Origins of life before the cell: echos from the past with broad implications in our future

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Abstract. The following pages refers to the origin of life, but the discussion focuses far beyond finding the place where it probably started, and moves toward some intriguing questions and some of its broad implications for evolution itself. Can life flourish in all its complexity from a single proto-organism model that thrive thanks to natural selection at an individual level? Or, is there any implicit constraint in the mechanisms that drives evolution in the first steps of precelular life to allow community-based, collaborative abiogenic systems that differ from cellular life as we know it? As we will discuss here, it seems pertinent to expand some evolutionary concepts that seems to reach the limits of the discipline, and can be helpful to link the abiogenic world where life probably emerge, and the Darwinian cellular world ruled by the natural selection. With some of these questions in mind, we are obliged to at least consider the implications of this answers for the future exploration of the space, particularly within the field of applied astrobiology, a discipline that will have to tackle the problem of how a minimal viable community of microorganisms or precelullar forms, can thrive and cross the Darwinian threshold that allow life to take over a planet, by creating a Biosphere. A key question for the future of life beyond the boundaries of our planet.

Keywords: Evolution, Origin, Life, Cell, Environment, History.

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Introduction

The origin of life is one of the Holy Grails of science. Trying to solve this mystery is not only essential to understand our origin, but it also helps understanding the place of terrestrial life in the cosmos and its place in the future. This deep context gives rise to a question with great implications for evolution itself: Can life flourish in all its complexity from a single proto-organism model that prevailed thanks to natural selection at an individual level? Or else, are there any implicit restrictions in the evolvability of early life that lead us to assume that life started from a collaborative community system ruled by evolutionary organisms acting at a group level? As you will see here, addressing these questions lead to reconsider the evolutionary mechanisms responsible for the formation of life as we know it.

The origin: Here or there? A sterile discussion

Currently there are two sets of hypotheses on the origin of life, which can be grouped by the place of the events: the first one states that the origin happened somewhere in the cosmos (panspermia) and the second one that the origin happened here on our planet (abiogenesis). The first set of hypotheses states that the origin of life took place outside our planet and that life was sowed on Earth by some sort of mechanism, from meteorites to intelligent beings (Warmflash and Weiss, 2005; Munévar, 2013). This hypothesis assumes that the emergence of life is an improbable, maybe singular, event that only happens in some places of the universe. Therefore, the Earth in itself does not have the conditions needed to originate it and needs to import it from somewhere in the Cosmos. By placing the issue outside the planet, any chance of knowing how life originated gets clouded, since the initial variables they work with would be unknown and the possible scenarios to propose a model would be infinite. In its less radical form, panspermia sets out that organic molecules, fundamental blocks for the formation of life, were sowed on Earth by the accumulation of impacts of space material. This allowed the formation of the first life forms given the planet's favorable conditions (Kvenvolden et al., 1970; Luisi, 2006). This is not absurd: around 15,000 tons of space material enter the Earth every year, that is, 41 tons of meteors, micro-meteors and micro-asteroids a day, 70% of which lies in the sea (Rogers, 1993; Nesvorny et al., 2011). This diverse material coming from space contains some traces of organic compounds identical to those produced by life (Deamery and Pashley, 1989; Warmflash and Weiss, 2005; Luisi, 2006).

The second set of hypotheses, abiogenesis, tries to explain the origin of life as emerging from organic and inorganic molecules present on Earth, which interacted and formed the molecule systems able to create self-organization and self-replication processes that finally led to the formation of a discrete cell entity that originated all known life (Luisi, 2006; Egel et al., 2011). Abiogenesis researches allow emphasizing that the emergence of life occurs within a probabilistic context and that the Earth, as a habitat, offers the right conditions to be within this probabilistic framework. There is no standardized model for abiogenesis. Some models propose mechanisms from chemiosmosis systems in marine hydrothermal vents, through photoactive systems in shallow waters to pre-cell worlds based on clay, zinc, sulfurs or iron (Luisi, 2006; Srinivasan and Morowitz, 2009; Egel et al., 2011). So far, no model has demonstrated stronger arguments than the others and, consequently, each one of them solves some issues, but loses ground on other fronts: compartmentalization, energy availability, geologic time window, consistency with the conditions on early Earth, self-replication, self-sustainability, organic material synthesis and transmission of information, to name only a few. Recently, synthetic biology has tried to address the issue of abiogenesis by using to different approaches with intriguing results. In one of them, the scientists modified a cell to find out what the minimum components are that allow due performance by using a "top-to-bottom" methodology, be it by suppressing part of the genome or introducing a synthetic one (Srinivasan and Morowitz, 2009; Gibson, 2010). The other experimental approach tried to synthesize a minimal, functional and completely artificial protocell based on self-replicating lipid vesicles with incorporated genetic material able to synthesize a minimum metabolome that, according to some authors, should be possible in a few years (Zimmer, 2009; Chiarabelli et al., 2012). No matter how interesting they may seem, the success of these experiments would only indicate that the abiogenesis process is possible; however, it does not solve some of the main questions about the origin of life: In what part of the abiogenesis process does evolution start? Are the same principles of evolution we see around us applicable to the origin of life? Can life emerge from a single and improbable successful replicant?

Abiogenesis and metabolism

Among the multiple abiogenesis models trying to explain the origin of life there are some that defend the early appearance of genetic information and others that argue that genetic information was the step following the appearance of abiogenic metabolism (Luisi, 2006). The chicken-and-egg problem is not part of the objective of this reflection; however, as will be analyzed below, it is possible to build some bridges between the possible abiogenic origins of metabolism and genetic information as mechanisms for cell self-sustainability and self-replication.

When we talk about the origin, most of the efforts are based on studying universal cell characteristics. Thus, the more spread and conserved a function, metabolic pathway or cell structure, it is more probable that it will invoke its origin. The "central biochemical pathway," as commonly referred to in textbooks, refers to the metabolic pathways present in yeasts and bacteria, pathways widely spread in nature, dating back to the early forms of cellular life (Romano and Conway, 1996; Karp, 2010). This central pathway includes: the gluconeogenic/glycolytic pathway[1] (Embden-Meyerhof-Parnas), and its alternative pathway in prokaryotes (the Entner-Doudoroff pathway), the pentose-phosphate pathway and the tricarboxylic cycle (Krebs Cycle). The Krebs Cycle is paramount for our discussion. All the essential components of cellular life can arise from this cycle: amino acids, purines,

pyrimidines, fatty acids, phospholipid isoprenoids and porphyrines (Smith and Morowitz, 2004). In addition, their universality is overwhelming: the 11 carboxylic acids of the Krebs Cycle are the central nucleus of the aerobic metabolism of the entire life and its function is distributed among the three-domain system: archaea, bacteria and eukaryote. Thus, the sequence of reactions flows oxidatively through modern phototrophs and oxygen-dependent heterotrophs, but reductively in most chemolithoautotrophs (Smith and Morowitz, 2004; Srinivasan and Morowitz, 2009). Studies in anaerobic organisms suggest that the Krebs Cycle may have evolved more than once, and although theoretically there are other alternatives for this cycle, the known configuration is the most efficient one (Melendez-Hevia et al., 1996). In fact, five critical steps behave like nodes from which all the anabolic pathways arise for the synthesis of cellular components; therefore, its canonical model gives rise to the entire metabolome, which supports its efficiency in biochemical and thermodynamic terms (Srinivasan and Morowitz, 2009).

The Krebs Cycle has traditionally been cataloged as a key problem in cellular evolution because its complexity can be hard to explain by using gradualist selective processes: How can natural selection explain the formation of a complex biochemical structure with multiple coupled steps, when an intermediate structure has no obvious adaptive function? Is this a typical case of irreducible complexity? We must make clear that the universality of the cycle must not be understood as an exclusive consequence of the evolution of all life from a common ancestor, but rather as a solution imposed on life within the context of organic chemistry, likely to be in the environment on early Earth (Smith and Morowitz, 2004). The pieces to put together the jigsaw of the Krebs Cycle already existed in the context of abiogenic organic chemistry and the only thing life had to do was to join the pieces. For instance, the steps for the production of carboxylic acids can result from spontaneous abiogenic processes (Melendez-Hevia et al., 1996; Davis, 2002). Thus, for example, traces of materials such as oxalate, succinate,

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[1] Some enzymes participating in the lower portion of the glycolytic-gluconeogenic pathway (the portion called main pathway) are extremely phylogenetically conserved and widely distributed among the three domains of life. The enzymes of this main pathway are: triose phosphate isomerase (TPI), glyceralhdehyde 3-phosphate deshydrogenase (GAPDH), phosphoglycerate kinase (PGK) and enolase (EC). The universal, highly conserved distribution of the main pathway portion of the glycolytic-gluconeogenic pathway supports the concept that this pathway evolved "from bottom to top", that is, towards gluconeogenesis, in completely anaerobic environments that remind us of the hypothetical habitat of the common cellular ancestor.

maleate and glutarate were found in the Murchinson meteorite. All of them are compounds of the Krebs Cycle (Kvenvolden et al., 1970). The same compounds have been spontaneously synthesizedin the laboratory with experiments similar to the pioneering abiogenesis Model proposed by Urey and Miller in 1952 (Luisi, 2006). The reactions of this cycle, from a biogenic context viewpoint, are ruled by chemical and thermodynamic restrictions (Melendez-Hevia et al., 1996; Davis, 2002). There is strong dependence on the concentration of each intermediate for the organized sequence of steps without deviating from the central cycle, since, given the sufficient concentration of an intermediate, the latter spontaneously becomes the next one. According to Smith and Morowitz (2004), this is explained by the fact that the canonic form of the Krebs Cycle is statistically favored by several possible redox patterns, especially if the analysis is made within the context of the conditions of the early Earth. According to said authors, the modern pattern of the Krebs Cycle is the most efficient solution in biochemical and thermodynamic terms, and its appearance in the abiogenic context explains its universality and evolutionary strength. The implicit ability of life to increase the efficiency of reactions by natural selection allowed adding and interconnecting new and diverse metabolic pathways; these complementary and alternative pathways undoubtedly moved from or to the Krebs Cycle as we know it (Smith and Morowitz 2004). As suggested, the abiogenic restrictions on early Earth imposed the core guidelines for terrestrial cellular metabolome and the genome, guardians and scenario of evolution, simply allowed maintaining the most efficient pattern in operation.

Abiogenesis andgenetic information

No matter how interesting these considerations on the prebiotic metabolism may be, there must be a way to store the information from the environment to efficiently self-sustain and self-replicate life forms. Without that process, evolution simply cannot occur. Life, as we know it

today, stores this information in complex chains of nucleic acids that need that one of their functional products, catalytic proteins, replicate in new sequences of nucleotides while metabolically self-sustain the system: a new chicken-and-egg dilemma. Is there a molecule capable of storing information and having catalytic capacity at the same time? Yes, that molecule is RNA and the discovery of its catalytic capacity, thanks to the finding of ribozymes and the peptidyl-transferase activity of RNAr, changed the theories on the early evolution of life (Luisi, 2006; Murray et al., 2009; Lincoln and Joyce, 2009). Due to its dual capacity, it was suggested that the origin of the age of genetic information was based on RNA; said hypothesis is known as the "RNA world," in which this molecule was in charge of replication and the catalysis before the beginning of cellular life (Bernhardt, 2012).This hypothesis is not problem-free: it is extremely labile, the repertoire of catalytic functions is reduced and, as it is a complex molecule, its spontaneous synthesis in abiotic conditions seems thermodynamically contradictory (Bernhardt, 2012). However, ribozymes with only seven nucleotides with catalytic capacity have been discovered. This indicates that small RNA chains with catalytic capacity could have been synthesized in an abiogenic manner (Bernhardt, 2012).The proof of this RNA pre-cellular world seems to come from the world of viruses: several key genes contained in the virus genomes in charge of the morphogenesis and replication are shared by many groups of RNA virus and they do not exist as any known life form (Koonin et al., 2006). But how did the bridge between nucleic acids and proteins started to be built? The first step seems to have been the appearance of RNAt, which appeared from a hairpin-shaped RNA, maybe with catalytic functions, which formed a duplex structure thanks to the symmetry of the interactions between base pairs (Di Giulio, 1992). The functions of this structure are unknown, but laboratory experiments suggest that the RNA catalytic repertoire is not as simple as it was thought to be (Bernhardt, 2012; Nagaswamy, 2003). How do amino acids enter here? Some of these compounds could be abiogenically

synthesized by copying the "central biochemical pathway". Szathmáry proposes that the first abiogenic amino acids were used as co-factors for the catalytic activities of RNA; in fact, it seems that the primordial RNA system was covalently bonded to some of the earlier amino acids (Di Giulio, 1998; Szathmary, 1999). It is not strange then that some authors suggest that the ribosome region with peptidyl-transferase activity, in charge of building the polypeptide chains, developed from this same duplicated RNA hairpin-shaped system (Tamura, 2011). With this scarce evidence and conjectures a bridge seems to be built between the RNA world and amino acids, future construction blocks of the world of proteins.

To go from nucleic to polypeptide acid, the information needs to be translated and to do so a code is needed. One of the most fascinating questions arises then: How did the genetic code form? It is not surprising that this question has intrigued the scientific community so much. The genetic code is organized in 64 codons that translate 20 aminoacids and is almost universal to all sorts of cellular life forms from the very first common cellular ancestor, and although there are few exceptions, the central nucleus is generally conserved through all the other domains of life, including viruses (Koonin, 2009). Crick suggested that the genetic code is a "frozen accident" that simply remained fixed because all life forms share a common ancestor; in other words, the universality of the genetic code is nothing but an epiphenomenon due to the singularity of the last common cellular ancestor (Crick, 1968; Koonin, 2009). Any subsequent radical change in the code would be eliminated by natural selection, since the reassignment of codons would have lethal effects on the organism due to deleterious pleiotropic changes in the proteome, and this finally allowed setting the code (Koonin, 2009). However, this explanation is unsatisfactory from the epistemological standpoint, since it turns in to a blind alley because it is inexplorable from an experimental point of view. The same relative flexibility of the code put the insight of the frozen accident to the test, as there are more than 20 variations of the code that have proved to

be adaptive, which indicates that the code has evolvability (Koonin, 2009; Moura et al., 2009; Moura et al., 2010). There are three hypotheses to explain the origin of the genetic code that were thoroughly revised by Koonin (2009), which are not mutually exclusive (Di Giulio, 2005; Koonin, 2009). The first one is the stereochemical theory, in which the assignment of codons is defined by the physical-chemical affinity between amino acids and accompanying codons (anticodons).This hypothesis is supported by experimental data showing that at least 8 out of the 20 aminoacids select the sequences of their anticodons according to, among other things, their polarity affinity (Yarus et al., 2009). Nevertheless, the statistical significance and validity of that association between the RNA and the amino acids is still questionable and the hypothesis needs more experimental validation (Ellington et al., 2000). The second one is the theory of adaptation, which suggests that the structure of the genetic code was shaped under selective forces that designed the code so as to minimize the effect of synthesis errors and the function of the translated proteins (Koonin, 2009). This hypothesis is supported by the fact that the cannon code is very robust against punctual mutations, a property that could well come from the established code and be shaped by selection processes and not be an explanation of its origin itself. The third hypothesis is extremely interesting, since it manages to build the bridge between the origin of the genetic code and the origin of cellular metabolism. It is known as the co-evolution hypothesis (Di Giulio, 2004; Wong, 2005). This hypothesis suggests that, within the context of prebiotic synthesis only a small group of amino acids, which can be the result of the first abiogenic organic synthesis, can be produced. Therefore, the evolution of a translation mechanism should start by using this small group and spread to others (Wong, 2005). Codon assignment developed progressively, following metabolic relationships between amino acids. In its original form, Wong proposed that the evolution of the genetic code took place in three critical moments (Koonin, 2009; Wong, 2005). In a first stage, the eight amino acids that can be

detoured from the "central biochemical pathway" were incorporated. In a second stage, seven other amino acids biochemically derived from the original prebiotic amino acids were added. The last phase took place when the last five amino acids were added through non-cannon, more complex synthetic pathways. It is worth noting that, although there is some evidence in favor (Di Giulio, 2004, 2008), it has not been demonstrated that the co-evolution hypothesis is strong enough from a statistical viewpoint. However, the hypothesis makes sense in the light of what has been previously described on abiogenic metabolism and thermodynamic restrictions imposed to the possible pre-metabolic pathway designs: thus, the entire group of stage 1 can be synthesized in abiotic conditions reenacting the early Earth (Kobayashi et al., 1990). In addition, amino acids such as glutamate and aspartate only require one to two reactions from the "central biochemical pathway," whereas aromatic amino acids, such as the tryptophane require fourteen steps (Karp, 2010; Smith and Morowitz, 2004); this suggests that complex synthesis amino acids must have appeared long after the synthesis of amino acids from the "central biochemical pathway" (Davis, 2002). In any event, evidence is still scarce and none of the models have been accepted as the rule. Ellington et al. have a lapidary reflection on it: *"we may never know the exact nature of the scene of the frozen accident because the transition from the RNA world to the protein world obliterated virtually all of the comparative biochemistry that might have been used to chart descent, we may have to forever remain agnostics about the code's origins, and to assume ignorance as the only viable scientific alternative"* (Ellington, 2000). A sound position, but, what if the important thing is not to disentangle the succession of events that led to the origin of the code, but rather understand the evolutionary mechanisms that allowed its appearance and put all the pieces described in this jigsaw together? These reflections have deep epistemological implications, as will be described in this text.

Space exploration and the sowing of life in other worlds: Are they essential to understand the origin of life?

Panspermia theory tries to explain the origin of life as a product imported from outer space and, as previously stated, said phenomenon is beyond our knowledge. A more fructiferous discussion arises by experimentally addressing the inverse process: taking terrestrial life to outer space to explore not only the intriguing future applications, but also the deep implications that may arise about the origin and evolution of life. The accidental conveyance and viability of organic, even biologic material through space is not impossible. For instance, despite NASA's political restrictions of planet protection aimed at trying to reduce the content of microorganisms carried in each mission, they transport several thousands of spores and bacteria. These measures are taken to prevent microbian contaminants from Earth from reaching a celestial body and endanger the hypothetical native life (David, 2011). Proof of this is the existence of polyextremophile organisms that withstand the adverse conditions of space; two significant examples of this are the tardigrades and the *Deinococcus radiodurans*. The former are a phylum of tiny animals that endure conditions of extreme pressure, desiccation and temperature. They have been recovered after space travels, showing that they can grow again and multiply thanks to a process called cryptobiosis (Goldstein and Blaxter, 2002; Jonsson et al., 2008). The latter is the intriguing bacterium *Deinococcus radiodurans*, which is capable of tolerating a radiation dose 500 times higher than the lethal dose for humans. This strange feature seems to be the result of an adaptation to protect and repair the genome after long periods of desiccation (Zahradka et al., 2006; Slade et al., 2009). Although intriguing, these extreme examples of endurance are useful for these organisms to tolerate adverse conditions to then grow again when the environmental conditions are optimal for their growth. Can any organism not just withstand but also grow

and reproduce in such a hostile environment such as one on a different planet? Two recent studies show that some bacteria can grow in conditions similar to those found in Mars. *Serratia liquefaciens*, a widely spread generalist bacteria, and bacteria of the genus *Carnobacterium* from the Siberian permafrost can grow in conditions of anoxia, high CO_2 content, low atmospheric pressure and low temperature (Nicholson et al., 2013; Schuerger et al., 2013). Although the growth of these two groups of microorganisms seems possible in Mars, these conditions are just four of seventeen threats that any life form would have to survive to in the red planet, including the most dangerous of all, radiation (Matson, 2013). Why are these experimental approaches of space exploration relevant to biology in general? Firstly, any experiment seeking to study the growth and maintenance of one single isolated life form in another planet would be an empiric approach to one of the radical versions of the panspermia hypothesis, as it would allow investigating if an extremophile life form is able to start the evolution process if the conditions are suitable on the surface of the new home (Rampelotto, 2010). More than giving a solution to the enigma of the origin, these experiments will allow understanding the mechanisms that may explain how life can persist in the cosmos and thrive in a new home. However, as will be described below, this "lonely pioneer" model that starts evolution is contrary to what we have learned on the evolutionary mechanisms that may explain life before the cell. No matter how successfully a life form can resist extreme conditions by itself, terrestrial life is intrinsically relational and community-based. Each cellular life form known, from an ontological viewpoint, has been shaped by the environment where it evolved and by its ecological relationship with other species. Stating this argument as a metaphor, no matter how complex a known life form may be, is just a note in the score, and only makes sense in the general context of the symphony of terrestrial life. However, an unsuccessful experiment of this kind would not be a failure, since it produces data to start designing a minimum viable ecosystem that may thrive by itself in another planet. The unexpected success of

an experiment like this would open, due to the possible serendipitous results, new, still unthinkable perspectives for the study of the origin of life even for future applications of astrobiology inside and outside the planet (Munévar, 2013). With these ideas in mind, it is time to explore and finalize the origin and organization of life as a collaborative phenomenon, a discussion that allows building bridges between non-life and life with deep implications on evolution itself.

Everything was and is connected

What evolutionary mechanisms can then explain the origin of life, not to create an improbable individual, but to shape a continuous process leading to the formation of the complex, majestic and omnipresent life as we know it? One of the key issues on the study of the origin of life is to actually build a bridge between non-life, apparently exclusively determined by the law of physics and chemistry, and life, determined not only by these laws, but also by evolutionary mechanisms, such as natural selection. But how can the evolutionary processes that govern life be extended to non-life? Authors have suggested that the theory of evolution should be analyzed in physicochemical terms to allow establishing a direct link between abiogenesis, no matter where the construction materials came from, and the evolution of known life. Pross proposes this extended formulation based on the concept of dynamic kinetic stability applied to replicative and collaborative organic chemical systems. Said systems can show emerging properties of complexity and organization (Pross, 2011), as supported by theoretical and empiric (*in vivo* and *in silico*) experiments (Sievers and von Kiedrowski, 1994; Lee et al., 1997; Yao et al., 1998; Kindermann et al, 2005; Lincoln and Joyce, 2009; Vasas et al., 2012). For this dynamic kinetic stability to exist there must be a population of replicants in continuous change to allow maintaining a pool of many probable designs and models in continuous cooperative inter-catalytic interaction over time. This process can only be maintained over time if there is a constant flow of stable energy in a

geological window of time to couple non-life with emerging cellular life. Since they are not lineal, said systems can be subject to sudden fluctuations due to environmental or physical changes that cause different coordinated interactions inside it and increase the organization and complexity; the greater the deviations from the state of equilibrium, the wider the correlations and interrelations that make these properties of evolution and self-organization possible (Sheliepin and Marín, 2005). For example, the abiogenesis models based on geothermal phenomena offer geological windows of time of thousands to millions of years, where thermodynamically favorable geothermal exergonic reactions have enough time to couple with organic abiogenic synthesis and allow the appearance of the pieces of a replicative system consistent with the pre-cellular scenario (Martin and Russell, 2003; Martin et al., 2008). These properties allow concluding that abiogenesis and evolution, more than two discrete steps, are a physicochemical continuum that allows the emergence, persistence and evolution of complex life. However, a key piece of the jigsaw is still missing: are Darwinian natural selection mechanisms responsible for this transition process? Or, is there any other mechanism that rules the evolutionary process that led to the emergence of the first cellular life form? The simplest known cellular form, the *Mycoplasma genitalum* bacteria, needs 270 of its 380 genes to be able to function properly. It is evident then that the minimum conceivable cell today is very complex in molecular terms and needs a lot of genetic information to be functional (Griffiths, 2007). Based on phylogenetic analyses, it is believed that the common cellular ancestor had, at least, from 250 to 600 genes (Doolittle, 2000). This means that the probability that our common cellular ancestor had evolved from a single replicator by natural selection seems absurd. Life as we know it today evolves mainly by natural selection and is made up by defined organisms (species) that are reproductively incommensurable with other organisms and transfer their genes to the new generations in a vertical manner (Dawkins, 1976). What if in the beginning of life the environment did not select the most suitable individuals? What if evolution was a community-based phenomenon? Recently, some significant progress has been achieved in the synthesis of minimal individual life forms, especially based on self-replicating lipid vesicle with incorporated genetic material capable of synthesizing a minimum metabolome, which promise to be the gateway to synthetic cellular biology (Hanczyc, 2004; Deamer, 2005; Chiarabelli, 2012). However, none of these models, although capable to self-sustain and self-replicate, seems to predict that they will be able to evolve towards greater diversity and complexity. If life as we know it today seems to be individualistic, competitive and vertical, the evolutionary scenario where it occurred seems to be community-based, collaborative and horizontal (Yao et al., 1998; Jain et al., 2003; Koonin et al., 2006; Koonin and Novozhilov, 2009; Egel, 2011, 2012; Pross, 2011;Vasas et al., 2012). This process seems to spread from non-life to life. *In silico* studies have shown that community-based, collaborative evolution is not an exclusive pattern of genetic material replicants and can be extended to groups of chemical compounds where the accumulation of adaptations can occur. This evolution phenomenon occurs if the network of chemical reactions accumulates enough "nuclei" of viable reactions to allow the system become more complex and suitable (Vasas, 2012). Applying the same idea, Vetsigian, Woese and Goldenfeld suggest an evolutionary model of the genetic code where the sub-populations of elements from nucleic acids capable of transmitting genes horizontally allow the formation of an almost universal and robust genetic code (Vetsigian et al., 2006). The idea of maintaining the continuous horizontal flow of genetic information between basic replicant communities provides the means for the emergence of clusters of similar codes, which start to compete for niches; this community-based evolutionary process finally leads to the appearance of an almost universal code (Vetsigian et al., 2006; Butler et al., 2009). These two studies, added to Pross' extended evolution theory (Pross, 2011), allow building a bridge between the properties of complex systems described above

(Sheliepin, 2005), the abiogenic metabolic synthesis (Martin and Russell 2003), the emergence of genetic information in the RNA world, (Bernhardt, 2012; Koonin and Novozhilov, 2009) and the consolidation of the cellular evolutionary scenario (Woese, 2002; Goldenfeld and Woese, 2007). In this pre-cellular scenario, the horizontal gene transmission dominated the landscape of evolution, allowing the viable maintenance of a community of replicants by way of the shared use of protein innovations (Woese, 1998). As the cell designs became more and more complex and molecularly and genomically interconnected, a critical point was reached, where the vertical transmission of genetic material started to gain significance to preserve the discretion of the most successful systems (Woese, 2002). Thus, the new cellular function system becomes increasingly incommensurable with the genetic material of the community and, consequently, more resistant to the horizontal transmission of genes. At that moment, a point of no return when we can talk about individuals and species is reached and the reconstruction of the tree of life can start, thus starting the Darwinian evolution predominantly ruled by natural selection of individuals. As Woese (1998) put it more than one decade ago "*The universal ancestor is not a discrete entity. It is, rather, a diverse community of cells that survives and evolves as a biological unit.*" This is how the common universal ancestor was born. Hence, we can start the phylogenetic reconstruction of the several taxonomic groups in the model known as the tree of life (Darwin, 2010). Do these hypotheses, conjectures, theories and findings have any relevance today? Yes, especially regarding the structure of the theory of evolution (Weiss and Buchanan, 2011). We are not saying that the insight of early microbial evolution as a community-based, collaborative and horizontal phenomenon is threatening Darwin's theory as Einstein's physics did with Newton's one in its day (Kuhn, 1971). As mentioned by Gould (2004), the structure of the theory of evolution is still there. However, phenomena such as the horizontal transmission of genes, which had already put microbiologists on their heads

(O'Malley and Boucher, 2005), deserves a revision of the structure to incorporate said mechanisms to the theoretical structure, not as an occasional curiosity, but as an essential evolutionary mechanism to explain the diversity and complexity of known life (O'Malley and Boucher, 2005; Goldenfeld and Woese, 2007). The indelible marks of these mechanisms and their radical importance in the transformation of life over time are there before our very eyes. They are hidden in the omnipresent and ancient virome responsible for the horizontal transmission of genes through all the ecosystems since before the cells existed to our days (Suttle, 2005; Koonin et al., 2006). It is in the endosymbiosis events that produced complex quantum jumping such as the formation of the first photosynthetic and heterotrophic aerobic eukaryote cells (Cavalier-Smith, 2006a). They are within that 25 to 50% of the proteome of each organism that has undergone at least one event of horizontal transmission in its phylogenetic history (Jain et al., 2003; Gogarten and Townsend, 2005). They are present in the mechanisms of collaborative and community-based evolution not limited to the early stages of life and continue operating today, not only at a species level but at supra-organismal levels (Weiss and Buchanan, 2011). Consequently, it is not strange that some authors suggest that animals should no longer be considered as "individuals" in ecological and physiological terms due to the immense diversity of symbionts that made up their organisms and are essential for their biological functions (Gilbert et al., 2012). These symbionts are indispensable in the immunology and metabolism of each species (Qin et al., 2010). It has even been demonstrated that the microbiome has determined the evolution of structures, such as the appendix (Laurin et al., 2011; Smith et al., 2013) and is indispensable for the complex development of some organs, such as the intestine (Gilbert et al., 2012). Cooperative complexity has made possible the evolution of adaptive traces at all levels, going beyond the individual, and is a fundamental principle from cells to ecosystems (Weiss et al., 2009; Weiss and Buchanan, 2011; Gilbert et al., 2012).

Edward O. Wilson has demonstrated that the spread of individual natural selection to group selection has allowed social insects, such as the ants, to become the most significant animal organism in terms of biomass in the biosphere thanks to the development of eusociality as a distinctive feature (Nowak et al., 2010). In this multilevel evolution model, the only one that can explain "*the greatest threat to Darwin's theory*" (Darwin, 2010; Wilson, 2012) the concept of individual is left aside and replaced by a concept of super-organism, where sterile worker ants are nothing but extensions of the phenotype of the queen, or else, alternative extra-somatic expressions or its genome (Nowak et al., 2010; Wilson, 2012).

All of them are some theoretical and empiric problems addressed from the non-traditional evolutionary approach, which has allowed explaining problems difficult to address from the classic evolutionary hypotheses.

Conclusion

As we have tried to show here, the study of the origin of life must continue to look beyond the discussion on the place of origin of the construction material of the first cells. Although the development of the first completely synthetic cell form shows that life can arise from purely abiogenic processes, the development of said cell still does not allow seeing any bigger picture. From these first steps, the study of the origin of life can also be focused on the evolutionary mechanisms that may allow community-based, collaborative abiogenic systems to take this big jump and generate minimum ecosystems that can thrive and generate discrete life forms adapting to different habitats as described by Darwin more than a hundred years ago. As shown in the previous paragraphs, the findings on the evolution of the first metabolic pathways and the origin of the genetic code are brimful of evidence pointing at collaborative, horizontal, non-Darwinian mechanisms as being responsible for the origin of life, from abiogenesis to proto-cellular life, to the diffuse network of highly organized microbial ecosystems that,

in successive eons, is transformed into the tree of life by Darwinian mechanisms.

The new approaches to the origin of life and microbial micro-cosmos threaten to restructure our vision on life itself and evolution, not to say that Darwinism is wrong, but to teach us that evolution is a dynamic process that uses several mechanisms to allow life establishing deep interconnections that we are just starting to understand. These approaches not only allow knowing the possible chain of events between the origin and the diversity of life, but also allow opening new fields of development and research in synthetic biology and astrobiology to understand which the minimum parameters are to allow life to thrive away from home in the future. Will we be able to listen to these echoes from the past to understand the biology of the future?

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Conflict of interest statement

Authors declare that they have no conflict of interests.

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