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Peer Review

# Review of: "What Is Life: A Biochemist's View"

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**Reviewer Comments on "What Is Life: A Biochemist's View"**

*Continuity, communication, and the status of viruses*

General assessment

The manuscript offers an interesting and potentially publishable contribution to the long-standing question of how life should be defined. Its central proposal - that organic life is an uninterrupted, thermodynamically open metabolic continuum sustained by flows of matter, energy, and reducing power - is clearly stated. The emphasis on continuity is particularly valuable. It distinguishes biological organisms from artificial systems that can be powered down and restarted, and it highlights the unbroken metabolic connection between present organisms and the earliest forms of life. My comments below are intended to broaden this framework rather than to dispute the importance of thermodynamics.

Metabolic continuity and communicative continuity

A complementary line of inquiry developed during the twentieth century in the humanities and the life sciences around language, signs, codes, and communication. These concepts have become increasingly relevant to biology through fields such as biosemiotics, code biology, and biocommunication. Signals and communication are not merely descriptive metaphors added to molecular biology: they concern differences that are produced, recognized, and interpreted by living or replicating systems in specific contexts. It has therefore been argued that signs and communication have accompanied life throughout its history (Sebeok, 2001; Sharov et al., 2015), that communication is a defining characteristic of life (Witzany, 2019), that life is physics plus chemistry plus communication (Witzany, 2015), and even that life itself is the action of signs (Emmeche & Kull, 2011).



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The manuscript could be strengthened by placing its concept of metabolic continuity alongside the continuity of biological information, signals, and communicative processes. Present-day life is continuous with the remote past not only because metabolism has never been globally interrupted, but also because biological information has never been reset between generations. Genomes are continually altered by mutation, recombination, horizontal transfer, and selection; nevertheless, each genome is historically derived from earlier genomes and is interpreted by cellular systems inherited from previous cells. This is not continuity as unchanging identity, but continuity through transformation. The same applies to biological codes and signals: their uses and meanings evolve, yet sufficient compatibility is retained for organisms, cells, and mobile genetic elements to interact. Life does not contradict fundamental physical laws, but it is guided by rules, which determine how signals should be interpreted by social agents sharing physical context and history.

Viruses as a critical case

The treatment of viruses provides the clearest opportunity to connect the two perspectives. In the thermodynamic account, the metabolically inert virion is classified as non-living, whereas the virus-host association becomes a living thermodynamic system once cellular metabolism supports viral replication. The virus is therefore described as oscillating between non-living and living states. This is an illuminating formulation, but it may also conflate the virion - the extracellular particle - with the virus understood as a complete, temporally extended process.

From a biosemiotic perspective, the virion does not become alive when it enters a cell. Rather, the virus functions as a context-dependent signal, or as a set of signals, interpreted by a heterogeneous cellular system (Gómez et al., 2015). In Peircean terms, the viral signal vehicle participates in a triadic relationship with an object and an interpretant. Viral entry can reorganize pre-existing molecular interactions and release cellular activities that were previously repressed, transforming a latent pathological state into an active one. On this account, the cell is not simply a metabolic apparatus that temporarily animates the virus. It is an active interpretive system whose history, molecular organization, physiological state, previous infections, and environmental context influence the outcome of infection.

This distinction matters because thermodynamic openness is necessary for viral replication but does not, by itself, explain the specificity or meaning of viral action. It cannot fully account for why the same virus produces cytolytic, persistent, or abortive infections in different cellular contexts, or why a viral signal is effective in one host but not another. Cross-species transmission, and even interactions that cross domains of life, also indicate that biological languages can change their rules of use without

becoming completely mutually unintelligible. Viral infection can therefore generate new, context-dependent biological meanings while remaining grounded in deeply conserved molecular affinities and codes.

Recommendation

I encourage the author to incorporate the continuity of signals and biological communication as a complement to metabolic continuity. Doing so would not weaken the thermodynamic proposal. On the contrary, it would distinguish the material conditions that make life possible from the historically inherited sign-mediated rule-governed processes that organize and direct living activity. The manuscript's treatment of viruses would then become especially powerful: instead of presenting the virus only as an entity that alternates between living and non-living states (two ontological states), it could examine the virus-host relationship as a continuous metabolic process that also involves signal recognition, contextual interpretation, and cellular self-transformation. With this conceptual expansion and clarification, the manuscript would make a stronger contribution to contemporary discussions of the nature of life.

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## Declarations

**Potential competing interests:** No potential competing interests to declare.