SIMULATING EVOLVABLE SYSTEMS OF SELF-REPLICATORS

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Abstract

One of the important features of the origin of life on Earth was the appearance of a self-replicating molecule since it could form the ancestors of information containing molecules such as RNA and DNA. Understanding of chemical behaviors of replicators can give insights to the first replicator and studies in synthetic replicators can provide a broad understanding. Living systems reside out of equilibrium and nonlinear dynamical chemical systems could provide simpler analogues to biological systems. Here, I am presenting a chemical system which has been experimentally shown to give rise to self replication[1]. The system is based on molecules which exhibit dynamical covalent chemistry based on di-thiol bonds re-arrangements. At first smaller macro-cycles are formed, followed by formation of larger macro-cycles due to di-thiol exchange. Once rings of a specific size (6, hexamer) are formed they begins to self-assemble by stacking onto each other to form fibers. As longer and longer fibers are formed, they begin to break and causing to system to exhibit exponential growth and replication. Such a complex system can be systematically studied using mathematical models of chemical dynamics. I will also discuss how such a system can be extended to give rise to oscillations. All in all, self-replicators can help us to understand the formation of the first stable information containing molecules, and this approach can help to demonstrate the chemical behavior of self-replicators.

Introduction: Self-Replicators

Self-replication is any behavior in which an identical copy of a system is made, and this is the underlying mechanism of life since nucleic acids and cells maintain their continuity by making copies of themselves. In this mechanism, building blocks (nucleotides for nucleic acids) form the replicator, and this replicator catalyzes the formation of its own copy. The formation of self-replicating molecules is supposed to involve three distinct problems;

1. The way that the pieces from which nucleic acids are composed came into existence on the primitive earth (Miller and Orgel, 1974),
2. To join nucleotides in a purely chemical fashion,
3. Origin of the biological organization, that is, of molecules that not only can come together by chance, but also can go on to make more or less faithful copies of themselves and do other interesting things (the genetic code) Figure.

By focusing on the second problem, we examine how building blocks come together to form larger molecules and fibers, self replication and dynamics of these reactions.

Replication Mechanism

In the full model, monomers containing thiol groups form trimers by oxidation. What follows is the formation of different cyclic species -*tetramer, pentamer, hexamer*- by disulfide exchange reactions. When two hexamers are stacked, a nuclei is formed and elongation occurs with the addition of more hexamers. The only elongation path after nuclei formation is not the hexamer stack, a fiber acts as a catalyst for trimer and hexamer formation by capturing free building blocks and add another autocatalytic step. In this way, the fragmentation of the elongated fiber will increase the number of fiber ends to which the monomers will be attached so that the fragmentation will cause an exponential replication.[1] In some cases, the concentrations begin to oscillate. Unlike models in which the evolution of the entire system is modeled, we are working on a simpler model of the same system (Figure 2) to observe chemical oscillations.

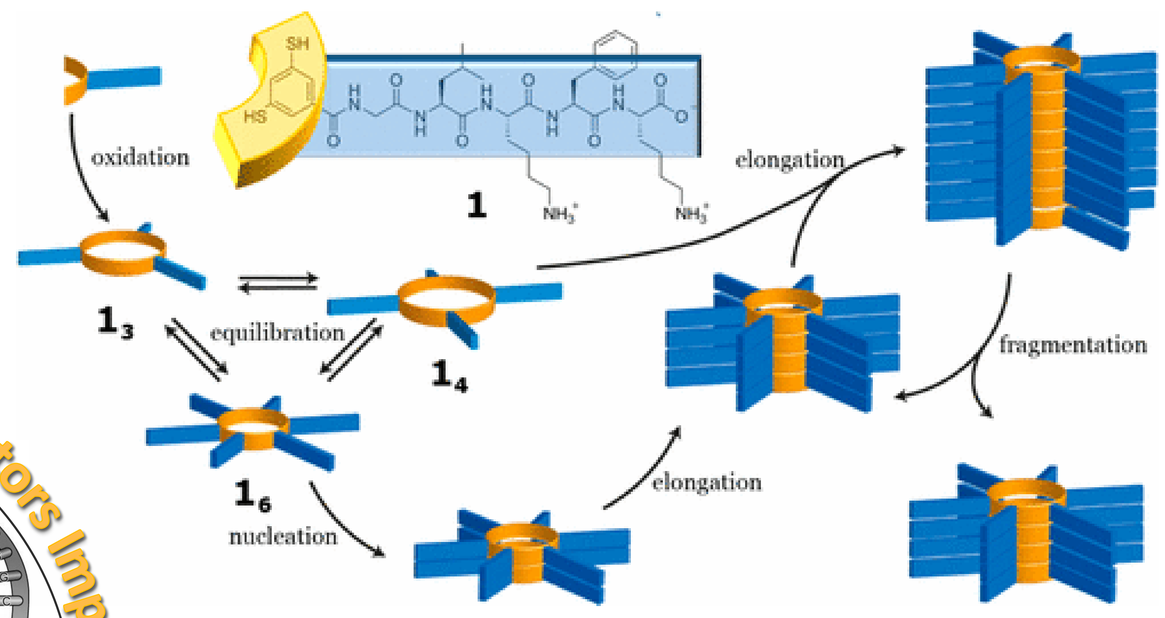
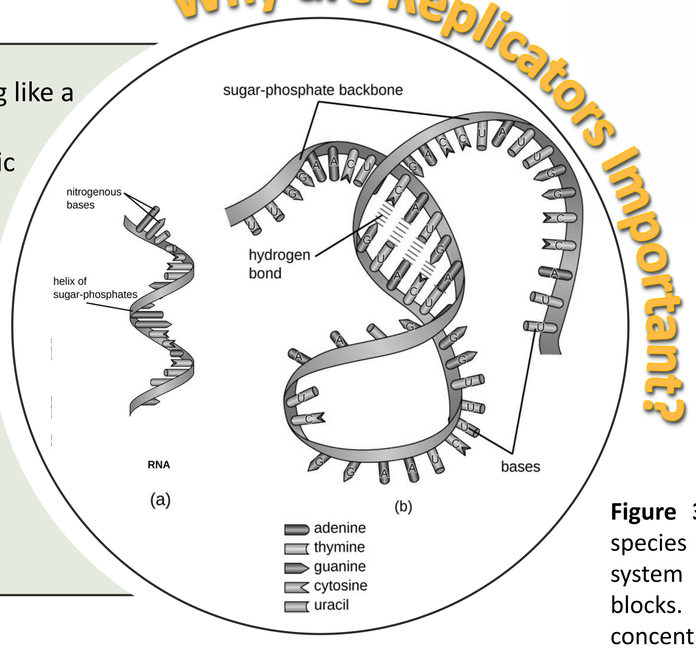


Figure 1: The full model: Scheme of the oxidation of monomers towards tri/tetra/hexamers and elongation/fragmentation of fibers.[2] Monomers oxidizes to trimers, disulfide exchange reactions takes place between cyclic species. The hexamers can self-assemble into stacks or fibres, which have an autocatalytic effect on their own formation; monomers can also stact to the fiber ends and form cyclic species.

Why are Replicators Important?

The first self-replicating molecule was something like a contemporary nucleic acid. RNA (a) stands out because it has the potential to catalyze enzymatic reactions by special foldings (b) such as proteins, as well as carrying genetic information as DNA does. RNA may not be as good as storing information as DNA, being less stable, or as versatile as proteins, but more or less compatible with the molecule we seek at the origin of life. This is one of the first things a living cell needs; The presence of a simple structure specialized in storing information and catalyzing reactions involving its own formation, especially in the absence of proteins yet.



Chemical Oscillations

Oscillatory reactions take place where the concentration of some species increases and decreases periodically over time. (Figure 5) Nonlinear systems with multiple feedback loops have been found to exhibit chemical oscillations. An understanding of oscillatory processes at molecular level is of great importance, as it holds the key to the mystery of complex phenomena like sleep induction in animals, circadian clocks and etc. Since self-replication can also have multiple feedback, positive and negative, and this complex behavior is crucial for biological systems, we are trying to capture how the replicator oscillates. The connection between theory and experiment is made through mathematical models derived from the dynamics of replicator with the help of numerical integrations.

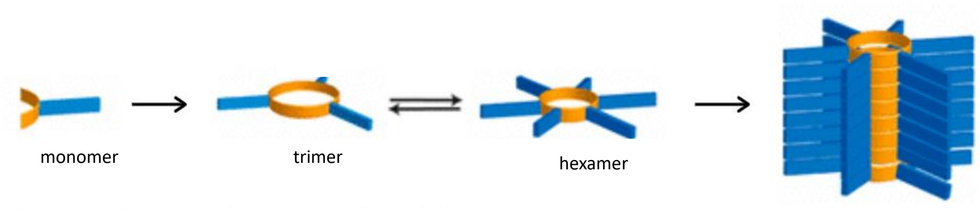
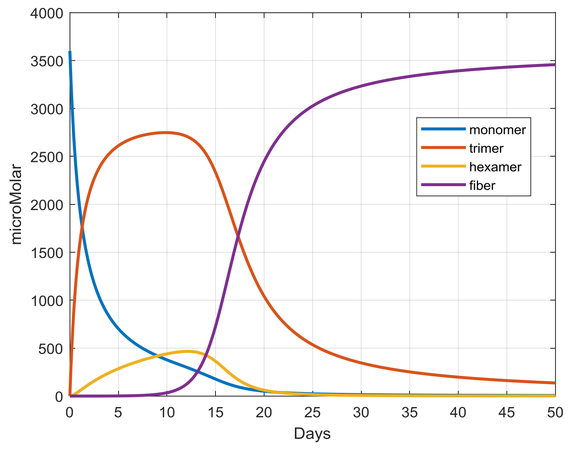


Figure 2: The simplified model of the full model shown in Figure 1. In the simple model, only 4 types are studied (Monomers, trimers, hexamers and fiber.). Simple model makes it easier to work on the system with fewer parameters.

Figure 3 (right): The chemical dynamics of the species in the simple model shown in Figure 2. The system initially has 3600 micromolar of building blocks. The graph shows the change in concentration of species over time.



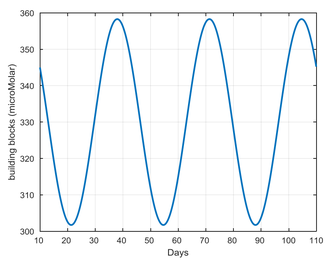


Figure 5: An oscillating system.

Conclusion

A self-replicator needs to act as a catalyst that catalyzes the transformation of its building blocks into intermediate molecules and the elongation of itself. This is a mechanism underlying the formation of information containing functional polymers, such as nucleic acids. To better understand these mechanisms synthetic replicators can be used and mathematical modeling of the dynamics can bridge between theory and experiments. It is still an important question; was the first replicator RNA, or did there exist a replicator molecule, the ancestor of RNA (proto-RNA)? We don't know the answer, but simulating evolvable systems of replicators with mathematical models will facilitate our understanding.

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