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Introduction. Artificial protocells

What makes a cell? How are cells able to replicate themselves in a stable manner? How did cellular life emerge on our planet?

The answer to these fundamental questions lies at the base of biology. Cellular life is the basic unit of living organization and defines the presence of a stable information reservoir connected through the external world by a well-defined boundary.

Inside the cell, chains of computations and chemical reactions take place, sustained by self-assembled molecular machines. At the cell membrane, the environment and the cell communicate with each other through proteins that are able to detect small concentration changes and send the appropriate signals. But modern cells are very sophisticated entities and extracting the logic of cell organization from them is a gigantic effort. In order to answer these questions, we need to look at cells in a more basic level: a reduction of complexity is needed.

Protocells, roughly defined as the simplest instances of autonomous cell-like structures, have been a matter of exploration for decades. Although most of the original work in this area was largely theoretical, the end of the twentieth century was marked by very active experimental research on minimal cells.

One approach has been the top-down strategy, where living organisms (the simplest life forms) are being selectively modified to reduce their genome complexity. Such a minimal genome would be the smallest one able to sustain reproduction and growth under a given set of external constraints (mainly available molecules). The second approach is the bottom-up one, very much in the tradition of research into the origins of life. Under this approach, extremely simple life forms are built from basic chemical components, including lipids and a basic metabolism but also information-carrying molecules (such as DNA or RNA). The top-down approach has been improving as progress has been made, mainly within the arena of vesicle-based assemblies. Although these approaches have yet to build a truly autonomous self-replicating system, advances are taking place at high speed and the synthesis of a living protocell seems to be closer than ever. The new field of synthetic biology might well accelerate such achievement.

The twilight zone separating living from non-living matter is also the boundary separating a simple molecular assembly from molecular cooperation. Somehow, self-reproducing cellular systems are able to do so by properly coupling the cell container with metabolism and information. Such coupling is likely to rely on well-defined (but largely unknown) thermodynamic and kinetic constraints.

Understanding the nature and number of such constraints requires a better knowledge of the internal organization of candidate protocell models. This special issue presents several novel approaches to this problem, with special emphasis on understanding the logic of protocell structure and how it couples with self-reproduction.

The models and views presented here suggest that building protocells should be the probable outcome of future research. In this context, theoretical approaches might help by paving the way for the emerging field of protocell systems biology.

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One contribution of 13 to a Theme Issue ‘Towards the artificial cell’.