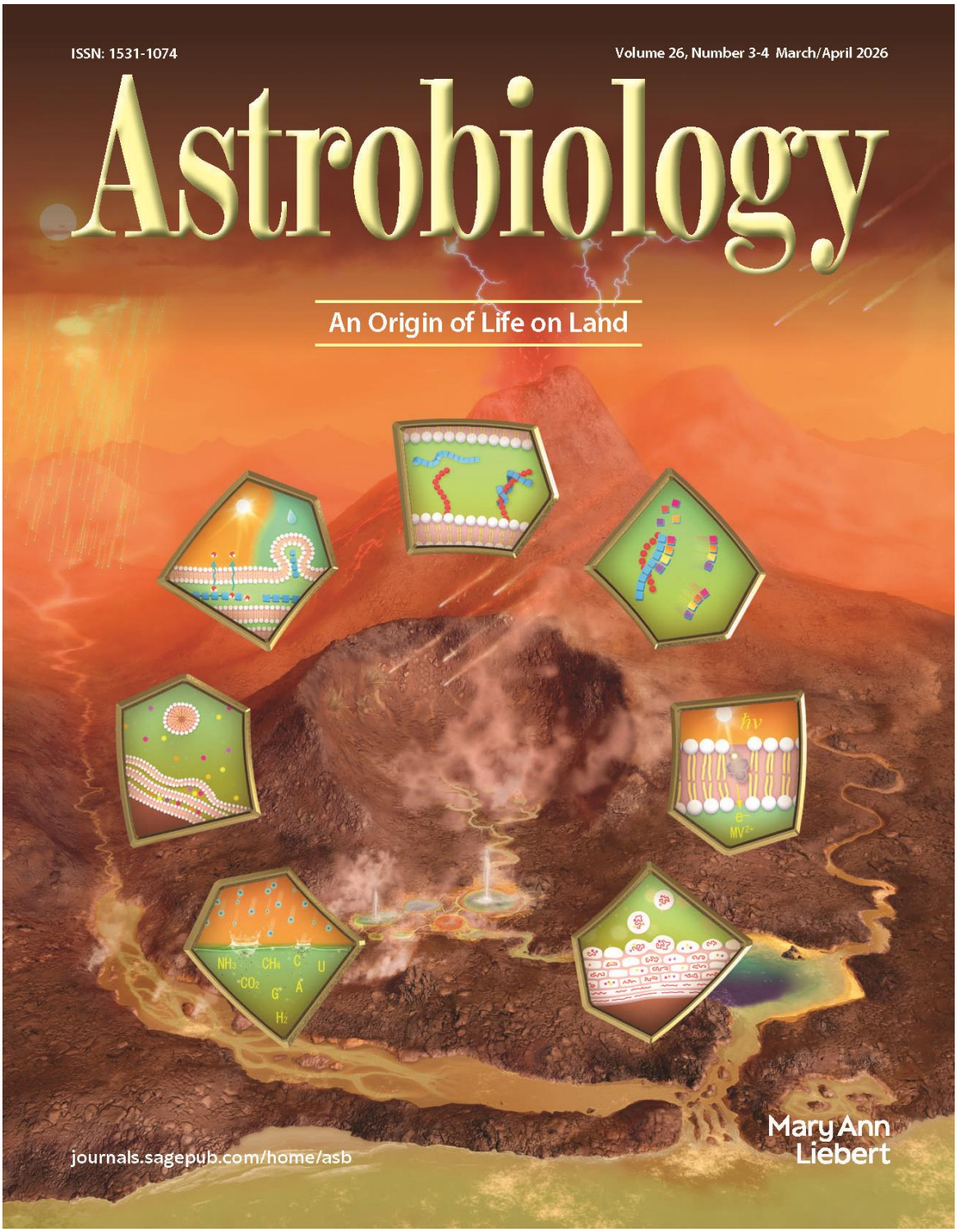


The cover depicts an idealized volcanic landscape in the Hadean Era (~4 Ga) in which life may have originated. A faint young sun is partially obscured by a lightning-generating ash plume from active volcanic cones beneath a CO_2-rich, nitrogen-bearing supergreenhouse atmosphere. Meteorites and carbonaceous dust fall onto a dominantly basaltic, iron-rich surface. A caldera hosts a hydrothermal field of interconnected pools with variable chemistry. These pools concentrate, mix, and cycle organic building blocks and trace

metals, promoting polymerization and protocell assembly. Over time, protocells acquire increasingly functional traits, evolving into the first microbial communities capable of colonizing diverse environments.

Downstream, early life enters cooler hydrothermal crater lakes and transient saline estuaries that empty into iron-rich green oceans. Braided river systems with hotspot-infused sediments provide additional settings for protocell assembly and dispersal. Turbulent, saline shorelines act as strong selective barriers to cellular communities, which when surmounted enable global colonization.

These environments constitute “urable zones” supporting distinct stages of prebiotic chemistry. The inset circle (clockwise from lower left) illustrates a hypothesized end-to-end origin-of-life scenario:

- Delivery and concentration of organics into hot spring pools and other aqueous settings from meteorites, dust, atmospheric and hydrothermal synthesis.
- Amphiphiles form micelles and membranous compartments; wet–dry cycles produce multilamellar matrices on subaerial mineral surfaces.
- Evaporation lowers interlamellar water activity enabling condensation reactions that form polymers; rehydration encapsulates polymers into protocells.
- Interlamellar mobilization drives combinatorial formation of functional polymers (short RNAs, peptides), enabling the first catalytic and informational systems.
- Template-directed polymerization transfers sequence information.
- Exogenously sourced pigments in membranes absorb light, generating reducing power for primitive metabolism.
- Progenote-like protocell aggregates propagate, exchange genetic innovations, and evolve toward cellular division and transition into the microbial world.

Although laboratory and fieldwork evidence supports individual stages, integration into a fully coupled system is a key challenge for future work. Image by Bruce Damer and Ryan Norkus with scientific input from David Deamer and Martin Van Kranendonk.

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Hypothesis Article

A Multilamellar Lipid–Polymer Progenitor Can Promote the Assembly of Improbable Functional Polymer Complexes at Life's Origins

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Abstract

The original conditions from which primitive life emerged on the early Earth were likely to be dilute mixtures of organic compounds in aqueous solutions. A significant challenge for origins of life research is to discover the reactions that allowed such mixtures to become increasingly complex with products such as polymers that had structural and functional properties related to biology. The chances are low that potential reactants could find one another in dilute solutions composed of thousands of different molecular species. To improve the probability of such encounters, we have investigated a novel condition that both concentrates and organizes potential reactants and encapsulates polymeric products to form protocells. The condition involves a source of freshwater that falls as rainfall precipitation on land masses such as volcanic islands. The water dissolves exogenously and endogenously available organic compounds and feeds into hydrothermal fields where the solutions undergo cycles of evaporation and rehydration, a process easily observed today. Most researchers would agree that monomers such as amino acids and nucleotides would be present in the mixture, but less attention has been paid to the self-assembly of amphiphilic compounds that are also essential components of widely studied protocells. Here, we hypothesize how a closely related medium—multilamellar lipid–polymer (LP) matrices exposed to wet–dry cycles—can act as a progenitor and drive three essential processes: concentration of monomers, polymerization by synthesis of ester and peptide bonds, and promotion of interactions between peptides and nucleotide oligomers. We propose that such matrices represent "combinatorial engines" that can generate otherwise improbable functional complexes. After characterizing the sources of organics, the geochemical settings, and energetic environments in which such an LP progenitor can assemble, we present a conceptual model system that informs both chemical and computational experimental approaches to test this hypothesis. Key Words: Origin of life—Polymerization—Lipid membranes—Wet–dry cycling—Combinatorial selection—Functional polymer complexes. Astrobiology 26, 247–259.

1. Introduction

A significant challenge to research on the origin of life was presented by Leslie Orgel who offered strong arguments for the implausibility of metabolic cycles arising spontaneously on the prebiotic Earth. Orgel argued that complex reaction sequences such as the reverse citric acid cycle were highly unlikely to have arisen without some form of genetic information to guide their organization:

> *"There is no agreement on the extent to which metabolism could develop independently of a genetic material. In my opinion, there is no basis in known chemistry for the belief that long sequences of reactions can organize spontaneously—and every reason to believe that they cannot. The problem of achieving sufficient specificity, whether in aqueous solution or on the surface of a mineral, is so severe that the chance of closing a cycle of reactions as complex as the reverse citric acid cycle, for example, is negligible." (Orgel, 1998)*
>
> *"To postulate one fortuitously catalyzed reaction, perhaps catalyzed by a metal ion, might be reasonable, but to postulate a suite of them is to appeal to magic." (Orgel, 2000)*

Although Orgel was referring to metabolism, his comments apply equally well to the series of steps underlying protein synthesis and particularly to the origin of the ribosome itself. The leading scenario for abiogenesis, the RNA world (Gilbert, 1986), converges on the central role of ribozymes composed of RNA or ancestral prototype nucleotides able to form homochiral, supramolecular polymeric assemblies (Cech et al., 1981; Karunakaran et al., 2019). To support their emergence, such assemblies must undergo

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selection for specific catalysts, genetic information storage, and expression (Li et al., 2022). RNA–peptide world scenarios extend this hypothesis by proposing that the first protobiological functions arose through assembly of short RNA-like strands associated with polypeptides (Müller et al., 2022).

The ribosome is the link between the RNA world and the last universal common ancestor. It is a remarkably complex molecular machine. But how did it first emerge? Although there are many ideas, little is known about the process by which the first primitive ribosomes assembled in the chaotic environment of the early Earth. One thing to keep in mind is that even within this chaos, there could have been a "proto-ribosome" involving interacting peptides and nucleic acid oligomers that can be simulated by chemists and biophysicists.

Models of ancestral ribosomes suggest that the first protein translation machinery was a bricolage (Seelig and Chen, 2025), a distributed set of short strands of RNA, peptides, and RNA–peptide assemblages running an energy-driven informationally directed *stochastic relay race*. The participants in this race somehow passed coded instructions, catalysts, and substrates through semi-random encounters to generate populations of the earliest proteins. In the words of Seelig and Chen:

> *"A bricolage that formed the first coded protein synthesis machine from unrelated functional parts would only persist during natural selection if its product, the first coded peptide (that is, a short protein), provided an immediate selective advantage to the survival of the [proto]cell." [our modification]*

Collectively, the earliest stages of translation (initiation, elongation, and termination) would have been carried out with such a low level of efficiency that it would be dwarfed by the complexity of even the earliest living cells. In the prebiotic world, such systems must merely be good enough for the system to adapt against environmental stresses, grow and reproduce. A self-sustaining proto-ribosomal bricolage will have the following properties: (1) the bricolage itself and yields of functional products are maintained against environmental stresses, (2) the components of the bricolage can be reproduced, and (3) a data store that provides the coded instructions for the components is available as the "genetic material" proposed by Orgel. Preliminary maps of the gradual evolutionary accretion of ancestral ribosomes have been proposed (Lanier et al., 2017). However compelling these proposals may be, we agree with Orgel that their spontaneous emergence by a fortuitous combination of a chain of two or more catalytic systems, let alone an entire bricolage, is highly improbable in dilute solutions, perhaps even "to appeal to magic." This seemingly insurmountable hurdle presumably applies more generally to chemical reactions performed in laboratory water because that is the medium employed by most researchers. The incorporation of self-assembled structures of amphiphilic compounds into the medium coupled with wet–dry cycles can markedly increase the chances that a sequential series of reactions will occur because the components of the system remain sequestered and concentrated in defined compartments rather than diffusing randomly. This allows vast numbers of microscopic experiments to occur, and the rare ones that are selected for robustness will survive, while inert systems will be recycled back into the surrounding bulk.

2. Section 1. Converging Lines of Evidence That Support an Origin of Life on Land

The narrative of life's origin begins with two primary questions: where did the ingredients for life come from, and how did organic compounds accumulate in sufficient concentrations to assemble into the self-reproducing structures of primitive living systems? Clues to answering the first question come from analysis of samples recently returned from the asteroid Bennu (McCoy et al., 2025), which confirmed that the monomers required for life's origin are synthesized by nonbiological chemistry and would have plausibly been delivered to the early Earth. The theme of this special issue "*An Origin of Life on Land*" was chosen to explore how such organic compounds could accumulate and then become increasingly complex in hydrothermal fields associated with volcanic land masses. This scenario is supported by the discovery of ancient geyserite in Western Australia's Dresser Formation (Djokic et al., 2017, 2021), which confirmed the presence of microbial communities thriving in a freshwater hydrothermal spring 3.5 billion years ago. Drill core samples in the same region have since revealed a varied and extensive subaerial volcanic landscape with well-preserved stromatolites that provide additional evidence of microbial communities a few hundred million years after life would have presumably originated. Lastly, elemental abundances in these drill core samples confirm the presence of mineral nutrients considered to be essential for the origin of life (Van Kranendonk et al., 2021).

2.1. Sources of organic compounds in the prebiotic environment

There are at least two possible sources of organic compounds available on the prebiotic Earth. The first is endogenous geochemical reactions in the early Earth's crust and atmosphere that produced highly reactive chemicals such as formaldehyde and hydrogen cyanide that entered secondary pathways leading to more complex compounds such as amino acids (Miller, 1953) and nucleobases (Oró, 1960). Although it has been common to think that formaldehyde can react with itself in the formose reaction to form a variety of carbohydrates, Sutton et al. (2025) have challenged certain aspects of this hypothesis. Fatty acids, for example, can be synthesized by the Fischer–Tropsch reaction in which carbon monoxide is passed through a hot iron catalyst (Nooner et al., 1976). Although primary compounds involved in living systems have been synthesized spontaneously from reactions in the laboratory, there is no direct evidence that such reactions did in fact provide organic compounds to support the emergence of the first life on the early Earth. Therefore, an endogenous source of monomers is not a certainty but instead is an inference from laboratory results.

An alternative to endogenous synthesis is the previously mentioned exogenous delivery of organic compounds from extraterrestrial sources. We can be confident that this was occurring in the later Hadean, a period proposed for life's beginning approximately 4 billion years ago, because such delivery is still happening today. The evidence that supports this hypothesis comes from three linked observations. Radio astronomers have identified $\sim$200 organic compounds concentrated in molecular clouds that give rise to stars and solar systems (Allamandola et al., 1989; Öberg et al., 2011). In

our own solar system, organics accumulate as thin icy films on the surfaces of dust particles that became increasingly concentrated during assembly of the particles into aggregates, which formed the rocky planets of the inner solar system, Mercury, Venus, Earth, and Mars.

The organic composition of carbonaceous meteorites and dust grains illustrates the compounds that would have been available in the prebiotic environment. Figure 1 (left) lists carbonaceous components of the Murchison meteorite, which itself accreted from dust grains in the early phases of the solar system. A similar suite of organics has recently been identified in pristine material returned by the OSIRIS-REx mission from the Bennu asteroid (right). One major study reported a diverse suite of organic molecules in the samples: all 5 nucleobases, 14 proteinogenic and racemic amino acids, ammonia, carboxylic acids, amines, and ~10,000 nitrogen-bearing species (Glavin et al., 2025). Observation of the veined mineral systems that encapsulated these potential prebiotic building blocks indicated that they were likely precipitated during cyclic evaporation of brines (McCoy et al., 2025). Prebiotically important inventories were also discovered in samples returned by the Hayabusa2 mission from the Ryugu asteroid (Potiszil et al., 2023). The composition of these samples bears a resemblance to the suite of organic compounds in carbonaceous chondrites such as the Murchison meteorite (Pizzarello and Shock, 2010). These findings are consistent with our hypothesis that the primitive forms of life may have originated at least, in part, from exogenous infall accumulating on subaerial volcanic land masses on the Hadean Earth.

2.2. Membrane-bounded volumes as an alternative medium to bulk aqueous solutions

The structures and functions of a living cell are carried out by chemical and biochemical reactions in aqueous solutions. As a result, most origins of life research are performed with the assumption that the reactions occurred in relatively dilute concentrations of reactants in aqueous solutions. Because of their prominence as monomers of biopolymers such as proteins and nucleic acids, the properties of amino acids and nucleotides have been the focus of much experimental work. However, there is another organic species that has received less attention, which are amphiphilic compounds such as monocarboxylic acids and their monoglycerides. The monocarboxylic acids participating in living systems are classified as acids because of the carboxyl group that can release hydrogen ions into aqueous media: $–COOH \Leftrightarrow –COO^- + H^+$. As the length of the hydrocarbon chain increases to 10 or more carbons, monocarboxylic acids become amphiphilic and begin to assemble into a variety of structures as depicted in Figure 2.

No other biochemical compounds have this property, so a brief description of the structures may be helpful. What follows focuses on monocarboxylic acids as examples, although the properties of these compounds are shared with many other amphiphilic molecules. When monocarboxylic acids 10 or more carbons in length are associated with metabolism, they are often referred to as fatty acids. Most lipids, including fatty acids, are classified as surfactants because they tend to accumulate at air–water interfaces as monomolecular layers with the hydrophilic head groups interacting with the aqueous phase and hydrocarbon tails directed upward away from the interface. The molecules in solution also have a property called critical micelle concentration (CMC). All fatty acids can exist in aqueous solution as individual molecules, but, at a certain concentration, the hydrocarbon tails begin to aggregate and form nanoscopic spheres called micelles. The CMC varies with chain length and temperature and so does the ability of the compounds to form monolayers. Micelles and monolayers are the simplest examples of self-assembly of amphiphilic compounds. At concentrations above the CMC, fatty acids begin to assemble into bimolecular membranes that form compartments known as vesicles. This concentration is referred to as the critical vesicle concentration (CVC). Finally, when vesicles in freshwater evaporate, they fuse into a multilamellar matrix that captures solutes and polymers between the layers of lipid head groups in the matrix. Significantly, this is a reversible process. When the film becomes rehydrated in the wet phase of a wet–dry cycle, enlarging compartments containing concentrated solutes swell and bud away from the matrix into the bulk-phase aqueous medium. This reversible cycle between vesicles and multilamellar matrices is a key aspect of our hypothesis.

2.3. Prebiotic properties of Darwin's warm little ponds

In a letter to his friend Joseph Hooker, Charles Darwin speculated that life began in a "warm little pond" (Darwin,

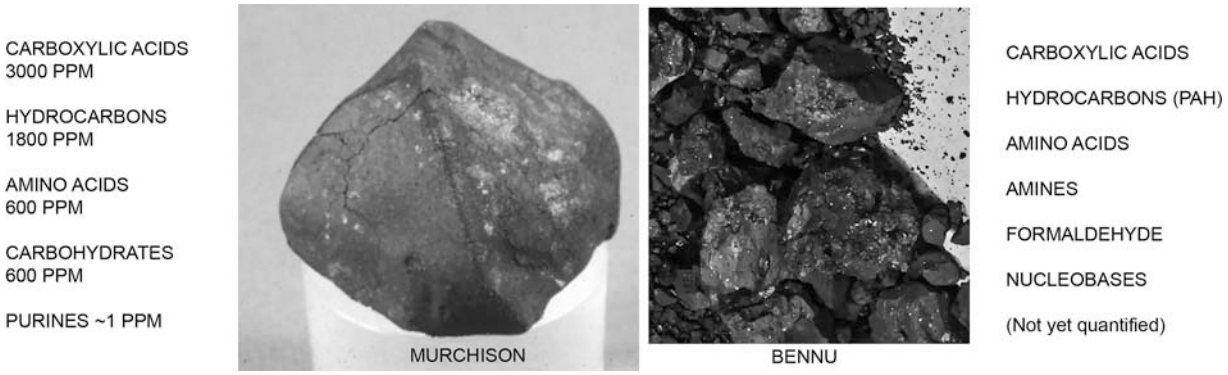


FIG. 1. Left: The Murchison meteorite and other carbonaceous chondrites contain thousands of organic carbon compounds that compose ~1% of its mass. Right: The Bennu sample returns confirmed many of the same compounds present (credit: the authors and NASA).

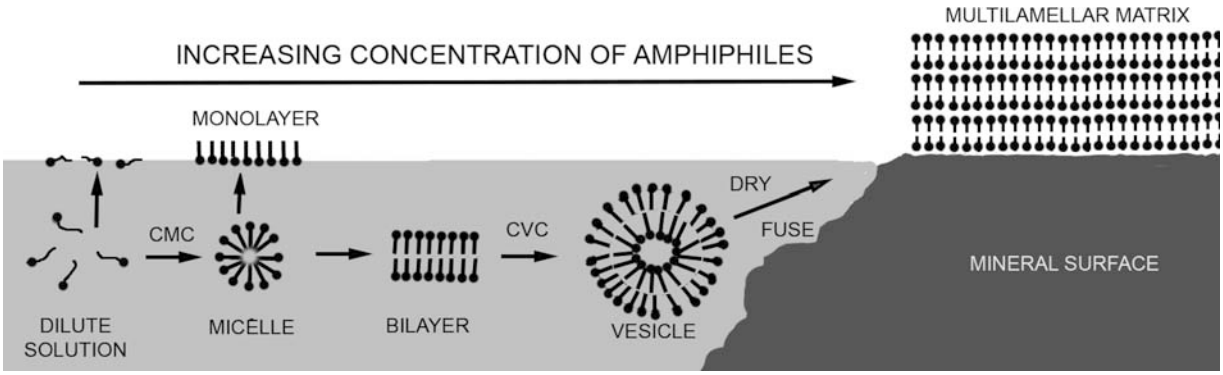


FIG. 2. Representation of distinct structures formed in sequence by amphiphiles such as fatty acids as their concentrations increase.

1871). On Earth today, as in the ancient past, air–water–mineral interfaces are abundant in aqueous systems. Basaltic mineral surfaces on volcanic land masses characterized the subaerial landscape on the early Earth as continents formed. Hydrothermal fields with geyser activity and hot springs would support small pools supplied with freshwater rainfall distilled from the surrounding salty seawater. Carbon dioxide and sulfur dioxide are major components of volcanic gases and become weak acids when dissolved in water, so the water circulating in hydrothermal fields is typically moderately acidic, with a pH ranging from 2 to 5. The concentrations of common cations such as sodium, potassium, calcium, and magnesium are in the millimolar range, with accompanying anions of sulfate, chloride, and silicate (Deamer et al., 2019). Hydrothermal fluids in hot springs and pools surrounding geysers circulate and undergo multiple cycles of evaporation to a dry state in response to heat and low relative humidity, followed by rehydration from rainfall, diurnal dew formation or periodic hot spring, and geyser activity. The cycling frequency is as short as minutes when caused by geyser splashing or steam exposure, to hours due to fluctuating levels of pools fed by pulses from hot springs, or over days to weeks in seasonal cycles of evaporation followed by rainstorms.

Figure 3 (left) shows a small boiling pool at Orakei Korako, New Zealand, fed by geyser upwelling and draining into other pools, an example of the mixing of potential dissolved reactants through diverse chemical conditions. Such "fitness landscapes" of pools (Van Kranendonk et al., 2026) can support different stages of prebiotic reactions. Figure 3 (right) presents an artist's rendering of a similar pool in a volcanic landscape of the Hadean Earth, also fed by local geysers. Small, freshwater pools like this would provide the "Goldilocks" conditions for prebiotic chemistry, as suggested by Powner and Sutherland (2011). These conditions incorporate variable chemical compositions and pH, as well as elevated temperatures maintained by underlying magma (Bada and Lazcano, 2002). Organic compounds provided by exogenous extraterrestrial infall would have accumulated as dilute solutes in these pools with wet–dry cycles concentrating them as dry films on surrounding mineral surfaces.



FIG. 3. Left: Contemporary volcanic hot spring pool at Orakei Korako, New Zealand (photo: the authors). Right: Artist's rendering of a hot spring pool on a volcanic Hadean land mass. Both settings are fed by geyser-driven upwelling via inflow channels and are also connected to a field of pools beyond.

As suggested by these dynamics, a multilamellar lipid matrix forming at air–water–mineral interfaces will have multiple opportunities to exist in three distinct phases: aqueous vesicles, moist gels, and dry films. These phases will extend from the edge of the pool onto exposed mineral surfaces and present a continuous gradient of hydration, with dry multilamellar phases farther from the water's edge and a moist phase at the water line where vesicles either bud off during hydration or fuse into the multilamellar phase during evaporation. It is important to note that wave action, geyser surges, and rainfall infusion can cause vesicles to be distributed downstream, often into networks of connected pools. The vesicles are present as vast populations of protocells with encapsulated polymers, each different in composition and available to undergo a form of combinatorial selection (Damer and Deamer, 2015).

Energy sources beyond wet–dry cycles include condensing agents and thermal cycling (Powner et al., 2010). Light energy would also be available to drive photochemical reactions, such as the generation of proton gradients across protocell membranes (Milshteyn et al., 2019; Summers and Rodoni, 2015), and enable nucleotide synthesis (Gilboa et al., 2024; Powner and Sutherland, 2011). Lim and Fahrenbach (2020) and Adam et al. (2021) provide excellent reviews of studies of radiolysis as a driver of closed-loop and hierarchical abiotic chemical networks implicated in life's origins. Finally, Nan et al. (2024) demonstrated photochemical carbon fixation by iron–sulfide clusters on mineral surface environments simulating hot springs. In summary, a major advantage of prebiotic chemical and physical processing in land-based environments is that diverse organic reactants and energy sources would have been continuously available on early Earth.

3. Section 2. Self-Assembling Lipid Systems Forming in Land-Based Pools

3.1. Protocell formation

Most investigations of polymerization processes are carried out in three-dimensional volumes, such as aqueous solutions of activated monomers. The reactions occur in a single process that includes initiation and an end point when the chemical potential is depleted, and the system comes into equilibrium. Polymer products that have been synthesized then begin to undergo the slower hydrolytic back reaction. The chemistry of polymerization reactions is well understood in terms of industrial products, but the much more complex processes that synthesize biomolecules still have significant gaps, one of which is the topic addressed here. The origin of life required primitive polymers, yet how were they synthesized from non-activated monomers before the advent of enzymes and catalyzed metabolism?

We reserve the word *protocell* for membranous compartments formed by amphiphilic compounds like fatty acids or phospholipids that encapsulate polymers such as nucleic acids or peptides. We refer to empty compartments as vesicles. Abiogenesis was likely to have been enabled through multiple reaction cycles, substrates, and end products interacting with one another in shared microscopic volumes, rather than a series of independent reactions in bulk-phase aqueous solutions. Protocells exposed to wet–dry cycles would have fragile membranous boundaries composed of prebiotically available fatty acids. They would have a transient existence in which their assembly would occur rapidly through budding, followed by a slower dispersal and recycling of their components in the wet phase. Protocells' friability means they were likely to have been an ephemeral stage in prebiotic evolution in which structural stability would be a strong selective factor. This logically invites the following questions:

1. What medium and associated energy-driven cycles can generate a continuous flux of protocell populations yet also support the return and re-accumulation of their polymer contents for a subsequent round of protocell generation?
2. Can this medium also serve as a primary synthesizer of protocells' polymer contents?
3. Are the selective processes presumed to act on protocells in solution augmented by additional selection within this generative medium?

Because their boundary structures are fused and mixed with every wet–dry cycle, the membranous compartments of individual protocells have a more or less uniform composition. Therefore, the most important selective factors in populations of protocells are variations of their polymeric contents. During the earliest stages of protocell formation, encapsulated polymer populations never stay associated with a single compartment because of the fusion and mixing that occurs during the intermediate, multilamellar phase. The unit of selection might therefore not solely be the protocell in the aqueous phase. Alternatively, it is the cycling stream of encapsulated polymers, coupling between lipid-bounded wet–dry encapsulation, which would collectively engage the battery of available selective processes driving molecular evolution (Damer and Deamer, 2015). The medium that generated both protocells and their polymer contents could benefit from being distinctly named and studied.

3.2. Progenotes and a hypothesized lipid–polymer progenitor

An applicable name was already proposed for this medium, the *progenote*, a neologism Carl Woese and George Fox introduced back in 1977. Woese defined a progenote as a hypothetical transitional form leading to living cells in which the expression and sharing of the first genetic material were characterized by "lateral transfer, not vertical inheritance" and that it "...cannot have been a particular organism, a single organismal lineage. It was communal, a loosely knit, diverse conglomeration of primitive cells that evolved as a unit" (Woese, 1998, 2002).

We paraphrase Koonin's (2014) summarization of Woese's definition of a progenote as being a community of primitive entities...

> *"with imprecise, 'statistical' translation, and multiple, small genomic segments, conceivably present in multiple copies in each (proto)cell ... [which] divided through the simplest imaginable mechanism, namely physical pinching of the membrane vesicles ... [and that as such] 'organisms' (molecular species) subject to selection must have preceded the cellular life forms [and] could have been represented by small, virus-like replicons that populated abiogenic lipid vesicles." [our modifications]*

Koonin then concluded that "once such growing replicons reached the level of complexity sufficient for the formation of cells, the major evolutionary transition to cellular life forms... Woese's *Darwinian threshold* would be crossed."

Here, we provide a more in-depth biophysical and geochemical foundation of Woese and Koonin's progenote scenario, which we first introduced in Damer (2016). The challenge is to understand how a mixture of self-assembled, random-sequence, varying-length polymers might become organized into the finely tuned molecular systems of the first living cells. For brief periods, these polymers occupy temporary protocell compartments and gradually, through selective processes, gather the machinery necessary to initialize the transition to living cells capable of self-regulation, growth, and reproduction.

As a way to constrain the argument, we adopt an additional term: the *progenitor*. In the context of astrobiology, a progenitor would be a medium or substrate from which protocell populations and eventually microbial communities can emerge. In fact, this term has been used previously in origins of life investigations by Cartwright and Russell (2019) and Duval et al. (2019), who described the mineral Fougèrite as "The not so simple progenitor of the first cells." Fougèrite is also called green rust, and in a later treatment, Russell (2021) referred to it as a "first seed of life... a 'makeshift' protocell." These colleagues recognized that in the highly dispersive environments of deep-sea hydrothermal vents, a concentrating matrix of compartments is required to support pH and temperature gradients, as well as maintain solutions of concentrated reactants.

An alternative to a mineral substrate would be an aggregate of membranous structures composed of amphiphiles

that continuously assemble from natural exogenous and endogenous feedstocks. If these become concentrated in small hydrothermal pools subjected to periodic cycles of wetting and drying, the amphiphiles will self-assemble into distinct structures as illustrated in Figure 4 including aqueously immersed vesicles (left) and aggregating moist vesicles (center) transitioning to dried multilamellar bilayers (right). As membranous vesicles fuse into multilamellar sheets, solutes are captured in between films, forming a "bathtub ring" around the mineral edges or bottoms of pools. The transition of vesicles to a multilamellar matrix is a unique property of amphiphilic compounds driven solely by evaporation of the aqueous phase. In the dry state, reduced water activity and elevated temperatures provide an energy source for condensation reactions within the layers, which allows the synthesis of ester and peptide bonds.

This system constitutes a primitive chemical factory capable of producing a continuous supply of short encapsulated polymers composed of random sequences of amino acids and nucleotides. This *lipid–polymer (LP) progenitor* could sustain the emergence of the progenote as originally proposed by Woese and Fox (1977). The LP progenitor acts as the surrounding, protective, and concentrating proto-niche (Damer, 2019) within which emergent biological circuitry constituting the progenote emerges. This process must be entirely driven by selection across innumerable generations of protocells and cycling polymer streams (Deamer et al., 2023).

3.3. Proposed properties of an LP progenitor

Figure 5 details how solutes and polymers are processed through lipid vesicles and multilamellar matrices during the initial formation of an LP progenitor. The initial stage of evaporation causes empty vesicles to aggregate and fuse into multilamellar structures. Previous research demonstrated that water-soluble compounds present in solution outside the vesicles are captured between alternating layers of the multilamellar phase (Deamer and Barchfeld, 1982; Shew and Deamer, 1985). It is significant that the multilamellar structure is not a solid. Instead, the hydrocarbon chains are fluid, and the structures are referred to as liquid crystals. As evaporation continues, the increasingly concentrated monomers pass through a "moist" phase in which they diffuse within a confining interlamellar volume (inset A). As the system enters the dry state (inset B), the trapped monomers form two-dimensional films. If the monomers are purine nucleotides, Himbert et al. (2016) reported that they undergo base stacking into linear arrays. Such ordering effects have the potential to promote polymerization processes by overcoming entropic hurdles that enable reactions that cannot occur in dilute aqueous solutions.

As the system undergoes rehydration in the wet phase of a cycle, water molecules return to the layers of hydrophilic polar head groups and the lamellae swell, thereby expanding the interlamellar gap (inset C). In this second moist phase, newly synthesized polymers have an opportunity to interact and combine into potentially functional structures (see further treatment in Section 3). Full rehydration then causes the outer layers of the lamellae to bud off from the main mass as a mixture of empty vesicles and polymer-containing protocells (top right).

Not shown but described previously in Damer and Deamer (2015, 2020) is that the protocells, empty vesicles, and free solutes can undergo continuous cycles of dehydration to a multilamellar phase and rehydration to a vesicular phase. In each cycle, through fusion, contents of returning protocells are deposited back into the lamellar matrix for subsequent processing. We refer to this process as *coupled phases* because polymers and other solutes are continuously retained within lipid boundaries, coupling between lamellar and vesicular compartments. The result of this cycling is a version of a *kinetic trap* that permits rates of polymer synthesis to exceed the rates of degradation (Ross and Deamer, 2016). Experimental studies in the laboratory and volcanic hydrothermal fields have demonstrated that inventories and lengths of polymers grow through cycles in the presence and absence of lipids (Deamer et al., 2019; Hassenkam and Deamer, 2022; Rajamani et al., 2008). The formation of polymers in a prebiotic setting is a cornerstone of the LP progenitor proposal, and the mechanisms underlying it are detailed next.

3.4. Polymerization of mononucleotides by phosphodiester bond formation

For cellular life to begin, there must have been a nonenzymatic polymerization reaction in which phosphodiester bonds linked mononucleotides into oligomers of single-stranded nucleic acids. The polymerization of nucleotides is basically a condensation reaction in which phosphodiester bonds are formed that link the monomers into linear strands

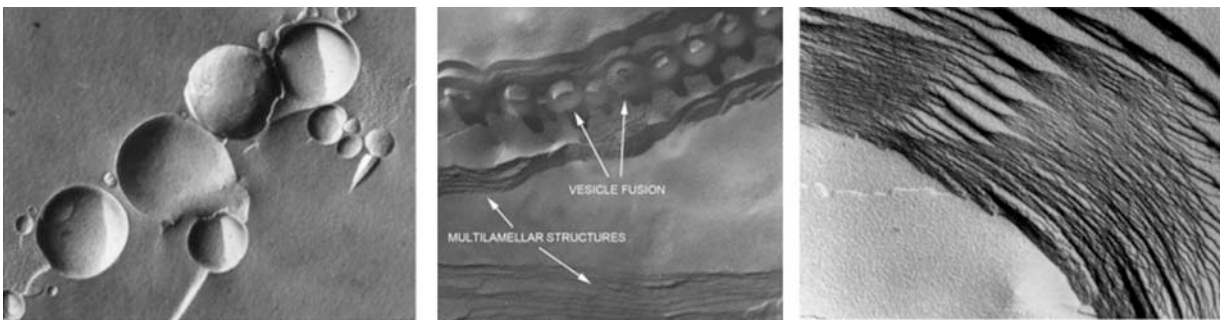


FIG. 4. Freeze-fracture images of lipid vesicles (left), vesicles aggregating and fusing into multilamellar structures (center) and a dehydrated multilamellar lipid matrix (right). Each lamellar line in the matrix is a lipid bilayer approximately 5 nm thick (credit: the authors).

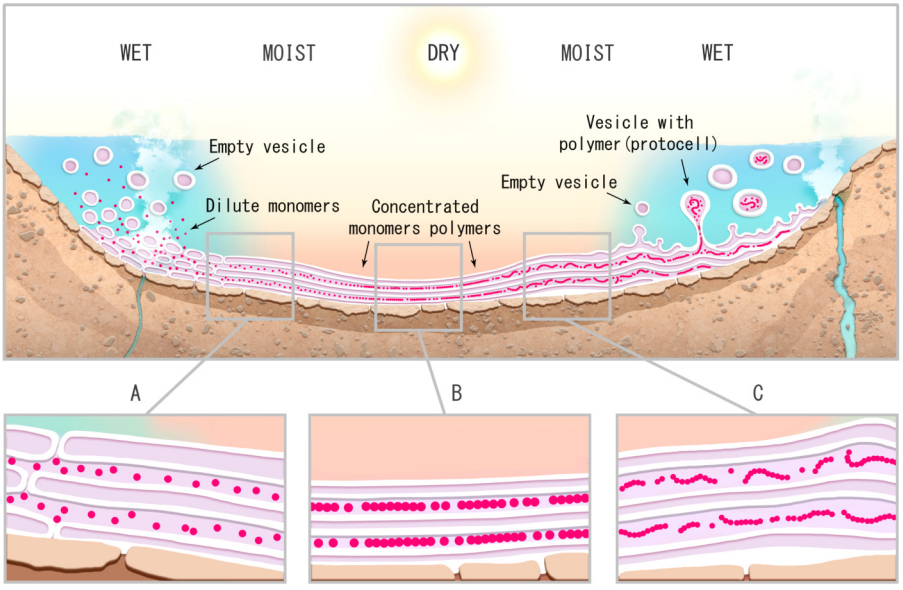


FIG. 5. Illustrating left to right through time, a lipid–polymer progenitor forming and processing entrapped solutes and polymers through wet, moist, and dry phases at the mineral edges of a freshwater, hydrothermal pool.

capable of containing genetic information in base sequences. However, for this reaction to occur in aqueous media, the monomers must be chemically activated with an appropriate leaving group. Orgel and coworkers pioneered the use of imidazole esters of mononucleotides and demonstrated that these chemically activated monomers in aqueous solutions spontaneously produce short oligomers, mostly dimers and trimers. Significantly, imidazole esters can assemble on RNA templates to produce longer complementary RNA strands up to 30 nucleotides in length (Inoue and Orgel, 1983; Orgel, 1998). This result is a clear indication of how an organizing surface, in this case RNA strands acting as templates, can enhance a polymerization reaction.

The question posed here is whether an alternative organizing medium could provide additional order that promotes polymerization processes. We posit that ordinary mononucleotides, not chemically activated, produce polymers ranging from 20 to over 100 nucleotides in length within a liquid-crystalline matrix. This process depends on the thermodynamic prediction that it should be possible to drive phosphodiester bond formation in the absence of activated substrates by producing conditions in which water can be removed from the reactants. Fluctuating environments in the form of wet–dry cycles have long been considered as possible sources of free energy for "uphill" polymerization reactions. Verlander et al. (1973) showed that anhydrous heating of nucleotides could drive the formation of mixed 2′–5′ and 3′–5′ phosphodiester bonds. These researchers also explored this possibility but were only able to achieve dimers and trimers in low yields. Usher and McHale (1976) proposed that cycles of heating and drying, followed by rehydration, could lead to phosphodiester bond formation and promote the accumulation of 3′–5′ bonds in the system due to the relative lability of 2′–5′ bonds to hydrolysis.

However, anhydrous conditions do not spontaneously produce long polymers when monomers are dried at ordinary temperatures. The reason is that potential reactants lack activation energy and tend to be immobilized within the solid matrix of a dry bulk phase, so that reactive groups rarely come into contact to undergo condensation reactions. But if a microenvironment not only concentrates monomers and also permits diffusional mobility, with activation energy provided by elevated temperatures, it is possible that polymers can be synthesized that cannot form under ordinary conditions of polymerization. To this end, we have been testing the hypothesis that lipid microenvironments impose order on monomers such as mononucleotides so that they form extensive chains linked by phosphodiester bonds. Such an ordering effect is illustrated in Figure 6, which shows the result of X-ray diffraction analysis of adenosine monophosphate (5′-AMP) within a multilamellar matrix a of a phospholipid (Toppozini et al., 2013). The structure on the left shows the organized matrix with a layer of AMP, while the panel on the right shows a schematic multilamellar lipid matrix (A), a diffraction pattern of an X-ray beam passing through a thin film of the matrix on a silicon support (B), and the molecular structures of the phospholipid (C) and adenosine monophosphate (D). A neutron scattering study also established that mononucleotides were mobile within a fluid lipid matrix (Misuraca et al., 2017).

RNA-like polymers are defined here as oligomers of monoribonucleotides linked by both 3′-5′ and 2′–5′ phosphodiester bonds. We have determined that polymer yields are improved if the reaction conditions incorporate multiple dehydration–rehydration cycles. Elevated temperatures are used to provide activation energy for the condensation reaction, so the process is carried out in the absence of oxygen that can damage the lipid components. As introduced in Section 1, several experimental studies have demonstrated that wet–dry cycling of non-activated RNA monomers can drive the formation of RNA-like polymers. In early work, Rajamani et al. (2008) showed that repeated drying and rehydration of 5′-monophosphate nucleotides in the presence of lipid multilamellar matrices produced polymers ranging from 25 to 100 nucleotides in length. Under more reactive

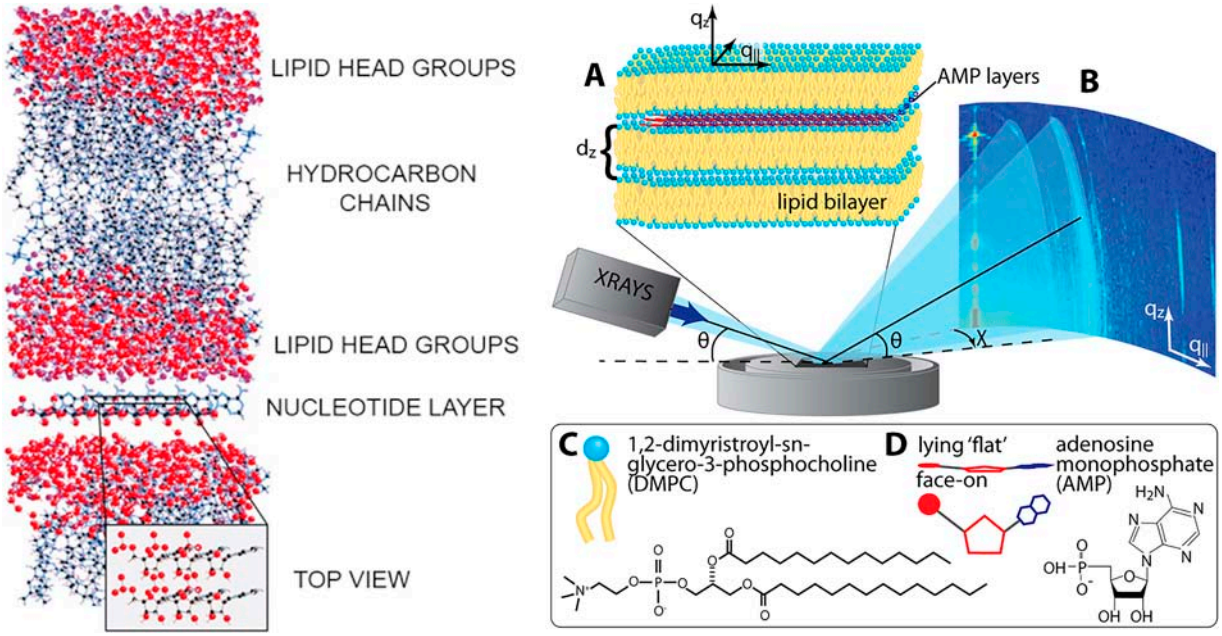


FIG. 6. Left: Molecular model of adenosine monophosphate organized within a multilamellar matrix composed of dimyristoylphosphatidylcholine. Right: The diffraction patterns were obtained by passing an X-ray beam through a thin film of lipids and nucleotides that was dried on a silicon substrate (Toppozini et al., 2013).

conditions, such as cycling in the presence of ammonium chloride and other salts of monovalent cations, polymer lengths exceeding 300 nucleotides have been observed (Da Silva et al., 2015). Further studies revealed that RNA strands formed in these settings can form ring structures (Fialho et al., 2020; Hassenkam and Deamer, 2022). In addition, our group has conducted these experiments in actual volcanic hot springs (Deamer, 2021; Deamer et al., 2019) and observed polymer products. Degradative reactions, such as depurination, have also been reported in such settings (Šimonis et al., 2026). Significantly, these polymerization reactions do not require activated monomers. Instead, they involve ester-bond synthesis driven by the chemical potential of water activity cycles. Other workers have also formed peptides and depsipeptides through wet–dry cycles (Forsythe et al., 2015), by gentle hydration–dehydration regulated by deliquescence (Campbell et al., 2019), and by using phospholipids as an organizing matrix (Joshi et al., 2021). Also of note is that evaporative drying of decanoic acid membranes with serine ethyl-ester has been found to increase the initial rate of serine–serine formation, compared with drying with a shorter fatty acid unable to form bilayers (Todd et al., 2022).

In summary, nanoscale liquid-crystalline structures readily assemble from a variety of amphiphilic compounds. Solutes ranging from low molecular weight dyes to macromolecules as large as proteins and nucleic acids are entrapped within the multilamellar matrix produced by dehydration of lipid vesicles. Furthermore, if the monomers have the potential to undergo polymerization reactions, the order imposed by the nanoscale matrices promotes reactions that cannot occur in solution. Future studies of such reactions will provide valuable insight into guided polymerization that may lead to the formation of novel, functional polymeric products.

3.5. Membrane–polymer colocalization

Roy Black and coworkers have demonstrated that organic solutes can also interact with lipid membranes and propose that *colocalization* of polymers with membranes provides a concentrating medium, permitting interactions not feasible in bulk solution. Their early work (Black et al., 2013) showed that adenine has a stabilizing effect on fatty acid membranes. Cornell et al. (2019) observed similar effects of certain amino acids and propose that this colocalization sets up "a positive feedback loop in which amino acids bind to self-assembled fatty acid membranes, resulting in membrane stabilization and leading to more binding… [and that] high local concentrations of molecular building blocks at the surface of fatty acid membranes may have aided the eventual formation of proteins" [our modification]. This polymer–membrane mutualism may represent a structurally enhancing collective phenotypic property as the first step of the long evolutionary march to microbes. Black (2026) has extended this work to propose a simple system in which colocalized oligonucleotides could direct *de novo*, templated novel peptide synthesis in a minimal, primitive version of the ribosome.

Oligonucleotide colocalization with membranes is also garnering more attention, and recent experimental studies provide compelling evidence that short RNA strands (under 50 nucleotides) can stably associate with fatty acid membranes when paired with simple peptides, particularly cationic strands rich in lysine or arginine. These peptides create localized electrostatic fields that can attract and hold negatively charged RNA near the membrane surface, increasing the likelihood of molecular interactions and potential ribozyme activity (Kamat et al., 2015). Other researchers have developed amphiphilic localized complexes composed of lipophilic peptides covalently linked to short RNA sequences. These nucleopeptide complexes enable the RNA to

remain anchored to the lipid bilayer while potentially interacting with internalized reactants (Lopez et al., 2024). The coupling of RNA's sequence-specific recognition with peptide-driven membrane localization provides a plausible model for early protocell systems where compartmentalization, catalysis, and replication could have co-occurred. These findings reinforce the idea that hybrid colocalized structures could bridge informational and structural roles in prebiotic systems, particularly when organized by primitive amphiphilic matrices.

4. Section 3. Testing the LP Progenitor Hypothesis

> *"The localization of short polynucleotides to membranes could promote a variety of catalytic processes of RNA, ranging from faster nonenzymatic template copying to faster assembly of oligonucleotides into multi-component ribozymes. Determining mechanisms for RNA–membrane association is a fundamental step towards the goal of demonstrating increased RNA reactivity in the presence of vesicle membranes." Kamat et al. (2015)*

We agree with Kamat et al. (2015) that an association of RNA with membrane structures is worth investigating and suggest some preliminary experimental approaches to ribosome assembly that serve as a test of the hypothetical LP progenitor model system, both chemically and computationally.

4.1. Chemical tests

Held et al. (1973) first demonstrated that the 30S ribosomal subunits of *Escherichia coli* could be disassembled into their RNA and protein components. If the components were then mixed, they spontaneously reassembled into functional subunits. A year later, Held et al. (1974) showed that the assembly process occurred in specific stages, a hierarchy rather than random associations. More recently, Nikulin et al. (2000) were able to use X-ray diffraction to establish the molecular structure of the initial ribosome assembly step in which the S15 ribosomal protein of the S30 subunit binds to 16S ribosomal RNA. Significantly, the binding involves positive charges on amino acids in the protein (lysine and arginine) interacting with the negatively charged phosphates of the 16S RNA. We propose that this kind of electrostatic interaction can be used to test whether a multilamellar lipid matrix is able to promote and stabilize the assembly of protein–RNA complexes.

The goal of the experiment is to better understand the electrostatic interactions between peptides and RNA, such as those that would be involved in the assembly of primitive ribosomes. Carroll (1972) described one such possibility, and its simplicity suggests that it would be a useful model system to investigate how peptides can bind to RNA in a multilamellar lipid matrix. Carroll reported that polylysine mixed in approximately a 1:1 ratio with polyuridylic acid formed aggregates with greatly enhanced circular dichroism (CD), which means that the anionic RNA polymer forms a helical structure when it binds to the cationic polylysine. Measuring the CD spectral changes that accompany the complex formation is a convenient way to monitor the process.

The control will be to mix the polylysine and polyuridylic acid in the bulk-phase solution that Carroll described, and the experimental test will be to compare those results with the same components in the presence of phospholipid vesicles that undergo exposure to wet–dry cycles that capture the components in a multilamellar matrix. If there is no difference between the control and experiment, we would conclude that the multilamellar condition does not affect the interaction between RNA and polylysine, but if there is an apparent difference, the experiment could be expanded to compare the following variations:

- Length and concentration of polymers required to form stable complexes.
- Kinetics of association in the bulk-phase and multilamellar phase.
- Stability of the complexes over time in both phases.
- Effect of temperature on the process.
- Effect of ionic conditions including pH and concentration of ionic solutes.

The prediction is that there will be a minimal length for stable complexes to form in the bulk phase, but this minimum will be reduced in the multilamellar phase. There will also be an optimal pH because both polymers have groups (phosphate and amines) with pKas that are neutral or ionic depending on the pH. The most stable complexes will occur in the multilamellar matrix and be maintained when the matrix reverts to the vesicular state because concentrated polymers will remain in the vesicles when the matrix is rehydrated. If these predictions are fulfilled, it will encourage a similar approach for testing whether multilamellar matrices can promote the binding of the S15 protein to 16S RNA.

4.2. Computational tests

Coarse-grained molecular dynamics (MD) and Monte Carlo computational simulations provide a tractable way to test how short peptides anchored to lipid bilayers or freely dispersing in interlamellar gaps can form complexes with RNA oligomers. Studies on relaxation, diffusion, and translocation dynamics of single linear polymer chains in membranous confinement (Milchev, 2011), surface density (McGeachy et al., 2018), and diffusion (Guo and Gai, 2010) of free-floating or colocalized peptides inform these approaches. These studies suggest that substantial numbers of polymers can interact in confined interlamellar volumes. Mathematical and computational work may support predictions that rare functional polymer complexes can also form in these matrices with a substantially higher likelihood than in bulk solution or in protocell interiors.

To illustrate, Figure 7 presents a minimal conceptual model system for how short polymers, such as an oligonucleotide P1 and a peptide P2, could first arise from a random pool of monomers by condensation reactions during wet–dry cycles and then diffuse within a confined interlamellar aqueous gap. A "combinatorial engine" would naturally arise within these gaps as they can facilitate a mobilizing aqueous medium (Misuraca et al., 2017) that would promote numerous polymer–polymer encounters, a small proportion of which might form functional and possibly catalytic complexes C, at a stochastic rate r. P3 depicts amino acids and peptides that in previously referenced studies by Black et al. (2013) and Cornell et al. (2019) become colocalized on membranes and could also extend into the interlamellar gap,

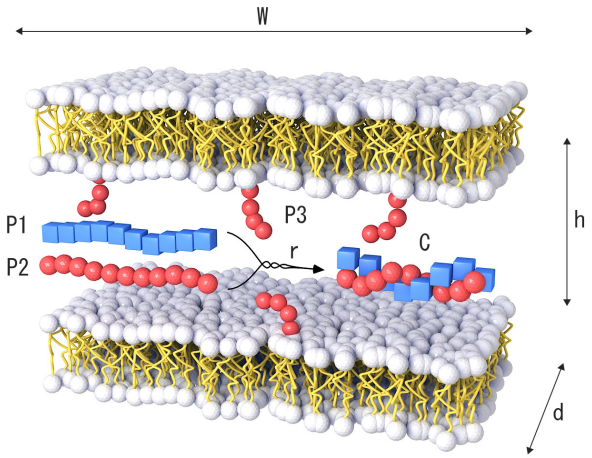


FIG. 7. Conceptual model system to guide computational and chemical simulations: interlamellar gap volume (w × d × h), polymer P1 (oligonucleotides) and P2 (peptides) undergoing a stochastic encounter rate (r), forming a paired complex C. Membrane-colocalized peptides P3 can provide additional points of interaction and formation of functional nucleopeptide complexes.

thereby able to react with freely diffusing polymers. Combining this finding with that of Kamat et al. (2015) and Lopez et al. (2024) who demonstrated that lipophilic peptides can attract RNA to form nucleopeptide complexes, a small fraction of these complexes might express catalytic or informational capabilities. These functional complexes could operate on available substrates such as small molecules diffusing into the lamellae and provide primitive components of a self-sustaining proto-ribosomal bricolage (Seelig and Chen, 2025). The products of such bricolages could provide selective advantages for protocells forming in a subsequent hydration phase.

Greatly enhanced probabilities for the emergence of functionally relevant polymer complexes from random-sequence pools plausibly address Orgel's challenges and are the central tenet of the LP progenitor hypothesis. In a concentrating lamellar medium where cycling inputs of substrates, formation of polymers, sources of energy, and a high frequency of combinatorial encounters are all co-present, the emergence of autocatalytic sets also seems more likely and are considered by some investigators to be essential for life's origination (Hordijk et al., 2010). The large potential number of polymers involved makes it probable that such complexes and networks of interactions can occur in a reasonable time frame. In one study, McGeachy et al. (2018) measured lipid bilayer adsorption of octapeptide sequences such as Lys_8, with observed optical surface mass densities that suggest the presence of millions of colocalized peptides/cm^2. Even within a relatively small set of interconnected hydrothermal pools undergoing wetting and drying, many square meters of multilamellar films would be available to accommodate such interactions.

By treating the interlamellar gap as a well-defined, two-dimensional confined environment, this model system provides parameters that can be tested computationally, including monomer concentrations, synthesis of polymers having varying lengths, interlamellar diffusion of free-floating or membrane-colocalized polymers, and encounter radii for possible pairings. *In silico* simulations can then track the rates of polymer–polymer encounters and, given binding free energies, lead to estimates of the fraction of products that result in stable, functional complexes. Coarse-grained MD simulations could then predict how confinement, concentration, and wet–dry cycling can influence these rates and promote the spontaneous arising of potential catalytic activity. By framing these simulations with prebiotically realistic chemical and environmental inputs, computational models can enrich the LP progenitor hypothesis with chemically testable predictions, suggesting how an interlinked series of sustainable catalytic cycles might have emerged at life's beginnings.

5. Conclusions

To respond to Leslie Orgel's challenge related to the improbability that long sequences of primitive metabolic reactions could organize spontaneously, we propose an alternative to performing experiments in dilute, bulk solutions. Multilamellar lipid matrices allow exploration of combinatorial catalytic complexes formed by RNA oligomers interacting with peptides. Such matrices are inevitable in a mixture of amphiphilic compounds and potential monomers that would accumulate in freshwater hydrothermal fields associated with volcanic land masses. A matrix forming during a dry down phase organizes and concentrates potential reactants, thereby promoting the synthesis of polymers that can pair into rare catalytic complexes. Also, in the interlamellar medium, these complexes will have continuous access to substrates and energy sources. In subsequent rehydration cycles, the lamellar matrices bud off vast numbers of protocells that contain initially random collections of these polymers. Protocells and the cycling polymer streams populating them become natural experiments that undergo testing, selection, and possible amplification to generate the first chemical systems related to life's origin.

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Authors' Contributions

B.F.D. conceptualized the original hypothesis and produced the initial draft of the essay and figures. D.W.D. contributed to critical revisions, added key references and figures, and refined the discussion with supporting experimental evidence. Both authors approved the final version of the article.

Author Disclosure Statement

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