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COMMENTS ON THE ORIGIN OF CHIRALITY IN PROTEIN AMINO ACIDS

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ABSTRACT

We discuss chirality of protein amino acids from the point of view that it may have originated from a phase transition from a racemic mixture into an optically pure state, in which Bose-Einstein condensation may act as an amplification mechanism. The original theory is due to Salam. In the present work we suggest a new role for phase transitions in the context of biochemistry. Following Quack we distinguish parity violation of two kinds (*de facto* and *de lege* symmetry breaking). While the Salam phase transition corresponds to parity violation of the second kind *(de lege),* the phase transition we discuss in this work corresponds to parity violation of a third kind. This is suggested by recent experimental phenomena which correlate chiral symmetry breaking and pattern formation (spontaneous symmetry breaking that separate an initial racemic mixture into right- and left-handed space domains by means of the condensed medium). Tentative comments are given on the eventual design of possible experiments that may test this new hypothesis.

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1. THE ROLE OF BROKEN SYMMETRY IN BOTH INERT AND ANIMATED MATTER

Perhaps amongst the basic sciences one of the most intriguing problems is that of chemical evolution and its main consequence, namely the origin of life. One possible way to approach the outstanding questions in this field of research is with the help of symmetries. Broken symmetries, in particular, underlie the phenomenon of *cooperative phenomena*. This may be illustrated in the case of superconductivity. In general the role of broken symmetries is well understood in the properties of inert macroscopic matter (Anderson, 1972).

Molecules, on the other hand, behave rather differently from macroscopic matter in the sense that there are no sharp transitions between symmetric and asymmetric states in molecules (Barron, 1992). In condensed matter the situation is different, since there is the possibility of *cooperative effects*. Thus, in the solid state, for instance, we can observe rather sharp transitions between symmetric and asymmetric states of the complete macroscopic sample (cf., Sec. 4 below).

It seems evident that an important further stage in our understanding of the basic sciences in terms of symmetry concepts is to consider systems, such as the macromolecules of life, which are regular *but contain information* (which is at the basis of the fundamental step leading from chemistry to biology). This remark may be understood in terms of the four bases of the nucleic acids (T or U, C, A, and G)- the sequence of these symbols can encode a message, thereby a property of living organisms arises that goes beyond physics and chemistry, namely that of information (Eigen and Winkler-Oswatitsch, 1992). One possible way to approach these biological problems is to investigate extant relics of the primordial chemical (Barron, 1993a) and biological events (Chela-Flores, 1994). The chirality of protein amino acids is a universal phenomenon observed in organisms from all the kingdoms, from Monera to Animalia. Indeed, such universality has been referred to as the first principle of biochemistry (Crick, 1981). The study of possible origins of biochirality is the main subject of this work.

2. SOURCES OF THE OPTICAL PURITY OF PROTEIN AMINO ACIDS

The bases of chirality in biology (protein amino acids, sugars in nucleic acids, and lecithins in the cellular plasma membrane) are not well understood, in spite of many efforts spanning over 30 years. It still remains as an open question whether the optical purity of protein amino acids, in particular, is a result of at least one of the following possibilities:

- *Parity (P) violation [of the first kind], alternatively called 'de facto' symmetry breaking In such case the ground state does not show the same symmetry as the Hamiltonian; the two possible ground states are not completely stable, but instead they have a finite energy at which they interconvert by the tunnel effect* (Quack, 1993).

- *P violation [of the second kind] alternatively called 'de lege' symmetry breaking. This is due to P breaking in the Hamiltonian as, for instance, shown by the electroweak interaction* (Quack, 1993).

To these two cases we would like to add a further possibility,

- *P violation [of a third kind].*

This phenomenon is suggested by recent experiments which correlate chiral symmetry breaking and pattern formation. In other words, we maintain that this form of P breaking consists of spontaneous symmetry breaking that may separate an initial racemic mixture into right- and left-handed **space domains.** This phenomenon may be due to the affinity of the individual amino acids to the condensed medium that may be acting as a substrate to the racemic mixture. In such case spontaneous P breaking may be able to induce phase separation by the stability provided by the amino acid substrate.

We focus attention entirely on the breaking of the discrete P symmetry, since it can produce a difference in rates for enantiomeric processes. In fact, the electroweak interaction may be considered as a truly universal chiral influence in the sense of Barron (1986), i.e., P odd, T even. This is relevant both in reactions that have reached thermodynamic equilibrium, as well as in the case of kinetic control, in which case reactions have not yet reached equilibrium. In this situation we have unequal energy barriers for the production of chiral enantiomers from a prochiral molecule.

In principle, one would *a priori* anticipate certain difficulties arising from possible violations of microscopic reversibility (and the Principle of Detailed

Balance). Such anomaly may be expected in the physical cases in which T violation is taken into account. This may be understood simply by recalling that in the enunciation of microscopic reversibility molecular processes and their reverse (obtained by T reversal) will take place on the average at the same rate, provided in the definition of the two processes we use equal ranges in μ space [i.e., the phase space for any individual kind of molecule contained in the system, (Tolman, 1938)].

However, it has been demonstrated that no fundamental thermodynamic principles are violated even if we consider that T violation may induce differences in rate constants for enantiomeric processes (Barron, 1987).

Hence it is not under discussion whether, in principle, it is reasonable to search for the basis of phenomena governing the source of abiogenically produced L-amino acids that may have set biochemistry on its singular asymmetric mode in all organisms that are known to date.

3. PHYSICAL MECHANISMS FOR THE ATTAINMENT OF BIOLOGICAL CHIRALITY BASED ON THE BREAKDOWN OF P SYMMETRY

It is just for the reasons given in the previous section that we are entitled to restrict our search of further physical mechanisms for the attainment of chiral amino acid purity to the breakdown of the P symmetry. Further discrete symmetry violations to be incorporated eventually in the standard electroweak interaction theory, such as additional CP violating terms, probably can add no new elements to our discussion in view of the general validity of baryon number conservation, as follows from two recent papers of this topic (Barron, 1993b; Quack, 1993).

In view of the importance as we have argued so far, of studying the P-violating sources of chirality in biochemistry, a new possibility of retrieving optically pure amino acids from a racemic mixture should be given careful consideration. It has been suggested that protein amino acid chirality may occur by means of a phase transition induced by P violation of the second kind (Salam, 1991, Chela-Flores, 1991, Salam, 1992). The theoretical discussion of this important contribution should centre on whether there exist possible mechanisms for amplifying the rather small chiral bias (Ulbricht, 1981) underlying the phase transition theory. This point shall be touched upon in the following section.

4. COMMENTS ON BOSE-EINSTEIN CONDENSATION AS A NOVEL AMPLIFICATION MECHANISM

One of the principal difficulties in understanding the asymmetry of biomolecules is the question of the amplification mechanism that would boost a primordial small physical effect (Thiemann, 1981; Keszthelyi, 1981a; 1981b). New suggestions of amplification mechanisms should be considered in addition to the earlier possibilities such as those considered in the past:

(a) Amplification of the Vester-Ulbricht processes, namely amplification mechanisms that may apply to the interaction of polarized particles with biomolecules, and

(b) Amplification of the Yamagata processes, namely those processes (such as those discussed in this work) in which the breakdown of the dicrete P symmetry is considered as a possible source of biochirality.

In addition, we have:

(c) Amplification known as the Kondepoudi-Nelson catastrophic mechanism (Kondepoudi and Nelson, 1985), According to this proposal the small electroweak energy difference between the enantiomers is sufficient to determine which of the two single-enantiomer reaction sequences was adopted at the metastable stage in the flow reactor that is off thermodynamic equilibrium.

In the past Bose-Einstein condensation has been suggested to be relevant in the macromolecules that may have played a role in the origin of life (Chela-Flores, 1985). The recent seminal suggestion of Salam that Bose-Einstein condensation may act as a novel amplification mechanism still suffers from a difficulty: the underlying theory requires that large activation energy barriers be overcome in the process of turning a racemic mixture into optically pure amino acids. This requires that the phase transition may induce molecular changes that lead to the breaking of chemical bonds.

Amongst various options that the phase transition hypothesis may be faced with is that the origin of life may be extraterrestrial, provided that the critical temperature is too small for the phase transition to have been supported by the environment of the early Earth.

5.SPONTANEOUS SEPARATION OF CHIRAL PHASES IN CHEMICAL EVOLUTION AND THE ORIGIN OF LIFE

On the other hand, these difficulties should be balanced with many arguments that militate in favour of the Salam phase-transition theory (Chela-Flores, 1991). In the Salam suggestion the second order phase transition, due to P violation of the second kind, induces a racemic mixture into a chirally pure collection consisting of one enantiomer (preferentially stabilized by the P-violating weak neutral current interaction).

We would like to suggest the possibility of an alternative model incorporating P violation of the third kind, in which the phase transition acts on a racemic mixture of amino acids inducing *spontaneous separation* of the chiral phases due to the environment.

The ground states of the two optical pure phases are taken to differ in energy (the L-amino acid having the lower ground-state energy) according to the quantum chemistry calculations (Mason, 1992):

In fact, it has been found that a small electroweak energy increment adds to the binding energy of a given state in one enantiomer and subtracts from that of the corresponding state of the other, giving an electroweak binding energy difference ΔE_{ew} between the two optical isomers.

This rationalizes the observed bias of protein amino acids for the left-handed chirality, a phenomenon that has been preserved by biological (i.e., neodarwinian) evolution. The interpretation of the postulated phase transition provided in this note does not suffer from the difficulty of implying large activation energy barriers for the production of optically pure amino acid concentrations from an initial primordial racemic mixture.

If, on the other hand, extraterrestrial origin of biochirality is envisaged, a more compelling argument in favour of the present proposal is that, as pointed out above, molecules behave rather differently from macroscopic systems in the sense that,

> *There are no sharp transitions (such as those considered in the original Salam proposal) between symmetric and asymmetric states in (free) molecules.*

6. RELATION BETWEEN CHIRAL SYMMETRY VIOLATION AND PATTERN FORMATION

The BCS-like phase transition which we are now postulating to exist in the amino acids occurs at a certain critical temperature $T_{c.}$ Preliminary experiments reporting negative results (Navarro Gonzalez, *et al.,* 1993; Figureau *et al.,* 1993) have attempted to find the value of T_c for the original theory. This situation motivates the search of further insights into the sources of biochirality.

We are suggesting that one possible insight may be found in the connection between chiral symmetry breaking and pattern formation. This phenomenon has recently been the subject of significant progress:

It has been observed that two-dimensional liquids composed of achiral units can spontaneously separate into right- and left-handed regions. This induces a breakdown of natural mirror symmetry, an effect which is related to ferroelectricity at the interfaces (Schwartz, 1993).

However, one of the important aspects of these experiments is that a new example has been provided, in which structure and symmetry at the molecular level have implications at the macroscopic level.This phenomenon has been observed at molecular length scales in some experiments (Eckhardt *et al,* 1993). The molecular lattice of a racemic organic monolayer has been imaged and was observed to separate into separate chiral regions.

We assume that the connection between chiral symmetry breaking and pattern formation may occur in bulk three-dimensional systems such as amino acids.

A temperature gradient would induce a racemic mixture of amino acids, through the Bose-Einstein condensation into a regime of spontaneously broken mirror symmetry, in which the chiral phases may be separated. This, we conjecture, should manifest itself physically through pattern formation.

7. DISCUSSION AND CONCLUSIONS

A new generation of experiments are suggested with the use of, for instance, the scanning electron microscope. The purpose of these experiments would be the search of pattern formation due to the phase transition in a racemic mixture of amino acids in an appropriate substrate that may have been present on the early Earth, during the Hadean Era. This suggestion is in analogy with chiral symmetry breaking in

Langmuir monolayers and smectic films (Selinger *et al.,* 1993), as discussed in Sec. 6. Clearly, the present paper does not have a proper suggestion as to the specific nature of the appropriate primordial substrate of the amino acids, in which separation of their chiral phases may have occurred due to the phase transition. However, we cannot rule out the possibility that the electroweak interactions may have introduced a chiral bias to the substrate itself, and that the effect of the phase transition may be to enhance the affinity of the amino acid for the substrate.

In this context it is timely to recall that L-leucine and L-aspartate have been reported to bind stereospecifically to bentonite, which is a colloidal clay. This is a remarkable result since D-leucine and D-aspartate do not seem to exhibit any selective absorption in the same clay (Bondy and Harrington, 1979). Hence this type of experiment goes beyond the known result that polar organic molecules can be absorbed on clay mineral surfaces (Weiss, 1969). Yet work with Na-montmorillonite at various hydrogen ion concentrations failed to detect any protein amino acid adsorption. (Frieble *et al,* 1980, 1981). This approach is mentioned only as an illustration of how, subject to experimental verification, pattern formation may be studied in terms of a phase transition in a racemic mixture of amino acids, provided the mixture itself be in the presence of an appropriate physically realistic Archean substrate. From the evidence that we have reviewed it seems that other substrates may be considered.

A further example that may orient experiments on the phase transition comes from the fact that quartz crystals (one of the commonest minerals of the earth's crust - 12 per cent by volume) are enantiomorphic or rotary polar. This asymmetric property is caused by the spiral structures of silicon-oxygen tetrahedra in the crystalline form of quartz (Mottana *et al.,* 1983): This mineral has been studied for almost sixty years as a possible chiral environment. More recently attention has been paid to quartz as a possible source for the introduction of a bias into a previously racemic mixture of amino acids (Bonner, 1979). Such chiral physical force environments have been studied in terms of the absorption of DL amino acids on the surfaces of left- and right-handed quartz crystals, with the result that small net chirality may be generated this way, although this effect is quite small.

The purpose of the author in writing these comments is in the hope of highlighting the possibility of retaining the advantages of the amplification mechanism proposed by Salam, while focussing attention on a role of the novel phase transition (of the third kind) we are proposing in this paper.

This line of thinking avoids the considerable difficulty of overcoming large potential barriers, which the preliminary experiments have not seen. Indeed, according to Quack (1993), for chiral molecules the asymmetry in the effective potential induced by the P-violating effect (of the second kind) can be estimated to be of 20 orders of magnitudes smaller than the potential barriers themselves.

We would encourage others to throw some light on the nature of the possible chemical nature of the substrate (whether it may have been quartz, a colloidal clay or some other mineral substrate) that would support the putative amino acid phase separation due to the postulated P-violating effect of the third kind. This would be of invaluable help in the design of new experiments, possibly with the help of the scanning electron microscope in the search of characteristic pattern formation.

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