

Piet Herdewijn & M. Volkan Kiskürek (eds.): *Origin of Life: Chemical Approach*, Zürich: VCHA & Weinheim: Wiley-VCH, 2008, xii + 418 pp. [ISBN 978-3-906390-50-5]

Whereas the question 'What is life?' has been the province of philosophers, the related question 'What is the origin of life?' falls within the scope of chemistry and can be investigated experimentally. Life can be considered to have originated from the organization of organic molecules in a thermodynamically open system, far from equilibrium that requires a constant input of energy and material. It needs energy to escape from equilibrium, allowing spontaneous evolution, and several dynamic processes should become irreversible. The fully integrated system is extremely complex, and no single experiment or theory can explain how one of these processes was 'born' and how it contributed to the origin of life. However, experiments have been carried out and continue to be designed to support theories that certain molecules or chemical processes could have been involved in the origin of life. Hence, the subtitle of the volume under review here is quite appropriate. A wide variety of competing theories and experimental results are argued and described in this book.

Origin of Life: Chemical Approach is most appropriately dedicated to the memory of two of the leading pioneers in the subject – the recently deceased Leslie E. Orgel and Stanley L. Miller. It is a reprinting of most of the articles of a special issue of *Chemistry & Biodiversity* (2007, no. 4) titled "On Chemistry Leading to Life's Origin", edited by Piet Herdewijn of Katholieke Universiteit Leuven, Belgium and M. Volkan Kiskürek of Verlag Helvetica Chimica Acta, Zürich. A brief summary of Miller's and Orgel's most important contributions should help the potential reader to appreciate and understand the questions and answers dealt with in the book under review here.

Scientists have long speculated about how life could have arisen on Earth, but practical experiments had been few and unsuccessful until recently. Russian biologist and chemist Aleksandr Ivanovich Oparin is considered the father of modern investigations on the origin of life because in 1924 he suggested that the earliest living organisms might have been generated from chemical precursors, a suggestion proposed independently at about the same time by the British geneticist and evolutionary biologist John Burdon Sanderson Haldane.

The discovery of methane in the atmosphere of Jupiter led the two scientists to propose that the primitive Earth had possessed a strongly reducing atmosphere containing methane, ammonia, hydrogen, and water vapor. In this primordial or prebiotic soup molecules of increasing complexity could be built up progressively. The synthesis and accretion of organic compounds could continue until primitive life forms were attained. The theory was neglected until the 1950s when it was resurrected by 1934 Nobel chemistry laureate Harold Clayton Urey, who assigned 23-year-old University of Chicago graduate student Stanley Lloyd Miller to test it experimentally (J.P. Adloff & G.B. Kauffman, 'Stanley Lloyd Miller (1932-2007), Exobiology Pioneer', *Chemical Educator*, 12 (2007), 279-284).

An experiment to prove the Oparin-Haldane theory required a reducing atmosphere simulating the prebiotic soup, a source of energy to trigger chemical reactions, and an analysis of the compounds that might be produced. For Miller the first condition was straightforward: a mixture of methane (CH₄), ammonia (NH₃), hydrogen (H₂), and water vapor (H₂O). Second, experiments employing electric discharges in gaseous mixtures had been performed previously, and he assumed that the atmosphere of the early Earth was the site of intense electric phenomena such as flashes of lightning and *aurorae boreales*.

Third, various kinds of organic compounds could be expected, but Miller considered that it would be most appropriate to search for amino acids, the precursors of proteins – the ‘building blocks of life’ or the ‘precursors of life’, which could be separated and identified by paper chromatography.

Miller sealed the gaseous mixture inside an array of glass and two flasks. Water vapor produced by heating or boiling simulated evaporation from the oceans. The prebiotic soup passed repeatedly through the reaction chamber where it was subjected to a continuous electrical spark discharge. The water-soluble reaction products passed through a condenser and dissolved in the ‘ocean’. After Miller ran the experiment continuously for a week, the water in the flask was found to contain the amino acids glycine, α -alanine, and β -alanine; and possibly aspartic acid after reactions had produced simpler compounds – formaldehyde and hydrogen cyanide.

Miller’s report positively impacted not only the scientific community but also the general public as well. It catapulted the field of exobiology – the study of life beyond the Earth or the study of the origin of life on Earth. This experiment, immediately recognized as a classic, was only the beginning of future work in the field. It opened the field of prebiotic organic chemistry and engendered an immense interest in academic circles and in the public. Almost overnight it transformed the study of the origin of life into a respectable field of inquiry. Despite the brilliant beginning, neither Miller nor others were able to take the next step, that of providing a plausible mechanism by which these chemicals could have been assembled into living cells or the macromolecules, DNA, and proteins on which cells depend. However, as *Origin of Life* clearly demonstrates, research in this area is being carried out by numerous scientists.

On the theoretical front, during the 1960s Leslie E. Orgel and other scien-

tists began to pose questions about the biochemical origins of deoxyribonucleic acid (DNA), the nucleic acid that contains the genetic instructions used in the development and functioning of all known living organisms (J.P. Adloff & G.B. Kauffman, ‘Leslie E. Orgel (1927-2007): Pioneer Researcher on the Origin of Life’, *Chemical Educator*, **13** (2008), no. 4, 248-256). Its peculiar helical molecular structure had been unraveled by James D. Watson and Francis H. C. Crick in 1953, and its role as a repository of genetic instructions was becoming more widely understood. Orgel was one of the first scientists to argue that DNA is too complex to be the first storehouse of genetic information and to suggest that it was probably preceded by RNA. The latter would be the first replicative molecule, passing on the genetic blueprint to future generations. Orgel and other scientists suggested that RNA had previously served a more elemental role in creating a library of genetic information ultimately to allow organisms to replicate.

These ideas became broadly known as the ‘RNA World’ theory, which was explored more deeply in Miller and Orgel’s book (*The Origins of Life on the Earth*, Prentice Hall: Englewood Cliffs, 1974). The theory referred to a hypothetical stage in the origin of life on Earth during which proteins were not yet engaged in biochemical reactions and RNA carried out both the information storage task of genetic information and the full range of catalytic roles necessary in a very primitive self-replicating system. Nevertheless, the RNA World gave rise to a paradox: Information contained in DNA is necessary to make proteins, the large molecules that carry out most cellular activities, but proteins are also necessary to make DNA. This posed what Orgel termed a ‘chicken and egg’ conundrum. Which came first: DNA or proteins?

Among current theories of the origin of life, one is discussed in Herdewijn and Kisakürek’s book by Günter

Wächtershäuser, an award-winning chemist turned patent lawyer, who is Honorary Professor at the Universität Regensburg, mainly known for his 'Iron-Sulfur World' theory, in analogy with the 'RNA World' theory. He postulates that life on Earth had hydrothermal origins, a theory consistent with the hypothesis that life originated near hydrothermal vents on the sea floor. One of the key ideas advanced by Wächtershäuser is that an early form of metabolism predated genetics, metabolism meaning a cycle of chemical reactions that produce energy in a form that can be harnessed by other processes. The idea is that once a primitive metabolic cycle was established, it began to produce ever more complex compounds by autocatalytic cycles. This 'metabolism first' scenario is opposed by the alternative 'replication first' hypothesis, whose proponents believe that life originated from the spontaneous emergence of the first, supposedly RNA-based 'replicators'.

In the following essay Armen Y. Mulkidjanian (Moscow State University) and Michael Y. Galperin (National Institutes of Health) contrast the 'replication first' and 'metabolism first' hypotheses and conclude that the theories complement rather than contradict each other and suggest that life on Earth emerged from a 'metabolism-driven replication'.

Origins of Life is an international venture that includes 25 essays by 64 authors from 14 countries. The essays deal with a variety of topics and approaches to fundamental studies in the field. In the introductory essay, 'What Is Life? A Brief Historical Overview', Antonio Lazcano (National Autonomous University of Mexico) defines life in terms of evolution and the role of chemistry in the evolutionary process. He summarizes the question from a wide variety of sources, both scientific and non-scientific, and concludes, "Research in the origin and nature of life is doomed

to remain, at the best, as work in progress" (p. 12).

The essays that follow describe and explain a wide variety of theories and experiments such as chemistry and selection; evolution of the pioneer organism; chemical aspects of synthetic biology; ribozyme catalysis in the RNA world; intractable mixtures and the origin of life; spontaneous replication; the chemical etiology of nucleic acids; interstellar amino acids; the HCN-tetramer, which is a "classic" in the prebiotic chemistry of HCN; autocatalytic feedback with organic products acting as ligands for activating metal centers from which they arise; shaping of origin and evolution of life by the contingency of environmental conditions; hypothesis that small molecules ("molecular midwives") and alternative backbone linkages facilitated the emergence of the first RNA-like polymers of life; possibilities bridging the gap between "naked gene" theories and metabolic theories in which complex systems self-propagate by growth and fragmentation; *in vitro* and *in vivo* studies; chiral meteoritic amino acids in the induction of selective traits in molecular evolution; assembly of potential RNA precursors, focusing on methods for stereoselective C-C bond construction by aldolization and related processes; possible role of pseudo-peptide-DNA mimics like PNA (peptide nucleic acid) in the prebiotic origin of life prior to an RNA world; aminopropyl nucleic acids as potential catalytic polymers that may evolve into RNA; achiral informative polymers as RNA predecessors; and the homochirality of nucleic acids.

We are still far from getting a definitive answer to the most fundamental question in science, because every theory such as the 'RNA world' hypothesis, the role of astrobiology, the function of minerals as primitive catalysts, the uniformity of life in the universe, has its supporters and opponents.

According to the editors, this compilation "gives an overview of the present

'state of the art', written by the eminent 'players' in the field. We realize that several topics are not really covered and would like to apologize for this deficiency. We are hoping, however, that the enthusiasm with which the authors have agreed to contribute to this volume will inspire further pioneers of this creative domain of 'explorative chemistry' to present their ideas and/or experimental data" (pp. VII-VIII).

In my opinion, Herdewijn and Kisakürek have eminently succeeded in attaining their goal. I heartily recommend *Origin of Life: Chemical Approach*, which reviews much of the theoretical and experimental work of the past two decades, while simultaneously, because of the variety of approaches, emphasizing that considerable further work remains to be done. It should be invaluable to chemists, philosophers, students, and anyone working in or interested in this field of research that seeks to answer one of the most fundamental and complex questions in science.

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