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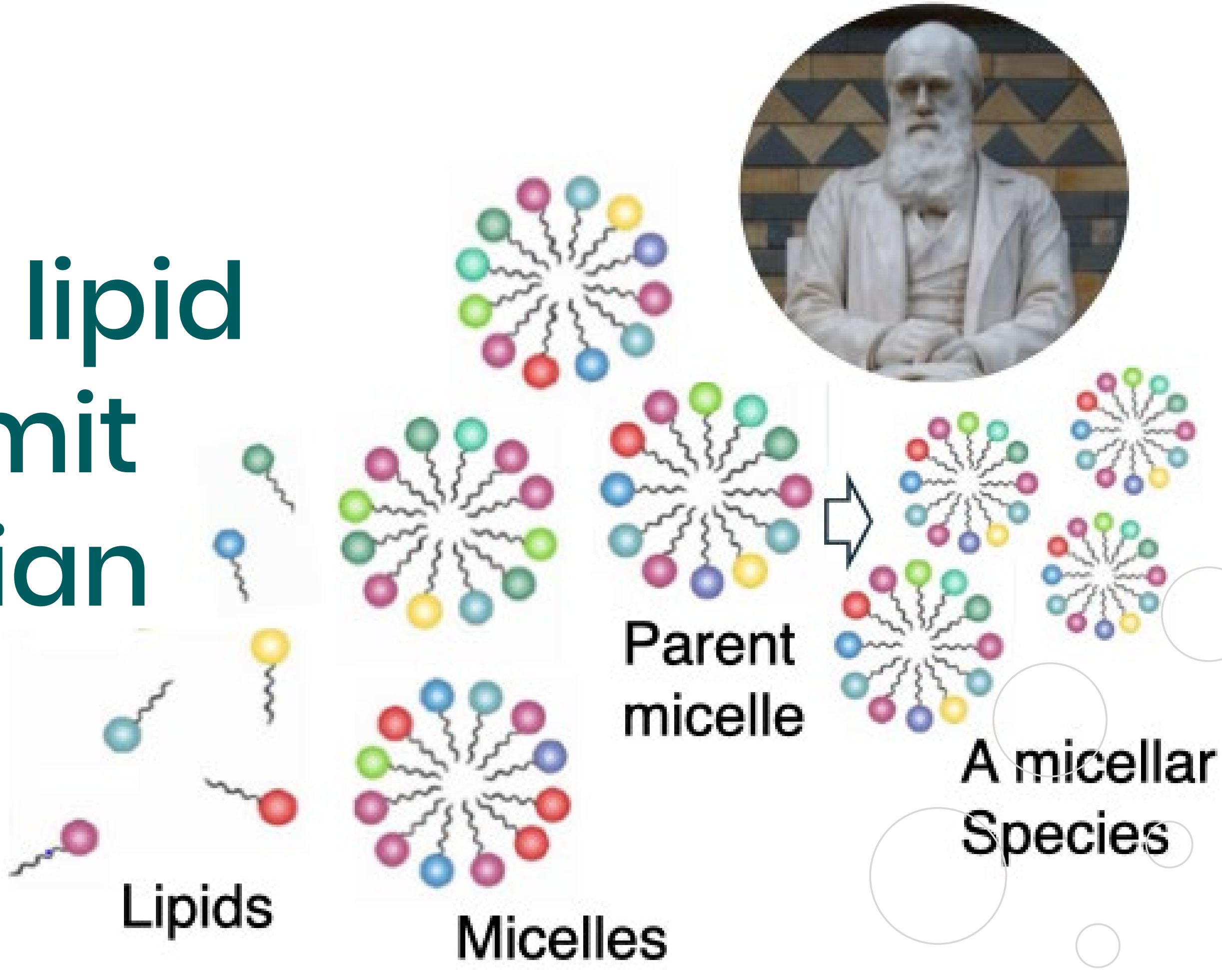
Reproducing lipid micelles permit early Darwinian evolution



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LIFE SCIENCES & BIOLOGY

The origin of life has puzzled science and philosophy for thousands of years. While the prevailing scientific narrative is of an 'RNA world' or 'polymers first' approach, Prof Doron Lancet's group of the Weizmann Institute of Science in Rehovot, Israel, present an alternative, describing a 'lipid world' scenario as a plausible origin for life, in which lipid micelles (simpler structures than cell-like vesicles) could have been nanoscopic protocell precursors. Core to the theory is that these micelles could exhibit catalysis and compositional self-reproduction, passing information through the mixture of their lipid components rather than through a genetic sequence.

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Lipids at Life's Dawn

One of the largest questions humans still grapple with is the origin of life on Earth. How did a chaotic mix of non-living chemicals spontaneously give rise to the first entities capable of reproducing and evolving? For decades, the prevailing scientific narrative — often dubbed the 'RNA world' or 'polymers first' hypothesis— suggested that life began when complex, self-replicating molecules like RNA somehow emerged from the primordial soup. These molecules were thought to have been the crucial starting point, later becoming enclosed within membranes to form rudimentary cells.

However, this traditional view faces significant challenges. Prof Doron Lancet and collaborators explain how totally impossible it is that complex polymers, like RNA, could spontaneously form with the necessary specific sequences and structures needed for replication, in the midst of the chaotic and disordered early Earth environment. Furthermore, no single molecule, not even DNA or RNA, can self-reproduce in isolation, as they rely on the intricate machinery of the entire cell. This raises the question: would it be reasonable to assume that prebiotic chemicals could possess capabilities beyond those of modern biomolecules?

The 'Lipid World' Scenario

Lancet and collaborators present an alternative perspective, often called the 'lipid world' or 'lipid first' hypothesis, that proposes a more parsimonious beginning for life. Instead of starting with complex information-carrying polymers, this view suggests that life emerged from much simpler, spontaneously self-assembling structures made of lipid-like molecules.

Also known as amphiphiles or surfactants, lipids are molecules with both a water-attracting head ('polar') and a water-repelling tail ('apolar' or 'hydrophobic'). These compounds were surely abundant on early Earth, as evidenced by analyses of meteorites, or chemical reactions shown to occur in suboceanic vents. A key property of lipids is their ability to spontaneously self-assemble in aqueous environments, energetically driven by the tendency of their hydrophobic tails to cluster away from the water. This self-assembly can create various structures, including nanoscopic spheres called micelles, and larger spheres with a watery core called vesicles. Unlike highly constrained biological polymers, lipid self-assembly is promiscuous, meaning any type of amphiphile, biological or not, can join together to form these structures.

Micelles as Protocells

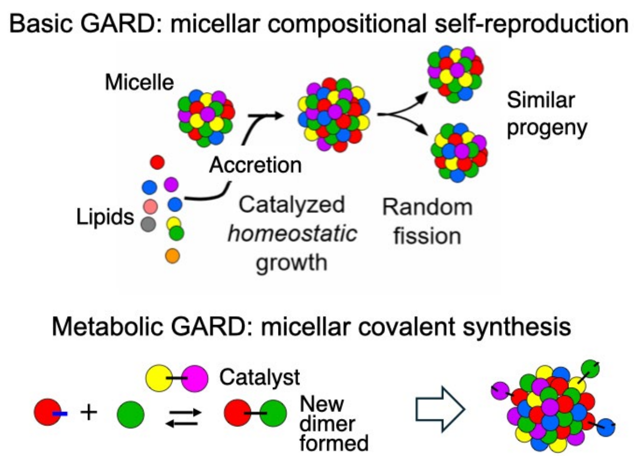
With their enclosed water filled core, vesicles have long been considered prime candidates for early protocells, due to their resemblance to modern cells. But this research highlights the compelling possibility that nanoscopic lipid micelles could have been even earlier precursors to life. In fact, micelles are simpler, typically composed of only a few hundred lipid molecules arranged in a single layer, with the hydrophobic tails facing inwards and the polar heads facing outwards onto the water. They lack the water containing centre of vesicles.

Despite their simplicity, micelles possess several advantageous attributes in the earliest stages of evolution. Their nanoscopic size means they contain fewer molecules, making their composition more sensitive to change, and potentially facilitating interactions between components. They have a high surface-to-volume ratio, enhanced reactant concentrations, promote all against all molecular networking and portray huge diversity of compositions. Their ability to form from a diverse range of lipids makes them compatible with the chemically heterogeneous disorganised chemistry that we predict to have existed on early Earth.

Catalytic Network Begets Reproduction

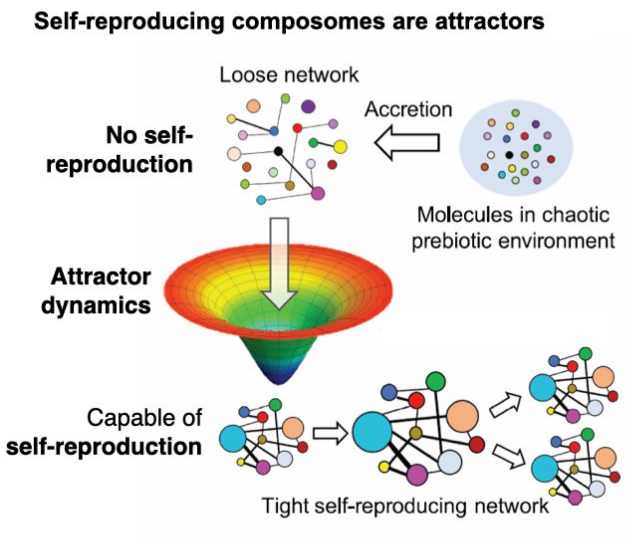
For any entity to be considered a precursor to life, it must be able to facilitate chemical reactions through catalysis. Lipid molecules have proven to be simple catalysts ('lipozymes'). Micelles provide a unique arena for that, significantly enhancing reaction rates, due to concentration, surface effects, and polarity gradients. These catalytic capabilities mean that micelles effectively harbour mutually catalytic networks. In such a network, molecules within the micelle catalyse the entry, formation, or modification of other molecules, helping to maintain and grow the whole structure.

A critical characteristic of life is self-reproduction. Micelles can grow by incorporating more lipid molecules from their environment (accretion) or by synthesizing/modifying lipids internally. Subsequently, micelles often split into two or more parts, resulting in offspring assemblies. However, meaningful reproduction requires that new assemblies inherit characteristics from the parent. Since micelles lack a genetic sequence like DNA or RNA, the solution is passing information through composition. Reproduction in this context means the micelle grows while maintaining stable internal concentration relations (homeostatic growth), which is then transferred to the 'progeny' assemblies upon fission. This compositional information is akin to non-genetic (epigenetic) inheritance in present-day cells.



The GARD Model and the Power of Attractors

To quantitatively explore catalytic networks and reproduction, the Graded Autocatalysis Replication Domain (GARD) model was developed. This simulation model studies the dynamic behaviour of mutually catalytic networks within lipid assemblies. This model is purely based on computational chemistry, allowing simulations of the kinetic behaviour of micelles and vesicles. A key finding of this model is that certain rare compositions exhibit self-reproduction. These stable, reproducing entities are termed 'composomes'. Although a random composition is unlikely to be a composome, the simulations revealed something crucial: reproducing composome states are dynamic attractors. Attractor dynamics means that a system tends to settle into stable states. In the GARD model, this means that from practically all initial random compositions, after a limited number of growth and fission events, the assembly will reach a stable composome.

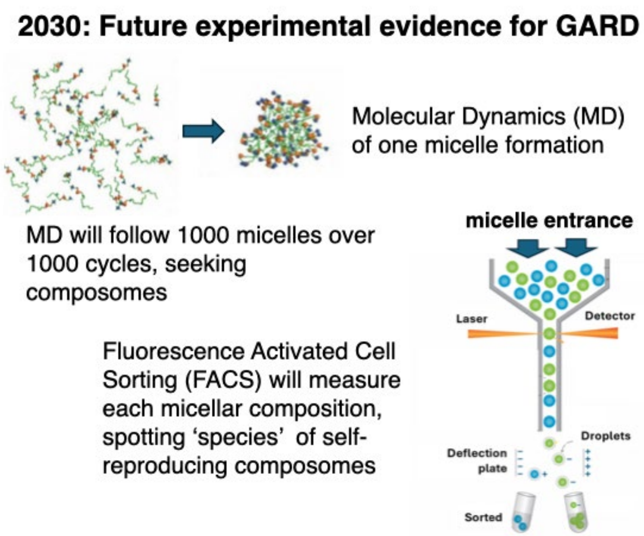


The above finding is profoundly significant for the origin of life. It suggests life's emergence doesn't require an impossibly lucky chance event. Instead, inherent chemical dynamics can spontaneously guide random assemblies towards reproduction. The presence of these attractor states vastly increases the probability that reproducing entities would arise, en route to life's origin.

Simulations also indicated repertoire diminution as assemblies approach attractors: the number of molecule types decreases, often leaving potent catalysts – in a manner analogous to modern cells which utilise a relatively small subset of the vast assortment of chemical compounds available.

Early Evolution and the Path to Complexity

The capacity for compositional reproduction in micelles, opens the door to compositional mutations. Exponential growth of micellar counts having similar composition with some variation would constitute 'proto-species'. This in turn, will allow natural selection, providing a foundation for primeval Darwinian evolutionary attributes. If micelles with certain compositions reproduce more successfully than others (due to more effective catalytic networks, for example), their proto-species would become more prevalent. This scene allows a departure from the view that Darwinian evolution requires complex biopolymers like DNA or RNA; it could have begun at a much simpler stage.



This also suggests a plausible path for increasing complexity. Once reproducing micellar entities exist, they can evolve. This evolution could drive the gradual emergence of more complex catalytic networks, the seeds of metabolism. Such micellar catalysis could facilitate the synthesis of more complex molecules, e.g. building of amino acids into peptides or nucleotides to increasingly long RNA. Some lipid modifications could lead to structural changes, potentially triggering the transition from micelles to the more complex vesicular form.

From Micelles to Vesicles and Towards Cells

The transition from simple micelles to the more cell-like vesicle protocells is a necessary step towards modern life. For example, sufficiently endogenously catalytic modification of one-chained lipids into two-chained molecules within a micelle could induce a shift to vesicular structure.

How would larger vesicles acquire the complex catalytic networks needed for reproduction and evolution? This requires the crucial synchrony between membrane growth and the growth of the internal aqueous content. The micellar hypothesis offers a solution. Reproducing micelles, already containing functional catalytic networks, could fuse with existing non-reproducing vesicular membranes. This fusion would transfer network components and catalytic capabilities from the micelle to the vesicle and allow its membrane to reproduce. This process of transferring compositional information via fusion is seen as analogous to horizontal gene transfer or epigenetic inheritance in modern biology.

At this point any molecule in the watery volume inside the vesicle will not be coupled to the membranal network. However, gradual mutations in the membrane could lead to increasing control of catalytic molecules in the membrane that will begin to control the composition of the inner volume. This will eventually allow synchronous compositional reproduction that encompasses both membrane and the internal metabolism, a renowned challenge in the field.

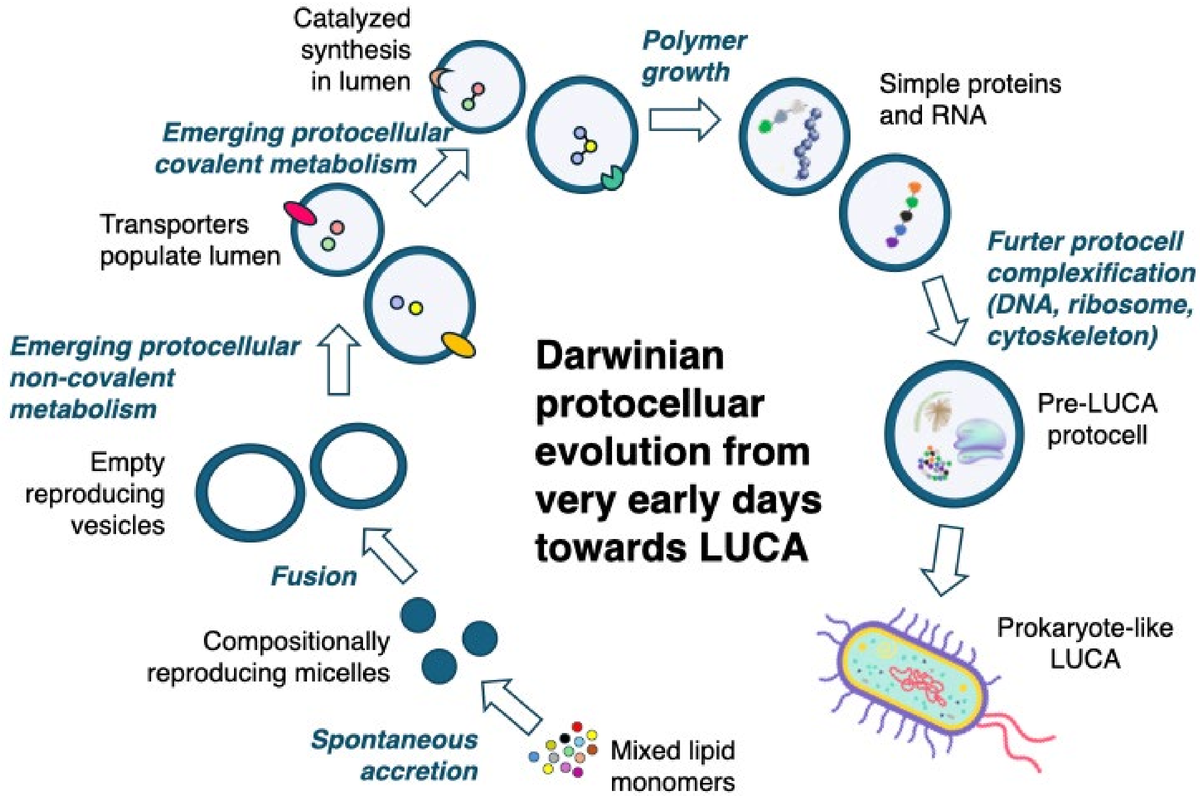
This stepwise progression (starting with simple, spontaneously forming, reproducing micelles) that gradually builds complexity towards vesicular protocells (membrane and inner content) presents a much more plausible chemical path from chaotic non-living matter to life than scenarios relying on the sudden appearance of complex biopolymers.

A Plausible Path from Lipids to Life?

Prof Lancet's idea portrays the first steps of life not as a singular, improbable event involving the perfect assembly of complex machinery, but as an emergent property of dynamic, self-organising chemical systems. It suggests that the fundamental attributes of life (catalysis, reproduction, and containment) could have been integrated from the very beginning within simple micellar structures. The subsequent evolution towards the sophisticated, biopolymer-based life we see today —including the central dogma of biology— could then be seen as a result of this initial, more primitive form of Darwinian evolution, rather than a prerequisite for it.

While the journey from these early protocells to complex modern cells is still a vast area of research, focusing on the self-reproduction and evolutionary potential of simple, dynamic, supramolecular lipid assemblies provides a tangible and scientifically rigorous path forward in deciphering the origins of life.

Article written by Joseph Earley, PhD



MEET THE RESEARCHERS

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Prof. Doron Lancet is an Israeli computational biologist and geneticist. He holds a B.Sc. in chemistry and physics from the Hebrew University and a PhD in Chemical Immunology from the Weizmann Institute of Science, followed by postdoctoral training at Harvard and Yale. He established and headed the Crown Human Genome Center there for two decades until 2015. Prof. Lancet pioneered research on the chemistry, biochemistry, genetics, and evolution of olfaction and deciphering human disease genes. He and his team developed GeneCards, a world-renown web-based compendium of human genes. He is known for his work on Abiogenesis, developing GARD – a novel computer-simulated kinetic model for prebiotic evolution that offers an alternative view to the RNA-first scenario. His awards include the Takasago, Hestrin, Wright, and Landau Prizes. He is a member of the European Molecular Biology Organization and was on the World Human Genome Organization Council.

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Roy Yaniv obtained his BSc in Biology and MSc in Cell Biology and Immunology from Tel-Aviv University, Israel. He is currently a scientific consultant in the field of the origin of life in Lancet's laboratory, located at the Weizmann Institute of Science, Israel. In parallel with his work at the Weizmann Institute, he also serves as a scientific editor at the Davidson Institute of Science Education in Israel, a non-profit organisation dedicated to promoting and nurturing scientific education. Additionally, he heads the post-production editing department at Henry Stewart Talks (HSTalks), a company that provides audio-visual presentations in biomedicine and life sciences to institutions globally.

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FURTHER READING

A Kahana, and D Lancet. Self-reproducing catalytic micelles as nanoscopic protocell precursors. *Nature Reviews Chemistry*, 2021 5.12: 870-878. DOI: https://doi.org/10.1038/s41570-021-00329-7

A Kahana, L Segev, and D Lancet. Attractor dynamics drives self-reproduction in protobiological catalytic networks. *Cell reports physical science*, 2023, 4.5. DOI: https://doi.org/10.1016/2023.101384

R Yaniv, D Lancet. Life's Emergence by Protocellular Mutually Catalytic Networks, *Guidebook for Systems Applications in Astrobiology*, Vera M. Kolb Ed. 2023, CRC Press. https://doi.org/10.1201/9781003294276-13

C Mayer, D Lancet O.Markovitch, The GARD prebiotic reproduction model described in order and complexity, Life, 2024 14(3), 288; https://www.mdpi.com/article/10.3390/life14030288/s1