Experimental Model Protocells Support a Heterotrophic Origin of Life

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Keywords Heterotrophy • Protocell • Origin of Life • Prebiotic

Life can be divided into two categories, those that acquire their nutrients and those that make their own, i.e. organisms are either heterotrophic or autotrophic. The question is then, which of these two forms of life are simpler and thus more likely to have arisen first? Historically, heterotrophy has been viewed as the more likely starting point (Oparin 2003), due in part to its perceived simplicity. However, simplicity in cellular structure requires greater complexity in the environment, in the form of nutrients, to compensate for the cell’s inability to produce its own nutrients. The availability of abiotically synthesized nutrients in the environment is supported by simulated prebiotic syntheses of amino acids (Miller 1953), nucleobases (Oro 1961), nucleotides (Powner et al. 2009), sugars (Ricardo et al. 2004), and lipids (Hargreaves et al. 1977). However, many are unconvinced by such arguments and instead believe that early life could not have survived off of “free lunch” (Morowitz 1992). In other words, cells that are incapable of providing for themselves would have quickly exhausted the nutrients available in their surroundings and died. Therefore, only autotrophic organisms could have survived the environments of early Earth. The two opposing views, not surprisingly, have led to two different modes of research. The heterotroph supporters tend to focus on the creation of self-replicating systems dependent upon provided energy sources, and the autotrophic supporters often focus on geochemical cycles that mimic contemporary biochemical paths. In short, heterotrophy versus autotrophy emerges as replication-first versus metabolism-first arguments.

One strategy to resolve this debate is to try to build model protocells in order to evaluate which paths are compatible with the measured behavior of model protocells of specific
compositions. The approach is attractive in that it attempts to piece together life rather than to characterize cellular components in isolation. However, those that attempt to build protocells often have different views as to what threshold needs to be crossed for life-like properties to emerge. Much of the protocell experiments are aimed at creating self replicating systems (Szostak et al. 2001), which is in contrast with those that contend that life is a self sustained entity that does not necessarily require replication (Luisi 2003). The latter has been coined autopoiesis. Of these two protocell perspectives, the replication model fits more easily within heterotrophy, whereas the autopoiesis model seems better accommodated by autotrophy, although interesting examples of heterotrophic-like autopoiesis exist (Zepik et al. 2001). The allure of heterotrophic, replicating protocells is its apparent simplicity and compatibility with Darwinian evolution. However, the autopoietic perspective may more closely describe what we recognize as life (Luisi 2006).

A simple parameter to evaluate in order to gain insight into the likelihood of heterotrophic and autotrophic origins is membrane permeability. Highly impermeable membranes give compartments sealed off from their surroundings and thus are incapable of acquiring or releasing material. Such a protocell needs to rely on internally synthesized nutrients and thus would be an autotroph. Permeable membranes, conversely, allow for the uptake and release of nutrients and waste. Therefore, such a heterotrophic protocell could survive by acquiring externally supplied nutrients. A series of permeability studies of membranes composed of prebiotically plausible, monoacyl lipids, such as fatty acids, show a high degree of permeability and selectivity (Hargreaves and Deamer 1978; Chen and Szostak 2004b; Sacerdote and Szostak 2005). Fatty acid vesicles even allow for the passage of nucleotides in the absence of specific transport machinery (Walde et al. 1994a; Chen et al. 2005; Mansy et al. 2008). In summary, the permeability properties of model protocell membranes composed of fatty acids are amenable to heterotrophic, but not autotrophic, processes.

Since model protocell membranes are permeable to nucleotides, they can be used to create heterotrophic cell-like structures capable of genetic replication. Remarkably, only four components (fatty acids, primer, template, and activated nucleotides), excluding salts and buffers, are required to generate a system that acquires nutrients, i.e. activated nucleotides, to fuel compartmentalized copying of a nucleic acid template (Mansy et al. 2008). The permeability properties of the system are dependent upon the lipid composition of the membrane. The permeability advantages of fatty acid membranes complement well other properties, such as their ability to easily form boundary structures (Gebicki and Hicks 1973; Hargreaves and Deamer 1978), grow (Bercelaz et al. 2001; Hanczyc et al. 2003; Chen and Szostak 2004a), replicate (Walde et al. 1994b; Hanczyc et al. 2003; Zhu and Szostak 2009), and compete for resources (Chen et al. 2004). Fatty acid vesicles are also stable enough to survive temperature fluctuations that melt and anneal duplex nucleic acids (Mansy and Szostak 2008). Prebiotically plausible fatty acid vesicles allow for the emergence of a variety of life-like properties that also commit the resulting cell-like structure to heterotrophic means of survival.

What has been briefly described is a one sided story. Unfortunately, few attempts to generate autotrophic protocells or protocellular systems composed of less permeable diacyl phospholipids have been reported. This is in spite of interesting data that show that light driven reactions in the presence of weak acids can generate pH gradients across diacyl phospholipid membranes (Deamer and Harang 1990; Deamer 1992; Sun and Mauzerall 1996). Diacyl phospholipid systems are also attractive due to their increased stability to a wider variety of conditions. It seems likely that our understanding of protocellular processes would be enriched if more effort were expended in developing such autotrophic systems.
If one were to base their opinions on experimental evidence, then the conclusion drawn likely would be that life had a heterotrophic beginning. This, of course, does not mean that it is correct. Instead, the paucity of data indicates the need for more protocell experiments so that each data set can be better evaluated against competing theories. Nevertheless, the protocell perspective may, to a certain extent, avoid the posed question of the nature of Earth’s first cells. One could envisage the appearance of heterotrophic protocellular structures that then evolve into autotrophic cells (rather than protocells). In this case, the evolution of metabolism would likely have been coupled with the evolution of increasingly impermeable membranes (Szathmary 2007). Similarly, focus on the emergence and evolution of a single protocell type may be misguided. Perhaps mixtures of cell-like structures, some of which are better described as autotrophic while others as heterotrophic, is a more realistic view of evolution. One hopes that through experimental research, we will be better able to answer such questions.

Acknowledgments
SSM is supported by the Armenise-Harvard foundation.

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The Autotrophic Origins Paradigm and Small-Molecule Organocatalysis

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Keywords Autotrophic Origins • Organocatalysis • SMILES • Computational Chemistry

Autotrophy and heterotrophy: disentangling the issues

All origin of life paradigms suppose at some level that cells have incorporated organic molecules that were once of abiotic origin. The distinction between primordial organosynthesis through high-energy processes quite different from those of biochemistry, and geochemical processes posited to be continuous with biochemistry, has become framed as a distinction between “heterotrophic” and “autotrophic” origin scenarios. The naming draws on an analogy with heterotrophy versus autotrophy of organisms, which is