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Excerpt
More Information

1 Building Blocks

All living organisms, from microbes to humans, are made of the same basic building blocks, consisting mainly of sugars, amino acids, fatty acids, and nitrogenous bases, altogether little more than fifty distinct, small chemical species, of molecular weights rarely exceeding 200. What largely differentiates organisms chemically is the manner in which these building blocks join into larger assemblages, mostly polysaccharides, proteins, lipids, and nucleic acids. A number of additional compounds peculiar to certain sets of organisms exist – chlorophyll in plants is an example – but these are most likely products of later evolution. In its earliest forms, life probably was made of little more than the universal building blocks found in all living organisms today.

Prebiotic Chemistry

This remarkable singularity goes back to the very beginnings of life, conveying a central message whose meaning did not catch the attention of biologists until 1953, when Stanley Miller observed the spontaneous formation of a number of amino acids and other typical biological constituents in a laboratory situation he and his mentor, the celebrated chemist Harold Urey, believed to be representative of the conditions that prevailed on the primitive Earth at the time life first appeared (Miller, 1953). Even though serious doubts have since been voiced about its underlying assumption, Miller's achievement remains a major landmark in the history of biology. It opened the new field of prebiotic chemistry and sparked a large number of interesting experiments.

Perhaps even more importantly, Miller's findings highlighted the possibility that the building blocks of life could have been the products of natural chemical phenomena, mandated by local physical–chemical conditions. This possibility should not have come as a surprise, for it was consistent with the view, already solidly established at that time, that living processes take place naturally, without the intervention of some special "vital force." But, with rare exceptions, biochemists in those days hardly bothered with the origin of life, which they relegated to the realm of the unknowable, not worth experimenting on or even thinking about.

Cosmic Chemistry

Surprisingly, nothing like the sensation created by Miller's experiments greeted the later, much more startling discoveries showing the presence of a variety of organic molecules in extraterrestrial sites never visited by any living organism. Detected by radioastronomical spectroscopy, by spacecraft-borne instruments sent to passing comets and other parts of the solar system, and by detailed analyses of meteorites that have fallen on Earth, these organic substances now number in the hundreds, creating a host of fascinating problems for the scientists who attempt to explain their formation (for two comprehensive reviews, see Botta and Bada, 2002; Ehrenfreund et al., 2002).

From the ultra-rarefied interstellar spaces, where hours may go by before an atom encounters another atom, to the tiny dust particles that float in space, to the material that makes up protoplanetary disks around new-forming stars, to the comets and asteroids that condense from this material, to the surfaces of planets and their moons orbiting around a star, there exists a gradation of complexity, ranging from small assemblages of a few atoms – such as the hydroxyl, methyl, and methylene radicals, water, methane, carbon monoxide, methanol, formaldehyde, cyanide, cyanate, isocyanate, and thiocyanate, to mention only a few – to a wide variety of larger molecules, including, in addition to a considerable amount of "junk" (as judged by a biochemist), amino acids, sugars, purines, pyrimidines, fatty acids, and other typical biological constituents, some engaged in more complex associations.

These observations have now reached the stage of laboratory experimentation. In France, the group of Guy Ourisson has obtained a wide variety of biological building blocks by high-energy bombardment of graphite targets with molecular beams of the desired atoms, simulating plausible interstellar events (Devienne et al., 1998, 2002). In another approach, two groups, one American (Bernstein et al., 2002) and the other European (Munoz Caro et al., 2002), have found that a number of amino acids arise spontaneously in simulated interstellar ice analogues containing water, methanol, and ammonia as main components, with, in addition, hydrogen cyanide in one case (Bernstein et al., 2002), and carbon monoxide and carbon dioxide in the other (Munoz Caro et al., 2002), exposed to UV irradiation at very low temperature and under very high vacuum.

There has been much discussion concerning the possible destruction of extraterrestrial organic molecules upon entry into the atmosphere, and later impact, of their carrying body, whether comet or meteorite (Botta and Bada, 2002; Ehrenfreund et al., 2002). It is generally believed that, even though such destruction may have been important, a sufficient proportion of the incoming material would have been spared, providing abundant building blocks for the origin of life on our planet. A partial contribution by terrestrial chemistry is, however, not excluded.

The general conclusion that emerges from all these findings is that *the building blocks of life form naturally* in our galaxy and, most likely, also elsewhere in the cosmos. The chemical seeds of life are universal. The first singularity that we detect is thus the consequence of the basic laws that govern the transformations of matter in the universe; it is clearly of *deterministic* origin (mechanism 1).

This conclusion presupposes that the products of cosmic chemistry (and of terrestrial prebiotic chemistry) did indeed serve to initiate the development of life on Earth. The remarkable similarities between these products and the building blocks of life would seem strongly to support this assumption. Nevertheless, as will be mentioned in Chapter 5, a theory vigorously advocated by some investigators holds that life started from scratch, so to speak, that is, from carbon dioxide and other simple materials developing into increasingly complex compounds by pathways that prefigured in some respects the reactions of present-day metabolism. As we shall see, these are very interesting proposals, which include a number of valuable aspects. But the assumption that the products of prebiotic chemistry may have had nothing to do with the initiation of life on Earth – and, therefore, that their similarities with the building blocks of life are a meaningless coincidence – does seem difficult to accept.

Note, however, that not all the products of cosmic chemistry are used for the construction of life. For example, α-aminobutyric acid and α-aminoisobutyric acid, which are present in fair abundance in the Murchison meteorite and in Miller's experimental flasks, are not found in living organisms. On the other hand, ubiquitous compounds, such as the amino acids tryptophan and histidine, have not so far been identified among products of cosmic chemistry and may never be, having appeared later in the development of life. Thus, selection and innovation are two key notions that have to be added to determinism at an early stage in our appreciation of life's building blocks. A remarkable singularity, in this connection, is the fact that life often uses only one of the two possible isomers whenever molecules exhibiting the phenomenon of chirality are employed. Known as homochirality (Greek for "same-handedness"), this trait, which is considered by many as one of the most mysterious properties of life, deserves to be examined in some detail.

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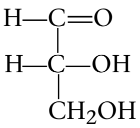
2 Homochirality

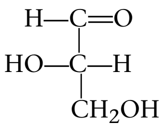
It has been known since the days of Pasteur (famous, notably, for the separation of two forms of tartaric acid) that molecules containing an asymmetric carbon atom, that is, a carbon atom bearing four different groups, can exist in two forms that are to each other like one hand to the other (*cheir* means hand in Greek) or like an object to its image in a mirror. When aqueous solutions of such molecules are traversed by a beam of polarized light, the polarization plane of the light is rotated by a certain angle. The value of this angle, adjusted to the concentration of the solution and to the thickness of the liquid layer traversed, is known as the specific rotatory power, or optical activity, of the substance; it is the same in absolute value, but of opposite sign, for the two forms. By definition, the optical activity is said to be positive when the polarization plane of the light is rotated to the right, and negative in the opposite case. The two forms, known as enantiomers (*enantios* means opposite in Greek), are designated *d*, for dextrorotatory (*dexter* means right in Latin), and *l*, for levorotatory (*laevus* means left in Latin).

Following a proposal made at the beginning of the last century by the German chemist Emil Fischer, the nomenclature based on optical activity was replaced by one based on structure. Stereoisomers (*stereos* means solid in Greek) replaced optical isomers. Fischer based his classification on the two forms of glyceraldehyde, designating by D the *d* form of this substance, in which the central OH group lies at the right in the planar projection of the molecule (the aldehyde group being written on top), and by L the *l* form, in which this group lies at the left:



$$\begin{array}{c} \mathrm{H{-}C{=}O} \\ | \\ \mathrm{H{-}C{-}OH} \\ | \\ \mathrm{CH_2OH} \end{array}$$

D-glyceraldehyde

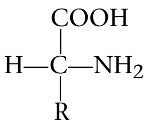


$$\begin{array}{c} \mathrm{H{-}C{=}O} \\ | \\ \mathrm{HO{-}C{-}H} \\ | \\ \mathrm{CH_2OH} \end{array}$$

L-glyceraldehyde

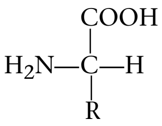
Fischer classified sugars according to this rule, the prefix D being given to the form in which the OH group attached to the penultimate carbon atom (next to the terminal CH_2OH) lies at the right, and the prefix L being given to the corresponding enantiomer. In this convention, the letters D and L no longer indicate the sign of the optical activity. For example, whereas D-glucose is dextrorotatory, D-fructose, which combines with glucose to form sucrose, the common sugar, is levorotatory. So are D-ribose and D-deoxyribose. Optical rotation, when indicated, is represented by a sign, for example, D-(+)-glucose, D-(−)-ribose, and so on.

This nomenclature was extended to α-amino acids, the position of the α-amino group (the carboxyl group being written on top) serving to distinguish the D and L forms:



$$\begin{array}{c} \mathrm{COOH} \\ | \\ \mathrm{H{-}C{-}NH_2} \\ | \\ \mathrm{R} \end{array}$$

D-amino acid



$$\begin{array}{c} \mathrm{COOH} \\ | \\ \mathrm{H_2N{-}C{-}H} \\ | \\ \mathrm{R} \end{array}$$

L-amino acid

As it happens, L-amino acids are levorotatory, at least in neutral solution (they become dextrorotatory in an acidic medium). So, in their case, L corresponds to *l*.

In living organisms, most of the complex substances (polymers) constructed from chiral building blocks (monomers) are homochiral, that is, contain molecules of the same stereochemical handedness. Proteins are made exclusively of L-amino acids (except for glycine, which is not optically active). Among nucleic acids, RNA contains only D-ribose, and

DNA D-deoxyribose. Starch and glycogen are homochiral combinations of D-glucose, and so on. There are exceptions. For example, D-amino acids are found, alongside L-amino acids, in murein, the main constituent of eubacterial cell walls, and in a number of bacterial peptides and related substances; they are even found in significant amounts in higher organisms (Fujii, 2002).

The remarkable homochirality of central biological constituents has been the object of much discussion and speculation. Actually, there are two separate problems, represented by the "homo" and "chirality" parts of the term. The use of building blocks of the same (homo) chirality for the construction of biological macromolecules can be largely explained by the fact that these macromolecules would not display their characteristic properties if they were not so constructed. Proteins made of the two kinds of amino acids could not adopt typical structures, such as α-helices or β-sheets, that are essential to their biological properties. Heterochiral nucleic acids most likely would not be replicable (Schmidt et al., 1997). Thus, whatever the starting situation, one would expect homochirality to emerge by selection. This question will be examined in subsequent chapters.

The key problem raised by biological homochirality concerns the "choice" between enantiomers. It cannot possibly be due to the fact that building blocks were available in only one chiral form for the early life-forming processes. Uncatalyzed chemical syntheses of chiral substances invariably yield racemic mixtures, that is, equal amounts of the two isomers. Among catalysts, enzymes are almost unique in being chirally specific. This property is so remarkable that the artificial creation of chiral catalysts has been considered sufficiently noteworthy to warrant awarding of the 2001 Nobel prize in chemistry to their inventors. The fact that nature sometimes uses the two enantiomers of chiral substances (see above) further suggests that both isomers must have been available originally. It seems almost certain, therefore, that the first building blocks made by cosmic and terrestrial chemistry were racemic. The "choice" must have occurred subsequently.

How this could have happened is not known. A possibility not widely entertained but nevertheless worthy of consideration is that the first catalysts involved in the utilization of the building blocks for assembly reactions were already chirally specific. A related possibility, to be considered in Chapter 8, is that the chirality of RNA may have determined the chirality of the proteins; in other words, the "choice" of D-ribose for the synthesis of RNA dictated the "choice" of L-amino acids for the assembly of proteins. This would simplify matters by reducing the "choice" to the sole ribose molecule, instead of nineteen amino acids, making it a true singularity.

According to many workers in the field, this "choice" could be a typical example of a frozen accident (mechanism 5). Two equally probable alternatives presented themselves. Pure chance decided in favor of one, which, once adopted, could not be reversed. But were the two alternatives equally probable?

This question has attracted the attention of a number of physicists, who have looked into possible mechanisms whereby given enantiomers could be preferentially synthesized or, more likely, destroyed by such phenomena as parity violation or asymmetric irradiation, in particular UV circular dichroism (for a brief review, see Jorissen and Cerf, 2002). The resulting enantiomeric excess, although small, would have been sufficient to tip the scale in favor of the more abundant enantiomer at the time selection occurred.

The analysis of meteorites has revealed a systematic and often considerable excess of L- over D-amino acids (Botta et al., 2002). This fact was generally attributed to inevitable contamination by debris from living organisms until the finding, in 1997, that some amino acids that are not used for protein synthesis may sometimes also show an excess of the L form, though much more modest than that observed for proteinogenic amino acids (Cronin and Pizzarello, 1997). The possibility of a slight cosmic bias in favor of L-amino acids, at least in the neighborhood of the solar system, therefore cannot be excluded. Interestingly, a recent study has shown that such a bias is catalytically communicable: The chirality of four-carbon sugars (tetroses) formed from glycolaldehyde by amino-acid-catalyzed aldol condensation was found to depend on the chirality of the amino acids (Pizzarello and Weber, 2004).

We must leave this matter to experts. Its main relevance, from the point of view of this book, besides its obvious theoretical interest, is to extraterrestrial life. Could there be other life forms containing the same basic constituents as terrestrial organisms, but of opposite chirality? Should such forms one day be discovered, their chirality would be strong evidence of their independent origin.

3 Protometabolism

Given a steady supply of organic building blocks, whether delivered from outer space or formed locally, what goes on next depends on prevailing physical and chemical conditions, as exemplified by Earth, Europa, Titan, and, perhaps, Mars, which all have undergone different histories while probably all receiving the same array of cosmic building blocks. Under the conditions that existed on Earth some four billion years ago – assuming life arose on our planet – the building blocks entered into a complex set of chemical interactions that initiated a long road that finally was to lead to the first primitive living cells. These early chemical processes are generally referred to as prebiotic, or abiotic, chemistry. They will be designated *protometabolism* in this book, in order to indicate that they preceded present-day metabolism and gave rise to it.

The pathways of protometabolism are unknown, but they can be approached, theoretically and experimentally, with the help of what is known of present-day life. There are good reasons to believe, for example, that RNA was the first bearer of replicable genetic information,[1] only

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[1] The possibility that RNA may itself have been preceded by some simpler, replicable, information-bearing substance has been repeatedly evoked. A whole literature exists on the topic, which has produced a number of findings that are interesting from the chemical point of view but not obviously relevant biologically. Being unsupported by direct evidence, these suggestions will not be considered in this book.