The quest to unravel the mysteries surrounding life’s origin continues to captivate scientists. In fact, the central question revolves around how an abiotically formed mixture of non-living chemicals (no-life) gave rise to the early self-reproducing and evolving living cells, called protocells (lipid). In simpler terms, the question is: what bridged no-life to life? Alexander Oparin’s book, The Origin of Life, pioneered a scientific approach to these questions; yet, 100 years later, scientists are still grappling with the profound question of how life, with its remarkable ability to replicate and evolve, emerged from the chaotic mix of chemical compounds on our early planet.

THE ABOGENESIS CONUNDRUM
The central debate in this field of abiogenesis is the study of how life could have arisen spontaneously and naturally from non-living substances. The popular answer revolves around two major complementary lines of study: one focuses on the prebiotic synthesis of life-like small molecules, and the other centres on the prebiotic synthesis of RNA, a complex molecule believed to have the capacity for self-replication. However, there is currently an unbridged chasm between a mixture of numerous scattered organic compounds, large and small, and the formation of the first reproducing protocells.

To resolve this problem, we need spontaneously formed containers. It is widely accepted that key molecules capable of forming such containers are lipid molecules. Such amphiphilic assemblies can gather specific molecules from the complex mix of chemicals around them. But there is another challenging aspect to this: figuring out how these early assemblies could make copies of themselves, in the case of vesicles, including both the outer lipid shell and the chemical content inside. Two decades ago, Professor Doron Lancet from the Weizmann Institute of Science, Israel, and colleagues began the unravelling of this enigma.

THE LIPID SALVATION
In living cells today, there are four main classes of small organic molecules: amino acids (building blocks of proteins), nucleobases (building blocks of DNA and RNA), sugars, and lipids. It is only lipids that can readily form labile (easily breakable) multi-molecular ensembles, such as the membranes surrounding cells and protocols as well as the much smaller micelle particles, which are known to be simple efficacious chemical factories, competing with present-life complex proteins. Primordial lipid ensembles thus provide both compartmentalisation and chemical specificity that might lead to self-replicative lipid protocells. The reason lipids can perform such marvels is their amphiphilic nature; they consist of two parts: water-attracting heads and water-repelling tails. This laid the foundation for Lancet’s ‘lipid first’ alternative for the famous ‘RNA first’ argument.

THE ROLE OF LIPID MICELLES
A novel perspective in the research on the origin of life has thus ushered in a paradigm shift. Rather than exclusively focusing on the study of how certain molecules might have formed before life existed, scientists are now exploring how simple lipid molecules, copiously present in ancient oceans, could have autonomously come together.

Catalysed accretion

Scientists are now exploring how simple lipid molecules, copiously present in ancient oceans, could have autonomously come together. However, this organisation is not in terms of spatial position or order of amino acids as in a protein. Instead, the organisation is expressed in terms of composition. In a simplified example, imagine an environment in which all types of lipids have the same concentration. Upon micelle growth driven by molecule accretion, the network dynamics are capable of biasing their lipid composition would remain stable as they get bigger. This is called ‘homeostatic growth’; another capability of reproducing living cells. When these entities split into two, the offspring are very similar to each other, just like when living cells reproduce. One of the most important findings of the research is that the catalytic networks within lipid micelles (a team of molecules working together, where certain molecules speed up the entry of some others) might have enabled self-reproduction, meaning micelles could reproduce themselves by a mechanism analogous to metabolism in living cells (Figure 2) (Lancet, D., Zidovetzki, R., Markovich, O., 2018).

THE GRADED AUTOCATALYSIS REPLICATION DOMAIN (GARD) MODEL
Over the span of 20 years, Lancet and his team developed the Graded Autocatalysis Replication Domain (GARD) model – a computational chemistry approach that simulates the chemical reactions and processes that could have occurred in the prebiotic era. The GARD model builds upon the earlier foundations of the Collectively Autocatalytic Set (CAS) model (Kauffman, SA, 1986), which predicts that catalytic networks may give rise to self-reproduction. GARD adds quantitative layers to CAS, providing a chemical kinetics understanding of how complex mutual catalysis can lead to self-reproduction.
The team highlights that the transition from non-life to life involved chemical entities that possessed catalytic properties, which can lead to self-reproduction. These capabilities are considered crucial steps in the emergence of life because they set the stage for the development of more complex, organised, and self-sustaining systems, all having catalysis as their foundation, eventually leading to what we recognise as living organisms. The team developed a model for reproduction at life’s origin via spontaneous selective clustering of small lipid molecules in the prebiotic environment.

The GARD model represents a crucial advancement in the study of life’s origin. Its simulations predict the dynamic behaviour as described above, which leads to a reproduction point, termed ‘composome’ (Figure 2). GARD demonstrates the feasibility of self-replication much before the advent of utterly complex molecules such as DNA and RNA, as well as catalysis ahead of complex proteins. This opens new avenues for exploring the emergence of life-like behaviour at very early stages.

Experimental findings published over the last few years, as summarised (Kahana, A, Lancet, D, 2021), strengthen the foundation of the GARD model and emphasise the plausibility of early emergence of life-like networks. They bridge the gap between primordial soup and early protocols as described in empirical observations, bringing us closer to understanding the origins of life on Earth. Significantly, GARD simulations also predict that the reproducing point would be reached much more readily than expected, because that point is a dynamic attractor, a state toward which a network tends to progress (Kahana, A, Maslov, S, Lancet, D, 2021). GARD simulations predict the dynamic journey of how life began, but also suggest the potential for a shift from simple micellar protocols to more complex vesicular counterparts. They point out that it is possible to envisage the chemical steps that would lead to new functionalities, including metabolic-like syntheses of new metabolites, vesicular membrane transporters, as well as RNA and its translation device (Kahana, A, Lancet, D, 2021).

CHARTING NEW HORIZONS

The GARD model, as described by Lancet, provides the dynamic journey from simple lipid micelles to complex protocols, offering new insights into how life may have originated and evolved on Earth. It highlights the significance of locally available compounds coming together to form complex, life-like entities. Lancet and his team not only provide a novel understanding but also open up new avenues for research in the domain.

Bio

Professor Doron Lancet completed his BSc degree in biology at Ben-Gurion University, and his MSc and PhD on the GARD origin of life model with Professor Doron Lancet at the Weizmann Institute of Science, both in Israel. He is now studying for his PhD in chemistry at the University of Glasgow, UK in the laboratory of Professor Lee Cronin. The main focus of his current research is the origin of life and assembly theory for mapping chemical complexity space.

Research Objectives

The team developed a model for reproduction at life’s origin via spontaneous selective clustering of small lipid molecules in the primordial environment.

References

- Segre, D, Lancet, D, 2005b, Evolvability of life (EMBO reports, 10), 217-222. doi.org/10.1038/sj.embo.7400007

Personal Response

What do you believe are the most promising implications of your research on the origins of life for our understanding of life’s emergence on Earth and potentially, elsewhere in the Universe?

Our research provides a rigorous chemical framework that constitutes a complete path from simple chemistry to bacterial complexity. We demonstrated that spontaneously formed amphiphilic assemblies, initially nanoscopic micelles, will naturally undergo chemical catalytic modifications, leading to self-reproduction. This generates a population with some mutations (quasi-species) that can undergo natural selection and therefore, portray early Darwinian evolution. Along this path, micelles can evolve into more elaborate vesicular protocols that can endogenously synthesise new and larger molecules, leading to self-reproduction. This opens a new avenue for exploring the emergence of life-like behaviour at very early stages.