Chapter 10
Life

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Abstract From the eighteenth to the twentieth century, most theories in life sciences are characterized by particular conceptions of life. In this paper, we discuss them by analyzing how they have been mobilized by some authors in the studies of specific topics in life science. From Buffon to the theories on the origins of life of the second half of the twentieth century, examining closely the approaches of J.-B. Lamarck, L. Pasteur, C. Darwin and C. Bernard, we will observe how the problems of the nature of the living matter, of spontaneous generation, of molecular dissymmetry, of stop of metabolism and of the origin of life constitute the context of important thoughts on the nature of life.

Defining life is an ambition which is sha-red between philosophers, biologists and physicians. The notion of life easily calls for diachronic syntheses bringing forth conceptions ranging from Aristotle to molecular biology. Georges Canguilhem (1995) has thus shown how life was successively considered *as animation, as mechanism, as organization* and then *as information*. The approach hereby proposed analyzes the ways in which the origin of life has been envisaged for three centuries. The reflections on the primordial limit of life will therefore be analyzed for the purpose of revealing some of the most fundamental conceptions about life, and this will be accomplished starting from three successively explored issues.

From the first microscopic observations to the contributions of biological chemistry, with reflection on the nature of the protoplasm, the theoretical and empirical researches of the material basis of life, from Buffon to Pasteur, as well as Claude Bernard, founded the belief of the eighteenth and nineteenth centuries on this very strict limit of life which constitutes its own origin.

Moreover, it was in the nineteenth century that life was historicized. Thus, once with evolutionism, which was added to developments in physiology, biology saw itself sustained by two dimensions, namely the historical and the nomological ones.

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The challenge for the epistemologist was to analyze the way in which they were related, or even inseparable.

It is on the basis of this double identity of life that in the twentieth century a reductionist approach was developed, even though synthetic perspectives were being elaborated for the purpose of understanding evolution. Research on the origin of life, together with the prebiotic chemistry, which emerged in the 1950s, appeared initially as an additional attempt to reconstruct the life of this reductionist approach. Soon after, a new field of study which is still active nowadays opened up concerning the evolution of matter in a prebiotic world and simultaneously a renewal of the fundamental reflection on life came out into the open.

1 The Beginnings of Microscopy in Biological Chemistry: An Approach of the Material Basis of Life

In the eighteenth and nineteenth century, reflecting on the nature and the organization of life was a major preoccupation in life sciences. It engaged empirical approaches thanks to microscopy, which revealed structures on a scale hitherto unsuspected, due also to chemistry, which identified the protoplasm of albuminous bodies and on account of theoretical approaches as well, especially illustrated by theories such as Buffon's organic molecules, or later the cell theory.

1.1 See and Consider the Microscopic Scale

The seventeenth and eighteenth centuries were the background of a confrontation with a new scale of the material nature of living beings revealed by the invention and development of microscopy. The possibility to observe very small beings, invisible up until then, as well as the opportunity to observe previously ignored anatomical details represented an opening towards what could be called a new world.

In this context, certain problems were recomposed, such as that of spontaneous generation. The microscopic beings made the object of an empirical approach, linking together microscopic observation and experimentation, which directly questioned their generation.

That is what fueled the discussion between Lazzaro Spallanzani and John Tuberville Needham about the origin of animalcules. Their work is indeed fundamentally different from that carried out about a century earlier by Francesco Redi, who tried to block the reproductive cycle of flies by preventing them to lay eggs in the observed medium. As for Spallanzani and Needham, they conducted a change of scale in the problematization and discussed the possibility of the animalization of matter into animalcules. The spontaneous generations were considered then in the context of this microscopic space which proved to be likely to accommodate new experiments (Spallanzani 1769).

1.2 The Elemental and Fundamental Components of the Living Matter

According to Canguilhem (1995), definitions of life have been sought in Linnaeus and Buffon, but to no avail. It would nevertheless be proper to be less sharp about the French naturalist. A more comprehensive view of his work would certainly reveal the conception of life which he had developed and which was an essential foundation to build his theory on. It is well known that his *Histoire Naturelle* contains, from its second volume, concepts constantly present in the whole theory of the naturalist.

Thus, very early in his work[1] Buffon (1749) laid the material basis of his conception of life by describing the *organic molecules* which he saw as the constituents of all animals and plants. It was a fundamental concept for him, who believed that the organic was the most ordinary work of nature and life was in fact one of its physical properties. The definition he gave to them while he still called them organic parts clearly describes their function:

> It appears to me very probable […] that there really exists in nature an infinity of small organized beings, similar in every respect to the large organized bodies that appear in the world; that these small organized beings are composed of living organic parts which are common to animals and vegetables; that these organic parts are primitive and incorruptible; that the assemblage of these parts forms what in our eyes are organized beings; and consequently that reproduction, or generation is only a change of form made and operating through the mere addition of these resembling parts alone, as the destruction of the organized being by death or dissolution is produced by the division of these same parts (Buffon 1749: t. 2:24).

The organic molecules ensure the continuity of the organization over time through the action of the *interior mold*, transmitted from one generation to another. Buffon approached hence the notion of life in a highly conceptual manner, which allowed him to simultaneously take into account the current materiality of life and its temporality. And thus he said:

> For species is an abstract and general word, whose object exists only in the succession of times, and in the constant destruction and equally constant renewal of beings. It is in comparing nature today with that of other times, and present individuals with past individuals, that we have obtained a clear idea of what we call species (Buffon 1753, t. 4: 384–385).

There is certainly no precise definition of life in Buffon's work, but it wouldn't be wrong to state that it is contained within the conceptual structure of his theory.

Apart from Buffon's work proposed here as an example of reflection on the materiality of the fundamental constituents of life, for a long period of time, stretching from the end of the seventeenth century to the beginning of the nineteenth century, there was tension between the empirical results of microscopic observation and the possibility to conceptualize, to consider, the elements of this new world. This tension was conducted through the interpretation of multiple microscopic observations which lacked, however, explanatory concepts (Hooke 1665; Spallanzani 1769).

[1] Available online on www.buffon.cnrs.fr/ (edited by Pietro Corsi and Thierry Hoquet).

In the early nineteenth century, the affirmations based especially on the observation of plants, tried to lay the foundation for a universal interpretation of the microscopic structure of living beings. Thus, Charles-François Brisseau de Mirbel, for example, considered the plant as a space filled with sap and containing a network of membranes pierced with numerous pores and filled with sap. René Dutrochet, for his part, identified cells in the walls of larger cells which could be observed at the microscope and he considered them as the constituents of the fundamental plant structure. François Raspail stated shortly after that, in his opinion, these cells could have emerged from the wall of preexisting cells.

Finally, note that the concept of cell, as it is used today, was coined in two stages. In a first stage, it was used in the late 1830s in the observations made by Matthias Schleiden of a cytoblast (nucleus) systematically present in all the cells, and in the generalization of this fact in animals, carried out by Theodor Schwann in 1839. In a second stage, in the 1850s, the explanation of cell formation by division was proposed independently by Robert Remak and Rudolf Virchow.

After a long period of observation, the perception of life at a microscopic scale created the conditions, in the second quarter of the nineteenth century, for the invention of this new conceptual framework, which became from that moment on inevitable in any discussion on the living matter. If the cell referred to a fundamental frame for conceptualizing life, it goes without saying that new questions emerged correspondingly. What place should it be given within the organism? What about the matter which characterizes life or which constitutes the cell?

1.3 Claude Bernard: Life Between Environment and Protoplasm

Throughout his work, Claude Bernard has sought to dismiss the cumbersome alternative of vitalism vs. materialism. In his *An Introduction to the Study of Experimental Medicine* (1984), the rejection of this opposition had a double role. Indeed, apart from the clarification which he provided about the proper philosophical position of the physiologist, this rejection allowed him to define physiology as based on the methods of physics and chemistry, but one of its particular stakes was to master the complexity of life while studying it.

The study of this complexity engaged Bernard in a conceptual line of thought which resulted in the formulation of a set of additional definitions of life. His *Lectures on the Phenomena of Life Common to Animals and Plants* introduced in 1878 the synthesis of his ideas. He simultaneously asserted that "life is creation" and that "life is death". As a physiologist, he based himself in concrete terms on a balance between two kinds of phenomena within the living matter:

> 1° The phenomena of *vital creation* or *organizing synthesis*; 2° The phenomena of death or *organic destruction*.

Moreover, life must be understood in relation to the environment surrounding it. It is the result of "a close harmonious relationship between exterior conditions and the pre-established constitution of the organism. It is not by a struggle against the cosmic conditions that the organism develops and maintains its existence; on the contrary, it is by an adaption and blending with these cosmic forces" (Bernard 1966: 66–67).

The living being is in agreement with the general cosmic forces, "it is a member of the universal concert of things, and the life of the animal, for example, is only a fragment of the total life of the universe." This relationship between the organism and the cosmic conditions determined him to establish a distinction between three forms of life, revealing a gradation on the autonomy of the organism in relation to the conditions of the external environment. (1) Latent life: "life is not manifest"; (2) oscillating life: "variable manifestations depend on the external environment (the case of a tree)"; (3) constant life: "life with free manifestations which are independent of the external environment" (Bernard 1966: 201).

But in his approach to life, Bernard knew how to change the scale and place the cell at the base of the organization. Indeed, in his opinion, it is in the protoplasm that the explanation of life must be sought. It is the only "active and working" matter. It is here that one must look for "the explanation of life, as well as for vital reactions greater than the sensitivity of movement" (Bernard 1966: 201).

In doing so, Bernard registered his opinion on the concept of life in the framework of an observation on the structuring of the most nomological part of biology, that is to say, of physiology (Gayon 1993). Moreover, while questioning the explanation of life at the scale of the matter, he produced elements on its functioning and determined the object on which a reflection on the origins could be carried out.

1.4 Pasteur and the Barrier Between Nonlife and Life

Pasteur's work is marked by his ability to address extremely concrete biological problems and to place them in fundamental issues at the same time. One of these is the barrier between nonlife and life. For Pasteur, this barrier was effectively insurmountable and he believed that molecular dissymmetry, the living nature of ferments, as well as the absence of spontaneous generation aimed to prove this. Beyond the immediate goals of the research he conducted, it was thus a reflection on life of the most fundamental kind which he consistently maintained.

From his early work on the tartaric acid, when he treated with molecular dissymmetry, Pasteur said: "Life is dominated by dissymmetric actions of whose enveloping and cosmic existence we have some indication. I can even foresee that all living species are primordially, in their structure, in their external forms, functions of cosmic dissymmetry" (1994: 38). This statement isolated the life from the symmetric molecular world, that is to say, from the inert world and imposed a continuity of life which he summarized by continuing with this statement: "life is the germ, and the germ is life" (*ibid.*). This conviction will structure much of his later work. Thus, in the debate on the nature of ferments, he sustained his interpretations on the same conceptions and concluded that only life could produce the observed transformations. Finally, his position in the famous controversy on spontaneous generations brilliantly reinforces this idea of an insurmountable barrier, of life that can only come from life, from the germ, and he believed that through his experiments, he had struck the deathblow to the spontaneous generation from which it would never recover.

The impossibility of spontaneous generations is equally a structural result for biology as well as a fact which imposed the need to consider the redevelopment of a problematic field so as to conceive the origin of life. The matter which constitutes the latter is obviously of the same nature as that which composes the inert bodies, but the complexity of its organization and of the mechanisms involved made it impossible to hope seeing life emerge in the laboratory.[2] It is, once again, a matter of the complexity of life. Claude Bernard noted this complexity and made it a characteristic of life, being, at the same time, the objective of the study and an inevitable constraint for the experimenter. As for Pasteur, he associated these two aspects for the purpose of establishing a barrier between the inert and life, the latter being studied through the methods of physics and chemistry, but its complexity remained for him in part insurmountable.

1.5 The Research of the Physical Basis of Life

In 1868, Thomas Huxley, who, beside the fact that he was one of Darwin's main advocates, was primarily a zoologist and a physiologist, had collected his thoughts on the living matter in a lecture entitled *On the physical basis of life*. It was in fact Pasteur's limit that was taken under consideration. Huxley was indeed against the spontaneous generation and in his study on the living matter, he attempted to elucidate the question of which were the complex chemical constituents, carriers of the fundamental characteristics of life?

Like Bernard, he rejected the alternative of vitalism vs. materialism. It has to do with clarifying the complexity characteristic of life and it was on the scale of the matter that he considered the issue. Although Huxley was a convinced evolutionist, his demonstration rests here on life at present form and the task which he set himself was to demonstrate that the albuminous bodies play the most fundamental role in the cell and that it is on them that life lies.

The limit set by Pasteur applies to current nature but it does not explicitly deny that a process of complexification of matter could have taken place at the origin of life, where the questions of the nature of living matter and those of evolution intersect. Therefore, for example, Huxley himself and the German biologist Ernst Haeckel admitted that the substance discovered in 1857 on the ocean floor of the North Atlantic by the British ship *Cyclops*, was living. It was Huxley who named it *Bathybius haeckelii* when he studied it toward the end of 1867 or early 1868. For him, it was the evidence of a possible crossing of the limit between the nonliving and the living, a primordial step of the general phenomenon of the evolution. Similarly, for Haeckel, the existence of *Bathybius* was a crucial fact, the real corner-

[2]About the current work to "reconstruct" life in the laboratory, see Heams on synthetic biology, Chap. 20, this volume. *(ed. note)*.

stone of his monistic conception (Haeckel 1897: 15). However, if this episode of *Bathybius* had an important echo at the time, it died down in 1876 when a chemist showed that the substance was not living and that it was nothing more than calcium sulfate. Thus vanished the hope of an empirical evidence for the existence of a transition between the inert and life.

The positions of Bernard, Huxley or Haeckel, each in their theoretical or specific experimental background, illustrate another change of scale. Indeed, the cell, an inevitable fundamental structure, is nothing but a structural container, and the matter which constitutes it, the protoplasm, is itself complex and the holder of the properties which characterize life. It will be one of the aims of biological chemistry, active from the end of the nineteenth century and which will become biochemistry, to elucidate these issues.

2 The Nineteenth and Twentieth Centuries and the Historicization of Life

In the nineteenth century, the life sciences were marked by the development of the evolutionary thought. Darwin's work represented a turning point by revealing certain modalities of the historicity of life and it was associated with the abandonment of spontaneous generation so as to impose the framework of a new way of thinking about the origin of life.

2.1 Time of the Earth and Life Time

As it was emphasized above, an important part of Buffon's theoretical thinking was based on the organic molecules, but his ambition to explain life in a more global theory will assert itself more clearly in the *Epochs of Nature* (1779), in which Buffon recorded the history of the Earth in a sagittal time, grounding his arguments on the irreversibility imposed by the cooling of the globe. Once it cooled down enough, the Earth carried organic molecules in large quantities during a period of great fertility and they were at the origin of spontaneous generation. Then, the species this way produced remained faithful to their original interior molds.

Therefore, Buffon registered life in the time of the Earth, but without including in his conception of life the notion of irreversible change over time which he applied to the globe. Indeed, it has often been said, and it must be repeated that Buffon did not imagine any form of evolution for the living. When he suggested a sagittal history of the Earth, he maintained nevertheless the species as a fixed frame within which possibly reversible variations were conceivable but that nothing in them led to a passage from one species to another. For Buffon, the spontaneous generations were thus a step in the implementation of prototypes of species and he did not describe them; he justified them simply by the high fertility of the Earth.

Diderot's conception on life which was developed a bit later, but remained partly unpublished at the time, showed a different approach from Buffon's, but it had nevertheless influenced him. The philosopher took interest in the changes which regarded life, but neglected the geological setting. His belief which took shape in *D'Alembert's Dream* was also expressed in unpublished notes from his lifetime which constitute his *Elements of Physiology* and the first part opens with the words: "Nature has made only a very small number of beings that she has infinitely varied, perhaps from a single one, by combining, mixing and dissolving from which all the others have been formed" (Diderot 1994: 1261). He explained later how, in his opinion, the chain of beings is a chain of transformations: "We must classify beings from the inert molecule, if there is one, to the living molecule, to the animal-plant, to the microscopic animal, to the animal, to man."

Diderot was convinced by the idea of a "productivity" of nature and this was what created his vision of the ongoing transformation of life. "The vegetation, the life or the sensitivity and the animalization are three successive operations and the vegetable kingdom could very well be and have been the primary source of the animal kingdom, which could, in its turn, have the primary source in the mineral kingdom, and the latter to have come from the original universal matter" (*ibid.*: 1261–1262).

The work of Jean-Baptiste Lamarck was marked by the development of his theory of the modification of the organization with perfection. In 1802, while formulating the basic principles of his theory, he relied on a definition of life that allowed him to describe the state of the matter on which the transformations that resulted in changes at the scale of the organism and, therefore, of species, could be exercised. In his opinion, life was thus "an order and a state of things in the parts of all the bodies which possess it. Life allows or makes possible the performance of organic movement, and, as long as it subsists, effectively counteracts death." (Lamarck 1802: 71).

The animalization of the gelatinous matter begins with the installation, under the influence of "uncontainable" fluids – "the caloric and electrical matter[3]" – of the vital orgasm which is "a particular tension in all points of the soft parts of these living bodies, which holds their molecules at a certain distance between them, [...] and which they are susceptible to lose by the simple effect of attraction, when the cause which holds them apart ceases to act."

This animalization is nothing more than the spontaneous generation, which is located at the base of the series and constitutes a permanent beginning, because the matter thus animated can be transformed under the influence of "containable" fluids this time – gases and liquids[4] – when their action is repeated for a long time.

Having this way conceived a permanent commencement of the series, Lamarck did not, however, formulate any successful opinion on the primordial origin of life. His long-standing chemical theories, which he never really gave up and because of

[3] They are uncontainable because "no known body would know how to retain them" (Lamarck 1802: 107).

[4] "These other fluids, which are water charged with dissolved gas, or with other tenuous substances, the atmospheric air, which contains water, etc." (Lamarck 1802: 107).

which he believed that all the bodies came from combinations produced by living matter, probably prevented any approach to the primordial origin (Tirard 2006).

2.2 Darwin's **The Origin of Species***, the Modalities of a History of Life*

When he wrote *The Origin of Species*, Darwin did not give any circumscribed definition of life. However, it is through his conception of descent with modification that he gave the characteristics of life. Let us remember the last lines of *The Origin of Species*: "There is grandeur in this view of life, with its several powers, having been originally breathed into a few forms or into one; and that, whilst this planet has gone cycling on according to the fixed law of gravity, from so simple a beginning endless forms most beautiful and most wonderful have been, and are being, evolved" (Darwin 1985).

It can be noted here a crucial indication regarding the commencement of the development of an infinite number of forms produced by laws which are operating around us:

> These laws, taken in the largest sense, being Growth with Reproduction; Inheritance which is almost implied by reproduction; Variability from the indirect and direct action of the external conditions of life, and from use and disuse; a Ratio of Increase so high as to lead to a Struggle for Life, and as a consequence to Natural Selection, entailing Divergence of Character and the Extinction of less-improved forms (*ibid.*)

Darwin's theory in its entirety led to the introduction of a time and historicity in the conception about life. His theory revealed the contingency of evolution, the unpredictability of the stages of the process and the possibility of a retrospective explanation. This historicity of life and especially the "non-repeatability" is particularly highlighted in 1969 when Darwin, in a letter to the botanist Hooker, wrote about the impossibility of spontaneous generations while providing at the same time a scenario for the origin of life:

> It is often said that all the conditions for the first production of a living organism are now present, which could ever have been present. But if (and oh what a big if) we could conceive in some warm little pond with all sort of ammonia and phosphoric salts, – light, heat, electricity &c, present, that a protein compound was chemically formed, ready to undergo still more complex changes, at the present day such matter would be instantly devoured, or absorbed, which would not have been the case before living creatures were formed. (Calvin 1969: 4).

Darwin's words reveal to us that at the end of the nineteenth century, life could be approached according to the different aspects of its historicity, that is to say, both at the scale of the evolution of life in general and at that of its physical basis. Both aspects were united in questioning the origin of life. It was indeed a matter of understanding how the transition from the inert matter to living matter could be included in the global process of evolution. The ground for a problem that is still active today was thus laid.

2.3 Considering the Origins of Life

The second part of the nineteenth century has therefore constituted a key period of reconstruction of the beliefs about the origins of life (Tirard 2005). In the context of the Darwinian evolutionism, the rejection of the spontaneous generation led to an important problem because it was a matter of describing the entirely finished process of the emergence of life.

The authors of that period, Darwin himself, Herbert Spencer, Huxley, Haeckel, as well as a handful of writers from the beginning of the following century devised a progressive evolution of matter which allowed imagining the passage of the inert mineral to the living organic matter. This theory was retrospectively qualified as evolutionary abiogenesis. The developments in organic chemistry, particularly with the syntheses, – the biological chemistry studied for its part the living matter -, through further exploration of the colloidal state, especially from Thomas Graham to Wilhelm Ostwald in particular, represent many contributions which structured the descriptions which are often brief but which strive to assert that the current mechanisms could clarify the primordial process.

These propositions are also rarely contextualized, in the sense that they are not truly taking into consideration the conditions of the terrestrial environment in which the first reactions would have occurred.

Let it be noted, however, that this abiogenetic approach has been, for four decades, in fierce opposition to the *Panspermia*[5] theory revived in the 1870s by William Thomson (Lord Kelvin) and Hermann von Helmholtz. Thomson's interest for this theory was undoubtedly motivated by his opposition to the theory of evolution and he preferred to assert the idea that life was eternal and universal, like matter, rather than to let the evolutionary conceptions prevail. In the early twentieth century, the methods of the panspermia became more refined with the theory of Svante Arrhenius (1910) according to which particles of life of a very small size were scattered into space by being pushed by the cosmic radiation pressure. This suggestion was massively abandoned after the work of the biologist Paul Becquerel, published in 1910, which showed that structures such as the seeds and spores could not resist to certain harsh conditions of the space and especially to exposure to ultraviolet rays.

2.4 Molecules Carriers of History

Around Mendel's work, rediscovered in 1900 and extensively amended by Morgan in 1910, the incipient genetics had structured a concept of gene which designated an entity located on the chromosome and capable of mutation, as well as of recombination. The laws of genetics that were associated to it seemed to reveal the possibility of

[5] According to the panspermia theory, after its cooling, the Earth was seeded with seeds of life from outer space.

a nomological dimension of heredity within the living.[6] The link with the historical dimension of life, that is to say of evolution, did not appear until several years later, notably due to population genetics. Towards the middle of the twentieth century, biology was thus part of a double movement which consisted at the same time, on the one hand, in considering a "synthetic theory of evolution" and, on the other hand, in developing a molecular biology to study the mechanisms involved in heredity.

The empirical data acquired from the 1940s until the middle of the 1960s generated new concepts which revolutionized the understanding of life. The sequence of nucleic acids which structured the gene gave a material character to the information and the gene was thus objectified (Morange 1994). The nucleic acids and proteins have been from then on the objects upon which lay a new representation of life, because the method of reduction seemed to have led to an understanding of the living matter on which the explanation of life might have lay. Simultaneously, the gene also asserted itself as a fundamental entity in the mechanisms of evolution. It was therefore the double support of constancy and of variation, both a nomological and a historical object.

3 What Prebiotic World? Or the Twentieth Century and the Reflection on the Origin of Life

With this molecularized approach, the chemistry and biology of the twentieth century produced the scenarios of a possible evolution of matter, the scenarios of the origin of life being conceived in light of ever more precise data delivered by the present living matter and by a specific experimental approach.

3.1 Scenarios for the Evolution of Matter

The interwar period was marked by the formulation of several scenarios of the origin of life on Earth, the most remarkable of which were those of the Soviet alexandre I. Oparin, in 1924 and 1936 (Oparin 1924, 1938), as well as of the British J.B.S. Haldane in 1929 and, a short while later, of the French Alexandre Dauvillier starting from the late 1930s (Haldane 1991).

The two texts of the 1920s, written independently, are suggestions to situate the origin of life in the context of the evolution of the planet and of the matter on its surface. The two authors described the synthesis of organic molecules in the primitive conditions of the atmosphere, which, in Oparin's view, led to more or less voluminous drops of an organic gel and, in Haldane's opinion, to half-living molecules, the synthesis of which was imagined as what he called the prebiotic soup. Oparin thoroughly completed his theory in 1936. He mobilized the notion of coacervate, developed some years earlier by the Belgian H.G. Burgenberg de Jong (1932), and

[6] See Heams ("Heredity"), Chap. 3, this volume. *(ed. note).*

described how these spherical elements could be isolated in solutions and constitute models of primordial cells. Dauvillier, for his part, formulated a photochemical theory of life (Dauvillier and Desguins 1942) in the late 1930s and the 1940s.

Finally, the scenario established by John D. Bernal (1951) should be noted as well, conceived in the 1940s but published in 1951, in which he adopted the main models of his predecessors, suggesting, however, that the first reactions had taken place on the clayey bottom of liquid stretches, the mica having served both as support and catalyst.

All these approaches share in common the inclusion of the evolutionary abiogenesis in the broader context of the history of the Earth and take into account the geological data which allowed to define the primordial conditions.

3.2 From Reductionism to Prebiotic Chemistry

In the early 1950s, the work on the origin of life committed to the path of chemical syntheses in conditions assumed to correspond to those that predominated on the primordial Earth, thus founding the branch of chemistry called prebiotic.

It was the reductionist approach to life that opened the possibility of such a reverse movement consisting of attempts to reconstruct the molecular constituents of living matter.

In 1951, the biochemist Melvin Calvin exposed a solution of carbon dioxide to γ radiation and obtained formaldehyde. This synthesis was the first to be conducted in compliance with conditions considered as prebiotic. However, his interest was soon questioned by Harold Urey who stated in 1952, as Oparin had done before him, that the primitive atmosphere could not contain CO_2 and had to be reducing. He advocated for synthesis experiments starting more particularly with methane (Urey 1952). In 1953, one of his students, Stanley Miller, obtained amino acids from a mixture of ammonia, hydrogen, methane and water vapor, exposed to electric shocks for a week (Miller 1953). The success of this experiment had a significant impact and opened up promising prospects for the experimental exploration of scenarios meeting the prebiotic conditions, the reducing composition of the primitive atmosphere constituting one of the crucial conditions of the prebiotic experimentation setting of the 1950s to the 1970s.

A three-phase model was gradually established. The first involved the synthesis of organic molecules starting with mineral compounds, the second consisted in the production of polymers and the third was the synthesis of the compartments prefiguring the cells. In 15 years, the work in conditions called prebiotic had illustrated these phases particularly with proteinoids (Fox and Harada 1958) and then with microspheres.

It is remarkable that the attempted syntheses seemed conditioned by biochemical and paleontological milestones imposed by nature as it is today. In a first stage, the amino acids and the carbohydrates have certainly undergone the main syntheses, but rapidly, the importance of nucleic acids having been revealed by molecular biology, nitrogen bases of DNA, then of RNA were produced, with the synthesis of adenine in 1960 and the synthesis of uracil in 1961.

In the early 1970s, geochemical data encouraged the reevaluation of the theory of the reducing atmosphere, revealing that the primitive atmosphere must have contained carbon dioxide, fact which had been denied until that moment. These new initial conditions were reminiscent of the historic nature of the object of study and thus, of the epistemological specificities of the implemented methods.

Chemistry, which came from the field of nomological sciences, called itself prebiotic. It became in fact a historical science and tested former potentialities.[7] The initial conditions being reviewed, a new field of possibilities was needed from then on to be explored (Tirard 2002).

3.3 A RNA World?

In 1986, the reflection on the origin of life was the framework of an innovative suggestion. Noting the autocatalytic properties of some RNAs, Walter Gilbert (1986) suggested the idea of a primordial RNA world which would have preceded the DNA world. He himself formulated a series of arguments in favor of his theory. The autocatalytic properties of RNA made the enzymatic proteins useless at the beginning of evolution. The self-insertion of introns[8] and the existence of transposons[9] allowed some form of recombination and constituted the mechanisms of a molecular evolution. The same transposons prefigured a form of sexual reproduction. The copy errors of self-replicating molecules were a form of mutation and also constituted a mechanism of evolution. Finally, the replication took place due to the sample in the "soup of nucleotides".

This suggestion had the merit to overcome for good the problem in which the informational molecule, the DNA, and the catalysts, the proteins fought for the status of the original molecule, while being dependent on one another at the same time. The RNA, for a long time relegated to the rank of mere intermediary, became this original molecule, which allowed the formulation of a complete scenario: the first step involved progressive mechanisms due to recombinations and mutations of the RNA; the second consisted in the synthesis of proteins, the RNA serving as model; in the third, the synthesized proteins turned out to be the best enzymes and, finally, the DNA appeared.

This suggestion, still often accepted in broad outline, remained nonetheless the subject of debate. Very quickly after its publication, criticisms were brought: what were the environmental conditions compatible with the existence of RNA in solution? The necessary molecules for the functioning of the system needed to be

[7] On the nomological and historical sciences, see Lecointre Chap. 19, this volume. *(ed. note)*.

[8] Noncoding parts of the DNA present in the sequence of a gene.

[9] Or "transposable elements". Sequences of DNA which change position in the DNA molecule.

available close by. When did the membranes appear? When and how did the genetic code appear? (Joyce 1991).

The hypothesis of the RNA world did not exempt from a questioning on the previously present systems. The RNA itself is in fact very complex and it seemed unlikely that it could have constituted the first system that appeared. This reflection on the possibility of anterior systems different from those known in nature as it is today, from which to draw inspiration, was initiated in the 1960s by Graham Cairns-Smith (1966).

He suggested imagining a series of shifts between systems which would successively replace one another; he called *genetic takeover* this succession of systems in which the first ones could disappear without trace once supplanted by the following. With this hypothesis, he suggested that the first informative system could have been entirely mineral and founded on mica. The concept of genetic takeover thus took into account the need to think this time around about what preceded the cell life. The more recent suggestion made by Günter Wächterhäuser (1988) involved the idea of a surface metabolism mobilizing the pyrite.

Regarding the phenomena of this prebiological period, it is possible to ask whether "the domain of validity of the Darwinian explanation could be extended from biological to prebiological? [And] is the evolution before and after the constitution of the genetic code the same?" (Canguilhem 2000: 116–117). This problem has effectively generated fundamental theoretical positions over several decades. Manfred Eigen (1992), for example, suggested with his hypercycle theory that during the cyclical repetition of reactions, errors occur and thus generate the chemical evolution; a Darwinian chemical evolution could then explain the prebiological steps of the origin of life. The possibility of a Darwinian explanation extended to prebiological remains debatable however, and the cell stage is frequently imposed as the one standing at the origin of recognized life; life being the only form to which the Darwinian evolution can be applied.[10]

3.4 The Origin of Life Between Contingency and Universality

Today, the Earth is the only place in the universe where life is known to exist. As for the conception of life, this uniqueness generates epistemological constraints within the historicity of the phenomenon. Ideally, the solution to such a historical problem should depend on the use of trace fossils of primordial processes that preceded the first cells, but they are nonexistent. The prebiotic experimentation tested therefore possibilities in the field of the historical contingency imposed by the complexity of every stage. Canguilhem noted the distinctive philosophical nature of speculations made by science to explain the transition between "*assumed* initial conditions [and] a *given* circumstance, the fundamental structure of present organisms" and he also

[10] In addition to Sect. 3, we will refer to Sect. 1.1 of Heams's chapter on synthetic biology, Chap. 20, this volume. (ed. note).

highlighted the consequences of the absence of traces by saying that, in this field, "the laboratory notebook replaces the history of nature" (Canguilhem 2000: 116–117). The prebiotic chemistry, as we have seen, is a historical science; it tests possibilities and tries to retrace the steps of a contingent path.

This contingency of the phenomenon can be brought into debate and this was precisely the case during the opposition between Jacques Monod (1970) and Ernst Schoffeniels (1973). The first built on the idea that life was highly improbable and that it could have been drawn only once in a "game from Monte Carlo", while the second advocated anti-hazard and considered that life mandatorily resulted from chemical properties of molecules.

As for the prebiotic chemists, they have been for the most part convinced since the 1950s that life forms could be present in the universe. Nowadays, the aim of astrobiology or of exobiology is to carry out the search for life in the universe and for its conditions of possibility. What form would have a life outside of Earth? It is not easy to build on what we know of life on Earth to answer this question, but nevertheless the search for signs of life in the universe has been launched. The theoretical research on a definition of life trying not to be limited to known life finds particular resonance in this most universal approach to life, which can especially be liberated from the notion of evolution as criterion. The autopoietic systems of Francisco Varela (1989), characterized by their ability to continually renew their own constituents or their own organization, are one such example. The more recent approach by Tibor Ganti (2003) which is based on the identification of absolute or real criteria of life could be illuminating as well. According to him, a living system has to be an individual unit, to perform metabolism, be intrinsically stable, possess a subsystem carrying information which is useful to the system in its entirety, and the processes which are inherent to it must be regulated and controlled (see Szathmáry 2007).

Strangely, this quest for universality does not mention the possibility of the historicity of systems considered to be living, which, in the terrestrial life, has emerged as one of its remarkable features. This historicity, as a capacity for evolution, is in fact potential because it ensues fundamental characteristics of life. In this case, perhaps it is possible to consider as Michel Morange did (2003) that life is "molecular structure, metabolism and reproduction."

4 Conclusion

Should we define or reflect on life? The search for a definition of life is hampered by the difficulty to describe in a few words a phenomenon whose limits, both temporal, related to its beginning, and spatial, related to its distribution in the universe, we know little nowadays. Any definition of life claims to be confronted with universality, yet it is precisely the perception of the universality of life that we lack. It would be ideal to confront the definitional suggestions with the past reality of the primordial life and the current reality of life elsewhere. Can a consensus be found around the various criteria? In any case, we should avoid falling into the tendency denounced by Canguilhem of being limited to a reflection on the research of the aforementioned criteria, because, according to him, we would then neglect the reflection on this "singular power of nature" that is life.

In the context of the work on the origin of life that has been of particular interest here, is the definition of life a prerequisite? It turns out that the absence of a consensus among experts does not prevent in the least the progress of the said work. Some even question the need to define life (Reisse 2007: 1–4). The theories about the origin of life constitute in fact a field in which a general reflection on the limits of life is developed, which questions concepts which allow, among other things, to think about life. It is less a matter of defining life than it is of considering it in the broadest possible manner. As a common issue in many areas of specialty, the origin of life constitutes a heuristic problematic field by stimulating the renewal of fundamental questions about life.

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