MINIREVIEW

The Origin of Life and the Left-Handed Amino-Acid Excess: The Furthest Heavens and the Deepest Seas?

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The origin of life is an extraordinary problem that leads back to the structure and dynamics of the cosmos and early development of organic molecules. Within that wider question lies an unsolved problem that has troubled biologists for 150 years. What is the origin of the dominant presence of left-handed stereoisomers of amino acids in nature even though their synthesis normally results in an equal mixture of the right- and left-handed molecular forms? We propose that asymmetric Earth rotation caused at dawn and dusk circularly polarized UV light (CPUVL) of opposite polarity and reversed temperature profiles in the oceans. Destruction of the D-isomer by CPUVL at dusk in a sea surface hotter than at dawn created a daily L-isomer excess protected from radiation by nightfall, preserved by down-flow (diffusive, mechanical) into cold, darker regions, eventually initiating an L-amino-acid excess embodied in early marine forms. Innumerable mechanisms have been proposed for the origin of L-chiral dominance in amino acids and none proven. Since the thalidomide tragedy, homochirality of amino acids has been a growing practical issue for medicine. Understanding its origin may bring further and unexpected benefits. It may also be a modest pointer to the possibility of positive answers to whether intelligent life will have the capacity to continue to protect itself from conditions inimical to survival. Exp Biol Med 231:1587–1592, 2006

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Introduction

While the physicist ponders the uniqueness of singularity, the biologist addresses the equally nebulous problem of how life started and developed, two implausible events seemingly unrelated and each imbued with its own set of unknowns yet closely and inevitably intertwined, fueled by an increasing overlap of research in astronomic and geocentric physics, chemistry, and biology. When and how did life's macromolecules come to be on Earth? The pioneering work of Miller and Urey was the first to address, in an empiric way, organic compound synthesis in early Earth (1). This issue continues to attract attention, including modifications of the original work (2) and involvement of cosmic dust and other materials in protoplanetary systems (3). Essentially, a number of questions can be posed regarding the beginnings of life's macromolecules. Was it the result of universal or local events? In what earthly environment did they and life itself evolve? Is life's origin rooted in lightning strikes into a mass of organic molecules? What was the dividing point between the prebiotic and biotic periods? Did biotic development originate in an oxygen-lacking, reducing atmosphere present on Earth three or four billion years ago, much like that today in the outer planets of our solar system? The Earth's environment when life arose was very different from what it is today. We still do not have a clue as to what the first cells were like and how they formed, even though the age of the Earth and evidence of life has been dated on the basis of the presence of algae in Western Australian rock formations, and knowledge of the chemistry of macromolecular biochemical polymerization expands steadily.

Of additional interest are important issues, such as the hypothesis of panspermia (a cosmic location and possible

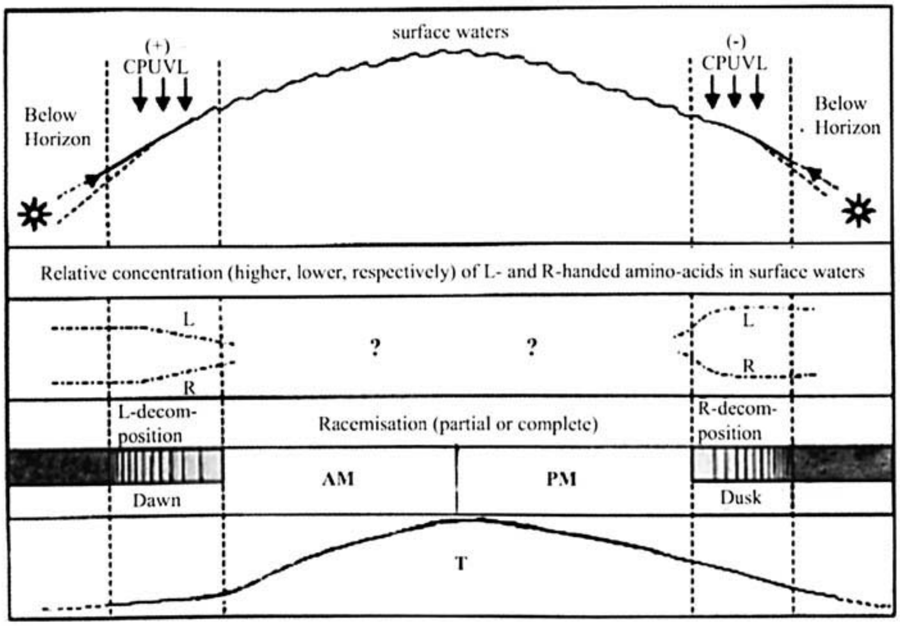

Figure 1. Schematic diagram of proposed diurnal differences in the relative concentration of right- and left-handed amino acids in prebiotic surface waters due to the asymmetric influence of Earth's unidirectional rotation on the combined effect of optical activity and temperature at dawn and dusk.

source of biochemistry and "life" as commonly defined) and the immediately critical issues of the role of Earth and its environment in not only the development but also the continued evolution of life (4) and in the origin of biological dominance of terrestrial, stereoisomeric left-handed amino acids. Although only a small segment of the large jigsaw of unknowns, the latter phenomenon is more than a center of scientific curiosity. It is the background to efforts of pharmaceutical chemists and engineers to avoid clinical tragedies and to improve drug efficiency by evading natural enzymatic destruction of potential medicines (5–7). It is also an established tool for aspects of biological, geological and climatological dating.

The Homochiral Conundrum

More than 150 years ago, Louis Pasteur demonstrated that generally only left-handed amino acids and right-handed sugars are of biochemical significance. The homochirality conundrum continues to attract attention and has been the study of many reviews and discussions (8–12). This one-handedness (homochirality), now critical in the structuring of genetic coding, may have been dominant from the earliest development of the latter. Certainly in most living organisms today, biochemical activity takes place in a framework of almost pure homochirality, the molecular conformations of L-amino-acids and D-sugars usually being preferred in nature over their respective enantiomers (mirror images), right-handed or left-handed, respectively (13). This is normally in contrast to *in vitro* production of amino acids, which at reaction equilibrium usually provides equal numbers of L- and D-acids.

One solution to the homochiral conundrum is that bio-organic material found its way to Earth *via* impacts of comets, meteorites, and dust particles during the first 100 million years of the solar system formation. However, an Earthly origin and evolution of genetic material can also be argued, beginning with local, raw organic materials and proceeding to the first building blocks, the precursors of nucleotides, nucleotide formation, the RNA precursors, RNA, and finally to DNA. This complex structural process certainly takes place now on Earth, and specific amino acids are an essential part of it. We should note that molecular evolution, at least as posed in Darwinian terms, is beyond the scope herein but clearly critical to this process (14–17).

It is noteworthy that an excess of L-amino acids has been found in certain meteorites (18), suggesting a cosmic preference for L-amino acids even before there was life on Earth. Local mechanisms, by which homochirality may have originated on Earth, have also long been suggested. These are added to from time to time, and a number of recent reviews have focused on this issue of chirality (19–22).

However, how an initial excess of L-amino acids came about and was maintained against rapid racemization due to high temperatures and solar and other radiation (23) remains a mystery. Initiation was either random (24) or brought about by a preexisting force or matter with an asymmetric attribute (13, 25).

We now propose that with the assistance of ocean bed morphology, two different mechanisms created a prebiotic excess of L-amino acids. Essentially, this thesis proposes that diurnal, asymmetric optical and temperature conditions caused by asymmetric (unidirectional) planetary rotation, together with a geomorphology conducive to the existence of deep, warm waters beneath colder higher layers, may have participated in an earthly origin of L-amino-acid essentiality (Fig. 1). The question of whether L-amino-acid excess was pre- or postbiotic in origin and of the part possibly played by polymerization processes in amplifying an initial, homochiral amino-acid excess will not be considered here. In line with many opinions, L-amino-acid excess will be assumed to have been prebiotic in origin.

An exhaustive review of the associated literature is not intended herein; however, we should note that between 1929 and 1945, several resolutions of racemates in solution were achieved by asymmetric photodestruction of one antipode alone because of its preferential absorption of energy from circularly polarized monochromatic light of opposite chirality (13, 26, 27). Furthermore, although all universal physical forces were once regarded as intrinsically symmetric and unable alone to discriminate between left- and right-handed chirality, the universal weak nuclear interaction has been found to show a left-handed asymmetry explainable in terms of elementary particle physics. Arising from this, electron polarizing effects have been calculated to be a cause of destabilization and lysis of only one of an enantiomeric pair. The weak nuclear interaction with the electromagnetic vectors creates an electroweak force that is regarded as the source of left-handed chiral excess (13, 28), as greater stability is imparted by it to the left-handed enantiomer. However, though published decades ago and much discussed, the minuscule calculated left-handed parity violation in respect of amino acids has not been confirmed experimentally (13, 28). Indeed, the scale of the results of the various mechanisms proposed to date for the initiation of selective chiral excess is so small that, without the existence of parallel processes for amplification of the results (29, 30) and for prevention of concurrent racemization, their significance is in doubt.

In light of the proposals here, it is also of specific interest that the latter universal physical asymmetry is claimed to support a cosmic origin for terrestrial left-handed biodomination (18, 26, 30, 31). Astronomical optical findings also may indicate a cosmic rather than a terrestrial origin (32, 33), but both approaches, terrestrial (including nonoptical candidates for initiation of homochirality) and cosmic, remain problematic, as does the survival of a presumed initial very minute chiral excess in the face of the known effects of one or more cosmic or terrestrial racemizing agents (18).

The overall uncertainty is compounded by an apparent total rejection by some of the possible involvement of circularly polarized light in the initiation of terrestrial homochirality (31). Even though the presence today of circularly polarized ultraviolet light (CPUVL) in the photic zone of Earth is relatively very small, it has not yet been shown to be less likely a cause of a significant homochiral excess under prebiotic conditions than electroweak asymmetry (13, 28, 34). Although circular dichroic wave bands of opposite sign follow each other at successive frequencies along the wavelength ordinate and cancel out, it was suggested but not stated as irrefutable that this prevented photoresolution of a racemic mixture of amino acids in dilute solution by broadband CP white light. Furthermore, it was also acknowledged that narrowband CP radiation as well as monochromatic can cause selective resolution of a racemic mixture (31). How narrow a "narrow band" may be will not be considered here. Work continues on the possible effect of UV circular polarization on organic molecules identified in specific cosmic conditions. This has suggested the existence of optical mechanisms for UV light polarization of a strength capable of providing an enantiomeric excess considerably greater than has been found under current terrestrial conditions (33) or has been taken into consideration in respect of the latter. The nature of prebiotic light radiation (which may have been more similar to the cosmic than to the terrestrial today) and other conditions then pertaining and of interactions between them are still too unclear to conclusively deny that CPUVL of a suitable bandwidth could have been involved in the initial creation of an excess of L-amino acids. The latter debate will also not be considered further, as it is not necessarily relevant to the model proposed here, as a whole. Also, even the strongest support for any specific, selective geochemical resolution of a racemic amino acid does not abrogate the possibility that a number of factors, independently or in concert, may have been involved in initiating terrestrial L-chiral dominance. Indeed, this is more likely true than not.

In the conditions of today, the UV light penetrating the atmosphere is limited, but it does penetrate into the sea, particularly away from the coastline, and exhibits considerable plane polarization due to aerosol scattering and reflection off the sea surface, particularly during the hours of low solar inclination (35). The circular component in polarization, whether due to molecular or aerosol scattering, was counterclockwise at dusk (a mean of –0.03%) with the sun inclined between 3° and 6° below the horizon (34). Although UV was not measured at dawn, it may reasonably be assumed that dawn CPUVL would be of opposite sign to that at dusk, as was found for the IR radiation. Innumerable littoral pools could also be a participant in the mechanism proposed here, as they would be regularly swept by evening tides caused by a variety of disturbances to hydrostatic equilibrium. If, as others have suggested, such pools were a source of high concentrations of amino acids due to evaporation and consequently also possibly a crystalline source of enantiomeric excess, evening tidal washing into deeper cooler waters could be protective against intense daytime destruction and racemization.

The proposed model integrates two different asymmetries resulting from the rotation of Earth: CPUVL with opposite signs at dawn and dusk and a sea with opposite temperature profiles at the start and end of daily solar radiation. As expected, the coldness of night water stretches into the dawn light; the hotter water of day continues into dusk, as is confirmed by parallel measurement of diurnal natural light and water temperature. The latter is important, as higher temperature increases the rate of photolysis. It is proposed that these asymmetries resulted in daily L-amino-acid excess at nightfall in the upper layer of the sea surface. As the suggested excess-creating process was initiated at a surface upper layer of sea covering most of Earth and the possibly minute excess was thence protected from racemization by a deep ocean sink, the small volume of the upper layer relative to the great bulk of the oceans would not, over eons, be of consequence for the mechanism proposed. CPUVL radiation of positive sign led to destruction of L-amino acids at dawn, but because of the relatively cold water temperatures going into sunrise, this would be less than the destruction of the D-isomer by CPUVL at dusk in a sea surface still at a temperature higher than that at dawn. Under racemic conditions of intense UV radiation, cosmic ionizing radiation, electric discharges, and peak midday surface temperatures, the daily excess-creating mechanism described above would not be likely, alone, to establish a particular chiral dominance. This would be true no matter how large or minute an excess was created by this or any other mechanism; it would need protection to accumulate. Each day, at least some of the L-isomer excess created at dusk was preserved by cooling of the waters and disappearance of solar radiation after nightfall.

The postulated preservative action would be reinforced during the night by a downward migration (diffusion and mechanical mixing) of the L-amino-acid excess into even colder, darker regions. These were deep enough to remain cold during the hottest prebiotic day and at a temperature at which even a residual racemization would almost cease. Thus, a daily stereoselection at sunset could have initiated an eventually irreversible asymmetry in the deep marine ratio of L- and D-amino-acid enantiomers. This would provide a cyclically replenished and eventually dominating supply of L-amino acids during the development of early marine life forms. The model is probably not unfavorable to views that life as we perceive it originated in a suitable proximity to deep hydrothermal sources. It will also be noted that any left-handed excess engendered by the electroweak force or by any other mechanism and still present at the sea surface at dusk would also be protected from racemization by this process.

The proposed model constitutes a dynamic process inviting computer and laboratory simulation. Most of the data are accessible quantitatively for testing its fundamental predictions, such as surface and subsurface UVL levels and circularity of CPUVL, racemization rate for amino acids in water, enantiomeric excess from asymmetric photolysis, and percentage of asymmetric photodecomposition. As was stated earlier, prebiotic conditions are still unknown, and ultimately all models will need to be tested under a wide range of conditions, including light quality and quantity, concentration, temperature, and pressure. These conditions must include extreme environments and in a nonequilibrium situation (such as would likely exist in respect of a deep ocean sink in accord with this hypothesis). The model also suggests another, later link with an eventual emergence of life from the ocean. Did the postulated downflow of a left-hand–dominated molecular stream provide an upward trail *via* which, because of population pressure on deep-sea essential L-amino acids, early life forms eventually migrated to the sea surface and shores—the first case of Malthusian economics?

A Wider View

The origin of chirality is but one example of the many enigmas important to the development of life and survival. These enigmas will be illustrated by several brief overviews that will reflect the relationships to the structure of the universe and possible relationships to the origin of life (23). First, according to our understanding of cosmic microwave background (CMB) data, the universe is nearly "flat" (36). This thesis constitutes the basis of a number of cosmological models wherein the average density of the universe is very close to the critical value. However, there is muted debate as to whether, during the early period of the universe, some curvature was required for it to expand. More critically, a flat universe demands a cosmology that contains matter far in excess of that currently found (i.e., the missing matter problem). Indeed, with evidence that the expansion of the universe is rapidly increasing, the problem with missing matter becomes even more dramatic. These two difficulties have been dealt with by introducing two *ad hoc* solutions: the existence of dark matter (DM) and the concept of dark energy, the use of which allows theory to conform with results at the cost of introducing a negative element (i.e., not any of the other categories of variables included in the theory). This poses the philosophical problem of the impossibility of proving a negative and draws the same skepticism that formed one of the bases of the attack on the Ptolemaic model of the heavens (e.g., the Byzantine proliferation of cycles, epicycles) to make it conform to data.

Second, one of the most difficult issues with respect to matter is the large amount of so-called missing mass, best exemplified by DM. The so-called dark matter describes matter that is unobservable but for its gravitational effects. Cold dark matter (CDM) has been used by a large number of laboratories to explain the large-scale structure of the universe (36). The data are based on a number of experimental observations, especially those on galaxies and large-scale structures and on CMB detection. However, the data on actual measurements of CDM, well summarized (37–39), do not fit with current models. Study of galaxies in a region within the first several kiloparcsecs reveals a density profile much less than current model simulations (40, 41) and again falls short of the mark.

Third, and as an example of overall structure, studies of dwarf galaxies in the local group reveal far fewer of them than one would expect in current models of CDM simulation. This again is particularly a problem in smaller masses (42, 43). When the best hydrodynamic simulations, with computer modeling, are used in the study of the halo properties of galaxies, the end result is that the galaxy disk is too small and has too little angular momentum for the latest observational data (40). Moreover, cosmological modeling that includes CDM yields cuspy halos that are too centrally concentrated (44). This is against the current cosmological dogma.

Fourth, the search for ways of making the existence of DM fit the observed data has led to further modification, such as either removing the cold properties of CDM or introducing more exotic assumptions, in order to permit the use of CDM to fit results to data on large scales while maintaining the fit of data with predictions on small scales. The only way this can occur is when fudge factors are introduced to explain the density in halo formation in CDM. This uses a cosmological constant called LCDM, or a tilted model called TLCDM (linear versus tilted linear CDM). However, such factors then require further modifications of standard cosmological constants (45). The use of DM has also led to a suggestion that Newtonian dynamics need modification (MOND). Although MOND may explain some of the problems with DM, it is still another fudge factor with its own pitfalls (46).

Fifth, any understanding of the origin of life may ultimately reflect back to the age of the universe. The use of Hubble's constant and data on a number of globular clusters suggests that some of those are considerably older than our current estimate of the universe. Again, arguments have been made to reconcile this with current theory but at the expense of introducing tweaks and adjustments that have limited or no support—outside of the fact that they allow the theory to be reconciled with the experimental findings. Evidence that the universe is diverse and exists differently today than in the distant past is based on the appearance of quasars. However, if red-shift data are correct, the majority of quasars thus far studied occupy a spherical annulus surrounding the Earth. This has implied to some that the Earth is near the center of the universe. The latter, while perhaps philosophically attractive to some, is extraordinarily unlikely and suggests that our understanding of quasars is either incomplete or incorrect, and therefore their use to assess the validity of the current cosmological model may be erroneous. Red shifts have been shown to be inaccurate for estimating galaxy distance because of velocities relative to the Hubble flow (47). This has led to assumptions about the geometric distribution in cosmological models, providing an additional artifact of anisotropy when applied at large distances. It is clear that large red shifts lead to distortions based on our current analysis, although these may someday be corrected by better empiric data. The implications of this can be significant and have been coined "the finger of God effect" (47). Other problems relate to an additional fudge factor, the so-called Great Attractor. This factor comes about because of unexplained, peculiar radially symmetric patterns of voids in deep red-shift galactic surveys from the Hubble space telescope, which also seem to show galaxies moving in the wrong direction when compared to cosmic microwave data.

Against the background outlined above of continuing uncertainty, even possibly confusion, concerning the most fundamental physical characteristics of the universe, current thoughts and concern on the origins of life or any of its elements remain speculative. In 1961, astronomer Frank Drake proposed a method for estimating the number of civilizations in the Milky Way that may be detectable from Earth. However, we should not forget the thesis that increasing intelligence is not necessarily advantageous for the survival of a species and, we could add, also of civilizations. Furthermore, without presupposing the nature of species or civilizations, if any, in the far reaches of the universe, a similar restriction on the development of intelligent life, if any, could also apply there. To some, the search for life on other planets, in other galaxies, is a pointless and unappreciated pursuit (48, 49). To others, it is a world of boundless curiosity (a characteristic itself possibly vital to survival), a world the future of which, like that on Earth, is dependent on the ability to respond to the environmental alterations that necessitate and determine evolution (50). The existence of life forms in the extremes of Earth's environment comes as no surprise to the biologist (51). The simpler a life form is, the more pliable it may be in face of environmental challenge. Understanding the fundamental principles of the biological issues, of which homochirality is but one, has far-reaching consequences.

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