

Proto-Neurons from Abiotic Polypeptides

Subjects: Biology

Contributor: Panagiotis Mougkogiannis, Andrew Adamatzky

To understand the origins of life, we must first gain a grasp of the unresolved emergence of the first informational polymers and cell-like assemblies that developed into living systems. Heating amino acid mixtures to their boiling point produces thermal proteins that self-assemble into membrane-bound protocells, offering a compelling abiogenic route for forming polypeptides. Recent research has revealed the presence of electrical excitability and signal processing capacities in proteinoids, indicating the possibility of primitive cognitive functions and problem-solving capabilities. This review examines the characteristics exhibited by proteinoids, including electrical activity and self-assembly properties, exploring the possible roles of such polypeptides under prebiotic conditions in the emergence of early biomolecular complexity. Experiments showcasing the possibility of unconventional computing with proteinoids as well as modelling proteinoid assemblies into synthetic proto-brains are given. Proteinoids' robust abiogenic production, biomimetic features, and computational capability shed light on potential phases in the evolution of polypeptides and primitive life from the primordial environment.

Keywords: proteinoids ; origin of life ; proteins

In this review article, the aim is to offer a thorough summary of the existing research on proteinoids, while also sharing significant experimental advances from the laboratory that contribute to the current knowledge. The article will explore the history of prebiotic chemistry experiments on abiotic polypeptide formation and self-assembly, investigate the proposed evolutionary mechanisms, and analyze the structure and function of these proto-biopolymers. The analysis will cover experimental findings on proteinoids assembly, structure, and excitability dynamics, examining emerging activity patterns including electrical signaling exhibited by these thermal polypeptide systems.

Thermodynamic Perspectives on Life's Origins

The concept of non-equilibrium thermodynamics provides a framework for understanding how life may have originated from abiotic chemical processes ^{[1][2][3][4]}. Sidney Fox's groundbreaking research showcased the spontaneous formation of proteinoids and protocells in thermal environments, providing valuable evidence for the dissipative models of biogenesis ^[5]. Using thermal polymerisation of amino acids to produce protein-like microspheres capable of catalysis, signalling, and self-assembly, Fox's proteinoids mimic the characteristics of living cells ^[5]. According to the theory of non-equilibrium thermodynamics, life originated as a dissipative structure that was far from equilibrium and was driven by the absorption of solar photons ^[6]. Proteinoids are in line with this perspective because their synthesis involves using thermal energy to produce organised biomolecular systems. The protocells that have been proposed function as photon absorbers, thereby increasing the production of entropy. Proteinoids offer a thermodynamically feasible pathway to cellular structures that are compatible with life, taking advantage of non-equilibrium conditions. Although there are still unanswered questions regarding the environmental conditions necessary for protocell development, Fox's proteinoids provide a conceptual demonstration of how lifelike entities can spontaneously self-organize under thermodynamic forces. The thermal production of proto-biopolymers and the subsequent assembly of protocells demonstrate possible mechanisms that connect equilibrium and living states.

Requirements for Early Biomolecular Systems

Our understanding of the transition from prebiotic chemistry to organised, functional biomolecular systems capable of evolution is rapidly advancing ^{[7][8][9][10]} but still limited. There are likely several key requirements that need to be fulfilled. First, the ability to encode information into reproducible polymer sequences would have been essential ^[11]. The RNA world hypothesis suggests that RNA was the initial informational polymer ^{[12][13][14]}. However, there are still uncertainties surrounding the abiotic synthesis of RNA. Moreover, the presence of membranes would have facilitated compartmentalisation, creating specific locations for reactions to occur and enabling selective permeability ^[15]. Amphiphilic molecules, such as lipids, possess the capacity to self-assemble and form vesicles that encapsulate other molecules. Moreover, it is likely that thermodynamic forces played a crucial role in driving the self-organisation of networks that became progressively more complex. Energy could have been supplied by geological and chemical gradients, while

molecular assembly may have been facilitated by inorganic mineral surfaces. According to Pross and Pascal ^[16], the presence of primitive molecular recognition, catalysis, and feedback mechanisms would have allowed for the development of basic metabolism, responsiveness, and growth dynamics. The thermal proteinoids concept developed by Sidney Fox effectively meets several of these criteria ^[5]. The process of polymerisation from amino acids, followed by self-assembly into membrane-bound protocells, and the resulting lifelike chemical properties provide valuable insights into the formation and functioning of the earliest peptide-based biomolecular systems ^{[11][16][17][18]}. The upcoming sections will discuss proteinoids as models for the abiotic polypeptides that could have formed the informational and compartmental infrastructure of early life.

References

1. Pascal, R.; Pross, A.; Sutherland, J.D. Towards an evolutionary theory of the origin of life based on kinetics and thermodynamics. *Open Biol.* 2013, 3, 130156.
2. Bartlett, S.J.; Beckett, P. Probing complexity: Thermodynamics and computational mechanics approaches to origins studies. *Interface Focus* 2019, 9, 20190058.
3. Liang, S.; De Los Rios, P.; Busiello, D.M. Non-Equilibrium Chemical Reactions Under Non-Isothermal Conditions: Kinetic Stabilization, Selection and Thermophoresis. Master's Thesis, Section of Physics, École Polytechnique Fédérale de Lausanne, Lausanne, Switzerland, 2020.
4. Kleidon, A.; Lorenz, R.D. Non-Equilibrium Thermodynamics and the Production of Entropy: Life, Earth, and Beyond; Springer Science & Business Media: Berlin/Heidelberg, Germany, 2004.
5. Fox, S.W. Thermodynamic perspectives and the origin of life. In *Quantum Statistical Mechanics in the Natural Sciences: A Volume Dedicated to Lars Onsager on the Occasion of his Seventieth Birthday*; Springer: Boston, MA, USA, 1974; pp. 119–142.
6. Michaelian, K. Non-equilibrium thermodynamic foundations of the origin of life. *Foundations* 2022, 2, 308–337.
7. Ruiz-Mirazo, K.; Briones, C.; de la Escosura, A. Prebiotic systems chemistry: New perspectives for the origins of life. *Chem. Rev.* 2014, 114, 285–366.
8. Ruiz-Mirazo, K.; Briones, C.; de la Escosura, A. Chemical roots of biological evolution: The origins of life as a process of development of autonomous functional systems. *Open Biol.* 2017, 7, 170050.
9. Frenkel-Pinter, M.; Samanta, M.; Ashkenasy, G.; Leman, L.J. Prebiotic peptides: Molecular hubs in the origin of life. *Chem. Rev.* 2020, 120, 4707–4765.
10. Mann, S. Systems of creation: The emergence of life from nonliving matter. *Accounts Chem. Res.* 2012, 45, 2131–2141.
11. Bernhardt, H.S. The RNA world hypothesis: The worst theory of the early evolution of life (except for all the others). *Biol. Direct* 2012, 7, 1–10.
12. Robertson, M.P.; Joyce, G.F. The origins of the RNA world. *Cold Spring Harb. Perspect. Biol.* 2012, 4, a003608.
13. Joyce, G.F.; Orgel, L.E. Prospects for understanding the origin of the RNA world. *Cold Spring Harb. Monogr. Ser.* 1993, 24, 1–25.
14. Orgel, L.E. Some consequences of the RNA world hypothesis. *Orig. Life Evol. Biosph.* 2003, 33, 211–218.
15. Sacerdote, M.; Szostak, J. Semipermeable lipid bilayers exhibit diastereoselectivity favoring ribose. *Proc. Natl. Acad. Sci. USA* 2005, 102, 6004–6008.
16. Pross, A.; Pascal, R. The origin of life: What we know, what we can know and what we will never know. *Open Biol.* 2013, 3, 120190.
17. Deamer, D. The role of lipid membranes in life's origin. *Life* 2017, 7, 5.
18. Barge, L.; Branscomb, E.; Brucato, J.; Cardoso, S.; Cartwright, J.; Danielache, S.; Galante, D.; Kee, T.; Miguel, Y.; Mojzsis, S.; et al. Thermodynamics, disequilibrium, evolution: Far-from-equilibrium geological and chemical considerations for origin-of-life research. *Orig. Life Evol. Biosph.* 2017, 47, 39–56.