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Physical aspects of mirror symmetry breaking of the bioorganic world

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Abstract. Current hypotheses concerning the breaking of mirror symmetry in the bioorganic world are reviewed critically. Two interrelated aspects of the problem, matrix structured homochiral macromolecules and enantiospecific functions capable of keeping homochiral structures replicating, are discussed. Two basic approaches to symmetry breaking, namely evolutionary selection and asymmetric origin scenarios, are considered, whose underlying hypotheses are shown to be inherently inconsistent.

1. Introduction

There are numerous examples in the history of life sciences showing that some properties of biological structures and functions are not only unique but, at first sight, also in conflict with generally accepted physical concepts. One of them is the optical activity of bioorganic materials first discovered by Louis Pasteur some 150 years ago [1 – 3]. It is worth noting that the rotation of linearly polarized light on its passing through matter was a new and somewhat enigmatic phenomenon at that time because optical activity was actually described no sooner than the quantum theory of interaction between light and matter had been developed. But even then, in the middle of the last century, Pasteur's works were of paramount importance because they fostered the understanding that optical activity is first and foremost a function of the properties of molecules and molecular structures in relation to mirror reflection [4, 5].

It is a well-known fact that the process of mirror reflection (spatial inversion) allows spatial structures to be categorized into two classes. One of them includes objects whose spatial structure is non-invariant with respect to the mirror reflection; in other words, a structure arising from mirror reflection of a preexisting object is incompatible with this object whatever shifts and turns may be used to match one to the other. Included in this class are molecules having neither symmetry plane nor symmetry centre. They can exist in the form of two mirror antipodes called 'dissymmetrical' by Pasteur and currently referred to as chiral (from the Greek word '$\chi\varepsilon i\rho$' — a hand), just because right and left hands provide a visual image of mirror-antipodes. It is these molecules that show optical activity. The other class comprises achiral molecules whose structure has both a symmetry plane or a symmetry centre which makes it invariant with respect to mirror reflection. Such molecules exhibit no optical activity.

It seems opportune to note in a paper published in such journal as this that it is common in Russian physical literature, especially in that on elementary particle physics, to use the term 'kiral'nost' (transliterated English word 'chirality' coined by Lord Kelvin from '$\chi\varepsilon i\rho$' [6]). There is not much sense in discussing here which way of spelling the Russian term should be considered correct ('kir' or 'khir' as the first syllable). Suffice it to say that we shall use throughout this paper the term 'chirality' universally accepted by chemists and biologists, because we are largely concerned with organic molecules.

Also, a few words about optical isomers of chiral molecules are in order. Figure 1 shows an aminoacid molecule

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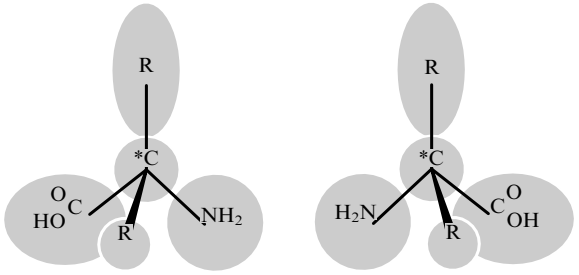


Figure 1. Spatial structure of a chiral molecule with one asymmetrical centre C*.

whose tetrahedral structure contains the asymmetrical centre, a carbon atom C*, linked to four different substitutes. Such molecules are known to form polymeric protein chains which serve as the most important functional structures of the cell called enzymes.

If a molecule has one asymmetrical centre, then only two optical isomers are possible, that is two mirror isomers referred to as enantiomers and designated as L (left) and D (right) respectively. Molecules with N asymmetric centres always have 2^N optical isomers which can be categorized into 2^{N-1} different pairs of enantiomers†. For example, a molecule of sugar (pentose) may have 4 asymmetric centres. Hence $2^4 = 16$ optical isomers, or 8 different pairs of corresponding L and D enantiomers, are possible. Each pair represents a substance with specific chemical properties and has its own name. One pair shown in Fig. 2 is called ribose. The same is true of deoxyribose, one of the pentose optical isomers having 3 asymmetrical centres.

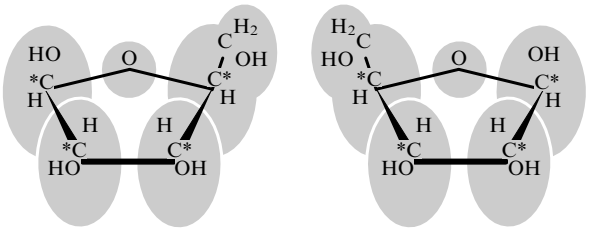


Figure 2. Spatial structure of ribose — a chiral molecule with 4 asymmetrical centres.

Both ribose and deoxyribose play key roles in cell biochemistry. Their nucleic derivatives, nucleotides, are building blocks of such important 'informational' macromolecules as RNA and DNA. Similar to subunits of macromolecular chains of enzyme proteins, nucleotides of DNA and RNA are chiral, each being able to exist in both L and D forms outside a biopolymeric structure.

Now, it is appropriate to pass from optical properties of individual molecules to those of the medium. In the case of diluted solutions, mirror reflection of the medium as a whole is equivalent to a simple substitution of all the molecules by their mirror-antipodes. When molecules are achiral, the medium is invariant with respect to mirror reflection and optically inactive. Conversely, if molecules are chiral but the mixture contains L and D enantiomers in equal concentrations, such a mixture is referred to as racemic and is also invariant with respect to mirror reflection and optically inactive. However, if concentration of one enantiomer exceeds that of the other, the mirror reflection is no longer an identical transformation and the mixture becomes optically active. A mono-enantiomeric solution shows maximum optical activity and is considered to be optically or chirally pure. Therefore, optical activity of a solution suggests an excessive amount of one of the enantiomers of the chiral compound.

When examining dissolved metabolic products, Pasteur found out that they were optically active. Moreover, he demonstrated, using a racemic nutrient solution, that certain bacteria feed on one substrate enantiomer leaving the other in the solution. He arrived at a most important conclusion that the molecular basis of life is both chiral and asymmetric [1, 2].

What do we know about this now, when we seem to know all about at least simple organisms, e.g. bacterial cells, except perhaps how they came into existence?

The reader certainly knows that polymeric chains giving rise to the double-stranded DNA structure may comprise millions of nucleotide units; similar RNA chains consist of hundreds and thousands of nucleotides, and enzyme molecules include a few hundreds of aminoacid residues each. These biopolymers play a key role in the most striking and fundamental biological function, cell replication. DNA bears complete information about the cell's structure and composition and 'knows' what is to be done to reproduce itself and all constituent components of the cell while enzymes are responsible for operations necessary to carry out the programme. In a sense, DNA and enzymes play different roles [7], the former being an information carrier and the letters are functional carriers. RNAs are peculiar molecules in that their role is intermediary between those of DNA and enzymes, and they can sometimes act as either of them [7, 8]. This makes them universal informational and functional carriers.

However, in terms of chirality, these biopolymers have one singular property in common, that is nucleotide units of RNA and DNA have only D-configuration (contain only D-ribose and D-deoxyribose, respectively) whereas enzymes are built of L-enantiomers of aminoacids. In other words, DNA, RNA and enzymes have homochiral primary structures. There is no exception to the rule as far as main biological macromolecules are concerned.

To avoid misunderstanding, it should be emphasized that 'L' or 'D' designation of selected aminoacid and sugar enantiomers is the corollary of 'random choice memory' in the development of stereochemistry even though it is not the best one from the physical point of view because the sole fundamental physical source of mirror asymmetry in nature, weak interactions, 'prefers' L-aminoacids and D-sugars [9, 10]; in this sense, enzymes, RNA, and DNA macromolecules consist of units with the same 'chirality sign'.

Also, it is worthwhile to note that, unlike sugars in RNA and DNA and aminoacids in enzymes, other chiral cell components are known to occur in either enantiomeric form. Specifically, some bacteria have been shown to contain L-sugars and D-aminoacids produced as metabolites in biochemical reactions although they are not incorporated in DNA, RNA, and enzymes. Therefore, the bioorganic world at large is lacking in chiral purity; rather each biological species has an individual 'enantiomeric portrait' which

† In fact, some of optical isomers of multi-centre molecules may be achiral.

characterizes its metabolic patterns [11, 12] and is reproduced by replication†. Such a property is due to the fact that certain groups of enzymes can perform enantioselective functions, if necessary. Such enzymes distinguish between enantiomers of a chiral substrate as, for instance, they did in Pasteur's experiments in which bacteria were grown on racemic media or directly controlled the enantiomeric composition of chiral organic substances during biosynthesis. Interestingly, systemic enantiomeric regulation is equally possible since some enzymes are able to decompose 'unnatural' enantiomers which arise spontaneously in ageing or may be induced by adverse environmental factors, e.g. ionizing radiation [13 – 16].

Enantiomeric configuration during RNA, DNA, and enzyme biosynthesis is under stringent control. For example, there is no more than one wrong unit per $10^6 - 10^8$ ones in a DNA molecule. On the whole, metabolism is programmed to selectively use L-aminoacids and D-sugars in the synthesis of the key macromolecules. Nevertheless, requirements for enantiospecificity become less rigorous at the 'periphery', i.e. as distance grows from the 'centre' of cell metabolism — the mechanism of replication for information and functional carriers. Biological activity of organic compounds depends not only on their chemical formulas but also on their optical isomery. This fact underlies the mechanism of action of some pharmaceutical products, e.g. antibiotics, and pharmacologists are well aware of differential effect of the different enantiomeric forms of the same drug [17]. Talidomide's tragedy is a sad illustration of what is likely to happen whenever this fact is disregarded: trials of its optically pure form provided good results whereas production of the racemic form and its further use led to most serious disorders in many people. The cause was the presence of a different enantiomer with equally high but 'negative' biological activity.

To summarize, chiral specificity of the bioorganic world has two most important aspects. First, the structural one, that is homochirality of macromolecules playing a key role in the mechanism of biologcal replication. Second, the functional aspect, that is enantioselectivity of functions which support replication of homochiral macromolecules. It should be once again emphasized that, despite the fact that primary structures of functional and information carriers are identical in terms of chirality, the enantioselective functions they realize are not universal and vary from one biological species to another, while their evolution is maintained by genetic mutations.

2. Problems

Chiral specificity of the bioorganic world is often thought to reflect mirror symmetry breaking responsible for life with a given 'sign of chirality', in the absence of any evidence of 'mirror-antipode life [18 – 22]. However, this immediately raises a question to be answered: Is the cause of symmetry breaking related to chemical, prebiological or biological evolution?

Intuitively, these stages of molecular evolution should differ. Anyway, what they have collectively brought about is the unique polymeric world of homochiral macromolecules with most remarkable structural and functional properties. Therefore, we believe that the really important problem is how homochiral molecules, as complex as it is necessary to be adequate to the complexity of information and functional biological carriers, came into being. The way this problem is approached may largely, if not wholly, determine trends in further research on the possible cause of mirror symmetry breaking the biosphere.

Generally speaking, structural and functional properties of RNA, DNA, and enzymes are very specific. At first sight, it may seem very strange that chiral specificity makes it so difficult to account for the appearance of such macromolecules in the course of evolution. Indeed, why should the factors responsible for the appearance of homochiral structures be more puzzling than those which made ribose, deoxyribose, and aminoacids the chemical basis for information and functional carriers? Or more puzzling than those known to have contributed to the realization of present genetic texts, i.e. a collection of nucleotide sequences in RNA and DNA together with the corresponding set of specific biological functions? Finally (although this list of questions is easy to continue), why should homochirality of carriers be considered more enigmatic than the absence of an alternative to currently operative mechanisms of encoding, transcription and translation of genetic information? In other words, bearing in mind the origin of chiral specificity of the bioorganic world with special reference to homochiral structures and enantiospecific functions, what is the difference between this problem and that concerning the appearance of any other type of specificity of structures and functions as complicated as biological ones?

2.1. Complexity of homochiral structures

Let us consider macromolecular chains of L and D monomers containing N units. The number of all chains (M) differing in L and D sequences, i.e. the number of all possible optical isomers of a given macromolecule, is 2^N and grows exponentially with increasing length N. Comparison of M and the characteristic scale of particle number fluctuations under standard laboratory conditions (10^{12}) shows that M becomes of the same order of magnitude at $N \approx 40$. Thus, if chain N is no longer than a score of units, it is possible to choose such conditions for the chain formation when all conceivable sequences including homochiral ones are realized.

We call macromolecules of such length the structures of the chemical level of complexity. The problem of emergence of specific sequences at this level has no special sense because, given a certain chemical mechanism of macromolecule assemblage, the probability for any pre-set sequence, e.g. a homochiral one, to appear is not infinitesimal, even when the choice of units is purely random. In other words, the formation of homochiral structures of the chemical level of complexity does not require special functions.

However, there are serious statistical limitations for chains comprising as many as 150 monomers. Indeed, comparison of M and a number of cosmological scale, e.g the number of bioorganic molecules on the Earth (10^{23}) [23], reveals that M becomes of the same order of magnitude at $N \approx 130$. This means that each real sequence containing 150 units or more is certain to be 'unique' for the overwhelming majority of such sequences cannot be realized in principle, simply because even our Universe is too small for that. At this level of complexity referred to as biological or biochemical, since it is in the first place characteristic of enzymes, DNA, and RNA, the relative number of realizable sequences is very small regardless of physical or chemical conditions. There is

† After all, the term 'chiral purity of the bioorganic world', extensively used in the literature, seems to be inadequate.

no 'sorting out' of all possible variants in biological evolution. Moreover, the number of variants is so small that 'random choice memory' [23, 24] means only that in principle any variant is suitable among those from which selection is possible.

Some important evolutionary features of specific sequences ensue from the molecular quasispecies theory [25 – 27].

Let us consider polymeric chains of length $N \gg 1$, each representing a certain word I_i ($i = 1, 2, \ldots, 2^N$) written in a given two-letter alphabet. Let us further imagine a set of functions which allows copies of sequences to be obtained. Correct replication of each sequence I_i is possible with a probability $\Omega_{ii} = p^N$, where ρ is the relative probability of correct replication of an individual unit. Let us suppose, for simplicity, that ρ is independent of the unit type (letter of the alphabet) and its ordinal number in the chain. Mutant sequences I_k are likely to arise in the process of copying sequences I_i. The probability of mutant sequences is $\Omega_{ik} \sim q^{d(i,k)} p^{N-d(i,k)}$, where $q = (1-p)$ is the probability of mutation at a single step of chain synthesis and $d(i,k)$ is the so-called Hamming distance, i.e. a minimal number of consecutive point mutations allowing transition from I_i to I_k.

Let us consider relative concentrations

$$x_i(t) = \frac{c_i(t)}{\sum\limits_i c_i(t)}\,, \quad i = 1, 2, \ldots, 2^N\,,$$

where $c_i(t)$ is the concentration of I_i, assuming that the total concentration of all sorts of polymeric chains is maintained due, for instance, to a flow of matter across the system:

$$\sum_i c_i(t) = c_0 = \text{const}\,.$$

Equations of the model which provide the basis for examining the process of sequence selection has the form

$$\frac{\mathrm{d}x_i}{\mathrm{d}t} = (A_i\Omega_{ii} - B_i - \varphi_0)\,x_i + \sum_{k\neq i} A_{ki}\Omega_{ki}x_k\,,$$

$$i,k = 1,2,\ldots,2^N\,, \qquad (1)$$

where parameters $A_i\Omega_{ii}$ and B_i define replication and degeneration rates of chains I_i respectively, φ_0 is the velocity of outflow I_i from the system, and $A_{ki}\Omega_{ki}$ defines the rate of I_i synthesis by replication of the sequence I_k.

In order to understand how selection occurs, let us assume that a set of sequences $\{I_i\}$ taken at an initial moment can be reproduced without mutations with different efficiency $\{A_i\}$, i.e. $\Omega_{ii} = 1$, while $\Omega_{ik} = 0$ for all $i \neq k$.

The total concentration of polymeric chains being constant, the quantity φ_0 is equivalent to mean reproducibility $\bar{E} = \sum_i (A_i - B_i)\cdot x_i(t)$. Then, it is easy to see from (1) that only concentrations of those sequences for which $(A_i - B_i) > \bar{E}$ will grow. Concurrently, concentrations of sequences with lower reproducibility will decrease which will result in a rise of average reproducibility $\bar{E}$. This process will continue until only sequence I_0 with maximum reproducibility coefficient remains. Thus, given the absolutely correct replication ($p = 1$), the stationary sequence distribution resulting from selection will be a δ-function for the sequence with maximal reproducibility.

In case of mutations ($p < 1$), selection dynamics is essentially different. The overall pattern of this change is shown in Fig. 3 [27]. The concentration of sequence I_0 decreases with decreasing replication accuracy ρ while concentrations of mutant sequences grow (starting from the sequence differing from the progenitor one in only one mutation, then two mutations, etc.). At small $q = (1-p)$, when 'mutation jumps' are realized only at small Hamming distances, the stationary distribution is a peak of finite width which describes a set of mutant sequences localized around the original sequence; in other words, the distribution broadens and undergoes a shift towards high-probability mutants. However, the probability of 'jumps' at a greater Hamming distance significantly increases with decreasing replication accuracy, not only because the quantity q grows but largely due to the exponential growth of the number of ways through which such big jumps can be realized when the sequences are sufficiently long. For this reason, replicative functions mainly produce mutant copies, starting from a certain error rate level q_c, and the stationary distribution undergoes degeneration to the homogeneous one, with the maximum amount of sequences with $N/2$ mutations (due to the combinatorial factor), smaller number of them with $(N/2 - 1)$ mutations, etc. Thus, mutations are selected till a certain critical value $q_c = 1 - p_c$ is achieved which is called the error threshold [27].

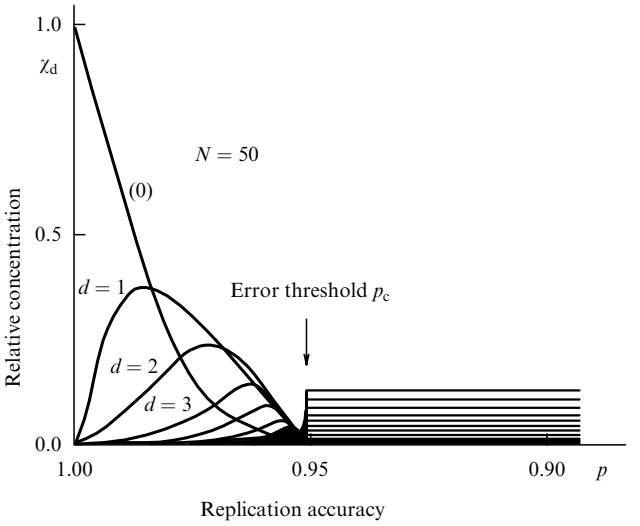


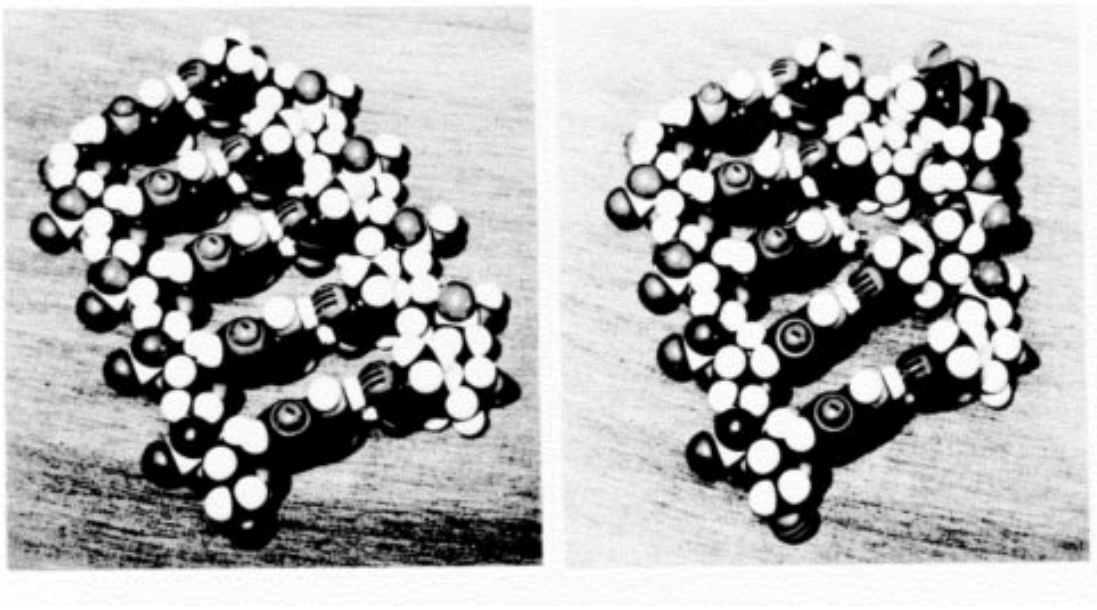
Figure 3. Dependence of concentrations of wild-type (0) and mutant ($d = 1, 2, 3, \ldots$) sequences on replication accuracy.

Evidently, this feature is immaterial at the chemical level of evolution because the probability of even purely random synthesis of any sequence of the chemical level of complexity is not essentially low. However, in the case of biological evolution, it gives rise to a most important condition: evolution of information carriers of the biological level of complexity is feasible only in the presence of specific functions.

Equally important is the fact that the error threshold q_c is a function of length of the chains being copied:

$$q_c = \alpha N^{-1}, \qquad \text{where} \quad \alpha \sim 1\,. \qquad (2)$$

To explain the physical sense of this condition it is sufficient to note that as long as the statistics of errors in copying obeys the binomial distribution the mean number of errors $\langle m\rangle$ in a single copy of length N is N_q and the critical condition (2) simply means $\langle m\rangle \sim 1$, i.e. the *average number of errors in a single copy must not exceed unity*. This is a major condition of



a b

Figure 4. (a) A double-stranded template replica for homochiral complementary chains (poly-A)-(poly-T), (b) A double-stranded structure with an inserted (poly-T) chiral defect.

evolution for sufficiently complex macromolecules. It has been shown in [27, 29] that condition (2) is essential for the evolution of sequences containing a few tens of units (e.g. when $N = 50$), that is for macromolecules which appear to be main objects of the biological rather than prebiological stage of evolution.

Naturally, a question arises: could homochiral macromolecules arise (through mutations and selection) in the course of Darwinian evolution of a world of heterochiral sequences formed as a result of the polymeric takeover of a prebiological racemic medium?

2.2. Homochirality and template replication

Polymeric chains of RNA and DNA are known to be templates on which complementary copies are synthesized. This property of biological information carriers underlies the replicative function, and any homochiral A, T(U), G, and C nucleotide sequence can serve as a matrix suitable for assembling a complementary replica from of the same nucleotides into a complimentary macromolecule†.

Is there a relationship between chirality of units in information carriers and the matrix mechanism underlying the 'read out' of genetic information? A qualitative answer to this question was obtained in [30, 31] from molecular models constructed to simulate two fragments of double-stranded structures (poly A) $\Leftrightarrow$ (poly-T) (Fig. 4a, b). One of the fragments (Fig. 4a) had both strands built up of units with the same 'sign of chirality', and each acted as a template for the synthesis of a complementary copy. In the second fragment (Fig. 4b), one strand (poly-A) was homochiral (as in the previous case) whereas the other (poly-T), complementary to the former in terms of nucleotide composition, contained the so-called 'chiral defect', i.e. a T-unit differing in chirality from the remaining T-components in the same chain. It turned out that if such a mirror-antipode nucleotide is incorporated into poly-T, the position of its nitrogenous base proves to be turned with respect to the normal position for complementary coupling through an angle of about 100°. As a result, pairing between the nitrogenous base of the chiral defect and the base of the corresponding unit in the defect-free chain becomes impossible unless chemical bonds between the chiral defect and neighbouring units of the same chain are broken. However, it appears from the model in Fig. 4b that the most important result is not simply the impossibility of complementary pairing between the chiral defect and a 'normal' unit of a homochiral matrix‡ but the complete loss of the template profile by the replica in the vicinity of the chiral defect.

The same was inferred from the results of direct experimentation on abiogenic (non-enzymatic) matrix oligomerization of nucleotides [32]. Synthetic homochiral poly-G templates were placed in two C nucleotide solutions, a racemic one and a chirally pure solution containing C enantiomer of the same optical configuration as units in the matrix chain. In both cases, the length distribution of poly-C homochiral replicas was evaluated after their synthesis on the homochiral poly-G template.

Oligomerization of nucleotides in the chirally pure solution yielded homochiral copies of around 20 units in length whereas in the racemic solution, this process was substantially suppressed. In the latter case, the length of the replicas was the same as under spontaneous oligomerization in the absence of a template and was restricted to a few units. Further studies of distributions thus obtained [32 – 34] showed that matrix oligomerization of nucleotides in the racemic solution was blocked by the very first defective nucleotide whose nitrogenous base was joined to the complementary base of the corresponding unit in the template chain by hydrogen bonds.

† A, T(U), G, and C stand for adenine, thymine (uracyl in RNA), guanine, and cytosine which give rise to two complementary pairs, A↔T(U) and G↔C.

‡ Such a result can be obtained by inserting a homochiral but non-complementary partner, e.g. A opposite A or T opposite T.

In a sense, this situation is opposite the case of the molecular models where one of the chains *a priori* contained a chiral defect which made it impossible to obtain a double-stranded structure (analog of matrix oligomerization) without cleavage of bonds throughout the defective chain. Here, the chiral defect first couples to the appropriate link in the matrix chain but its subsequent binding interaction with the neighbour units of the replica was equally impossible for the same reason.

Thus, in the vicinity of the chiral defect, an information carrier loses its main property to serve as a template for the synthesis of complementary molecules. This is the principal difference between the chiral defect and mutations which also disturb the complementary conformity between template and replica components, but the structure of the newly synthesized mutant replica retains its matrix properties and may be used to copy duplicate sequences.

Can matrices be other than homochiral chains? Generally speaking, they cannot. One can certainly imagine a macromolecular chain whose matrix relief arises from an orderly alternation of L and D units [35, 36]. However, even in this case, the appearance of a chiral effect (disordered enantiomer alternation) would lead to a similar result, that is, the loss of matrix properties of the chain in the vicinity of the defect. For the realization of the template-based mechanism for encoding and reading out genetic information, it is important that the chain always contain an orderly rather than random sequence of enantiomers, the type of the sequence (homochiral or heterochiral) being immaterial.

In the first place, this is essential from the evolutionary point of view because selection of information carriers through replication requires not only template (chirally specific) sequences but also a set of enantioselective functions capable of maintaining assemblage of such structures. It is for this reason, that the problem of the origin of rather complex homochiral macromolecules is of special interest in any evolutionary theory.

2.3. Complexity of enantiomeric functions

Let us assume the relative probability of the chiral defect to emerge during a single step of chain formation to be q. Let us further introduce the parameter $\gamma = (1 - 2q)$ which characterizes enantioselectivity of the function responsible for the synthesis of a homochiral chain.

How will enantioselectivity γ of the replicative function alter with growing complexity of homochiral carriers?

Starting from the prebiological level of complexity involving lengths of $N \approx 50 - 150$ units, the average number of chiral defects must not exceed unity to avoid infinitesimal probability of homochiral chain assemblage due to the error catastrophe. Then, it ensues from (2) that

$$\gamma > 1 - 2\alpha N^{-1}, \quad \text{where} \quad \alpha \sim 1. \tag{3}$$

Let us redefine parameter γ on the assumption that all kinetic parameters of homochiral chain synthesis having a sense of reaction rate constants are proportional to the Arrhenius factors:

$$q = \frac{\exp(-E_1/kT)}{\exp(-E_1/kT) + \exp(-E_2/kT)} \quad \text{and} \quad \gamma = \text{th}\left(\frac{\Delta E}{2kT}\right).$$

Here, E_1 and E_2 are activation barriers which preclude incorporation of units with incorrect and correct chirality respectively; $\Delta E = (E_1 - E_2)$ is the energy of chiral discrimination for the enantioselective function responsible for the chain synthesis; T is the temperature.

Condition (3) restricts from below discrimination energy ΔE of enantioselective functions which are necessary to avoid the error catastrophe during the assembly of chiral chains of length N (Fig. 5).

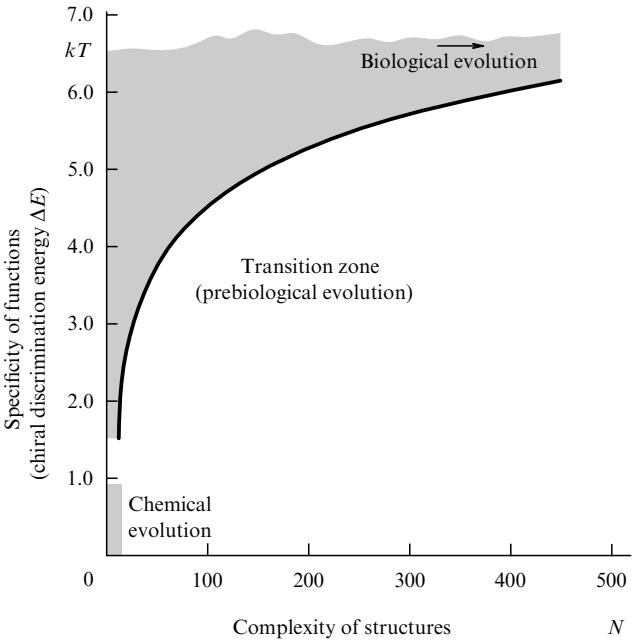


Figure 5. The shape of limitation on chiral discrimination energy of enantioselective functions. The shaded area corresponds to the synthesis conditions for homochiral sequences of length N.

Enantioselectivity of functions maintaining both formation and evolution of homochiral structures of the chemical level of complexity has no interesting singularities ($\Delta E < kT$). Moreover, as noted above, evolution of short homochiral chains does not require selective functions.

On the contrary, the biological level of complexity ($N > 150$) imposes strong limitations; specifically, discrimination energy of enantioselective functions must be significantly higher than kT ($\Delta E \approx 6 - 8\,kT$). This condition can be met only in case of the 'solid' microenvironment of interacting molecular fragments in which their mobility is greatly restricted by dense package [37 – 40]. Therefore, macromolecular carriers of functions of the biological level of complexity must first and foremost be able to ensure rigid and reproducible orientation of interacting molecular fragments during transfer of charges, atoms, and atomic groups in an elementary act of chemical transformation.

In a world of sufficiently long (and flexible) polymeric chains, there is no fundamental contradiction between the complexity of functional carriers and the requirements for selectivity of functions which they perform. Polymeric globules are structures with such properties. Note also, that the low boundary of discrimination energy undergoes but little change when N ranges from hundreds to millions of units, and an increase in the complexity of information carriers in the whole range characteristic of biological macromolecules does not require alteration of physical properties of macromolecular structures which determine

the type of functional carriers. One and the same class of functionally active structures with sufficiently high functional adaptivity is able to ensure evolution of information carriers containing from thousands (e.g. RNA-like) to tens of millions of units (DNA-like).

Therefore, in the world of simple molecules and long polymeric chains, conditions for evolution of information structures are not in conflict with the possibility for the appropriate functions to be realized.

However, there are some non-trivial requirements intrinsic in the prebiotic level of complexity. On the one hand, discrimination energy of enantioselective functions must be naturally higher than kT; hence, macromolecular carriers of such functions, similar to those of biochemical functions, must be sufficiently 'dense' and rigid structures. On the other hand, the low boundary of discrimination energy drastically grows with increasing N; therefore, the same structures must have special properties to be able to enhance their enantioselectivity even at a small rise in the complexity of information carriers.

Template polynucleotide chains like RNAs appear to meet these requirements, being information carriers subject to evolutionary selection by means of complementary template replication [41 – 43] and, like protein enzymes, showing specific activity [8, 44 – 46]. Finally, specific activity of RNAs depends on their spatial structure which is in turn determined by double-stranded fragments of complimentarily paired chain sections; for relatively short nucleotide sequences containing around $50-150$ units, the probability of the formation and stability of complementary double-stranded fragments with secondary structure is essentially dependent on the chain length [29]. Therefore, there is every reason to regard the RNA-world as a model of a class of macromolecular carriers which could probably serve as a source for transition towards structures and functions of the biological level of complexity, non-trivial in terms of realization conditions. However, it should be emphasized that all the properties of polynucleotide templates so attractive from the prebiological standpoint are relevant only so far as homochiral chains are concerned, just because only such chains possess matrix properties. In fact, the problem is why it is homochiral templates that have come into being.

3. Scenarios

Two fundamentally different scenarios have been proposed to account for chiral specificity of the bioorganic world. One holds that an initially racemic organic medium gave rise to functional carriers lacking in chiral specificity that were able to maintain evolution of complex macromolecules; at later stages of evolution of such primary 'achiral biosphere', there was, for unknown reasons, a striking change in the type of information and functional carriers which resulted in the appearance of a class of homochiral structures that filled up the entire organic range available at that time [47 – 49]. In other words, chiral specificity of the bioorganic medium is a result of evolution of structures and functions of the biological level of complexity.

The second scenario is exactly reverse. Its underlying assumption is that symmetry breaking of an organic medium was somehow broken already at the stage of chemical evolution, and certain homochiral structures formed as a result of polymeric takeover of such asymmetric medium, and afterwards they gave rise to homochiral structures from which informational and functional carriers were selected [20, 21, 50 – 55]. In other words, chiral specificity of the bioorganic world is a result of evolution of structures and functions of the chemical level of complexity.

3.1. Two hypotheses: Specificity of functions or specificity of medium

No matter which way was used to achieve chiral specificity of structural and functional carriers, general requirements ensuing from the conditions of evolution for sufficiently complex homochiral molecules must have been fulfilled. The most important of these conditions is dictated by the catastrophe of errors [27].

It has been shown in a previous paragraph that if homochiral macromolecules are to be formed in a racemic medium, enatiospecific functions must be present as early as the prebiological stage of evolution.

Now, let us consider the homochiral chains-assembly process in an asymmetric environment, i.e. in a medium with chiral polarization $\eta = (x_L - x_D)/(x_L + x_D)$ (x_L and x_D are concentrations of enantiomers). In this case, the relative probability q of a chiral arising defect per chain-assembly step depends not only on enantioselectivity γ of the mechanism responsible for the selection of enantiomers from the medium and their selective incorporation into the chain but also on chiral polarization of the medium η. Assuming that unit attachment acts are independent events and bearing in mind that we deal here with no other situation,

$$q = \frac{(1-\eta)(1-\gamma)}{2(1+\eta\gamma)},$$

and the condition (2) necessary to avoid the error catastrophe takes the form [54]:

$$\eta > 1 - \frac{\alpha'(1+\gamma)}{N(1-\gamma)}, \quad \text{where} \quad \alpha' \sim 1. \tag{4}$$

This simple condition gives an idea of how the properties of the medium (η) and the enantioselectivity of functions (γ) should change in order that homochiral macromolecules might have arisen and evolved towards a higher degree of complexity (N). The shaded area in Fig. 6 corresponds to those η and γ values for which the number of chiral defects in chains of length N is of the order below unity. It is actually a zone of the characteristic width of order N^{-1} adjacent to absolute values $\eta = 1$ and $\gamma = 1$. The result is explicit because η and γ are two independent parameters similarly affecting the probability of chiral defects. Note that this area is very narrow even for a transition from the chemical to biological level of complexity ($N \approx 50 - 150$).

Thus, what is needed to avoid the error catastrophe during the formation of sufficiently complex homochiral macromolecules, regardless of whether it occurs at the prebilogical or biological stage of evolution, is either chiral purity of the organic material from which macromolecular carriers are constructed or enantiospecific functions able to maintain an assembly of homochiral structures [33, 34, 54, 55].

Therefore, there are only two types of evolutionary trajectories (Fig. 7) corresponding to the two above scenarios of the origin of chiral specificity of the bioorganic world that satisfy the condition (4).

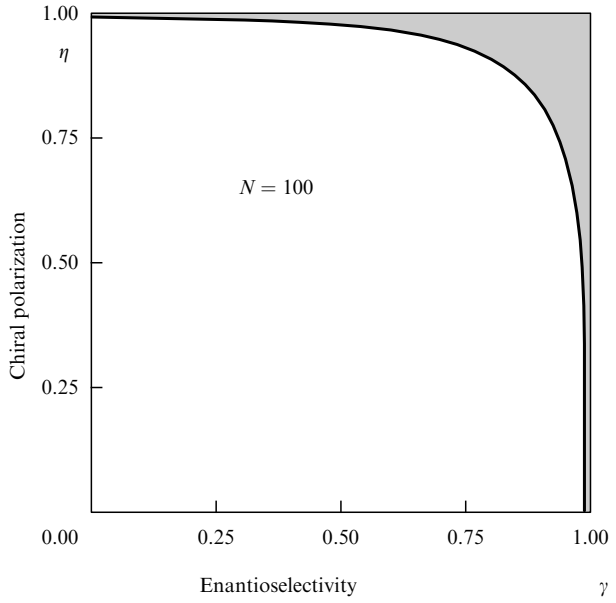


Figure 6. The shape of limitation on chiral polarization of medium η and enantioselectivity of functions γ. The shaded area corresponds to the synthesis conditions of a homochiral sequence with a fixed length ($N = 100$).

3.2. The evolutionary selection scenario

The trajectory (*1*) in Fig. 7 corresponds to evolution in a racemic medium which first gives rise to specific functions of the biological level of complexity and thereafter to homochiral carriers of these functions. The main problem here is to identify at least one chirally non-specific type of macromolecular carriers which, similar to enzymes, could perform specific functions. By analogy with RNA, it may be supposed that they could be sought for in the world of achiral matrix structures. In principle, such structures exist at the chemical level of complexity [56 – 58]. The main difficulty arises here not in connection with chemical constructions, but is due to the absence of the idea of an evolutionary coordinate, the motion along which would allow to avoid an error catastrophe at the prebiological stage, during the creation of information and functional carriers of a biochemical level of complexity. What we mean is alternative chemistry of living matter which remains a moot question of great theoretical and applied interest even though the few attempts at its solution have failed to produce any promising results [59 – 62].

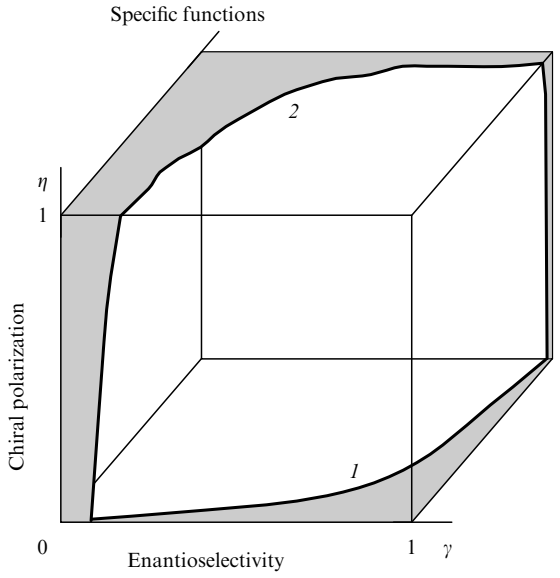


Figure 7. Two types of evolutionary trajectories: (*1*) trajectories satisfying the evolutionary selection hypothesis, (*2*) trajectories satisfying the assymetrical origination hypothesis.

It is equally important to account for the realization, in the course of hypothetical achiral evolution, of such 'big mutations' that have modified mechanisms of encoding, transcription, and translation of genetic information. Note that the theory of molecular evolution based on the Darwinian selection principle does not describe such events, and the hypothesis of evolutionary mechanism for chiral specificity of the bioorganic world will be *an ad hoc* hypothesis as long as these questions remain unanswered.

3.3. The asymmetrical origination scenario

Condition (4) provides basic principles for the asymmetric scenario of the emergence of homochiral carriers [trajectory (*2*), Fig. 7].

First, the polymeric takeover stage must be proceeded by the formation of a chirally pure (not simply asymmetric) medium which requires mechanisms of strong mirror symmetry breaking in geochemical or cosmochemical areas [33, 34, 53].

Second, the chirally pure medium must be maintained not only at the stage of polymeric takeover and formation of homochiral macromolecules, but also at the stage when a class of structures playing the role of informational and functional carriers (e.g. RNA-like structures) is separated from a large amount of newly-formed homochiral macromolecules and later in the course of further evolution until enantiospecific functions responsible for the replication of homochiral structures appear. The chiral purity condition recede only after these functions are formed [54, 55].

In other words, all stages of molecular evolution, from the polymeric takeover of an organic medium to the appearance of informational and functional carriers of the biochemical level of complexity, need a chirally pure environment. Hence, another important problem is concerned with the stability of mirror symmetry breaking mechanisms in a monomeric media in relation to those evolutionary processes that are supposed to have led to the formation of macromolecular carriers of enantiospecific functions.

These problems are considered below.

4. Asymmetrical factor or spontaneous symmetry breaking

The principal feature of chiral chemistry is mirror symmetry of electromagnetic interactions. As a rule, they make the only real contribution to the intramolecular interaction between electrons and nuclei, which explains why the states corresponding to L and D enantiomeric configurations are created by the symmetrical double-well potential. 'As a rule' refers to the contribution of a weak interaction which violates the parity and is, strictly speaking, responsible for symmetry breaking of the double-well potential. However, the ensuing difference between reactivities of enantiomers is so small

$(10^{-15} - 10^{-17}kT)$ [20, 22] that it is normally regarded as purely symbolic under laboratory conditions†.

Enantiomeric configurations being invariant with respect to the operation of spatial inversion, $|\mathrm{L}\rangle$ and $|\mathrm{D}\rangle$ states have no definite parity and are therefore non-stationary. Such are their symmetrical and asymmetrical combinations:

$$|+\rangle = \frac{1}{\sqrt{2}}\left(|\mathrm{L}\rangle + |\mathrm{D}\rangle\right), \qquad |-\rangle = \frac{1}{\sqrt{2}}\left(|\mathrm{L}\rangle - |\mathrm{D}\rangle\right).$$

This means that from the quantum point of view, there must exist oscillations (tunnelling transitions) [64] between enantiomeric configurations, with characteristic frequency

$$\omega_{\mathrm{th}} \sim \exp\left\{-\frac{Q\sqrt{2mE}}{\hbar}\right\},$$

where m is the tunnelling mass, E and Q are the height and the width of the tunnelling barrier, respectively. This explains why a chirally pure compound undergoes transformation to a racemic one for time $t \gg \omega_{\mathrm{th}}^{-1}$ at temperatures near absolute zero.

As far as compounds with an asymmetric carbon atom are concerned, inversion of the enantiomeric configuration is feasible only when the chemical bond is broken and the characteristic time of tunnelling transition is very large (from hundreds of thousands to tens of millions of years) [53]. This time is far longer than the duration of elementary chemical transformations induced, for example, by thermal excitations at room temperature; it is possible to neglect tunnelling racemization at such a time scale typical of 'terrestrial chemistry'‡. In this case, however, it is necessary to bear in mind that the same thermal excitations lead to above-barrier transitions between enantiomeric states (thermoactivated racemization) with characteristic frequency

$$\omega_{\mathrm{r}} \sim \exp\left\{-\frac{E}{kT}\right\}$$

proportional to the Arrhenius factor. For this reason, thermoactivated racemization predetermines the tendency to the thermodynamically equilibrated ratio of enantiomer concentrations even when other chemical transformations are absent.

Thermodynamic potential F for an ideal enantiomer mixture has the form

$$F = (\varphi_{\mathrm{L}} x_{\mathrm{L}} + \varphi_{\mathrm{D}} x_{\mathrm{D}}) - kT(x_{\mathrm{L}} \ln x_{\mathrm{L}} + x_{\mathrm{D}} \ln x_{\mathrm{D}}),$$

where φ_{L} and φ_{D} are the ground state energies of L and D enantiomers respectively. In the symmetrical (achiral) external field $\varphi_{\mathrm{L}} = \varphi_{\mathrm{D}}$, the minimal F value corresponds to a racemic mixture with maximal entropy.

Therefore, two fundamental physical laws: the conservation of parity in electromagnetic interactions and the second law of thermodynamics, lead to one of the basic propositions in chiral chemistry according to which only racemic products are formed in the absence of asymmetrical inducers.

Note that racemic mixtures are produced in natural synthesis of organic compounds as, for instance, during volcanic eruptions or in outerspace and also under experimental conditions designed to simulate the primitive Earth's environment [20, 69 – 71]. For all that, symmetry of chemical transformations can be broken by external asymmetrical fields or when far from thermodynamic equilibrium. We shall consider these two options as applied to the simplest model of an evolving organic medium [54] made up of two subsystems: Q, in which L and D monomers are formed from an achiral substrate, and P, in which polymeric structures are assembled (Fig. 8). The connection between these subsystems is due to the transition of enantiomers from Q to P and characterized by enantioselectivity γ and intensity $K_p = \tau_0\tau_p^{-1}$ (the ratio of the characteristic time τ_0 of chemical transformations in Q to the characteristic time τ_p of macromolecular synthesis in subsystem P). The change in parameters γ and K_p from $(\gamma, K_p) \ll 1$ to $(\gamma, K_p) \approx 1$ corresponds to the prebiotic stage of evolution.

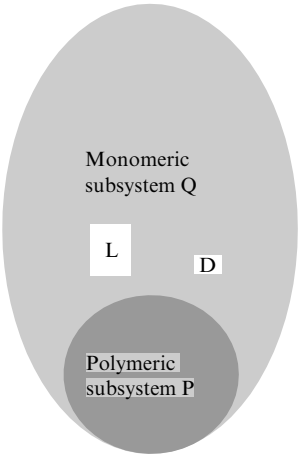


Figure 8. The simplest representation of the Q–P model of prebiological medium evolution.

4.1. Symmetry breaking at the 'thermodynamical branch'

Let processes yielding chiral products in the course of chemical evolution ($K_p = 0$) maintain the subsystem Q at the thermodynamical branch (in other words, in the absence of asymmetrical effects, subsystem Q tends to the racemic state with characteristic relaxation time τ_{r}). The dimensionless parameter $K_{\mathrm{r}} = \tau_0\tau_{\mathrm{r}}^{-1}$ serves as a measure of 'racemization factor' (RF) [53].

In this case, the asymmetrical state Q may result only from the effect of a chiral (asymmetrical) field imposed upon Q. A measure of this effect is the 'advantage factor' (AF) [53]

$$g = \left|\frac{k_i^{\mathrm{L}} - k_i^{\mathrm{D}}}{k_i^{\mathrm{L}} + k_i^{\mathrm{D}}}\right|,$$

where k_i^{L} and k_i^{D} are rate constants of mirror-coupled channels of the reaction in Q which is sensitive to asymmetrical impact. Note that $\tau_0 \sim (k_i^{\mathrm{L}} + k_i^{\mathrm{D}})^{-1}$.

It has been shown in Refs [51, 53] that chiral polarization of subsystem Q in the presence of AF is described by solutions

† It is tempting to hypothesize that the violation of the parity by weak interactions has eventually become the primary cause for mirror asymmetry of the bioorganic world and has probably predetermined the choice of the 'sign of chirality'. This idea has been most ardently discussed for several decades (see, for instance, reviews [53] and [63]).

‡ Racemization time may be large enough due to the interaction of chiral molecules with the environment even at low temperature, when the reaction occurs through the tunnelling mechanism [65 – 68].

of a simple equation (independently on the type of chemical transformations, which determines the relaxation to the racemic state in the absence of AF):

$$-K_r\eta + g(1-\eta^2) = 0\,. \tag{5}$$

For this reason, chiral polarization at the thermodynamical branch depends only on the AF to FR ratio. Strong violation of mirror symmetry ($g \ll 1$) is possible even at small AF, provided $(g/K_r) \gg 1$.

The enantioselective capacity is inherent in a variety of natural chiral factors, e.g circularly polarized electromagnetic radiation ($g \sim 10^{-2}$) or mineral surfaces ($g \sim 10^{-1} - 10^{-3}$ [20, 72] having the chiral structure as in quartz. In the general case, they can arise from different combinations of electromagnetic, weak, and gravitational interactions [63]. There are elegant selection rules [73 – 76] which allow for distinction between combinations that are 'true' asymmetrical factors capable of altering the reactive capacity of enantiomers and 'false' ones unable to do the same (e.g. a constant magnetic field). True chiral factors created by the interactions which conserve parity exist as mirror-antipode pairs (right- and left-circularly polarized radiation or 'right' and 'left' modifications of quartz crystals); on the whole (e.g. in the Universe), such as AF-antipodes exhibit symmetrical distribution. Their asymmetrical action is apparent only within some geochemical or cosmochemical area, hence the term 'local' is applied to them.

Apart from local AFs, there are global ones created by weak interactions ($g \sim 10^{-12} - 10^{-17}$) [63, 77]. Their action is asymmetrical everywhere, which accounts for their special importance. Nevertheless, it should be emphasized that they are so small that the (g/K_r) ratio for such factors does not exceed 10^{-9} [51, 53, 78, 79]. Even at the most optimistic RF estimates. Therefore, the condition $(g/K_r) \gg 1$ can be realized under the local AFs only.

For all that, we shall not confine ourselves to examining only local AF. Let us assume that, in a certain geochemical or cosmochemical area asymmetrically affected by a chiral physical factor, both a chirally pure medium and the conditions for its polymeric takeover have formed. As a result, there is an asymmetrical polymeric world (subsystem P) in which homochiral macromolecules contain monomers with a definite 'sign of chirality'.

If such a world undergoes evolution towards formation of enantiospecific functions, the states of Q are described by an equation

$$-K_r\eta + (g - K_p\gamma)(1-\eta^2) = 0\,, \tag{6}$$

having a simple sense: AF is now opposed by enantioselective pressure $K_p\gamma$ with which the polymeric subsystem P affects the monomeric medium due to the enantioselective (asymmetrical) outflow of L and D monomers from Q to P.

The condition for conservation of the chirally pure state Q in the course of evolution of the polymeric system P has the simple form

$$\frac{(g - K_p\gamma)}{K_r} \gg 1 \tag{7}$$

and depends not only on RF and AF but also on the enantioselective pressure. At first, when $(g/K_r) \gg 1$, and enantiospecific functions are absent, condition (7) is also fulfilled. Therefore, if $(g - K_p\gamma)/K_r \sim N$, the takeover of a chirally pure medium by polymers may lead to the formation of rather long (N) homochiral chains. However further on in stage, when the polymeric subsystem undergoes evolution towards formation of enantiospecific functions ($K_p\gamma \to 1$), condition (7) breaks down, in the first place due to a small g value. The chirally pure state of the medium can be maintained throughout the stage of the formation of enantiospecific functions only if $g \approx 1$, that is, by asymmetrical factors whose enantioselective action is compatible with functions of the biological level of complexity. But such physical factors are simply nonexistent.

Therefore, had the chirally pure state been achieved in a certain geochemical or cosmochemical area due to chemical (kinetic) reinforcement of asymmetrical impact, it would not have remained stable at the next stage of formation of enantiospecific functions. This makes impossible the formation of homochiral molecules due to strong symmetry breaking at the thermodynamical branch of chemical evolution, largely due to the error catastrophe by the loss of chiral purity of the monomeric medium during transition to the structures of biological level of complexity.

4.2. Nonequilibrium systems

It has been shown that the symmetry of macroscopic states of a chemical system is subject to spontaneous breaking when it is not in thermodynamic equilibrium [50 – 53, 80 – 83], due to the loss of stability by the racemic (symmetrical) state and the appearance of stable chirally polarized (asymmetrical) states. In this case, symmetry breaking can be accounted for by kinetics of chemical processes which determines types of stable attractors far from the equilibrium.

However, what we need for our purpose is a general equation that would describe spontaneous symmetry breaking in chemical systems, by analogy with Eqn (5), regardless of the means of its realization. Such an equation for the parameter of order η which directly reflects the symmetry of chiral system states was constructed in terms of the theory of bifurcations [50, 53, 82] and takes the classical form in the theory of phase transitions of the second kind:

$$-\eta^3 + (1-\rho)\eta = 0\,, \tag{8}$$

where $0 \leqslant \rho < \infty$ is the controlling parameter which in turn depends on other parameters responsible for the kinetics of reactant transformations in the system. Figure 9a presents the

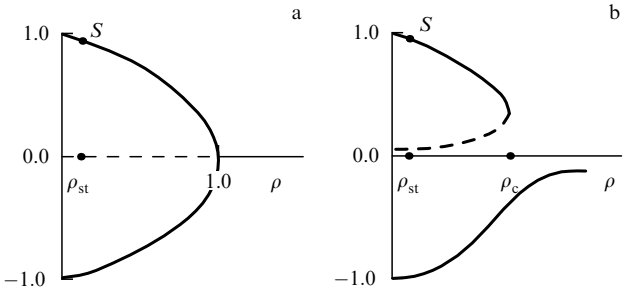


Figure 9. Dependence of chiral polarization η of stable states of the monomeric subsystem Q on the controlling parameter ρ: (a) at the chemical stage of evolution, (b) at the prebiotic stage of evolution. The position of point S corresponds to the medium state at the moment of primary polymeric takeover.

bifurcation diagram which makes clear how chiral polarization of stable states of the system alters with a change the in controlling parameter ρ. At $\rho > 1$, there is only one stable state — racemic ($\eta = 0$). This interval of ρ values corresponds to the thermodynamical branch of conditions. However, at $\rho < 1$, system dynamics depends on asymmetrical attractors, i.e. mirror-coupled stationary states $\eta = \pm\sqrt{1-\rho}$. As soon as ρ becomes smaller than the critical value $\rho_c = 1$, the racemic state loses stability which leads to the so-called spontaneous mirror symmetry, which is broken when either of the two mirror-antipode asymmetrical states is realized with equal probability, provided the system was initially in the racemic state. Chiral polarization grows with a decrease in controlling parameter ρ; the state with a high degree of chiral purity, for instance $\eta \approx (1 - N^{-1})$ for $N > 150$, is attained at the sufficiently small $\rho \sim N^{-1}$.

There are numerous schemes of L and D enantiomer transformations with this property. As a rule, they simulate diverse of autocatalytic processes including both corresponding chemical transformations and self-consistent interactions between coherent radiation and optically active molecules [83 – 86]. Formal rules for the choice of such schemes and the construction of theoretical models from them have been reviewed in [53]. Important properties of such processes will be discussed in the next section. Here, we shall confine ourselves to examining the possibility, in principle, of using the idea of spontaneous symmetry breaking for the substantiation of the hypothesis of asymmetrical origin of the biosphere.

Let us suppose that the kinetics of the formation of some classes of chiral organic compounds accounts for a change in stable attractors in the monomeric subsystem Q given on these classes by way of spontaneous symmetry breaking. Let us further assume that in the course of chemical evolution (in the absence of the polymeric subsystem P), the controlling parameter ρ has attained values corresponding to the degree of chiral purity necessary for the formation of sufficiently complex homochiral structures while the polymeric takeover of the chirally pure medium by polymers has resulted in the creation of a polymeric world able to evolve towards the formation of enantiospecific functions. Assuming that changes K_p and γ corresponding to evolution of the polymeric subsystem P are as slow as compared with the processes in Q, it can be demonstrated that the bifurcation equation which describes states in Q will now have the form [54, 87]

$$-\eta^3 + (1-\rho)\,\eta - K_p\gamma\,(1-\eta^2) = 0\,. \qquad (9)$$

In this equation, as in Eqn (6), the enantioselective pressure $K_p\gamma$ with which the polymeric subsystem P acts on the monomeric environment due to the specific selection of enantiomers plays the role of an external chiral field imposed upon Q. The bifurcation diagram satisfying Eqn (9) is shown in Fig. 9b.

Now, the problem of sustained evolution can be formulated in the following way [54]. Let the controlling parameter ρ has attained (in the absence of enantiospecific functions ($\gamma \ll 1$, $K_p \ll 1$)) be near-zero values $\rho_{st} \sim N^{-1}$, the state of necessary chiral purity $\eta \approx (1 - N^{-1})$ has established (point S in Fig. 9a), and a polymeric subsystem P with sufficiently long homochiral chains has appeared. The critical value at which a branch of stable states Q (containing point S) emerges is shifted to zero (Fig. 9b) with growing enantioselective pressure ($K_p\gamma \to 1$), until the origin point of this branch coincides with point $S(\rho_c = \rho_{st})$. Let this moment be described by a certain $\gamma = \gamma_c$. Then, with the further growth in γ point S will be beyond the branch of stable states, and the monomeric medium will lose its chiral purity. The question is whether this results in the necessary enantioselectivity of functions responsible for the synthesis of macromolecules in P ($\gamma \approx 1 - N^{-1}$), prior to the moment when point S abandons the stable state branch. The answer is given by the relation $\gamma_c \approx (1 - N^{-1})$ which indicates that the subsystem Q retains its chiral purity throughout the entire range of enantioselectivity changes from $\gamma \ll 1$ to $\gamma \approx 1 - N^{-1}$.

Therefore, if spontaneous symmetry breaking leads to the conditions necessary for the formation of homochiral structures of the biochemical level of complexity, the same mechanism may support such medium conditions till the appearance of enantiospecific functions able to maintain evolution of homochiral structures.

It is important to emphasize that the chirally pure state of the subsystem Q loses stability precisely when functions with the necessary enantioselectivity arise. On the one hand, such functions allow the processes to evolve regardless of the medium state. Interestingly, on the other hand, the same functions lead to the 'annihilation' of all important information about the non-trivial sequence of evolutionary events which has been responsible for their creation.

Thus, spontaneous mirror symmetry breaking is the sole mechanism which is not in conflict, at least in principle, with the hypothesis of asymmetrical origin of the biosphere. A 'minor' problem that remains to be solved is for which processes and under which conditions the evolutionary trajectory (*2*) was realized (Fig. 8).

5. Mirror symmetry breaking in the class of autocatalytic functions

It is clear that autocatalytic processes underlying evolution at the prebiological and biological levels are of special interest. That such processes could have led to mirror symmetry breaking in living nature, apart from their being responsible for other events, was conjectured by many authors [88 – 90], but Charles Franck was the first to substantiate this idea [80].

Far from denying its fruitfulness, we would like to illustrate difficulties of its applying to the problem of origin of chiral specificity of the bioorganic world.

One of them is related to the fact that uncorrelated autocatalytic functions do not cause symmetry breaking. Indeed, let us imagine two mirror-antipode subclasses of a certain class of objects capable of replication and selection. The evolution equations have the form analogous to (1):

$$\frac{\mathrm{d}x_i^{\mathrm{L}}}{\mathrm{d}t} = (A_i^{\mathrm{L}}\,\Omega_{ii}^{\mathrm{L}} - B_i^{\mathrm{L}} - \varphi_0)\,x_i^{\mathrm{L}} + \sum_{k\neq i} A_{ki}^{\mathrm{L}}\,\Omega_{ki}^{\mathrm{L}}\,x_k^{\mathrm{L}}\,,$$
$$i,k = 1,2,\ldots,2^N\,,$$

$$\frac{\mathrm{d}x_i^{\mathrm{D}}}{\mathrm{d}t} = (A_i^{\mathrm{D}}\,\Omega_{ii}^{\mathrm{D}} - B_i^{\mathrm{D}} - \varphi_0)\,x_i^{\mathrm{D}} + \sum_{k\neq i} A_{ki}^{\mathrm{D}}\,\Omega_{ki}^{\mathrm{D}}\,x_k^{\mathrm{D}}\,,$$
$$i,k = 1,2,\ldots,2^N\,,$$

The fact that variables x_i^{L} and x_i^{D} are concentrations of mirror antipodes provides additional symmetry relations $A_i^{\mathrm{D}} = A_i^{\mathrm{L}}$, $\Omega_{ii}^{\mathrm{D}} = \Omega_{ii}^{\mathrm{L}}$, $B_i^{\mathrm{D}} = B_i^{\mathrm{L}}$; that is, all kinetic parameters related to evolution of 'enantiomeric' individuals of the i-th species are identical.

In order to see symmetrical properties of solutions of the evolution equations, it is sufficient to pass to variables

$$\eta_i = \frac{x_i^{\mathrm{L}} - x_i^{\mathrm{D}}}{x_i^{\mathrm{L}} + x_i^{\mathrm{D}}} \quad \text{and} \quad \theta = (x_i^{\mathrm{L}} + x_i^{\mathrm{D}})\,.$$

In this case,

$$\frac{\mathrm{d}\eta_i}{\mathrm{d}t} = 0\,,$$
$$\frac{\mathrm{d}\theta_i}{\mathrm{d}t} = (A_i\,\Omega_{ii} - B_i - \varphi_0)\,\theta_i + \sum_{k\neq i} A_{ki}\,\Omega_{ki}\,\theta_k\,.$$

Selection within either of the mirror-antipode subclasses may facilitate the distribution which consists of a set of mutants of the progenitor species exhibiting maximum reproductive capacity. However, chiral polarization of the class as a whole undergoes no change as a result of such evolution and remains the same (on the average) as the given initial one. The mechanism of the Darwinian selection as the selection of kinetically advantageous autocatalytic functions does not lead to mirror symmetry breaking [91, 92].

5.1 Is it conceivable that a symmetrical Biosphere exist?

Now, we shall demonstrate that correlated autocatalytic functions can lead to mirror symmetry breaking. It has already been mentioned that the theoretical grounds for this idea were developed in [80]. One of the models considered by the author includes two irreversible stages: enantiospecific catalytic synthesis of mirror-antipodes from a certain achiral substrate A

$$\mathrm{A} + \mathrm{X_L} \xrightarrow{k_1} \mathrm{X_L} + \mathrm{X_L}\,, \quad \mathrm{A} + \mathrm{X_D} \xrightarrow{k_1} \mathrm{X_D} + \mathrm{X_D} \tag{10a}$$

and enantioselective transformation of enantiomers to a catalytically inactive product B

$$\mathrm{X_L} + \mathrm{X_L} \xrightarrow{k_{-1}} \mathrm{B}\,, \quad \mathrm{X_D} + \mathrm{X_D} \xrightarrow{k_{-1}} \mathrm{B}\,, \tag{10b}$$

$$\mathrm{X_L} + \mathrm{X_D} \xrightarrow{k_{-2}} \mathrm{B}\,. \tag{10c}$$

Let us discuss this model after the addition of non-selective transformation of mirror-antipodes to the catalytically inactive product B†:

$$\mathrm{X_L} \xrightarrow{k'_{-1}} \mathrm{B}\,, \quad \mathrm{X_D} \xrightarrow{k'_{-1}} \mathrm{B}\,. \tag{10d}$$

In this form, the Franck model describes the evolution of a population of mirror-antipode biological species $\mathrm{X_L}$ and $\mathrm{X_D}$:

$$\frac{\mathrm{d}x_{\mathrm{L}}}{\mathrm{d}t} = (k_1 c_{\mathrm{A}} - k'_{-1})\,x_{\mathrm{L}} - k_{-1}(x_{\mathrm{L}} + x_{\mathrm{D}})\,x_{\mathrm{L}} - (k_{-2} - k_{-1})\,x_{\mathrm{L}} x_{\mathrm{D}}\,,$$
$$\frac{\mathrm{d}x_{\mathrm{D}}}{\mathrm{d}t} = (k_1 c_{\mathrm{A}} - k'_{-1})\,x_{\mathrm{D}} - k_{-1}(x_{\mathrm{D}} + x_{\mathrm{L}})\,x_{\mathrm{D}} - (k_{-2} - k_{-1})\,x_{\mathrm{D}} x_{\mathrm{L}}\,. \tag{11}$$

Here, x_{L} and x_{D} are the numbers of the respective species, c_{A} is the amount of the achiral substrate‡, and k_i are the parameters having the sense of rate constants characterizing respective transformations.

The first term on the right-hand side of each Eqn (11) corresponds to processes of reproduction and natural death of individuals, the second one to 'demographic pressure' experienced by each species because of limited resources, and the third term describes peculiar 'annihilation', i.e. reciprocated elimination of mirror-antipodes, for example by toxic chiral metabolites produced by each species in course of vital activities. The fact of $\mathrm{X_L}$ and $\mathrm{X_D}$ are mirror antipodes is reflected in the invariance of Eqns (11) with respect to $\mathrm{X_L} \leftrightarrow \mathrm{X_D}$.

It should be emphasized that Eqns (11) do not contain cross-terms typical of population models in which they describe production of individuals through mutagenesis because of zero probability, at the biological level of complexity, of an event in which all units of macromolecular informational and functional carriers of an individual offspring would undergo inversion relative to macromolecular units of a parental individual. In other words, biological replication is an absolutely enantiospecific autocatalytic function.

In variables (η, θ), Eqns (11) have the form

$$\frac{\mathrm{d}\eta}{\mathrm{d}\tau} = \frac{k_{-2} - k_{-1}}{k_1 c_{\mathrm{A}} - k'_{-1}}\,\theta\eta(1 - \eta^2)\,,$$
$$\frac{\mathrm{d}\theta}{\mathrm{d}\tau} = 2\theta - \frac{k_{-2} + k_{-1}}{k_1 c_{\mathrm{A}} - k'_{-1}}\left(1 - \frac{k_{-2} - k_{-1}}{k_{-2} + k_{-1}}\,\eta^2\right)\theta^2\,, \tag{12}$$

where $\tau = (k_1 c_{\mathrm{A}} - k'_{-1})\,t/2$ is dimensionless time§. It directly follows from the first equation that there are two types of stationary solutions: $\eta = 0$, describing the symmetrical co-existence of mirror-antipode species, and $\eta = \pm 1$, which describes a totally asymmetrical monospecific population. At $(k_{-2} - k_{-1}) < 0$, only the symmetrical state $\eta = 0$ (stable) exists whereas at $(k_{-2} - k_{-1}) > 0$, there are two types of stationary states of which only 'chirally pure' states $\eta = \pm 1$ show stability [80].

Had prebiological evolution resulted in the creation of two mirror antipode branches of life, the impossibility of their co-existence could have been due, for example, to biochemical incompatibility of metabolic products of mirror antipode species [93].

However, this argument should not be taken as an explanation of mirror symmetry breaking in the biosphere. It is cited only by way of illustration of the fact that, at the biological level of complexity where evolution of species is directed by correlated (enantiospecific) autocatalytic functions, these functions may lead to broken mirror symmetry of the biosphere at large. It is therefore appropriate to emphasize once again that the asymmetrical biosphere is a natural phenomenon rather than a paradox, unlike the existence of homochiral macromolecules of the biochemical level of complexity.

5.2. Chemical autocatalysis

Now, let us go back to the problem of spontaneous mirror symmetry breaking at the chemical stage of evolution, a key idea in the hypothesis of asymmetrical life origins.

† This process is a 'neutral' one [53] and does not change the model's behaviour (10a-c).

‡The amount of the achiral product A is assumed to be constant.

§ $k_1 c_{\mathrm{A}} > k'_{-1}$

Of course, the Franck model (10a-c) helps to understand that autocatalytic processes far from thermodynamical equilibrium may be responsible for instability of the racemic state. However, from the chemical point of view, the model is too formal even if it does not involve the controlling parameter, that is at any value of $(k_{-2}-k_{-1})>0$ only chirally pure states $\eta=\pm1$ remain stable. It will be shown below that this feature of Franck's model is due to the absolute enantiospecificity of autocatalytic synthesis of mirror-antipodes (processes 10a) which is in line with the biological interpretation of the model but at variance with the processes at the chemical level of complexity.

It is worthwhile to note that many modifications of the original Franck model have been suggested [94 – 101] to introduce, in a variety of ways, the concept of control over the passage through the critical point, but these attempts largely reflected the personal views of the authors rather than general principles of enantioselective catalysis. Moreover, all parameters including such 'reservoir variables' as achiral substrate concentrations (see for instance [80, 85]) or mixing rates [102] were treated, at least in theory, as controlling parameters; the problem is which one can be modulated in a given model.

We would like to emphasize that such an approach may prove crucial, in the first place for the use of spontaneous symmetry breaking in the evolutionary context. Indeed, it was implicitly proposed in the above discussion of the asymmetrical origin scenario due to spontaneous symmetry breaking that the controlling parameter ρ is possible to modulate regardless of enantioselectivity of the processes responsible for the synthesis of macromolecular carriers. In the beginning, at the chemical stage of evolution when enantioselectivity of chemical transformations was low ($\gamma \ll 1$), it was necessary to make the controlling parameter ρ tend to 0 (point S in Fig. 9a, b) and afterwards direct evolution of homochiral functional carriers to the formation of enantiospecific functions, while maintaining the monomeric medium in the chirally pure state. For this reason, whether ρ and γ are really independent parameters deserves special investigation.

Let us examine the autocatalytic stage the complete scheme of which for processes at the chemical level of complexity has the form

$$\begin{aligned} &\mathrm{A}+\mathrm{L} \underset{k_{-1}}{\overset{k_1}{\rightleftarrows}} \mathrm{L}+\mathrm{L}, \quad \mathrm{A}+\mathrm{L} \underset{k_{-2}}{\overset{k_2}{\rightleftarrows}} \mathrm{D}+\mathrm{L}; \\ &\mathrm{A}+\mathrm{D} \underset{k_{-1}}{\overset{k_1}{\rightleftarrows}} \mathrm{D}+\mathrm{D}, \quad \mathrm{A}+\mathrm{D} \underset{k_{-2}}{\overset{k_2}{\rightleftarrows}} \mathrm{L}+\mathrm{D}; \end{aligned} \tag{13}$$

where k_i are rate constants for respective biomolecular transformations. Unlike (10 a-c), this scheme meets two basic requirements. First, it takes into consideration that the enantioselective capacity of any chiral catalyzer is restricted, and the catalytic activity of each enantiomer leads to the formation of both L and D products. Second, the necessary kinetic correlation may arise owing to reversibility of the catalytic stage.

It is worthy of note that scheme (13) is actually the generalized Franck model for catalytic trnsformations with arbitrary enantioselectivity; in the case of absolute enantioselective transformations, i.e at $k_2=k_{-1}=0$, this scheme is converted to scheme (10 a-c).

On the assumption that concentration c_{A} remains constant, properties of model (13) can be obtained from equations

$$\begin{aligned} \frac{\mathrm{d}\eta}{\mathrm{d}\tau} &= \left[\frac{K}{2}\,\gamma_-\theta+\gamma_+-1\right]\eta-\frac{K}{2}\,\gamma_-\theta\eta^3\,, \\ \frac{\mathrm{d}\theta}{\mathrm{d}\tau} &= \theta-\frac{K}{2}\,(1-\gamma_-\eta^2)\,\theta^2\,, \end{aligned} \tag{14}$$

where $\gamma_+=(k_1-k_2)/(k_1+k_2)$ and $\gamma_-=(k_{-2}-k_{-1})/(k_{-2}+k_{-1})$ stand for enantioselectivity of direct (+) and reverse (−) reactions respectively, $\tau=c_{\mathrm{A}}(k_1+k_2)\,t$, and $K=(k_{-1}+k_{-2})/(k_1+k_2)$ is the reversibility parameter of the autocatalytic stage. However, it is enough for our purpose to write the bifurcation equation in the form

$$-\gamma_+\gamma_-\eta^3+(\gamma_++\gamma_--1)\,\eta=0\,. \tag{15}$$

Therefore, the controlling parameter ρ included in Eqn (5) is

$$\rho=\frac{(1-\gamma_+)(1-\gamma_-)}{\gamma_+\gamma_-}$$

and depends only on enantioselective catalytic transformations. The critical point $\rho_{\mathrm{c}}=1$ at which the racemic state loses stability is defined by condition

$$\gamma_++\gamma_-=1\,. \tag{16}$$

As soon as the total enantioselectivity of catalytic transformations exceeds unity, the racemic state becomes unstable, and the system enters one of the two mirror-coupled asymmetrical states $\eta=\pm\sqrt{1-\rho}$. Note that the chirally pure state occurs only when γ_+ or γ_- value is close to unity. Specifically, the state with chiral polarization $\eta\approx(1-N^{-1})$ sets in at

$$\gamma_++\gamma_->1, \quad \max\{\gamma_+,\gamma_-\}>(1-2N^{-1})\,. \tag{17}$$

Real processes involve monomolecular stages, besides bimolecular ones. This explains why a change in the achiral substrate level affects symmetry breaking conditions.

In order to assess the contribution of such stages, they must be simulated using a simple scheme

$$\mathrm{A} \underset{k_{-3}}{\overset{k_3}{\rightleftarrows}} \mathrm{L}, \qquad \mathrm{A} \underset{k_{-3}}{\overset{k_3}{\rightleftarrows}} \mathrm{D}. \tag{18}$$

Given the same assumptions as in (14), equations for processes (13) – (17) have the form

$$\begin{aligned} \frac{\mathrm{d}\eta}{\mathrm{d}\tau} &= \left(\frac{K}{2}\,\gamma_-\theta-\frac{2\delta_+}{\theta}+\gamma_+-1\right)\eta-\frac{K}{2}\,\gamma_-\theta\eta^3\,, \\ \frac{\mathrm{d}\theta}{\mathrm{d}\tau} &= 2\delta_++(1-K\delta_-)\,\theta-\frac{K}{2}\,(1-\gamma_-\eta^2)\,\theta^2\,, \end{aligned} \tag{19}$$

where $\delta_+=k_3/(k_1+k_2)\,c_{\mathrm{A}}$, $\delta_-=k_{-3}/(k_{-1}+k_{-2})\,c_{\mathrm{A}}$.

Let us suppose that the contribution by (18) is small ($K\delta_+$, $K\delta_-\ll1$), and the behaviour of model (19) is similar to that of model (14). Then, in the first approximation in $K\delta_+$ and $K\delta_-$, the critical point $\rho_{\mathrm{c}}=1$ is given by the relation

$$(1-K\delta_+)\,\gamma_++(1-K\delta_-)\,\gamma_-=1\,. \tag{20}$$

To clarify the physical sense of the multipliers in front of γ_+ and γ_-, let us suppose that the controlling parameter ρ

adjoins ρ_c from the side of the thermodynamic branch, when the racemic state

$$\eta = 0, \qquad \theta = 2K(1 + K\delta_+ - K\delta_-)$$

is stable. By estimating from (19) a fraction of catalytic acts in this state, it is easy to show that $(1 - K\delta_+)$ is a part of enantioselective synthetic acts whereas $(1 - K\delta_-)$ is a fraction of enantioselectve acts of decay of the chiral product. Therefore, the multipliers in front of γ_+ and γ_- in (20) have the sense of statistical weights of enantioselective transformations at the time of passing the critical point $\rho_c = 1$ (of the total number of them in the system). As the achiral substrate concentration c_A grows, the fraction of enantioselective (catalytic) acts tends to unity. Therefore, relations obtained from (14) represent the estimated lower boundary of the degree of enantioselectivity of catalytic stages necessary to reach the critical point ρ_c.

Is there experimental evidence confirming spontaneous symmetry breaking in chemical processes? This issue has long been a matter of many discussions [103 – 111]. Quite recently, Soal et al [112] reported a chemical analog of the Franck model that enabled them to observe enhanced enantiomeric excess in an autocatalytic reaction. Details of the experiment can be found in the original publication. We would like only to note that there is no serious reason to question the possibility of spontaneous symmetry breaking at the chemical level of complexity (in addition to the biological one), at least in the class of autocatalytic functions.

However, the most important conclusion ensuing from the above data on symmetry breaking conditions is that chiral purity necessary for the evolution of structures with length ($N > 150$) can be achieved only if catalytic processes responsible for spontaneous symmetry breaking possess a high degree of enantioselectivity ($\gamma > 0.995$) comparable with that of biological functions.

This inference underlies the main discrepancy in the hypothesis of asymmetrical origin of the biosphere. On the one hand, the idea of spontaneous symmetry breaking was used to support the mechanism of the formation of a chirally pure medium at the chemical stage, before enantiospecific functions arise. On the other hand, for the chirally pure medium to form, autocatalytic functions of the chemical level of complexity must exhibit enantioselectivity comparable with that of biochemical functions.

Of course, this discrepancy does not invalidate the hypothesis of asymmetrical origin, but it emphasizes the crucial obstacles which stand in the way.

6. Conclusion

The present publication was not designed to comprehensively discuss all the attempts at solving the problem of mirror symmetry breaking in the bioorganic world. For this, the reader is referred to excellent recent reviews [21, 53, 63]. However, we deem it appropriate to comment on those traditional approaches which, for the majority of researchers, are directly related to the essence of the problem.

There are three principle questions.

— Did symmetry breaking occur in the course of chemical or biological evolution on Earth? Or, was it not a sequel to earlier events in the Universe which might have been of crucial importance for the origin of life at this planet?

— What was the possible cause of symmetry breaking: effect of a chiral physical field or a spontaneous break?

— What was responsible for the 'sign of chirality' of the biosphere: a causative factor or an merely?

Let us start from the most popular view of the phenomenon termed in the literature in a variety of ways: 'homochirality', 'biochirality', 'chiral purity', and finally 'mirror asymmetry' of the bioorganic world†. These terms reflect a historically formed opinion about the existence of two molecular worlds: the symmetrical racemic world of nonliving nature and the totally asymmetrical, 'chirally pure' world associated with living nature. It needs to be emphasized, however, that it would be incorrect to make use of this distinction without due regard for the complexity of objects that form both worlds.

To proceed, there is the mirror symmetry problem. Doubtless, biological systems are characterized by the prevalence of some enantiomers of chiral compounds over others. However, this fact in itself cannot be interpreted as symmetry breaking. It only suggests that enantiospecific functions, similar to specific ones in biology at large, are subject to strong unification because changes in phenotypic traits during evolution are rare events. The only fact which may be interpreted as mirror symmetry breaking is the absence of a mirror-antipode 'life form'. Therefore, so far as such a variety of symmetry breaking is concerned, it should be borne in mind that in the bioorganic world it is apparent only at the population level.

It would be helpful to discover a universal mechanism that possibly underlay asymmetrical formation and accumulation of chiral organic compounds and could be naturally realized either on Earth or in the space. At the same time, the fundamental problem: how specific hypothetical features of chemical evolution could predetermine the origin of only one branch of life, remains beyond the scope of most publications.

Attempts at the solution of this problem over more than a century have generated numerous explanations for asymmetrical accumulation of primary organic matter that cover virtually the entire range of possible causes, from the effect of circularly polarized light at the Earth's surface or polarized gamma-radiation by neutron stars in space to asymmetrical formation of 'right' and 'left' forms of optically active crystals due to 'poor' mixing of large-scale racemic objects. Actually, there are two classes of factors able to break symmetry in chemical systems: effects of chiral fields (both local and global ones) and spontaneous symmetry breaking. At present, there is no doubt that many natural factors can be responsible for asymmetrical synthesis of chiral organic compounds.

How universal or effective one or another natural chiral factor may be is debatable. This issue is still discussed in the literature [21, 63]. However, the question of whether asymmetrical synthesis of chiral compounds is possible under natural conditions has conclusively been given an affirmative answer.

Characteristically, substantial progress in our knowledge about mechanisms of asymmetrical synthesis does not appear to be conducive to the solution of the problem of the asymmetrical bioorganic world, largely because we do not know the basic relationship between asymmetry at the level of

† Far from being satisfied with such terminological diversity, we have introduced one more definition: 'chiral specificity of the bioorganic world'.

simple organic molecules that may have arisen in course of chemical evolution and chiral specificity of biological macromolecules intrinsic in the living nature.

In contrast to the traditional approach to this problem, we are inclined to directly relate chiral specificity of biological macromolecules to that level of complexity at which it is apparent. We use as a starting point the fact that informational and functional carriers playing a key role in biological replication are homochiral polymers. In the macromolecular world, these structures are characterized by a level of complexity at which any specific sequence is unique. Hence, the fundamental question as regards the origin of homochiral structures adequate to biopolymers in terms of complexity.

A major theoretical problem in this context is to describe evolution of information structures and specific functions in increasing of their complexity [113, 114, 115]. This task is not trivial since the number of evolving objects grows exponentially with increasing complexity and becomes physically infinite even for macromolecules as long as tens of units (as a matter of fact, 50 or more). This may result in specific dynamical patterns, with the error catastrophe being one possibility. However, we have so far had but vague idea about the evolution of complex systems to be able to answer the first of the questions posed above.

Nevertheless, there are several points which enable us to judge about the relevance of the idea that asymmetry of the bioorganic world is the result of mirror symmetry breaking at the chemical stage of evolution.

First, the action of chiral physical factors, regardless of whether they are local or global and of the conditions in which their effects are apparent, could not be of serious consequence in terms of mirror symmetry breaking in the bioorganic world for such factors are intrinsically unable to ensure sustained evolution of homochiral structures towards the formation of enantiospecific functions, largely because of growing enantioselective pressure. Therefore, the traditional problem of choice between asymmetrical factors and spontaneous symmetry breaking must be solved in favour of the latter.

Second, evolutionary dynamics at the prebiological stage may have the aspect of spontaneous symmetry breaking. However, there is are no grounds for accepting the most widely known version of such scenario [50, 53, 55] according to which the appearance of a chirally pure medium at the chemical stage of evolution and its subsequent polymeric takeover could collectively provide conditions for the straightforward realization of prebiological transition. The reason is that in the case of spontaneous symmetry breaking in chemical systems, at the level of simple molecules, the necessary level of chiral purity is attained only for the processes whose enantioselectivity is commensurable with the enantioselectivity of functions of the biochemical level of complexity. Therefore, the discussion needs to be confined to the prebiological stage, specifically to symmetry breaking in a class of processes which could play a crucial role in the transition from structures and functions of the chemical level of complexity to informational and functional carriers of the biological type.

Finally, the last traditional question is whether a certain chiral physical field could be responsible for the choice of the 'sign of chirality' of the bioorganic world, that is for the fact that RNA and DNA are built up of right-handed (not left-handed) nucleotides while enzymes are composed of left-handed (not right-handed) aminoacids. It should be emphasized from the very beginning that in a mirror-antipode world, macromolecules built up of left-handed nucleotides and right-handed aminoacids should be as good as the existing ones. Therefore, this problem is not of crucial importance in the context of prebiological evolution. It rather reflects the desire to search out the cause for every event.

Very soon after the discovery of the parity violation in weak interactions, it was conjectured that there must be a relationship between the asymmetry of the living nature and fundamental asymmetry in the Universe, on the grounds that polarized products of β-decay can, in principle, ensure asymmetrical synthesis of chiral molecules [116]. However, numerous attempts to validate this hypothesis (see [63]) yielded-have no appreciable result, while many authors appear to have lost interest in it.

Nevertheless, the idea of such a relationship is too tempting to be given up for good. The renewal of interest is due to the results of calculations indicating that the contribution of weak interactions to the interaction between the electrons and the nucleus of the asymmetrical centre in a chiral molecule results in a relative shift of the ground state energy of enantiomers [10, 117 – 119]. Notwithstanding that this shift is actually insignificant and does not exceed $10^{-15} - 10^{-17}kT$ for such simple molecules as aminoacids and sugars, the above calculations showed that the ground state energy of L-aminoacids and D-sugars is lower than the energy of their mirror antipodes. Living nature has chosen one and the same configuration of chiral molecules — the most stable one!

Another idea concerns the possibility for the infinitesimal difference between reactive activities of enantiomers to be enhanced in large-scale chemical systems [120, 52]. Unlike asymmetrical synthesis induced by polarized products of β-decay, this case implies spontaneous symmetry breaking as the key mechanism of the process. The idea is based on the 'anomalously high sensitivity'† of a chemical system to the effect of a constant chiral field in the vicinity of the critical point. Near ρ_c, in the so-called 'strong field' region [121], mean chiral polarization $\langle\eta\rangle$ and the squared fluctuation amplitude of this value $\langle\eta^2\rangle$ grow similarly, in proportion to time t. Therefore, the signal to noise ratio $\langle\eta\rangle(\langle\eta^2\rangle)^{-1/2} \sim \sqrt{t}$, and even a very weak chiral field may cause a marked enantiomeric excess if the system remains for a long time close to the critical point.

We dwell shall not optimistic estimates obtained by the authors of this idea [52, 120, 122]. Their criticism can be found in [123 – 127] and [53]. However, it seems appropriate to emphasize that a common feature of critical phenomena in simple chemical systems with evolutionary dynamics in the prebiological period has yet to be confirmed.

The processes which account for the creation of structures and functions of the biochemical level of complexity are far from being clear. Moreover, we do not know in full what their 'biochemical level of complexity' is. Nevertheless,, we believe that the relationship between two unique properties of biological macromolecules, homochirality and potential for replication, may be used as 'Ariadne's clue' in an attempt to pass through the labyrinth of the prebiological stage of molecular evolution. This issue needs to be addressed in future studies.

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† The term has been coined by the authors [52, 120].

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