The Origins of Life: The Metabolism First, Replication First, and Compartmentalization First Theories

INTRODUCTION

The origin of life (OOL) is a scientific problem that spans multiple disciplines, such as chemistry, biology, and thermodynamics, and includes many theories that will be discussed in depth. It investigates the source of life on Earth, specifically the natural processes that allowed organic life to arise from non-living matter. While it is generally agreed that life arose from a single primitive life form, there is little evidence that demonstrates how this occurred.\textsuperscript{1,2} A highly speculative field of study, the OOL has been debated since the early 19th century.

Life’s emergence from non-living matter is poorly understood. There is a consensus among the scientific community that nature evolved from non-living matter through a step-by-step process.\textsuperscript{3} The OOL scientific community is focused on determining these steps. To do this, researchers examine the chemical and environmental conditions necessary for the emergence of life.

The conditions in the early Earth environment could have allowed for the occurrence of prebiotic chemistry and the emergence of biologically relevant molecules. Although there are current theories of how life arose, they consist of some paradoxes that need to be discussed. Overall, the OOL theory is vital for understanding life today.

EARLY EARTH ENVIRONMENT

The early Earth environment plays an important role within the OOL theory. One of the first people who theorized the OOL was Harold Urey, who proposed...
that life arose from countless natural experiments of increasing complexity that involved many different combinations of molecules, light, and energy. Despite many attempts to understand these processes, there is still much speculation. One part of the problem is that these processes would have occurred on a young and primitive Earth, whose characteristics were vastly different from those of the present. Understanding the environment where such processes would have occurred is essential to answering questions about how they occurred. However, early Earth coincides with the end of the Hadean era and the beginning of the Archean era (Figure 1), an eon that has little evidence to indicate what the environment was like. Current theories aim to describe the conditions found on early Earth and the resulting prebiotic chemistry.

In 2002, the earliest evidence of life was discovered in the form of fossilized stromatolites that date back to 3.45 billion years ago (Gya). Stromatolites are rock-like structures formed by cyanobacteria. The age and simplicity of the fossilized organisms suggest that the origin of life occurred at the beginning of the Archean Era, between 4 and 2.5 Gya. Older stromatolite fossils were discovered in 2017. These fossils were tubular microorganisms found in iron and silica-rich rocks dating back to 4.28 Gya. This discovery suggests that the origin of life could have occurred at the end of the Hadean Era, from 4.54 to 4 Gya. According to the geologic time scale (GTS), the Hadean Era covers the formation of Earth, the moon, and the primitive oceans and landmasses. Overall, these fossilized remains support the general assumption that life began between the end of the Hadean and the beginning of the Archean Eras.

**Earth’s Early Atmosphere**

Some of the strongest evidence for the characteristics of early Earth have been identified through the use of detritus zircons. Zircon (ZrSiO4) is a mineral that is common in the crust of the Earth and can occur in all three rock types: sedimentary, igneous, and metamorphic. Detrital zircon refers to sedimentary rocks which have been exposed by erosion. Detrital zircons are highly durable, heat resistant, and provide information about the chemical characteristics of the environment from which they formed, as they have an extremely stable bonding structure. This makes them useful in determining the characteristics of Earth during the Hadean Era. The discovery of detrital zircons in mid-western Australia has led to evidence suggesting that the first oceans and continental crust formed on Earth as early as 4.4 Gya, which falls into the Hadean Era.

Experiments conducted in 1952 and 1953 by Stanley Miller and Harold Urey aimed to model the disequilibrium chemistry that would have resulted from electrical discharges, or ultraviolet radiation, being absorbed in highly reduced atmospheres consisting of methane, ammonia, and water. The experiments were based on the conclusion that early Earth likely had a reducing atmosphere because of its high temperature and concentration of hydrogen. This would have reduced the likelihood of highly reactive free oxygen particles. It was unlikely that the atmosphere contained more than trace amounts of carbon, nitrogen, oxygen, and hydrogen, other than as CH4, H2O, NH3 (or N2) and H2. This idea was supported by the Miller-Urey experiment in 1953, which tested the chemical origin of life under conditions stimulated to mimic those believed to be present on early Earth. One-step reactions of the mixture components (CH4, H2O, NH3, H2) produced compounds such as HCN and CH3O, which were then able to form biomolecules such as amino acids and glycine, as shown in Equations (1) and (2), respectively. The experiment was able to produce 11 out of the 20 known amino acids and was part of the first chemical evidence of abiogenesis, or life emerging from inorganic substrates. In 2007, scientists re-examined sealed vials from the original experiments and identified more amino acids than previously reported, classifying more than 20. The discovery of more amino acids is linked to increased efficiency in detection equipment and procedural techniques.

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\begin{align*}
\text{CO}_2 & \rightarrow \text{CO} + \text{O}^* \\
\text{CH}_4 + 2[\text{O}] & \rightarrow \text{CH}_3\text{O} + \text{H}_2\text{O} \\
\text{CO} + \text{NH}_3 & \rightarrow \text{HCN} + \text{H}_2\text{O} \\
\text{CH}_4 + \text{NH}_3 & \rightarrow \text{HCN} + 3\text{H}_2
\end{align*}
\]

(1)

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\begin{align*}
\text{CH}_3\text{O} + \text{HCN} + \text{NH}_3 & \rightarrow \text{NH}_2\text{CH}_2\text{CN} + \text{H}_2\text{O} \\
\text{NH}_2\text{CH}_2\text{CN} + 2\text{H}_2\text{O} & \rightarrow \text{NH}_3 + \text{NH}_2\text{CH}_2\text{COOH}
\end{align*}
\]

(glycine)

More recent evidence published in 2011 by Trail et al., has suggested that early Earth’s atmosphere may not have been as reducing as originally thought at the time of the Miller-Urey experiment. Major volcanic eruptions during early Earth would have released nitrogen...
(N₂), carbon dioxide (CO₂), hydrogen sulphide (H₂S) and sulphur dioxide (SO₂) into the atmosphere, and likely played a critical role in determining its composition.¹⁷,¹⁸ Identities of molecular species in magmatic outgassing, the release of gas from volcanoes, depend on the partial pressure of oxygen. The partial pressure of oxygen depends on the magmatic characteristics of the volcanoes.¹⁷ Volcanic melts that have oxygen partial pressures close to that defined by the iron–wüstite buffer, a signature in the rock that indicates it has little oxygen, would yield volatile species similar to that of the Miller-Urey atmosphere (CH₄, H₂, H₂S, NH₃ and CO).¹⁷,¹⁸ Conversely, melts close to the fayalite– magnetite–quartz buffer signify that the rocks would have had a higher oxygen concentration and would have been similar to present-day conditions with H₂O, CO₂, SO₂ and N₂ gases.¹⁷ The oxidation state of samples from the Hadean era magmatic melts are consistent with that of the fayalite–magnetite–quartz buffer, suggesting that the atmosphere was less reducing.¹⁷

Earth’s Early Oceans

The climate of the Earth’s oceans is an important component in understanding the emergence of life. Liquid water likely originated on Earth when it cooled enough for water vapour in the atmosphere to condense.¹⁹ Evidence for the characteristics of such oceans is typically found using isotope ratios. This is a method of comparing the relative abundance of isotopes in samples, such as rocks and water, to elucidate the characteristics of the samples such as age.¹⁹,²⁰ Using the ratio of ¹⁸O to ¹⁶O isotopes found in fossils or rocks, researchers are able to determine the temperature at the time the organism existed or the rock was formed.¹⁹ Using Equation (3), as seen below, the δ ¹⁸O value corresponds to the ratio of both oxygen isotopes in the sample divided by the ratio of a standard, which is anything that has a known isotopic ratio.¹⁹,²⁰ Obtaining temperature estimates from oxygen isotopes is based on equilibrium isotope fractionation, the partial separation of isotopes at chemical equilibrium.²⁰,²¹ The heavier isotope, ¹⁸O, condenses in the liquid phase of water, and the lighter isotope ¹⁶O, is found in the vapor phase of water. A δ ¹⁸O above one indicates a higher number of ¹⁸O isotopes, and therefore a cooler climate, while a δ ¹⁸O value below one indicates a higher number of ¹⁶O isotopes, and therefore a warmer climate.¹⁹,²⁰,²¹ The δ ¹⁸O values of Archean marine sediments are tens of times lower than values today, suggesting a warmer environment.¹⁹ A hot early Earth is supported by other evidence, with oceanic temperatures calculated to be approximately 70 °C.²⁰,²¹ As well, this result is supported by silicon isotope ratios which have been interpreted as showing evidence of ocean temperatures ranging from 60 to 80 °C.²¹ Converting δ ¹⁸O to a temperature value in degrees Celsius (°C) is done using Equation (4), where correlates to the temperature in °C and correlates to the δ ¹⁸O value computed with Equation (3).¹⁹,²⁰,²¹

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\delta O_{18} = \left( \frac{\alpha_{18}}{\alpha_{16,\text{sample}}} - 1 \right) \times 1000\%
\]

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T = 16.5 - 4.3\delta + 0.14\delta^2
\]

The pH of the Earth’s early ocean is highly debated due to opposing experimental evidence. In 2013, Blatter et al. interpreted Archean calcium (Ca²⁺) isotopes to reflect high Ca²⁺ alkalinity ratios, suggesting that an alkaline ocean with a high pCO₂ value was unlikely.²² On the other hand, Friend et al. in 2008 argued the existence of an alkaline ocean due to the presence of alkaline earth elements (e.g. Mg²⁺ and Ca²⁺ isotopes) that corresponds with high pH environments.²³

THE ORIGIN OF LIFE

Life is generally characterized by three requirements: (1) the ability to reproduce, (2) the ability to evolve, and (3) the presence of metabolism.²⁴ In present living organisms, these functions are operated by biopolymers, such as DNA and RNA, proteins, and phospholipids in highly balanced, syndicate systems that have evolved over billions of years.²⁴,²⁵

The OOL theory proposes that life began in the form of simple elements.¹² Through chemical evolution, identifiable structures like amino acids, nucleotides, and fatty acids formed.¹²,¹³ These early molecules developed the ability to perform actions that mimicked modern metabolism, replication, and evolution.¹,¹²,²⁶ Eventually, they converged to form the last universal common ancestor (LUCA).²⁶ Overall, the origin of life can be summarized into three basic stages: (1) the origin of biological monomers, (2) the origin of biological polymers, and (3) the evolution from molecules to cells which are able to metabolize, reproduce, and evolve.²⁶ While this statement is a general outline for the OOL, there is little scientific evidence which connects these steps.¹,¹²,²⁶ For this reason, many theories have arisen to suggest which aspect of life could have emerged first.¹,²⁶

A popular theory is the ‘prebiotic soup theory’, proposed in 1929 by Alexander Oparin.¹,²,²⁷ This theory suggests that life arose in the ‘primordial soup’ of the early Earth environment and that organic molecules in the soup reacted in an increasingly complex fashion.²⁷ While recent research has changed what was hypothesized about the early Earth environment since the theory’s proposal, the soup theory remains central to the scientific community’s understanding of the OOL.²⁷

Three of the most current popular theories are: (1) the Metabolism First Theory, (2) the Replication First
Theory, and (3) the Compartmentalization First Theory. The following sections will consider the evidence for each theory.

**METABOLISM, RNA, OR COMPARTMENTALIZATION FIRST?**

Metabolism is a chemical process that occurs within a living organism in order to maintain life. In present-day organisms, metabolic systems employ enzymes, receptors, biomolecules, and cofactors that react in various ways to create energy to fuel life processes. Life today also has genetic material, RNA and DNA, which are blueprints for producing proteins and enzymes. Finally, life can also be characterized by compartmentalization and the ability of eukaryotic cells to regulate energy conversion and ion concentrations with the help of lipid membranes. These three aspects are essential for life to occur and would have been required for the LUCA to arise, but the order in which these aspects developed is highly debated.

The debate in which aspect of life arose first is commonly referred to as the ‘origin of life paradox’. For life to have arisen, there must have been a genetic molecule, RNA or DNA, capable of transferring blueprints for making effective proteins and enabling the ability to pass on changes to the next generation. Nevertheless, RNA and DNA cannot function without the help of proteins to replicate, transcribe, and translate. As well, these reactions require some form of a compartment to separate them from other molecules that could affect the process. However, membranes that act as compartments in cells today are made of lipids that require proteins to be synthesized. Therefore, while the following sections outline some of the evidence supporting each theory, the question of which aspect of life came first cannot be answered definitively. The emergence of these aspects could have happened in conjunction with each other, or in a different way that has not yet been theorized.

**Metabolism First Theory**

The Metabolism First Theory suggests that self-sustaining networks of metabolic reactions may have been the first forms of simple life. This idea of self-sustaining networks was first introduced by Dr. Stuart Kaufmann, who proposed the idea of autocatalytic sets as a method for the emergence of life. Autocatalysis is the phenomenon where a group of chemicals react and create products that catalyze their own formation, thus creating a self-sustaining set (Figure 2).

Initial chemical reaction pathways could have produced more complex chemicals that were then able to catalyze their own formation. Eventually, these react...
ists, but it is limited in the scope of temperature and reliability.\textsuperscript{40} This is due to the tendency of proteins to denature at high temperatures (~41°C).\textsuperscript{41} In experiments using the water-soluble functional group carbodiimide as the condensing agent, short oligonucleotides were formed but the reactions were slow and inefficient.\textsuperscript{39,46} Another problem arises from the relative complexity of ribozymes, which cannot self-assemble without the presence of a polymer backbone.\textsuperscript{44}

Compartmentalization First Theory

The Compartmentalization First Theory refers to the introduction of a simple cell membrane or other methods of compartmentalization occurring as the first step towards the OOL.\textsuperscript{42} The theory questions how any chemical reaction, whether forming molecules or reaction networks, could have arisen if there was no way to concentrate constituents.

The belief that there needed to be a concentrating mechanism for life to arise cannot be singularly attributed to the Compartmentalization First Theory. It has been suggested that there had to be some mechanism of concentrating necessary elements and molecules for prebiotic chemistry to occur and for life to emerge.\textsuperscript{27, 43, 44} Alexander Oparin suggested that liquid droplets, formed at the bottom of Earth’s early ocean due to differences in water density, could have contained a high enough concentration of constituents to eventually turn into living cells.\textsuperscript{45} Other theories have suggested that perhaps iron-sulphide bubbles, which were compartments that formed on the ocean floor near hydrothermal vents, could have acted as primitive membranes at life’s origin.\textsuperscript{45} They could have grown by inflation due to the hydrostatic pressure of the fluid from the external environment, as well as by osmosis catalyzed by organic and inorganic molecules trapped within the bubbles.\textsuperscript{46} The idea that life may have started in membrane-less micro-droplets, like iron-sulphide bubbles, has been highly researched and is generally an accepted theory.\textsuperscript{29} While life could have started in membrane-less micro-droplets, eventually, a simple organic membrane would have needed to develop, as modern-day cells are characterized by a bilipid membrane.\textsuperscript{29, 47, 48} Modern-day cells are made of amphiphilic lipid molecules that self-assemble into a membrane when exposed to a polar environment.\textsuperscript{47, 48}

Self-assembly in mixtures of a single species has been heavily investigated in the last two decades, as it offers a simple explanation for the spontaneous emergence of lipid membranes for the OOL.\textsuperscript{29} Groups of similar fatty acids lead to a more efficient self-assembly process under a broad range of conditions. However, some problems arise with more complex mixtures of amphiphilic material, such as fatty acids of different lengths and constitutions. While the mixtures will still self-assemble into aggregate structures, their half-life is four to nine times shorter than that of vesicles formed from single type mixtures.\textsuperscript{29} Additionally, they have a smaller aqueous volume enclosed in the vesicle, which would affect how well these membranes concentrate inorganic and organic substituents.\textsuperscript{47} On the other hand, complex mixtures of fatty acids and their derivatives are considered more likely to have contributed to the source pool for compartmentalization processes at the OOL.\textsuperscript{29} This is because it would be very unlikely for only one type of fatty acid to be outputted initially, and for the reaction to be stable enough to output a large enough number of these fatty acids to form a membrane.\textsuperscript{29, 47} The consequences of this, along with the lack of evidence confirming the emergence of a supportive framework, have led to uncertainty about the Compartmentalization First Theory. As mentioned previously, the lifespan of vesicles formed from complex mixtures is shorter than that of single type mixtures.\textsuperscript{29} In general, longer lifespans of molecular products and structures increases the probability that they will react with other molecules and form the next step in the OOL.\textsuperscript{29} This duality suggests that more evidence is required to elucidate some of this theory’s inherent complications.

CONCLUSION

Will it ever be possible to determine the exact moment when life arose? Most likely not. The answer to the question of when life arose is limited to fossilized evidence of microscopic organisms; this enables the window of time for when life could have arisen to be narrowed, but it has yet to offer any definitive evidence of the LUCA.

Although it will likely never be known when life on Earth first arose, it is still important to research how life on Earth arose. Life is built on several molecular components and understanding how these components have formed helps to answer some of the questions around the nature of these building blocks. Therefore, a deeper understanding of the OOL has applications to genetic therapy, drug development, and cures for diseases that require an understanding of biological systems.\textsuperscript{49, 50, 51}

This literature review discussed the early Earth environment and some of the main theories underlying the OOL theory, specifically those pertaining to what aspect of life occurred first: metabolism, compartment, or genetic material. Due to the speculative nature of the OOL theory, the belief of how life emerged will continue to change with the discovery of new chemical mechanisms and evidence. Future research will hopefully be able to further the understanding of the geochemical inventory of Hadean Earth and how it would be able to fuel the processes and stages involved in chemical evolution. Therefore, the OOL is an extremely complex puzzle in the scientific community. Future
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REFERENCES