieces required for RNA transcription and protein translation, two fundamental cellular reactions, from a disperse and inactive mixture and locally confine them for long periods of time. By applying a temperature gradient to an air-water interface a local water cycle is created. Molecules in the solution are concentrated at the warm side of this interface by the combined effects of microscale evaporation and capillary flows. The findings not only shed light on a possible mechanism by which the first archaic reaction networks could have formed but it will also allow to create interacting and cooperating multicellular expression systems without the barrier of cell membranes and offer a novel paradigm for long-term feeding of transcription-translation systems.



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High-yield prebiotic RNA polymerization in 2′,3′-cyclic nucleotides mixtures under mildly alkaline wet-dry cycling

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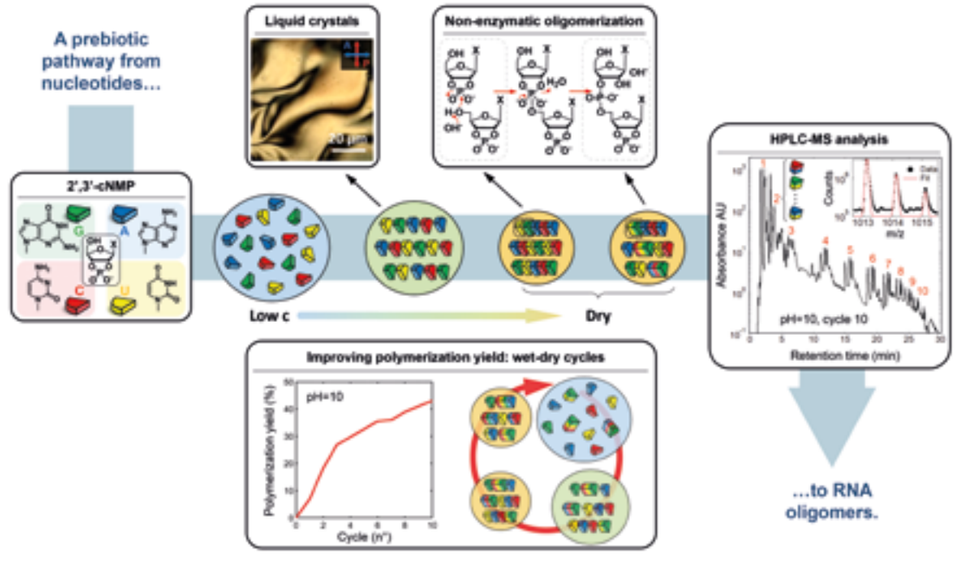
The spontaneous formation of RNA oligomers from single nucleotides is one of the most crucial, yet unsolved, steps for the investigation of the origin of Life. So far only low reactivity has been observed for non-activated nucleotides. Here we report that, in the absence of any condensing agent or external activator, 2′,3′-cyclic nucleotides efficiently polymerize upon dehydration-rehydration cycles at room temperature and in a mild alkaline pH range, with up to 70% monomer conversion for guanosine. Microscopy observation during drying indicates that the guanosine reactivity is enhanced over the other nucleobases by its self-assembly propensity: A, U and C polymerize up to 20-35% and no liquid-crystalline structure was detected. Repeated wet-dry cycles, where only water is added, increase the oligomerization yield and the polymer length for each nucleobase. Performing cycles at pH ≥ 11 favors a balanced inclusion of all four nucleotide species in the oligomers that, in turn, self-assemble in a long-range ordered supra-molecular structure. The spontaneous nature of the supra-molecular assembly and the high-yield oligomerization reaction make the reported process a promising candidate to explain the prebiotic origin of RNA oligomers on early Earth.



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Non-Enzymatic Kinetic Error Correction in Nucleic Acid Replication through Asymmetric Cooperativity

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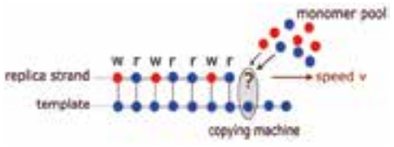
Accurate nucleotide sequence replication is essential for self-replicators in primordial environments, where each nucleotide incorporation presents a potential for error. Modern cells have attained remarkably low error rates, as minimal as 10^(-9), through the use of sophisticated enzymes that utilize kinetic proof-reading mechanisms. However, the emergence of life must have occurred without the presence of such complex enzymes. We propose a theoretical model of a non-enzymatic kinetic error correction mechanism utilizing asymmetric cooperativity, a novel kinetic property that actively rectifies errors immediately after they arise. Our analysis utilized a time-continuous absorbing Markov chain to assess the fidelity of progeny strands by incorporating kinetic discrimination. Our findings indicate that kinetic asymmetry improves the accuracy of progeny strands when the system operates beyond thermodynamic equilibrium, driven by an influx of energy.



Studies on Peptido RNA Formation and Single-Nucleotide Translation

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What the molecular origins of translation were is unclear. The earliest organisms capable of RNA-induced protein synthesis must have possessed a much simpler form of molecular machinery than the ribosomal apparatus. Based on the experimental observation of unencoded formation of amino acidyl and peptido RNAs from amino acids and nucleotides in condensation buffer, we are studying RNA-directed or -catalyzed peptide coupling and peptido RNA forming reactions on different levels of complexity. This includes di- and tripeptide-forming reactions on RNA templates directing the synthesis of specific peptides. Further we are investigating the three-dimensional structure of peptidoyl RNAs by one- and two-dimensional NMR.

Theory of RNA replication and evolution

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We aim to develop a theoretical framework that can account for RNA replication and evolution in homogeneous and heterogeneous systems. It is known that evolution is due to the error-prone replication processes of genetic material performed by replication machinery translated from the same genetic material. Even if the understanding of how the complexity of primitive self-replication molecules develops through Darwinian evolution still remains a mystery with regards to the origins of life, the ability to evolve is thought to be a key feature which distinguishes living things from non-living molecules.

Specifically, in our project we want to investigate how spatial heterogeneities of different kinds, like phase-separated mixtures with liquid droplet-like compartments, could play a role in providing spatially confined micro-environments which allow for the co-evolution of RNA replicators together with parasitic RNAs. This coexistence could create a robust RNA replication network which might have the chance to evolve into the complex replication machinery of cells. We build our model upon a client-scaffold theoretical framework, which is able to decouple the phase separation of a solvent-scaffold mixture from the reaction kinetics of dilute clients [1], [2].

[1] Sudarshana Laha. Chemical reactions controlled through compartmentalization: Applications to bottom-up design of synthetic life. PhD thesis, Technische Universität Dresden, Dresden, Max Planck Institute for the Physics of Complex Systems, 2023.
[2] Jonathan Bauermann, Sudarshana Laha, Patrick M. McCall, Frank Jülicher, and Christoph A. Weber Journal of the American Chemical Society 2022 144 (42), 19294-19304 DOI: 10.1021/jacs.2c06265

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Sequence motif dynamics in RNA pools

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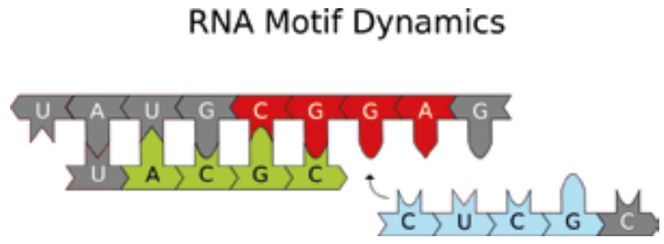
In RNA world scenarios, pools of RNA oligomers form strongly interacting, dynamic systems, which enable molecular evolution. In such pools, RNA oligomers hybridize and dehybridize, ligate and break, ultimately generating longer RNA molecules, which may fold into catalytically active ribozymes. A key process for the elongation of RNA oligomers is templated ligation, which can occur when two RNA strands are adjacently hybridized onto a template strand. Detailed simulation of the dynamics in RNA pools is computationally expensive, due to the large variety of possible species and reactions. Here, we develop a reduced description of these dynamics within the space of sequence motifs. We then explore to what extent our reduced description can capture the behavior of detailed simulations that account for the full dynamics in the space of RNA strands. Towards this end, we project the dynamics into a motif space, which accounts only for the abundance of all possible four-nucleotide motifs. A system of ordinary differential equations describes the dynamics of those motifs. Its control parameters are effective rate constants for reactions in motif space, which we obtain from the rate constants for the processes underlying the full dynamics in the space of RNA strands. We find that the reduced motif space dynamics simulation permits an efficient and surprisingly accurate computation of observables that characterize the informational dynamics of RNA pools in sequence space. This approach could also provide a framework to rationalize and interpret features of the sequence dynamics observed in experimental systems.



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Phase separation directs polymerization and selects sequences

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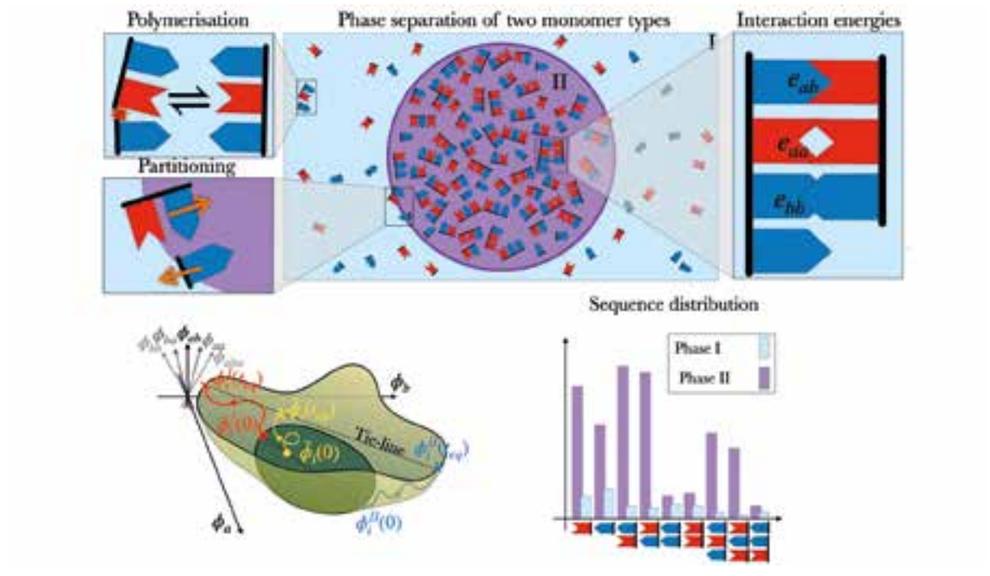
Sequence distributions of hetero-polymers, such as RNA and DNA, are essential for information storage, catalyzing chemical reactions, and regulating functions in living cells and at the molecular origin of life.
Since most of the possible hetero-polymers sequences are dysfunctional, a key question is which physicochemical mechanism can direct polymerization and the selection of specific sequences. Interestingly, phase-separated condensates were shown to direct various chemical processes including polymerization of homopolymers, raising the question whether condensed phases can provide mechanisms for sequence selection. To answer this question, we use non-equilibrium thermodynamics and describe reversible polymerization of different monomers to sequences at non-dilute conditions prone to phase separation. We find that when sequences nucleate and polymerize, their interactions give rise to phase separation boosting the enrichment and depletion of specific sequences. Importantly, pathways for sequence selection can emerge when maintaining the system away from equilibrium. These results suggest that condensed phases can act as hubs for Darwinian-like evolution toward functional sequences.



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Testing emergence of life hypothesis in early Earth analog experiments: Abiotic hydrogen produced in an iron sulfur chemical garden rescues a methanogen from hydrogen limitation

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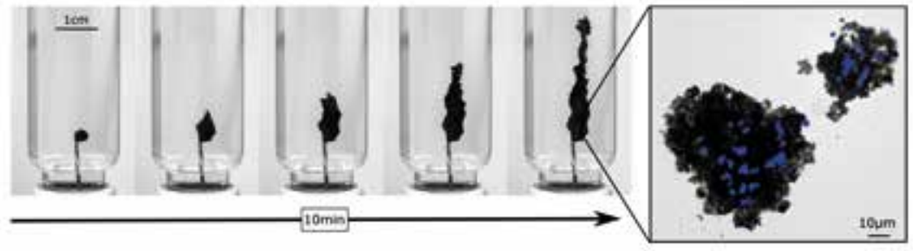
The emergence of life on Earth holds one of the biggest secrets mankind has yet to unravel. The methanogenesis pathway is at the forefront of possible metabolisms present in an ancient anoxic environment. But experimental evidence linking the abiotic formation of hydrogen necessary for methane production, and a plausible organism like a methanogen using the hydrogen for metabolism, is scarce. We show, that high temperature anoxic iron sulfide chemical gardens consisting of mostly mackinawite (FeS) and greigite (Fe3S4) not only produce abiotic hydrogen, but also offer the reactive space for Methanocaldococcus jannaschii to attach to the iron sulfur particles and use the hydrogen to form methane. Experiments also reveal that sufficient abiotic H2 is produced in the Fe-S chemical gardens to rescue M. jannaschii culture from H2-limitation, and even provided sufficient energy for the methanogens to reach exponential growth. Under these conditions, gene expression analysis showed that the methanogenesis pathway was overexpressed in the Fe-S chemical gardens compared to controls. These findings provide experimental support linking two origin of life theories: (1) that the methanogenesis pathway would have been an energetically favored metabolism in primordial hydrothermal vents, and (2) that the origin of life occurred in an "iron-sulfur world".



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Spatio-temporal control of nucleic acid catalysis with active droplets

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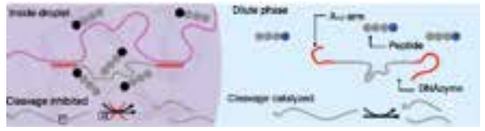
Cells use transient membraneless organelles to regulate biological reaction networks. For example, stress granules selectively store mRNA to downregulate certain protein expressions in response to heat or oxidative stress. Models mimicking this active behavior should be established to better understand in vivo regulation involving compartmentalization. Here we use active, complex coacervate droplets as a model for membraneless organelles to spatiotemporally control the activity of a catalytic DNA (DNAzyme). Upon partitioning into our peptide-RNA droplets, the DNAzyme unfolds and loses its ability to catalyze the cleavage of a nucleic acid strand. We can transiently pause the DNAzyme activity upon inducing droplet formation with fuel. After fuel consumption, the DNAzyme activity autonomously restarts. We envision this system could be used to up and down-regulate multiple reactions in a network, helping understand the complexity of a cell's pathways. By creating a network where the DNAzyme could reciprocally regulate the droplet properties, we would have a powerful tool for engineering synthetic cells.



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Bacterial histone HBb compacts DNA by bending

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Histones are DNA-binding proteins and play a pivotal role in DNA packaging and gene regulation in eukaryotes and archaea. While eukaryotic histones form octamers constituting the nucleosome core, archaeal histones assemble into elongated superhelices upon DNA binding. Recently, histone homologues were discovered in bacteria, prompting our investigations into their structural and functional properties. Here, we present the crystal structure of histone HBb from the predatory bacterium Bdellovibrio bacteriovorus in both apo and DNA-bound forms. Our findings demonstrate that dimeric HBb bends DNA upon binding utilizing interaction interfaces akin to its eukaryotic and archaeal counterparts. Employing a range of biophysical and biochemical methods, we confirm HBb's sequence-independent DNA binding and compaction by bending. Moreover, we unveil genome-wide binding of HBb across B. bacteriovorus DNA, and show that HBb is essential for bacterial survival, suggesting a role in DNA organization and gene regulation. The distinct DNA-binding properties of the bacterial histone HBb, which show similarities yet distinct differences from their archaeal and eukaryotic counterparts, highlight the diverse functions of histones in DNA organization across all domains of life.

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Optimal harvest of chemical work from cyclic environment

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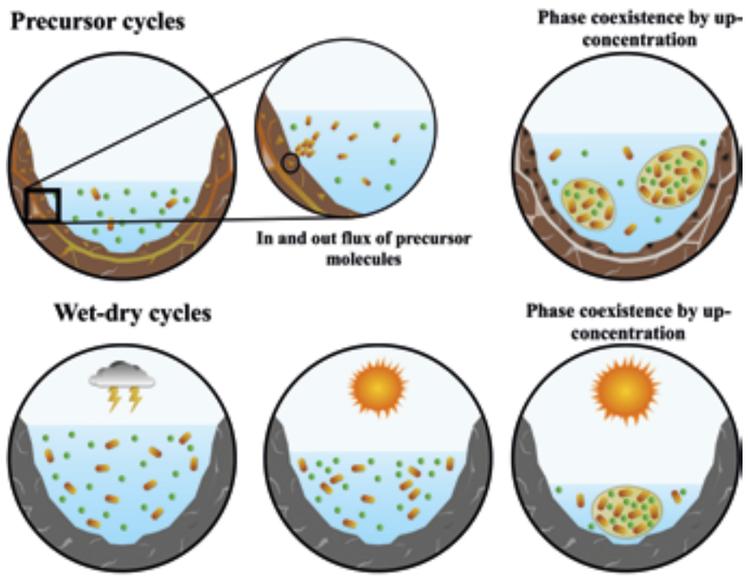
Here, we study the question of how chemical reactions can optimally harvest chemical work from external reservoirs that cycle periodically. To answer this question, we use nonequilibrium thermodynamics and describe precursor and wet-dry cycles. Due to interactions among the constituents, chemical reactions are non-dilute, and phase separation can occur. We find a resonance behaviour, where the optimal chemical work and efficiency are maximised, and investigate the role of interactions and cycles on this resonance. For symmetric interactions, precursor cycles are found to enhance chemical activity more effectively than wet-dry cycles, whereas wet-dry cycles are more beneficial for asymmetric interactions. Our work sheds light on which cycles can speed up the chemical processes of constituents depending on their interactions. Thus, cycles in non-dilute systems can promote the formation of specific constituents and their chemical reactions, paving the way for selection and Darwinian evolution of molecules in cyclic systems.



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G4 World hypothesis: booting up life with ribosome

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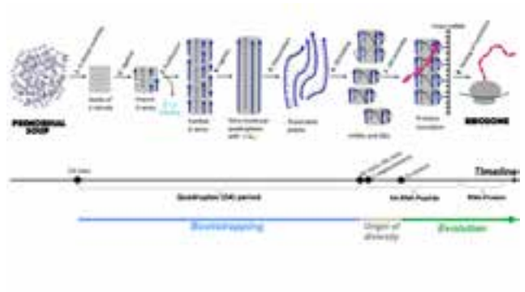
Information represents the crux of the Darwinian evolution. Without it, Earth would remain chemical evolution's playground with forever chaotic prebiotic soup. The information gave a chance to its carrier – the ab initio polynucleotide that self-emerged from the chaos, folded into the very first phenotype, and booted up open-ended Darwinian evolution. How was the information encoded? What was the nucleotide sequence and length of the information? What kind of message it carried? How was it produced?
To address these questions, the ground zero of information must be found – the process that generated the very first message for free. For RNA World hypothesis this turned out to be an impossible task due to the fact that RNA sequences, capable to fold into the ribozymes (catalytic RNA), are the heteropolymers with enormous Shannon entropy leading to the mega-astronomical RNA pool. Besides the fact that creating the gigantic RNA pools is incomprehensible, RNA World requires natural selection before emergence of Darwinian evolution. Only unparadoxical way to generate a message is to initiate the bootstrapping process by a polynucleotide with zero Shannon entropy, or a homopolymer. At first glance, this sounds impossible since the biological information is usually attributed to the heteropolymers containing at least two bases. However, zero Shannon entropy doesn't mean absence of an information – it only drops astronomical number of options to single message. The message singularity ideally fits to the bootstrapping, which must be spontaneous and very simple process. Recently proposed G4 World hypothesis (Kankia, 2023,Which came first: the chicken, the egg, or guanine? RNA 29, 1317) suggests that role of the ab initio polynucleotide, capable to bootstrap Darwinian evolution, could be played by poly(G). The presentation will analyze the emergence of the information that boots up Darwinian evolution through ribosome and answers above listed questions.



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Kinetics and Coexistence of Autocatalytic Reaction Cycles

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Biological reproduction rests ultimately on chemical autocatalysis. Autocatalytic chemical cycles are thought to have played an important role in the chemical complexification en route to life. There are two, related issues: what chemical transformations allow such cycles to form, and at what speed they are operating. Here we investigate the latter question for solitary as well as competitive autocatalytic cycles in resource-unlimited batch and resource-limited chemostat systems. The speed of growth tends to decrease with the length of a cycle. Reversibility of the reproductive step results in parabolic growth that is conducive to competitive coexistence. Reversibility of resource uptake also slows down growth. Unilateral help by a cycle of its competitor tends to favour the competitor (in effect a parasite on the helper), rendering coexistence unlikely. We also show that deep learning is able to predict the outcome of competition just from the topology and the kinetic rate constants, provided the training set is large enough. These investigations pave the way for studying autocatalytic cycles with more complicated coupling, such as mutual catalysis.

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Chemically fueled motions

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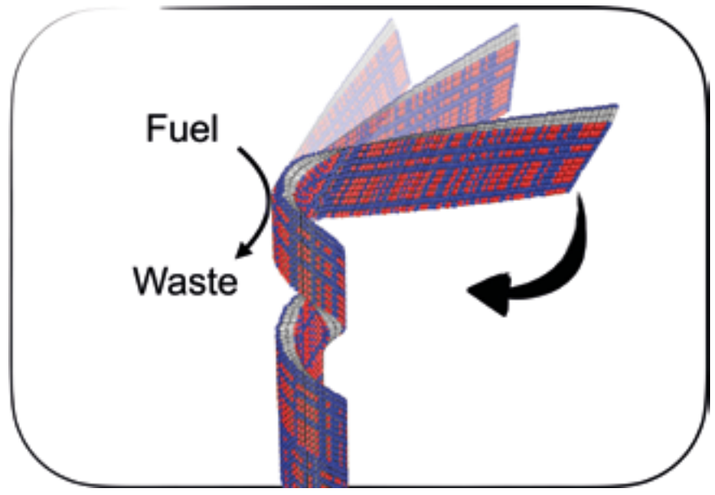
Biology uses the interplay of non-equilibrium chemical reactions and assemblies to regulate function and structure. This allows a cell to harvest chemical energy to maintain structural order, store energy, and perform work, like the ATP-fueled actin-myosin complex responsible for contractions in the cytoskeleton or the ATP-fueled bacterial flagellar rotational motor. In such biological systems, chemical energy is transduced to mechanical energy, like directional motion. Synthesizing and developing similar energy-transducing systems from the bottom up by making use of the interplay of chemical reactions and assemblies has been a longstanding goal for chemists. However, so far, no examples of synthetic supramolecular systems rival the dynamic behaviour observed in biology. There exist no chemically fueled motors that operate on the supramolecular level like the ATP-fueled bacterial flagellar rotational motor or supramolecular fibres that oscillate like the microtubule. Part of the reason is that we currently cannot design chemical reactions that affect a supramolecular process. Therefore, our goal in this project is to understand how chemical reaction cycles can regulate a supramolecular process. Next, we use this knowledge to understand several new supramolecular behaviours that we observe by coupling chemical reactions and assemblies, like the rotational motion of chemically fueled ribbons.



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Template-based copying in chemically fueled dynamic combinatorial libraries

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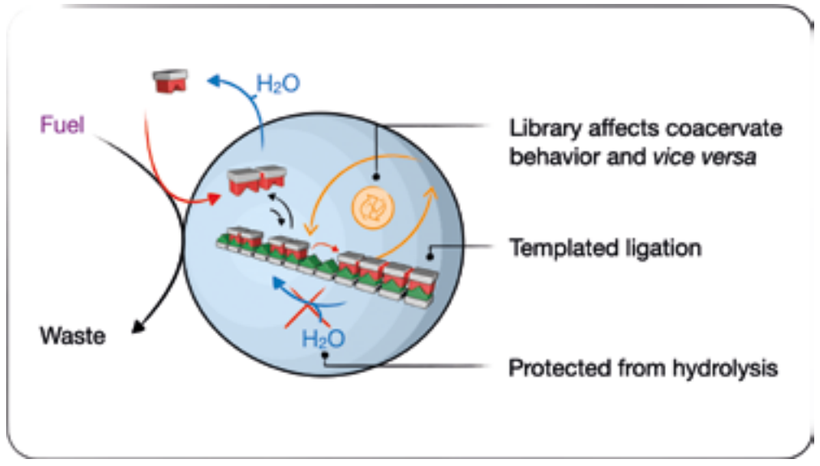
Life as we know it originates from a pool of molecules, but how? Finding answers is accompanied by technological breakthroughs, opening the door to new approaches in materials science, medical science, and biotechnology. These arising opportunities and curiosity drive scientists, including me, to find answers to the following questions. How can an abiotic world, governed by the laws of thermodynamics, be transitioned to a world of living matter, maintained by the constant supply of energy far from equilibrium? Can we realize such a transition de novo in the lab? Can we synthesize de novo life? Dynamic combinatorial libraries have especially become an appealing tool to study mechanisms by which life's molecules have been selected from prebiotic molecular mixtures and, most recently, to start synthesizing (de) novo life.

Despite the great progress of the field, degradation and- and reuse pathways have long not been integrated into combinatorial libraries. However, life uses those degradations and- and reuse pathways to convert energy to sustain itself. Therefore, our research aims to develop chemically fueled dynamic combinatorial libraries, i.e., combinatorial libraries that operate out of equilibrium by converting chemical fuel. Our overarching aim is to test the role of those fuel-driven libraries in synthesizing de novo life. Specifically, we aim to test what physical and chemical mechanisms help evolve the combinatorial libraries towards greater complexity and de novo life. For this, we need to answer the following research questions: What is the role of hydrolysis, i.e., more general degradation? Which role plays templation and compartments? Do physical and chemical interactions between templates and molecules result in reciprocal feedback, driving open-ended evolution? (Kriebisch et al., J. Am. Chem. Soc. 2021, 143(20), 7719–7725, Kriebisch et al, Research Square, 2023)



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The UV-driven Functionality of Coenzyme NAD

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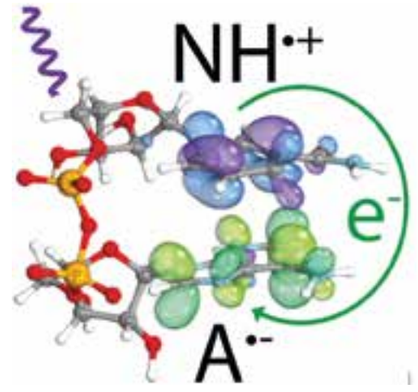
The coenzyme, nicotinamide adenine dinucleotide (NAD), plays a vital role as a charge carrier in biology. Despite its vital role in, e.g. in the production of ATP, the photochemistry of both NADH and NAD+ is poorly understood. Here, we used ultrafast UV-pump, mid-IR probe spectroscopy combined with accurate quantum-chemical calculations to investigate photochemical events in the reduced (NADH) and oxidized (NAD+) forms. This synergistic approach allowed us to unambiguously identify a long-lived charge-separated state as a transient intermediate state of UV-induced NADH for the first time, thereby unifying contradictory mechanisms from the past decades in a big picture. An efficient population of the long-lived charge-transfer state can also initiate secondary photochemical reactions, which can affect the photostability of cells. In NAD+, we found ultrafast photorelaxation as the only deactivation channel. Therefore, the NADH/NAD+ system can be considered a storage system of photon energy, such as sunlight, which can be chemically switched on and off by redox reactions. These processes occur in all living organisms exposed to sunlight and might have acted as an early enzyme function prior to the emergence of cells. The photochemical pathways demonstrated in this work elaborate functions of NAD in chemistry and molecular biology as an electron donor, FRET agent or redox pair switch, which have previously not been considered.



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A Prebiotic Pathway to Nicotinamide Adenine Dinucleotide

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Enzymes play a fundamental role in cellular metabolism. A wide range of enzymes require the presence of complementary coenzymes and cofactors to function properly. While coenzymes are believed to have been part of the last universal ancestor (LUCA) or have been present even earlier, the syntheses of crucial coenzymes like the redox-active coenzymes flavin adenine dinucleotide (FAD) or nicotinamide adenine dinucleotide (NAD+) remain challenging. Here, we present a pathway to NAD+ under prebiotic conditions starting with ammonia, cyanoacetaldehyde, prop-2-ynal and sugar-forming precursors, yielding in situ the nicotinamide riboside. Regioselective phosphorylation and water stable light activated adenosine monophosphate derivatives allow for topographically and irradiation-controlled formation of NAD+. Our findings indicate that NAD+, a coenzyme vital to life, can be formed non-enzymatically from simple organic feedstock molecules via photocatalytic activation under prebiotically plausible early Earth conditions in a continuous process under aqueous conditions.

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Emergence of homochirality via template-directed ligation in an RNA reactor

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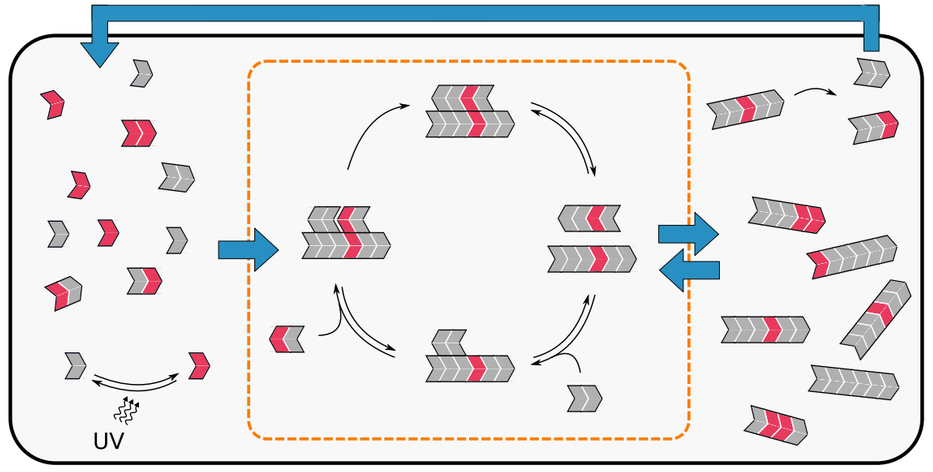
RNA in extant biological systems is homochiral; it consists exclusively of D-ribonucleotides rather than L-ribonucleotides. How the homochirality of RNA emerged is not known. Here we use stochastic simulations to quantitatively explore the conditions for RNA homochirality to emerge in the prebiotic scenario of an RNA reactor, in which RNA strands react in a non-equilibrium environment. These reactions include the hybridization, dehybridization, template-directed ligation, and cleavage of RNA strands. The RNA reactor is either closed, with a finite pool of ribonucleotide monomers of both chiralities (D and L), or the reactor is open, with a constant inflow of a racemic mixture of monomers. For the closed reactor, we also consider the interconversion between D and L monomers via a racemization reaction. We first show that template-free polymerization is unable to reach a high degree of homochirality, due to the lack of autocatalytic amplification. In contrast, in the presence of template-directed ligation, with base pairing and stacking between bases of the same chirality thermodynamically favored, a high degree of homochirality can arise and be maintained provided the non-equilibrium environment overcomes product inhibition, for instance, via temperature cycling. Indeed, if the experimentally observed kinetic stalling of ligation after chiral mismatches is also incorporated, the RNA reactor can evolve towards a fully homochiral state, in which one chirality is entirely lost. This is possible because the kinetic stalling after chiral mismatches effectively implements a chiral cross-inhibition process. Taken together, our model supports a scenario where the emergence of homochirality is assisted by template-directed ligation and polymerization in a non-equilibrium RNA reactor.



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Formation of reactive 2‘,3‘-cyclic phosphate ribonucleosides by phosphorylation with trimetaphosphate and their subsequent polymerization, in presence of amino acids

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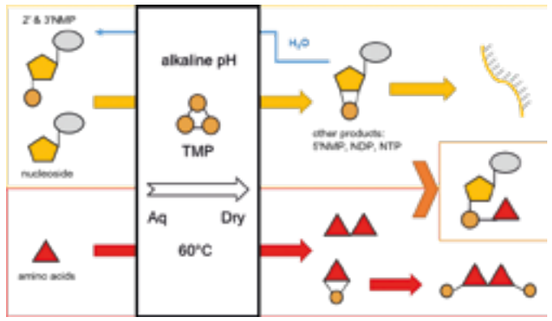
The phosphorylation of ribonucleosides into ribonucleotides, followed by RNA formation, are crucial steps for the emergence of life. In prior work, we demonstrated RNA oligomerization from ribonucleosides 2‘,3‘-cyclic phosphates (2‘,3‘-cNMP) by drying from an alkaline solution. In those conditions, the reaction of polymerization is in competition with the reaction of hydrolysis: part of the 2‘,3‘-cNMP undergoes phosphate ring opening, which results in 2‘- and 3‘-monophosphate ribonucleosides, unreactive toward polymerization.
2‘,3‘-cNMP can arise from hydrolysis of RNA or prebiotic nucleoside phosphorylation. We observed nucleoside phosphorylation using trimetaphosphate and drying from an alkaline solution. The efficiency and regioselectivity of the reaction can be further enhanced by small molecules like urea and amino acids. Additionally, a fraction of nucleoside 2‘ and 3‘-monophosphate can also convert back to 2‘,3‘-cNMP, the prebiotic RNA precursors. In the same condition, we also observed the phosphorylation of amino acids and the formation of short peptides.



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Modeling Chemical Reaction Systems using Rule-Based Stochastic Simulations

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A common approach to modeling systems of chemical reactions is to transform them into a set of coupled ordinary differential equations (ODEs) that are then numerically solved, in order to obtain trajectories for the change of concentration of the involved species. While this is sufficient for small reaction systems there are nevertheless several shortcomings when attempting to model larger, more complex reactions systems. These include failing to address concepts like the concurrency of reaction processes or considering potential side reactions that are not accounted for by the initial assumption of reactions. One solution is to move to stochastic models, e.g. using Gillespie-type algorithms [1] to solve the ODE system, but this still requires an a priori assumption of a chemical reaction network. However, recent advancements made in rule-based modeling [2,3] allow for a different, more realistic approach at modeling complex systems of chemical reactions. As the name suggests, at the center of this type of modeling framework lies the assumption that chemical reactions can be formalized as general rules that are furthermore assigned rates with which they might occur which then allows for a so called network free Gillespie algorithm [4]. In this poster an approach is presented that furthermore attempts to ground the estimations of these rates in thermodynamic calculations as well as topological properties of the molecules. For future works, such a basal form of kinetic modeling, that should ideally be informed by experiments, will be required in order to understand how potential feedback mechanisms in the system influence the selection of particular pathways from a larger set of possibilities. In the long run such exploitative computational approaches may help to elucidate the control mechanisms that enabled the switching from precursor pathways to the biochemical pathways observed today

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Formation of reactive 2‘,3‘-cyclic phosphate ribonucleosides by phosphorylation with trimeta-phosphate and their subsequent polymerization, in presence of amino acids

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Ribonucleic acid (RNA) possesses unique properties among nucleic acids such as its capability to carry genetic information in many viruses and its catalytic abilities such as cleavage of other RNA molecules. It is suspected thatRNA played an essential role in the first stages of molecular evolution of life based on these remarkable features[1,2]. The main principle of the RNA world hypothesis is the absence of enzymes composed of amino acids. RNA replication is considered as one of the most fundamental prebiotic processes. It was discovered that nucleotides activated with imidazole derivatives may play a major role in non-enzymatic replication on the young Earth. Unlike triphosphates (NTPs), they are able to extend the primer without enzymes[3]. It was also shown that in the presence of 2-aminoimidazole activated monomers and helper trinucleotides the primer extension was efficient for all 4 canonical nucleotides, however the A:T pair exhibited the poorest quality of the process[4]. Here I will present results of molecular dynamics investigation of potentially prebiotic self-replicating RNA oligomers along with DFT calculations. I performed classical molecular dynamics simulations of systems containing imidazolium bridged dinucleotides consisting of guanine, inosine, adenine and 2-thiouracil nucleotides. Moreover, thio-uracil was also present in the complementary strand in the system with adenine. Based on the MD simulation results, I conducted geometry optimizations and binding affinity calculations of selected structures with DFT-D3. These structures were obtained from RMSD-based clustering analysis of the trajectories. My work shows that conformation of imidazolium activated dinucleotides plays a significant part in the quality of the self-replication process.

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Mineral assisted flavin reduction as a stepping stone towards a redox cofactor network

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Modern cells are harmonious chorus of sequential reactions that create a network of self-regulating feedback-loops. Most of these reactions are facilitated by enzymes that enable, direct and combine otherwise slow reactions to be utilized in metabolism. In the context of origins of life this would pose a problem since the chemical reactions leading to life could not benefit from complex molecules such as enzymes. Before the emergence of enzymes, cofactors could have played a crucial role in participating and facilitating the reactions of protometabolism, possibly connecting energy and compounds by geochemistry with proto-biochemical reactions (1). The conditions of early earth water-rock interactions could have hosted an environment for the formation of basic protometabolic networks based on cofactors and other metabolites.
This project is aiming to map possible reactions and functional boundaries of redox cofactors that are central to metabolism in Hadean hydrothermal environments, and to explore if multilateral co-factor-facilitated reactions could have been the basis of early metabolism. Cofactors such as nicotinamide dinucleotide/mononucleotide (NAD, NMN), flavins (Riboflavin, FMN, FAD) are evolutionary conserved and thus ideal candidates for protoenzymatic redox reactions (2). So far, we have tested FAD, FMN, and Riboflavin reduction under several abiotic conditions (pH and temperature, various buffers, minerals and atmospheres) showing some robustness of flavins under several conditions. In a next step, we are trying to connect flavins with other other metabolites and cofactors they come across with in (autotrophic) metabolism.
Finding information on the singular nodes, trends and functions of these cofactor-based networks could help to illuminate the bigger picture and help to bridge the gap between geo- and biochemistry.

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Exceptionally opposing trends in carbon and hydrogen isotope fractionations of chemoautotrophic sulfur-oxidizing bacteria at shallow hydrothermal vents

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Early life forms likely depended on environments with pronounced redox gradients to support chemoautotrophic processes. Hydrothermal systems found on Earth today, offer similar conditions for chemoautotrophs to thrive. However, adaptation mechanisms are necessary to sustain life in such extreme environments. This study focuses on the metabolic adaptations of chemoautotrophic sulfur-oxidizers in shallow-water hydrothermal vents off Kueishantao (Taiwan). We explore these metabolic adaptations through analyses of stable carbon and hydrogen in lipid-derived fatty acids from sediments and fluids collected at the venting sites.

As an adaptation to extreme environments, chemoautotrophs can use the reductive tricarboxylic acid (rTCA) cycle for CO2 fixation. This carbon fixation pathway is more energy efficient and discriminates less against 13C than the Calvin-Benson-Bassham (CBB) cycle. The presence of chemoautotrophs using the rTCA cycle is supported by highly abundant C16:1ω7c, C18:1ω7c, and C18:1ω9 fatty acids that are strongly enriched in 13C resulting from extremely low carbon isotope fractionations of as low as -0.5‰ in the vent fluid (Maak et al. 2024, EGUsphere [preprint]). At the same time, these fatty acids demonstrate significant hydrogen isotope fractionation of as high as -300‰. In contrast, fatty acids with 13C values of -23.2 ± 0.6‰ (iso- and anteiso-C15), indicative of the CBB cycle, show δ2H values of -208 ± 4‰.

This strong difference, with minimal to no fractionation for carbon uptake and high fractionation for hydrogen is likely driven by the thermodynamically challenging conditions of hydrothermal vents. The combined analysis of $\delta^{2}H$ and $\delta^{13}C$ isotopes enables us to differentiate between metabolic pathways and carbon sources, providing insights into the adaptation strategies of chemoautotrophs. This approach might also enable us to identify similar metabolic signatures in paleoenvironmental samples, enhancing our understanding of ancient ecosystems.

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‚Life' in the Origins of Life

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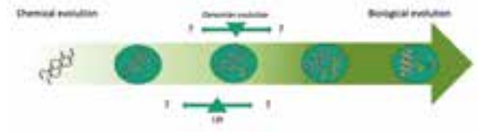
The unexamined assumptions about the nature of life in origins of life research constrains the research programs pursued in the field. Hence, exploring what these assumptions are and engaging with their justification is a necessary step towards a more philosophically informed practice of origins of life research.

Many have argued for the redundancy of a definition of life, because it is arbitrary at what point a complex chemical system can be called living, and because spending too much time trying to figure it out distracts from the true aims of origins of life research: understanding the transition from chemistry to biology. However, I argue that this critiques of 'life definitionism' do not work. Firstly, a definition may be ultimately arbitrary and still not be redundant, but informative. Secondly, it is unclear what 'the transition from chemistry to biology' amounts to if not the transition from chemical systems to biological systems. Thirdly, and more crucially, while origins of life research does not concern itself with functional definitions of 'life' or specific microstructural features of life, it does usually posit the minimal chemical requirements for a system to evolve towards a living system. These are often embodied in protocell models.

Protocell models throughout origins of life research consist of the functional integration of a compartment, a metabolism, and a mechanism of inheritance. The reason why they are picked out as having a predominant role in our account of origins is that they are the minimal system that can undergo natural selection. These 'microstructural identities' of protolife, then, are associated with a specific view of life: evolution by natural selection is the primary and sufficient process by which life acquires complex adaptations and exhibits all its distinctive behavior. I suggest that this needs to be evaluated in the context of recent debates about evolutionary theory which suggest that evolution by natural selection is not sufficient to account for evolutionary trajectories, and may require an extension. These ideas are brought together as the extended evolutionary synthesis. The question I posit is what the bearing of this for origins of life research may be.



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NADH-mediated primordial synthesis of amino acids.

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The pathways potentially responsible for the abiotic synthesis of amino acids differ from those found in living organisms.(1) This contrast leaves a gap between bottom-up approaches aimed at understanding how life began and research on the emergence and development of metabolism. (2) Identifying non-enzymatic versions of crucial metabolic reactions seems a powerful strategy to shed some light into this gap, and the use of natural cofactors can play a vital role in facilitating these chemical processes in the absence of enzymes.(3) Nicotinamide adenine dinucleotide, or NAD+ (together with its reduced form NADH), is an essential coenzyme for redox reactions that are fundamental in the biochemistry of all living cells. Our research group has focused on the formation of amino acids via reductive amination as model reaction to investigate the non-enzymatic redox capabilities of nicotinamide systems without enzymatic support.(4) Our emphasis was on understanding the interaction between nicotinamide systems and the reaction environment. We employed DFT calculations and spectroscopic data analysis for this purpose. The calculations indicate that this reaction goes through an iminium intermediate with the potential to increase the low reactivity of NADH as a hydride donor toward the carbonyl group of □-ketoacids. In summary, these findings demonstrate the possible role of NADH in amino acids primordial synthesis through a pathway that is reminiscent of the chemoautotrophic theory. This example establishes a significant link between modern and ancient chemical processes used to form these crucial building blocks in an early protometabolism.

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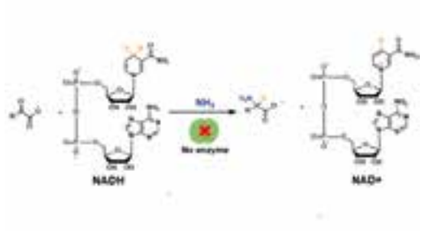

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Geothermal non-equilibria drive ionic and pH gradients

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Rocks and their constituent phases likely played an essential role as molecular feedstock during the emergence of life on earth. We aim to combine this geological scenario with physical non-equilibria such as thermal gradients, offering unique opportunities for molecular selection.

Prebiotic reactions often require a defined set of ion concentrations. One example is the activity of some important RNA enzymes that vanishes without divalent magnesium salt, whereas an excess of monovalent sodium salt reduces enzyme function. However, leaching experiments show that relevant geomaterials such as basalts release mainly sodium and only little magnesium. A ubiquitous non-equilibrium solution to this problem are heat flows through thin rock fractures, driving thermogravitational convection and solute thermophoresis. The superposition of both effects actively enriches magnesium ions against sodium and establishes a habitat for ribozyme function from basaltic leachates [1]. The process plausibly occurs within systems of connected rock cracks, which increases the strength and stability of the selective accumulation. Interestingly, thermal gradients also lead to the formation of pH gradients in mixtures of only formic acid and sodium hydroxide, which can be understood and predicted by a separation of timescales [2].

While phosphate is essential to all life, its prebiotic accessibility poses major problems. For instance, one of the most abundant phosphate minerals on the early Earth, Apatite, is insoluble at the neutral and alkaline pH values compatible with nascent life. We show that heat flows can spatially separate the constituents of Apatite, phosphate and calcium, under acidic conditions. The neutralization of the phosphate-enriched and calcium depleted fraction yields considerable amounts of free phosphate. The resulting concentrations are sufficient to form more reactive phosphate species such as trimetaphosphate upon heating. Using a variety of minerals, glasses, and clays, we show which surfaces can promote such reactions.

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Robustness of collectively encoded genomic information

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The precise inheritance of genetic information through generations is a key concern for origins of life studies. Modern life relies on replicating single long oligonucleotides like DNA, but this mechanism faces difficulties in prebiotic conditions lacking evolved enzymes. Alternatively, some hypotheses suggest that short oligomers could collectively transmit information, but this concept lacks experimental and computational validation. Here, we demonstrate the suppression of mutations through cooperation among oligomers. We designed short DNA oligomers that encompass information from a "virtual circular genome." These oligomers possess overlapping bases, allowing them to function as both primers and templates in thermal cycling processes, along with enzymatic primer extension. Through a combination of experiments and simulations, we observed that mutant oligomers replicate more slowly than their wild-type counterparts. This can be explained by a "binding partner effect," in which wild-type oligomers are more likely to have partners that act as primers for their extension. Our findings highlight the advantages of collectively encoding genomic information in the origins of life context.

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Whence the demise and fall of the RNA World?

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A widely promulgated concept for the fundamental ancestor-descendent relationship at life's origin, and thus the onset of Darwinian evolution, is the RNA World hypothesis. If Darwinian evolution on Earth began with a simple RNA molecule which had the ability to replicate itself, in the long run this must have given way to DNA perhaps via an intermediate RNA(±Peptide) World. This could happen once DNA appeared and became the preferred informational molecule for all extant biology. Yet, making sense of this transition is confounded both by the intervening 4 billion years of biological evolution, and a scarce ancient (pre-3.2 Gyr) geologic record. Here, we explore whether the relative instability of RNA to thermal stresses, salt content, pH, variable UV sensitivity and an overall narrow available suite of metabolic styles, strictly limited the range of suitable habitats for RNA World organisms; they were susceptible to marginalization, assimilation and effective extinction. We propose that main factors responsible for the transition from the RNA±Peptide to DNA+-Peptide World included (i) overall changes in the geosphere (e.g. heat flow, crustal type, nutrient availability); (ii) transient global heating of the hydrosphere by late accretion bombardment viz. "thermal bottlenecks"; and, (iii) competition from, and perhaps predation by, metabolically diverse and genomically nimble emergent DNA+Peptide organisms.

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Controlling transport for RNA enrichment in 2D alkaline chimneys

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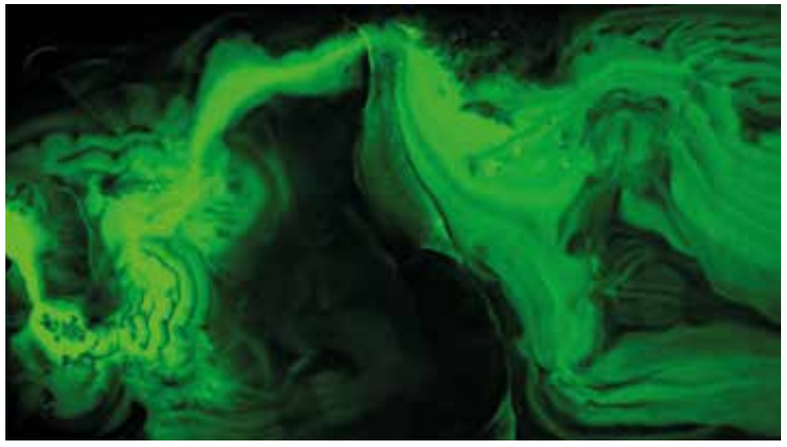
Alkaline vents at the prebiotic ocean floor are hypothesized as a setting for the emergence of life. These alkaline vents (AVs) produce chimneys with intricate hierarchical architectures and steep pH gradients. Within the AV chimneys, intricate flow networks facilitate complex transport of organic molecules and other compounds. For the emergence of life, enrichment and synthesis of organic molecules, in particular nucleic acids, needs to be facilitated. Yet, the location within the AV chimneys and the necessary flow conditions to overcome the concentration problem are still unknown.

Our recently established microfluidic two-dimensional (2D) model of alkaline chimneys allows us to directly observe chimney architecture, fluid flow, and molecule transport and enrichment. By combining optical tracking with numerical methods, we aim to establish a quantitative model of transport through the AV chimney. Experimental 2D chimneys will be optimized using predictions from the quantitative model and tested for enrichment of organic compounds. Finally, the effects of a dynamic chimney environment will be probed by periodically changing inflow salt concentration and tracking the impact on denaturation and hybridization of nucleic acids. Through this combination of experiments and quantitative modeling, we aim to uncover the physical prerequisites for the enrichment of nucleic acids and the creation of dynamic environments facilitating replication at the origin of life.



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Formation of Hierarchical Microcompartments through Autocatalysis and Coacervation Interplay

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Biological systems are organized in space and time through the interplay between chemical reactions, diffusion, phase separation, and self-assembly. Decades ago, Alexander Oparin hypothesized that coacervates formed by liquid/liquid phase separation on early Earth could be a key to the origin of life. These coacervates would act as permeable compartments that support primitive metabolism. The interaction between non-linear reactions (autocatalysis) and liquid-liquid phase separation is particularly interesting because of the emergence of functional properties and structures through instabilities, which are hard to predict theoretically without the help of experimental model systems.

In this work, we studied systems where chemical autocatalysis is coupled to complex coacervation and the formation of oil-in-water droplets. The autocatalysis is driven by a nucleophilic chain reaction and is coupled to complex coacervation with polyacrylic acid (PAA) through the formation of tri- and tetra-cationic species. Interestingly, we observed the formation of hierarchical colloids when we used reactants that can form oil droplets in addition to coacervate droplets. Structure of these complex colloids and the mechanism underlying their formation were studying with use of fluorescent microscopy, NMR spectroscopy, Raman spectroscopy, dynamic light scattering (DLS) measurements, confocal imaging, and molecular dynamics simulations. In addition to PAA, a model RNA molecule - polyuridylic acid (PolyU) demonstrated autocatalytic formation of coacervates and hierarchical colloids. This work illustrates a mechanism for the formation of complex, hierarchical microstructures by kinetically controlled self-assembly regulated by nonlinear chemical reaction networks. Such experimental system could serve as a model for future origin of life related studies where these compartments could autocatalytically reproduce their content and divide to sustain Darwinian evolution.

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Autocatalytic reaction between HCN and cysteamine creates hydrophobic liquid compartments

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The origin of life remains one of the most intriguing and interdisciplinary problems in science. Hydrogen cyanide (HCN) is a key molecule in prebiotic chemistry, known for its versatile reactivity and ability to form building blocks. However, macroscopic system-level phenomena arising from HCN reactivity, such as autocatalysis, oscillations, pattern formation, and phase separation have received less attention and remain underexplored. In our study, we investigated the interaction between HCN and cysteamine, revealing three important aspects: (i) autocatalysis driven by pH increase and the catalytic properties of the second liquid phase, (ii) liquid-liquid phase separation, and (iii) formation of analyzable oligomers instead of insoluble polymers typical for HCN reactions. The second liquid phase demonstrated the ability to extract certain hydrophobic substances from the solution, increasing their local concentration in microdroplets. This can accumulate certain compounds in high concentrations and create conditions for protometabolism. The study of intermediates arising in this simple system also allows us to better substantiate the possible pathways of HCN transformations under prebiotic conditions. Our system is valuable as a prebiotic model showcasing several key phenomena simultaneously, enabling us to explore the integration and participation of other prebiotic molecules (such as cofactors), the role of phase separation in prebiotic processes, and the transformation pathways of hydrogen cyanide. This enhances our understanding of the transition from simple high-energy molecules to more complex, thermodynamically stable compounds, offering valuable insights into the chemical evolution necessary for the origin of life.

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Route to Biopolymers via Mixed RNA-Aminonitrile Building Blocks

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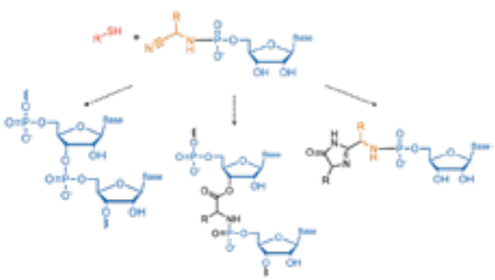
To transition from RNA world to RNA-protein world, there likely existed a predisposed way of interaction between RNA nucleotides and amino acids or related species. We show that aminonitriles, the Strecker precursors of amino acids, are strongly favoured to attack the activated 5'-phosphate of AMP at pH 6. The resulting aminonitrile-phosphoramidate (ANPN) species is stable compared to aminoacyl-nucleotides. Thiol addition to the nitrile group unlocks different pathways that could result in RNA polymers, polypeptides, or RNA-aminoacyl-bridged polymers. ANPN-RNA building blocks could in future serve as the substrate of an in-vitro selected ribozyme catalysing a primordial form of translation.



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Phosphate-Driven Systems Chemistry

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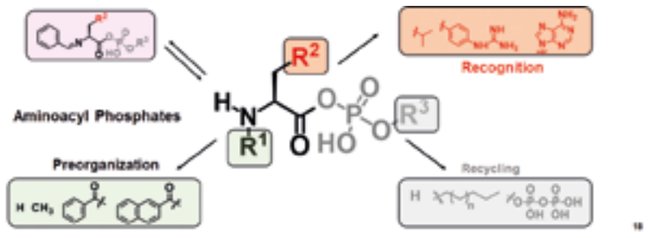
Phosphates and phosphate esters underpin biological information transfer, signal transduction and contribute to the energetics of life. Biochemical energy carriers, such as triphosphates, (ATP, GTP) drive selective processes, by incorporating chemical information (Adenine vs. Guanine) in their structure. These recognition elements match with complex machineries through a variety of non-covalent interactions, enabling specific functions. We aim to develop roles for phosphates outside of biology and capitalize on the idea of providing chemical information within abiotic phosphates to control selectivity and reactivity in chemical reaction networks.1,2 The information is provided by chemical functionalization of energy-rich aminoacyl phosphate esters (Figure 1), whereby the information encodes structural assembly of phosphates prior to their consumption, or transfer large chemical groups onto self-assembling species, enabling activation of various pathways. In particular, we explore the ways in which phosphate esters give rise to spontaneous and selective peptide oligomerization in water, as a result of the construction of autonomous phase changes. Moreover, depending on the chemical nature of peptide nucleophiles used in the network, we demonstrated the construction of non-equilibrium assemblies. Within these systems, the transfer of energy and reactivity from phosphates activates cascade reactions, involving multiple high-energy molecules. Incorporating structural elements around non-biological phosphates and coupling them to dynamic chemistry represents an unexplored opportunity to impact reaction networks, by developing phosphate-driven supramolecular systems chemistry.



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Nonenzymatic RNA replication in a mixture of ‘spent’ nucleotides

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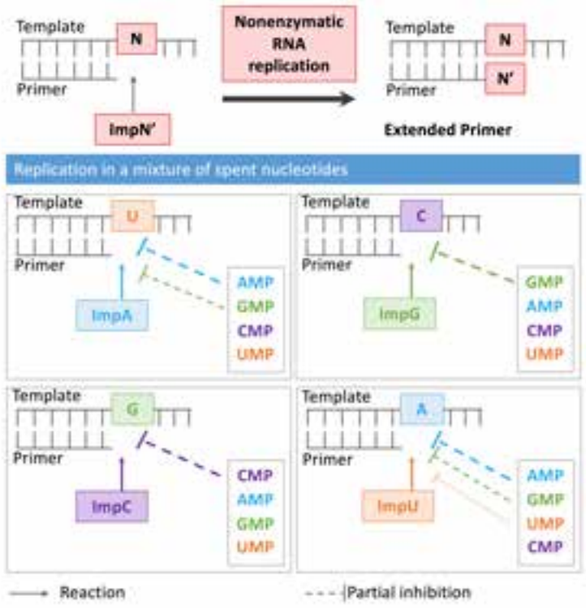
Nonenzymatic template-directed replication would have been affected by co-solutes in a heterogenous prebiotic soup, due to lack of a sophisticated correction machinery. Unlike in contemporary biology, these reactions use prebiotically plausible chemically-activated nucleotides, to extend a template-bound primer, which undergo rapid hydrolysis into corresponding nucleoside monophosphates (‘spent’ monomers). These nucleotides that are present as co-solutes cannot extend the primer but continue to base pair with the template, thereby interfering with replication. Given this, we aimed to understand how a mixture of ‘spent’ ribonucleotides affected nonenzymatic RNA replication. We observe inhibition of primer extension in the presence of the spent nucleotide mixture, wherein the predominant contribution came from the cognate Watson-Crick monomer. Furthermore, a potential sequence dependence of the inhibitory effect was observed. Thus, our study highlights how nonenzymatic RNA replication would have been directly affected by pertinent co-solutes, with ramifications for the emergence of functional polymers in a putative RNA World.



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Hydrothermally reducing nicotinamide di- and mononucleotide and implications for the emergence of metabolism

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Metals could have predated enzymes in their functions. Previously, minerals found in natural hydrothermal systems were shown to promote the production of all intermediate products of the linear acetyl-CoA pathway from CO2 and hydrogen (H2), functioning as both cofactors and enzymes1. Organic redox cofactors such as nicotinamide dinucleotide (NAD) might have preceded the enzymes that use them as electron donor and acceptor for redox reactions in modern metabolism. Theoretical work proposes that cofactors could help to build a non-enzymatic metabolic network2. The role of (di)nucleotides in emergence of life theories has been resurfacing in emergence of life theories – from both RNA- and metabolism-focused sides2,3. And the reason seems obvious: these organic cofactors could function as a missing link between the informational and the metabolic part of life. We see such organic cofactors also as a missing link between geo- and biochemical reactions, being able to bridge mineral-assisted and enzymatic catalysis.

Many cofactors shown to be most conserved within metabolism consist of an active group, responsible for redox reaction or alkyl-transfer, and adenosine nucleotides (mono or diphosphates). But what is the role of this nucleotide "tail"? Does it predate enzymes or is its functioned connected to the emergence of enzymes? To investigate the evolution of cofactors and the function of these nucleotide "tails" in a prebiotic environment, we studied and compared NAD to its ADP-free metabolite, nicotinamide adenosine mononucleotide (NMN). We were able to show that tail seems to prevent over-reduction of the cofactor when strong heterogeneous catalysts are used, but with weaker catalysts, NMN seems to be the more efficient hydride acceptor. We deduce from these results that the adenine nucleotide tail is essential for the targeted reduction of the 1,4-position, as well as for the stability of this specific reduction product. Nevertheless, under less catalytically effective conditions, NMN is more easily reduced which could constitute an advantage in a prebiotic context. As we were able to show that both nicotinamides are able to reduce ketoacids non-enzymatically with comparable efficiencies, we conclude that the role of the nucleotide tails (at least in the case of nicotinamide nucleotides) coincide rather with the environmental conditions and associated reaction partners than with enzymatic evolution.

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Non-enzymatic formylation of H4F: implications for the emergence of autotrophic metabolism

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The Wood-Ljungdahl pathway, also known as the reductive acetyl-CoA pathway, has been proposed to be one of the oldest carbon fixation pathways and is found in methanogenic archaea and acetogenic bacteria (1). It consists of two branches. The first is the methyl branch in which CO2 is reduced stepwise first into formate and then into a methyl group attached to a cofactor carrier (tetrahydromethanopterin, H4MPT, for Archaea and tetrahydrofolic acid, H4F, for Bacteria). The second is the carbonyl branch, in which CO2 is reduced to CO. Both branches converge with CoA to form acetyl-CoA. The role of these cofactor carriers is pivotal in this process, but their role in a prebiotic context is still poorly understood. These folates might have preceded those enzymes – as a transitional process between inorganic catalysts such as mineral surfaces, to the enzymatic process we know today (2).Our aim in this project is to explore whether the formation of the methyl group can occur in a stepwise fashion non-enzymatically using mineral catalysts and conditions akin to the ones found in hydrogen rich hydrothermal systems during the Hadean period. Building upon the work previously conducted in our lab we use high-pressure reactors combined with H2/CO2 atmosphere to methylate the cofactor starting from the formylation of the compound followed by a cyclization and two reduction steps. Here, we show that in the presence of formic acid the reaction proceeds for the first two steps non-enzymatically, bypassing energy requirements found in Acetogens, thanks solely to the chemical and physical properties of the cofactor and its medium (4). We also show that the concentration of C1 donor required is in line with the amount of formate generated by abiotic CO2 fixation in serpentinizing hydrothermal systems (3).

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Tuning the catalytic function of lipopeptide assemblies using nucleobases

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An important question about the role of catalysis in systems chemistry (1) relates to the way in which biohybrid catalysts could be tuned and optimized (2), most likely through the establishment of well-defined supramolecular structures in aqueous media.
In this poster presentation, we report functional hybrid molecules consisting of a H-(D)Pro-Pro-Glu tripeptide (3), derivatized with both a fatty acid and nucleobases. The combination of simple biological components allows to merge the peptides catalytic properties with the capacity of lipids to induce self-assembly, and that of nitrogenous bases to provide structural ordering (4). The biomolecule hybrids self-assemble in aqueous media into nanotubes displaying catalytic activity in a model reaction between butanal and nitrostyrene. The higher degree of ordering in the supramolecular structures induced by nucleobase pairing allows to increase the catalytic activity and diastereoselectivity of the assemblies, resulting in a 95% conversion and a d.r. ratio of 10:1 of the conjugate addition product. The present results point to the significant control, directionality and ordering that nucleobase interactions can provide in the self-assembly of biologically inspired supramolecular catalysts. (5)

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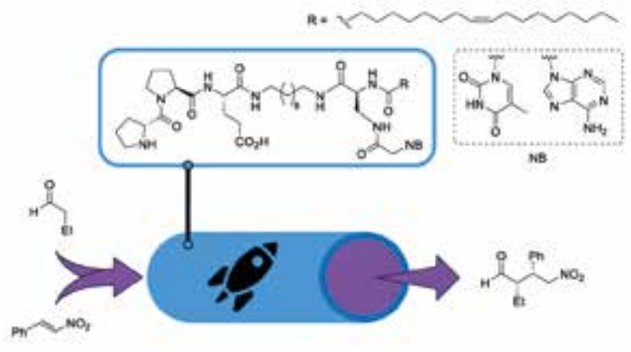

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Amino acids catalyze RNA formation under ambient alkaline conditions

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RNA and proteins are the core molecules of life. The sequence of mRNA encodes the protein sequence, and proteins orchestrate the replication of nucleic acids. How this synergistic relationship arose remains an unanswered question. Amino acids have not yet provided an evolutionary advantage to nucleic acid synthesis. This relationship has been assumed as a late development during RNA evolution. Here we show that amino acids substantially improve the yield of RNA polymerization from prebiotically plausible ribonucleoside-2′,3′-cyclic phosphates. The amino acid catalysis of RNA polymerization was base-selective, increased the compositional oligomer sequence diversity and favoured the formation of natural 3′,5′ linkages. It was most efficient at pH values close to the pKaH of the amines and correlated with sidechain hydrophobicities, suggesting a general acid-base mechanism akin to ribozyme-catalyzed RNA-hydrolysis. This is confirmed by the observed general base-enhanced polymerization of G and U nucleotides. The copolymerization of G/C/A/U with valine resulted in a substantially increased oligomer yield and compositional diversity. The catalytic effect of proteinogenic amino acids on RNA oligomerization suggests the reactivity of amino acids and RNA was united earlier than previously thought, and their association likely predates the genetic code.

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Spontaneous formation of prebiotically relevant molecules from nucleotide-amino acid mixtures

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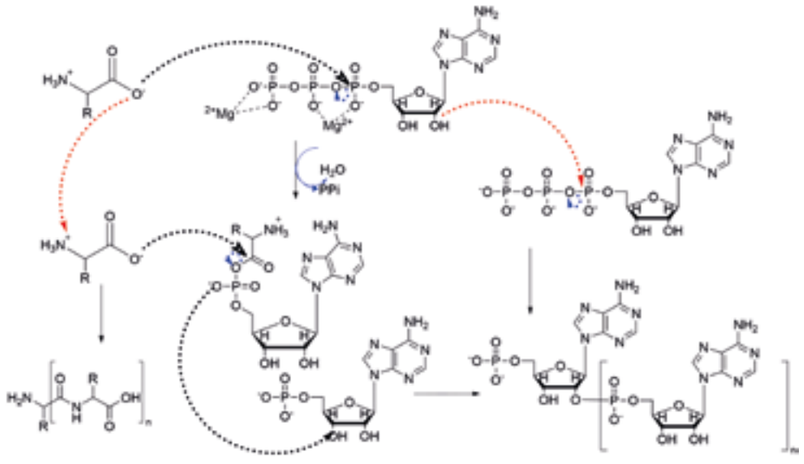
Previous origins of life studies have demonstrated the presence of amino acids and nucleotides in the same prebiotic milieu. In this context, we set out to understand the interplay of amino acids with nucleotides under prebiotically pertinent reaction conditions, especially for its implications for biomolecular evolution. We started with characterizing the non-enzymatic formation of activated or charged amino acids (AMP-aa), an important first advance towards translation, mainly using glycine. We also characterized the cross-catalytic effect (e.g., on oligomerization potential), if any, stemming from the simultaneous presence of these two biochemically important monomers in the reaction milieu. Qualitative analysis indicated the formation of longer AMP oligomers and peptides (glycine oligomers). Pertinently, quantitative analysis indicated a greater abundance of peptides in the presence of nucleotides than in reactions that looked at amino acid oligomerization in isolation. We also characterized the various possible linkages between AMP-aa that could result in such reactions where there is no stereochemical control. We extended this to also elucidate the synthesis of AMP-aa using other amino acids, including aspartic acid, lysine, glycine, and tryptophan. Overall, we used a nonenzymatic approach to characterize the formation of molecules relevant to life's early evolution. We make a compelling case for how processes involving co-solute interactions between biomolecules would have set the stage for an increase in molecular complexity, a prerequisite for the eventual emergence of a cellular entity. In summary, our research illuminates the biochemical dynamics that could have contributed to the genesis of life on Earth, providing valuable insights into the initial phases of biochemical evolution.



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Comprehensive Analysis of Soluble Organic Matter and Volatiles on meteorites – seeing the bigger picture by looking from different angles

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Introduction: Meteorites contain complex organic chemistry that reflects the chemistry on the parent body under stress of heat, water alteration and shock events [1][2]. Some of the molecules formed on a meteorite's journey potentially play an important role in the molecular evolution towards the emergence of life after being transported to Earth via meteoritic impact [3].
Obtaining insight into this complex mixture as well as the chemical dynamics at which the organic compounds form and react helps to better understand how pre-biotic molecular evolution works.

Summary: Different meteorites were exposed to temperature stress. While heat was applied, the volatiles desorbing from the material were ionized via a dielectric barrier discharge ionization (DBDI) ion source (called SICRIT and produced by Plasmion) and analyzed with Fourier-transform ion cyclotron resonance (FT-ICR MS). In addition to this, the change in soluble organic matter (SOM) imposed by the heat can be observed by comparing the state before and after the heating.
In a fist step towards this characterization, we show here the analysis of SOM via a setup that can analyze minute amounts of sample while at the same time providing an additional perspective on the chemical diversity by employing DBDI ionization, which shows different selectivity compared to the standard approaches of electrospray ionization in positive or negative mode. The data shows that the ion source provides good insight into the N-containing molecules within the mixture, which makes it suitable for the heating experiments that are expected to have a big impact on exactly these types of molecules.

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Framboid-like pyrite traces mineral-fluid-organic interactions in hydrothermal sulfide systems

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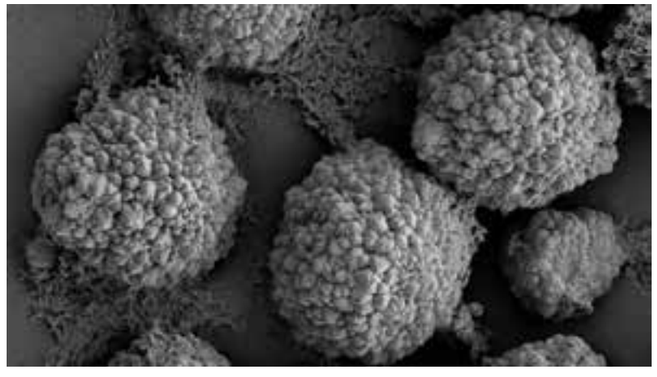
Life originated from interactions between minerals, fluids, and organic molecules, most likely in a hydrothermal context. Magnetite is a widespread mineral in hydrothermal systems and was suggested to mediate critical prebiotic reactions, including Fischer-Tropsch-type abiotic organic synthesis and enantiomeric selection. Unraveling the interactions between magnetite, organic matter, and fluid-bound species under conditions representing hydrothermal systems on the early Earth may thus be essential to understanding the origin of life. The products of hydrothermally driven magnetite transformation may be relicts of such interactions in the rock record. However, these products are poorly constrained. Here, we show experimental data on the hydrothermal sulfidation of abiogenic and biogenic (i.e., organic matter-associated) magnetite nanoparticles (sulfide/Fe=4, 20-80°C, pH 7-10) in the presence of different sulfur species (sulfide, S0, polysulfides). We characterized the resulting precipitates with analytical imaging techniques, mineralogical methods, and geochemical approaches (e.g., SEM-EDS, FIB, µ-XRD, Raman spectroscopy, sequential Fe extraction). Our experiments yielded pyrite with various distinct morphologies, including framboid-like spheroids. We demonstrate that the variability in pyrite morphologies resulted from the modulation of pyritization rates by pH and the interrelated effects between organic matter and S0 (crystalline or colloidal). Notably, framboid-like pyrite was exclusively produced from the sulfidation of organic matter-associated magnetite. While commonly considered a potential fingerprint of microbial sulfur cycling, our results show that framboid-like pyrite may also trace the hydrothermal sulfidation of organic matter-associated magnetite, providing a valuable tool for unraveling the nature of mineral-fluid-organic interactions in deep time.



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Initiation of DNA Unzipping Through Sequence-Kinetics

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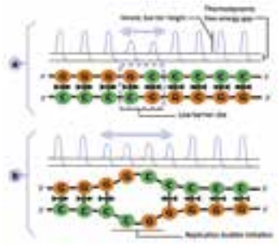
The replication of DNA, the primary polymer responsible for information storage within cells, is a crucial event occurring once per cell cycle. The initiation of this process entails the separation of double-stranded DNA (dsDNA), resulting in the formation of a replication bubble, wherein both strands become accessible for the attachment of monomers to construct the daughter strand. Despite extensive investigation into DNA replication, the sequence dependency of unzipping initiation site, called origin of replication, remain elusive. We employed a theoretical model known as the Asymmetric Cooperativity Model and conducted simulations of dsDNA unzipping using a Markov Chain method to understand the sequence dependency of origin of replication. By considering an asymmetric nearest-neighbor kinetic cooperative effect among base pairs within DNA, the model elucidates the localized melting of DNA at palindromic sites with skewness in purine-pyrimidine content, thus offering valuable insights into the dynamics of replication initiation.



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Collective adaptability in a replication network of minimal nucleobase sequences

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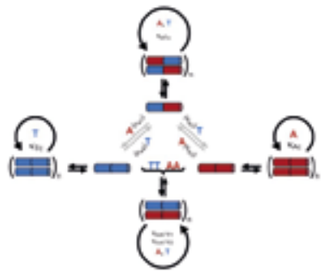
A major challenge for understanding the origins of life is to explore how replication networks can engage in an evolutionary process. Herein, we shed light on this problem by implementing a network constituted by two different types of extremely simple biological components: the amino acid cysteine and the canonical nucleobases adenine and thymine, connected through amide bonds to the cysteine amino group and oxidation of its thiol into three possible disulfides. Supramolecular and kinetic analyses revealed that both self- and mutual interactions between such dinucleobase compounds drive their assembly and replication pathways. Those pathways involving sequence complementarity led to enhanced replication rates, suggesting a potential bias for selection. The interplay of synergistic dynamics and competition between replicators was then simulated, under conditions that are not easily accessible with experiments, in an open reactor parametrized and constrained with the unprecedentedly complete experimental kinetic data obtained for our replicative network. Interestingly, the simulations show bistability, as a selective amplification of different species depending on the initial mixture composition. Overall, this network configuration can favor a collective adaptability to changes in the availability of feedstock molecules, with disulfide exchange reactions serving as 'wires' that connect the different individual auto- and cross-catalytic pathways.



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Enhancing polymerization of prebiotic building blocks by activation chemistry and wet-dry cycling

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Prebiotic chemistry is limited by several factors as concentration or availability of starting materials on the early Earth. On top of that, many artificial and natural activation agents are too complex to have been a part of prebiotic reaction networks. To overcome this problem, amino acids might help reaching ideal environmental conditions, enhancing prebiotic reactions like polymerization of nucleotides. Depending on their specific side groups, they can buffer the pH towards more acidic or basic conditions, provide the system with hydrophilic or hydrophobic moieties and act as proton or electron donors. Recent work in our group demonstrated, that by the addition of Valine, the polymerization of nucleotides as 2',3'-GMP can be enhanced by 40%. [1]
By using wet-dry cycles and including other prebiotic plausible "activating agents" as trimetaphosphate or volcanic rocks, a better control of the polymerization should be accomplished. Preliminary experiments suggest that by adding valine to a mixture of 2',3'-GMP and 2'3'-CMP, the cyclic end of the polymers can be preserved, while at the same time the ratio of C and G polymers stays constant. These new findings reveal that under these conditions there might be a control over the polymerization pattern.

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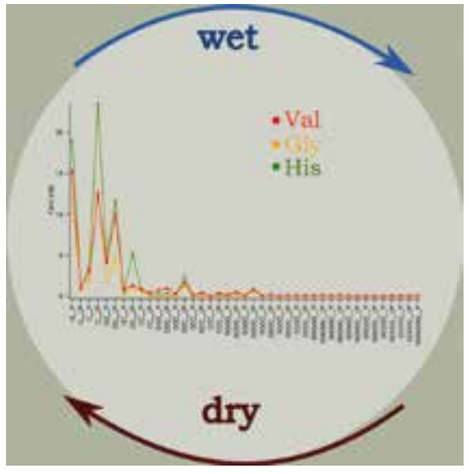

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Origin of the genetic code: RNA library screening for self-aminoacylating tRNA precursors

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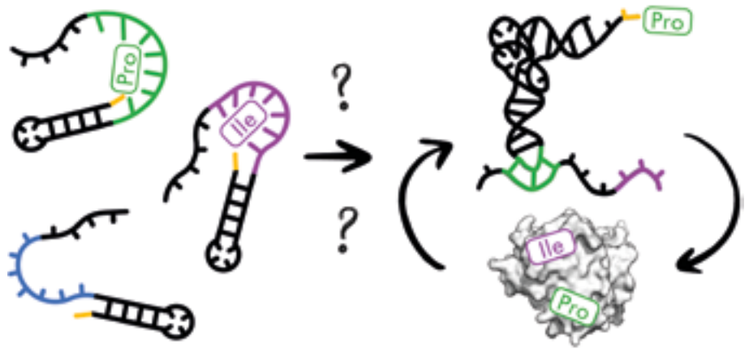
Every extant organism uses mostly the same genetic code of three successive nucleotides called 'codons' to encode each amino acid. Transfer RNAs (tRNAs) translate one codon at a time into a sequence of amino acids to form proteins. This is being achieved by base-pairing of a tRNA's anticodon with an mRNA's codon. tRNAs carry the amino acid matching to their anticodon at their 3'-end and proteins are needed to recharge a tRNA's amino acid once it was incorporated into the nascent protein. As such a system is too complex to appear at once in a prebiotic setting, we investigated its origin as well as the origin of the genetic code itself by verifying Hopfield's testable hypothesis of a tRNA-precursor that could charge itself with the correct amino acid by using its anticodon as a chemical sensor. The proposed 'Hopfield fold' suggested an alternative folding of a tRNA sequence which brings their anticodon-loop in close proximity of their 3'-end. We conducted kinetic sequencing of Hopfield folds with anticodon-loops consisting of seven randomized nucleotides resulting in 16,384 parallely tested sequences. Thereby, we could identify sequences that undergo specific and efficient self-charging when in solution with D-/L-lysyl-, L-alanyl-, and glycyl-adenosine monophosphate as well as L-lysyl-cytosine monophosphate.



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Evolution at the Origins of Life?

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Evolutionary theory has a tremendous explanatory power when it comes to understanding the biological world. Its central Darwinian logic is fairly straightforward, even though the theory itself is multifaceted. This has led to numerous evolutionary research programs in various fields, ranging from economics, to epistemology, to the origins of life.

In this project, I focus on evolutionary theory as applied to origins of life research. The central question is 'How, if at all, can evolutionary theory be applied to the pre-biological emergence and development of life?' Answering this question requires solving several issues surrounding three core parts: (i) the extension of evolutionary theory from a theoretical and philosophical perspective, (ii) the conceptualization of the transition from prebiotic chemistry to cellular life, and (iii) the current use of evolutionary terminology by the origins of life community.

For this poster, I will focus on the second part of the project. This second part is the more empirically oriented counterpart of the first: rather than looking at what it means from a theoretical and conceptual perspective to apply evolutionary theory to a field other than its field of origin, which is organismal biology, the second part is aimed at elucidating in what ways the various concrete steps in the origins and early development of life that have been proposed so far might be evolutionary. Questions include: What does it mean for a protocell to be evolutionary? How are these protocells related to LUCA? And could there be such things as evolutionary prebiotic chemical reaction networks preceding the protocellular stage?

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The cyanide-free formation of amino acids and amides from acetylene, ammonia and carbon monoxide in aqueous environments in a simulatedn Hadean scenario

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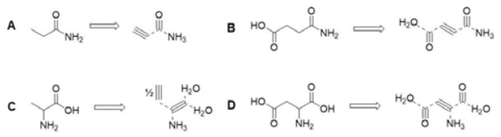
Amino acids are one of the most important building blocks of life. During the biochemical process of translation, cells sequentially connect amino acids via amide bonds to synthesize proteins, using the genetic information in messenger RNA (mRNA) as a template. From a prebiotic perspective (i.e. without enzymatic catalysis), joining amino acids to peptides via amide bonds is difficult due to the highly endergonic nature of the condensation reaction. We show here that amides can be formed in reactions catalyzed by transition metal sulfide from acetylene, carbon monoxide and ammonia under aqueous conditions. Some α- and β-amino acids were also formed under the same conditions, demonstrating an alternative cyanide-free path to amino acids in prebiotic environments. Experiments performed with stable isotope labeled precursors, like 15NH4Cl and 13C-acetylene, enable accurate mass spectroscopic identification of products and their composition from the starting materials. Transition metal sulfide catalyzed reactions seem to offer a promising alternative pathway for the formation of amides and amino acids in prebiotic environments, bypassing the challenges posed by the highly endergonic condensation reaction. This finding sheds light on the potential mechanisms by which the building blocks of life could have originated on early Earth.



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Binding Affinity of RNA-Peptide Conjugates to RNA duplexes

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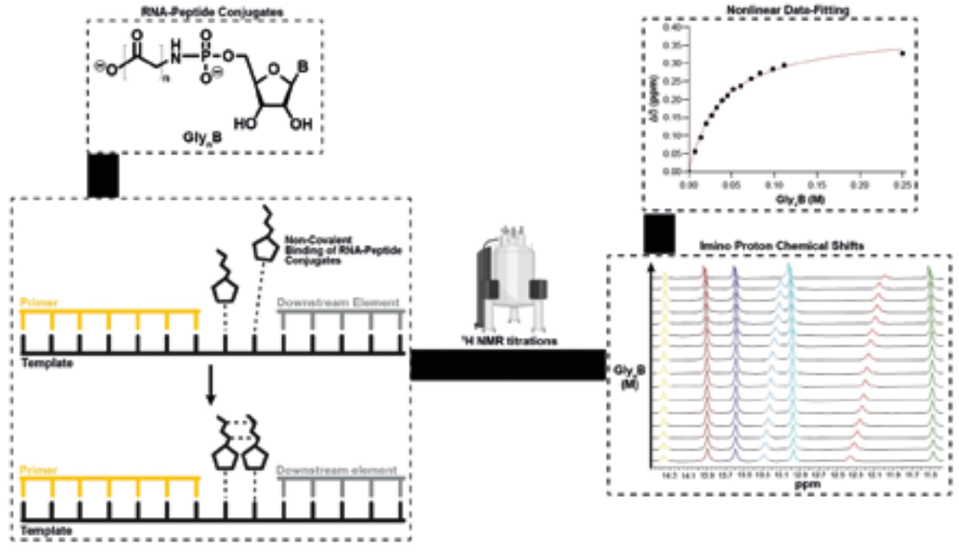
RNA-based self-replicating systems are thought to precede extant biology, with nonenzymatic template-directed RNA copying offering a possible mechanism by which molecular Darwinian evolution was initiated. The limitations in efficiency and fidelity of nonenzymatic template-directed RNA replication, however, prevent us from understanding how this system could be capable of undergoing natural selection. Integrating peptide and amino acid functionality into RNA-controlled nonenzymatic template-directed replication in the form of RNA-peptide conjugates has been observed to enhance the rate of copying – the mechanism is not well understood and must be studied further. My project aims to measure the thermodynamic parameters for the binding of various conjugates to polymeric RNA duplexes. Understanding the plausibility of this system will assist in understanding how the RNA world may have evolved into proto-metabolism processes resembling biochemistry as we know it today.



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Combined Network and High Resolution Mass Spectrometry Analysis of the Formose Reaction Reveals Mechanisms for Emergent Behaviors

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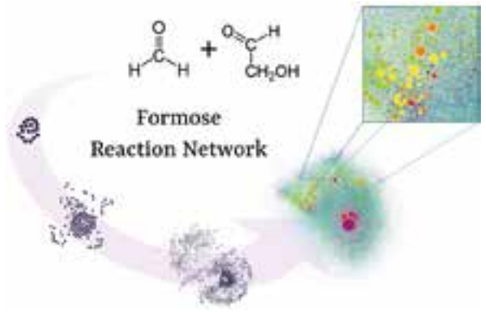
The formose reaction (FR) autocatalytically converts simple plausibly prebiotic feedstocks into molecules of biological interest, including ribose. Autocatalysis is a hallmark of life, thus various studies have explored the formose reaction with respect to the origins of life. The FR is robust under appropriate conditions, occurring readily at low temperatures from a variety of substrates, and has been implicated in the generation of meteoritic organic compounds. We explored the FR here using a combination of in silico modeling techniques and high resolution mass spectrometry. The models match experimental results well, and point to the FR being much more complex than previously modeled or measured, and help explain the FR's potential to generate homochirality and primitive compartments, both of which are also hallmarks of life, before the emergence of the complex directed molecular encoding suggested by the RNA World model. These results suggest the FR requires further study with regard to the origins of life, and its importance may lie in the way it enables and coordinates emergent chemistries, rather than the particular products it generates, such as ribose.



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Coacervate protocells selectively localize ions and create distinct reaction microenvironments

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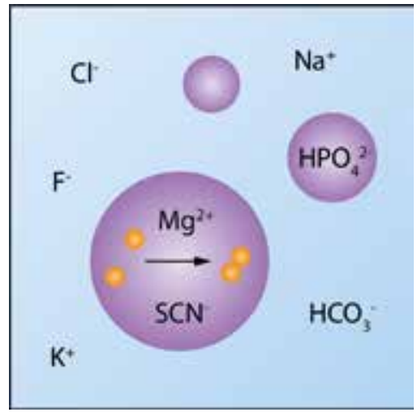
Coacervate protocells can catalyse prebiotic reactions by concentrating reactants and by altering the rate constant using their local microenvironment that is distinctly different in terms of polarity, crowding, pH and water activity. To understand how specific coacervates could modulate prebiotic reactions, a proper characterization of the local environment is crucial. Many prebiotic reactions require specific ions to function, such as Mg2+ for folding of RNA or metal ion catalysts. However, a thorough understanding of how specific ions can accumulate inside coacervates and their effect on the local environment is currently lacking.
In this work, we investigate the effect of a wide range of ions on coacervate protocells made of an arginine-rich peptide and ATP. We use NMR spectroscopy to quantify the local concentration of ions inside coacervates, as well as the concentration of all other coacervate components, allowing us to elucidate for the first time the total molecular composition of coacervates. We find that coacervates selectively localize ions that bind to various chemical moieties in the coacervate-forming molecules, following the law of matching water affinities and valency of the ions. ClO4-, SCN-, Li+ and Mg2+ are enriched in the coacervates, while F- and K+ are excluded. Using NMR chemical shift-based binding assays, we found that ClO4- and SCN- bind to the guanidinium and □-carbon of the arginine-rich peptide, while Li+ and Mg2+ bind to the phosphates of ATP. Excluded ions show no or weaker binding. The selective binding of ions creates a local chemical environment that is enriched in specific ions, which we show to significantly affect ion-dependent processes inside the condensate, such as nucleic acid partitioning and folding. We further find that prebiotically relevant coacervates retain their highly concentrated microenvironment even at elevated salt concentrations, making them robust catalytic compartments at the origins of life.



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Solutions of ferrous salts protect liposomes from UV damage: implications for Life Origin

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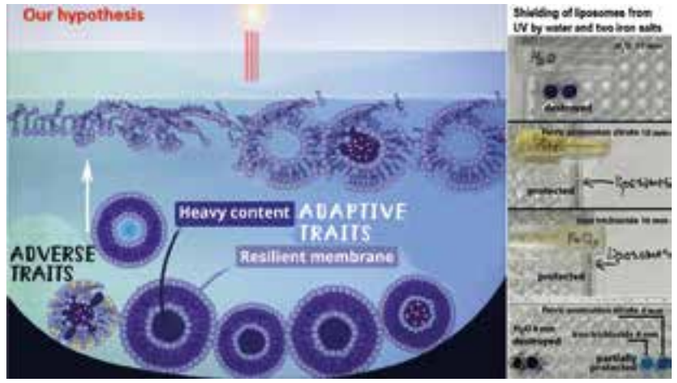
The recognized scenarios of Life Origin, e.g., RNA and pre-RNA Worlds, Metabolism First, assume the occurrence of multiple events that must align strictly consecutively in time and space, i.e., appeared as a multistage process. However, such co-occurrence of multistage processes raises strong skepticism, e.g., by A.I. Oparin and L.E. Orgel. The above models also require co-occurrence of encapsulation, rendering them implausible. An alternative model, Lipid First, avoids these impediments because of the unique ability of amphiphiles for self-assembly into liposomes. We further have advanced this concept by offering a new hypothesis (Astrobiology 2023, 23, 344-357) that relies only on natural and ever-present phenomena: solar UV radiation, day/night cycle, and gravity. The new hypothesis comprises the necessary prerequisites for Darwinian evolution: adaptive traits and selective forces. The model suggests that liposomes formed on the surface of the Archean water pools are destroyed by the solar UV radiation unless they acquire two adaptive traits – the heavy content that sinks the liposomes to the bottom of the pool and facilitates protection from UV and the formation of resilient autocatalytic membrane composition that ensures liposomal survival, mutation, fusion, and proliferation. The hypothesis makes two testable predictions: 1) ferric salts of Archean waters attenuate the UV, and 2) that attenuation protects the liposomes from solar UV destruction. Our previous study (Astrobiology 2023, 23, 741-745) tested and confirmed the first prediction. In the present study, we report the confirmation of the second prediction. In particular, it was established that 10 mm of FeCl3 and (NH4)5[Fe(C6H4O7)2] solutions at a concentration of 2.5 g/L, believed to be close to that in Archean waters, completely protected liposomes from UV damage. These results reinforce our hypothesis that the Sun UV radiation and gravity could be the major selection forces for the abiogenesis.



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Regulation of nucleic acid hybridization by coacervate protocells

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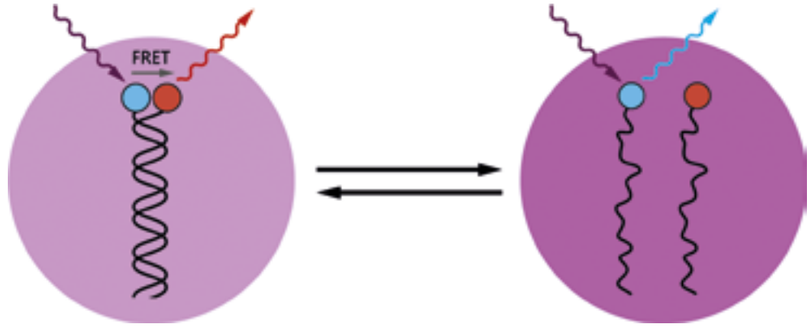
Short RNAs are believed to have been essential in the emergence of life, both as an information carrier and ribozyme catalyst. To transfer the information in the RNAs, they must have been replicated. Self-replication has been investigated as an enzyme-free replication mechanism that could have occurred on early Earth. In self-replication, the RNA would function as a template, that would catalyze the formation of its complementary strand. However, one of the remaining challenges with this theory is that product inhibition occurs after the first replication cycle, effectively rendering the RNA template unusable.
In this work we explore the use of coacervate protocells as a potential solution to overcome this issue. We investigate how coacervates made from various homo-peptides, with varying lengths, can sequester, and subsequently influence the hybridization of DNA and RNA. Using FRET microscopy, and fluorescence spectroscopy, we measure the relative differences in hybridization of short DNAs and RNAs. We find that coacervates with increasing lengths of poly-K and poly-D will result in relatively higher hybridization of a short DNA, while the coacervates made of poly-R and poly-D showed comparatively little effect. Interestingly, this is opposite to the previously described effect on RNA, where increasing lengths of poly-K and poly-D resulted in de-hybridization of the RNA.
By reversible peptide coupling, we aim to actively switch between different peptide lengths. This would give us control over the nucleic acid hybridization, and could be used to overcome product inhibition during self-replication. Furthermore, depending on the conditions applied, it would be possible adjust peptide lengths while keeping the coacervates intact, or to completely dissolve, and then form them again, providing additional control over compartmentalization.



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Insights into the emergence of life on earth – carbonaceous matter in ~3.5 Ga hydrothermal barites from the dresser formation (pilbara craton, australia)

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7 Swedish Museum of Natural History, Sweden

The conditions and processes underlying the abiotic-biotic transition remain blank spots in understanding of how life emerged on Earth. Some of the oldest rocks and minerals on our planet contain carbonaceous matter (CM), potentially providing valuable insights into the earliest evolution of metabolism in an environmental context. However, proving the origin and syngeneity of CM in very ancient geological records is challenging [1, 2]. In this study, we examine CM in ~3.5 billion-year-old barites from the Dresser Formation (Pilbara Craton, Western Australia) [1]. Field observations indicate that bedded barite likely formed from hydrothermal fluids discharging into underwater caldera settings [3]. These bedded barites, found in association with stromatolites, contain notable amounts of CM (total organic carbon ~ 0.3 wt% [2]). We identified three distinct CM populations using light microscopy coupled with high-resolution Raman imaging: (i) abundant CM flakes at the edges of barite crystal growth bands, (ii) CM dispersed within barite crystals, and (iii) a minor fraction of CM in 50–300 µm wide secondary quartz veins intersecting the barite crystals. Peak metamorphic temperature reconstructions using Raman spectra indicate that the major CM populations observed at crystal growth bands and within the barite are syngenetic, whereas, the minor CM fraction in the secondary quartz veins represents a later addition to the barite deposit. Analyses using near edge X-ray absorption fine structure (NEXAFS) and solid-state nuclear magnetic resonance (NMR) reveal that the CM is highly aromatic (with only a minor aliphatic proportion), consistent with advanced thermal maturity. These findings strongly argue for a biological origin of CM resulting from multiple metabolic pathways.

References:
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[2] Mißbach, H. et al. (2021). Nature communications 12, 1101
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Basaltic glass as prebiotic phosphate source

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Phosphate is considered one of the most important building blocks for the emergence of life but concentrations in water were likely too low for prebiotic reactions. Modern science is still searching of a reasonable source material as most minerals are either hardly soluble, or occur in too small quantities. As volcanoes supply thermal energy and new material from the earth's mantle, we propose that volcanic glasses can act as the missing link bringing together global availability, high solubility, and a suitable environment.
Here we investigate the capability of mafic magma, the source of most Hadean and Archean komatiites and tholeiites, to accumulate phosphate in the melt phase. The magma can quench in contact with air or water, creating highly reactive volcanic glass, which can act as a phosphate source for prebiotic chemistry via leaching processes.
We synthesized two glass species at 1600°C mimicking an average basaltic composition of 2.2 – 3.8 Ga old Archean rocks with P_2O_5 concentrations up to 8 wt.%. Binodal decomposition produced inclusions enriched with magnesia and phosphate during the cooling of one glass. Scanning electron microscopy and ion chromatography revealed high solubility of the glass at various pH and temperatures. Polymerization experiments at 180°C delivered di- and triphosphate concentrations up to 15 nmol/g, corresponding to a yield of up to 3%. Finally, we investigated the capability of the leachate to produce activated carbamoyl and imidazole phosphate. Resulting concentrations peaked after one day at mild conditions, with yields of ~15 and 40% respectively.

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Bridging the gap between chain formation and genetic copying of RNA

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The copying of RNA sequences is the template-directed reaction underlying replication. It is interesting to ask how such a process may have occurred in a prebiotic context to ensure the transmission of genetic information. Selective and efficient incorporation of activated monomers has previously been demonstrated, using immobilized template/primer systems. We have expanded this work to enzyme-free ligation of dimers and trimers to an RNA primer using in situ activation conditions. With these conditions we achieved a successful copy of up to 12 nucleotides with C and G rich sequences. Further, new modes of activation of nucleotide monophosphates was studied, including forming aminoacidyl nucleotides and screening their reactivity by measuring their hydrolysis in aqueous buffer. The aminoacidyl nucleotides were then successfully employed in primer extension, demonstrating that they can replace xenobiotic leaving groups used thus far, leading to a more plausible scenario for enzyme-free copying and eventually replication of RNA sequences.

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Chiral selection by non-enzymatic oligomerisation of 2‘,3‘-cyclic nucleotides

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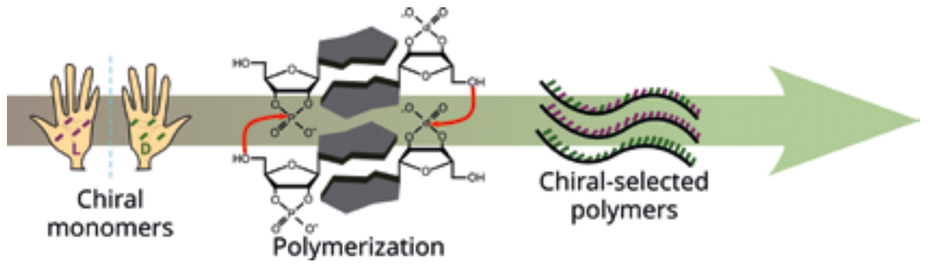
The key biomolecules of life, i.e nucleic acids and proteins are composed of (barring a few rare exceptions) monomers of one chirality, L for amino acids and D for sugars and nucleotides. Different mechanisms have been proposed to resolve the mechanism by which chirality emerges and is amplified at the origin of life. (1) Here we explore whether chiral-selection could be driven by the simple, dry-state polymerization of 2′,3′-cyclic nucleotides. (2, 3). We show that for the polymerization of the guanosine nucleotides, homochiral polymers are preferred over heterochiral polymers, likely due to its propensity to form higher order structures. Recent works have shown that adenosine nucleotides and mixtures of GC/AU/GCAU also form higher order structures with repeated wet-dry cycles and enhance polymerization. (3) Here we explore whether such conditions are chiral-selective for the dry-state oligomerization of 2′,3′-cyclic nucleotides.

References:
[1] Sallembien Q, et al. (2022) Chem. Soc. Rev. 51, 3436
[2] Dass, A., Wunnava, S., Langlais, J., et al. (2023): ChemSystemChem 5, e202200026.
[3] Rout, S., et al. Amino acid catalyzed RNA formation under ambient alkaline conditions. In prep.
[4] Fontana, F., Langlais, J. et al. High-yield prebiotic RNA polymerization from mixture of all four 2′,3′-cyclic nucleotides under mildly alkaline wet-dry cycling. In prep.



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Investigating the Role of Amyloids in the Origin of Life

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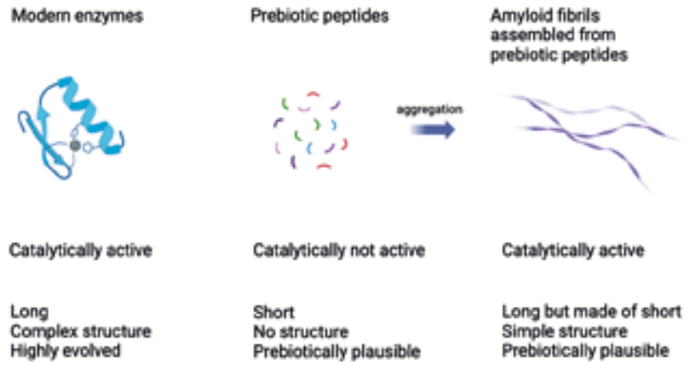
Our research focuses on developing experimental methods and strategies to examine the potential roles of amyloids in the earliest forms of life. Amyloid-forming peptides are prime candidates for evolutionary precursors of proteins due to their small size, stability, ability to self-assemble with closely related sequences, and potential for catalysis and information transfer.

In 2014, Rufo et al. described amyloids capable of enzyme-like catalysis of acyl ester hydrolysis, suggesting that assembling short peptides might drive catalytic reactions before the evolution of longer enzymes. To further understand the catalytic potential of amyloids and their possible roles in the emergence of life, we are developing a method to screen populations of peptide sequences for the ability to form catalytic amyloids. Utilizing an in-vitro transcription-translation system, we synthesized a library of 40 modifications of the original IHIHIQI peptide described by Lengyel et al. We tested these peptides for their ability to promote tandem hydrolysis/oxidation reactions—specifically the oxidation-reduction of 2′,7′-Dichlorofluorescein diacetate (DCFH-DA) to 2′,7′-Dichlorofluorescein (DCF).

Our experiments identified multiple IHIHIQI variants with either enhanced or attenuated catalytic functions. Based on these findings, we are developing a high-throughput, evolvable system aimed at improving catalytic properties in terms of both catalytic efficiency and substrate scope. This research advances our understanding of how early molecular evolution might have progressed, shedding light on the potential roles of amyloids in the origin of life.



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Acyl Phosphates as Chemically Fueled Building Blocks for Self-Sustaining Protocells

Oleksii Zozulia, Christine M. E. Kriebisch, Brigitte A. K. Kriebisch, Héctor Soria Carrera, Kingu Rici Ryadi, Juliana Steck, and Job Boekhoven
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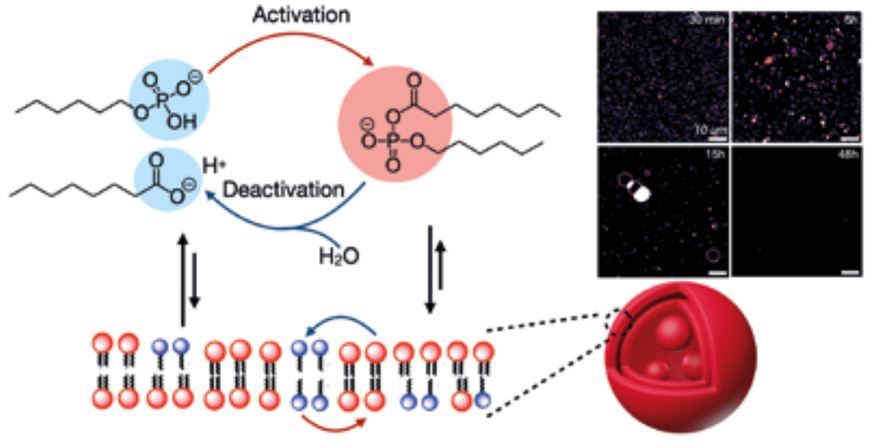
Lipids spontaneously assemble into vesicle-forming membranes. Such vesicles serve as compartments for even the simplest living systems. Vesicles have been extensively studied for constructing synthetic cells or as models for protocells—the cells hypothesized to have existed before life. These compartments exist almost always close to equilibrium. Life, however, exists out of equilibrium. In this work, we studied vesicle-based compartments regulated by a non-equilibrium chemical reaction network that converts activating agents. In this way, the compartments require a constant or periodic supply of activating agents to sustain themselves. Specifically, we use activating agents to condense carboxylates and phosphate esters into acyl phosphate-based lipids that form vesicles. These vesicles can only be sustained when condensing agents are present; without them, they decay. We demonstrate that the chemical reaction network can operate on prebiotic activating agents, opening the door to prebiotically plausible, self-sustainable protocells that compete for resources. In future work, such protocells should be endowed with a genotype, e.g., self-replicating RNA structures, to alter the protocell's behavior. Such protocells could enable Darwinian evolution in a prebiotically plausible chemical system.



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Robert J. Mayer	TUM, DE	A Mechanistic Approach to Prebiotic Chemistry: Coenzymes, Chirality, and Catalysis	Session G	13:55	28
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Ralph E. Pudritz	McMaster University, CN	Atmospheric HCN production and the emergence of the RNA world on early Earth	Session C	14:20	17
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#	Last Name	First Name	Email Address	Title
1	Aikkila	Paula	p.aikkila@physik.uni-muenchen.de	Physical selection pressures to drive early molecular evolution
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3	Burger	Ludwig	ludwig.burger@tum.de	Efficiency of Replication in Oligomer Pools Encoding Prebiotic Circular Genomes
4	Callaghan	Kimberley	kimberley.callaghan@unimelb.edu.au	Accelerating non-enzymatic template directed primer extension for the production of DNA and RNA
5	Cherepashuk	Ivan	cherepai@natur.cuni.cz	Exploring the Interplay between Random Peptide Libraries and Decanoic Acid/Decanol Vesicles
6	Dänekamp	Felix Taiyang	f.daenekamp@physik.uni-muenchen.de	2',3'-cP RNA Replication by Ligation
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8	Das	Souradeep	das.souradeep@students.iiserpune.ac.in	Dynamical interactions among coexisting protocellular populations result in emergent properties with selective advantages
9	Dherbassy	Quentin	quentin.dherbassy@gmail.com	Metal-Pyridoxal Cooperativity in Nonenzymatic Transamination
10	Diaz-Espinoza	Rodrigo	rodrigo.diaz.e@usach.cl	Self-assembly of Prebiotic Peptides into Catalytically Active Amyloids
11	Dimitrova	Stella	dimitrova.stella76@gmail.com	Enantiomer excess differences in carbonaceous chondrites organic content. A systematic review of the literature data.
12	Floroni	Alexander	alexander.floroni@physik.uni-muenchen.de	Cell-free expression localized and activated at heated air-water interfaces
13	Fontana	Francesco	francesco.fontana3@studenti.unimi.it	High-yield prebiotic RNA polymerization in 2',3'-cyclic nucleotides mixtures under mildly alkaline wet-dry cycling
14	Ghosh	Koushik	kg.22ph1103@phd.nitdgp.ac.in	Non-Enzymatic Kinetic Error Correction in Nucleic Acid Replication through Asymmetric Cooperativity
15	Giannakopoulos	Nikolaos	nikolaos.giannakopoulos@oc.uni-stuttgart.de	Studies on Peptido RNA Formation and Single-Nucleotide Translation
16	Gomez	Samuel Santhosh	samuel.gomez@uni-a.de	Theory of RNA replication and evolution
17	González Martínez	David	david.gonzalezm@uam.es	NADH-mediated primordial synthesis of amino acids.
18	Harth-Kitzerow	Johannes	jharthki@mpa-garching.mpg.de	Sequence motif dynamics in RNA pools
19	Haugerud	Ivar Svalheim	ivar.haugerud@gmail.com	Phase separation directs polymerization and selects sequences
20	Helmbrecht	Vanessa	v.helmbrecht@lrz.uni-muenchen.de	Testing emergence of life hypothesis in early Earth analog experiments: Abiotic hydrogen produced in an iron sulfur chemical garden rescues a methanogen from hydrogen limitation
21	Holtmannspötter	Anna-Lena	anna-lena.holtmannspoetter@tum.de	Spatio-temporal control of nucleic acid catalysis with active droplets
22	Hu	Yimin	yimin.hu@tuebingen.mpg.de	Bacterial histone HBb compacts DNA by bending
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24	Kankia	Besik	bkankia@chemistry.ohio-state.edu	G4 World hypothesis: booting up life with ribosome

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26	Kriebisch	Brigitte	brigitte.kriebisch@tum.de	Chemically fueled motions
27	Kriebisch	Christine	christine.kriebisch@tum.de	Template-based copying in chemically fueled dynamic combinatorial libraries
28	Kufner	Corinna	corinna.kufner@cfa.harvard.edu	The UV-driven Functionality of Coenzyme NAD
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30	Lacoste	David	david.lacoste@gmail.com	Emergence of homochirality via template-directed ligation in an RNA reactor
31	Langlais	Juliette	juliette.langlais@physik.uni-muenchen.de	Formation of reactive 2',3'-cyclic phosphate ribonucleosides by phosphorylation with trimeta-phosphate and their subsequent polymerization, in presence of amino acids
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45	Patki	Gauri	patki.gauri@students.iiserpune.ac.in	Nonenzymatic RNA replication in a mixture of 'spent' nucleotides
46	Pereira	Delfina	delfina.pereira@mpi-marburg.mpg.de	Hydrothermally reducing nicotinamide di- and mononucleotide and implications for the emergence of metabolism
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48	Puente Arribas	Alonso	alonso.puente@estudiante.uam.es	Tuning the catalytic function of lipopeptide assemblies using nucleobases
49	Rout	Saroj	s.rout@physik.uni-muenchen.de	Amino acids catalyze RNA formation under ambient alkaline conditions

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51	Ruchti	Stefan	stefan.ruchti@helmholtz-munich.de	Comprehensive Analysis of Soluble Organic Matter and Volatiles on meteorites – seeing the bigger picture by looking from different angles
52	Runge	Eric	eric.runge1@uni-goettingen.de	Framboid-like pyrite traces mineral-fluid-organic interactions in hydrothermal sulfide systems
53	Sahu	Parthasarathi	partha.d4e3@gmail.com	Initiation of DNA Unzipping Through Sequence-Kinetics
54	Sanz Sánchez	Marcos	marcos.sanz@uam.es	Collective adaptability in a replication network of minimal nucleobase sequences
55	Schmid	Almuth	almuth.schmid@physik.uni-muenchen.de	Enhancing polymerization of prebiotic building blocks by activation chemistry and wet-dry cycling
56	Schmitt	Christian	sh401@uni-heidelberg.de	Origin of the genetic code: RNA library screening for self-aminoacylating tRNA precursors
57	Schoenmakers	Ludo	ludo.schoenmakers@kli.ac.at	Evolution at the Origins of Life?
58	Seitz	Christian	c.seitz@tum.de	The cyanide-free formation of amino acids and amides from acetylene, ammonia and carbon mo-noxide in aqueous environments in a simulatedn Hadean scenario
59	Senthilkumar	Tejaswi	z5207725@ad.unsw.edu.au	Binding Affinity of RNA-Peptide Conjugates to RNA duplexes
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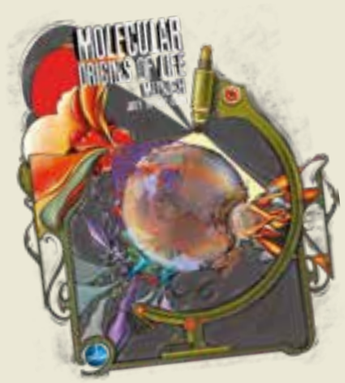

SAVE THE DATE

MOM 2025 (online)
July 16th – 18th 2025

FRIDAY, 19 JULY, 2024

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8:55	**Kerstin Göpfrich** Engineering a synthetic protocell with RNA origami
9:20	**Christine Keating** Before cells: Prebiotic compartments based on phase separation and molecular self-assembly
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10:55	**Andres Jäschke** Probing the Origin of the Genetic Code by High-Throughput Sequencing
11:20	**Eugene V. Koonin** On the origin of cells, genomes and viruses
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13:55	**Judit E. Šponer** The role of crystallization in prebiotic polymerization processes
14:20	**Ralph E. Pudritz** Atmospheric HCN production and the emergence of the RNA world on early Earth
14:45	**Discussion**
15:05	**Coffee Break**
Session D	**Chair: Philippe Schmitt-Kopplin**
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15:55	**Klara Hlouchova** Possible roles of peptides in early life
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16:20	**Job Boekhoven** Template-based copying in dynamic combinatorial libraries out of equilibrium
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17:30	**Closing remarks**