

## Author Response

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### Definition of Life: Navigation through Uncertainties

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I am pleased to receive such multifaceted response (1-19) to my paper (20). It helped me to better realize what exactly I have done. Perhaps, the main thing is original motivation: how from 123 uncertain definitions of the uncertain phenomenon described in uncertain terms to derive a consensus, without engaging in the debates, which so far did not bring the consensus. As P. L. Luisi put it: “the concept of life is too vague and general, and loaded with a number of historical, traditional, religious values” (21). The debates, therefore, have been intentionally excluded from my analysis. No semantics, logics, semiotics, and alike, nor philosophy in general were involved. With all respect to philosophy, mother of sciences, I chose to keep away from it, with the risk of becoming “non-scientific”, and engaged in the word-count approach, “vocabulary method instead of insight” (4), which has never been tried for definition of life. The first consequence, of course, is an understandable avalanche of protests, but a comparable flow of praise as well.

Thus, the main motivation and the main point of the disputed paper was to bypass centuries-long philosophical debates on the definition of life, “lacking the cohesiveness” (13), which, as I see it, continue to lead nowhere, and suggest an entirely new approach on a new ground, well away from the old territory. This point is not appreciated by most of the comments dragging instead back to the weathered grounds (1, 2, 4, 6-16, 18, 19). “The risk with this minimalistic definition is the failure to meet the essential logical requirement of a definition” (8). Yes, indeed, as it was not geared to the traditional routines of definitions.

Another intention in deriving the minimalistic definition was to find, hopefully, a practical guide towards potential minimalistic models of life. The resulting three-word definition is considered by many as incomplete. A whole variety of *definitia* to supplement it is offered: *heritable* variations (3), information, energy, environment, thermodynamic inversion (5), error threshold (6), self-directing and self-speeding (7), exchange with the environment, kinetics and self-assembly (11), cell (11, 15, 18) (I do not consider cell as unit of life, see below), adaptive evolution (13), selection (14, 18), metabolism (16), lack of purpose, evolvability (18), and ‘Love’ and ‘Soul’ (10). The last one deserves special comment. Following Cartesian body/soul division I focused, as many others before, at the body (structure, mechanisms). The soul, as well as mind, consciousness, love remain firmly in the philosophical and theological realm. Apart from additional defining words full alternative definitions are suggested as well (*e.g.*, 3, 4, 10).

Accepting the above suggestions would completely sterilize and smear the original idea of the paper. A fable of S. Mikhalkov “Elephant-painter” suits here as ironical metaphor. The elephant’s landscape painting was criticized by other

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animals for lacking Nile, and snow, and kitchen-garden... (22). The spectrum of the suggested additions to the definition also vividly illustrates the starting point of the paper: derivation of the consensus definition of life by the way of traditional disputes leads only to further inflation of the definitions and to accumulation of disagreements.

“The minimized definition fails to illustrate the myriad of possibilities of life’s emergence” (16). The minimized definition is not to illustrate, but to suggest what is common for that myriad. Another comment is “the question ‘What is Life?’ hardly can be considered scientific. Falsification is impossible” (6). But would not we still try to imitate life as close to its essence as possible? Why should we surrender to Popperian bounds, if current working hypotheses continue bring fruits of new knowledge?

The philosophical disputes are often about terminology at the expense of essence. Several comments are actually, terminological (which term is better to use): Description instead of definition (1), evolution instead of variation (7), processes instead of properties (are not self-reproduction and mutation both processes?), understanding instead of definition (14), and other. Is it, really, important how exactly one or another thing is called when a simple (“naïve” some would say) common sense picture is to be drawn? Few self-explanatory words are put together, describing what would be the target in the search for minimal system/process/network/transition at the border between life and non-life. The “enchancing exercise” (2) of word count is meant as the way out of terminological multinode net, to the simplest “what to look for”. The recipe, whether right or wrong, should be minimalistic, and one such recipe is offered. I hope that the definition suggested will be useful in the search for the border, and I am glad that this hope is shared, though not by all (see below).

I did abandon the rival grounds after suggesting the nine *definientia*. They may serve as, again, a tentative minimal set of relevant terms (notions, categories) to continue the debates, perhaps, on more fruitful basis. I did so with some “curtness” (7) since, after all it is not exactly my territory. The suggested minimal definition is, obviously, debatable, and “the final assertion of the definition of life needs more cautious and deeper consideration” (7). One possible outcome is the construction with self-directing and self-speeding (*ibid*). I suspect, however, that the debates would not go far away from the minimalistic definition (if only one-two words are added).

“Lack of sensitivity to the precise meanings of words” (14) is common criticism. The 123 definitions are all fuzzy (2) in various degrees. They emanate from enormity of the problem, and belief that only humble *descriptions* (1) may be suggested. The vocabulary of the definitions is fuzzy as well,

often giving different names for the same thing, not mentioning the eternal disagreements what would be the meaning of this or another word. The attempt to classify the words, as in the disputed word-count paper, may only be fuzzy as well as the concluding definition., as it is, indeed (7, 19), The word “force” is good example (14). Strictly, it is not energy, however, the only word group it may belong to is Energy. After all, force is  $dv/dt$ , and  $v^2$  is energy. Another example is uncertain meaning of “exact replication” (19). Again, it may belong, obviously, to Reproduction, rather than to any other of the nine groups, irrespective of what exact meaning would be given to it. “Evolution and changes are not synonyms” (17). Yes, but the suggested groups of words with similar meanings are not groups of synonyms. The “clear” Darwin’s formula “descent with modification” (19) is as fuzzy as self-reproduction with variations. Yet one more example of different understanding is derivative nature of complexity: it is asked by one commentator “why complexity (information) is a product of self-reproduction with changes (evolution)” (12), while according to another comment (7) it goes without question: “certainly, the sentence “the complexity (information) can be considered as product of 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”. Viruses “are in the strictest sense incapable of “self”-reproduction” (16). But the strictest sense is avoided intentionally, otherwise none of the words of the Reproduction group will go together. And no groups will be formed at all.

One argument against the alleged redundancy of the minimalistic definition is that “error-free replication (more precisely, any information transmission process) is impossible” (6). This is clear case of misunderstanding: the “variation” in the definition is meant, of course, as inherited propagated variation, not just error, that is mostly lethal.

Classification of definitional properties (8) is a whole universe of uncertainties. Every single classifying word would invite disputes. For example, does “metabolism” belong to Chemistry, or to Life, or to System? The most frequent words of the vocabulary are “life” and “living”. Strictly speaking, they do not belong to the same group of meanings, though common sense (or intuition) would put them together. How to classify the words without coming to absurd extremes of a definition (all inclusive definition, or meaningless one-two word stumps, like “living matter”, or “system and environment”)? By suggesting those nine groups of related words I have taken a risk to find a golden middle that suits *my* intuition and common sense. And I do have reasons to believe that it is close to the intuition and common sense of many.

The end result of the “anthropomorphic consensus polling” (2) – nine or so word groups that could serve as *definientia* – is,

essentially, there, no matter how accurately the groups are gathered. Excessive sensitivity to precise meanings would end, perhaps, in up to hundreds of word groups, to completely blur the target.

Is the definition so loosely constructed, vulgar for scholastic perception, even non-scientific (e.g., 9, 16, 17), useful in any way? Opinions divided. There are few on the positive side (e.g. 1, 5, 6, 9, 12), while many disagree (2, 15-17). Does that definition have a heuristic power (6), and what it is useful for? One opinion is “the distinction between living and non living systems is a matter of belief and not science, it is not only hopeless but useless to try to define this indefinable state” (17). And “How can we use Trifonov’s novel definition of life in guiding us toward a better understanding of life?” (12). “I have not seen that efforts to define life have contributed at all to that understanding” (J. Szostak, 15). Yet, the Szostak’s definition “self-sustained chemical system capable of undergoing Darwinian evolution” is broadly quoted. It, thus, has something in it that appeals to researchers of life. Is not that a manifestation of some better understanding? My own definition helped me to realize, for example, that cell, probably, would not be needed as part of minimal definition. Thus, the efforts to imitate the minimalistic life, perhaps, do not have to include the attempts to build the cell, as, say, in the work of Szostak (23). As it is put correctly in (14), “we have to be clear about why we want to define life: is the purpose to be able to make and modify life, or is it to understand how life itself came into existence?” I thought of pursuing both targets. In the process of construction of the minimalistic life, hopefully, guided by the minimalistic definition, one certainly will arrive to better understanding. The definition quite likely has “potential to yield genuine biological insights” (6). “This definition can indeed be applied as a practical guide in topical origin-of-life research” (9). An immediate concrete example is recent experiment with synthesis of  $G_n$  on template of  $GCC_n$ , checking whether  $G$  would be occasionally incorporated opposite  $G$  as well, thus, evaluating possibility of mistakes in the presumably ancient replication system (24). This system based on  $GCC_n$  has been suggested as the “minimal process” (17) in (20 and references therein). The mentioned work is part of an effort to design minimalistic system (process) in accordance with the minimalistic definition.

Questioning the usefulness of the definition inevitably puts the whole work under question. Indeed, some comments are firmly negative (14, 19). Some, however, consider it as an important contribution, resolutely so (1, 4, 5, 7, 12), or reluctantly (14). At the same time a frequent motif is that the definition of life is simply impossible (1, 5, 15, 19).

The methodology of the word-count work is, generally, accepted with interest. The extreme negatives are given by “The ranking of words according to frequencies seems blind

to the underlying logical relationships” (4), and “There is no genuine scientific justification behind this approach and no guarantee that the numerous compared definitions are not all based on common misconceptions” (6). Yet it is “delightfully clever, objective and quantitative approach to defining life” (3), and “sound analytical effort applied rigorously on a comprehensive body of literature” (11). More moderate criticism relates rather to suggestions on improvement: “Trifonov should not stop at the very first *principal component* of his statistical vocabulary filtering approach” (2). This suggestion is, unfortunately, unrealistic as the statistical ensemble for the possible second component would be too small. Supplementing the list of definitions by data from other sources would be justified (3) but these data have to be not single individual definitions, like the one by V. Kunin (25), as suggested in (13). I operated with known *collections* of definitions, which I did not compile myself, not to get excessively biased. Property classification should have been performed (8). Weighted measures of information capacity of various words should be used, and structured method for clustering rather than intuition only (12). Inclusive capacity of the groups has not been estimated (19). “Attempt to seek components that are both necessary and sufficient cannot be accomplished through the clustering procedure” (12). At this point I would disagree, since the clustering was not used for that purpose in the paper. Rather some straightforward (non-scientific!) intuitive reasoning. The above suggestions are acknowledged and will be considered in future work.

Several cases of the “Is that life?” category popped up in the discussions.

“Frost tracery on a window pane or frostwork-type mineralizations in cave deposits” (2) is suggested as a non-life example that fits to the definition. I would not agree with this, since the replication of ice crystals shows variety of shapes, but *the same* variety that does not change. Each crystal type reappears unchanged. The indivisible pair self-reproduction/variation, of course, implies that the variation is copied in the next reproduction cycle. Thus, the statement that “self-reproduction *without variation*” would be entirely fictitious, in that it can never be realized as a natural process (2), is trivial. It simply says that every copying is non-exact. But is the copying mistake always inherited? Another example of the confusing non-life phenomenon with life is “the soap bubble divided into two smallest bubbles” (19). There is no variation component in it, and it is division, rather than replication. Sterilized cat and frozen bacterium (4), as well as mules (8, 11) are just manifestations of life, or aberrant forms of life – not a challenge to any general definition. The fossil that “continues to exist in museums and in the memory does not die” (10). But it does not live either, as it does not make copies. On the other hand, “a computer virus performs self-reproduction

with variations. It is not alive” (9). By my definition it is. I thought that the two key features are “applicable not just to “earthly” life but to any forms of life imagination may offer, like extraterrestrial life, alternative chemistry forms, computer models, and abstract forms” (20). Similarly, considering the generality of the definition it is wrong to state that I “pound on the RNA-world drum” (13).

In conclusion, after reading the comments I realized that although what I have done is not in the main stream of research on definitions of life, and not fully justified methodologically, the result, as fuzzy as it is, and, thus, questionable for some (but complimented by others) gives the tentative self-explanatory concise answer to the questions “what is that we are all looking for”, and “what to do to get it”, although exact wording may need some brushing to become academically approved. “The reader interested in the subject of defining life and explaining its early evolution will find sufficient substance in (20) to make this article worth reading and instructive” (13).

I am grateful to all commentators, who joined my humble efforts to move towards elusive target – origin of life – for many suggestions and thoughts to contemplate. I hope to continue the discussions beyond this time- and space-wise brief exchange, as many questions remain unanswered.

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