CHIRALITY AND LIFE

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Abstract. The crucial role of homochirality and chiral homogeneity in the self-replication of contemporary biopolymers is emphasized, and the experimentally demonstrated advantages of these chirality attributes in simpler polymeric systems are summarized. The implausibility of life without chirality and hence of a biogenic scenario for the origin of chiral molecules is stressed, and chance and determinate abiotic mechanisms for the origin of chirality are reviewed briefly in the context of their potential viability on the primitive Earth. It is concluded that all such mechanisms would be non-viable, and that the turbulent prebiotic environment would require an ongoing extraterrestrial source for the accumulation of chiral molecules on the primitive Earth. A scenario is described wherein the circularly polarized ultraviolet synchrotron radiation from the neutron star remnants of supernovae engenders asymmetric photolysis of the racemic constituents in the organic mantles on interstellar dust grains, whereupon these chiral constituents are transported repetitively to the primitive Earth by direct accretion of the interstellar dust or through impacts of comets and asteroids.

1. The Crucial Role of Chirality and Chiral Purity

It is well known that the essential biopolymers associated with life are made up of chiral monomer units characterized both by unique homochiralities (*i.e.* L-amino acids occur in proteins and D-sugars in RNA and DNA) as well as by absolute chiral purity (*i.e.* no 'unnatural' enantiomeric D-amino acid or L-sugar monomer units are found in these biopolymers). Why are chirality and chiral homogeneity so fundamental for the existence of life? Two hallmarks of life, the synthesis of specific proteins mediated by DNA and RNA and the replication of DNAs to pass on genetic information, rely upon a precise fitting together (complementarity) of the polymeric chains involved. Two decades ago Miller and Orgel (1974) suggested that, while replicating double-stranded nucleic acids would be possible with either pure D- or pure L-ribotides, they would be impossible with *mixtures* of the two, and Goldanskii and Kuzmin (1988) later showed with molecular models that the substitution of 'unnatural' L-sugar enantiomers in double-stranded ribotide helices disrupted the H-bonding between their bases in such ways that complementarity was impossible. Joyce and coworkers (1984) have validated such conclusions experimentally with the demonstration that the template-directed oligomerizations of nucleotides by a chirally pure template proceeded readily if the monomers had the same chirality as the template, but was far less efficient with monomers of opposite chirality. Other examples of the importance of chiral purity during oligomerization are found in studies on the polymerization of γ-benzyl glutamate N-carboxyanhydride (NCA) into poly(γ-benzyl glutamate), where it has been shown that the introduction of D-glutamate units into the chain of the L-polymer weakened its α-helix secondary structure (Blout *et al.*, 1957), that the polymerization rate of DL-NCA was only

5% that of the enantiomerically pure L-NCA (Blout and Idelson, 1956), that a mixture of only 5% of L-NCA in 95% D-NCA polymerized only 1/3 as rapidly as did pure D-NCA, and that the degree of polymerization of DL-NCA was only 20% of that achievable with pure D-NCA (Idelson and Blout, 1958). Similar observations have been made by Weingarten (1958) in polymerizations involving the N-carboxy anhydrides of L- and DL-lysine, and by Kulkarni and Morawetz (1961) in the polymerization of methacrylglutamic acid. We have additionally found (Blair and Bonner, 1980) that partial polymerization of $D \neq L$ mixtures of leucine NCAs results in the preferential formation of the homochiral polymer, while Weber (1989) has recently observed that L-glyceric acid polymerizes more rapidly than does DL-glyceric acid, and that the yields of the L-polymer are markedly decreased when small amounts of D-monomer are present during polymerization. As regards polypeptides with β-sheet secondary structures made from alternating hydrophobic and hydrophilic monomers, Brack and Spach (1979) have concluded that monomers of opposite chirality progressively decreased the formation of β-structures as they were progressively introduced into the chains, and that the polymer itself consisted of β-sheet portions highly enriched in one enantiomer, with the remaining enantiomerically less pure chains in a random state. Such findings have made it abundantly clear that the chiral homogeneity of monomer units leads not only to vastly more rapid polymerization but also to higher yields of longer polymer chains, and that homochiral polymer chains form preferentially.

Additional advantages accrue to homochiral polymers over chirally heterogeneous polymers once they are formed. Thus Blair et al. (1981) found that homochiral poly-D- (or L-)-leucines were considerably more stable to hydrolytic degradation than was poly-DL-leucine, and that partial hydrolysis of leucine polymers made from an excess of one enantiomeric monomer resulted in the preferential hydrolysis of the less chirally homogeneous polymer constituents and the preservation of the more homochiral ones. Similarly, Brack and Spach (1980) observed that the random coil segments of their enantiomerically impure β-sheet polymers hydrolyzed preferentially, with the more homochiral segments being more stable. This greater hydrolytic stability of enantiomerically pure peptides has been emphasized as a factor in the possible abiotic enantiomeric enrichment of optically impure primitive polypeptides having either the α-helix (Blair and Bonner, 1981) or the β-sheet (Brack and Spach, 1981) secondary structure. Barbier and Brach (1992) have recently shown the importance of homochiral β-sheet or α-helix polypeptides in promoting the enzyme-like hydrolysis of oligoribonucleotides. Finally, it has been observed recently that a homochiral 16-unit self-complementary β-sheet oligopeptide is able to self-assemble spontaneously to form a stable macroscopic membrane, and it is speculated that such spontaneously formed membranes might compartmentalize and eventually establish closed environments for primitive metabolism (Zhang et al., 1993). It has not yet been established, however, if such spontaneous self-assembly into membranes can occur with analogous heterochiral polypeptides (Rich, 1993).

2. Chirality and the Prebiotic Environment

Pace (1991) has recently pointed out that speculations as to the origin of life have hitherto paid 'little heed to the constraints that might be imposed by the physical setting'. As will be apparent below, a similar criticism can be leveled at all hypotheses (and experiments) to date which pertain to the origin of chirality. Historically, from ideas proposed by Haldane and Oparin in the 1920s and experiments of Miller and Urey in the early 1950s, the 'dilute soup' scenario for the prebiotic environment and the origin of life has gradually developed (Shapiro, 1986). This argued that the action of such energy sources as lightning, solar radiation and radioactivity on the reducing atmosphere of the primitive Earth gave rise to the key molecules associated with life, and that these gradually accumulated in the primitive ocean to produce a dilute 'primordial soup' (devoid, incidentally, of chirality (Miller and Orgel, 1974)) from which life ultimately emerged. While this conventional primordial soup paradigm for the prebiotic 'physical setting' has proved comfortable and persistent, recent findings suggest a need for its drastic reappraisal, particularly as regards the need for chirality.

A significant peril to prebiotic chirality, of course, was racemization. Keszthelyi *et al.* (1979) have emphasized that process leading to chiral molecules must occur 'within a much shorter time interval than the racemization time', and Bada and Miller (1987) have estimated that the half-life for amino acid racemization is 10^5 – 10^6 years at ambient temperatures, rates which are dramatically increased in solution by metal ions, alkaline conditions and ionizing radiation (Bonner and Lemmon, 1978).

An even more formidable prebiotic nemesis to chirality, perhaps, was the primeval environment itself. It is now recognized that, contrary to providing a suitable locale for the life-nurturing 'warm little pond' of Darwin or an evolving 'primordial soup', the primitive Earth was a planet which 'endured rampant volcanism, scorching heat, and a murderous bombardment from comets and asteroids' during its first 700 million years (Waldrop, 1990), a conclusion recently featured as part of the cover story of a popular news magazine (Nash, 1993). Twenty years ago Sagan (1974) suggested that such conditions could shorten the period available for the origin of life to 'only a few hundred million years – perhaps much less', and later authors (Maher and Stevenson, 1988; Sleep *et al.*, 1989; Oberbeck and Fogelman, 1990) have concluded that the intervals between annihilating impacts became great enough for life to emerge and proliferate only about 3.8 Gyr ago, and that the maximum time needed for the subsequent origin of life was as little as 6 to 165 million years (Oberbeck and Fogelman, 1989). How much shorter, then, must have been the time interval available for development of the substantial homochirality imperative for primitive self-replicating biopolymers, and how might such chirality have originated?

3. Terrestrial Origins of Chirality

While the indispensable role of chirality has been largely ignored in most specula-
tive scenarios for the origin of life, the general association of molecular asymmetry
(chirality) with living matter has been appreciated since Pasteur (1860) pointed it
out over 130 years ago. It is thus not surprising that during the intervening years
numerous theories have been proposed and experiments undertaken bearing on
the the question of the origin of the first chiral molecules in Nature. We have
surveyed the literature pertaining to these questions exhaustively in four recent
reviews (Bonner, 1972, 1988, 1991, 1992), which should be consulted for greater
details. Here we shall merely summarize very briefly the more important aspects of
these theories and experiments, and endeavor to evaluate their intrinsic relevance
in the context of the current knowledge the prebiotic environment outlined above.
In doing so, we should bear in mind that mere logical hypotheses or even exper-
imental demonstrations of mechanisms which prove effective for creating chiral
molecules under contrived and controlled laboratory conditions might be totally
irrelevant in a realistic prebiotic setting.

3.1. BIOGENIC THEORIES

Hypotheses that life arose in a racemic environment and that homochirality devel-
oped only later have had numerous adherents during the past 60 years (see Bonner,
1972, 1988, 1991), and as late as 1987 it was argued that the origin of chiral
molecules on Earth 'must have occurred at the time of the origin of life or short-
ly thereafter' (Bada and Miller, 1987). It should be emphasized, however, that
there is no experimental evidence whatsoever supporting such speculations, and
the requirements of homochirality and chiral purity for the self-replication of
biopolymers would appear to render all such hypotheses quite untenable. Indeed,
as indicated above, both theoretical and experimental data support the early con-
tention of Terent'ev and Klabunovskii (1957) that 'life cannot and never could
exist without molecular dissymmetry', the more recent conclusions of Avetisov
et al. (1985, 1991) that even the simplest self-replicating systems could originate
only in a medium already possessing a high degree of chiral purity, and those of
Goldanskii and Kuzmin (1988) and Avetisov and Goldanskii (1991) that a biogenic
scenario for the emergence of chiral molecules is 'non-viable even in principle'.
In short, whether we are dealing with a 'DNA-world', a 'RNP-world', a 'RNA-
world', or a 'Pre-RNA-world' (Marcus and Olsen, 1991), all the evidence points
to one conclusion: No Chirality – No Life.

   The early panspermia hypothesis of Arrhenius (1903), postulating that life on
Earth originated by seeding with extraterrestrial microorganisms, has more recently
claimed both numerous adherents as well as detractors (see Bonner, 1991; Marcus
and Olsen, 1991). In any case, the hypothesis is inherently sterile in that it merely
displaces the origin of chirality and life to a more remote time and more distant
locale.

3.2. ABIOTIC RANDOM MECHANISMS

Random or chance mechanisms for the abiotic origin of chiral molecules are those which have an equal probability of producing an excess of either the D- or the L-enantiomer in the product formed.

3.2.1. Spontaneous Symmetry Breaking

Frank (1953) suggested a mechanism for spontaneous symmetry breaking in a system in which one enantiomer was a catalyst for its own production and an anticatalyst for that of its antipode, such that any random fluctuation in the 50:50 population of a racemic mixture would result kinetically in the eventual dominance of the enantiomer originally in slight excess and the disappearance of its antipode. Many analogous mathematical models, which contained feedback steps that amplified the randomly favored enantiomer, were subsequently proposed (see Bonner, 1988, 1991, 1994). Of such models only Calvin's (1969) scheme for 'Stereospecific Autocatalysis' has been validated experimentally, and that only in the context of spontaneous resolution under racemizing conditions. This involves the random crystallization of one enantiomer from a rapidly equilibrating mixture of enantiomers, with seeds of the crystalline product then acting as 'feedback catalyst' for further crystallization of the randomly selected enantiomer. The resulting '2nd Order Asymmetric Transformation', first demonstrated in this context by Havinga (1954), may in principle lead eventually to the total conversion of the racemate into crystals of the randomly preferred enantiomer. While this process has been demonstrated in several experimental systems, and while it has been shown capable of producing essentially optically pure products (Bonner, 1994), its prebiotic relevance is quite dubious however. Barring an unlikely immediately subsequent solid state reaction, the resolved crystalline enantiomer, produced by spontaneous resolution in its aqueous prebiotic environment, would necessarily racemize on redissolving before undergoing the next step of its chemical evolution in this environment.

3.2.2. Asymmetric Adsorption on Quartz

Asymmetric adsorption on quartz, the preferential adsorption of one enantiomer of a racemate onto one of the morphologically right-, (+)-, or left-handed, (−)-, crystal forms of quartz, was first proposed as potentially responsible for the origin of chiral molecules in Nature over 50 years ago (Karagounis and Coumoulos, 1938). Early reports claiming the successful partial resolution of racemates on exposure to (+)- or (−)-quartz were later challenged by Amariglio et al. (1968), who were unable to duplicate the positive observations and concluded that they resulted from experimental artifacts. Using D- and L-amino acids as 'prebiotically realistic substrates', we subsequently showed (Bonner et al., 1974, 1975) that the phenomenon was indeed a valid one provided that non-aqueous solvents were employed under conditions rigorously excluding moisture, results which were later

confirmed by others. However, the equal abundance of (+)- and (–)-quartz on Earth (Frondel, 1978; see Section 3.3.3.3) and the scrupulously anhydrous conditions required to enable the occurrence of measurable asymmetric adsorption on quartz render the mechanism totally implausible in any realistic prebiotic environment.

3.2.3. Asymmetric Adsorption and Polymerization on Clay Minerals

Early reports of the stereoselective adsorption of amino acids by kaolinite (Jackson, 1971) and of the stereoselective polymerization of aspartic acid catalyzed by kaolinite (Degens *et al.*, 1970) were subsequently shown to be erroneous using more definitive analytical techniques (Bonner and Flores, 1973, 1975; McCullough and Lemmon, 1974), and Freibele *et al.* (1981) were later unable to find any evidence for stereoselectivity in the adsorption of several amino acids onto montmorillonite under a variety of conditions. Analogous claims for the preferential binding of 'natural' D-sugars over their 'unnatural' enantiomers by montmorillonite (Bondy and Harrington, 1979) were likewise subsequently shown to be due to experimental artifacts (Youatt and Brown, 1981). Thus there is no experimental evidence whatsoever to date supporting any stereoselective effects on prochiral or racemic substrates attributable to clay minerals.

3.2.4. Solid State Asymmetric Synthesis in Chiral Crystals

Certain non-chiral organic substances may, like quartz, crystallize randomly as enantiomorphic crystals. If a non-chiral organic substance intimately incorporated into one form of such an enantiomorphic crystal can react with itself or with another symmetrical reagent to form a chiral product, the latter is found to be optically active. In short, the chirality of the crystal lattice imposes a preferred chirality on the products of such solid state reactions occurring within the crystal. The possible implication of such 'lattice-controlled' solid state asymmetric syntheses to the terrestrial origin of molecular chirality has been suggested by several authors, and the principles behind them have been extensively reviewed (Addadi and Lahav, 1979; Addadi *et al*, 1979; Green *et al*,, 1975, 1979; Ramamurthy and Venkatesan, 1987; Scheffer and Pokkuluri, 1991; Vaida *et al.*, 1991). Somewhat related asymmetric effects have been observed in asymmetric syntheses performed on surfaces of non-chiral centrosymmetric crystals which may be delineated by enantiotopic faces (Chenchaiah *et al.*, 1982; Vaida *et al.*, 1989), and the enantioselective occlusion of amino acids onto the enantiotopic faces of centrosymmetric glycine crystals has likewise been suggested as another mechanism for the origin and amplification of chirality (Addadi *et al.*, 1985; Weissbuch *et al.*, 1984, 1988). While stochastic processes such as those above are unquestionably capable of generating chiral products, they have invariably required either esoteric reactants and/or carefully contrived experimental conditions, which again would seem to make their relevance in a realistic prebiotic environment quite dubious at the least.

3.3. ABIOTIC DETERMINATE MECHANISMS

Determinate mechanisms for the abiotic origin of chirality presuppose that some non-random external chiral agent or force may influence the reactions of racemic or prochiral substrates in such ways as to yield products having a predetermined chirality. In short, the handedness of the external agent induces a specific chirality in the products of reactions occurring under the influence of the agent.

3.3.1. Electric, Magnetic and Gravitational Fields
In the mid–1800s Pasteur first investigated the possibility that magnetic and gravitational fields might induce the formation of chiral molecules, but his experiments were uniformly unsuccessful. Between 1939 and the mid–1980s a number of later investigators have claimed positive results in producing chiral molecules with both electric, magnetic, gravitational and centrifugal fields, either by themselves or in combination. These controversial experiments and conclusions have engendered considerable and sometimes acrimonious debate, and the 'successful' experiments have never been duplicated independently (see Bonner, 1988, 1991). Barron (1987), examining the above conflicting reports in terms of his concepts of 'true chirality' and 'false chirality', has pointed out that the above experiments involved fields characterized by 'false chirality' and would not be expected to induce the formation of chiral products in reactions which proceed to equilibrium. Later Takehashi *et al.* (1986) made the astonishing claim that asymmetric electrolytic reductions occurred at a mercury cathode with optical yields of up to 25% in a magnetic field of 0.168 T perpendicular to the cathode. These claims were subsequently refuted by Bonner (1990), who found that the products from such reductions were totally racemic even in a magnetic field of 7.05 T. He further emphasized the applicability of the 60 year-old dictum of Jaeger (1930) stressing that, to be effective, such externally applied fields must act not as mere accompanists, but must actually *initiate* the reactions in question, which would be impossible without them. Thus to date no experimentally substantiated asymmetric reactions have been observed under the external influence of any of the fields described above.

3.3.2. Circularly Polarized Light
Circularly polarized light (CPL), an electromagnetic wave whose electric vector traces a right- (RCPL) or left-handed spiral (LCPL) along its direction of propagation, on the other hand, does represent an agent characterized by 'true chirality'. Over 100 years ago both LeBel and van 't Hoff suggested that CPL might be responsible for the origin of chiral molecules in Nature, but it was not until 50 years later that Kuhn and Braun (1929) finally accomplished the first CPL-induced stereoselective reaction, the asymmetric photolysis of racemic ethyl α-bromopropionate, $CH_3CH(Br)COOC_2H_5$. Since that time innumerable successful experiments have been performed using R- and LCPL. Experimentally, CPL has proved capable of generating chiral molecules by any of three mechanisms: a) asymmetric pho-

toequilibration (partial photoresolution), b) photochemical asymmetric synthesis, and c) asymmetric photolysis. Asymmetric photoequilibrations and photochemical asymmetric syntheses are of negligible prebiotic relevance, since 1) they have been confined only to esoteric substrates having no apparent relation to biological systems, and 2) they are limited both practically and theoretically to the production of only trivial (< 1%) enantiomeric excesses (e.e.s). Asymmetric photolysis, on the other hand, the preferential photodestruction of one enantiomer of a racemate over the other by CPL, is potentially pertinent prebiotically since it is applicable to any racemic substrate having absorption bands in the visible or ultraviolet spectral regions. Since the two enantiomers of a racemate photolyze at different rates with CPL, interruption of the photolysis before completion yields a residue enriched in the more photostable enantiomer. E.e.s as high at 20% have been observed experimentally in the products of such photolyses, and much higher ones are possible theoretically (Balavoine *et al.*, 1974).

As to the availability of CPL at the surface of Earth, a number of CPL sources and production mechanisms have been suggested and/or observed, but all suffer from one or both of two disadvantages: 1) they are extremely weak both in the intensity and the net handedness of the CPL produced, and 2) they are subject to randomization over periods of time and/or with different geographical locations or geological features on Earth's surface (see Bonner, 1988, 1991; Bonner and Rubenstein, 1990). Thus even the well-documented and efficient process of asymmetric photolysis would probably prove ineffective in creating chiral molecules in the prebiotic *terrestrial* environment. Extraterrestrial CPL will be discussed later on.

3.3.3. Mechanisms Based on Parity Violation

These stem from the 1956 prediction of Lee and Yang that the principle of parity might be violated in 'weak interactions' such as those involved in the β-decay of certain radioactive isotopes. This prediction, verified experimentally a year later, has spawned numerous investigations regarding its possible applicability to the origin of the unique chirality of biomolecules, which itself represents a violation of the parity principle at the biological level.

3.3.3.1. The Vester-Ulbricht Hypothesis

In 1957 Vester and Ulbricht (Ulbricht, 1959) pointed out that longitudinally polarized electrons emitted with parity violation during β-decay produce circularly polarized 'Bremsstrahlen' photons when they impinge upon matter, and suggested that these in turn might induce stereoselective photochemical reactions by usual CPL processes such as those described above. Numerous investigators have tested this hypothesis by examining the products remaining after the irradiation of a variety of racemic substrates with the Bremsstrahlen from an assortment of radioactive β-ray sources (see Bonner, 1988, 1991). However, in none of these

investgations was there any evidence beyond experimental error for the formation of chiral products.

3.3.3.2. Direct Stereoselective Interactions with Chiral Particles

Supplementing the above experiments involving β-decay Bremsstrahlen, a number of investigations have been undertaken in search for *direct* stereoselective interactions of racemic substrates with a variety of artificially produced spin-polarized chiral subatomic particles, including electrons, protons, positrons and muons (see Bonner, 1988, 1991). None of the chiral particles examined, however, showed any reproducible evidence whatsoever beyond experimental error for stereoselective interactions with chiral organic or inorganic substrates, and as such would be of no prebiotic importance.

3.3.3.3. Parity Violating Energy Differences

Over 25 years ago Yamagata (1966) predicted that, due to the intrinsic parity violation in a pair of enantiomers (*i.e.* one is not composed of anti-matter), there should be a small 'parity violating energy difference' (PVED) between enantiomers. He also argued that this PVED should give rise to minute differences in the physical and chemical properties of enantiomers and that, properly 'accumulated', these consequences of the PVED might explain the configurational one-handedness of the biosphere. These ideas, subsequently elaborated and quantified (see Bonner, 1988, 1991), have led to the *ab initio* calculations that PVEDs favor the populations of 'natural' enantiomers (L-amino acids, D-sugars and their polymers) over their 'unnatural' mirror-image counterparts to the extent of *ca.* 1 part in 10^{17} (Mason and Tranter, 1985). This minuscule excess (which corresponds in magnitude to one star out of all the stars in a million of our 100-billion-star Milky Way galaxies, or one second out of all the time since our Solar System was formed) is then alleged by some yet undemonstrated mechanism to be capable of amplification to the present state of biomolecular homochirality.

Another alleged consequence of PVEDs (Mason, 1986) is the 1.4% excess of (–)-quartz (50.7%) over (+)-quartz (49.3%) reported for 17738 samples gathered world-wide (Palache *et al.*, 1962). We should appreciate that the standard deviation ($\pm \sqrt{n}$) from the strictly random (50:50) population of (–)-quartz in a sample of this size is ± 133.2. Since one would thus expect the random number of (–)-quartz samples in this collection to be 8869 ± 133 (*i.e.* $\pm 1.5\%$), we see that the 1.4% excess of (–)-quartz reported is within the standard deviation for the number of samples surveyed. Be that as it may, the alleged PVED-generated excess of (–)-quartz asserted above completely ignores a later study (Frondel, 1978) reporting 50.17% (+)- and 49.87% (–)-quartz in 27053 samples examined. We thus conclude that the terrestrial distribution of (+)- and (–)-quartz is random and offers no support whatsoever for the still-reiterated (MacDermott and Tranter, 1989) PVED-engendered excess of (–)-quartz.

The most recent suggestion for symmetry breaking based on PVED effects is that of Salam (1991), who postulated a Bose condensation phase change of 'unnatural' enantiomers into their allegedly more stable 'natural' configurations below some critical low temperature. Recent careful experiments subjecting racemic cystine to 0.1 K temperatures, however, have so far failed to detect the predicted phase transition (Figureau *et al.*, 1992).

We thus find no experimental evidence to date for any efficacy of PVEDs in producing enantiomeric excesses. Moreover, in view of the incredible minuteness calculated for PVED effects as well as the failure of all other pertinent experiments involving parity violation, we must tentatively agree with the conclusions of Goldanskii and Kuzmin (1988) and of Keszthelyi (1984) that all mechanisms based on parity violation are incapable of leading to prebiotic symmetry breaking or to the production of chiral molecules. These would thus have been ineffectual on the prebiotic Earth.

4. Chirality Amplification

While the above mechanisms for the generation of chirality would appear uniformly implausible or impossible on the primitive Earth, several have nevertheless been shown experimentally to be capable of generating small e.e.s. If any of these *were* operative in the prebiotic era, it is clear that additional abiotic mechanisms for the subsequent amplification of such small e.e.s must have been available to achieve the high degree of chiral homogeneity thought necessary for the emergence of self-replicating biopolymers. We have discussed the question of chirality amplification extensively (Bonner, 1988, 1991), and we mention here briefly the prebiotic relevance of only those mechanisms which have been validated experimentally.

Mathematical models involving autocatalytic feedback steps, originally proposed for the spontaneous generation of chirally pure molecules by random processes, would of course be equally applicable to the enrichment of small e.e.s resulting from determinate mechanisms. However, the only experimentally demonstrated autocatalytic amplification scheme, spontaneous resolution by crystallization under racemizing conditions, has been shown to be an implausibile mechanism in the prebiotic environment (Section 3.2.1). Other recently proposed schemes for the autocatalytic enrichment of e.e.s, which have had little or no experimental success and which are also quite unrealistic in the prebiotic environment have been reviewed recently (Bonner, 1994).

When an optically impure compound reacts incompletely with itself or with a second chiral substance, either the product or the unreacted starting material will have an e.e. greater than it had at the outset. Such e.e. enrichments by 'kinetic resolution', reviewed recently by Kagan and Fiaud (1988), however, have generally required specific and contrived experimental conditions for their success, making them also of dubious prebiotic relevance. The same criticism applies to the novel and efficient enantiomeric purification scheme reported by Lahav *et al.* (1976)

involving the difference of a topochemical solid-state photodimerization reaction of an enantiomeric crystal and racemic compounds.

Solubility differences between a racemate and its constituent enantiomers are known to permit e.e. enhancement during the partial evaporation of a solution or the partial precipitation of a solid from a solution where the original concentrations of the enantiomers are unequal. While these processes have been treated theoretically and observed experimentally in a few instances (Morowitz, 1969; Thiemann, 1974), they have not received extensive study. This is unfortunate, because such processes would intuitively appear as potentially viable in the prebiotic environment.

The most widely studied mechanism for the enhancement of small e.e.s is polymerization. Based on the original suggestion of Wald (1957) that the secondary α-helical structure of a growing polypeptide chain might dictate the subsequent selection of chirally similar amino acid monomers being incorporated into the chain, this mechanism has now been shown to result in e.e. enhancement during polymerizations resulting in both α-helix and β-sheet structures (see Section 1 above). Finding that the partial polymerization of a $D \neq L$ mixture of an amino acid (derivative) followed by the partial hydrolysis of the resulting polymer could result in truly impressive e.e. enrichment, Blair and Bonner (1981) later suggested that repetitive polymerization-hydrolysis reactions, driven by environmental dry-wet cycles, might serve as a mechanism for the abiotic genesis of homochiral polypeptides. While the amino acid derivatives used in the above polymerization studies of e.e. enhancement were clearly unrealistic for the prebiotic Earth, the fundamentals established suggested that such processes might be viable and would have the distinct advantage of leading in principle directly to the homochiral polymers of our current biosphere.

5. Extraterrestrial Sources of Terrestrial Chirality

If the various mechanisms discussed above for the *terrestrial* genesis of chiral molecules are either impotent *per se* or non-viable in the turbulent and hostile prebiotic enviornment, then we can only conclude that the origin of the chirality available on Earth during the brief time interval prior to life must have been both *extraterrestrial* and repetitive. Following the original suggestion of Oró (1961) that organic matter might have been transported from outer space to Earth by comets, it is now generally accepted that infalling exogenous organic material complemented terrestrially formed endogenous organics in providing the prebiotic precursors of biomolecules on Earth (Chyba and Sagan, 1992). Furthermore, Delsemme (1991–1992) has recently argued convincingly that late cometary impacts provided all of the molecules which now comprise the biosphere, including the atmosphere and oceans. Huebner and Boice (1991–1992) have concluded that the complex organic molecules in comets could have provided some prebiotic molecules which were essential for the origin of life, while Oberbeck and Aggarwal (1991–1992) have

proposed that comets may have been more important than endogenous agents for the initial evolution of amino acids.

Khasanov and Gladyshev (1980) were the first to suggest that *chiral* molecules might be formed in outer space by some unspecified 'conjoint stereospecific effect of a magnetic and other molecule-orienting field'. Three years later we proposed a detailed scenario for the production of chiral molecules on interstellar grains, followed by their transport to Earth (Rubenstein *et al.*, 1983; Bonner and Rubenstein, 1990). In this scenario the plasma of electrons around the neutron star remnant of a supernova are accelerated to near relativistic velocities by the prodigious electric fields, then constrained to move in a circular orbit by the colossal magnetic fields of the rapidly rotating neutron star, and thus emit polychromatic synchrotron radiation. Synchrotron photons are known to be plane polarized in the plane of the orbiting electrons, but elliptically and circularly polarized at angles above and (of opposite handedness) below the orbit plane. This situation would result in vast domains of space in the universe 'above' and 'below' the neutron star which would be illuminated by oppositely handed polarized synchrotron radiation of all, including photochemically relevant, wavelengths.

Greenberg (1984) has proposed a detailed hypothesis for the development of organic mantles on interstellar dust grains. He postulated that ultraviolet radiation causes the photolysis into free radicals of small interstellar molecules frozen as 'ices' on the dust grains, and that after slight warming these trapped radicals eventually recombine on the grains to form mantles containing larger, even polymeric, molecules. He later supported this hypothesis by conducting laboratory simulations of the first stages of the sequence, irradiating such frozen 'ices' with ultraviolet light at 10 K and obtaining artificial grain mantles containing numerous identifiable organic molecules, some of which were capable of chirality (Agarwal *et al.*, 1986; Briggs *et al.*, 1992).

We have combined these concepts into a unified scenario for the extraterrestrial formation of chiral molecules by postulating that the ultraviolet CPL components of the synchrotron radiation from the neutron star photolyze the racemic constituents of the organic mantles of interstellar grains in molecular clouds to form chiral molecules in the mantles by the familiar and efficient process of asymmetric photolysis, which Greenberg (1992) has recently found to be viable even at interstellar temperatures. Earth could then accrete these interstellar grains with their chiral mantles as the solar system passes periodically through the clouds while rotating about the center of our galaxy, and could thus accumulate vast quantities of exogenous organic matter with certain of its constituents having a uniform chirality, unracemized since formation due to the cold interstellar temperature. Another plausible mode of delivery might be the incorporation of such grains with their chiral mantles into comets or asteroids, followed by impact delivery to Earth during its turbulent prebiotic era. As regards asteroids and meteorite fragments, the presence of non-protein along with protein amino acids in the Murchison meteorite has been taken as indicative of their extraterrestrial origin, as has the fact that these

amino acids (and in particular isovaline, which is non-racemizable by α-proton abstraction), have proved to be approximately racemic (Kvenvolden *et al.*, 1971, Oró *et al.*, 1971). Our subsequent findings (Bonner *et al.*, 1979a,b) that amino acids, including isovaline, are highly subject to *radioracemization* by ionizing radiation, however, has led us to argue that the question of the primordial enantiomeric compositions of amino acids in meteorites is a fundamentally indeterminate one. The fascinating unconfirmed report of Engel *et al.* (1990) that L-alanine exceeds D-alanine by *ca.* 18% in the Murchison meteorite, with the ^{13}C content of each enantiomer consistent with an extraterrestrial origin, would, if substantiated, lend credence to the above scenario for the extraterrestrial generation of optically active amino acids. As regards comets, Chyba (1990) has suggested that the primitive oceans had a cometary origin, and Greenberg *et al.* (1989) have argued that the fluffy morphological structure of comets would provide a basis for their capability of delivering organic constituents to Earth in a form unmodified by the impact event. Thus it would seem likely that many of the uniformly chiral molecules in comets, formed as above and having low e.e.s, could be transported to Earth's primitive oceans with their enantiomeric compositions essentially pristine. The dilution of such extraterrestrial chiral molecules to insignificance by racemic terrestrial counterparts could, of course, be overcome by the ongoing influx of exogenous chiral molecules provided by repetitive cometary impacts during Earth's initial period of heavy bombardment. In any case, after whatever mode of delivery, the low e.e.s of such extraterrestrial chiral molecules could be subsequently enhanced terrestrially by suitable amplification, sequestration, and protection mechanisms into whatever state of homochirality was needed for rudimentary self-replication, thus finally setting the stage for the origin of life.

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