MIRROR SYMMETRY BREAKING IN BIOCHEMICAL EVOLUTION

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Abstract. The problem of origination of molecular asymmetry in biochemical evolution is discussed. The theoretical analysis shows that chiral purity of biomolecules has the biological significance for self-reproduction of organisms. The models of spontaneous symmetry-breaking in molecular systems are given. The aspects of various stages of biochemical evolution associated with the development of chiral polarization are analysed.

A. Introduction and General Remarks

The three-dimensional structure of many biologically important molecules (amino acids, sugars, nucleotides) possesses a specific property of chirality of 'handedness' (from the Greek χειρ, the hand), i.e. the molecules may exist in two mirror-antipodal forms. One can hardly imagine anything more similar than mirror-image antipodes. Therefore, it would be natural to expect equally frequent occurrences of mirror-twin molecules (enantiomers or enantiomorphs) in nature. However, this is the case solely in inanimate nature. Living organisms employ only levo-(L) amino acids in proteins and dextro-(D) sugars in nucleic acids. Among proteins and ribonucleic acids built by the organism, there is a tremendous number of chiral monomers, all of them having the same chirality.

For more than a century the nature of the asymmetry of the molecular portrait of organisms has been discussed from diverse standpoints.

The hypothesis of asymmetric 'élan vital' being refuted there are two more approaches in explaining the chirality of biomolecules.

According to the hypothesis of abiotic origin, asymmetry of the biomolecular world is merely a reminescence of those stages in the chemical evolution which accompanied the nascence of the world of organisms. In this case, either as a result of incomplete symmetry of the environmental conditions or as a result of chance, the asymmetry of molecules was created by the physical world in the process of the chemical transformations which accompanied the origination of life.

The second approach, the hypothesis of biotic origin, assumes that the asymmetric chemical composition of the organisms is the result of the struggle for existence, in which they survived due to exhibiting the type of ordering prerequisite for the vital activity, namely, chirally pure molecules. Let us briefly consider these two hypotheses, see Figure 1.

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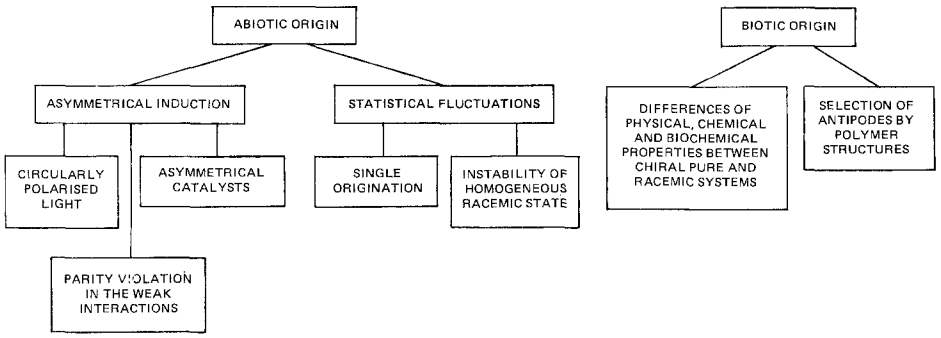

Fig. 1. Hypotheses of the origin of molecular asymmetry.

A1. HYPOTHESIS OF ABIOTIC ORIGIN

The hypothesis of abiotic origin assumes the symmetry of the molecular world to have been broken before the origination of life either due to (a) asymmetric physical induction, or (b) as a result of chance.

(a) Origination of Optical Activity Due to Physical Induction

The pertinent data to the asymmetry in biology, if considered in their purely external aspect, suggest an intrinsic difference between the dextral and sinistral (Weil, 1966). In this connection, many researchers since the time of Pasteur tried to explain the molecular asymmetry of the biosphere by the conditions under which the world of organisms had originated, *viz.*, by the causal internal asymmetry of the Earth or of the fields and radiations. In 1930, W. Kuhn (Kuhn and Braun, 1929; Kuhn and Knopf, 1930) showed that liquid consisting of unequal quantities of antipodal molecules may be enriched with one of the antipodes, depending on whether the polarization of the light the liquid is irradiated with is right-handed or left-handed. Investigations continuing the work initiated by W. Kuhn are reported in a number of original publications and surveys (Bonner, 1972).

Unequal quantities of antipodes originate also when they are synthesized on the surface of asymmetric catalysts (thus, it is known that such crystals as quartz, which makes up about 20% of the Earth's crust, can exist in enantiomorphic asymmetric forms) (Klabunovsky *et al.*, 1951; Tsuchida *et al.*, 1936; Akabori, 1960(b); Fukawa, 1962). It may be supposed that within certain areas of the Earth's surface there existed unequal quantities of left-handed and right-handed polarized light, or of left-handed and right-handed mineral catalysts, and these physical factors imparted molecular asymmetry to the world of organisms during its nascence. Locally there are places where L-quartz, for example, predominates. However, so far no predominance has been found on the Earth to lie with a particular sort of such external chiral agents, and it may be stated that the asymmetric inductors we know of could have broken the symmetry of molecules to a very small extent and within quite limited areas only. Even if in one place the predomi-

nance might happen to lie with one of the antipodes, their distribution in general had to be random.

For 20 years the space surrounding us has been known to be asymmetrical: the discovery of parity non-conservation showed that weak interactions of elementary particles are asymmetrical. Mirror symmetry in the microworld is destroyed (Lee and Yang 1956).

Almost immediately after the discovery of the parity non-conservation in weak interactions, a hypothesis was advanced that, possibly, the physical world had created molecular chirality, starting from the asymmetry of the nuclear level. If so, and the asymmetry of molecules is a consequence of the chirality of weak interactions, then, irrespective of the place and time, similar processes must impart only one type of chirality to the molecules.

The possibility of projection of weak interactions upon the molecular world was predicted by T. Ulbricht (1959). According to Ulbricht, in view of the parity non-conservation, emitted electrons are chiral (longitudinally polarized). Interacting with a substance, the electrons stimulate bremsstrahlung which contains chiral (circularly polarized) photons. Irradiation of a molecular system with such photons leads to the appearance of unequal quantities of mirror-antipodal molecules (Ulbricht, 1959). Though sufficiently extensive experiments are carried out to confirm this hypothesis, from the theoretical standpoint it is rather difficult to obtain a measurable enrichment of a molecular system with one of the antipodes, and possible effects are extremely small.

A second possibility of microworld asymmetry manifestations in macroscopic processes is the participation of weak interactions in the electron-nucleus interactions. (The possibility of such manifestation at the macroscopic level was first predicted by Ya. B. Zel'dovich (1959) who showed that a substance can be optically active owing to the non-conservation of parity in atomic transitions). In such a case, the asymmetry of interactions must lead to physical nonequivalence of the right- and left-handed molecules throughout the space. However, these effects are so insignificant, that, although the sensitivity of the experimental techniques is very high, they have not been detected as yet.

Overall, it may be noted that so far there are no explanations for the origination of the molecular asymmetry due to physical induction: those effects which are observable experimentally are capable of inducing only very insignificant and quite local asymmetry. The effects which are in principle suited for a general standardization of the asymmetry have not yet been confirmed experimentally.

(b) Origination of Optical Activity as a Result of Chance

At an early stage of discussion of the problem, a hypothesis was formulated that optical activity of biological materiad had formed as a result of chance. According to this hypothesis, the incipiency of life depended on the formation of the first autocatalytic molecule or aggregate. By chance they originated in one of the enantiomeric forms and

such casual asymmetry, being inherited by the progeny, has propagated in the biosphere.

In the light of our present-day conceptions about the origin of life this hypothesis is under criticism; self-reproduction as a property of living matter can be attributed only to the complicated organized system of metabolic processes developed in the course of long and complicated evolution (Oparin, 1957).

Another hypothesis belonging to the category of ideas which associate the origin of asymmetry with random processes, namely, with statistical fluctuations, is the hypothesis of spontaneous splitting of antipodes in physico-chemical transformations. According to this hypothesis, under certain conditions symmetrical, homogeneous distribution of antipodes may become unstable. Therefore, the appearance of a product containing a greater quantity of one antipode than of the other may become a regular result of the physical system dynamics.

Mathematical presentation of this hypothesis was offered by F. Frank and his colleagues (see Section C.1). Theory shows that under certain conditions there is a possibility of fluctuations in chirality developing into the macroscopic asymmetry of products. Theoretically (Hochstim, 1975), statistical fluctuations as factors initiating the symmetry breaking had to outbalance the possible fundamental asymmetry of the dextral and sinistral.

As processes capable of realizing such behaviour, reference is usually made to the experiments which have been known since the time of Pasteur, on crystallization of a saturated racemic solution of antipodes; in these experiments for certain antipodal pairs splitting of the antipodes in crystals is observed (Secor, 1963). It should be noted, however, that such processes cannot be regarded as the only resource for the origination of asymmetry, since they require quite stringent conditions and can ensure only local breaking of symmetry in separate areas of the system or within separate intervals of time; as a whole, they preserve symmetrical distribution of the antipodes.

A.2. HYPOTHESIS OF BIOTIC ORIGIN

The hypothesis of the biological origin of chirality assumes that the very nascence and development of life ruined one type of the chirality of molecules. G. Wald has demonstrated that if only chiral purity of biological polymers is supposed to be necessary for the organisms to function normally, then as a result of the struggle for existence the chirality of the monomers employed in the survived organisms will be standardized not only in every individual biopolymer, but also in the organism and in the population of organisms – in the entire biosphere (Wald, 1957).

Such explanation rests on the assumption of a particular value of the chiral purity of biological polymers for the functioning of organisms. G. Wald proceeded from the experiments which had shown that polymers built from chaotically distributed levo- and dextro-amino acid residues are less stable and grow poorly (Blout *et al.*, 1957; Lundberg and Doty, 1957; Idelson and Blout, 1958). However, chirally impure structures may have the same advantage. First, as with any physical regularity, the necessity of the same

chirality of monomers for the stability of polymer structures is of a statistical character. A certain quantity of monomers having a 'foreign' chirality can be introduced without destroying the α-helical structure. In organisms where we deal with chiral purity, any infinitely small quantity of an admixture is eliminated. Moreover, in recent years success has been achieved in finding a new type of a stable helix of polypeptides, which is a sequence of regularly alternating D- and L-amino acid residues (Spach, 1974). Such configurations are found in some simple organisms, but in higher stages of development nature neglected this opportunity. Thus, the question as to why chiral purity of molecules is a requisite for organisms has remained open.

A.3. GENERAL REMARK

The results briefly considered above provide abundant material which is rather mosaic in character. Works in this field can be quite definitely classified in accordance with the main hypothesis concerning the origin of the asymmetry, to the substantiation of which they are directed. In contemporary literature the following alternative is considered: optical asymmetry originated in physico-chemical systems either before the biological era or in the biological epoch (Ulbricht, 1962; Bonner, 1972).

As a matter of fact, however, such an alternative does not exist. It is easy to see that the conceptions concerning the biotic and abiotic origin of the molecular chirality of organisms are mutually complementary. Explaining the specific ordering encountered in the present-day organisms, we usually say that it has been assimilated and is reproduced by the organisms as a result of memorizing a random choice; this type of ordering had once opened the combination lock in the door leading to the survival. If, in considering the symmetry breaking in the chemical evolution, we try to understand what it was that helped in choosing this key, the question of the biological significance of the chiral purity of molecules becomes reduced to the question of which lock was thus opened.

In our opinion, setting the problem about the biotic or abiotic origin is in contradiction with the present-day conceptions about the origin of life. The origin of optical activity was considered to a considerable extent apart from other aspects of the molecular evolution. The asymmetry of the molecular architecture of living systems is one of the most characteristic features of their organization. Its coming into being and development can be considered neither separately from the evolution of the inanimate to the animate form of matter, nor without the application of the general strategic method of solving the problem of the origin of life, formulated in the works by A. I. Oparin (1924; 1957).

In this paper we shall try to formulate principles for drawing a comprehensive picture associating the problem of symmetry breaking in the molecular evolution with the contemporary science about its course. We shall show that the origination of chiral asymmetry must be considered as an evolutionary process closely linked with the most basic aspects of the origin of living systems, and that the origination of the chiral purity of organisms should be considered not as a most improbable and casual event, but as a consequence of the evolution of living matter, which could not fail to take place.

The problem of the origin of asymmetry can be linked with the development and functioning of the metabolic network of modern organisms and with those problems which are encountered in the laboratory synthesis of biologically active substances.

B. Biological Aspects of Chiral Purity of Molecular World of Organisms

The origin of asymmetry of molecular systems of organisms cannot be explained only by casual features of chemical evolution on the Earth. This becomes apparent if one considers the significance of molecular asymmetry in the metabolic network of modern organisms.

Laws of development of any physical system are statistical in character, and any spontaneous or induced symmetry breaking must be necessarily accompanied by errors as a result of the process, i.e. by foreign antipodal forms being present in the final state in small but finite amounts. (Chemically, this means that no equilibrium constants are infinite in non-living nature, regardless of how far reactions may be shifted towards one of the antipodes.)

On the contrary, in the complex metabolic processes associated with the functioning and reproduction of organisms at the molecular level, a completely unambiguous reproduction of the chiral purity of biologically important molecules can be observed.

To understand how the development of living matter affected the development of this chiral univocality of the molecular apparatus (even if some features of the broken mirror symmetry might be inherited from the preceding evolution stages), as well as to understand the important features of the reproduction of organisms at the molecular level, it is necessary to consider the problem of the biological significance which the chiral purity of molecules has for organisms.

B.I. VIEW UPON SYMMETRY BREAKING IN MOLECULAR WORLD OF ORGANISMS

It is difficult to analyze problems associated with the chiral purity of metabolic systems, since the appearance of foreign enantiomeric forms is never encountered in the most important sections of normally functioning metabolism.

(a) Factors Eliminating the Appearance of Non-natural Enantiomeric Forms in Metabolism

Stereoselectivity of the synthesis of biomolecules. The univocality of the work of the molecule-synthesizing systems of the organism is connected not only with the univocal arrangement of various structural units of the synthesized molecules, but also with the univocal reproduction of their chirality. It is ensured by both spatial and time organization of biosynthesis.

Selectivity of the ferment system to the chirality of the structural units (promotion of proper and suppression of wrong reactions) is ensured by the evolutionarily developed

capability of recognizing fragments with different chirality by the conformational machine of biomolecule-regulators. The accuracy of such recognition is conditioned by the organization of the ferment system in space. In many investigations *in vitro* a strong reaction of the spatial organization of higher order macromolecular systems to the inclusion into them of racemic elements (in particular, destruction of spatial structures of the type of α-helices, associated with the enzymatic activity) has been found. This may be a peculiar protective mechanism against contamination of molecule-synthesizing systems by an undesirable antipode. In the protection of the chiral purity of molecules time-organization of the biosynthesis takes place. Participation of a catalyst, however strongly stereospecific, in an isolated system cannot ensure the asymmetry of products being maintained for a long time; after temporary breaking of the product symmetry there follows a stage of equalization of the content of the left-handed and right-handed forms (Kuhn, 1958). In living systems, enzymatic reactions are connected with integrated metabolic channels. Products are created in a complex of processes in which each new stage is controlled by a new enzyme, the complex including active transport among various parts of the cell, etc. As a result, in biosynthesis the organism does not allow contact with the enzyme catalyzing every stage to be continued, and the product is thus protected against possible racemization (Urbricht, 1962).

Biosynthesis of modern organisms, as a result of evolution, is organized in a manner so as to protect metabolism against possible errors in the chirality of molecules.

(b) Stereoselectivity of destruction and withdrawal from metabolism

In this respect it is of interest to analyze the role played by such an enzyme as oxidase of D-amino acids, and also the presence of nonnatural forms in nonmetabolic channels of organisms. (For more details see Urbricht, 1962.)

Practically all organisms contain stereospecific enzymes which oxidize D-amino acids. The role of this enzyme appears to be rather unclear. "It is a curious fact that this enzyme acts only on nonnatural forms of amino acids. Maybe this enzyme has yet unknown and important biological functions" (Fruton, 1959). The enzyme was also supposed to be a rudimentary residue of evolution (Atkinson and Fox, 1952).

Taking into account the aspects of the molecular asymmetry under consideration, such an enzyme system, adjusted to destroy undesirable antipodes, is of interest as a possible mechanism serving to protect the chiral purity of the biosystems. Interesting results were obtained by Birkhofer (1940), when he investigated the occurrence of oxidase of D-amino acids in various organisms. In organisms feeding on optically active products produced by these very organisms the concentration of D-oxidase is minimum, whereas, in cases of an organism feeding on products of other organisms (with the chain of reactions organized in a more complicated manner, where the probability of racemization is higher, for instance, as a result of necrosis) the enzyme controlling the destruction of the undesirable D-form is contained in greater amounts (Birkhofer and Wetzel, 1940).

The second method for eliminating the D-form is in cumulating it in those structures

which do not participate directly in metabolism. A relatively frequent occurrence of D-amino acids was found in bacteria, particularly in cell walls (Ulbricht, 1962). Some authors are of the opinion that the utilization of D-amino acids in cell walls is a specific means for eliminating the undesirable antipodes from places dangerous for metabolism.

The undesirability of contamination of molecular systems by foreign antipodes (even in extremely small quantities) exists not *per se*, but in the measure chirally impure formations may enter structures controlling the processes of biosynthesis. In these systems and related processes there exist systems which protect their chiral purity.

(c) Chiral Purity and Diseases

There are few theoretical conceptions and little experimental data concerning the connection between disturbances in the functioning of organisms and chiral impurity of molecular material, particularly where related to the problem of malignant growth.

In the work of K. Miescher (1955), optical asymmetry was included in the complex of the biopotentials controlled with a sufficiently high accuracy. From this point of view, functional disturbances (e.g. such as malignant growths) are associated with a disturbance in the system of biopotentials, namely, with a transition to a state more chaotic than is the norm (Schmidt, 1941).

W. Kuhn (1958) suggested that, from the point of view of the molecular asymmetry, normal functioning is associated with the highest degree of chiral purity rather than simply with non-racemism. In the opinion of W. Kuhn, if the required minimum (of the accuracy of chiral purity) cannot be maitained, the consequence will be malignant growth or death.

F. Kögl reported to have found an abnormal content of nonnatural D-forms of amino acids in malignant tumors (Kögl, 1949). The procedures employed by Kögl were subject to severe criticism, since, in the opinion of many authors, his procedures involved a possibility of racemization not related to the disease (Dittmar, 1939). For this reason, evidently, this trend has not developed any further. However, it is felt that the works of F. Kögl in the main (namely, in the establishment of a connection between malignant growth and contamination of the amino acid system with a nonnatural enantiomer) are not erroneous. From this point of view, as well as from the general theoretical standpoint (see below), investigations in this direction must certainly be continued on an experimental level.

(d) General Comments

Some authors believe the resources for maintaining the molecular asymmetry in biosystems reside in physical differences of diastereomers (different solubilities, reaction constants), or in different stability of the spatial structures destroyed with the incorporation of foreign antipodes into macromolecules (Gause, 1940; Wald, 1957; Kuhn, 1958).

When considering the molecular architecture of modern metabolism, we are concerned not only with mirror symmetry breaking but also with an evolutionarily created, comprehensive and multiform complex of activities. This is realized at different levels of metabolism control and is directed to the strict protection of biosynthetic systems against the appearance of nonnatural enantiomeric forms. Hence, we are concerned with one more aspects of the biological organization of living matter at the molecular level. Consideration of this aspect of the biological ordering is necessary in understanding the normal functioning of living systems.

B.2. CHIRAL CODING IN ORGANISM AND INFORMATIONAL MEANING OF CHIRAL PURITY OF BIOMOLECULES

The development of life is connected with the formation of definite ordered structures at different levels of hierarchy, i.e. with the process that acted against the principle of entropy increase in nonliving matter.

When it is said that structures which can be encountered nowhere but in organisms are biologically ordered, it is usually implied that an organism is a definite unique arrangement of cells. A cell, in its turn, is likewise a definite and unique arrangement of biopolymers, and every biopolymer is a unique sequence of fragments. A structure encountered in an organism appears there as a result of having been chosen from a multiplicity of others, its only difference from those excluded from this particular structure is that it is "biologically meaningful." The structure having been chosen from a multiplicity of others, "the conversion of the unpredictable into the inevitable," is an act of creating information, the amount of which is determined by the number of alternative structures from which the one employed is selected.

In a rough approximation the amount of information required for the construction of unique structures (for example, in a human body) may be estimated thus (Blumenfeld, 1975):

1. Uniqueness of a multicellular organism being structures from cells:

$$I = \log_2(10^{13}!) \sim 4 \cdot 10^{14} \text{ bits}$$

(the choice of one of permutations of $\sim 10^{13}$ cells).

2. Uniqueness of a cell being structured from polymers:

$$I = \log_2(10^{8}!) \sim 2.6 \cdot 10^{9} \text{ bits}$$

(the choice of the only arrangement from the permutations of biopolymers in a cell). For all cells in the organism of man we have:

$$I \sim 2.6 \cdot 10^{22} \text{ bits}$$

3. Uniqueness of proteins and DNAs being structured from monomers:

$I \sim 1.3 \cdot 10^{26}$ bits for proteins;
$I \sim 6.10^{23}$ bits for DNAs

(the choice of unique sequences of $\sim 3 \cdot 10^{25}$ amino acid fragments and $\sim 3 \cdot 10^{23}$ nucleotide fragments in the organism of man).

Actually, when building its molecules, an organism makes a still more complicated choice. Each sequence of monomers may originate as a multitude of molecules which will differ from one another both in the relative content of D- and L-monomers and in their arrangement, i.e. in a peculiar binary (dextro-levo) chiral code.

When proteins and DNAs are being built in an organism, in addition to the selection of a sequence of monomers, chiral coding also takes place.

Selection of chirally pure molecules requires introducing one more type of ordering in 3 (Morozov, 1976b):

4. Uniqueness of the chiral code of biomolecules: With the length of a chain of chiral fragments being n, a unique sequence is to be chosen out of 2^n alternatives. The amount of information thus created is

$$I = \log_2 2^n = n.$$

For $\sim 3 \cdot 10^{25}$ amino acid fragments in the protein system of an organism this will amount to

$$I \sim 3 \cdot 10^{25} \text{ bits.}$$

Since relative amounts of information allow comparison of the scope of the choice carried out by the organism in building a unique structure, selection of the chiral code of biomolecules is comparable with that carried out in the creation of the genetic code.

Thus, at the molecular level of the organization of biosystems, there exists one more information reservoir, the filling in metabolism which is associated with the selection of molecules having a unique chiral code. The scope of selection of this type is comparable with the scope of selection performed by the molecular apparatus of the genetic code.

By analogy with the coding of a monomeric sequence of biomolecules, we shall call the selection of their chirally pure forms chiral coding.

B.3. SIGNIFICANCE OF CHIRAL PURITY OF BIOMOLECULES FOR SELF-REPRODUCTION OF ORGANISMS

Information is biologically meaningful only when it directly or indirectly influences the self-reproduction of an organism (Blumenfeld, 1975). If we immerse one of the DNA threads into a solution containing various nucleotides, a second thread will be assembled on the first one, the sequence of monomers in the second thread being univocally determined by the code of the initially immersed thread. The information contained in an enzyme in the form of a definite code represented as a sequence of monomers is written there "for the purpose" that the enzyme could, regulating the assembly of a daughter biomolecule, impart a definite ordering to it, i.e. properly arrange the monomeric units in it.

Chirality of the monomers employed in biomolecules makes the task of proteins and DNAs more complicated; they must not only look after the arrangement of various monomers in the skeleton of the molecule, but also select the chirality of these monomers. Indeed, the sign of the chirality of the three-dimensional structure of the fragments from which biomolecules are composed determines to a considerable extent, its spatial structure and, hence, its stability and biochemical properties. A molecule in which the arrangement of various monomers is correct, but the chirality of the monomers is wrong, is not fit for performing its functions. Not every enzyme can cope with the task of imparting a definite chiral code to the biomolecule in its synthesis. Only a chirally pure enzyme is capable of imparting to a molecule, when controlling its synthesis, a definite chiral code; hence the requirement of organisms in the chiral purity of biopolymers (Morozov, 1976b; 1977a).

This can be demonstrated by a simple example, by considering the ability of enzymes – regulators to chiral coding.

If a molecule-regulator of biosynthesis is chirally pure, all its active centres are built from monomers having the same chirality. When interacting with substrate molecules, such active centres can, in principle, distinguish between the D- and L-forms of the substrate (fitting of antipodes to the surface of chirally pure active centres is different). Consequently, although the regulating actions of the enzyme, caused by this association, may differ, the enzyme can promote a reaction with the required antipode and eliminate the undesirable form.

In the event a molecule-regulator contains a certain (even if rather insignificant) amount of monomers with a foreign chirality, the active centres may have a different stereoisomeric form. In particular, an active centre may be composed of two monomers, of which one has a D- and the other has an L-configuration. Such a meso-chiral (DL)-active centre of the enzyme principally cannot distinguish between the desirable and undesirable enantiomeric forms of the substrate. Both D- and L-antipodal forms of the substrate molecule (or their ensembles) are equally well or equally poorly fitted to the symmetrical structure of the meso-chiral active centre. If, for instance, in a reaction of enzyme catalysis chiral molecules are produced from an achiral or racemic substrate, and the active centre of the enzyme is mesochiral, the probability of origination of antipodal products is the same, and the system can produce only a racemic mixture of antipodes.

A similar situation also arises in more complicated enzymatic processes, where the chirally impure enzyme will build a unit with an erroneous chiral code into the final structure of the biomolecule.

A complicated pattern of the regulating action taking place in reactions of synthesis of biomolecules includes various rearrangements of the enzyme and its functioning parts. Even a single defect in the chiral purity of the regulator may lead to a plurality of units with an erroneous chiral code in the molecule being synthesized. As all states of a chirally pure regulator are chirally pure in case of any rearrangements, such a regulator is capable of distinguishing all types of the chiral code, and it can unambiguously construct a definite molecule. A hypothetical chirally impure enzyme will, instead, produce daughter

molecules that are stereoisomers having different three-dimensional structures and different biological activity. The use of such enzymes leads (with the number of reproduction acts being sufficiently small) to complete chaos in the structure of daughter molecules and to the loss of the initial molecular ordering.

For organisms to preserve the ordering of molecular information in those processes in which they sustain their existence and reproduce themselves, their enzyme system must be chirally pure. Chiral purity of biomolecules is one of the laws underlying the protection of biological information.

Observations show that even a chirally pure molecule may be rearranged differently within a sufficiently narrow range of environmental conditions. Reliability of the chiral coding requires that the synthesis conditions should be maintained within exacting limits, otherwise the enzyme may err in the chiral code. That is why the measures taken by organisms and by their communities to protect the chiral purity of molecular systems prove to be so thorough.

Chiral coding is a necessary element of the synthesis of biomolecules. Recognition of the chiral code is a necessary element of enzyme catalysis in living systems. Chiral purity of biomolecules is at the basis of protection of the main property of organisms: the ability to preserve and exactly transmit molecular information in their self-reproduction.

The problem of evolution of molecular world asymmetry can, therefore, be regarded as that of an integral process closely connected with the evolution of matter from the non-living to the living form.

C. Spontaneous Mirror Symmetry Breaking in Processes of Development

For a long time ideas have been entertained that any processes in which antipodes are created, undergo mutual transformations, or are destroyed under symmetrical conditions can lead only to racemization of chiral material. Accordingly, racemization is considered to be a spontaneous process, which establishes in any system, after a longer or shorter period of time, an equal amount of enantiomeric forms. Some well-known processes (such as modifications of Pasteur's experiments on spontaneous resolution of racemates in crystallization, origination of optical activity on the surface of symmetric catalysis (Isoda *et al.*, 1958) are regarded as an exception which is hard to understand (Strayer, 1966). The origin of optical activity is treated as a result of a rather low-probability chance (e.g., unambiguous reproduction of the initially asymmetric progenitor molecule and of its progeny) which acted against this "universal thermodynamical imperative" (Bonner, 1972; Thiemann, 1974).

An alternative point of view assumes that in the evolution of matter conditions could arise when homogeneous distribution of antipodal elements became unstable. In this case, the asymmetry of the final state could be established as a quite natural result of the system development, as a reaction to fluctuations even under symmetric conditions.

Mathematical presentation of this hypothesis and its theoretical predictions will be considered in this section, and conditions for the realization of such behaviour and the

relationship with the general process of evolution of matter will be considered in Section D.

C.1. CONCEPTS CONCERNING WAYS OF DEVELOPMENT TO ASYMMETRIC FINAL STATES

F. Frank (1953) was the first to formulate a mathematical model of evolution which could lead to the origin of asymmetry. He introduced two autocatalytically developing antipodal systems:

$$L \xrightarrow{K} L + L; \quad D \xrightarrow{K} D + D \tag{C.1.1}$$

with mutual suppression of antipodes through a certain lethal interaction:

$$L + D \xrightarrow{K_1} X \tag{C.1.2}$$

It turned out that the sum of concentrations of the antipodes could grow slower than the difference: a small deviation of the concentration ratio of the antipodes from unity could grow with time.

F. Seelig and P. Decker (Seelig, 1971; Decker, 1973) again demonstrated such a possibility, having considered the evolution of open systems in accordance with the reaction schemes:

$$\begin{array}{llll} A + L \overset{K_1}{\rightleftarrows} 2L & & A_L + B_L \overset{K_1}{\rightleftarrows} 2B_L & \\ A + D \overset{K_1}{\rightleftarrows} 2D & & A_D + B_D \overset{K_1}{\rightleftarrows} 2B_D & \text{(C.1.3; C.1.4)} \\ D + L \overset{K_2}{\rightleftarrows} (L, D) & & B_L + B_D \overset{K_2}{\rightleftarrows} (B_L B_D) & \end{array}$$

(where L and D are antipodes.)

The starting point (Seelig, 1971) was a theoretical model of enzyme kinetics, and it was the evolution of certain specific systems – "bioids" (Decker, 1973), capable of existing in several stationary states. With definite relations between the parameters, the states of such systems are stable when there predominates one of the enantiomeric forms. Similar models have been considered by some other authors (Hochstim, 1963; Seelig, 1970; Calvin, 1969), and the entire corpus of such models may be termed as models of aggressive behaviour of antipodes (Decker, 1973b). A detailed analysis of these models was given by A. Hochstim (1975).

In 1974 P. Decker (1974) presented a new type of kinetics – a "hypercompetitive model", in which "lethal" interaction of the antipodes was not present explicitly, but the competition of the antipodes in the process of self-reproduction was described by a higher than second-order reaction:

$$\begin{array}{l} A + (1+\delta)L \xrightarrow{k} (2+\delta)L \\ A + (1+\delta)D \xrightarrow{k} (2+\delta)D \end{array} \tag{C.1.5}$$

In this model the origination of asymmetric stable stationary states has been demonstrated as well.

In the above-described models, the essential factors are the role played by the interactions of chiral units and the difference in the results of such interactions, depending on whether they take place between identical or antipodal partners.

It is not difficult to see here the conditions necessary for the instability of racemic states and for the development with the spontaneous resolution of the antipodes. The same conditions are also essential for the dynamics of systems pertaining to another level: physico-chemical systems.

One may consider a thermodynamically controlled reaction of mutual transformation of antipodes or reactions of the production of chiral molecules from an achiral substrate, corresponding to the reaction schemes:

$$L \rightleftharpoons D; \qquad L \rightleftharpoons A \rightleftharpoons D \tag{C.1.6}$$

The dynamics of the chirality of each element of the system may be ensured both by simple intramolecular inversion and by an intricate complex of physico-chemical processes (various chemical reactions, diffusion of elements in the structure of the system, exchange of chiral fragments with the medium). At first sight it seems evident that, since the probabilities of the corresponding transitions are the same, the formation of a racemic mixture of antipodes should be expected to take place under any conditions. However, with allowance made for the interaction of the chiral particles of the system, the situation becomes drastically different (Morozov, 1977a).

In the work of Ya. B. Zel'dovich (1974a) it is shown that differences in the energy of interaction of L- and D-molecules may bring about stabilization of the same chirality of the hypothetical mesomorphic pseudoscalar medium.

In the work of L. Harrison the possibility of resolution of antipodes is demonstrated on a hypothetical model of the reaction of transformation of an achiral substrate into chiral products, this reaction being catalyzed by the symmetrical surface (Harrison, 1974). Autocatalytic behaviour is ensured by the adsorption of the molecules of one of the product enantiomers making the surface active for the predominant production of the same enantiomer.

The conditions of the resolution of antipodes caused by an analogous mechanism with the separation of a new phase are demonstrated in (Kabachnik *et al.*, 1976b).

In all such thermodynamically controlled physico-chemical transformations the development towards the asymmetrical state is routed by the energy nonequivalence of the interactions of the identical (LL and DD) and antipodal (LD) elements of the system.

Each of the works cited above has demonstrated the principal possibility for the spontaneous evolution towards one of the asymmetric states. The models as such, however, being based on quite concrete mechanisms, do not enable one to separate casual features from the general regularities in the development of the asymmetry. Yet, one thing is common to and unites all the schemes of this type: the resource for the autocatalytic development of the asymmetry consists in fluctuations and instability of

the racemic state, which arises as a result of the interaction of chiral elements, that are selective to the chirality of partners. This allows formulating a unified problem of regularities in the development of asymmetry in the evolution of chiral systems.

C.2. DISORDER–ORDER TRANSITIONS, CHIRAL POLARIZATION AS A PARAMETER OF ORDER, AND THE PROBLEM OF SPONTANEOUS MIRROR SYMMETRY BREAKING IN EVOLUTIONARY PROCESSES

The unity of the considered models becomes particularly apparent if in each model we do not trace the development of antipodal subsystems, but trace the evolution of a certain simple parameter which may be termed chiral polarization (Morozov, 1976a):

$$\eta = \frac{L - D}{L + D} \tag{C.2.1}$$

In this case, it turns out that all the models which give stable asymmetric solutions are reduced to the following equation:

$$\eta = a\eta + b\eta^3 \tag{C.2.2}$$

(The connection between the parameters a and b takes into account all specifics in the physical nature of the processes described by these parameters.) The sense of this unity becomes clear if we take into account that the development of asymmetry may be regarded as the evolution of a certain type of organization and described by the evolution of chiral polarization as a corresponding parameter of order. As the parameter of order, chiral polarization can be rigorously introduced as the mathematical expectation $\langle\eta\rangle$ for each element of the system. Distribution of the asymmetry will be taken into account by the function of spatial distribution $\eta(\vec{r})$. As ordering of the chirality distribution in the system or its subsystems, a corresponding correlation function may be introduced:

$$\eta^2 = \langle \eta \underset{x\to\infty}{(\vec{r})} ; \eta(\vec{r} + \vec{x}) \rangle$$

as it is usually done in fluctuation theories of phase transitions. Thus, we enter the sphere of the intensively developing theory of disorder–order transitions.

The development of this field in recent years has spared physicists the perplexity caused by nature of diverse manifestations of the asymmetry: an idea has been conceived, that symmetry breaking can take place spontaneously as a reaction to fluctuations because of the instability of the state which is symmetrical in the most general sense. The theory of spontaneous symmetry breaking is used in the physics of the '70's, particularly in the theory of quantized fields for explaining the breaking of the vacuum symmetry (which may furnish an explanation of the asymmetry of weak interactions).

The basic model of this theory can be presented as follows (Zel'dovich and Novikov, 1975): let the energy of the system be written as a series arranged according to

the parameter of order η:

$$F(\eta) = a_1\eta^2 + b_1\eta^4 + \ldots$$

(considerations of symmetry require taking into account only symmetrical terms of the expansion).

The taking into account of the interactions necessitates the inclusion, in addition to the term $a_1\eta^2$, of the term $b_1\eta^4$.

The condition of equilibrium $\partial F/\partial\eta = 0$ when $a/b > 0$ is satisfied only by the chaotic state $\eta = 0$. When $a/b < 0$, this state becomes unstable, whereas new stationary solutions $\eta = \pm\sqrt{|a/b|}$ define stable asymmetric states to one of which the system is bound to come as a result of development of fluctuations. Let us write down the dynamic equation for the parameter of order under the conditions of transition to the asymmetric state, taking into account the general relationship (Patashinsky and Pokrovsky, 1975):

$$\dot{\eta} = -\Gamma^{\partial F/\partial_\eta} \tag{C.2.3}$$

Then:

$$\dot{\eta} = a\eta + b\eta^3 \tag{C.2.4}$$

which is the simplest form describing the dynamics of the system whose evolution is connected with a spontaneous symmetry breaking.

The form (C.2.4) coincides with equation (C.2.2). Thus, the models considered previously belong to the class of general models of spontaneous symmetry breaking developed by contemporary physics. Its methods (regardless of the particular sense of transformation capable to realize the evolution of the asymmetry and of the levels of the organization of matter to which these processes pertain) allow the formulation and solution of a number of general problems concerning the critical conditions for the course of the processes of spontaneous symmetry breaking and of the development of the ordering of matter, associated with its chiral polarization.

Further, we shall consider those simplest criteria which are imposed on the conditions for the evolutionary processes to proceed with a route offered for the spontaneous development of chiral polarization.

C.3. CRITICAL TEMPERATURE

For a route to be offered for the asymmetric evolution, the equation parameters must satisfy the relationship $a/b < 0$. The fulfillment of this relationship depends on which processes are brought under consideration and which characteristics of space and time organization of the system are covered by these parameters.

The simplest form occurs in the reaction scheme (C.1.6) which describes the kinetics of the thermodynamically controlled symmetry breaking:

$$\dot{\eta} = \alpha\,[(T_c - T)\eta - T_c\eta^3] \tag{C.3.1}$$

For this system the critical temperature can be estimated at once as $T_c \sim zw$, where z is

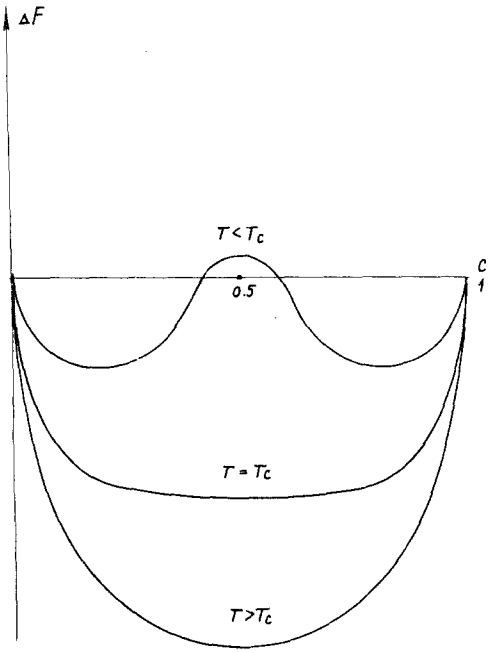

Fig. 2. Dependence of the free energy of a mixture of mirror antipodes on the composition and temperature. Above T_c racemic state is stable. Below T_c chirally polarized states are stable.

the coordination number and w is the energy selectivity of the interaction of antipodes in relation to their chirality.

In case of evolutionary models pertaining to more complicated systems (in particular, for open self-replicating systems) an analogous critical characteristic can be constructed from constants of corresponding transformational (see Figure 2).

C.4. CRITICAL CONCENTRATION

Let us consider the evolution of a system which, in addition to chiral elements, contains achiral material (substrate or solvent in simple chemical models, nutrient medium in the models of open systems). In the process of development, achiral material may be absorbed by the chiral colony by virtue of the reaction $L \rightleftharpoons A \rightleftharpoons D$.

In such a system the chiral polarization dynamics can be described by the following simplest equation which is a modification of equation (C.3.1):

$$\dot{\eta} = \alpha \left[(\Theta T_c - T)\eta - \Theta T_c \eta^3 \right] \tag{C.4.1}$$

where Θ is the relative content of the chiral material in the medium, described by the corresponding equation of the evolution; T_c is the critical temperature of the symmetry breaking in a system without the achiral material.

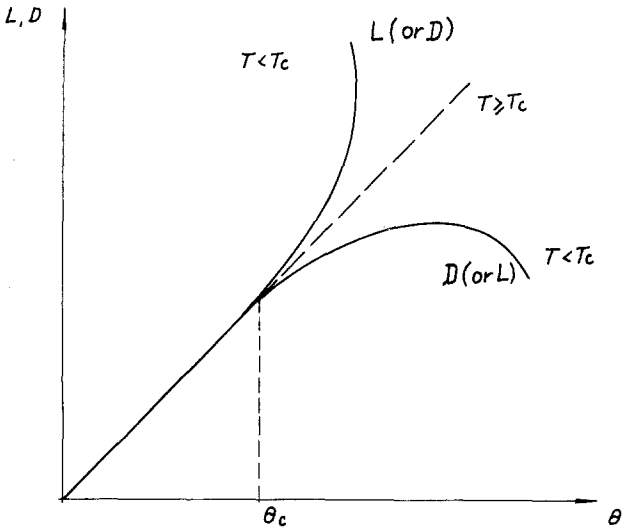

Fig. 3. Dependence of the concentration of optical antipodes L.D. in the developing system on their total concentration θ. θ_c is the critical concentration of the antipodes, above which the racemic state is unstable.

Stationary states of this system satisfy the relationships:

$$\eta_1 = 0; \quad \eta_{2,3} = \sqrt{1 - T/\Theta T_c}$$

$\eta_1 = 0$ is stable, if

$$T > T_c; \quad 0 < \Theta \leqslant 1 \tag{C.4.2}$$

$\eta_1 = 0$ is unstable, $\eta_{2,3}$ are stable, if

$$T < T_c; \quad \Theta > T/T_c \tag{C.4.3}$$

Thus we have established the existence of still another characteristic of the system, which has the sense of a critical parameter. In the temperature region wnere the system is in principle capable of developing with a spontaneous symmetry breaking, the possibility of development of chiral polarization arises only if the medium is sufficiently saturated with chiral material (see Figure 3).

C.5. CRITICAL COOPERATION

The condition obtained in Section C.4 places a lower limit on the quantity of chiral material in the medium capable of breaking the initial symmetry in the course of development.

Another characteristic which reflects the quality of the interactions of chiral particles is the cooperativeness of elements in the system of dynamic transformations.

P. Decker (1974) with the aid of the model of competition of antipodes (C.1.5) came

to the conclusion that the possibility of symmetry breaking, all other things being equal, is dependent on the order of the reaction by which the self-reproduction of the antipodes is described. If the self-reproduction of the asymmetry of each autocatalyst is described by the reaction of the type:

$$\begin{aligned} A + L &\rightleftharpoons 2L \\ A + D &\rightleftharpoons 2D \end{aligned} \qquad \text{(C.5.1)}$$

the development of chiral polarization does not take place. If the reaction of self-reproduction is of a higher order:

$$\begin{aligned} A + (1+\delta)L &\rightleftharpoons (2+\delta)L \\ A + (1+\delta)D &\rightleftharpoons (2+\delta)D \end{aligned} \qquad \text{(C.5.2)}$$

then spontaneous symmetry breaking is possible. Only the participation of more than two elements in the interaction (cooperativeness) makes symmetry breaking possible.

A similar conclusion was drawn by L. Harrison (1974) when he considered a hypothetical reaction of separation of antipodes on the surface of a symmetric catalyst: for the symmetry breaking to take place, it is necessary that at least two identical molecules of the chiral product should participate in the modification of an active centre.

The necessity of a high coordination number of interacting particles has been shown (Kabachnik and Morozov, 1976) for the separation of antipodes upon separation of a new phase. These particular results become understandable within the framework of the general theory of symmetry breaking, in which the general requirement is a sufficient degree of the cooperation of particles in the interaction (Stanley, 1971).

The influence of cooperation on the development of chiral systems can be illustrated by a simple example. Let us consider the conditions for the existence of stable chirally

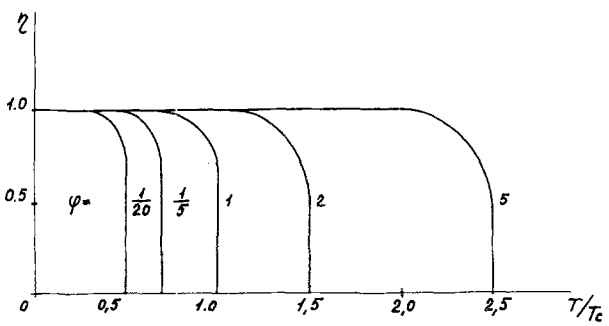

Fig. 4. Dependence of the ordering of chiral polarization of stable stationary states of a mixture of mirror antipodes on the degree of the system cooperativeness and on the temperature. The critical temperature below which the racemic state is unstable (T_c being the critical temperature when $\varphi = 1$) depends on the parameter of cooperativeness φ of the interaction of mirror antipodes. At each temperature $T < T_c$ there exists a certain critical value of the cooperation degree φ_c, such that less cooperated systems are stable in the states containing equal quantities of enantiomers; more cooperated systems ($\varphi > \varphi_c$) are stable only in asymmetric states.

polarized solutions in a model similar to that described by equation (C.2.2), but in which the number of partners interacting with each element of the system may vary.

To this end, we shall use the solution of the classical Ising's problem (Ising, 1925) for two-dimensional systems (Onsager 1944) (see Figure 4). The measure of the system cooperativeness φ is defined so that when $\varphi = 0$ the system consists of non-interacting linear chains (a non-cooperative system, which, as is known, is incapable of symmetry breaking); when $\varphi = 1$, the system is a square network, in which all the four nearest partners take equal part in the interactions; the intermediate values correspond to different degrees of cooperation. Figure 4 shows that with a definite value of T less cooperative systems $\varphi < \varphi_c$ will develop without symmetry breaking, while the evolution of more cooperated forms $\varphi > \varphi_c$ is impossible without the development of chiral polarization in them.

Thus, the complex of critical conditions for spontaneous symmetry breaking includes elements of spatial organization of the system and, therefore, it is necessary to analyze those features of evolution of matter, which are associated with the morphogenesis of the asymmetry.

C.6 CRITICAL SCALE OF MIRROR SYMMETRY BREAKING AND MORPHOGENESIS OF ASYMMETRY IN THE DEVELOPMENT OF MOLECULAR SYSTEMS

Let us consider the main features of the evolution of spatial order in the distribution of chiral polarization.

The development of the spatial structure of matter, initiated by the metastability of the initial homogeneous state is called morphogenesis. As regards the evolution of chiral polarization, one may speak about the morphogenesis of asymmetry and about the connection of the morphogenesis of asymmetry with the general morphogenetic aspects of the evolution of matter.

The simplest model of morphogenesis is the so-called morphogenesis of Turing (Turing, 1952):

$$\dot{x} = P(x, y) + D_x(\partial^2 x/\partial r^2); \quad \dot{y} = Q(x, y) + D_y(\partial^2 y/\partial r^2) \tag{C.6.1}$$

where $P(x, y)$; $Q(x, y)$ are nonlinear functions and D_x; D_y are corresponding diffusion coefficients. (When $D = 0$ the system of equations describes only local dynamics; when $D = \infty$ it describes the dynamics of the system as a whole.)

When $0 < D < \infty$ there exists the so-called problem of Turing, which is formulated as follows. Let $\bar{x}, \bar{y}$ be homogeneous stationary states of the system. Consider the reaction of the system, described by Equations (C.6.1) with the initial states $\bar{x}, \bar{y}$, to a set of fluctuations of various wavelength λ.

If there exists a range $\lambda_{c_2} < \lambda < \lambda_{c_1}$ such that the state $\bar{x}, \bar{y}$ is unstable with regard to the fluctuations whose wavelengths are within this range and is stable with regard to all other fluctuations, morphogenesis starts to take place (in the sense of Turing), and $\lambda \in \{\lambda_{c_1}; \lambda_{c_2}\}$ are the characteristic scale of the developing inhomogeneities.

The problem of Turing in the model of the evolution of chiral polarization has the form

$$\dot{L}\ ,\ \dot{D} = f(\dot{\eta})\ \ \dot{\eta} = a\eta + b\eta^3 + D_\eta(\partial^2\eta/\partial r^2) \tag{C.6.2}$$

Its solution gives an estimate of the critical scale of the system in which the morphogenesis of asymmetry is possible $r_c \sim \sqrt{D/a}$. All fluctuation inhomogeities of the chiral polarization with the size smaller than r_c are cancelled; fluctuations with a greater wavelength give way to the development of large-scale areas, where macroscopic quantities of asymmetric material may differ in the chiral polarization. This simplest problem allows an important conclusion to be drawn: for the mirror symmetry breaking and morphogenesis of the asymmetry to be ensured, the system in its development must pass through a certain critical size. The relationship between this critical characteristic, the internal structure of the system and the environmental conditions can be derived in a rather simple way. Thus, for the system (C.3.1) the critical size is defined as

$$r_c = \sqrt{D/\alpha(1 - T/T_c)\phi}. \tag{C.6.3}$$

Thus, in the organization of condensed media there exists an important aspect which is associated with the ordering of the material chirality and with its spatial distribution.

This circumstance must necessarily be taken into account when one considers the general aspects of the morphogenesis of chiral systems. Analyzing the development of the organization of matter, we must consider the interconnection of two aspects, of which one is associated with the ordering of the chirality of material, and the other, with its spatial ordering.

In the first place, evolution of inhomogeneity is a decisive factor in the origination of the metabolic network of living systems and in the incipience of life (Oparin, 1957). In the second place, no mirror symmetry breakings can be realized without the chiral material being cooperated to a sufficient degree; this, in its turn, can hardly be conceived of without the origination of heterogeneities at various levels, differing from the other medium by packing of the material.

The simplest cooperative effects in the interaction of fluctuations of two types of the system ordering in the fluctuation theory of phase transitions are described by the so-called Landau Hamiltonian (Patashinsky and Pokrovsky, 1975), in accordance with which the simplest model of dynamics will have the form:

$$\begin{cases} \dot{\eta} = a_\eta\eta + b_\eta\eta^3 + c\eta\varphi^2 \\ \dot{\varphi} = a_\varphi\varphi + b_\varphi\varphi^3 + c\varphi\eta^2 \end{cases} \tag{C.6.4}$$

or, taking into account diffusion terms,

$$\begin{cases} \dot{\eta} = a_\eta\eta + b_\eta\eta^3 + c\eta\varphi^2 + D_\eta(\partial^2\eta/\partial r^2) \\ \dot{\varphi} = a_\varphi\varphi + b_\varphi\varphi^3 + c\varphi\eta^2 + D_\varphi(\partial^2\varphi/\partial r^2) \end{cases} \tag{C.6.5}$$

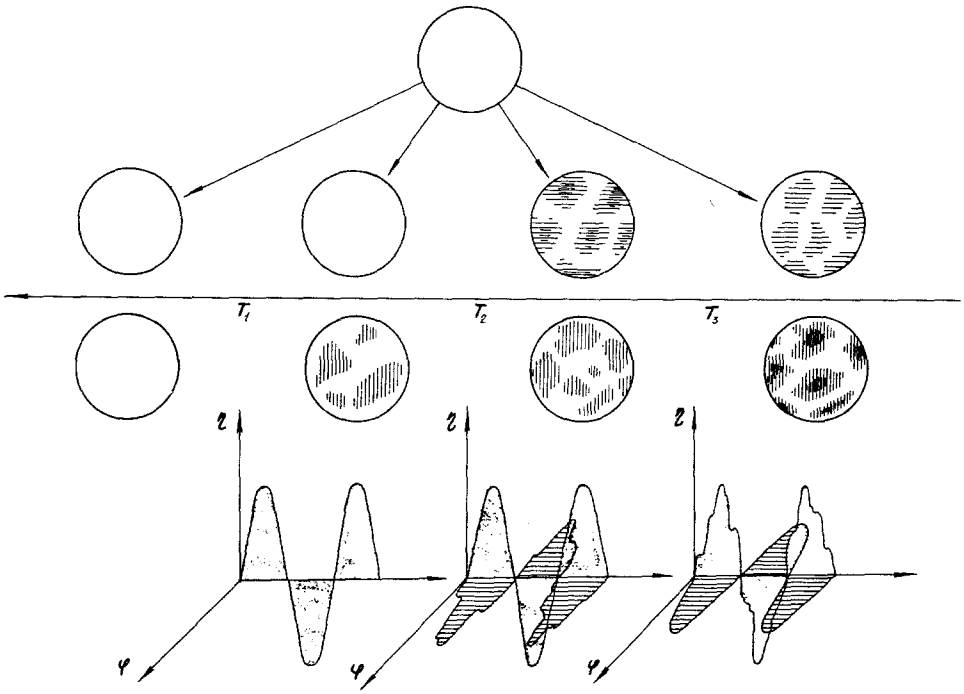

Fig. 5. Morphogenesis of a system, including the morphogenesis of chiral asymmetry as one of the types of ordering.
η is the parameter of chiral ordering:
φ is the parameter of order, characterizing the ordering of the spatial structure;
$T > T_1$ – any morphogenetic path is absent;
$T_1 > T > T_2$ – a morphogenetic path in which only spatial or chiral structure can arise;
$T_2 < T < T_3$ – an interference of the chiral and structural morphogenesis; the size of the structurally ordered areas being smaller than those with definite sign of the chiral polarization;
$T < T_3$ – an interference of the chiral and structural morphogenesis, the size of the ordered structures exceeding the size of the areas with the definite chiral polarisation.

Here φ, η are parameters of order (η is chiral polarization, φ is the parameter of order, characterizing the inhomogeneity of the spatial structure of the system: $\varphi = 0$ if the medium is homogeneous, $\varphi \neq 0$ if the medium is heterogeneous); a, b are parameters describing the cooperative interactions of the fluctuations of each of the parameters of order; c is the parameter of the interaction of the various parameters of order.

Some final results of the investigation of Turing's problem in this system are presented in Figure 5. Of interest is the general essential dependence of the character of morphogenetic processes on the internal characteristics of the interactions in the system and on the environmental conditions.

Figure 5 shows critical temperature levels in the intervals between which the type of morphogenesis differs. With the temperature lowering, there takes place a transition from the chaotic racemic state to the small-scale structuring of one of the parameters of order

and further to large-scale inhomogeneities, in which the spatial structure interferes with the chiral polarization.

Such a model may be an interesting subject for investigation. It contains sufficiently clear parameters which characterize the internal structure of the system (these characteristics can be studied through independent experiments) and external conditions. From the theoretical point of view, the development of the organization of systems is a result of the interaction of internal information (genetic information 'written' in the interactions of the elements) with the stochastic information of the environment (Decker, 1974). The model described above offers a possibility for analyzing the physical realization of such control, taking into account the dependence of the choice of the route for non-univocal morphogenesis on evolution conditions. This model may serve as a basis for discussing certain important aspects of mirror symmetry breaking in biochemical evolution and is discussed further in section D.

C.7. TERRITORIAL EVOLUTION OF ASYMMETRY

The territorial separation of the antipodes, considered above, does not completely solve the problem of evolution of asymmetry, a prerequisite stage is the annihilation of one of the antipodal colonies. Therefore, many authors regard the autocatalytic behaviour only as a means of preparing antipodal systems to complete symmetry breaking. According to this posit, territorial separation, by transferring the asymmetry from the molecular to the macroscopic level, changes the situation from statistics of large numbers to that of small numbers (Harrison, 1974). This makes the system more ready in the event of some accidental cataclysm which would destroy one of the antipodal populations.

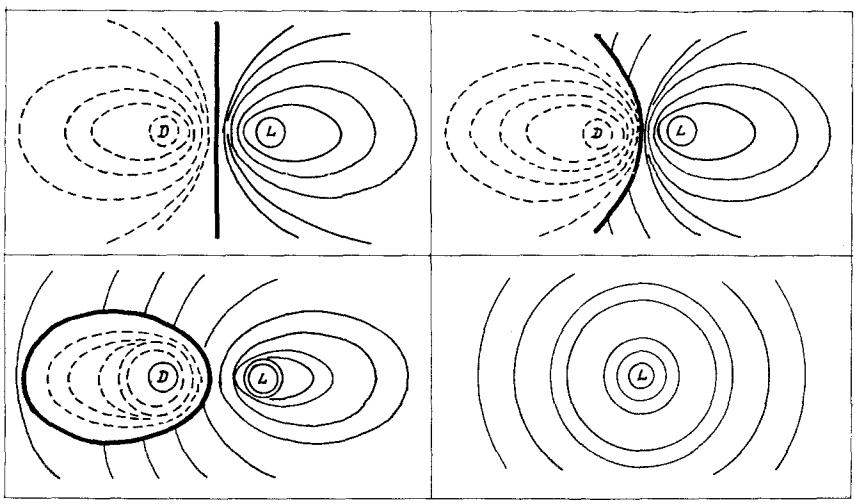

Fig. 6. Coalescence of antipodal colonies in the territorial development of a mixture of mirror antipodes.

However, this hypothesis is not required to understand the observed asymmetry; cooperative development of antipodal populations in space had resources of its own for producing the predominance of one of the antipodal forms.

F. Frank (1953) was the first to notice that territorial behaviour of antipodes leads to the formation of an interface between enantiomeric colonies, which differs in its properties from the rest of the medium, and that such an interface must have surface tension. Corresponding quantitative characteristics of the walls (thickness, distribution of components, surface tension, etc.) can be obtained theoretically (the analysis of similar boundary effects for other physical systems can be found, e.g. in Zel'dovich *et al.*, 1974a).

Such an interface between the antipodal domains of the system is stable only in the case of an ideally planar form. In the case of curvatures the boundary will move towards its concavity (the movement is analogous to that of soap film in foam). Because of this, in the system first domains originate surrounded by the antipodal colony, and then such domains disappear, being absorbed by the 'surviving' enantiomeric form. A qualitative picture of the behaviour, shown in Figure 6, can be described in sufficient detail theoretically.

The result of the territorial behaviour of symmetry breaking (except special cases of a rather specific initial topology) will be a spatially developed system with a sufficiently homogeneous domination of one of the antipodal forms.

Thus the theory of spontaneous symmetry breaking, as applied to the processes of evolution of chiral molecular systems, allows a combination of quite a number of ideas concerning the possibility of molecular asymmetry having a fluctuation origin. This theory enables one to proceed from general ideas about the origin of chiral polarization as a consequence of fluctuations and instability of symmetrical states to the quantitative regularities of these phenomena. The models of spontaneously broken symmetry reveal a whole complex of critical parameters of the system (temperature, concentration, cooperation, size, etc.), which, when attained, provide a possibility for chiral polarization to develop spontaneously. Combinations of the parameters of the models, limiting the transition to the instability of the homogeneous state and the transition from the symmetrical to the asymmetrical course of development, may be called 'chemical Reynolds numbers (Prigogin, Glensdorf, 1974) by analogy with the corresponding function in problems of hydrodynamics. These characteristics for both closed and open evolving systems are sufficiently complex in character and can be constructed on the basis of parameters describing the internal structure of the developing systems, stereospecificity of the interactions of antipodes, constants of chemical reactions, diffusion processes, spatial structure parameters, etc.

The elaborated theoretical concepts permit the data obtained by physical methods to be included in the system of controlling such processes under laboratory conditions and point ways to experimental simulation and study of those aspects of the evolution of systems, which are associated with molecular chirality. Proceeding from the models with spontaneously broken symmetry, it is possible to combine the experimental data accumulated in the fields of chemistry, physical chemistry and biochemistry and to ascertain the

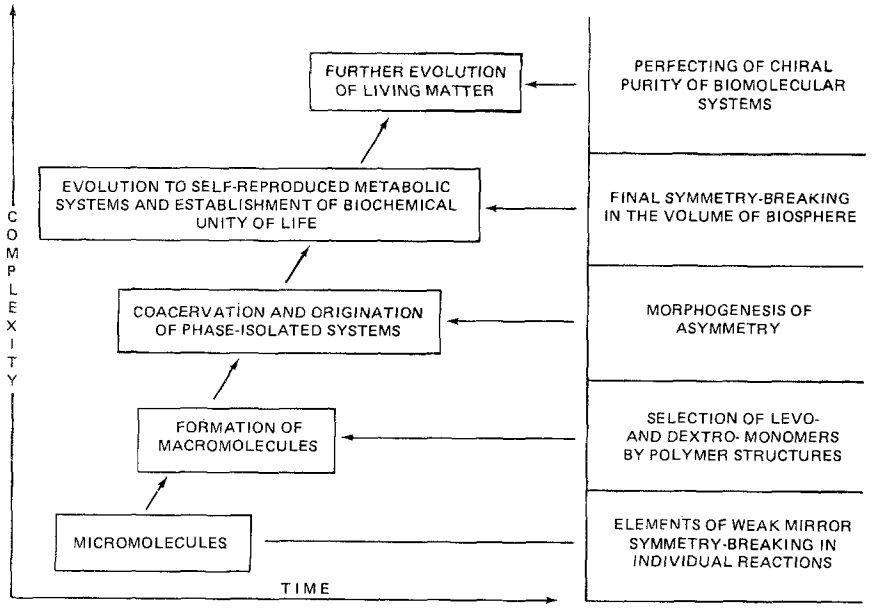

Fig. 7. Possible stages of the mirror symmetry breaking evolution in the model of the origin of life.

place held and role played by aspects related to chiral polarization in the general course of evolution of matter.

D. Mirror Symmetry Breaking and Development of Chiral Purity of Molecular World of Organisms as an Aspect of Biochemical Evolution

The material considered in the preceding sections allows a discussion of the role played by evolution of chirality in the general development of matter. The system of biological evolution according to A. I. Oparin can be schematically presented in the form shown in Figure 7.

The aspects of these evolutionary stages, associated with the development of chiral polarization will be briefly analyzed.

D.1. THE STAGE OF ORIGIN OF BIOLOGICALLY IMPORTANT MOLECULES

The possibility of symmetry breaking is essentially dependent on the physical structure of the medium in which the necessary transformations take place.

The gaseous phase, evidently, did not have a structure sufficiently cooperated for spontaneous symmetry breaking. The liquid phase may have displayed the minimum level of organization necessary for the realization of certain, although rather weak, elements of spontaneous origin of the asymmetry of reaction products. Through the use of nuclear magnetic resonance spectroscopy methods, success has been achieved in identifying both

local non-equivalence of L-L and L-D interactions of antipodes in liquid (Kabachnik *et al.*, 1976; Harger, 1977; Cung *et al.*, 1977) and, in a rather small but measurable degree, the statistics of the competition of antipodes in exchange processes. This competition is associated with a disturbance of homogeneity of the distribution of antipodes within the system (Morozov, 1976a).

Elements of such behaviour have also been detected at the chemical level (Wynberg and Feringa, 1976). Effects of this kind, which are capable, in principle, of leading to chiral polarization in the liquid phase (Morozov 1976a, 1977a), occur mainly in associated liquids. They provide conditions for the required aggregation of chiral material in exchange processes.

Ample opportunity for spontaneous chiral polarization effects is offered by the set of reactions in ordered liquids and liquid crystal media. It is known, for example (Buckingam *et al.*, 1969), that introducing microscopic chiral seeds into a symmetrical liquid crystal medium leads to the origin of macroscopic asymmetry of the mesophase as a whole, owing to torsioning of the cholesteric-type structure. Such medium structure may favour reactions to proceed predominantly in one (left-hand or right-hand) direction.

In principle, processes taking place *in the phase adsorbed on a solid surface* are endowed with the complex of factors required for symmetry breaking.

The series of reactions under definite conditions in this state may correspond to the behaviour with spontaneously broken symmetry (Bonner, 1972). One series of experiments may be noted, associated with the reaction of generating amino acids, which are catalyzed by a symmetrical surface (Isoda *et al.*, 1958). Through this work, in a series of experiments, optically active products have been observed to originate from achiral starting material.

In reactions proceeding with the isolation of a *solid phase* the effects of spontaneous splitting of racemates are sufficiently well-known (Secor, 1963) and are connected with individual aspects of the origin of asymmetry.

Under definite conditions, the reactions at this stage of evolution could have resources for chiral polarization originating within separate stretches of time and in separate reaction volumes. (On the whole in different sections, but the signs of the chiral polarization of separate parts had to be distributed statistically.)

D.2. THE STAGE OF ASSEMBLY OF MICROMOLECULES INTO MACROMOLECULES

This stage is fairly well investigated experimentally. As regards symmetry breaking, two important aspects of these processes may be noted – synthesis of polymers on symmetrical surfaces, and formation of a second spatial structure of the polymers.

S Akabori has considered a possible reaction for the synthesis of pre-protein macromolecules (Akabori, 1960a). The scheme includes condensation of polyglycine adsorbed on the symmetrical surface of kaolin and the subsequent reaction of substitution of side groups of glycine monomer units, which may lead to a whole series of amino acid

polymers. One of the main features of this synthesis is that polymer systems originating under symmetrical conditions contain mostly monomers of the same configuration. Explanation of this fact relates to the stage of binding polyglycine by the symmetrical surface. At this stage, achiral molecules of glycine (as one of the similar groups is nearer to and the other farther away from the surface) acquire chirality. At the same stage, steric conditions of the interaction of monomers with the similar virtual chirality are such that in bonding with the surface the polymer structure (the so-called *cis*-form of the adsorbed polymer) in accordance with the model of the spontaneously broken symmetry stabilizes the same chirality of all the monomer units. Subsequent substitution fixes this virtual chirality and standardization.

One of the main resources for the selection of monomers having the same chirality in the synthesis of macromolecules is the formation of a secondary spatial structure of polymers. The mechanism of this type may be called Wald's selection. G. Wald (1957) has taken into account two known circumstances of polymer chemistry: (a) the necessity of a secondary spatial structure (of α-helix type) for high rates and high degree of polymerization of polypeptides and their stable existence; (b) the impossibility of the existence of a stable spatial structure of such type without the monomers being used, having a sufficient degree of chiral purity. Generally speaking, this second requirement is not absolute. Wald has shown the connection between these factors to be a resource for the abiogenic synthesis of biologically important polymer systems – polypeptides and polynucleotides – to be accompanied by a standardization of chirality in the polymer chains being built. These processes have been studied sufficiently well experimentally, and their main properties are in fair agreement with the concepts about the mechanisms and conditions of spontaneous symmetry breaking (Morozov, 1977a).

The stages in the foregoing discussions prepared the molecular material for the evolution associated with higher levels in the hierarchy of the organization of matter. Needless to say, they did not have resources for the standardization of chirality in the entire evolutionary system. But the prepared material (within the scope of macromolecules or separate products of the reaction systems) had to standardize the chirality of smaller structural units.

D.3. THE STAGE OF COACERVATION OF MOLECULES AND OF FORMING PHASE-HETEROGENEOUS SYSTEMS

This stage is one of the main periods in the creation of the metabolic network, the development of which routed the development of living organisms. Such systems may be believed to create the best conditions for spontaneous chiral polarization. It may be hoped that the theoretical features of spontaneous mirror symmetry breaking in these processes will be investigated experimentally. There have been made, in particular, interesting experiments which demonstrate the possibility of chiral polarization of macroscopic quantities of a racemic liquid crystal (Young *et al.*, 1972). In this work it was observed that under definite conditions, the formation of more aggregated ordered areas

than forms in the rest of the medium, is connected with the predominant separation of one of the antipodes in it.

Analyzing the conditions under which this stage of evolution took place, one must consider the morphological process of both these aspects as a single whole, rather than treat the origin of optical asymmetry and phase-isolated protobiological systems as isolated processes. Different types of morphogenesis, shown in Figure 5, for one and the same 'genetic' structure of the system, are adapted to different external conditions. On the strength of the above, some speculations may be made and evidently substantiated experimentally, concerning the character of the external conditions enabling such a physico-chemical morphogenesis, the products of which are suitable for further evolution to metabolic systems capable of self-reproduction.

In the sphere of external parameters ($T > T_1$), the morphogenetic path is absent. In the sphere of ($T_2 < T < T_1$) with various relationships between the internal characteristics, there exists a path which leads either to inhomogeneities of the chiral polarization of the structureless medium or to elements of a spatial organization of racemic formations.

In the evolutionary sense such a path is unpromising, since in the absence of spatial coacervation it is impossible to conceive an evolution toward biochemical metabolism, while in the absence of chiral polarization, as it was shown in section B, there is no possibility for effective self-reproduction.

In the spheres ($T_3 < T < T_2$) and ($T < T_3$), the morphogenetic process is more complete. It is an interference of the chiral and structural morphogenesis. Two types of structures developing under these conditions substantially differ in their fitness for further evolution. Type (c), where chirality variations are realized on scales smaller than spatial inhomogeneities, offers material for a protoorganism in which separate parts are enriched with different antipodes. In view of difficulties to be encountered by such a system for building sufficiently chirally-homogeneous systems required for the development of self-reproduction, such a product of chemical morphogenesis is hardly adequate for further evolutionary stages.

In type (b) the size of coacervate formations is smaller than the scale of areas differing in chirality; this situation represents the spatial development of areas populated by chirally-homogeneous prebiological formations. In the light of reasons already discussed with this type of chemical morphogenesis a system originates which, on the one hand, is fit for development of a metabolic network, and, on the other, possesses a property (sufficient chiral homogeneity) prerequisite for the development of its self-reproduction.

D.4. THE STAGE OF EVOLUTION OF PREBIOLOGICAL SYSTEMS TO PRIMARY ORGANISMS AND OF FORMATION OF BIOCHEMICAL UNITY OF LIVING MATTER

This stage is a period during which the main features of the metabolic network self-reproduction have developed. The motive force in the process of selection and development of a metabolic network capable of self-reproducing at this stage (Oparin, 1957), was the

interaction of the initial systems (inherited from the preceding stages) with the external medium. Further, the mutual interaction of living systems, effected by way of exchanging the products of metabolism. This period – the transition from the pre- to the post-biological epoch – had formulated the biosphere as a self-reproducing system characterized by the biochemical unity of living matter.

Mirror symmetry breaking could take place only in separate parts of the physico-chemical system. The stage under consideration is decisive in the final breaking of mirror symmetry in the entire biosphere.

The main resources for this process could reside in the necessity, discussed in section B, for every metabolic system to have a homogeneous chirality for self-reproduction and the interactions of metabolic systems, which converted this requirement of individual organisms into an evolutionary requirement of their community.

Two aspects of this process are essential:

(1) The necessity for every self-reproducing system to use an identical chirality in the molecular apparatus of self-reproduction (which, as we now understand, is one of the main aspects of the protection of the self-reproduction process).

(2) The possibility of mutual poisoning with undesirable antipodes, when organisms employing material different of chirality start exchanging metabolic products, using long and complicated chains of chemical transformations.

Taking these aspects into account allows one to agree with the idea expressed by G. Wald, that a significant advantage exists, not only for each individual organism, but for the whole community in using a configurationally similar series of molecules. This idea was dramatically formulated by N. Pirie (1959): "In a competitive world that shop survives which standardizes the type of the screws employed, and organisms live in a competitive world."

Thus, the formation of biochemical unity of developing self-reproducing metabolic systems in the biosphere completes the picture of the spontaneous mirror symmetry breaking in molecular evolution.

From this point of view the observed total standardization of chirality in the modern biosphere may lead to the question "what asymmetry could cause this symmetry breaking?" but only if the evolutionary outlook on its origin is absent. The process that has broken the mirror in the molecular world of organisms proved to be the same molecular evolution which created life. The case would be different if it were possible to observe chiral forms of life on various planets. Then, provided that a predominance of one type of asymmetry were observed in the independently developing and non-interacting biospheres, the problem concerning the projection of fundamental asymmetry of the universe onto the molecular world could be posed again, proceeding from biochemical data.

At subsequent stages of biochemical evolution, the biological importance of chiral purity, discussed in section B having been taken into account, the selection of one enantiomer was responsible for the asymmetry of the molecular structure of organisms. When the presently observed system which is almost perfect in chiral purity was

established a perfect system of protecting it against changes in the processes of philo- and ontogenesis came into being.

Conclusion

The material presented above dispels doubts that the evolution of matter had both the need and the internal resources for creating such a type of biological ordering of organisms as the perfect chiral purity of biomolecular systems.

Only the basic principles of the concepts considered here are sufficiently substantiated theoretically and experimentally. Discussion of particular processes in which these resources can be realized is rather speculative in character. The theoretical concepts considered require integration with experimental material pertinent to different levels of the hierarchy of matter. Nevertheless, it is now clear that the strategy of these investigations must be not in the search for chances which may lead to the emergence of asymmetry, but in the study of the basic laws which link the processes of chiral evolution with the general evolutionary process and those processes for the functioning of modern organisms.

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