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Prebiotic chemistry: A fuzzy field

Gilles Bruylants, Kristin Bartik, Jacques Reisse *

Département d'ingénierie moléculaire et biomoléculaire, université Libre de Bruxelles, 50, avenue F.D.-Roosevelt, B-1050 Bruxelles, Belgium

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ABSTRACT

If prebiotic chemistry is defined as the study of the chemical steps, which lead to the first organisms, a clear-cut definition of "living organism" is needed. Unfortunately, no unambiguous and universally accepted definition exists for the concept "living". Under these conditions, fuzzy logic is probably the methodological tool that can best be used to handle questions pertaining to "the origin of life". A conventional scale must, however, be defined which interestingly enough, depends necessarily on our present-day scientific knowledge.

1. Introduction

Organic synthesis dates back to beginning of the 19th century but remains, 200 years later, an extremely active field of research with thousands of papers published each year. Millions of new molecules have been synthesized and described over the last 2 centuries. Chemists have developed methodologies, reactants, catalysts, solvents, which allow them to prepare almost any desired molecule. It can be said without any doubt that synthetic chemistry is a mature scientific field.

Synthetic biology is on the other hand a much younger field, its development having required preliminary knowledge concerning the nature and function of the molecular and supramolecular components of the living world. Of course, this knowledge is not yet complete but is already adequate for a scientist to work on substituting some of these components to obtain chemically modified living organisms. For obvious reasons, building or rebuilding genomes is an important aspect of synthetic biology. What is common to modern synthetic chemistry and synthetic biology is the fact that synthesis, when achieved, is the result of human design and that the products are obtained after days, weeks or years of hard work undertaken by a team of scientists who, from the start, had a clear idea about what they were trying to obtain.

In some aspects, prebiotic chemistry is very similar to synthetic chemistry. When Stanley L. Miller, knowing the importance of amino acids in the living world, succeeded in obtaining some of them, "simply" by generating an electric discharge in a gas mixture, he was performing a chemical synthesis [1]. This synthesis is generally taken as an illustrative example of prebiotic chemistry as the experimental conditions used by Miller were chosen not because they were the best to obtain amino acids but because they were considered similar to those which probably prevailed on the young Earth when life was not yet present.

If one caricatures, prebiotic chemistry could be described as inefficient synthetic chemistry performed under conditions which are generally far from optimal. The choice of these "poor" conditions is determined only by their supposed similarities with the natural conditions prevailing on the young Earth during the prebiotic period. Unfortunately, these conditions are very poorly characterized and furthermore, considering that the emergence of the first living cells was most probably a local event, many very different conditions could have prevailed simultaneously. Furthermore, nobody can imagine that all the events, which led to the first living cells, took place in a unique locus following a linear sequence. Prebiotic chemistry is supposed to reproduce the pathways by which matter complexity increased on the young Earth but these pathways were followed by chance; they were not

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* Corresponding author.
E-mail address: jreisse@ulb.ac.be (J. Reisse).

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designed and will remain forever unknown. Indeed, no fossils, no traces, nothing remains to substantiate one pathway with respect to others. The prebiotic chemist does not reproduce something he knows, he invents possible pathways, which are able to increase the complexity of the molecules or supramolecular systems on which he is working. This is where prebiotic chemistry clearly differs from synthetic chemistry.

2. Why is prebiotic chemistry a fuzzy field?

If prebiotic chemistry is defined as the study of the chemical steps, which lead to the first organisms, a clear-cut definition of "living organism" is needed. Unfortunately, as we discussed recently, no unambiguous and universally accepted definition exists for the concept "living" [2]. Clearly, this is not a problem for biologists who, from this point of view, are in a position very similar to the one of physicists. Physicists do excellent science without a definition for time, space or energy; biologists do excellent science without a definition for life! Nevertheless, for someone interested in the steps, which lead to the first organisms, the lack of definition of the final goal is a little disquieting: it introduces vagueness. Prebiotic chemistry is a fuzzy field!

Prebiotic chemistry could possibly also be defined as the study of the transition from "non living systems" to "living systems" but then a new problem arises: without a definition for "living" one cannot have a definition for "non living"! Is this really a problem? At first view, particularly for scientists trained in countries where Descartes is considered one of the founders of modern sciences, the response is "yes, this is a problem"! However, if we think about the way in which scientific research is performed, we are obliged to agree with the Dutch physicist H.A. Kramers when he says:

> *"In the world of human thought generally, and in physical sciences in particular, the most important and most fruitful concepts are those to which it is impossible to attach a well-defined meaning" [3].*

From our point of view, the absence of definition for "living" and "non living" is not a major problem in prebiotic chemistry; but it requires that the aim of prebiotic chemistry be clearly identified.

The search for the origin of the building blocks of living organisms is certainly one of the aims of prebiotic chemistry. These building blocks must, however, be clearly identified. Water is an important constituent of the living world but the search of the origin of water on the primitive Earth is not considered to be a sub-field of prebiotic chemistry. One could restrict the concept of building blocks to the organic constituents of living organisms, i.e., to molecules containing at least one C-H bond. If this definition is accepted, the study of the natural processes able to lead to the formation of C-H bonds could be described as prebiotic chemistry. The majority of prebiotic chemists would, however, certainly disagree with such a suggestion and it could be argued that, if such a broad definition of prebiotic chemistry is accepted, why should the study of the nucleosynthesis of carbon not also be included? This clearly highlights that a more precise definition of the expression "building blocks of living organisms" is required. Unfortunately, such a definition does not exist and this is another source of vagueness in prebiotic chemistry. Prebiotic chemistry is without doubt a fuzzy field!

Faced with the absence of a generally accepted definition of prebiotic chemistry, it is not surprising that the field is so frequently criticized by scientists who are not directly involved in it. For some of them, prebiotic chemistry is not even considered to be a "true" scientific field.

3. Towards the search for a certain consensus regarding the objectives of prebiotic chemistry and the tools required to reach these objectives

It is doubtful that the first cells were eukaryotic cells. They were more probably prokaryotes. These first cells were perhaps (certainly?) less complex than the simplest prokaryotic cells known today, one does not really know exactly what "less complex" means in this context! We simply have a "feeling" about what it could mean.

In front of so many diverse sources of vagueness, it becomes necessary to think about the methodological tools that can be used to solve questions pertaining to the origin of life. A fuzzy scientific field requires an appropriate logic. This logic exists and was introduced by Zadeh in the middle of the 1960s. It is called fuzzy logic [4]. This logic is not founded on the three axioms of Aristotelian logic, which take the form of three laws:

- the law of contradiction: *A cannot be both B and "non B"*;
- the law of excluded middle: *A must be either B or "non B"*;
- the law of identity: *A will always be A*.

If we agree on the fact that prebiotic chemistry is the study of the transition from "non living" to "living" systems and if we agree that this transition was a progressive process, it is evident that the first two axioms of Aristotelian logic could not have been valid during the transition period when some molecular systems were no longer "non living" but not yet "fully living", they were "partially living". As we have pointed out elsewhere, this will always be the case when one is interested by any problem related to the origin or evolution of something [2]. This has also been recently highlighted by others [5].

Lamarck and Darwin both pointed out that the concept of biological species is useful for classification, but only "for the sake of convenience" [6]. For them, this concept is not founded on any natural laws or rules, because if this were the case, species would always have been as they are today, separated by an interbreeding barrier and would have had to have been the consequence of a series of special creations, as discussed in the book of Genesis. For evolutionists like Lamarck and Darwin, the definition of biological species was conventional. Interestingly enough, scientists involved in prebiotic chemistry are exactly in the same situation: the barrier between the "non living" and the “living” world is conventional and when it is introduced, it is only “for the sake of convenience”. The fact that it is not possible to find an unambiguous definition for a “living system” is the direct consequence of the conventional nature of the borderline between “non living” and “living”. In exactly the same way as biologists find advantages in considering cats and dogs or humans and chimpanzees as different species, prebiotic chemists could perhaps find an advantage in reaching a consensus about the kind of problems which are definitively inside their field of research and the problems which are outside of this field. Vagueness is acceptable but an excess of vagueness is counterproductive!

4. On the conventional scale of “livingness”

In fuzzy logic, an object A can be member of various fuzzy classes with, for each class, an index, which defines its level of membership. In the cases of the fuzzy classes “living” and “non living”, an object A will be characterized by a life index (l_i) equal to 1 if A is only in the class “living” and by a l_i of 0 if it only belongs the class “non living”. In all other situations, the l_i of A will be a number between 0 and 1.

If we consider that the simplest systems for which $l_i = 1$ are prokaryotes, according to our definition, components of prokaryotes like ribosomes, genomes, membranes have a l_i less than 1 but higher than 0. One could even be more precise and stipulate that only molecules found in prokaryotes which have never been observed outside the living world have a l_i higher than 0. With this precision, the l_i of water is zero, as is the l_i of alanine, which has been found in carbonaceous chondrites (meteorites). It could be argued that enantiomerically pure alanine has never observed in a chondrite but since enantiomeric excess higher than 12% for some alpha methylated alpha amino acids have been observed in chondritic samples [7,8], it would be perilous to use the enantiomeric purity of a molecule to decide whether or not it has a l_i different from 0. With this definition for the zero value of the life index scale, we accept the fact that the l_i value of a particular molecule could depend on scientific knowledge (and its evolution); a molecular system never found until now elsewhere than in a prokaryote could be discovered tomorrow in a sample for which an abiogenic origin is unquestionable. We do not consider this possibility as a problem; it is indeed common in science to be obliged to adapt conventions and definitions following new discoveries. For examples, when in 1953, Stanley Miller conducted his famous experiment, he was trying to find the origin of the building blocks of all living organisms and he made the first, and certainly the most famous, prebiotic experiment. At that time, it was not yet known that amino acids were present in carbonaceous chondrites [8,9]. Today, someone performing the Miller experiment, even with modifications of the experimental conditions, is no longer performing prebiotic chemistry but is searching for the origin of amino acids in the parent bodies of chondrites.

If we remain at the level of very simple building blocks of prokaryotes like amino acids or nucleic bases like guanine or cytosine, the search for possible pathways leading to their spontaneous formation is not, according to our definition, of the type research which can be described as prebiotic chemistry. On the other hand, the search for pathways leading to the spontaneous formation of polynucleotides or proteins is today, and will remain perhaps for a long time, an issue of prebiotic chemistry. Similarly, the search for the possible origin of membranes, ribosomes or genomes can be considered as sub-domains of prebiotic chemistry.

According to our life index scale, supramolecular systems found in prokaryotes have a l_i higher than their individual components: condensation polymers like proteins, polynucleotides or polysaccharides consequently have a higher l_i than their constitutive monomers. It is, however, of fundamental importance not to limit ourselves to the constitutive molecules of the living cells and not to forget that a living cell is a dynamic system exchanging matter and energy with its environment and containing sub-systems characterized by well defined functions. The l_i of molecules, including macromolecules or even molecular complexes is necessarily smaller than life indexes of chemical systems able to exchange matter and energy with their surrounding, if these systems are the result of a spontaneous aggregation process. Similarly, polymolecular systems with a function, able for example, to synthesize other molecules by coupling an exergonic reaction to an endergonic synthesis reaction would be characterized by a higher l_i than a molecule. Of course, it would not be possible to give an absolute value for the l_i of these “partially living” systems but, at least, it could be possible to order them on the life index scale.

A l_i sequence does not necessarily, however, reflect a temporal evolution sequence. Exactly for the same reasons that chloroplasts or mitochondria are subcellular structures resulting from an involution of endosymbiotic bacteria [10], it is highly probable that the first living cells result from the fortuitous association of systems which, after association could have lost some of their previous characteristics or functions. The idea that systems with a higher l_i value necessarily appeared, during prebiotic evolution, after systems characterized by lower l_i cannot be considered as a general rule.

5. Experimental prebiotic chemistry: its present situation compared to its hypothetical future

Numerous papers are published every year describing experiments showing that amino acids, small peptides, oses or even nucleosides can be obtained under experimental conditions similar to conditions which could have prevailed, locally, on the young Earth. Generally, these papers are described as contributions to prebiotic chemistry. As we mentioned previously in this paper, when in 1953, Miller performed his synthesis of amino acids with an electric discharge in a mixture of gases, it was fully justified to consider this synthesis as a prebiotic experiment. By using the life index concept introduced in the previous paragraph, we could say that at that time, it was perfectly acceptable to give a l_i higher than 0 to amino acids. Nevertheless, the situation is different today because we know that amino acids are present in carbonaceous chondrites. [8,9]

The search for plausible prebiotic synthetic pathways leading to the molecular constituents (building blocks) of prokaryotic cells certainly remains an interesting activity but it is important to realize that this activity is devoted to the search for the origin of molecular systems with very low (if not zero) life indexes. Understanding how a brick is made does not mean that one knows how to build a brick house, especially without an architect, engineer and bricklayer!

The recent discovery of the amino acid glycine in dust coming from the comet Wild 2 led to the following comment by Dr. Carl Pilcher, Director of the NASA Astrobiology Institute:

> *"The discovery of glycine in a comet supports the idea that the fundamental building blocks of life are prevalent in space, and strengthens the argument that life in the universe may be common rather than rare" [11].*

This is a typical example of confusion between bricks and houses! Moreover, the discovery of glycine in comet dust is certainly not a big surprise since it is known for decades now that amino acids are present in carbonaceous chondrites. This discovery only confirms that the l_i of glycine must be taken as 0.

Today, the expression "experimental prebiotic chemistry" must be used preferentially to describe the search of pathways leading to the spontaneous formation of polymers, supramolecular systems, dynamic systems, coupled systems, i.e., systems with a significant life index. We must recognize that this kind of research is extremely difficult and, in front of this difficulty and in front of the risk of not obtaining results, it is tempting to continue to work on the plausible prebiotic pathways for the formation of amino acids, riboses or nucleic bases, i.e. to search for the origin of molecules with a life index equal to 0. Unfortunately, when working in this way, (prebiotic) chemists do not achieve their goal that remains the search for plausible mechanisms, which led to the progressive transition from systems with $l_i = 0$ to systems with $l_i = 1$! The future of experimental prebiotic chemistry consists in trying to reach the upper part of the life index scale, not to remain at the ground level.

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