

Juli Peretó

Cavanilles Institute for
Biodiversity and Evolutionary
Biology, and Department of
Biochemistry and Molecular
Biology, University
of Valencia, Spain

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Address for correspondence:
Institut Cavanilles de Biodiversitat
i Biologia Evolutiva
Poligon de la Coma, s/n
E-46980 Paterna, Spain
Tel. +34-963543666. Fax +34-963543670
E-mail: juli.pereto@uv.es

Controversies on the origin of life

Summary. Different viewpoints, many with deep philosophical and historical roots, have shaped the scientific study of the origin of life. Some of these argue that primeval life was based on simple anaerobic microorganisms able to use a wide inventory of abiotic organic materials (i.e. a heterotrophic origin), whereas others invoke a more sophisticated organization, one that thrived on simple inorganic molecules (i.e. an autotrophic origin). While many scientists assume that life started as a self-replicative molecule, the first gene, a primitive self-catalytic metabolic network has also been proposed as a starting point. Even the emergence of the cell itself is a contentious issue: did boundaries and compartments appear early or late during life's origin? Starting with a recent definition of life, based on concepts of autonomy and open-ended evolution, it is proposed here that, firstly, organic molecules self-organized in a primordial metabolism located inside protocells. The flow of matter and energy across those early molecular systems allowed the generation of more ordered states, forming the cradle of the first genetic records. Thus, the origin of life was a process initiated within ecologically interconnected autonomous compartments that evolved into cells with hereditary and true Darwinian evolutionary capabilities. In other words, the individual existence of life preceded its historical-collective dimension. [*Int Microbiol* 2005; 8(1):23-31]

Key words: autonomy · life definition · open-ended evolution · protocells

Introduction

Life is matter with two biographies: (i) ontogenetic, synchronic, developmental, individual existence, based on the autopoietic (i.e. self-building) properties of cells and their ecological (i.e. biogeochemical) consequences, and (ii) the historical-collective, diachronic, populational, evolutionary process. Metabolism and genetics are the two central pillars that sustain life. Every living being uses external sources of both energy and matter to fight against disorder, equilibrium, and death. Membranes and molecular machines located on the frontier between the inside and the outside control and manage flows of energy and matter for the benefit of the cell

itself. In current life forms, those activities are dependent on digital genetic records. Change, acquisition, and loss of fragments of the informative molecules are the basic mechanisms of evolution, i.e. the differential capacity for adaptation, survival, and reproduction. The historical persistence of genetic records depends absolutely on the metabolic and ecological abilities of organisms. A fundamental question is thus how the metabolic and genetic functions, which in terrestrial life forms are so intricately intertwined, came to be an integral part of the history of this planet. Which came first, the autopoietic or the hereditary properties of living matter?

What is life?

Although defining life is a difficult task, we recently proposed a definition that tries to join in a compact sentence both biographical aspects: "a living being is any autonomous

This article is dedicated to the memory of three illuminating scientists recently deceased: Ramon Margalef (1919-2004), Joan Oró (1923-2004) and Alfred Giner-Sorolla (1919-2005).

system with open-ended evolutionary capacities" [34]. The term "autonomy" refers to the relationship between the living being and its environment and their mutual modifications, as well as the capacity of a living being to use energy and matter to synthesize its own components, i.e. to self-construct, thereby building an identity separated from the ambient. In the simplest case, a living being is a cell (pioneering work on the minimal cell concept can be found in [25]). The term "open-ended evolution" refers to the capability of a living being to explore new functions and relationships with the ambient (including other living beings) and to adapt to diverse situations in an almost unlimited way. The range of physical conditions compatible with—using the words of Gold [13]—planetary infection by microorganisms is astounding: Wherever there is a useful energy source (for living beings, that means visible-light photons, certain inorganic chemical reactions, or organic matter) and liquid water, some form of biological activity can be found.

At the molecular level, biodiversity shows a no less striking biochemical unity: the same basic (cellular) organization, the recurrent use of DNA as hereditary material, the universal genetic code, and variations on the same bioenergetic mechanisms (i.e. chemical and chemiosmotic energy currencies). The most parsimonious explanation of those well-documented observations is that all current terrestrial life forms have the same late ancestor, the universal cenancestor—an idea that was already conjectured upon by Charles Darwin, based on much less evidence [4].

The origin of life

How can we approach the primordial steps of life evolution? In the "top-down" strategy, all known organisms are compared in order to reconstruct the genetic and metabolic makeup of the universal cenancestor. Thus, in the universal tree of life based on ribosomal structure, this essentially means comparing the two prokaryotic domains, *Bacteria* and *Archaea*, since the *Eucarya* domain is considered to be a chimera derived from prokaryotic partners. Molecular cladistic methods are among the most powerful tools available for making such comparisons, but the possibilities for going even further back in this type of retrospective study and venturing some careful guesses on stages preceding the universal cenancestor are limited. In the opposite direction, the "bottom-up" strategy starts with cosmochemical, planetary, geological, and any other useful source of evidence to reconstruct the ambient, chemical inventory and the processes involved in the origin of life. However, it is also possible to abstractly consider the primordial geochemical

conditions and then examine the theoretical principles that could apply to the oldest processes of matter organization. Mathematical models and computer simulations can help to define some general properties of the systems under consideration. Needless to say, many steps, stages, and transitions from chemical to biochemical evolution are, and will be for a long time, hot topics of scientific discussion. Table 1 shows a list of remarkable works devoted to the problem of the origin of life.

Ever since the historical contributions by Aleksandr I. Oparin, in the 1920s, the intellectual challenge of the origin of life enigma has unfolded based on the assumption that life originated on Earth through physicochemical processes that can be supposed, comprehended, and simulated; that is, there were neither miracles nor spontaneous generations. Thus, the scientific merits of Oparin's proposal are not in its details, which are always subject to change with the refinement of scientific knowledge, but in the possibility to experimentally test the plausibility of historical hypotheses and, even, to chemically implement very simple artificial life forms [18]. For example, in 1953, the Urey-Miller experiment [24] inaugurated the prebiotic chemistry research program [3]. Since then, many different reactions—notably, the synthesis of most amino acids, nucleic acid bases (as in the remarkable synthesis of adenine from hydrogen cyanide by Oró [28]), lipids, and other simple biomolecules—have been proposed to explain the abiotic origin of organic matter present in interstellar space [9], meteorites [9,20], comets [9,21], and the early *Archean* Earth (reviewed in [27]). Although some major abiotic syntheses are easier said than done, including the synthesis of very labile substances, such as sugars (e.g. ribose), or more sophisticated molecular arrangements, such as nucleotides (the abiotic combination of phosphate, [deoxy-] ribose and a base, in the correct positions, is far from trivial and can be well-considered as prebiotically inaccessible), the participation of mineral catalysts (e.g. clays as polymerization promoters [10] and borate as a sugar stabilizer [33]) facilitates some of the more difficult syntheses. Nonetheless, it is not only necessary to have a plausible scheme of abiotic synthesis for a biomolecule but also to explain how it would accumulate (i.e. present over enough time to be used) in the primitive planet [2].

Following Oparin's scenario, prebiotic organic molecules, either terrestrial or extraterrestrial in origin, built up in the oceans, thus promoting the organization of matter into primitive systems able to anaerobically thrive on environmental organics. In this scenario, life would have started with very simple anoxygenic and heterotrophic primordial cells. Difficulties regarding prebiotic chemical reactions in the atmosphere (since we still lack any robust evidence of its

Table 1. An essential library on the origin of life. (This is not an exhaustive list but mostly a personal choice)

Author (year of publication)	Title and reference	Remarks
Aleksandr I. Oparin (1924)	Proiskhozhedenie Zhizni. Moscovskii Rabotchii, Moscow	First work published by Oparin. First version in English published in 1967 by Bernal.
John B. S. Haldane (1929)	The origin of life. The Rationalist Annual for the Year 1929, edited by Charles A. Watts, p. 3-10	First work by Haldane, introducing the idea that the emergence of life was associated with the origin of viruses. The author also introduced the concept of prebiotic soup. Reprinted by Bernal in 1967.
Aleksandr I. Oparin (1938)	The Origin of Life. Translated and annotated by Sergius Morgulis. Macmillan, New York	The English version of the book published in Russian in 1936. First edition in Dover Publications, New York, in 1953. A Spanish version was published in Argentina by Editorial Losada in the 1960s.
Harold C. Urey (1952)	The Planets. Their Origin and Development. Yale University Press, New Haven	Arguments in favor of a reducing atmosphere for the early Earth, the starting point of Miller's classical experiment on abiotic synthesis of organic molecules in 1953, are presented at length.
Aleksandr I. Oparin (1957)	The Origin of Life on Earth. Translated by A. Synge. Oliver & Boyd, Edinburgh	One of the most complete accounts of the historical roots of the study life's origins, and scientific approaches that have been used. The Spanish translation from the Russian (Tecnos, Madrid, 1970) is probably the version best known by Spanish-speaking readers.
Aleksandr I. Oparin (1961)	Life: Its Nature, Origin and Development. Academic Press, New York	A remarkable book by Oparin, in which he discusses the relationship between the problem of the origin and the definition of life.
John D. Bernal (1967)	The Origin of Life. The Weidenfeld and Nicolson Natural History. Ed. by R. Carrington. Weidenfeld and Nicolson, London	A general review on the topic including as an appendix the English version of Oparin (1924) and the paper by Haldane (1929).
Leslie E. Orgel (1973)	The Origins of Life. Molecules and Natural Selection. John Wiley and Sons, New York	There is a Spanish version (Alianza, Madrid, 1975) of this review of prebiotic chemistry for a general reader.
Humberto Maturana and Francisco Varela (1973)	De máquinas y seres vivos. Una teoría sobre la organización biológica. Editorial Universitaria, Santiago de Chile	The original and seminal work on the "autopoiesis" concept. There is a second edition (1994).
Stanley L. Miller and Leslie E. Orgel (1974)	The Origins of Life on the Earth. Concepts of Modern Biology Series, ed. by W. D. McElroy and C. P. Swanson. Prentice Hall, Englewood Cliffs	An authoritative and classical review of the prebiotic chemistry experiments.
John Farley (1974)	The Spontaneous Generation Controversy from Descartes to Oparin. The Johns Hopkins University Press, Baltimore	One of the most complete account on the history of ideas on the origin of life, including a discussion on how cultural factors interfere with scientific views.
Engelbert Broda (1975)	The Evolution of Bioenergetic Processes. Pergamon Press, Oxford	One of the earliest and most wide-ranging reviews on the origin and evolution of energetic metabolism, including the classical hypothesis of photosynthesis preceding respiration.
Clair E. Folsome (1979)	The Origin of Life: A Warm Little Pond. Freeman, New York	A short and clear account that includes some original proposals for a chemical definition of life. There is a Spanish version (Reverté, Barcelona, 1981).
Francis Crick (1981)	Life Itself. Its Origin and Nature. Simon and Schuster, New York	Crick discusses the improbability of life emergence and provocatively proposes directed panspermia as a solution. Crick also considers how the discussion on the origin of life would be much simpler if a single molecule were both template and catalyst. This was in the year of the first description of a ribozyme.
Lynn Margulis (1984)	Early Life. Jones and Bartlett, Boston	The origin and early evolution of life by a great specialist in cell evolution. There is a Spanish version (Reverté, Barcelona, 1986) and a second English edition co-authored with Michael F. Dolan (Jones and Bartlett, Boston, 2002).
Robert Shapiro (1986)	Origins. A Skeptic's Guide to the Creation of Life on Earth. Summit Books, New York	Based on a criticism of the prebiotic soup, there is a very well written introduction to the subject.
Franklin M. Harold (1986)	The Vital Force. A Study of Bioenergetics. Freeman, New York	A brilliant presentation of bioenergetics and the chemiosmotic theory, including a chapter on the origin and early evolution of the cell.

(Continued)

Table 1 (cont.). An essential library on the origin of life. (This is not an exhaustive list but mostly a personal choice)

Author (year of publication)	Title and reference	Remarks
Christian de Duve (1991)	Blueprint for a Cell: The Nature and Origin of Life. Neil Patterson, Burlington	An original view from one of the most prominent cell biologists. The author introduces the concept of the “thioester world” as a scenario for early metabolism. The book contains a complete bibliography commented by de Duve.
Harold J. Morowitz (1992)	Beginnings of Cellular Life. Metabolism Recapitulates Biogenesis. Yale University Press, New Haven	Morowitz presents his ideas on the early emergence of cells, including a complete account of the minimal-cell concept.
John Maynard Smith and Eörs Szathmáry (1999)	The Origins of Life. From the Birth of Life to the Origin of Language. Oxford University Press, Oxford	This is a shorter and more popular version of the celebrated work by the same authors: The Major Transitions in Evolution (Freeman, Oxford, 1995). There is a Spanish translation (Tusquets, Barcelona, 2001).
Iris Fry (2000)	The Emergence of Life on Earth. A Historical and Scientific Overview. Rutgers University Press, New Brunswick	A comprehensive report with especially accurate scientific descriptions.
Christopher Wills and Jeffrey Bada (2000)	The Spark of Life. Darwin and the Primeval Soup. Perseus, Cambridge MA	An updated and wide view, including a good historical introduction.
Geoffrey Zubay (2000)	Origins of Life on the Earth and in the Cosmos. Second Edition. Academic Press, San Diego	An original, biochemically oriented view.
Tom Fenchel (2002)	The Origin and Early Evolution of Life. Oxford University Press, Oxford	An updated, brief- and well balanced story.
Athel Cornish-Bowden (2004)	The Pursuit of Perfection. Aspects of Biochemical Evolution. Oxford University Press, Oxford	An extensive and robust argument against intelligent design in metabolic evolution.

exact chemical composition and physical conditions) and uncertainties as to the accumulation of extraterrestrial organics have shifted the focus in search of other locations for primeval living processes. That is the source of interest in submarine hydrothermal vents as chemical cradles of life. In fact, some recent simulations indicate that organic matter can originate in those extreme ambients [11].

The proposal by Günter Wächtershäuser [41] of a thermophilic and autotrophic origin of life strengthened the attention focused on submarine chimneys (see Chap. 4 in [29]). This author suggested that the anoxic synthesis of pyrite was the energy and electron source for carbon dioxide fixation and the genesis of every organic component of nascent living matter. In other words, Wächtershäuser substitutes a primitive autotrophic and bidimensional metabolism on the pyrite surface for the prebiotic soup [23]. This is an acellular, genetically non-instructed metabolism, one that is favored by high temperatures and uses reduced sulfur gases that abound in submarine hydrothermal sources. There is experimental support for some of the chemical postulates but evidence is still lacking for many aspects of an autotrophic origin of life, including the ancestral character of the Arnon cycle [26,30]. A primordial chemolithoautotrophic metabolism based on the net synthesis of acetyl-CoA (Wood pathway) has been proposed as a link between a hydrothermal geochemistry and the most ancient biochemistry [35].

The entire diversity of processes and scenarios—the abiotic generation of chemical complexity in the primitive Earth, both endogenous (atmosphere, sea surface, submarine chimneys) and exogenous (meteorites, comets, interstellar dust particles), the roles of minerals (catalysis and stability) and of different energy sources (electromagnetic, chemical)—leads us, as Antonio Lazcano [19] has proposed, to an eclectic vision of the origin-of-life problem, in which the heterogeneity of mechanisms and conditions is essential to assembling a coherent historical narrative.

Confronted standpoints

There are several controversies regarding the origin of life, each with deep historical and philosophical roots (for a general discussion, see the book by Fry cited in Table 1, and references therein). In this sense, the scientific discussion of life's emergence does not differ from other intellectual conflicts in biology. Figure 1 summarizes the main subjects under debate.

Heterotrophic vs. autotrophic origins. Either life started as a simple system, taking advantage of a chemically complex environment, as suggested, among others, by Oparin and Haldane, or the early emergence of self-sustained systems

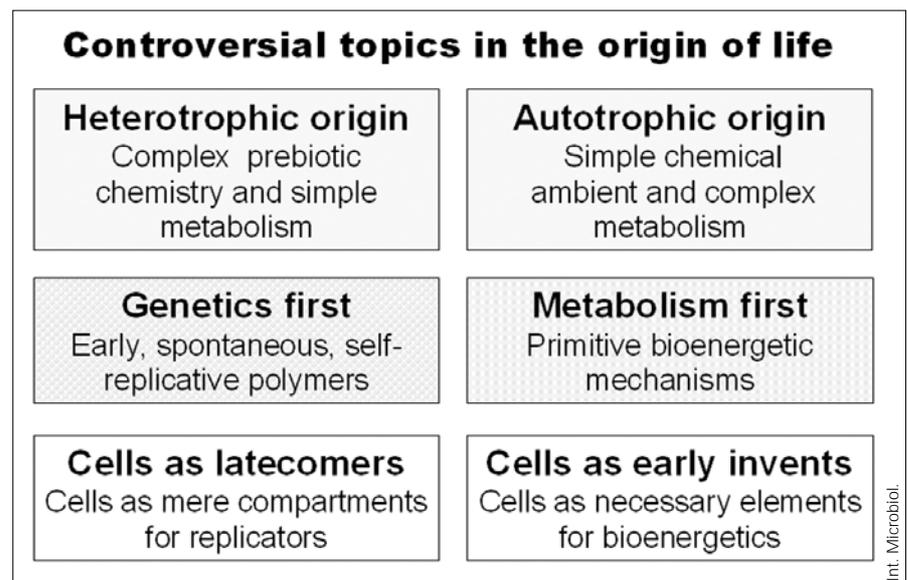


Fig. 1. Main controversial research topics in the origin of life.

was based on utilization of the simplest molecules available, as postulated by Wächtershäuser. If we consider that a heterotrophic metabolic chart is simpler than an autotrophic one (such a postulate still needs to be proved), then the first option is the more parsimonious, as admitted by most experts.

Replicators or metabolism first. This is a rather old debate, confronting supporters of an early origin of genes (even before their chemical nature was established, e.g. Herman J. Muller's ideas in the 1920s) with those advocating the emergence of proteins first (e.g. Leonard Troland in the 1910s) (see Farley's book cited in Table 1, and [18]). Many authors (including Manfred Eigen and Richard Dawkins) believe that the origin of life is equal to the origin of the first replicators, i.e. the first self-copying molecules. Theoretical and experimental insights (e.g. Leslie Orgel's classic assays on enzyme-free template replication; for a review, see [27]) and the discovery of catalytic RNA (Tom Cech's and Sydney Altman's description of the first ribozymes, in the early 1980s) brought about renewed interest in the idea of a spontaneous and early emergence of genetic polymers. This is one of the fundamental postulates of the RNA-world hypothesis, the alleged solution to the genetic version of the classical "chicken-and-egg" dilemma [8,42]. Nevertheless, other scientists take a different position: how would the origin of order (e.g. polymers synthesized from energetically and chirally pure monomers) have been possible without a plausible and efficient way for funneling energy through the system? Several authors, including Christian de Duve, David Deamer, Tibor Gánti, Harold Morowitz, Stuart Kauffman, Robert Shapiro, and Wächtershäuser, have argued for the appearance

of primitive self-catalytic metabolic networks as a first step towards the synthesis of replicators. Those self-organized prebiotic processes would have provided a scaffold for the emergence of genetics [36,37]. However, supporters of the replicator-first approach have refuted the metabolism-first proposals [1,32].

Early or late cellularization. Whether compartment formation was an early or late phenomenon during life's origins is a debate closely related to the above-mentioned controversy on the early origin of metabolism vs. genetics. Many advocates of an early emergence of replicators consider the cell as a mere physical compartment for segregating polymers of differential replicative abilities, albeit some authors have adopted intermediate positions [6]. However, ample biochemical evidence has shown that the cell is not a simple physical space enclosed by a semipermeable membrane. Instead, the inside is chemically and physically different from the outside medium because of the functionally active presence of phospholipid membranes and their molecular (protein) machines, i.e. the active players in bioenergetic transduction and control of the connection between inside and outside. In order to build its own components, living matter must be able to access outside resources through its biomembranes. The essence of bioenergetics lies in the asymmetric disposition of molecular machines on the cell membrane and the corresponding streams of chemical messengers allowing efficient coupling between primary energy sources (visible light, chemicals) and metabolic networks. Some proteins (electron transport chains, ATPases) synthesize bioenergetic currencies (either chemiosmotic or chemi-

cal) whereas others use those currencies to execute a wide range of cellular tasks: motility, biosynthesis of complex architectures, maintenance of identity against environmental fluctuations, heredity, etc. We certainly adhere to Franklin M. Harold's [15,16] incapacity to imagine any other way (not to mention acellular systems) to make and maintain complex structures exhibiting complex behaviors using solar energy or exergonic chemical reactions and simple building blocks. Thus, life would have been cellular *ab initio* (pp. 65–76 in [29]), although many controversial issues remain, including the chemical nature of membranes (e.g. see the theoretical models discussed in [31]) and the kind of primitive molecular transducers of primary energy sources and membrane transporters that would have been necessary to prevent an osmotic crisis [7] prior to the existence of intricate protein machines.

This contentious subject has even impregnated “bottom-up” strategies for the artificial (chemical) synthesis of life: those scientists interested either in the design of self-replica-

tive ribozymes [17] or in the chemical implementation of autopoiesis through self-organized and self-reproductive lipid vesicles [14,22]. Other researchers have tried to find common ground in chemical systems, such as vesicles containing both self-replicative ribozymes and ribozymes involved in the synthesis of the vesicle's amphipathic components [40]. Our understanding of the nature and origin of life will advance by closing with educated guesses the gaps between those approaches, both theoretical and experimental, and the “top-down” strategies aimed at imagining the simplest life forms [39].

A conjectured path for the transition from inert to living matter

Eörs Szathmáry [12] proposed distinguishing between units of life (entities showing self-maintenance) and units of evo-

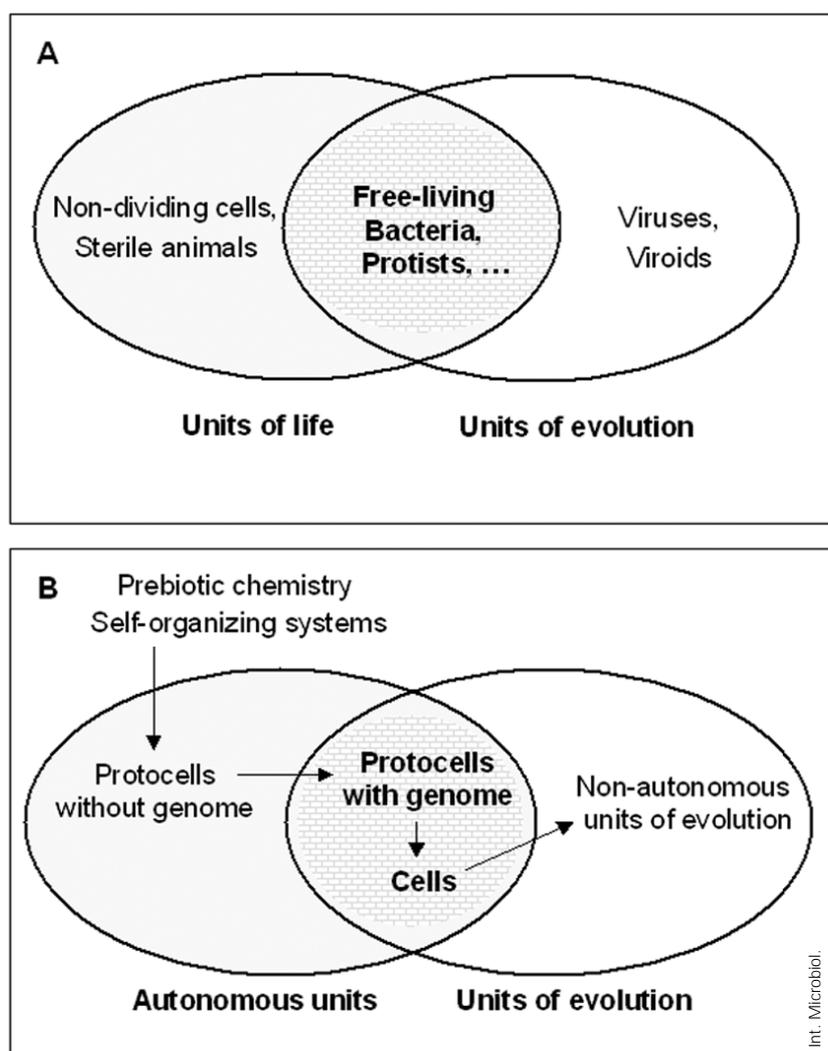


Fig. 2. Units of life and units of evolution: a genealogical perspective. **(A)** The concept of the units of life and evolution, after Szathmáry (see [12]). **(B)** A genealogical view ranging from self-organizing chemical systems, to autonomous units (protocells without genome), to autonomous and evolvable units (true Darwinian populations of protocells and cells). Eventually, after phenotype (proteins) and genotype (nucleic acids) decoupling and the invention of DNA, open-ended evolution started, giving rise to an enormous amount of diversity (see Fig. 1 in [34]). Some autonomous and evolutive units eventually lost their autonomy and became obligately dependent on other autonomous units (e.g. viruses and viroids).

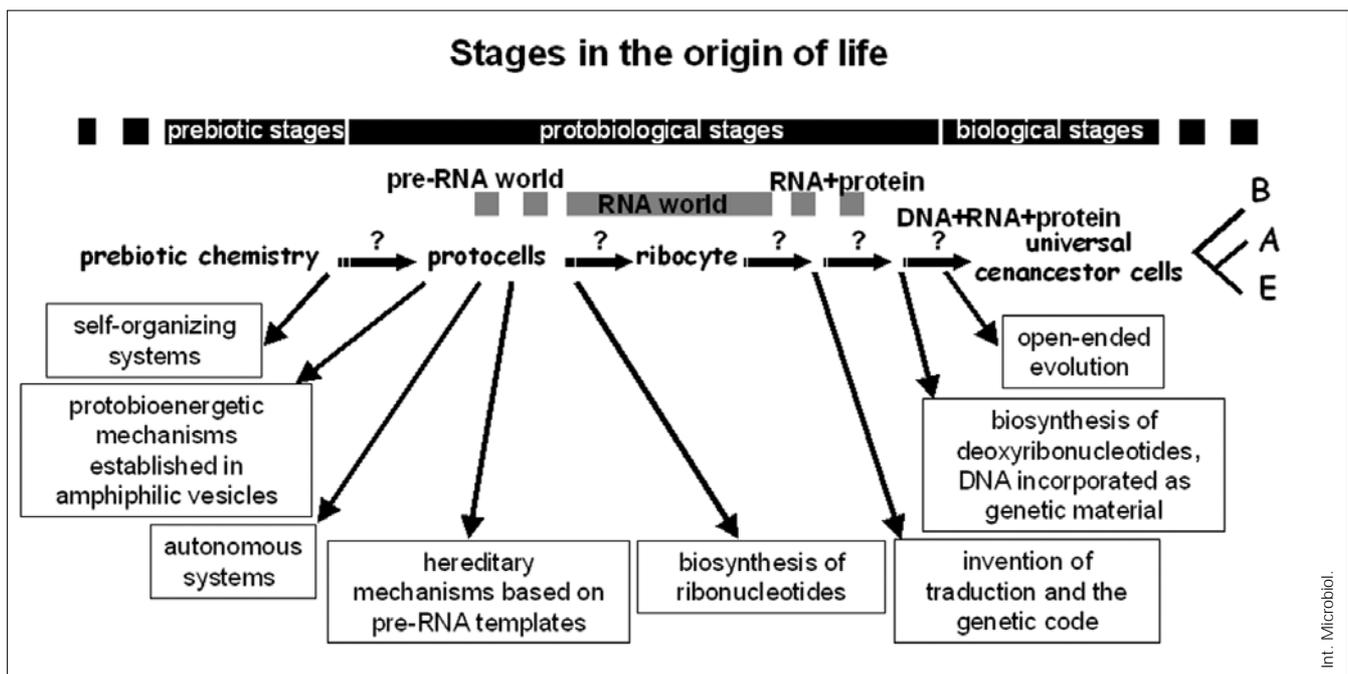


Fig. 3. A more detailed scheme of a hypothetical transition from prebiotic chemistry to cells. Protobiological stages comprise the origin of autonomous systems (protocells without genome), one-polymer protocells (including ribocytes [42], i.e. protocells based only in RNA) and the early phases of a two-polymer (RNA and protein) world. True biological stages started with DNA-RNA-protein cells and their open-ended evolutionary capacities, i.e. the origin of life [34]. Arrows with question marks indicate unknown processes. The scheme does not imply a temporal scale, e.g. the transition from early DNA-RNA-protein cells to the universal ancestor might have been more prolonged in time. B: *Bacteria* domain, A: *Archaea* domain, E: *Eucarya* domain.

lution (entities with replicable, mutable, and heritable instructions). Some typical examples of living beings (e.g. free-living bacteria) are both units of life *and* units of evolution, and are thus located at the intersection of the two categories. Nonetheless, borderline situations can also be imagined: units of life unable to evolve (sterile animals) or units of evolution strictly dependent on units of life (obligate parasites, such as viruses and viroids) (Fig. 2A). We have proposed a genealogical view of life (see Fig. 1 in [34]), one that can be combined with Szathmáry's scheme but which renames the units of life as autonomous units. In this case, the first step during the self-organization of matter in the primitive Earth would have been the emergence of units of autonomy, lacking the capacity to evolve in the Darwinian sense.

In other words, chemical evolution would have produced primitive self-maintaining chemical systems with rudimentary mechanisms of energy transduction but without digital (replicative and mutable) records. We call such "infrabiological" systems (Szathmáry's sensu [39]), involving a primeval association between metabolism and boundary, *protocells* (Fig. 2B). Once the genetic records were acquired and non-instructed metabolism was taken over by a genetically instructed one, an evolutionary stage was initiated [6] (Fig. 2B). A primordial version of these systems could have been a one-

polymer-dependent protocell, as in a *cellular* RNA world. It must be remarked that most proponents of this one-polymer scenario refer to a hypothetical *acellular* RNA world, which, in our opinion, is very implausible from a prebiotic perspective. The invention of RNA-catalyzed protein synthesis and the fixation of a code introduced a second key takeover: from a ribozyme-catalyzed primitive metabolism to dynamic control of metabolic networks by proteins. This major evolutionary transition allowed the phenotype (organization)-genotype (structure) decoupling so idiosyncratic to terrestrial life. A final, important takeover was the substitution of DNA for RNA as genetic material, which marked the beginning of the open-ended evolutionary process [34], and the universal ancestor cells as one of its consequences. Eventually, some autonomous units with open-ended evolutionary capacities completely lost their autonomy (i.e. their metabolic abilities totally vanished) and became obligate dependents on other autonomous units (e.g. viruses and viroids; Fig. 2B). Figure 3 presents a more detailed outline of processes involved in the origin of life following our proposal from prebiotic chemistry to protocells to cells. If we assume, like Simpson, that "the origin of life was necessarily the beginning of organic evolution" [38], then all the stages before the open-ended evolution phase should be considered as protobiological.

In summary, during individual life there is permanent communication with the environment, whereas during evolutionary history there is some (unidirectional) communication between past and present populations. As proposed here, during the origin of life the organization and mechanisms allowing a chemical system to be materially and energetically (ecologically) connected with the ambient, and equipped with the ability to self-construct, emerged first. This was before the appearance of complex chemical structures that provided the system with a temporal connection throughout successive generations. Paraphrasing Ramon Margalef, the ecological networks were, also at the very beginning, the cradle of evolution.

Future trends into the origin of life research will need a more fluid interaction between those proposing, “the origin of life was the origin of true heredity; we might even say the origin of the first gene” [5], and those claiming “no biopoietic scheme deserves to be taken seriously unless it provides both an explicit and sustainable energy source, and plausible means to couple the energy to the flow of matter through the emerging system” (p. 244 in [16]).

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References

- Anet FAL (2004) The place of metabolism in the origin of life. *Curr Op Chem Biol* 8:654-659
- Bada JL, Lazcano A (2002) The origin of life: some like it hot, but not the first biomolecules. *Science* 296:1982-1983
- Bada JL, Lazcano A (2003) Prebiotic soup-revisiting the Miller experiment. *Science* 300:745-746
- Darwin C (1859) *On the origin of species*. John Murray, London, p 484
- Dawkins R (2004) The ancestor's tale. A pilgrimage to the dawn of life. Weidenfeld & Nicolson, London, p 467
- de Duve C (2005) The onset of selection. *Nature* 433:581-582
- Deamer DW (1997) The first living systems: a bioenergetic perspective. *Microbiol Mol Biol Rev* 61:239-261
- Dworkin JP, Lazcano A, Miller SL (2002) The roads to and from the RNA world. *J Theor Biol* 222:127-134
- Ehrefreund P, Irvine W, Becker L, Blank J, Brucato JR, Colangeli L, Derenne S, Despois D, Dutrey A, Fraaije H, Lazcano A, Owen T, Robert F, ISSI-Team 2002 (2002) Astrophysical and astrochemical insights into the origin of life. *Rep Progr Phys* 65:1427-1487
- Ferris JP (2002) Montmorillonite catalysis of 30-50mer oligonucleotides: laboratory demonstration of potential steps in the origin of the RNA world. *Origins Life Evol Biosph* 32:311-332
- Foustoukos DI, Seyfried Jr WE (2004) Hydrocarbons in hydrothermal vent fluids: the role of chromium-bearing catalysts. *Science* 304:1002-1005
- Gánti T (2003) *The principles of life*. With a commentary by J Griesemer and E Szathmáry. Oxford University Press, Oxford, p 159
- Gold T (1992) The deep, hot biosphere. *Proc Natl Acad Sci USA* 89:6045-6049
- Hanczyc MM, Fujikawa SM, Szostak JW (2003) Experimental models of primitive cellular compartments: encapsulation, growth, and division. *Science* 302:618-622
- Harold FM (1986) *The vital force. A study of bioenergetics*. Freeman, New York, pp 168-172
- Harold FM (2001) *The way of the cell. Molecules, organisms and the order of life*. Oxford University Press, New York, chapter 11
- Joyce GF (2004) Directed evolution of nucleic acid enzymes. *Annu Rev Biochem* 73:791-836
- Lazcano A (1995) Aleksandr I Oparin: apuntes para una biografía intelectual. In: Morán F, Peretó J, Moreno A (eds) *Orígenes de la vida. En el centenario de Aleksandr Ivanovich Oparin*. Ed Complutense, Madrid, pp 15-39 (In Spanish)
- Lazcano A (2001) Origin of life. In: Briggs DEG, Crowther PR (eds) *Paleobiology II*. Blackwell Science, Oxford
- Llorca J (2004) Organic matter in meteorites. *Intl Microbiol* 7:239-248
- Llorca J (2005) Organic matter in comets. *Intl Microbiol* 8:5-12
- Luisi PL, Rasi PS, Mavelli F (2004) A possible route to prebiotic vesicle reproduction. *Artif Life* 10:297-308
- Maden BEH (1995) No soup for starters? Autotrophy and origins of metabolism. *Trends Biochem Sci* 20:337-341
- Miller SL (1953) A production of amino acids under possible primitive Earth conditions. *Science* 117:528
- Morowitz HJ (1992) *Beginnings of cellular life. Metabolism recapitulates biogenesis*. Yale University Press, New Haven, chapter 5
- Orgel LE (2000) Self-organizing biochemical cycles. *Proc Natl Acad Sci USA* 97:12503-12507
- Orgel LE (2004) Prebiotic chemistry and the origin of the RNA world. *Crit Rev Biochem Mol Biol* 39:99-123
- Oró J (1960) Synthesis of adenine from ammonium cyanide. *Biochem Biophys Res Comm* 2:407-412
- Peretó J (1994) *Orígenes de la evolución biológica*. Eudema, Madrid (in Spanish, available as PDF file: <http://www.valencia.edu/~orilife/Autors/Pereto/Pereto.htm>)
- Peretó J, Velasco AM, Becerra A, Lazcano A (1999) Comparative biochemistry of CO₂ fixation and the evolution of autotrophy. *Intl Microbiol* 2:3-10
- Peretó J, López-García P, Moreira D (2004) Ancestral lipid biosynthesis and early membrane evolution. *Trends Biochem Sci* 29:469-477
- Pross A (2004) Causation and the origin of life. *Metabolism or replication first?* *Origins Life Evol Biosph* 34:307-321
- Ricardo A, Carrigan MA, Olcott AN, Benner SA (2004) Borate minerals stabilize ribose. *Science* 303:196
- Ruiz-Mirazo K, Peretó J, Moreno A (2004) A universal definition of life: autonomy and open-ended evolution. *Origins Life Evol Biosph* 34:323-346
- Russell MJ, Martin W (2004) The rocky roots of the acetyl-CoA pathway. *Trends Biochem Sci* 29:358-363
- Segré D, Ben-Eli D, Deamer DW, Lancet D (2001) The lipid world. *Origins Life Evol Biosph* 31:119-145
- Shapiro R (2000) A replicator was not involved in the origin of life. *IUBMB Life* 49:173-176
- Simpson GG (1949) *The meaning of evolution. A study of the history of life and of its significance for man*. Yale University Press, New Haven, p 14
- Szathmáry E (2005) Life: in search of the simplest cell. *Nature* 433:469-470
- Szostak JW, Bartel DP, Luisi PL (2001) Synthesizing life. *Nature* 409:387-390
- Wächtershäuser G (1988) Before enzymes and templates: theory of surface metabolism. *Microbiol Rev* 52:452-484
- Yarus M (2002) Primordial genetics: phenotype of the ribocyte. *Annu Rev Genet* 36:125-151

Controversias sobre el origen de la vida

Resumen. El estudio científico del origen de la vida se ha moldeado desde diferentes perspectivas con profundas raíces filosóficas e históricas. Ciertas hipótesis suponen una vida primordial basada en microorganismos anaeróbicos simples que usaban materiales orgánicos abióticos (origen heterotrófico), mientras que otras postulan que se inició con organizaciones más complejas que se nutrían de moléculas inorgánicas simples (origen autotrófico). Muchos autores postulan que la vida empezó con una molécula autorreplicativa, el primer gen. Sin embargo, otros toman como punto de partida unas redes metabólicas autocatalíticas primitivas. Por último, la aparición de la célula misma es controvertida: ¿membranas y compartimentos tuvieron una incorporación temprana o tardía? Partiendo de una definición reciente de vida, basada en los conceptos de autonomía y evolución abierta, proponemos que, en un principio, las moléculas orgánicas se autoorganizaron en un metabolismo primordial localizado dentro de protocélulas. El flujo de materia y energía a través de dichos sistemas moleculares permitió la generación de estados más ordenados, o sea, la cuna de los primeros registros genéticos. De este modo la vida se inició con compartimentos autónomos interconectados ecológicamente que se transformaron en células dotadas de verdaderas capacidades hereditarias y evolutivas en sentido darwiniano. En otras palabras, la existencia individual de la vida precedió a su dimensión histórico-colectiva. [Int Microbiol 2005; 8(1):23-31]

Palabras clave: autonomía · definición de vida · evolución abierta · protocélulas

Controvérsias sobre a origem da vida

Resumo. O estudo científico da origem da vida foi moldado a partir de diferentes perspectivas sob profundas raízes filosóficas e históricas. Certas hipóteses pressupõem uma vida primordial baseada nos microrganismos anaeróbicos simples que usavam material orgânico abiótico (origem dos heterotróficos), enquanto que outras postulam que aquela se iniciou com organizações mais complexas que se nutriam de moléculas inorgánicas simples (origem dos autotróficos). Muitos autores argumentam que a vida começou com uma molécula auto-replicativa, o primeiro gene. Outros tomam como ponto de partida umas redes metabólicas auto-catalíticas primitivas. Por último, até mesmo a aparição da célula é controvertida: membranas e compartimentos tiveram uma incorporação prematura ou tardia? Partindo de uma definição recente de vida, baseada nos conceitos da evolução aberta, propomos que, no princípio, as moléculas orgánicas se auto-organizaram em um metabolismo primordial localizado dentro de protocélulas. O fluxo de matéria e energia através de tais sistemas moleculares permitiu a geração de estados mais ordenados, ou seja, o berço dos primeiros registros genéticos. Deste modo, a vida se iniciou com compartimentos autônomos interconectados ecológicamente que se transformaram em células dotadas de capacidades hereditárias e evolutivas no sentido darwiniano. Em outras palavras, a existência individual da vida precedeu a sua dimensão histórico-coletiva. [Int Microbiol 2005; 8(1):23-31]

Palavras chave: autonomia · definição de vida · evolução aberta · protocélulas

