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On the Origin of Molecular "Handedness" in Living Systems*

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Summary. Elementary particle effects (β-decay) provide at best only a weakly handed radiation in the biologically effective energy ranges. Global magnetic effects coupled to sunlight are randomized by paleomagnetic reversals. Hence a persistent terrestrial handed bias at possible local biopoetic sites offers a more promising explanation for the origin of the "handedness" of the molecules found among living systems on earth. Magnetite in lava flows maintains a handed bias for surface catalysis through many magnetic reversals. Magnetite contaminated with sulfur has already been proposed by Granick as a biopoetic site because it provides a weak source of chemical energy derived by photochemical conversion. Indirect evidence for this hypothesis has been provided by the molecular structure of ferredoxin - a single strand of the 14 primordial amino acids wrapped around an FeS core. Lava flows have been suggested as biopoetic sites by Fox, since their temperature and chemical composition might allow for the rapid synthesis of prebiotic compounds at the surface of the primitive earth. The additional fact that magnetite in lava flows also provides a persistent handed site for surface catalysis offers a further argument for the experimental investigation of this specific biopoetic environment.

Key words: Asymmetry - Biopoesis - Chirality - Geomagnetism - Handedness - Lava Flows - Magnetite - Optical Activity

Any non-planar molecule containing four or more distinguishable atoms or groups separated by finite distances has a conceivable non-superposable mirror counterpart (Fig.1a). These enantiomers would (granting parity conservation in relevant

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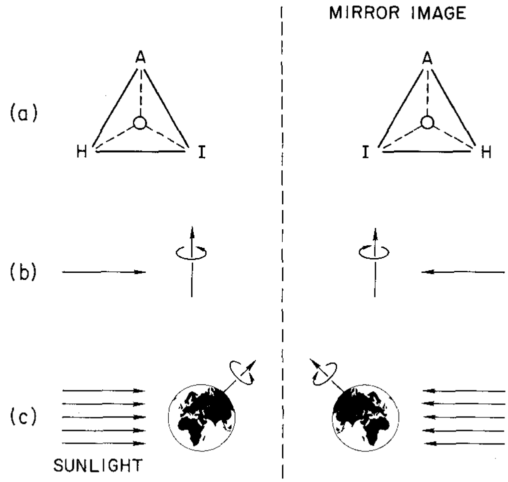

Fig.1
(a) Minimal three-dimensional configuration for non-superimposability: four distinguishable points not in a plane
(b) Minimal vectors required to distinguish left from right: a direction and an axis of rotation
(c) Illustration that our earth is handed both due to the relation between its axis of rotation and the direction of sunlight and due to the configuration of the continents with respect to the axis of rotation. The mirror image is not the world we live on in either respect

interactions) have identical energy levels in any reflection-invariant environment. Yet terrestrial living systems ordinarily use these parity-conserving interactions to organize a non-handed environment so as to enhance the occurrence of only one of two possible enantiomers. This property has even been advanced as a defining characteristic of life (Gause, 1941; Sayers & Eustace, 1930). Given a self-replicating molecule of one form, sufficiently stable to reproduce itself more than once (autocatalytic chain reaction) before degenerative processes reduce its molecular structure to an unbiased racemic mixture, there is no mystery why subsequent evolution from an original racemic environment should steadily increase the handedness of biologically active compounds. Nautral selection guarantees this statistically in the long run (Eigen, 1971). But proposed mechanisms for the origin of life from non-living matter (biopoesis) yield self-replicating systems of either handedness with approximately equal probability, and would thus result in two living ecosystems of opposite handedness competing for the same overall area but effectively isolated in terms of biologically active food supply. We know that interpenetrating ecosystems relying on different food chains are stable at higher levels of biological organization (Wald, 1957). The general theory of autocatalytic molecular evolution developed by Eigen (1971) suggests that in a single micro-environment only a single handedness can result from a single biopoetic event. Yet, this process could occur again at a geographically separated site, and if the time scale for diffusion from one biopoetic site to another is long enough, systems of opposite handedness could obviously result. Once established, one or the other system could achieve dominance and exterminate its enantiomeric competitor only by a selective advantage which depended on handedness. Mechanisms offering such selective advantage at the macroscopic level are even harder to conceive than mechanisms acting directly at the molecular level.

It life in fact originated in two enantiomeric forms, then a unique event at a later stage in evolution must have given a decisive selective advantage to one of them. R.Noyes (1972) has suggested that the development of photosynthesis relying on chlorophyll, which is associated either causally or temporally with the transition from a reducing to an oxidizing atmosphere around 3.2×10^9 years ago, could be such an event, since later photosynthetic life forms have several times the biochemical efficiency of more primitive forms. If this event was such as to imply a heritable handedness, then a selective advantage for one enantiomer would arise and lead to the inevitable evolution of biological compounds based on a single handedness. We are thus led to the conclusion that terrestrial life either originated on a primitive racemic basis, and that some subsequent unique handed event ultimately endowed one enantiomeric form with a great selective advantage at a later stage of evolution, or that there is some handed bias in the non-living environment sufficiently potent to favor the growth of one enantiomeric type at the expense of the other during the overall biopoetic process.

We turn our attention to the latter question of what type of handed environmental bias might have affected the origin of life. The minimal requirements for producing handedness are (a) that the environment contain two vectors, a polar vector defined by a line through two points and an axial vector defined by a rotation about some axis (since this suffices to distinguish left from right as is shown in Fig. 1b), and (b) that there be some specific mechanism by which this handedness can dominate over the statistical racemizing events in the biopoetic or evolutionary process. Prior to 1957, it was generally believed that the laws of nature are neither left nor right handed. Hence early speculations about the origin of handedness in biological compounds had to be connected to some macroscopic handedness of the terrestrial environment, such as those illustrated in Fig.1c, or relegated to the category of historical accident. But the discovery (Wu et al., 1957) that the β-decay of radioactive matter yields electrons of one dominant helicity, and consequently (via Bremsstrahlung) photons with a dominant handedness of circular polarization (Goldhaber et al., 1957) opened the possibility that this handedness of the environment could lead to handedness in biopoesis (Vester at al., 1959). Circularly polarized photons have been demonstrated to bias chemical reactions so as to produce a preponderance of molecules with one handedness (Kuhn et al., 1929, 1930a,b; Kagan et al., 1971; Bernstein et al., 1973) and theoretically this effect should persist down to the smallest intensities. Before a serious case for basing the origin of biological handedness on the non-conservation of parity can be made, however, it will have to be shown that (a) the handedness of the circularly polarized Bremsstrahlung will bias actual or hypothetical biopoetic reactions in the unique sense that will yield the observed handedness of terrestrial biological molecules, and that (b) such a bias will be of sufficient magnitude to override competitive racemizing effects.

A much less accessible way to make the β-decay hypothesis plausible would be the experimental demonstration that all living systems on planets which (like the earth) are composed of matter are of unique handedness (e.g. L-amino acids, D-sugars, etc.) while all living systems on planets composed of anti-matter are of the corresponding opposite handedness. This would be convincing since the helicity of electrons from the β-decay of anti-matter is the opposite of that of matter. Yet even were we to discover a biologically active planet composed of anti-matter, it would be a difficult object to study; any material probe would annihilate on contact. Since direct experimental proof for this origin of handedness in biopoesis will be hard to come by, we will confine ourselves to considering only macroscopic handed effects. One should bear in mind, however, that the bias produced by β-decay could be important, and that in the long run it could either enhance or mitigate against other biases in a unique direction.

The possibility of an environmental bias for the earth is easily seen, since the direction from the illuminated side of the earth to the sun provides a line while the earth's rotation provides an axis (Fig.1c). During the course of a year, the earth's axis changes by $\pm 23.5^{\circ}$ relative to this direction, but the average handed bias persists. As the sense of the revolution of the earth about the sun could not have changed since the solar system assumed approximately its present configuration without disrupting the orbits of the other planets, and as the sense of the earth's rotation about its own axis could not be significantly changed without releasing enough energy to destroy the surface of our planet, we assume that both have persisted for about 4.5×10^9 years (Stacey, 1969).

The existence of a macroscopic geometrical bias does not itself guarante a means for influencing the rates of chemical reactions. Thus most mechanisms which one can invoke do not reley on the rotation of the earth per se, but on the fact that the magnetic field of the earth is correlated in direction with the mechanical axis of rotation. For example, sunlight scattered by fluctuations in atmospheric density acquires both a linear polarization and, in the earth's magnetic field, a partial circular polarization; the handedness of the circular polarized scattered sunlight arriving at the surface of the earth persists throughout the period of illumination. Furthermore, chemical reactions taking place at the surface of the earth are influenced both by the local magnetic field and by the gravitational gradient, which again define a line and an axis. The effects of the gravitational gradient and the handedness of the magnetic field on reaction rates thus could provide a source of handed bias in the reaction products. Both of the above effects retain their sense throughout the day, but may vary differently with temperature and latitude. They could also couple to such macroscopic parameters as land-mass distribution and other geological features defined relative to the earth's axis of rotation. Thus to the extent that the earth's magnetic field is correlated with the direction of the earth's axis there could be a secular accumulation of reaction products of a particular handedness.

Unfortunately there is a difficulty connected with any mechanism which depends on the direction of the earth's magnetic field. It is now well established that the earth's magnetic field reverses polarity in a semi-random fashion (Cox, 1969; McElhinny, 1971). This fact, as well as the precession of the equinoxes, would appear also to negate Mörtberg's (1971) hypothesis for the abiotic origin of optical activity. Consequently, on the average, the handedness of the environment cancels out, except perhaps for macroscopic effects due to land-mass distribution. Since such geographical features shift only over periods of hundreds of millions of years due to continental formation and drift, they provide an environmental bias for much longer intervals than those between magnetic reversals. Thus, if we are looking for a very small but persistent handed bias, it appears that we might invoke the geographical asymmetry of the planet. The main difficulty here lies in imagining a mechanism by which these macroscopic features could couple in a handed way to a selective biopoetic process.

Although the arguments above do not lead to any very compelling model for the evolution of handedness, we present them both to review earlier speculations and to introduce a much more specific model for the origin of molecular handedness, which will be the focus of the remainder of this paper. Granick (1957) has proposed that the supply of chemical free energy, upon which any biopoetic process must rely, could be maintained steadily and over long periods of time by a particular inorganic system which substitutes for photosynthesis. This consists of magnetite crystals contaminated with sulfur which, when exposed to sunlight in an aqueous environment, concentrate electrons on one of the surfaces. Thus one surface of the mineral supplies energy for reduction reactions and the other for oxidation reactions. Prebiotic protein or nucleic acid polymers attached to such surfaces might therefore become active catalytic sites for further endothermic polymerizing reactions, and hence ultimately for self-replicating processes. Dramatic support for Granick's conjecture was subsequently provided by the discovery that all photosynthetic organisms retain to this day a molecule (ferredoxin) which functions as an electron carrier and consists of a single strand of protein wrapped around an Fe-S backbone (Tanaka et al., 1965). The primitive nature of this molecular fossil is clear from the fact that the amino acids in the chain comprise only those 14 amino acids which are coded for by the first two letters of the three-letter DNA codon, and not the remaining 6 amino acids which require all three letters. These 14 amino acids are arrived at by simpler metabolic pathways in the cell, while the remaining six require more complicated metabolic chains. Eigen (1971) makes it clear, both on grounds of chemical stability, and because of an evolutionary argument due to Crick, that the codon probably always consisted of three letters. But the metabolic fact mentioned above suggests that only the first two letters were used in the early stages of evolution. The fact that ferredoxin contains only the 14 amino acids of this early stage, an Fe-S chain, and is found with little variation in photosynthetic organisms thus provides indirect but powerfull evidence that it is a molecular fossil left over from Granick's mechanism for biopoesis.

The above focuses our attention on magnetite as a possible biopoetic site for an entirely different reason than the origin of handedness. However, magnetite crystals preserve, on the average, a magnetic axis aligned in the direction of the earth's magnetic field to which they were subjected at the time they were deposited. Being ferromagnetic, this local field at the surface of the crystals reinforces (in fact is much stronger than) the earth's magnetic field at precisely the spots where, if Granick's mechanism is viable, active biopoesis should occur. This could have a much stronger bias on the handedness of evolving molecules than any of the mechanisms considered above. To preserve a long-term bias it is necessary that this local field not reverse when the polarity of the earth's field reverses. In ore bodies the polarity of magnetite reverses with the changes of the polarity of the earth's field, but a percent or so bias persists. In the lava flows, the magnetization is frozen in and cannot be reversed by subsequent changes of the geomagnetic polarity (Cox, 1973). This fact is particularly interesting in that Fox (1964) has already proposed lava flows as the site of origin for many pre-biotic molecules. The polymerizing processes which he studied produce both peptide and nucleic acid chains at moderate temperatures and in brief time periods. Since in lava flows these processes would occur under a particular magnetic polarity, there might be a handed bias in the formation of these polymers. Thus particular geographic sites, active in early biopoesis, could acquire a prebiotic handedness which would persist through many reversals of the polarity of the earth's magnetic field. This long term persistence is important, since the aqueous environment within which the biopoetic processes occur could dry up and be reestablished many times before the threshold to self-replication was crossed, but now always carrying a secular increase in the unique handedness with each new episode. We therefore speculate, on the basis of the above lines of evidence, that the primordial biopoetic sites for the genesis of optically active prebiotic polymers might have been water pools containing magnetite produced by lava flows. We offer this hypothesis to our colleagues at this stage because it crosses many disciplines beyond our competence, and because we hope that it may stimulate both experimental and theoretical investigations in the future. We eagerly solicit criticism and discussion of these suggestions.

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REFERENCES

Bernstein, W.J., Calvin, M., Buchardt, O. (1973). J.Am.Chem.Soc. 95, 527
Cox, A. (1969). Sci. 163, 237
Cox, A. (1973). Private Communication to H.P.N.

Eigen, M. (1971). Naturwiss. 58, 465
Fox, S.W. (1964). Nature 201, 336
Gause, G.F. (1941). Optical activity and living matter, pp. 19-34. Normandy, Missouri: Biodynamica
Goldhaber, M., Grodzins, L., Sunyar, A.W. (1957). Phys.Rev. 106, 826
Granick, S. (1957). Ann.New York Acad.Sci. 69, 292
Kagan, H., Moradpour, A., Nicoud, J.F., Balavoine, G., Martin, R.H., Cosyn, J.P. (1971). Tetrahedron Letters 2479
Kuhn, W., Braun, E. (1929). Naturwiss. 17, 227
Kuhn, W., Knopf, E. (1930a). Z.physik.Chemie 7B, 292
Kuhn, W., Knopf, E. (1930b). Naturwiss. 18, 183
McElhinny, M.W. (1971). Sci. 172, 157
Mörtberg, L. (1971). Nature 232, 105
Noyes, R. (1972). Private Communication to H.P.N. (Aug.17)
Sayers, D.L., Eustace, R. (1930). The documents in the case. New York: Harper and Row Inc. A murder mystery whose solutions rests on the question of biologically generated optical activity.
Stacey, F.E. (1969). Physics of the earth. New York: Wiley
Tanaka, M., Benson, A.M., Mower, H.F., Yasunobu, K.T. (1965). None heme iron proteins, A. San Pietro, ed., pp. 221-224. Yellow Springs: Antioch Press
Vester, F., Ulbricht, T.L.V., Krauch, H. (1959). Naturwiss. 46, 68
Wald, G. (1957). Ann.New York Acad. Sci 69, 352
Wu, C.S., Ambler, E., Hayward, R.W., Hoppes, D.D., Hudson, R.P. (1957). Phys.Rev. 105, 1413

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