STATISTICAL FLUCTUATION VERSUS SPECIFIC MECHANISM AND THE ORIGIN OF THE LEFT-HANDED ASYMMETRY OF PROTEINS*

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Abstract. We point out an intrinsic weakness in the reasoning that adduces a statistical fluctuation as the origin of a left-handed, prebiotic stereoisomeric asymmetry which might have been the initial asymmetry that led to the left-handed asymmetry of proteins observed now on Earth. The argument in favor of a statistical fluctuation as the source of the asymmetry depends implicitly on the assumption of a very small number of terrestrial sites at which polymerization leading to protein formation took place. On the other hand, the probability that a left-handed prebiotic asymmetry produced by a specific mechanism was efficacious would have increased linearly with the number of terrestrial sites. Thus, on the basis of the greater likelihood of a large number of possible polymerization sites in the prebiotic era, a random fluctuation is deemed to be a much less probable source of a stereoisomeric asymmetry than a specific mechanism, particularly the mechanism that follows from the parity violating weak interaction.

1. Introduction

In an earlier paper [1] we explored the possibility that the almost complete left-handed stereoisomeric asymmetry observed in the protein molecules of living matter might be the result of a very small asymmetry induced, during the prebiotic era, in the monomer constituents of those molecules by a specific physical mechanism. Briefly, the mechanism suggested was that of Vester and Ulbricht [2] in which the interactions of electrons from nuclear beta-decay (having left-handed chirality) with the electrons of left-handed and right-handed chirality that were present in a racemic mixture of prebiotic monomers, e.g., amino acids, would have been slightly but not negligibly different for the two chiralities. Here, chirality is defined as the scalar product of electron spin and electron linear momentum.

One of the conclusions that followed from the analysis in [1] was that a very small, steady-state, left-handed prebiotic asymmetry, of order 10^{-8}, produced by the mechanism above, would have brought about an appreciable left-handed asymmetry in the proteins that largely completed their evolution after the end of the prebiotic era. A necessary condition for the efficacity of such a prebiotic asymmetry would have been the existence of a number of independent sites, 10^5–10^6 or more, at which accumulations of monomers were present and polymerization was possible. The asymmetry observed at present would then have resulted from chemical and biochemical processes building on that initial prebiotic asymmetry.

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An objection which might be raised against this conclusion is that such a small asymmetry, even if a steady-state condition, would have been overwhelmed by the random departures from strict racemic proportions. These departures could have occurred spontaneously at any site due to statistical fluctuations. Indeed, the occurrence of statistical fluctuations is often suggested as the actual means whereby a transient left-handed asymmetry, present purely by chance during the period of protein evolution, would have given rise to an initial asymmetry in the chain of events that led to the asymmetry observed now. For example, this suggestion was discussed more than fifty years ago by W. H. Mills [3]. One also finds it stated in passing in articles that survey the present understanding of the origin of life [4]. As still another more significant example, it has been the basis of models devised to explain the origin of the observed asymmetry by kinetic, nonlinear amplification of thermodynamic or other fluctuations in chemical processes [5].

There is, however, a simple but strong argument against fluctuations as the source of the initial asymmetry. To the best of our knowledge, this argument has not been applied explicitly to the subject addressed here. We wish in this note to discuss the argument and its implications.

2. Statistical Fluctuation

We assume that there were a number of independent, more or less spatially separated, sites at which chemical processes were taking place in the prebiotic 'soup' that occupied those sites. This assumption is necessary to indicate the absence of complete chemical continuity of the sites; i.e., to indicate the high probability that films or pools or lakes would have existed, as well as oceans, and that some of these would have been exposed to the decomposing effect of solar ultraviolet radiation while others, located in relatively isolated crevices or caves, would have been shielded from radiation and in reasonably stable temperature and humidity environments. It is useful to note for the purpose of illustration that 10^5 sites (see above) each of area, say, 100 cm^2 would constitute less than 10^{-11} of the surface area of a perfectly smooth Earth. Even in the larger sites, the rivers, ponds, and lakes, there probably would have been temperature and concentration gradients and different chemical compositions in passing from point to point.

Now, the assumed presence of chemically independent sites introduces a second variable (space) into the calculation of the effect of time-varying statistical fluctuations which significantly reduces the probability of an overall asymmetry of a given handedness arising from fluctuations. Most simply, this takes place because, at any site, it is equally likely that an excess of right-handed molecules will be present as that an excess of left-handed molecules will be present, due to a statistical fluctuation [6]. If these exhaust the total probability at a given site, and if there are n independent sites, then the probability that all n sites exhibit an excess of a given handedness at a given time is $(1/2)^n$, which rapidly becomes very small for increasing values of n. As a consequence, we are led to conclude that statistical fluctuations alone would give rise to

an equilibrium state in which the number of sites with left-handed excess would on average equal the number of sites with right-handed excess, providing the number of sites is not very small. If then one assumes, quite naturally, that polymerization and, ultimately, protein formation took place at a number of sites more or less simultaneously, the result is again, on average, equal numbers of right- and left-handed protein sites.

It follows then that to maintain the position in which left-handed dominance arose from a fluctuation-induced asymmetry requires the introduction of an arbitrary, non-statistical condition into what purports to be a strictly statistical phenomenon. Thus, to provide for such dominance, it is necessary to postulate a relatively small number of sites at which successful protein formation finally occurred. However, given a statistically significant number of independent sites, distributed randomly in chemical constitution, temperature, water content, pH, etc., there is no reason to assume that only one site, or only a very few sites, would have satisfied the conditions for successful polymerization wthin a finite time interval. Observe, again as a numerical illustration, that successful protein formation at as few as 20 sites would have reduced the probability of dominance by a single-handedness to $(1/2)^{20} = 10^{-6}$.

It is perhaps useful for the sake of emphasis to note that fluctuations at a given site might have been amplified so as to produce single-handed dominance at that site. Nevertheless, such an effect, if it took place at all, would not vitiate the conclusion reached above. For example, the number of, say, left-handed monomers present at any moment may have been larger than the mean value $\langle n_L \rangle$, the statistical standard deviation being $\langle n_L \rangle^{1/2}$, and similarly for right-handed monomers. Alternatively, a fluctuation may have come about because of polymerization processes, e.g., the transient formation and subsequent decay of a number of same-handed dimers, trimers, etc., which temporarily depleted the number of monomers of that handedness. It is conceivable that such fluctuations might have triggered some positive feedback mechanism [5] which would have contributed to an enhancement of the rate of production of polymers of a given handedness, and ultimately to local dominance of that handedness. In the absence of a parity-violating mechanism, and if more than a few independent sites existed, that dominance would again have been averaged out among the sites to yield equal numbers of left- and right-handed sites.

Of course, it cannot conclusively be ruled out that a statistical fluctuation at a single site was a precursor of the present asymmetry. Nevertheless, the requirement of a single site (or few sites) is arbitrary and not consistent with the assumption of a process dominated by statistics. In our opinion, the need for the restriction on the number of initial sites seriously weakens any attempt to account for the origin of a significant asymmetry by a statistical fluctuation.

3. Specific Mechanism

Indeed, the winner of the contest between a specific mechanism, such as polarized electrons from beta-decay, and a random fluctuation, would in large measure have

been determined by the magnitude of the number of independent sites that were present initially. If that number was of order 10^5 or more, then, as we claimed earlier [1], the effect of a small steady-state, prebiotic asymmetry $A(\sim 10^{-8})$ would have been significantly amplified; the amplification factor would have been N, where $N = n_1 n_2$ with n_1 ($\approx 10^3$) the number of chemical reactions or 'steps' in the polymerization process, and n_2 ($\approx 10^5$) the number of independent sites [7]. On the other hand, as we have shown above, the presence of even a relatively small number (e.g., 20) essentially independent initial sites would have very significantly diminished the probability that a statistical fluctuation was efficacious. For a small number of sites, the argument is inverted, as the limit of a single initial site demonstrates. Furthermore, the effective efficiency of the process of protein formation, averaged over many sites, need only be relatively small in magnitude, while that for very few sites must be of order unity, an improbable value for a statistical phenomenon.

As has been noted ([1], [2]), the sole parity (left-right) violating interaction known to be present in nature is the weak interaction which causes, among other things, the left-handed chirality of the negative electrons emitted in nuclear beta-decay. The cross-section for the parity-conserving electromagnetic interaction between an electron from beta-decay and a chiral electron in a stereoisomer is calculated (albeit with a crude model) to be smaller if both electrons have the same (in this case, left-handed) chirality than if their chiralities are opposite, i.e., left-handed for the (incident) beta-decay electron and right-handed for the (target) electron in the chiral molecule. Thus, the scattering of energetic beta-decay electrons by electrons in a racemic mixture of stereoisomers would lead to a larger decomposition (by ionization, etc.) of the right-handed stereoisomer than of the left-handed stereoisomer, and therefore to a resultant left-handed asymmetry.

We estimate that the resultant prebiotic asymmetry A is of the order 10^{-8}, or perhaps somewhat less [1]. In addition, the asymmetry $A(t_a)$ induced in present attempts to simulate the prebiotic situation in a laboratory experiment can be estimated [1] to be in the vicinity of 10^{-3} to 10^{-5} after a given time in an appropriately designed experiment ([1], [8]). An asymmetry of this magnitude induced in a racemic mixture would be undetectable by most current methods, which we believe accounts for the failure thus far of experiments aimed at producing and observing a positive effect in such a simulation [8]. In fact, the statistical fluctuations that occur randomly with time in any racemic sample employed in a laboratory experiment would generally exceed 1 part in 10^5, and would as a consequence mask the smaller, induced asymmetry unless asymmetry measurements were made continuously during the duration of the experiment.

4. Possible Experimental Method

What is needed is a method capable of continuous measurement of the stereoisomer content at the level of 1 part in 10^6 during the course of an experiment in which longitudinally polarized electrons irradiate a racemic sample. A method which suggests

itself is one in which the electron-bombarded gaseous sample is exposed to plane polarized light and the very small rotations of the plane of polarization are monitored frequently or perhaps even continuously. This technique is known to be capable of measuring angles of rotation of a plane of polarization as small as about 10^{-7} radian [9], and would therefore, in principle, be capable of measuring a steady fractional offset in polarization angle of magnitude corresponding to an asymmetry $A(t_a)$ of order 10^{-3} to 10^{-5}. To be numerically explicit, suppose each stereoisomer of a given racemic sample, if pure, would under appropriate circumstances rotate a plane of polarization by 1 radian. Then the rotation arising from a specific induced asymmetry $A(t_a)$ would lead to an angular displacement which, after a given time, would be of the order of 10^{-3} to 10^{-5} radian relative to the initial angle of rotation, and independent of fluctuations.

5. Summary

In this note we have pointed out an intrinsic weakness in the reasoning that adduces a statistical fluctuation as the origin of a left-handed, prebiotic stereoisomeric asymmetry. It is shown that the argument in favor of a statistical fluctuation as the asymmetry source depends critically on the implicit, arbitrary assumption of a very small number of sites at which the polymerization leading to protein formation took place; a large number of such sites, subject to independent statistical fluctuations, would have led on average to equal numbers of left-handed and right-handed sites. Thus, for instance, if there exist a number of planets in the universe that support life (presumably also based on the elements hydrogen, carbon, nitrogen and oxygen), and if the left- or right-handedness of the proteins or protein equivalents at each of those planets were the result of an initial statistical fluctuation, then we might expect, on average, equal numbers of planets with left-handed and right-handed protein dominance. On the other hand, the probability that a steady-state, prebiotic left-right asymmetry produced by a specific mechanism was efficacious would increase linearly with the number of planets, so that different planets would be characterized by proteins of the same handedness.

We are led to conclude, on the basis of the greater likelihood of a large number of possible polymerization sites on any one planet in the prebiotic era, that a random statistical fluctuation was a much less probable source of stereoisomeric asymmetry than a specific mechanism, particularly the mechanism that follows from the parity violating weak interaction.

References

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