COUPLED PHASES ENABLING COMBINATORIAL SELECTION OF COMPARTMENTALIZED MOLECULAR SYSTEMS: A PROPOSED MODEL FOR THE ORIGIN OF CELLULAR LIFE.

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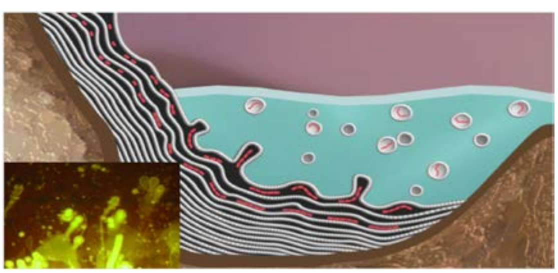
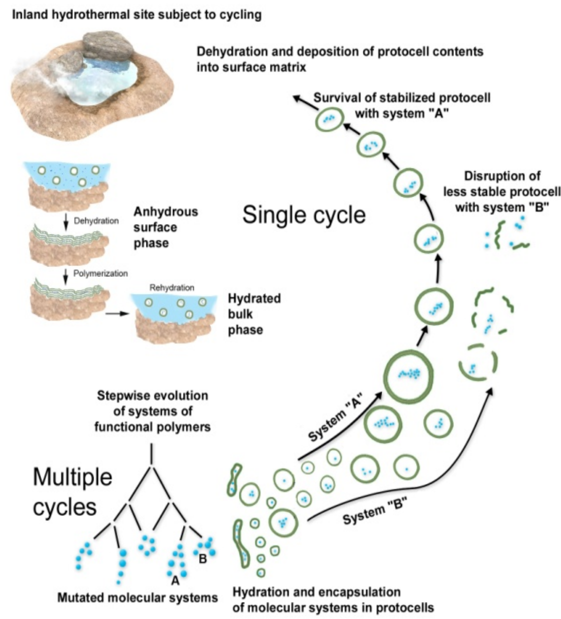
Introduction: We propose a model in which molecular systems driven by cycles of hydration and dehydration within pools in inland hydrothermal fields undergo chemical evolution in dehydrated films on mineral surfaces followed by encapsulation and combinatorial selection in a hydrated bulk phase.

Mechanisms for Polymerization: The pathway leading to the origin of life presumably included a process by which polymers were synthesized abiotically from simpler compounds on the early Earth, then were encapsulated to form protocells. Previous studies have reported that mineral surfaces can concentrate and organize activated mononucleotides [1], thereby promoting their polymerization into RNA-like molecules. However, a plausible prebiotic activation mechanism has not been established. We are exploring ways in which non-activated mononucleotides can undergo polymerization and encapsulation, and particularly the possibility that such reactions can be promoted by an organizing matrix. The organizing agents we are investigating include multilamellar liquid crystals and crystallization of monovalent salts, both of which promote synthesis of RNA-like polymers when exposed to cycles of dehydration and rehydration [2, 3]. The chemical potential driving the polymerization reaction is supplied by the anhydrous conditions in which water becomes a leaving group, with heat providing activation energy. As illustrated by the following figure, the polymeric products can be encapsulated in multiple microscopic compartments upon rehydration.



Combinatorial Chemistry Acting on Systems of Compartmentalized Polymers: Each compartment can be considered to be an experiment in a natural version of combinatorial chemistry that would be subject to selection: vesicles stabilized by functions of their contained polymeric systems could return those systems for new synthesis and amplification in the anhydrous phase.



Summary of Scenario: The above figure illustrates the coupled reactions and processing that occurs in hydrated and dehydrated phases. Because the system operates in continuous cycles, reactions do not proceed toward equilibrium but instead undergo a thermodynamic pumping of the system toward a steady state having ever increasing complexity. The polymers accumulate in kinetic traps because the rate of synthesis exceeds the rate of hydrolysis. The anhydrous lamellae concentrate monomers, then organize them in such a way that polymerization is promoted (on left). The resulting molecular systems are tested and selected for functions that enhance the viability of protocells in the dilute bulk phase (on right). The functions of a living cell therefore emerge first by chance, followed by selection and refinement with each cycle. We develop this further by proposing the mechanism for emergence of specific functional polymers plausibly possessing the necessary structures and functions for the transition to cellular life.

References: [1] Ferris JP (2006) *Phil. Trans. R. Soc. B 361*, 1777-1786. [2] De Guzman V. et al. (2014). *J Mol Evol 78*, 251-262. [3] Da Silva L. et al. (2015) *J Mol Evol 80*, 86-97.