

NEWS & VIEWS

ORIGINS OF LIFE

How leaky were primitive cells?

David W. Deamer

If the first cells were simple vesicles, how did nutrients cross their membranes without help from transport proteins? A model of a primitive cell suggests that early membranes were surprisingly permeable.

How life began remains an open question. There are now a dozen or more competing ideas that fall into two general categories: life began either as an autotrophic organism that used primitive metabolic pathways to make its own organic components, or as a heterotroph that incorporated carbon-containing nutrients already available in the environment. On page 122 of this issue, Mansy *et al.*¹ weigh in with a laboratory simulation that supports a heterotrophic origin of life — a cell-like vesicle that allows small, organic ‘nutrient’ molecules to pass through its membrane.

Recent progress in planetary science has provided a reasonably convincing description of what our planet was like at the time of life’s origin, sometime between 3 billion and 4 billion years ago. It was a world of global oceans peppered with volcanic land masses resembling the relatively newborn lands of today’s Hawaii and Iceland. The atmosphere was a mixture of carbon dioxide and nitrogen, with little or no oxygen, and the mean global temperature was much higher than that today, probably in the range 60–70 °C. Seas and lakes contained dilute mixtures of simple organic compounds, perhaps with thin films of oily hydrocarbons on the surface. But most importantly for a discussion of Mansy and colleagues’ work¹, local conditions were far from equilibrium — a constant flux of energy drove organic reactions towards ever-increasing complexity. This would ultimately have yielded various polymeric products, perhaps including prototypes of nucleic acids or proteins.

The result of this process would have been that vast numbers of microscopic assemblies of molecules (Fig. 1) appeared wherever organic compounds became concentrated at the interface between the atmosphere, water and mineral surfaces. In one scenario that might have led to the development of heterotrophic life, these assemblies took on a cell-like form — membranous compartments composed of bilayers, within which molecules are trapped. Such compartments are known to readily self-assemble from amphiphilic compounds (soap-like fatty acids and fatty alcohols) that



Figure 1 | Lipid self-assembly. A mass of phospholipid molecules (the building-blocks of cell membranes) extends tubular structures as it absorbs water, in a classic example of the self-assembly processes that might have led to the spontaneous formation of cell-like structures on prebiotic Earth. Mansy *et al.*¹ show that a protocell-like vesicle that self-assembles from simple organic molecules in a similar way doesn’t need proteins to transport molecules across its membrane.

are commonly found in experiments that simulate the prebiotic ‘soup’.

In this theory of the origins of life, each cell-like assembly had a different composition from the next. Most were inert, but a few might have contained a particular mixture of components that could be driven towards further complexity by capturing energy and small ‘nutrient’ molecules from the environment — the beginnings of a heterotrophic system. As the nutrient molecules were transported into the internal compartment, they became linked together into long chains in an energy-consuming process. Life began when one or more of the assemblies found a way not only to grow, but also to reproduce by incorporating a cycle involving catalytic functions and genetic information.

So far, so plausible. But there’s a problem: the membrane that forms the compartment of the

putative cell is also a permeability barrier. Small molecules that have no electrical charge (such as water and carbon dioxide) get across in seconds, but larger molecules (such as amino acids) that have electrically charged groups are a billion times less permeable. Modern cells solve this problem by integrating proteins into their membranes, with each protein specialized for transporting specific molecules such as amino acids, glucose or phosphate. But how did the first forms of cellular life overcome the permeability problem?

This is the question posed by Mansy *et al.*¹. Specifically, they ask how growing systems of polymers in primitive cells could have had access to nutrients in the external environment. To find the answer, the authors made membrane-bound compartments not just from modern phospholipids (the building-blocks of cells that have evolved to be virtually impermeable to ionic solutes), but also from mixtures of simpler molecules, such as fatty acids, fatty alcohols and monoglycerides (which might have been present on prebiotic Earth). Earlier work demonstrated that such mixtures produce surprisingly stable membranous vesicles^{2,3}.

Mansy and colleagues first investigated the permeability of the vesicles to ribose, the sugar component of RNA. They optimized the mixture of molecules in the vesicle membranes for maximal permeability to ribose, but minimal permeability to polymers such as DNA. In this way, the authors showed that membranes similar to those that might have formed on prebiotic Earth allow the passage of simple molecules, as would be essential for a functioning protocell.

They then trapped synthetic DNA molecules in the optimized vesicles. The DNA was designed to act as both a primer and a template for its own elongation, so that the primer spontaneously extends in the presence of the appropriate molecular building-blocks — nucleotides that are chemically ‘activated’ to undergo polymerization on the template. The template was a single strand of DNA that contained only cytosine bases, so the activated nucleotides had

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to contain the complementary guanosine bases. Mansy *et al.* added these nucleotides to the medium surrounding the vesicles, where they are analogous to the external nutrients required by a heterotrophic organism.

For vesicles composed of phospholipids, the authors observed no elongation of the encapsulated DNA primer on addition of guanosine-containing nucleotides to the external medium. This was to be expected, because the nucleotides were excluded from the interior volume. But the vesicles composed of simple amphiphilic molecules showed a remarkable elongation of the DNA primer over the course of 24 hours, as nucleotides were added one by one. This demonstrates that a primitive cellular compartment can be permeable enough to let a cell grow by allowing small molecules through the bilayer, yet stable enough to maintain the integrity of the internal mixture of functional polymers. Previous work^{4–7} has shown that a variety of polymerization reactions work beautifully when encapsulated in different systems, but Mansy *et al.*¹ establish for the first time that a simulated prebiotic protocell can work with an external source of reagents.

Arguably the most important aspect of this study is that it demonstrates that a heterotrophic origin of primitive cellular life is feasible. The next step is to devise some version of non-enzymatic replication in which a polymer such as DNA or RNA is completely reproduced within a vesicle using externally added substrates. That's a tall order, of course, but presumably not an impossible one — at some point in the pathway to the first cellular life, such a system must have arisen spontaneously.

Cells are the basic unit of all life today, and there is increasing reason to think that the first form of life was a primitive version of a cell, rather than a replicating molecule supported by a metabolic network⁸. Mansy and colleagues' work¹ suggests that the first cellular life might have sourced energy and nutrients from the environment, and that more complex, autotrophic lifestyles appeared at a later stage of evolution. We may never know for sure if this is true, but we certainly now have some compelling circumstantial evidence. ■

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1. Mansy, S. S. *et al.* *Nature* **454**, 122–125 (2008).
2. Apel, C. L., Deamer, D. W. & Mautner, M. N. *Biochim. Biophys. Acta Biomembranes* **1559**, 1–9 (2002).
3. Monnard, P.-A., Apel, C. L., Kanavarioti, A. & Deamer, D. W. *Astrobiology* **2**, 139–152 (2002).
4. Walde, P., Goto, A., Monnard, P.-A., Wessicken, M. & Luisi, P. L. *J. Am. Chem. Soc.* **116**, 7541–7547 (1994).
5. Noireaux, V. & Libchaber, A. *Proc. Natl Acad. Sci. USA* **101**, 17669–17674 (2004).
6. Ishikawa, K., Sato, K., Shima, Y., Urabe, I. & Yomo, T. *FEBS Lett.* **576**, 387–390 (2004).
7. Monnard, P.-A., Luptak, A. & Deamer, D. W. *Phil. Trans. R. Soc. Lond. B* **362**, 1741–1750 (2007).
8. Szostak, J. W., Bartel, D. P. & Luisi, P. L. *Nature* **409**, 387–390 (2001).

SOLAR SYSTEM

A shock for Voyager 2

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The Voyager 2 spacecraft has now followed Voyager 1 into the region beyond the end of the supersonic solar wind, where the influence of interstellar space is growing — so opening a new age of exploration.

Five papers^{1–5} in this issue, beginning on page 63, celebrate and record a notable event in the storied history of the Voyager space programme. Thirty years after its launch on 20 August 1977, Voyager 2 arrived at the 'heliospheric termination shock', adding important new data about this turbulent boundary in the outer Solar System to those collected by Voyager 1 four years ago^{6–8}.

For context, some Solar System geography is necessary. The Sun emits a supersonic flow of plasma (the solar wind) in all directions, carving out a vast spheroidal cavity in the interstellar plasma. This cavity is called the heliosphere, and is some 100–150 astronomical units (AU) in extent — an AU is the average distance from Earth to the Sun, about 150 million kilometres. The size of the heliosphere is determined principally by the properties of the solar atmosphere and the surrounding interstellar plasma, magnetic field and neutral particles. At large distances from the Sun, the solar plasma is so extended that it can no longer push back the interstellar plasma. Its supersonic flow, relative

to the interstellar medium, ends at a spheroidal shock wave, the termination shock, where the wind abruptly slows. The region of slower flow beyond the shock is the heliosheath. Here, the interaction of the solar plasma with the interstellar gas becomes dominant. The heliosheath ends at the heliopause, beyond which is the interstellar plasma. This entire system can be recreated in a kitchen sink, as shown in Figure 1.

Beginning on 31 August 2007 and ending the next day, Voyager 2 crossed the heliospheric termination shock several times, a feat made possible because this boundary is far from static and oscillates in and out. So the spacecraft has left the supersonic solar wind behind, and follows Voyager 1 into the heliosheath and on to the heliopause where they will probably arrive in the next decade or so (the distance to the heliopause is not yet known with any certainty, but is expected to be at about 130–150 AU from the Sun). The plasma analyser on Voyager 1 has long been inoperative. But that on Voyager 2 is working, and both spacecraft can measure plasma waves,

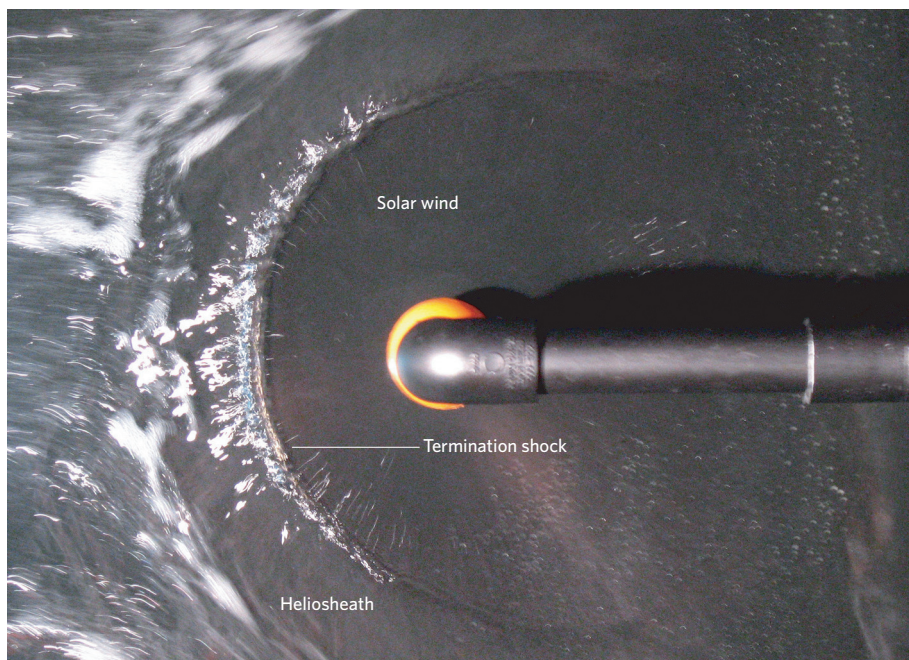


Figure 1 | The heliosphere in a kitchen sink. In this two-dimensional analogue, water flows down into the plane of the photograph from a tap (orange) and strikes a flat, inclined surface. The water radiates from the point of impact, much as the solar wind flows outwards from the Sun. It is eventually checked by surrounding water and forms a jump (a hydraulic bore, analogous to the termination shock) that is quasi-circular. The flow of the interstellar medium is represented by a uniform, slow flow of soapy water in from the left. The jump in this analogue is turbulent and dynamic, much as the termination shock is observed to be. (Analogue created by K. C. Hsieh, Department of Physics, University of Arizona. Photo by J. R. Jokipii.)