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Comment

Attempts to Define Life Do Not Help to Understand the Origin of Life

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Jack W. Szostak

Howard Hughes Medical Institute and Department of Molecular Biology and Center for Computational and Integrative Biology, Massachusetts General Hospital, 185 Cambridge Street, Boston, Massachusetts 02114

Attempts to define life are irrelevant to scientific efforts to understand the origin of life. Why is this? Simply put, the study of the 'origin of life' is an effort to understand the transition from chemistry to biology. This fundamental transition was the result of a lengthy pathway consisting of many stages, each of which is the subject of numerous scientific questions. Simple chemistry in diverse environments on the early earth led to the emergence of ever more complex chemistry and ultimately to the synthesis of the critical biological building blocks. At some point, the assembly of these materials into primitive cells enabled the emergence of Darwinian evolutionary behavior, followed by the gradual evolution of more complex life forms leading to modern life. Somewhere in this grand process, this series of transitions from the clearly physical and chemical to the clearly biological, it is tempting to draw a line that divides the non-living from the living. But the location of any such dividing line is arbitrary, and there is no agreement on where it should be drawn. An inordinate amount of effort has been spent over the decades in futile attempts to define 'life' – often and indeed usually biased by the research focus of the person doing the defining. As a result, people who study different aspects of physics, chemistry and biology will draw the line between life and non-life at different positions. Some will say there is no life until a well defined set of metabolic reactions are in place. Others will focus on spatial compartmentalization, on the various requirements for Darwinian evolution, or on the specific molecules of inheritance. None of this matters, however, in terms of the fundamental scientific questions concerning the transitions leading from chemistry to biology – the true unknowns and subject of origin-of-life studies.

Beyond the arbitrary nature of efforts to define the boundary between non-life and life, this effort is illusory for a deeper reason. As one focuses experimentally on any of the 'defining' properties of 'life', the sharp boundary seems to blur, splitting into finer and finer sub-divisions. As an example, let us look at the emergence of Darwinian evolution, which is often cited [*e.g.*, see Table II, in ref. 1] as a key aspect of the definition of life (with good reason, as Darwinian evolution is indeed the unifying characteristic of all of biology). Certainly once cells with genetically encoded advantageous functions existed, classically defined Darwinian evolution had begun, and most people would define such cells as alive. But what about the previous steps? Such cells would likely have been preceded by protocells, with replicating genetic information, but lacking coded functions that provided a cellular advantage. At this stage, replication with heritable variation would have existed, and whatever process drove replication would most likely have had biases that led to changes in the genetic structure of the population over time. Would that minimalist form of evolution qualify such protocells as being alive? Going back even further, consider genetic molecules replicating in solution

Corresponding author:
Jack W. Szostak
E-mail: szostak@molbio.mgh.harvard.edu

or on particulate surfaces – again, biases in replication would lead to selection for sequences that are better templates, *i.e*., easier to replicate. Even the assembly of the first genetic polymers would have had biases, leading to non-random population structures. Darwinian evolution itself emerged in a series of stages, step-by-step, gradually leading to the almost infinite potential for organismal variation seen in modern biology. And yet, to define a single point along the progression as *the* point at which Darwinian evolution first emerged would be difficult. More importantly, such a definition would not further our understanding of the transitions involved or the nature of the physical and chemical forces driving those transitions.

What is important in the origin of life field is understanding the transitions that led from chemistry to biology. So far, I have not seen that efforts to define life have contributed at all to that understanding.

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Reference

1. E. N. Trifonov. *J Biomol Struct Dyn 29*, 259-266 (2011).