The origin of life: from molecules to cells

How life on Earth really got its start

"It seems to me that it was much easier to determine the course of the stars observed in space, and to ascertain the distance, magnitudes, masses and movements of the planets belonging to our solar system, than to solve the problem of the origin of life."
Jean-Baptiste de Lamarck (1809) *Zoological Philosophy* p184

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Abstract

The origin of life is one of the biggest unsolved mysteries in the world. To explain the origin of all living species, an evolutionary tree of life was built, tracing back all organisms to the beginning of life. At the very beginning, stood our last universal common ancestor (LUCA). However, LUCA already was a fully formed organism and it must have also originated somewhere. It is believed that the first life forms originated from simple organic chemicals that through biochemical reactions developed life-like functions and eventually over time developed into fully functional organisms. Scientist have been investigating which biomolecules and processes happened to create life, by reducing life to only its essential properties as well as experimentally trying to recreate the early conditions on Earth. These processes have yielded several different theories on how life could arise based on RNA, peptides, lipids, or coenzymes. These theories study the different molecules and processes in isolation, which makes it easier to determine specific mechanisms. The downfall of this method is that it will never form a complete picture of the origin of life even if you would combine them, since it will leave out the interactions between the different components. The emergence of life from non-living compounds is a complex system, which cannot be fully understood if we only look at the components in isolation. Therefore, I propose that to unravel the secrets of the emergence of life on Earth and maybe even other planets, we should study the entire complex system as a whole. Complex systems can be studied with the assistance of mathematical models. A model of the origin of life could give some insight in the conditions needed for life to emerge that can be empirically tested.

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Introduction

"*An honest man, armed with all the knowledge available to us now, could only state that in some sense, the origin of life appears at the moment to be almost a miracle*" – Francis Crick (1981)

It was only a few hundred years ago when it was commonly accepted that small life forms could spontaneously generate from non-living matter. If you would, for example, put some grain or old rags in a dark corner, mice would spontaneously appear in that place as if by a miracle. However, if you like frogs more, just create a muddy spot and before you know it; it will be full of frogs. As science advanced, this theory of spontaneous generation was disproven as it became clear that these organisms would just go to those places and reproduce. Thus, the question where life came from remained unanswered and has captivated mankind for centuries. There have been countless theories and discussions on the origins of life. Then, around 70 years ago, the theory of evolution became accepted among scientists as the explanation for all changes that have transformed life on Earth from its origins up to the current diversity (Schrey et al. 2012). This theory was based on simple genetics and similarities between species and stated that all living species evolved from a common ancestor.

Upon further research, it became clear that all life shared the same biochemical properties as well. It was discovered that hereditary information was stored in DNA in all organisms (Henry et al. 2010). With the use of shared DNA, scientists were able to map out an evolutionary tree of life, all the way back to our last universal common ancestor (LUCA). LUCA was most likely a single celled organism that lived between three and four billion years ago (Poole et al. 2005). LUCA was not the first living organism that appeared on the Earth, but it is the earliest life form we could infer from shared characteristics from genomes of all known organisms (Russel & Hall 1997). We have traced life back to the first life forms, but where did these first life forms come from? Did they just appear by spontaneous generation?

It is believed that the first life forms appeared by abiogenesis, which is the process by which life has arisen from non-living matter. In particular, life is believed to have arisen from simple organic compounds which grew more complex over time by natural chemical processes (Kauffman 2011). All living systems are roughly made out of four different macromolecules: carbohydrates, lipids, proteins, and nucleic acids. Those molecules are dependent on each other to accomplish all biochemical processes associated with living systems (Rosslenbroich 2016). Scientists are researching the biomolecules and their reactions in isolation, in order to find a biomolecule that has multiple biochemical functions and could therefore start a series of events that could lead to life. However, when this molecule with multiple life-like functions is found, how does it answer the question of the emergence of LUCA?

In this essay, I will review the progress made in determining how abiogenesis can give rise to living systems. The first chapter covers the features that are necessary for living systems and how singular biomolecules could also show these characteristics. The second chapter will discuss the abiotic creation of the biomolecules and theories surrounding their possible roles in the creation of life. Lastly, I will review these theories and argue for how I think we could solve the problem of how the first living cells appeared on Earth.

Chapter 1: Identifying life

Identifying if something is alive might seem obvious and intuitive: a rock is not alive and a cat is. However, in biology and the search for the origin of life identifying the characteristics of life is not so straightforward. Life can be defined differently depending on the context and focus of study. In this chapter, I will go over general and biochemical characteristics that all living things have. These are also the characteristics that LUCA possessed. Multiple of these characteristics and biochemical reactions probably already existed in biomolecules and protocells before LUCA emerged. Therefore, after defining life, we will go over some of the characteristics of biomolecules that could indicate a pathway for the origin of the first organism.

There are some main characteristics identified that all living beings possess. First of all, living beings are structured and separated from the rest of the environment (Elani 2016). This allows living beings to maintain a constant internal environment regardless of their surroundings, or homeostasis in short. Next, living beings develop and can reproduce (Gómez-Márquez 2021). Furthermore, living beings exhibit some sort of metabolism, taking in compounds that provide them with energy to carry out the functions of a cell. Adenosine triphosphate (ATP) is the main compound that provides energy for all processes in living cells. Living systems are able to process information from the environment and respond accordingly (Cohen & Harel 2007). Finally, living things can adapt and evolve over time to external pressures (Tu & Rappel 2018). Apart from these general traits, all living beings on Earth also share the same biochemistry (Rosslenbroich 2016). They all have a cell as a unit of organization with lipids to form cell membranes. All organisms have their genetic material in the form of the same nucleic acids, and have the same building blocks for proteins that carry out functions in cells (Mistriotis 2021).

LUCA was inferred through shared genes as the starting point of our evolutionary tree. LUCA was believed to have emerged in the oceans near hydrothermal vents and to be an anaerobe (Russel & Hall 1997). Even though DNA was used to infer some characteristics and genes from LUCA, it is possible that at first LUCA had an RNA genome (Poole et al. 2005). The transitioning from an RNA genome to DNA could have happened later on, guided by certain viruses (Forterre 2002). Weiss and colleagues found through protein coding gene research that LUCA most likely inhabited a geochemically active environment rich in H_2, CO_2, and iron (Weiss et al. 2016). It is believed that LUCA used the Acetyl-CoA pathway for carbon fixation because of its chemical simplicity and the ability to release energy (Fuchs, 2011). The Acetyl-CoA pathway reduces CO_2 with hydrogen to form a methyl group and CO (Sousa & Martin 2014). The reaction is catalysed by different proteins and coenzymes and forms energy-rich chemical bonds such as thioesters (Martin & Thauer 2017) and ATP (Martin & Russel 2007). The cell membrane consisted most likely out of a mixture of lipids, which could eventually be synthesized by specific enzymes (Koga et al. 2007).

LUCA appeared most likely from a mixture of protocells with semipermeable membranes that were able to have horizontal gene transfer. The sharing of genes in these protocells allowed them to gain more abilities in metabolism and reproduction, until they eventually became the first fully realized cells (Glansdorf et al. 2008) capable of growth, adaptation, reproduction, and metabolism. There are still many controversies surrounding LUCA: was it a fully formed organism or was it still evolving the relations between genotype and phenotype, was it a prokaryote or protoeukaryote, was it thermophilic or mesophilic? Many of these questions remain unanswered (Glansdorff et al. 2008). On the other hand, what we do know is that LUCA had a range of different biomolecules all having their respective functions. These biomolecules must have appeared first through abiogenesis and already showed some functions that are similar to their functions in living systems. In order to discover how LUCA emerged, researchers have been looking for biochemicals and their interactions that could explain how life emerged.

There are four main biomolecules identified that life seems to be based around: nucleic acids, peptides, lipids, and carbohydrates. Simple molecules that were thought to have been present on early Earth were water, methane, ammonia, nitrogen, oxygen, formaldehyde, benzene, and carbon dioxide (Bernstein 2006). Experiments trying to simulate the conditions of the early Earth were successful in forming simple biomolecules, amino acids (Martin et al. 2007), and nucleic acids (Parker et al. 2014). Furthermore, amino acids (Koga & Naraoka 2017), nucleic bases (Krishnamurthy et al. 2022), and even carbohydrates have also been found to be present in carbon rich meteorites (Pizzarello et al. 2010), suggesting that the first precursors for biomolecules could have also come from space, similar to the belief that meteorites were the main source of all water now present on Earth.

There are four important properties molecules can have that can be described as properties of life. The first one is self-replication, which is the ability of a molecule to catalyse the formation of copies of itself (Sadownik et al. 2016). Next is the ability to catalyse the compounds it needs to replicate and to harness energy from external sources, or metabolism (Fani & Fondi 2009). Third is compartmentalization, which is the mechanisms by which the system prevents its contents from spreading into the environment (Keating 2012). Last, is adaptability, which is the ability of a system to grow and/or evolve over time. These characteristics present a minimal form of life. There has been progress on developing systems of biomolecules that exhibit some of these characteristics. Self-replicating molecules have been found and produced in vitro (Clixby & Twyman 2016). Moreover, scientists determined distinctive chemical and evolutionary routes for biochemicals to increase in size, gain more catalytic capabilities, and expand metabolic pathways, which could be seen as an increase in complexity (Kosikova & Philp 2017). Thereafter, the aim was to develop systems that would show more than one of the characteristics, such as replication and metabolism (Arsène et al. 2018). Despite the scientific progress made, we still have not found the pathway for the emergence of life. To do that, we should find systems of biomolecules that exhibit all these characteristics at the same time. The next chapter will take a deeper look at the four main biomolecules of life, to get a better understanding of their functions and characteristics.

Chapter 2: The four building blocks of life

It is believed that the four building blocks of life were abiotically formed in the early Earth from simple molecules, which formed monomers for all the biomolecules (Rotelli et al. 2016). It is still a bit unclear how exactly the monomers formed into polymers because the precursors and monomers did most likely not exist in high concentrations in the primordial soup (Sharov 2016). However, the polymers are generally more stable molecules than monomers, and this difference in stability might have stimulated the composition of probiotic macromolecules (Yakhnin 2013). The constant formation of polymers and decomposition of less stable polymers could eventually have resulted in polymers that could replicate and metabolise. This chapter will discuss the functions and theories of the important molecules of life for the emergence of the first living systems.

Paragraph 1: Peptides

we'll start with one of the most biochemically active biomolecules, peptides. Nowadays, proteins have countless functions and are essential for sustaining life, participating in almost all reactions in the cell. They provide structure and organisation in cells and are involved in DNA transcription and cell division. Proteins can transport molecules across cell membranes and within the cell, as well as throughout the entire body. Proteins are necessary for muscle contraction and other movements, they are a huge part of the immune system, and are the primary components in metabolism (Sleator 2012). In short, practically all processes in living systems involve proteins. Therefore, some scientists believe that proteins could have also played an important part in the early stages of the development of life. The "protein world" hypothesis takes this even further, suggesting that all life began around small peptides that formed a system of interactions and were also able to self-reproduce (Andras et al. 2005). This paragraph will discuss the formation and early interactions of proteins.

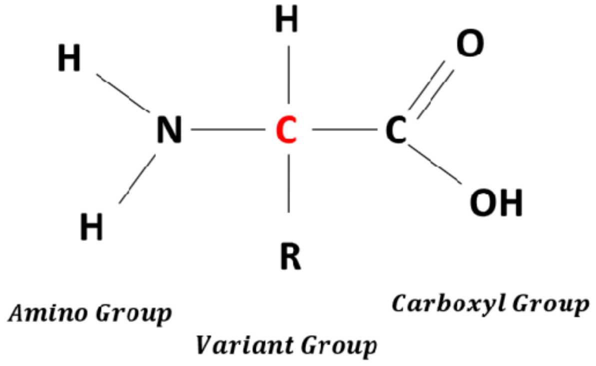

Figure 1: structure of an amino acid, around the central carbon (red) are an amino group, carboxyl group, and a group that varies between amino acids (R) (Aouniti et al. 2017).

All proteins in living systems today are polymers composed of 20 different amino acids. Amino acids are a basic organic molecule, made out of a central carbon to which an amino group, a carboxyl group, and a unique side chain are attached (Figure 1). The unique side chain gives the different amino acids their specific chemical properties and allows for different reactions with other molecules. There have been multiple experimental studies demonstrating the abiotic formation of multiple amino acids (Ménez et al. 2018, Takeuchi 2020). There have even been many different amino acids found in meteorites (Pizarello et al. 2010), suggesting that the building blocks for peptides were present on the early Earth and could have formed the first functional peptides.

Proteins are well known for their catalytic properties and metabolic functions. Most enzymes today are long polymers but that is not what scientists believe primitive peptides looked like. They propose that early peptides were only 3 to 8 amino acids long and consisted of only four amino acids; Gly, Ala, Val, and Asp (van der Gulik et al. 2009), because they were produced in abundance in experiments forming amino acids and were reported in meteorites (Ikehara 2014). Those early peptides could have promoted the catalysation of other early amino acids (Tretyachenko et al. 2022).

The problem with the peptides first hypothesis of life is that generally the proteins that are present in living systems today cannot replicate themselves. Therefore, scientists searched for mechanisms of self-replication for protein structures. One such peptide replication mechanism that has been shown to exist is by fibre elongation and breakage (Otto 2022). Otto and colleagues designed short peptides with amino acids alternating between hydrophilic and hydrophobic. These peptide chains were able to form beta sheets with each other, forming a cyclic structure that could be stacked on top of each other (Colomb-Delsuc et al. 2015). The process of stacking the molecules stimulates the synthesis of more of the peptide structures (Figure 2). The stacked formations can grow and form long fibres, which when agitated can break apart, forming more additional stacks that promote growth (Carnall et al. 2010). This enables the growth and replication of the molecules that make up the fibres, forming a pathway for proteins to replicate. These proteins can start to show evolutionary dynamics when starting with a mixture of peptides (Otto 2022).

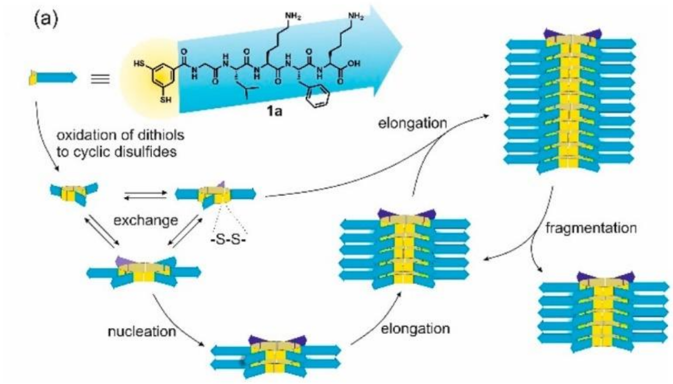

Figure 2: Schematic presentation of the mechanism by which self-assembly can drive self-replication in peptides (Otto 2022).

In conclusion, peptides have many catalytic functions and the first proteins could have eventually synthesized oligonucleotides and other biomolecules starting a pathway for the emergence of life. The system of elongating and breaking peptide fibres shows that peptides can also have the ability to self-replicate. Therefore, proteins could have multiple of the identified life-like characteristics. However, there are still some criticisms to this narrative of the origin of life. For example, proteins have limits to their catalytic abilities and often need assistance from cofactors (Bernhardt 2012). Furthermore, the discovered mechanisms of self-replication for protein structures are nothing like the mechanisms used in living systems today.

Paragraph 2: Carbohydrates

Nowadays, carbohydrates are mainly used as a source of energy in living systems. Carbohydrates are built from chains of sugar molecules, those chains can be short or long (Holesh et al. 2022). Sugars are one of the most common organic substances in nature and also one of the simplest biomolecules only containing carbon, hydrogen, and oxygen. Furthermore, sugars are involved in many reactions in the cell and are an important building block of nucleic acids, glycoproteins, glycolipids, ATP, and other coenzymes. In organisms today, sugars are mostly made by autotrophic organisms, during chemo-and photosynthesis.

In organic chemistry, sugars can be easily synthesised in an aqueous solution of formaldehyde, glycolaldehyde and a base as catalyst (Lamour et al 2019). Different bases can yield different kinds of sugars, including the sugars needed to form DNA and RNA (Steer et al. 2017). These sugars were formed in an aqueous solution suggesting that sugars can be abiotically created within the primordial soup. Additionally, NASA scientists actually discovered ribose, arabinose, and xylose in two different meteorites rich in carbon (Furukawa et al. 2019), and scientists replicated the processes needed to form these sugars on meteorites (Haas et al. 2020). All three discovered sugars can be found in biological life, and ribose is a crucial component of RNA. The extra-terrestrial sugars from meteorites together with sugars formed on earth could have contributed to the formation of RNA and other important biomolecules (Marcellus et al 2015).

In conclusion, sugars are an important source of energy and form building blocks for other biomolecules. A mixture of different sugars can be easily formed under abiotic circumstances. Therefore, it is probable that sugars existed in a pre-biotic environment (Nuevo et al. 2017). However, sugars are incapable of self-replication and cannot by themselves catalyse reactions. Therefore, sugars on their own are not capable of exhibiting life-like characteristics and are probably not the molecules that started life, but might be a component of the mixture of molecules that started life and had life-like functions.

Paragraph 3: Nucleic acids

Nucleic acids are large molecules that have an essential role in all living systems. The major function of nucleic acids today covers the storage and expression of heritable information. RNA can do more than store information; it can also catalyse reactions. This duality in the nature of RNA has many scientists convinced that life is based around the RNA molecule. The “RNA world” hypothesis is probably one of the most extensively studied pathways towards life and has gained some strong evidence (Robertson & Joyce 2012). This paragraph will look deeper into the formation and functions of RNA.

RNA is roughly made out of three separate building blocks, a nucleobase (adenine, cytosine, uracil, and guanine), a ribose sugar, and a phosphate (Figure 3a). Research suggests that cytosine and uracil could be formed by reactions of cyanoacetylene with cyanate (Robertson et al. 1995). The nucleobase adenine has also been found to be present in meteorites (Krishnamurthy et al. 2022). The three ingredients together can react to form a nucleotide (Biscans 2018). Alternative routes for the synthesis of nucleotides (Figure 3b) have also been proposed where the sugars and nucleobases are formed during

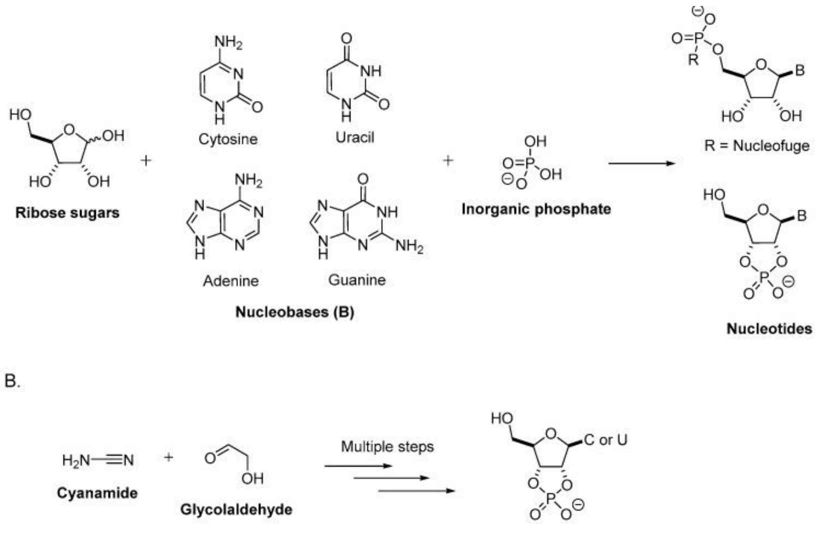

Figure 3: Schematic representation of the formation of nucleotides. A. production of nucleotides from a sugar and base. B. alternative route that uses cyanamide and glycolaldehyde (Biscans 2018).

the same process. Afterwards it can react with an inorganic phosphate to form a nucleotide (Anastasi et al. 2006).

The four different nucleotides can link together and form different RNA sequences (Kim et al. 2020). In a relatively cold environment, an RNA sequence can base pair with itself, forming an unique and sometimes complex shape. Outward facing bases that did not attach to itself can react with molecules in the environment catalysing reactions between them (Yokobayashi et al. 2020). A folded chain of RNA that can guide a specific chemical reaction is called a ribozyme. Functional ribozymes are generally considered to be long complex RNA sequences; however, they can also be as short as a few nucleotides (Vlassov et al. 2005). A strand of RNA can be replicated in a heating-cooling cycle, when free nucleotides are available. After each heating and cooling cycle, every other produced string will be a copy of the original. However, this process is not perfect and random mutations will occur, altering the sequence of the RNA strand. This means that a strand of RNA can reproduce and evolve on its own (Neveu et al. 2013). The function of a ribozyme is determined by the sequence associated with it, therefore if the sequence changes, the shape and function of the ribozyme will change as well. Research found that when RNA strands are replicated in a controlled environment, they will mutate and some of them gained catalytic properties that further evolved to be even more efficient (Popovic et al. 2021). One of these reactions was catalysing the reaction to make new nucleotides, therefore these RNA molecules have the ability to actively benefit their replication by forming more parts of itself (Arriola et al 2020). This suggests, that RNA can evolve and catalyse reactions beneficial for their own replication.

In conclusion, RNA molecules are able to have three out of the four characteristics of molecules that could indicate a pathway of life. These are the ability to replicate and mutate, to catalyse reactions in order to form the molecules it needs to grow and replicate. This makes the "RNA world" hypothesis quite plausible, but like all great theories there are some difficulties with this narrative of the origin of life. One of the problems is the notion that a large RNA molecule might be too complex of a molecule to have appeared in a prebiotic environment (Bernhardt 2012). In vitro studies of RNA have not yet achieved self-sustained RNA replication and transcription. Therefore, it has been suggested that RNA does not have the catalytic ability to sustain the RNA world (Le Vay et al. 2019). Thus, the hypothesis that RNA started all life seems plausible but is still incomplete.

Paragraph 4: Coenzymes

Proteins and RNA are reactive molecules that are able to replicate and catalyse reactions, and they are also both essential components of living systems. Therefore, scientists have hypothesized that life originated around either one of these molecules. However, a big criticism for both proteins and RNA is that they are large complex molecules that are quite unlikely to appear spontaneously in an abiotic environment (Bernhardt 2012). Thus, it seems more likely that at first there were smaller molecules that could catalyse metabolic reactions and eventually could produce the larger polymers we are familiar with. Within cells, most metabolic reactions need energy to function properly. Energy is transferred through adenosine triphosphate (ATP). ATP and other coenzymes assist enzymes to catalyse reactions more effectively, and many enzymes won't even function at all without coenzymes (Kirschning 2021). Even though coenzymes are not one of the four building blocks, they are essential to life and will therefore also be discussed.

ATP and nicotinamide adenine dinucleotide (NAD) are probably the most important coenzymes for energy transduction. NAD and other coenzymes have similar compositions, based on nucleotides. ATP is the smallest one and is a precursor to an RNA nucleotide, consisting of an adenine base attached to a ribose, which is attached to a triphosphate group (Figure 4). NAD is quite similar but is made out of two nucleotides that are bound together by their phosphate groups (Yadav et al. 2020). Because ATP is a building block of RNA, it can be abiotically synthesized during the same processes as nucleotides. NAD and other more complicated nucleotide-based coenzymes could have also formed in an early primitive metabolism before other polymers existed (Pinna et al. 2022).

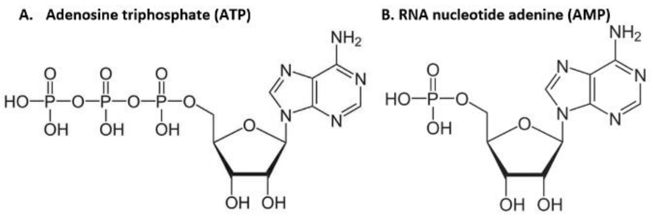

Figure 4: Comparison of the molecular structure of ATP (A) and (B) the RNA nucleotide for adenine also known as AMP.

The “coenzyme world” theory proposes that ATP and other nucleotide containing cofactors were at first the cofactors of ribozymes, before proteins replaced RNA as enzymes (Kirschning 2021). On the other hand, ATP and other cofactors were found to appear in many protein structures, suggesting primitive interactions with proteins (Sharov 2016). ATP is also known to increase concentrations of biomolecules in distinct locations within cells, thereby compartmentalising specific processes to one area (Guilhas et al. 2020). Furthermore, ATP assists the folding of proteins, which makes proteins more resistant to degradation and more likely to be functional. Therefore, it has been proposed that the most primitive proteins might have been selected and folded by nucleotide containing cofactors (Chu et al. 2022).

In conclusion, ATP and other cofactors are small biomolecules that have crucial functions in living systems. These functions are closely associated with both RNA and proteins, implying that ATP and other cofactors might have had critical roles in the emergence of life even before the emergence of peptides and RNA. However, the exact roles they played on the primitive Earth are still largely unresolved.

Paragraph 5: Lipids

Lastly, we’ll discuss the formation and biological importance of lipids. Lipids are a broad group of hydrophobic molecules including fatty acids, waxes, some vitamins, sterols, glycerides, and phospholipids. Triglycerides are used in energy storage in vertebrates. Phospholipids are essential parts of cell membranes and are involved in cell signalling, enzymatic reactions, and metabolism (Subbotin et al. 2022). Because lipids are the main component of cell membranes and are able to form membranous compartments in aqueous solutions, they are believed to be fundamental for the formation of compartmentalisation in early life forms. According to the “lipid world” hypothesis, the first process that happened in the emergence of life was the formation of liposomes, which are spherical vesicles that are made from lipid bilayers (Lancet et al. 2019).

The main components of cell membranes are amphiphilic lipids, meaning that they have a polar head and a non-polar hydrocarbon chain, in aqueous solutions the non-polar tails will attract each other and form membranous structures. In modern cells, the membranes are made out of phospholipids, these have a glycerol-phosphate group with two fatty acid chains attached that are anywhere between 14 and 24 carbon atoms long (Alberts et al. 2002). Because the phospholipids today are large molecules that need energy to be produced, it is believed that the first formed protocells were made out of a mixture of different, simpler amphiphilic lipids that could be formed more easily (Figure 5; Fiore et al. 2022). Short chain fatty acids have been detected in meteorites and could have been a precursor for the lipids in cell membranes (Lai et al. 2018).

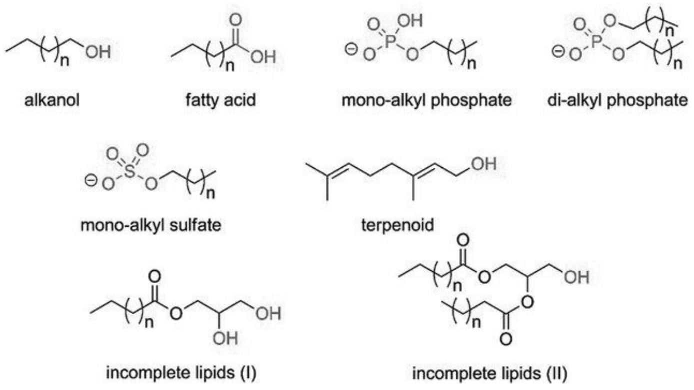

Figure 5: Plausible prebiotic lipid structures (Fiore et al. 2022)

Since phospholipids are amphiphilic, they are able to naturally form a structure in an aqueous environment, such as liposomes or membranes. Therefore, the emergence of lipid bilayer vesicles could have happened naturally (Deamer 2017). The "lipid world" hypothesis explains that during the formation of the liposomes they will encapsulate random molecules, which under damaging UV radiation could have started some sort of metabolism and growth in some of the liposomes (Subbotin et al 2022). However, lipids themselves cannot replicate by themselves or catalyse reactions, their main function appears to be in the compartmentalisation of life (Monnard et al. 2015). I think the process of the formation of liposomes that encapsulate molecules could have happened at any moment during the formation of life, encapsulating precursors to biomolecules or even entire metabolic pathways.

Chapter 3: The formation of life

In the last chapter, we confirmed that all of the biomolecules could be abiotically created. Furthermore, we discussed four theories around some of these biomolecules that could be a plausible pathway for the origin of life. All of those theories had some evidence and showed a credible route for the origin of life. In this chapter, I will discuss what I believe would be the most plausible theory in the origin. We will discuss more of the criticism for each theory and find out why I think neither one of these theories can be the correct one. Thereafter, I will introduce a new way of resolving the origin of life and argue for why I think this method would yield the most accurate results.

Starting off with the most researched theory, which has the most evidence backing it, the RNA world hypothesis. Most of the criticism of the "RNA world" hypothesis also holds true for the "peptide world" hypothesis (Bernhardt 2012). These are the criticisms that RNA and peptides are large and complicated molecules that would probably need assistance from other biomolecules to be created and that their catalytic properties are limited (Le Vay et al. 2019). Therefore, we looked at the "coenzyme world" hypothesis, because coenzymes are smaller molecules. They assist proteins to fold and catalyse reactions, and they are precursors for RNA (Chu et al. 2022). Because of this relationship, the coenzyme world theory could be connected to the "RNA-peptide world" hypothesis. The "RNA-peptide world" discusses the interactions between RNA and peptides and the early formation of transfer RNA, from which ribosomal peptide synthesis may have emerged (Müller et al. 2022). As coenzymes are nucleotide based and interact with proteins, it only seems logical that they also existed in the hypothetical "RNA-peptide world" and catalysed reactions between them. Lastly, the "lipid world" hypothesis explains mostly how early liposomes were formed. I don't think that the formation of liposomes were the very first processes of life. Cell membranes also contain proteins that mediate fundamental processes between the outside and inside of the cell (Overduin et al. 2019). Therefore, it would be more logical that there had already been some sort of early membrane protein before the lipid bilayer membrane was created.

All of the discussed theories have evidence that describe accurate biochemical reactions. Furthermore, there have even been experiments conducted investigating the biochemical reactions and the origin of life. None of them were actually successful in creating life itself but these did prove that biomolecules could be abiotically created and interacted with other molecules (Takeuchi 2020, Haas et al. 2020). Just like in the experiments, all of the individual theories fail to describe how LUCA actually emerged after the formation and reactions of their investigated biomolecules and pathways. All of these theories are mostly fixated on a specific molecule or specific process within the origin of life, while LUCA is a combination of all biomolecules and chemical processes that happened. On top of that, they present linear and simplified pathways. Therefore, I believe that none of these theories on their own could provide a plausible pathway for the origin of life.

So, if none of the theories work on their own, can we not just combine them to form a more complete picture? Well yes, but actually no. If we just combine them, we would get many starting molecules that would do their own thing. It would still be a theory were all the biomolecules exist in isolation and do not investigate the interactions between them. Additionally, we would still get a linear pathway for the emergence of life. Therefore, simply combining the theories would be problematic as well. The emergence of life is more than just the sum of all the parts needed for life. It is about the many different parts and their disordered reactions in a non-equilibrium state that give rise to feedback systems, order, and self-organization. Therefore, I do wholly believe that life arose as a result of a complex system and could be better understood through a systems theory perspective. Systems theory is an interdisciplinary theoretical perspective that studies complex systems. It is based around the principle that complex systems can be best understood in context of the relationships between the components and other systems, instead of analysing all components in isolation (Gibson 2013).

Complex systems are everywhere around us: each individual cell in your body, the brain, every organism as a whole, a colony of ants, entire ecosystems, the climate, the universe, cities, economics, and the internet are all examples of complex systems (Mitchell 2011). A complex system is built out of large collections of simpler components with simpler interactions, but can give rise to complexity. Take for example the colony of ants: they are able to interact with the environment as a whole and build large structures, maintain nests, grow fungi, and even farm aphids. This is collective behaviour that arises as a result of the interactions and feedback between them, not because of a leader that controls them. Every singular ant follows the same set of rules from which these complex behaviours will arise. When isolating one ant or even a group of a hundred, they will just wander around aimlessly. Only in a colony are they able to act like a single organism and interact accordingly with the environment. Therefore, the complex behaviour of the ant colony can only be studied when looking at the entire colony as a whole and not by only studying single ants.

The exact definition of a complex system is still being debated, some of the characteristics they can have are: they are mostly disordered and diverse, have numerous components, are in a non-equilibrium state, are robust, have feedback loops, can spontaneously give rise to order and self-organization, and are non-linear (Ladyman & Wiesner 2020). They can even have history and memory as well as adaptive behaviour in some cases. They have proven themselves to be a fundamental part of the world and are already addressing important problems in medicine and engineering (Alexander et al. 2020), for example, how pandemics develop and spread. Mathematical models are a tool to understand these complex systems and to make testable predictions, such as predictions about the weather (Pessoa 2021).

The emergence of life in early Earth conditions has many of the characteristics of complex systems. For this reason, I think we should approach the origin of life as a complex system. Therefore, the theories that only investigate a single molecule or process are not enough to get a complete understanding of the origin of life. Those theories and experiments are still important, as their discoveries are still essential in understanding the origin. The important parts of these theories are the underlying concepts and mechanisms that they are built around. If we could combine those interactions, with the conditions on the early Earth and the basic principles of chemical reactions in a mathematical model, we might gain more insight on the origin of life.

A mathematical model can be easily tweaked, to for example start with slightly different conditions and molecules. It could therefore be easier to theoretically determine what the ingredients, conditions, and reactions were on the early Earth and find out where on Earth life originated. It could even tell us if there is more than one pathway for the emergence of life. Furthermore, once life has been modelled, it can be confirmed by experimentally recreating the conditions shown in the model. I think this would be more efficient than scientists trying different methods and conditions in vitro, because the conditions in these experiments are mostly educated guesses on what the early environment on Earth was like. On top of that, the emergence of life could have happened over millions of years, and most scientists do not have the time to do experiments lasting that long. Thus, I think to get the most plausible pathway for the origin of life, we have to approach it as a complex system and make a mathematical model. Thereafter, we could recreate the conditions and confirm experimentally if it works.

Conclusion

"I think the next [21st] century will be the century of complexity. We have already discovered the basic laws that govern matter and understand all the normal situations. We don't know how the laws fit together, and what happens under extreme conditions. But I expect we will find a complete unified theory sometime this century. There is no limit to the complexity that we can build using those basic laws." — Stephen Hawking

One of the greatest challenges in evolutionary biology is probably understanding the origin of life. There have been countless theories addressing this problem. In this essay, I set out to find the best theory to this age-old problem, by critically looking at what life is and at different theories that surround the origin. I was expecting that by discussing the theories, I would determine which one was the most likely, and could answer the question with a scenario on how it most likely happened. What I found was quite the opposite: all of the theories seemed to be simplified pathways and would therefore not show the complete answer to the origin. The investigated pathways in the theories only show a small part of the entirety of the processes that happened.

I realised that the origin of life itself appears to be a complex system, just like every living system in the universe. Traditional approaches used to explain complex systems were to reduce it into smaller components. However, these approaches can fail in connecting the different parts and can lead to oversimplification (Ladyman & Wiesner 2020). For that reason, I think the best way to approach the problem of the origin is to investigate the complex system as a whole. Combining the different concepts and mechanisms discovered to build a realistic model for the origin of life. A model could investigate the many diverse microenvironments and the chemical possibilities that existed on the early Earth quicker than any experimental method.

Modelling the origin of life would be an immense challenge that could take decades. It requires a multidisciplinary approach that takes us beyond the boundaries of scientific disciplines. Therefore, I believe that such a huge task could only be completed by a multidisciplinary team of specialists, multidisciplinary scientists and innovative thinkers. Once completed and tested in experiments, the model for the origin of life could be one of the greatest accomplishments in science. Besides giving us a plausible pathway for the origin of life, the model could give us more insight on the conditions of early Earth, pathways that are a dead end, and the timescale it all happened on. More importantly, the model could help us to determine if there is other life in the universe and how we could find it. It could give us a range of different conditions that could be viable for life to emerge and what signatures to look for, which could help us narrow down the search for planets that could have life and maybe even verify if life ever existed on Mars. The universe is expanding and some places might already be forever out of reach. Unravelling the secrets of the origin of life would increase our chances of finding other life in places we can still reach, or we might finally come to the conclusion that we are all alone.

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