Bottom-up strategies towards the synthesis of minimal (living?) cells

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Abstract

There are several ways to approach the problem of assembling an artificial cell with just the necessary and sufficient ingredients so that it shows the main properties and behaviour of a minimal organism. Although the growing community of scientists interested in this issue agree that the level of complexity of the simplest living cells today is far too high, there is little consensus on how to proceed. The focus strongly depends on the conception of life --of minimal life-- dwelling in the mind of each researcher. Those who think that the major driving force of biological phenomena is Darwinian evolution tend to take up a *top-down* approach, and try to reduce the complexity of extant unicellular organisms (by various methods: knocking down secondary genes, stretching parasitic/symbiotic conditions,…), until they are no longer viable. Then, through the comparative analysis of a variety of such cases, the aim is to arrive at a common and indispensable genome core (nowadays thought to be around 200 genes), from which it would be possible to infer the central features of a minimal cellular system capable of Darwinian evolution (i.e., a type of system that should resemble the cenancestor of all living organisms on Earth). When the background conception, instead, is rooted in the idea that minimal living systems form and behave according to a characteristic material-dynamic organization (generally coined by the term 'metabolism'), which could emerge --in its most simple version--before full-fledged Darwinian evolutionary processes begin, the natural bias is to tackle the problem of the 'minimal cell' from a *bottom-up* physical-chemical perspective. Finally, a number of --more practical or engineering-inclined-- scientists are developing mixed or *semi-synthetic* approaches, in which biologically produced macromolecules (typically biopolymers) are combined with self-assembled lipid vesicles, or other supramolecular compartments, with the aim to analyse their interaction, mutual effects, or whether a particular (bio-)chemical reaction occurs under those bounded, compartmentalized conditions or not.

In my contribution I will try to throw some light into this multifarious research area, assessing the different lines of work, particularly with regard to their potential contribution to the problem of the origin of life. First, I will argue why attempts to *fabricate* life (i.e., synthetic biology) may provide new insights into the nature of life itself, different from the ones we already have (out of *describing* it, as biology has traditionally done). Then, according to a particular conception of minimal life and the process that leads to it [Ruiz-Mirazo et al. 2004; 2010], I will explain why strict bottom-up approaches constitute the most adequate way to tackle the *in vitro* implementation of a minimal self-maintaining cell, and why this should be the starting point for any process of origin of life. On these lines, a concrete *in silico* model will be proposed, to help illustrate two of the bottlenecks or major transitions that should be taken under consideration: (i) the transition from self-assembling fatty acid vesicles to self-producing protocells and (ii) the transition from structural lipid bilayers to functional 'lipid-peptide' membranes. Even in the case of accepting these as important landmarks in the problem of the origins of living systems, we can still debate whether a self-producing protocell with a functional membrane of this type (but still without genetic/hereditary mechanisms, i.e.: with limited evolutionary potential) would be alive or not.

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