**RESPONSE TO REVIEWERS 2 and 3**

Manuscript ID: Life-375954

Type of Manuscript: Article

Revised Title: The origin of the Prebiotic Information System in the Peptide/RNA World: A Simulation Model of the Evolution of Translation and the Genetic Code

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Chatterjee and Yadav: Response to the Reports of the Referee 2 and Editor’s Recommendations.

**General responses to Reviewer 2**

We are pleased that reviewer 2 provided us with thoughtful suggestions to revise the manuscript. Here is our detailed response to the comments and criticisms. We have made significant revisions of the manuscript in this version.

**1. There is no question about the lack of possibility of scientific proof of what happened between the origin of life on primordial Earth and the present times. However, the introduction of your article lacks such a large number of literature references of works of colleagues who worked for decades and years on questions for which you give answers without citing, that reading your introduction appears mainly as a lack of respect to these colleagues.**

**Your citations give respect to many works that are equally speculative as**

**your own. But those who worked experimentally to actually scientifically**

**clarify these questions you ignore in your citations. I take this as highly**

**superficial and badly mannered, sorry. I am very probably not the only one**

**who reacts like this. When reading your first version I started adding comments, in order to give you signs where citation work to experimental work is missing (without giving**

**the full citations, because it is too much work for me and, if you pretend to**

**write such an introduction, then this should be your effort to find these**

**original articles, read them and then cite in your manuscript, a lot of work that**

**you elegantly circumvented through what I call "storytelling"!). I transferred**

**these comments to your second version and stopped there, where I honestly**

**think that you should start your original work article at the earliest. The**

**introduction is very long, very superficial and lacks respect to many**

**colleagues.**

**This is the reason for why I rejected your first version as a review article, and**

**this is also the reason for why I cannot accept the introduction part of your**

**second version. I wrote on line 412 the comment "begin your article here".**

**However, this was a handwaving proposition. I must admit that I do not have**

**the time to go through the rest of the article with the same exactness as up**

**to that point. I suspect that you simply carry on in the same superficial, not**

**objective feebly scientific way of describing science as a "storyteller", rather**

**than a scientist. Storytelling is important in science, I agree, but with all due**

**respect to those colleagues that work hard experimentally to give some flesh**

**to these bare bones, and clearly stating as being speculative. It is not good**

**to mix objective truth with speculation, not good for anybody, including for the**

**imagine of a serious scientific journal.**

We respond: First, we thank referee 2 for your time and the second round of comments and criticisms toward the improvement of our manuscript. We greatly appreciate your input. It appears from your comments that the *Introduction* *and Background* of our paper was the weakest part of our manuscript and we have remedied that deficiency. We trimmed the introductory part 72%, from 18 pages to 5 pages, as you suggested, focusing more on the objective of the paper. Many of the narratives criticized by you have been eliminated from this focused version of the introduction.

**2. New citations: The reviewer recommended in his annotated criticism to cite the following papers in the introductory part:**

**(1) Boehnke and Harrison (2016), *PNAS*, on Late Heavy Bombardment;**

**(2) Powner et al., (2009), *Nature*, on RNA synthesis;**

**(3) Ritson and Sutherland (2012), *Nat Chem* on RNA synthesis.**

We respond: Although we have condensed the introductory part considerably, we have added these references in the revised version in appropriate places to update the revised manuscript. [see page 6, line 546 for reference 1, and page 12, line 994 and 997 for references 2 and 3].

**3. I propose the following, which should be the best for both the authors and**

**the image of Life as a scientific journal. Split this huge manuscript at least in**

**two parts. Submit the introduction storytelling part, where you have included**

**with care a maximal number of primary literatures on all the "statements" that**

**you give without citations (thus far), as a review article. Perhaps you should**

**even split this in two review articles: a geochemical and a polymerization**

**review article.**

We respond: You are right to point out the weakness of the long introductory part. We have shortened the introductory part considerably, omitting the ‘story telling section’ entirely (see previous responses), and highlighted the objective of the paper.

**4. In a second/third and original science article submit your original theoretical**

**work, which you claim to be new and unpublished. The form that you chose**

**here is much too long and mingles too much unsupported uncited**

**speculation with new original work.**

We respond: We have followed your advice in this version. We concentrated and consolidated the main theme of our paper on the ‘prebiotic origin of the information system.’

We updated the biological information system, revised the manuscript, and shortened the abstract accordingly to describe a novel model. We hope this time we are able to communicate to the readers more effectively.

**Reviewer 3:**

**Which insights are gained? What are the conclusions?**

We respond: Although the origin of the prebiotic information is not fully understood, the manufacturing processes of different species of RNAs and proteins by molecular machines in the peptide/RNA world require not only physical quantities, but also additional entities like sequences and coding rules. The demand for wide range of specific enzymes for catalysis of complex prebiotic chemistry was the main selective pressure for the origin of information system for creating programmed protein synthesis. These coded proteins are specific and quite different from random proteins generated by linking amino acids in vent environment. There is a great potential of application of numerical codons in bioinformatics in DNA mining. Our use of numerical codons provides a new way of looking at the central dogma, which becomes digital.