Designing a Protocell: Attempt at a Systemic Design Linking Information, Metabolism and Container

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Extended Abstract

Living cells are in many respects the ultimate nanoscale chemical system. Within a very small volume they can produce highly specific and useful products by extracting resources and free energy from the environment. They are self-assembled and self-organized, as well as capable of self-repair and self-replication.

Designing artificial chemical systems bottom up (artificial cells [1] or protocells [2-4]) endowed with these powerful capabilities are being intensively investigated. Usually such chemical systems are designed around the encapsulation of a set of genes along with a gene translation and protein generation unit, all confined within the boundaries of liposomes/vesicles [3, 4]. The generated artificial systems have many of the basic characteristics of a living system, but usually completely lack the gene mediated regulation functions that natural cells possess [5-7].

To address this issue, we are attempting to implement a simple, chemical system in which the regulation of the metabolism is truly mediated by information molecules [8, 9]. Our proposed system is composed of a chemical mixture of fatty acids that form bilayers (compartment), amphiphilic information molecules (polymerized nucleic acids -NAs), and metabolic complexes (photosensitizers). Due to the intrinsic properties of all its components, a chemical system will self-assemble into aqueous, colloid mixtures conducive to the necessary metabolic steps, as well as the non-enzymatic polymerization of the building blocks of the information unit. The metabolic reaction products (e.g., the container molecules) will in turn promote system growth and information replication.

In this scheme, the polymerized NAs acts as an information molecule mediating the metabolic catalysis (electron donor/relay system) with a ruthenium metal complex as a cofactor and sensitizer. The metabolic catalyst converts the hydrophobic precursor container molecules into amphiphiles, thus directly linking protocell metabolism with information. In a first experimental design, the NA chain has been replaced by a single nucleobase, 8-oxoguanine, which is tethered to one of the bipyridine ligands of the metal center [10].

We report the following major steps towards this chemical protocell: (1) the spontaneous formation (self-assembly) of chemical structures consisting of decanoic acid, its precursor, and the simplified NA-ruthenium complexes; (2) metabolism mediation by a nucleobase to effectively promote the photochemical assisted amphiphile synthesis, which continuously drive the system away from equilibrium; (3) the demonstration of reaction selectivity dependent on the nature of the information molecule since only one specific nucleobase has the required redox potential to allow the metabolism to function; (4) photochemical formation of amphiphiles that functions efficiently within the membrane, i.e., the protocell compartment; and (5) a demonstration of continued metabolic functionality after extrusion mediated container division.

The next steps are the integration of short nucleic acid oligomers as opposed to a single nucleobase as the information material to study their photocatalytic activity and attempts to adopt the underlying metabolic reaction to drive the polymerization of the oligomers, thereby yielding replication of the information molecules.

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