

Comment

Life: Self-Directing with Unlimited Variability on Self-Speeding

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In his recent report in this journal, E. N. Trifonov (1) suggests that life should be defined as “self-reproduction with variations”, based on a vocabulary analysis of previous definitions of life. The method is novel, and the conclusion is interesting. However, there are some problems in the analysis process, and the final assertion of the definition of life needs more cautious and deeper consideration.

The initial analysis, especially concerning the nine word groups (so-called “*defnientia*”), is impressive, which in some degree could reflect people’s common views up to now on the essential meaning of life phenomenon. This analysis leads to a collective definition of life as “metabolizing material informational system with ability of self-reproduction with changes (evolution), which requires energy and suitable environment” (referred to as “definition [1]” in the original paper).

As the author says, this collective definition, though comprehensive, should be worked on to reach a more concise one. This work is important because a satisfying definition should not be a collective one. However, the author does this work in a way of some curtness. For example, it is mentioned that “metabolism implies both energy and material supply which also represent environment”. Though this seems true, on the purpose of taking out the words “energy”, “material” and “environment” from the list, the author should say more than just one sentence, especially considering “metabolism” is a word with quite different interpretations. Furthermore, it seems that “self-reproduction (replication) ... implies metabolism ... as well” needs a more detailed explanation rather than “the self-reproduction ... can proceed only on condition that metabolism ... are in place”. Instead, in a view of “replication (reproduction) first” in the origin of life (*e.g.* 2, 3), a contrary statement could be expressed as “metabolism can proceed only on condition that self-reproduction are in place”, because enzyme-like functional molecules have to appear by chance again and again if they could not be produced in a self-reproduction system. If it is considered that metabolism does not need functional molecules complicated enough like enzyme but only simple ones, for example, produced in some assumed chemical autocatalysis reactions, then again, the meaning of metabolism needs more explanation in detail. In fact, approving the view of “replication (reproduction) first”, I agree to the taking out of “metabolism” from the list, but not because “self-reproduction” implies “metabolism is already in place”, instead, because metabolism could be a thing derived from self-reproduction during evolution. Certainly, the sentence “the complexity (information) can be considered as product of

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self-reproduction with change (evolution), on the evolutionary route from simple to complex” seems enough to justify the taking out of “complexity (information)” from the vocabulary list.

Based on the definition “life is self-reproduction with variations” (referred to as “definition [2]” in the original paper), if variations is considered as a word equivalent to evolution (as the author mentioned), along the logic line above, the final word left seems to be “evolution”. Apparently, evolution “can proceed only on the condition that self-reproduction is already in place”. Then, the most concise and conclusive definition should be “life is evolution”, or more explicitly “life is something capable of (Darwinian) evolution”, similar to some early suggestions (see 4, 5 for reviews).

However, this is apparently not a satisfying definition, because “Darwinian evolution” is *per se* a collective concept, only appearing as a concise expression. In other words, we still need to know what kind of things is capable of Darwinian evolution. In fact, seeking a concise expression should not be the only criterion to construct a satisfying definition. A clear definition should catch the most fundamental mechanism underlying the corresponding phenomenon. Therefore, the definition “life is self-reproduction with variation” should be appropriate but “variation” does not equal to “evolution”, instead, it is a feature accompanying “self-reproduction” which, together with the latter feature, leads to Darwinian evolution.

As a further consideration, however, we should notice that this definition remains not satisfying, because “self-reproduction” is a word typically used in the life science (biology), and should not be used to define life unless we admit that there

is some special rule for the life phenomenon over other phenomena in nature. In other words, we still need to know how things could self-reproduce in nature. In a recent report of ours (6), self-reproduction (replication) is explained in a chemical background. The main conclusions are: first, self-reproduction (replication) in the substantial world could not mean others but “an entity favors the production of its own”; second, the major chemical mechanism for such favoring is catalysis, which could be classed into the speed-favoring catalysis and the direction-favoring catalysis (*e.g.* the enzyme-like function is a speed-favoring one and the template-directing function is a direction-favoring one); third, correspondingly, self-reproduction could be either favoring its own production in speed (self-speeding) or favoring its own production in direction (self-directing), or a combination of them.

Let us talk about some scenario in the origin of life to explain these concepts. Life is very likely to have begun with RNA (or RNA-like) molecules (the RNA world hypothesis) (7, 8). Any RNA molecule could direct the chemical reactions of nucleotide-joining to produce its own species *via* an intermediate complementary sequence, under the mechanism of template-directing copying by base-pairing. That is self-directing. However, only some RNA molecules with characteristic sequences might spread in a pool of random RNAs in the competition for the limited common raw materials, due to their enzyme-like function (so-called ribozyme) favoring the self-directing process. Examples could be replicase ribozymes (catalyzing the template-directed copying) (8), nucleotide synthetase ribozymes (9), *etc.* That is self-speeding. It is just natural selection that works in this evolution, and would further work on further evolution, selecting for more or higher self-speeding features, upon the prerequisite that different characteristic sequences with these

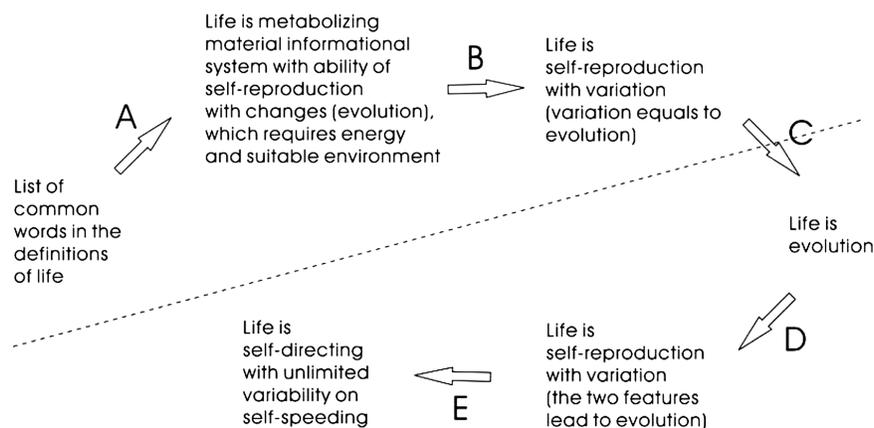


Figure 1: The scheme of the author’s logic (above the dashed line) and my further considerations in this comment (below the dashed line) concerning the definition of life. (A) Constructing the collective (consensus) definition according to the list of common words. (B) Constructing the concise definition by taking out “redundant” words. (C) Constructing the most concise and conclusive definition along the author’s logic. (D) Spreading out the meaning of (Darwinian) evolution to construct a clearer definition. (E) Spelling out the meaning of self-reproduction in a chemical background to construct a definition closer to the essence of life in nature.

features might appear by variation (in template-direct copying with some errors or other events, such as recombination). In modern life, DNA/RNA is the molecular base of the self-directing and RNA/protein is that of the self-speeding. We could image a bacterium as an entity absorbing raw materials to construct its own offspring (self-directing), in which process a lot of enzymatic reactions occur (self-speeding). When a variation on the self-directing (originating as the change of its genetic information) appears and if this variation could cause the change of the self-speeding (manifesting as the change of enzymatic efficiency or other phenotypes), Darwinian evolution might take place.

If it is emphasized that the Darwinian evolution should be ongoing forever, or say, “with an open end” (5), the variation of heredity should be unlimited (10), carried by molecules like DNA/RNA or similar polymers, and the corresponding variation of phenotypes should also be unlimited, carried by molecules like RNA/protein or similar polymers.

Then the definition should run in such a way as “living things are self-directing species with unlimited variability on self-speeding” or more concise “life is self-directing with unlimited variability on self-speeding”. This definition includes considerations on the chemical base of self-reproduction and

implies the most conclusive feature of life, *i.e.* Darwinian evolution. A scheme of the author’s logic and my further considerations in this comment concerning the definition of life is shown in Figure 1.

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