Introduction

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Humans in every civilization have always been intrigued by their origin and by the question of the origin of life itself. During thousands of years, the comforting theory of spontaneous generation seemed to provide an answer to this enduring question. In ancient China, people thought that aphids were spontaneously generated from bamboos. Sacred documents from India mention the spontaneous formation of flies from dirt and sweat. Babylonian inscriptions indicate that mud from canals was able to generate worms.

For the Greek philosophers, life was inherent to matter; it was eternal and appeared spontaneously whenever the conditions were favorable. These ideas were clearly stated by Thales, Democritus, Epicurus, Lucretius, and even by Plato. Aristotle gathered the different claims into a real theory. This theory safely crossed the Middle Ages and the Renaissance. Famous thinkers like Newton, Descartes, and Bacon supported the idea of spontaneous generation.

The first experimental approach to the question was published in the middle of the 17th century, when the Flemish physician Van Helmont reported the generation of mice from wheat grains and a sweat-stained shirt. He was quite amazed to observe that the mice were identical to those obtained by procreation. A controversy arose in 1668 when Redi, a Tuscan physician, published a set of experiments demonstrating that maggots did not appear when putrefying meat was protected from flies by a thin muslin covering.

Six years after Redi's treatise, the Dutch scientist Anton Van Leeuwenhoek observed microorganisms for the first time through a microscope of his own making. From then on, microorganisms were found everywhere and the supporters of spontaneous generation took refuge in the microbial world. However, Van Leeuwenhoek was already convinced that the presence of microbes in his solutions was the result of contamination by ambient air. In 1718, his disciple Louis Joblot demonstrated that the microorganisms observed in solutions were, indeed, brought in from the ambient air, but he could not convince the naturalists.

Even Buffon, in the middle of the 18th century, thought that Nature was full of germs of life able to scatter during putrefaction and to gather again, later on, to reconstitute microbes. His Welsh friend John Needham did many experiments to support this view. He heated organic substances in water in a sealed flask in order to sterilize the solutions. After a while, all solutions showed a profusion of microbes. The Italian priest Lazzaro Spallanzani argued that sterilization was incomplete. He heated the solutions to a higher temperature and killed all the microbes, but could not kill the idea of microbial spontaneous generation.

The controversy reached its apotheosis one century later, when Felix Pouchet published his treatise in 1860. He documented the theory of spontaneous generation in the light of experiments that, in fact, were the results of contamination by ambient air. Pasteur gave the finishing blow to spontaneous generation when he designed a rigorous experimental setup for sterilization.

The beautiful demonstration of Pasteur raised the fascinating question of the historical origin of life. Since life can originate only from preexisting life, it has a history and therefore an origin, which must be understood and explained by chemists.

It is always difficult to define what is meant by the word *life*. This is the first difficulty encountered by scientists who try to reconstruct the birth of life on Earth. The second difficulty is related to the factor time. Because of time flow and evolution, primitive life was different from life today and only hypothetical descriptions of primitive life can be proposed. Because of the limitations of time, prebiotic chemistry can never be repeated in the laboratory. Therefore, simulations may only represent possible supports for plausible hypotheses from the point of view of historical legitimacy. A way around these difficulties is to collect clues from different disciplines. Today, these clues are like pieces of a puzzle that we can begin to assemble. The purpose of this book is to integrate the most recent discoveries in astronomy, planetology, geology, paleontology, biology, and chemistry into plausible scenarios for a better understanding of the origins of life.

The minimal requirements for primitive life can be tentatively deduced from the following definition: Primitive life is an aqueous chemical system able to transfer its molecular information and to evolve. The concept of evolution implies that the system transfers its molecular information fairly faithfully but makes occasional accidental errors.

Since most of Earth's early geological history has been erased by later events, we remain ignorant of the true historical facts on Earth from the time when life started (Chapters 1 and 2). We must, therefore, imagine simple informative molecules as well as the machinery for information transfer. Both functions must then be tested in the laboratory.

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Water molecules are widespread in the universe as grains of solid ice or as very dilute water vapor. Liquid water is a fleeting substance that can persist only above 0 °C and under an atmospheric pressure higher than 6 mbars. Therefore, the size of a planet and its distance from the star are two basic characteristics that will determine the presence of liquid water. If a body is too small, like Mercury or the Moon, it will not be able to retain any atmosphere or, therefore, liquid water. If the planet is too close to the star, the mean temperature rises due to starlight intensity. Any seawater present will evaporate, delivering large amounts of water vapor to the atmosphere and thus contributing to the greenhouse effect, which causes a further temperature rise. Such a positive feedback loop could lead to a runaway greenhouse: All of the surface water would be transferred to the upper atmosphere, where photodissociation by ultraviolet light would break the molecules into hydrogen and oxygen. Loss of the atmosphere would result from the escape of hydrogen to space and the combination of oxygen with the crust. A planet that is far from the star may permit the existence of liquid water, provided that the planet can maintain a constant greenhouse atmosphere. However, water could provoke its own disappearance. The atmospheric greenhouse gas CO_2, for instance, would be dissolved in the oceans and finally trapped as insoluble carbonates by rock weathering. This negative feedback could lower the surface pressure and, consequently, the temperature to such an extent that water would be largely frozen. The size of Earth and its distance from the Sun are such that the planet never experienced either a runaway greenhouse or a divergent glaciation.

Present-day life is based on organic molecules made of carbon, hydrogen, oxygen, nitrogen, sulphur, and phosphorus atoms. However, primitive chemical information may have been stored in mineral crystals. This idea has been developed by Cairns-Smith at the University of Glasgow. According to this theory, some clays offered a potential repository for genetic information in the intrinsic pattern of crystal defects. These clays proliferated and their replicating defects became more abundant. Certain lines developed photochemical machinery producing nonclay species such as polyphosphates and small organic molecules. Natural selection favored these lines because the newly formed organic molecules modified the clay's properties in favorable ways, thus catalyzing synthesis of such lines. Organic polymers of specified monomer composition appeared but, at first, served only structural roles. Based-paired polynucleotides replicated, giving rise to a minor genetic material. This material proved to be useful in the alignment of amino acids for polymerization. Finally, the clay machinery was dispensed with in favor of a polynucleotide-based replication; a "genetic takeover" whereby nucleic acids became the genetic libraries. Unfortunately, since 1966 when Cairns-Smith

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began to advocate his interesting ideas, practically no experimental evidence has been provided to support such a primitive mineral genetic material.

It is generally believed, through analogy with contemporary life, that primitive life originated from the processing of organic molecules by liquid water.

Alexander Oparin, in 1924, suggested that the small, reduced organic molecules needed for primitive life were formed in a primitive atmosphere dominated by methane. The idea was tested in the laboratory by Stanley Miller (Chapter 3). He exposed a mixture of methane, ammonia, hydrogen, and water to electric discharges. Among the compounds formed, he identified 4 of the 20 naturally occurring amino acids, the building blocks of proteins. Since this historical experiment, 17 natural amino acids have been obtained via the intermediary formation of simple precursors such as hydrogen cyanide and formaldehyde. Spark discharge synthesis of amino acids occurs efficiently when a reducing gas mixture containing significant amounts of hydrogen is used. However, the true composition of primitive Earth's atmosphere remains unknown. Today, geochemists favor a nonreducing atmosphere dominated by carbon dioxide. Under such conditions, the production of amino acids appears to be very limited.

More recently, Günter Wächtershäuser suggested that life started from carbon dioxide. The energy source required to reduce carbon dioxide was provided by the oxidative formation of pyrite (FeS_2) from iron sulfide (FeS) and hydrogen sulfide. Pyrite has positive surface charges and binds the products of carbon dioxide reduction, giving rise to a surface chemistry (developed in Chapter 9). Experiments are presently being run to test this new hypothesis.

Deep-sea hydrothermal systems may also represent likely environments for the synthesis of prebiotic organic molecules (Chapter 4). Experiments have been carried out to test whether amino acids can be formed under conditions simulating hydrothermally altered oceanic crust.

Organic chemistry is universal. So far, more than 50 different organic molecules have been identified by radioastronomy in dense clouds of the interstellar medium. Synthesis of these molecules is thought to be initiated by collisions of high-energy cosmic ray particles with hydrogen and helium or by photochemical processes. The most important compounds for prebiotic chemistry that have been identified are probably hydrogen cyanide, formaldehyde, acetylene, and acetonitrile.

Comets also show substantial amounts of organic material. According to Delsemme's analysis, Comet Halley contains 14% organic carbon by mass. About 30% of cometary grains are dominated by the light elements C, H, O, and N, and 35% are close in composition to carbonaceous chondrites. Among the molecules identified in comets are hydrogen cyanide and formaldehyde.

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Comets, therefore, may have been an important source of organics delivered to the primitive Earth (Chapter 5).

The study of meteorites, particularly the carbonaceous chondrites that contain up to 5% by weight of organic matter, has allowed close examination of extraterrestrial organic material (Chapter 6). Eight proteinaceous amino acids have been identified in the Murchison meteorite among more than 70 amino acids. Engel reported that L-alanine was more abundant that D-alanine in the Murchison meteorite (see Chapter 6). This rather surprising result has been recently confirmed by Cronin. The latter found a racemic composition (equal mixture of L and D enantiomers) for norvaline and α-amino-n-butyric acid, which can racemize by abstraction of the C_α hydrogen atom. More interestingly, Cronin found enantiomeric excesses of about 10% for isovaline, α-methyl norvaline, and α-methyl isoleucine, which cannot racemize by proton abstraction. The enantiomeric excesses found in the Murchison meteorite may help us understand the emergence of a primitive homochiral life.

Homochirality of present-day life is believed by many researchers to be not just a consequence of life but also a prerequisite for life. Present terrestrial life is dominated by proteins, which catalyze biochemical reactions; nucleic acids, which carry genetic information; and a lipidic micellar system, which forms the cellular protecting membranes. Most of the constituents, that is amino acids, sugars, and lipids, contain at least one asymmetric carbon atom.

The 19 chiral proteinaceous amino acids belong without exception to the L-configuration class, whereas the two sugars found in nucleic acids are related to the D-series. The biopolymers themselves form asymmetric helical structures and superstructures, the α- and β-conformations of polypeptides, the A-, B-, and Z-forms of nucleic acids, and the helical conformations of polysaccharides.

Any chemical reaction producing chiral molecules in statistically large numbers that is run in a symmetrical environment yields a racemic mixture, that is, a mixture of equal quantities of right- and left-handed enantiomers. However, in view of the importance of optical purity in present-day life, it is difficult to believe that, at the beginning, a completely racemic life form arose using biomolecules of both configurations simultaneously in the same protocell.

Theoretical models of the origin of chirality on Earth can be divided into two classes, those which call for a chance mechanism and those which call for a determinate mechanism resulting from an asymmetrical environment originating from the universe or from the Earth.

The proponents of the chance mechanism argue that the notion of equimolarity of a racemic mixture is only relative. For a relatively small set of molecules, random fluctuations may favor one enantiomer over the other. Both theoretical and experimental models are available. In a rather simple kinetic

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model initially proposed by Franck, an open flow reactor, run in far-from-equilibrium conditions, is fed by achiral compounds and forms two enantiomers reversibly and autocatalytically. If the two enantiomers can react to form an irreversible combination flowing out of the reactor, by precipitation for instance, and if certain conditions of fluxes and concentrations are reached, the racemic production may become metastable and the system may switch permanently toward the production of either one or the other enantiomer, depending on a small excess in one enantiomer.

Spontaneous resolution of enantiomers via crystallization represents the most effective means of breaking chiral symmetry since optically pure enantiomers can be isolated on scales ranging from grams to tons with the help of homochiral seeds. Did terrestrial quartz, known to be an asymmetric adsorbent and catalyst, undergo such a spontaneous resolution during crystallization? Close examination of over 27,000 natural quartz crystals gave 49.83% L and 50.17% D.

Parity nonconservation has raised many hopes among those who call for a determinate mechanism. This fundamental asymmetry of matter has been examined from various aspects. For example, circularly polarized photons emitted by the slowing down of longitudinally polarized electrons might be capable of inducing degradation reactions or stereoselective crystallization of racemic mixtures. No experiment has convincingly supported these theoretical considerations for the origin of a dominant enantiomer on Earth. Either the results were shown to be artifacts or to be so weak that they are doubtful.

Parity is also violated in the weak interactions mediated by neutral bosons Z^0. All electrons are intrinsically left-handed (their momentum and spin are more likely to be antiparallel). The antimatter counterpart, the positrons, are intrinsically right-handed. Therefore, L-serine, made of left-handed electrons, and D-serine, also made of left-handed electrons, are not true enantiomers but diastereoisomers. There is a very tiny, parity-violating energy difference in favor of L-amino acids in their preferred conformations in water and in favor of D-sugars. The energy difference is about 3.10^{-19} eV, corresponding to one part in 10^{17}, for the excess of L-molecules in a racemic mixture at thermodynamic equilibrium at ambient temperature.

Other chiral force fields that could have been acting on the Earth's surface have been researched: Asymmetric synthesis and degradation have been achieved with circularly polarized light, and an original approach to enantiomer resolution – using Earth gravity and a macroscopic vortex – has been tested.

Unfortunately, the classical electromagnetic interactions, such as circularly polarized light or other fields that can be imagined acting on Earth, would probably never result in a very high yield of optically pure compounds. Such asymmetric force fields would also probably cancel their effects on a time and space average. The chiral (one handed) amino acids found in the Murchison meteorite push the problem of the origin of biological chirality out into the cosmos. Among the possible extraterrestrial sources of circularly polarized light, sunlight is generally discounted as probably being too weak and not of a consistent handedness for sufficiently long periods. According to Bonner and Rubenstein (1987), synchrotron radiation from the neutron star remnants of supernova events is a better candidate. Interaction of neutron star circularly polarized light with interstellar grains in dense clouds could produce chiral molecules in the organic mantles by partial asymmetric photolysis of mirror-image molecules.

Micrometeorites (Chapter 7), also referred to as cosmic dust or interplanetary dust particles, have been extracted both from black sediments collected from the melt zone of the Greenland ice cap and directly from Antarctic old blue ice. In the 50–100-μm size range, a constant high percentage of 80% of unmelted chondritic micrometeorites has been observed, indicating that many particles cross the terrestrial atmosphere without drastic thermal alteration. In this size range, the carbonaceous micrometeorites represent 80% of the samples and contain 2% carbon; they might have brought about 10^{20} g of carbon over a period of 300 million years, corresponding to the late terrestrial bombardment phase, assuming that the flux was 1,000 times more intense than today. This delivery represents more carbon than that now present in the biosphere (about 10^{18} g).

It is generally believed, based on analogy with contemporary living systems, that primitive life emerged as a cell, thus requiring, at the least, boundary molecules able to isolate the system from the aqueous environment (membrane), catalytic molecules providing the basic chemical work of the cell (enzymes), and informative molecules allowing the storage and the transfer of the information needed for replication (RNA).

Fatty acids are known to form vesicles when the hydrocarbon chains contain more than 10 carbon atoms. Such vesicle-forming fatty acids have been identified in the Murchison meteorite. However, the membranes obtained with these simple amphiphiles are not stable over a broad range of conditions. Stable neutral lipids can be obtained by condensing fatty acids with glycerol or with glycerol phosphate, thus mimicking the stable contemporary phospholipid. Primitive membranes could initially have also been formed by simple terpenoids (Chapter 8).

Wächtershäuser (Chapter 9) suggests that the carbon source for life was carbon dioxide. He proposes that the energy source required to reduce carbon dioxide was provided by the oxidative formation of pyrite from iron sulfide and hydrogen sulfide. An attractive point in this hypothesis is that pyrite has positive surface charges and binds the products of carbon dioxide reduction, giving rise to a two-dimensional reaction system, a surface metabolism that would be more efficient than a system in which the products can freely diffuse away.

Most of the chemical reactions in a living cell are catalyzed by proteinaceous enzymes. Proteins are built up from 20 different amino acids. Each amino acid, with the exception of glycine, exists in two enantiomeric forms, L and D, although only L-amino acids occur in proteins. Proteins adopt asymmetrical rigid geometries, α-helices and β-sheets, which play a key role in the catalytic activity. According to de Duve, the first peptides appeared via thioesters and began to develop their catalytic properties in a thioester world (Chapter 10).

In contemporary living systems, the hereditary memory is stored in nucleic acids built up with purine and pyrimidine bases, sugars, and phosphate groups. Nonenzymatic replication has been demonstrated by Orgel and his coworkers at the Salk Institute in California. The preformed chains align the nucleotides by base-pairing to form helical structures that bring the reacting groups into close proximity (Chapter 11). However, the prebiotic synthesis of nucleotides remains an unsolved challenge. Although purines and pyrimidines have been obtained in model syntheses, the formation of nucleosides is a difficult problem. Condensation of formaldehyde leads to ribose, among a large number of other sugars. The synthesis of purine nucleosides, the covalent combination of purine and ribose, has been achieved by heating the two components in the solid state, but the yields are very low. No successful preparation of a pyrimidine nucleoside has been reported. Nucleoside phosphorylation is possible by thermal activation but without any regioselectivity. Chemists are now considering the possibility that early living systems used simpler informative molecules. For example, ribose has been replaced by glycerol in the backbone of one such candidate. In the light of the first experiments, however, the chemistry of these simplified informative molecules does not appear to offer any advantages. The straightforward and selective formation of ribose diphosphates from glycolaldehyde phosphate suggests that pyranosyl-RNA may have been involved in the early forms of life. Intense experimental work quoted in Chapter 11 is presently being conducted in Eschenmoser's laboratory along this new avenue.

Even if clays did not participate in the early stages of life as informative molecules, they probably played a key role as catalysts. Efficient clay-catalyzed condensation of nucleotides into oligomers has been recently reported (Chapter 12). On the other hand, Cech at the University of Colorado found that self-splicing and maturation of some introns do not require the help of any peptidic enzymes. Fragments of introns markedly increase the rate of

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hydrolysis of oligoribonucleotides. They also can act as polymerization templates since chains up to the 30-mer can be obtained starting from a pentanucleotide. The catalytic spectrum of these ribozymes has been considerably enlarged by directed molecular evolution (Chapter 13). RNAs have been shown to be able to act simultaneously as informative and catalytic molecules. They are often viewed as the first living systems on the primitive Earth (RNA world).

However, since the accumulation of nucleotides under prebiotic conditions seems unlikely, many chemists are now tempted to consider that primitive life was supported by simpler informative molecules, and great efforts are devoted to autocatalytic systems (Chapter 14) including simple organic molecules and micelles.

To what extent can the nature of primitive life be illuminated by back-extrapolation of present-day life and particularly by biopolymer phylogeny? Firstly, a good picture of the common microbial ancestor would help to understand the different steps of evolution of early life. Recent advances in molecular phylogeny suggest that the first microorganisms were hyperthermophilic prokaryotes (Chapter 15), but arguments have also been provided suggesting that prokaryotes and eukaryotes emerged simultaneously from the same mesophilic common ancestor.

The geological record obviously provides important information. The isotopic signatures of the organic carbon of the Greenland metasediments bring indirect evidence that life may be 3.8 billion years old. The isotopic signatures are fully consistent with a biological origin and the remarkable diversity of the microflora discovered by Schopf (Chapter 16). Eleven species of cellularly preserved filamentous microbes, comprising the oldest diverse microbial assemblage now known in the geologic record, have been discovered in shallow water cherts interbedded with lava flows of the Early Archean Apex Basalt of northwestern Western Australia. This prokaryotic assemblage establishes that trichomic cyanobacterium-like microorganisms were extant and were both morphologically and taxonomically diverse at least as early as ~3.465 million years ago, thus suggesting that oxygen-producing photoautotrophy may have already evolved by this early stage in biotic history. The existence of the Apex microfossils demonstrates that the paleobiologically neglected Archean rock record is a fruitful source of direct evidence regarding the earliest history of life.

Unfortunately, the direct clues that may help chemists to understand the emergence of life on Earth about 4 billion years ago have been erased by the Earth's turbulent geological history, the permanent presence of liquid water, and by life itself when it conquered the whole planet. We remain ignorant of the true historical facts on Earth from the time when life started. Titan, the largest satellite of Saturn, offers a nice control of a planetary laboratory probably not modified by “living” systems. Titan’s organic chemistry is believed to have remained almost unchanged over geological periods. Its active atmospheric chemistry will be studied by the Huygens probe of the Cassini mission (Chapter 17).

The early histories of Mars and Earth clearly show similarities. Geological observations collected from Martian orbiters suggest that liquid water was once stable on the surface of Mars, attesting to the presence of an atmosphere capable of decelerating C-rich micrometeorites. Therefore, primitive life may have developed on Mars as well. Liquid water seems to have disappeared from the surface of Mars about 3.8 Ga ago. The Viking missions did not find any organic molecules or clear-cut evidence for microbial activities at the surface of the Martian soil. These experiments do not exclude the existence of organic molecules and fossils of microorganisms that may have developed on early Mars before liquid water disappeared. The Martian subsurface perhaps keeps a frozen record of the early evolution of life (Chapter 18).

References

Frank, F. C. 1953. On spontaneous asymmetric synthesis. *Biochim. Biophys. Acta* 11:459–463.

Bonner, W. A., and Rubenstein, E. 1987. Supernovae, neutron stars and biomolecular chirality. *BioSystems* 20:99–111.