Electroweak Bioenantioselection

A. J. MacDermott

*Physical Chemistry Laboratory, University of Oxford, South Parks Road,
Oxford OX1 3QZ, U. K.*

and

G. E. Tranter

*Wellcome Research Laboratories, Wellcome Foundation, Beckenham,
Kent BR3 3BS, U. K.*

This paper reviews evidence for the view that biomolecular chirality was determined not by chance but by the electroweak interaction. Other influences (such as the Earth's magnetic and gravitational fields, or circularly polarized light) are either falsely chiral or else even-handed on a time and space average, leaving the weak interaction as the only consistent universal chiral influence. Electroweak bioenantioselection could occur either through β-radiolysis or through the small parity-violating energy differences (PVED) between enantiomers. The PVED produces an electroweak enantiomeric excess of only 10^{-17}, but this can be amplified to homochirality within 10^4 years by the powerful Kondepudi mechanism. Calculations of the PVED show that the natural L-amino acids are more stable than their »unnatural« D-enantiomers, and natural D-glyceraldehyde and D-deoxyribose are also PVED-stabilized. The PVED can also explain the observed 1% excess of 1(—)-quartz, which, through pre-biotic mineral catalysis, could increase the electroweak enantiomeric excess to 10^{-4}.

1. INTRODUCTION

One of the hallmarks of life is its homochirality, terrestrial biochemistry being based on the L-amino acids and D-sugars to the virtual exclusion of their »unnatural« enantiomers, the D-amino acids and L-sugars. Despite this dominance of the »natural« enantiomers — the ratio of D- to L-glucose on Earth being estimated[1] as at least $10^{15} : 1$ — a few »unnatural« D-amino acids and L-sugars do occur with specific roles, as in bacterial cell walls (but not bacterial protein or nucleic acids) and antibiotics,[2,3] although the genetic nated by special enzymes, *e. g.* the ubiquitous D-amino acid oxidases;[6] there racemization of the L form.[4,5] Even in these cases homochirality is maintained, with the usually dominating enantiomers being excluded. The importance of homochirality in biological systems is underlined by the fact that the »unnatural« enantiomers often have destructive effects and must be eliminated by special enzymes, *e. g.* the ubiquitous D-amino acid oxidases;[6] there

is also speculation that molecules of the »wrong« chirality may play a role in the processes of ageing and carcinogenesis.[2,6]

An almost homochiral prebiotic chemistry is probably essential for the emergence of life because polymerization to form stereoregular biopolymers — in particular poly-D-ribonucleotides[7] and poly-L-peptides[8,9,10] — is found to proceed efficiently only in optically pure monomer solutions because addition of the »wrong« enantiomer to the growing chain tends to terminate the polymerization. Homochirality is certainly essential for an efficient metabolism, like the universal adoption of right-handed screws in engineering, and this was recognized by Fischer in his stereochemical »lock and key« hypothesis,[11] which showed that initial selection of a particular enantiomer in ancestral biomolecules would fix the handedness of the rest of biochemistry through diastereomeric interactions. There is evidence for such a diastereomeric connection between the L-amino acids and the D-sugars (for example through the conversion of D-glucosamine to L-alanine,[12] and, more generally, through the evolution of the genetic code[13]) which would seem to preclude a D-amino acid/D-sugar or L-amino acid/L-sugar biochemistry. Mirror-image D-amino acid/L-sugar life should, however, be just as viable as natural L-amino acid/D-sugar life, so the question arises as to whether selection of the latter was a »frozen accident«,[14,15] or as Pasteur believed,[16-18] the result of some universal chiral influence.

The universe is indeed pervaded by dissymmetry at many levels: Pasteur, who first established the connection between molecular and crystal dissymmetry in his famous resolution of tartrate crystals,[19] also noticed that the solar system is non-superimposable on its mirror image,[20] and it is now known that there is a predominance among spiral galaxies of rotation to the left with respect to the direction of recession.[21-23] More speculatively, the dominance of left cheeks in portraits[24] could be related to left-right brain asymmetry.

Past candidates for a chirally selective influence on biochemistry have included such supposedly chiral combinations as the Earth's magnetic and gravitational fields, or the Coriolis force and gravity. However, these influences can probably now be discounted because they are »falsely chiral« according to Barron's new definition of chirality.[25-27] A »truly« chiral system is one that exists in two distinct enantiomeric states that are interconverted by parity (space inversion) but not by time reversal. The hallmark of »true« chirality is natural optical rotation, which changes sign under space inversion but not under time reversal, that is, it is parity-odd, time-even. Absolute asymmetric synthesis can therefore be induced only by something with this same symmetry. Pasteur thought a magnetic field could be a chiral influence, but in fact its chirality is false because it is parity-even (being an axial vector) and time-odd (imagine it generated by a circular motion of electrons, which changes direction under time reversal). Curie first suggested[28] that collinear magnetic and electric fields might provide a chiral influence but again the chirality is false because the magnetic field is parity-even, time-odd, and the electric field parity-odd, time-even, giving overall a parity-odd, time-odd influence. It is therefore likely that experiments claiming asymmetric synthesis in this way[29]— or analogously from stirring (parity-even, time-odd) in the Earth's gravitational field (parity-odd, time-even)[30-32] — can be disco-

unted. However, it has recently been suggested[25,27,33,34] that these experiments should be re-evaluated because falsely chiral influences may be sufficient for asymmetric synthesis under conditions of kinetic rather than thermodynamic control. This is supposedly because under non-equilibrium conditions the changing entropy confers a preferred time direction which destroys any time-reversal symmetry,[35] but this view has been disputed.[36,37]

A good new example of a truly chiral influence is a uniform magnetic field (parity-even, time-odd) parallel to a (not necessarily polarized) light beam (parity-odd, time-odd), giving overall a parity-odd, time-even influence potentially capable of inducing asymmetric synthesis.[38–41] Recent preliminary results appeared to demonstrate this effect in the synthesis of hexahelicene,[42] more L molecules being obtained with the field parallel to the light beam, and more D with the field antiparallel. However the enantiomeric excess, at 0.07%, was just at the limits of detectability, and there has been some difficulty in reproducing the results. (We shall refer here to the asymmetry factor, $(L—D)/(L+D)$, of a chiral influence, meaning the enantiomeric excess or degree of polarization as appropriate.) Also, work on magnetic field effects employs large fields of about 1 T, compared with the terrestrial field of only 5×10^{-5} T.

A classic truly chiral influence is of course the circularly polarized photon, the enantioselective properties of which are well established.[43–45] Unfortunately, however, there is overall no natural predominance of either of the two circular components in the solar radiation reaching the Earth. Sunlight scattered from Jupiter and the other planets has a circular polarization of up to 0.01%, with oppositely-signed contributions from the northern and southern planetary hemispheres.[46] Sunlight reflected from the oceans in the Earth's magnetic field becomes elliptically polarized,[47,48] but equally and oppositely so in the northern and southern hemispheres. Recent measurements show that sunlight becomes about 0.1% circularly polarized at twilight as a result of multiple aerosol scattering, but equally and oppositely so at dawn and dusk, with the right circularly polarized component in excess at sunrise. This effect is particularly pronounced in the red and near infrared region,[49] but also occurs in the photochemically more significant visible and near UV region.[50] The overall even-handedness of this effect could be broken under certain special conditions, e. g. a pool of racemic amino acids on an east-facing mountain slope would be exposed preferentially to the right circular excess of solar radiation at sunrise, and — according to recent reports of asymmetric photolysis of racemic amino acids with circularly polarized 200—230 nm radiation[51,52] — could be expected to undergo enantioselective photolysis leaving the »natural« L-enantiomer in excess. This is no more than a »frozen accident« explanation, because life could equally have started in a pool on a west-facing slope, with the opposite effect.

Very recent measurements[53] indicate that in 1986 the slight right circular polarization of light from the north pole of the sun was not quite cancelled out by the corresponding left circular polarization of light from the south pole, leaving overall an excess right circular polarization of 10^{-6}. This effect is, however, transient, being influenced by the sun's magnetic field and sunspot cycle, with the sign of the excess polarization reversing every 11 years. It therefore could not have influenced biomolecular chirality unless biogenesis

occurred much more rapidly than generally believed — although the structure, strength and periodicity of the sun's magnetic field could have been different 3 billion years ago.

However, despite all these interesting possibilities afforded by sunlight, it must be borne in mind that the Kuhn-Condon sum rule for rotational strengths, $\Sigma_a R_{oa} = 0$, rules out a photochemical origin for biomolecular handendness from any broad-band source: the enantioselective effect of one CD band will be cancelled by that of another band of opposite sign, so that any effect averages to zero over the spectrum as a whole. Chiral photosynthesis therefore requires almost monochromatic light tuned to the wavelength of a major CD band maximum. The overall even-handedness of photosynthesis from a broad-band source could however be broken under certain special conditions, e. g. if there was only one absorption band which led to reaction, light from CD bands of opposite sign having no effect on the molecule.

2. THE WEAK INTERACTION: A TRULY CHIRAL UNIVERSAL INFLUENCE

Pasteur was correct in thinking that there is a universal chiral influence, because it is now known that elementary particles themselves have a handedness which is felt by the weak interaction. Fermions exist in two states of opposite helicity,[54] which are interconverted by parity, and correspond to spin and momentum vectors parallel (right-handed) or anti-parallel (left-handed). The two helicity states participate equally in the parity-conserving electromagnetic and strong interactions, which therefore do not feel the handedness of fermions, seeing them as »racemic«. However the weak interaction is parity-violating, as predicted in 1956 by Lee and Yang[55] and rapidly confirmed by observations of the handedness of β-decay electrons.[56] The two fermion helicity states do *not* participate equally in the weak interaction, which therefore sees fermions not as »racemic« but as more one hand than the other, to an extent proportional to v/c, the velocity of the fermions relative to the velocity of light.

Parity (P) is therefore violated since the weak interaction can distinguish the two helicity states — but CP (parity plus charge conjugation) is not violated, as it turns out that if a left-handed fermion participates preferentially (compared with the right-handed fermion) in the weak interaction, then the corresponding right-handed anti-fermion will participate preferentially (compared with the left-handed anti-fermion) to the same degree. As far as the weak interaction is concerned, therefore, particles and anti-particles have opposite handedness, and the dissymmetry that pervades the universe is therefore the fact that it is made of matter rather than anti-matter.

Barron's definition of true chirality has therefore been extended[26] so that true enantiomers are interconverted not by P, but by CP. Thus the true enantiomer of a left-handed electron is not a right-handed electron, but a right-handed positron. Radioactive β-decay — in which the parity-violating nature of the weak interaction was first confirmed[56] — is the decay of a neutron *via* the weak interaction into a proton, an electron and an anti-neutrino, and produces an excess, in proportion to v/c, of electrons with left-handed spin-polarization. The corresponding mirror-image process involving anti-particles would produce a corresponding excess of positrons with right-

handed spin-polarization. The electromagnetic and weak interactions were unified in 1967,[57,58] and whereas the former are mediated by massless photons, the latter are mediated by the massive $W^{\pm}$ and Z° bosons recently detected at CERN[59] and so are weak and very short range.

Although the weak interactions are weak, their parity-violating effects are all-pervading. Thus all atoms and achiral molecules are predicted to be very slightly optically active owing to the handedness of their constituent elementary particles.[60,61] Similarly, left and right-handed chiral molecules are not true enantiomers, but diastereoisomers: the true enantiomer of an L-amino acid is the D-amino acid made of anti-matter.[62] Left and right-handed molecules should therefore differ in, among other things, NMR chemical shifts, although these are just below current detection limits.[63]

In atoms, the weak interaction mixes states of opposite parity, notably s and p orbitals, so that Laporte's g—u rule for electric dipole transitions is no longer strictly valid. Further, a g—g or u—u magnetic dipole transition now has a small collinear electric dipole moment from the s—p mixing, and so the transition becomes optically active. This electroweak optical activity of free atoms is expected to be proportional to Z^6, where Z is the atomic number, and experimental studies of gas phase heavy metal atoms such as Tl, Pb, Bi and Cs give an optical rotation of the expected sign and order of magnitude.[64]

As a result of electroweak optical activity, the rotational strengths of two enantiomeric molecules, although oppositely signed, are no longer equal in magnitude, since the contribution of the common constituent atoms has the same sign for both enantiomers. This means that the circular dichroism is not quite the same for the two enantiomers, and so photochemical enantioselection is possible even with unpolarized light, especially since this efect of the weak interaction is present constantly, and so may be cumulative over extended time periods. The resulting enantiomeric excess is expected to be about 10^{-14} for light-atom biomolecules, and 10^{-7} for their complexes with heavy atoms.[65]

The symmetry-breaking effects of the weak interactions are very small, but could be amplified (see section 3) to produce today's homochiral biochemistry. The largest effect is the differential radiolysis of left and right-handed molecules by the predominantly left-handed electrons from β-decay.[66,67] Campbell and Farago[68] have recently reported differential absorption by camphor vapour of beams of left and right helically polarized 5-eV electrons, which gave an unexpectedly large asymmetry factor of 10^{-4} with an electron beam of 0.5% excess left helicity. Unfortunately there are problems in extrapolating this laboratory result to bioenantioselection in nature. β-Decay electrons are produced at relativistic velocities, and if they are to have any enantioselective effect they must be decelerated to energies gentle enough not to destroy the molecules indiscriminately. This is done very carefully in the laboratory, to preserve the helicity (which incidentally is proportional to the value of v/c at the moment of production of the β-electron, and not, as frequently misunderstood, to the instantaneous value at later times), but in nature deceleration involves scattering processes which are likely to spoil the helicity. A plausible natural β-emitter is ^{40}K, which is ubiquitous in terrestrial organisms,[69] but the short range (ca. 1 cm) of its β-electrons requires us to assume an early and quite intimate association between the pre-biotic

amino acids and potassium; this problem is circumvented if ^{14}C provides a source of handed β-rays from within the prebiotic molecules themselves,[69] but the only experiment so far on the self-radiolysis of ^{14}C-labelled amino acids yielded negative results.[70] An alternative to β-radiolysis is β-photolysis by the circularly polarized bremsstrahlung radiation associated with the deceleration of the electrons — but the degree of circular polarization falls off linearly with photon energy and is small at photoenantioselective energies.[71-74] Unfortunately, however, no reproducible bioenantioselective effects have been obtained from either β-radiolysis or β-photolysis,[75,76] although in theory the maximum asymmetry obtainable could be as large as 10^{-12}.[77,78] Furthermore, as with sunlight, the Kuhn-Condon sum rule probably precludes any enantioselective effect from β-photolysis unless the radiation is fairly monochromatic. There may also be an analogous sum rule for β-radiolysis, because Campbell and Farago[68] found resonances for polarized electrons analogous to CD bands for polarized photons.
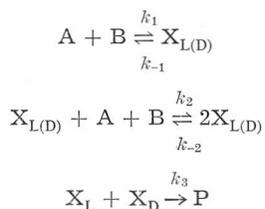
All the enantioselective mechanisms discussed so far rely on specific local conditions — the presence of β-emitters, circularly polarized light, magnetic fields, etc. — and the enantiomer selected depends on time and place. A global mechanism is afforded by the fact that because left and right-handed molecules are really diastereoisomers, not enantiomers, they differ slightly in energy.[79-83] This parity-violating energy difference (PVED) arises from weak neutral current interactions, mediated by the Z° boson, between electrons and neutrons. These interactions impart a parity-violating energy shift (PVES), E_{pv}, to the energy of a chiral molecule, and an equal and opposite shift, $-E_{pv}$, to that of its enantiomer, giving a parity-violating energy difference (PVED) of $\Delta E = 2E_{pv}$. The magnitude of ΔE is typically about 10^{-20} a. u., or 10^{-17} kT, as exemplified by the first *ab initio* molecular orbital calculation of the PVED, by Hegstrom, Rein and Sandars,[82] who considered a chirally twisted ethylene molecule. Although tiny, these energy differences represent the most promising possibility for electroweak enantioselection because they are present in all chiral molecules at all locations and at all times, thus providing a uniform background chiral bias. Before going on to discuss how the PVED is calculated (section 4), the PVEDs of biologically relevant molecules (section 5), and the prospects for finding larger PVEDs (section 6), we stop to consider that most important aspect of electroweak bioenantioselection — the necessary mechanism to amplify the initial enantiomeric excess from the weak interaction to eventual homochirality.

3. AMPLIFICATION MECHANISMS

Mechanisms proposed for the evolution of a nearly racemic system to optical purity fall into two classes: (a) catastrophic mechanisms in which a small chiral perturbation causes the system to bifurcate into one enantiomeric channel or the other over a relatively short time; and (b) those dependent upon a time-extended, uniformly cumulative process. The two types of mechanisms are not necessarily mutually exclusive, and indeed may act in concert, *e. g.* the small chiral perturbation from the PVED of a biomonomer might not in itself be large enough to determine the outcome of a bifurcation catastrophe, but it could well be sufficient to do so if it had already been cumulatively amplified to a larger size in the corresponding biopolymer.[84]

(a) Catastrophic Bifurcation by a Chiral Perturbation

The first chiral symmetry-breaking mechanism was that of Frank,[85] based on a kinetic scheme involving autocatalysis and enantiomeric antagonism, *i. e.* the presence of one enantiomer encourages production of itself, but inhibits production of its enantiomer. There have been several developments of this basic mechanism[86-90] including ones in which the two enantiomers have different reaction rates[91] (because unless the PVED is exactly the same in the reactants and transition state, the activation energies of enantiomers will differ). The most sophisticated scheme is that of Kondepudi, using non-equilibrium statistical thermodynamics.[92-94] He envisages an open-flow reactor system, such as a lake, fed by an input of achiral substances, A and B, with an output of enantiomers X_L and X_D and other products. The enantiomers form reversibly from the substrates, both directly (k_1) and autocatalytically (k_2), while cross-inhibition between the enantiomers results in their irreversible conversion (k_3) to products P:

$$A + B \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} X_{L(D)}$$

$$X_{L(D)} + A + B \underset{k_{-2}}{\overset{k_2}{\rightleftharpoons}} 2X_{L(D)}$$

$$X_L + X_D \overset{k_3}{\rightarrow} P$$

The scheme can accommodate unequal reaction rates for the two enantiomers, and can be extended[95] to include racemization, thermal fluctuations, and other factors such as asymmetric destruction rates of the two enantiomers by β-radiolysis or other environmental influences. With an input of A and B maintaining the substrate concentration at a constant or slowly increasing level, and a corresponding output of products, the system attains a dynamic quasi-steady state far removed from thermodynamic equilibrium.

The general solution of the integrated kinetics for the above scheme is found[92] to be a cubic equation in the enantiomeric excess of the chiral product, $(X_L - X_D)/(X_L + X_D)$. One root of the equation, correlating with a small input concentration of the substrates into the flow-reactor system, corresponds to an enantiomeric excess of zero, *i. e.* a racemic output. The other two roots correlate with a high substrate input and correspond to enantiomeric excesses of +1 or —1, *i. e.* the two homochiral reaction channels. As the input concentration is increased, the system reaches a transition point, where the racemic production process becomes metastable and the symmetry is spontaneously broken, with bifurcation into one or other of the oppositely-handed homochiral reaction channels. Without a chiral influence, the choice of homochiral reaction channel is arbitrary, but at the transition point the system becomes hypersensitive to small chiral perturbations or fluctuations, which may cause the bifurcation to become determinate. It is found[93,94] that thermal fluctuations damp out any initial trend toward the X_L or X_D homochiral production chanels unless $\Delta E/kT \gtrsim 10^{-17}$, where ΔE may represent either the difference in activation energies between enantiomers[93,94] or the PVED between enantiomers in an otherwise racemic substrate input.[96] ($\Delta E/kT$, some-

times called the electroweak advantage ratio,[84] is in fact equal, from the Boltzmann distribution, to the asymmetry factor or enantiomeric excess.) Since typical PVEDs are of the order of 10^{-17} kT, they should be just large enough to determine the outcome of the bifurcation under appropriate conditions: with realistic rate constants and concentrations, the PVED-stabilized homochiral reaction channel is selected if passage through the hypersensitive bifurcation region is slow, and takes place in a flow-reactor of substantial capacity. Specifically, Kondepudi estimates[95] that the PVED-stabilized series is selected with 98% probability if the transition occupies 10^4 years, during which time the input concentration increases from about 3×10^{-3} M to about 6×10^{-3} M in a flow system the size of a small lake of volume 4×10^9 L (1 km · 1 km · 4 m). Amplification can be achieved in the same time with lower reaction rates and concentrations if the lake is larger.

Some schools of thought continue to espouse the »frozen accident« viewpoint: Goldanskii[97] disputes Kondepudi's mechanism and Miller[98] believes that racemization annihilates any amplification effect. Of course »racemic« mixtures are not quite equimolar because of the PVED, so racemization is a problem only if it is fast compared with the amplification timescale. In fact, Kondepudi's mechanism can withstand a racemization half-life as low as $10^2 - 10^3$ years,[95] compared with typical values of $10^5 - 10^6$ years for most amino acids[98] (although values for some amino acids under certain conditions can be as low as 10^2 years).

Although typical PVEDs of 10^{-17} kT are only just large enough to be amplified, the amplification time and required lake volume are very sensitive functions of the PVED. An increase in the PVED of one order of magnitude decreases the amplification timescale by four orders of magnitude for a given lake volume, or alternatively decreases the required lake volume by two orders of magnitude for a given amplification time.[95] Thus, for the 1 km · · 1 km · 4 m lake, the amplification time would be reduced from 10^4 years to just one year if the PVED were increased to 10^{-16} kT. Care must be taken in reaching such conclusions, however: it does not follow that further increase of the PVED to 10^{-15} kT would result in amplification in 10^{-4} years, because the reactants would obviously take considerably longer than that to diffuse and distribute themselves uniformly through the large lake. Larger PVEDs — or the larger asymmetry factor of 10^{-12} theoretically available from β-radiolysis — would, however, enable the lake size to be reduced as well, so mitigating the reactant distribution problem and allowing the timescale to be further reduced. Thus, if the enantiomeric excess of 10^{-17} from the PVED requires 4×10^9 L and 10^4 years, that of 10^{-12} from β-radiolysis would require 40 L and 1 year, which could be checked on the laboratory scale.

But do such amplification mechanisms really exist in nature? Many polymerization reactions essential to life have precisely the required characteristics of autocatalysis and enantiomeric antagonism, and some enantiomeric enrichment has been demonstrated in the laboratory.[7-9] The results of Brack and Spach are particularly interesting. They showed[99,100] that if a pre-formed α-helix of L-amino acids is placed in a racemic amino acid mixture, mainly L-amino acids are incorporated in the subsequent polymerization, addition of a D-residue tending to poison the polymerization. Whereas in the case of the α-helix and other one-dimensional polymers amplification comes simply

from the fact that (all-L)-polymers form more easily than L polymers contaminated by occasional D residues, a much stronger effect is at work in the case of two-dimensional β-sheet formation. Here the inter-chain interactions are such that the β-sheet cannot form at all if even one D residue is incorporated.[101] Brack and Spach have obtained quite good experimental amplifications of a few percent using this effect.[102]

(b) Cumulative Chiral Amplification

The accumulation mechanism, proposed by Yamagata,[103] shows that a small difference in activation parameters for enantiomeric monomers, effective at each of n stages of polymerization or crystallization, results in a large enantiomeric excess in the n-omer, given by

$$(L_n - D_n)/(L_n + D_n) = n\varepsilon$$

where ε is the electroweak advantage ratio $\Delta E/kT$ for the monomers. ΔE refers[104] to the enantiomeric difference in either activation energy[103] or overall free energy change[105] for the addition of each unit. The cumulative mechanism requires the polymerization to be homochirally specific, but with no enantiomeric antagonism. Also, the monomers should be optically labile: if the monomers are not labile, stereospecific polymerization of an initially racemic mixture of monomers can only result in an equimolar mixture of the enantiomeric n-omers at the end of the polymerization; if, however, rapid racemization occurs, then as the monomers of the PVED-stabilized form are used up in the favoured polymerization, more will be formed in the racemization equilibrium, leading to an eventual excess of the favoured polymer. A transient enantiomeric excess may, however, be obtained even with non-labile monomers if the reaction is terminated before completion.[91,106]

These features of the cumulative mechanism are not usually applicable to biopolymerizations, which, as we have seen, are usually subject to enantiomeric antagonism and moreover usually involve non-labile monomers such as amino acids. However, the incomplete polymerization (ca. 50%) of the N-carboxyanhydride prepared from an unequal mixture of the D and L enantiomers of an α-amino acid produces a polypeptide mixture enriched in the enantiomer initially in excess. Subsequent incomplete hydrolysis (ca. 50%) of this polymer produces further enrichment.[107] A series of partial polymerizations and hydrolyses, resulting in a 3—14% optical enrichment of the polypeptide at each stage, thus provides a mechanism for asymptotic, cumulative convergence to homochirality.[107]

The cumulative mechanism is ideally applicable, however, to crystallizations, where enantiomeric antagonism is absent: optically pure single crystals of amino acids, for example, grow just as well from a seeded solution of the racemate as from a solution of the pure enantiomer.[108] Also, the requirement of optical lability is often fulfilled: quartz, for example, is labile in the sense of being a chiral crystal made up of achiral monomer units, which can add on to a growing crystal of either hand, and the two enantiomeric crystalline forms are interconvertible on melting or in solution. From Yamagata's formula, the enantiomeric excess in a crystal of n unit cells should be $n\varepsilon$,

where ε is the asymmetry factor for the individual unit cell. The implications of this for the role of chiral minerals in bioenantioselection will be discussed in section 7.

4. CALCULATION OF THE PVED

We begin with the parity-violating hamiltonian density

$$H_{pv} = J_\mu \cdot J^\mu \cdot G_F / \sqrt{2}$$

from quantum field theory,[54,82,109,110] where the weak neutral current J^μ is composed of electron, proton and neutron parts, and G_F is the weak interaction coupling constant. The expressions for the currents involve contributions containing the factor $(1 - 4 \sin^2 \Theta_w)$, where Θ_w is the Weinberg angle. Empirical values of $\sin^2 \Theta_w$ are 0.2156[64] and 0.23,[111] both close to the theoretical value of 0.25.[112] Using the theoretical value, the contributions with the factor $(1 - 4 \sin^2 \Theta_w)$ vanish, with the result that the electron and proton neutral currents have only axial vector components, while the neutron neutral current has both polar and axial vector components. Since the PVES, like the more familiar rotational strength, is a pseudoscalar (corresponding to the scalar product of an axial and a polar vector), only the axial vector electron current and the polar vector part of the neutron current contribute (intranuclear interactions obviously do not contribute as there is no spatial chirality within the nucleus). We therefore obtain

$$H_{pv}{}^{en} = (-G_F/2\sqrt{2})\, \overline{e}\, \gamma_\mu\, \gamma_5 e \, \overline{n}\, \gamma^\mu\, n$$

(using the sign convention[54] $\gamma_5 = i\gamma^0\gamma^1\gamma^2\gamma^3$, γ^0 hermitian, γ^i anti-hermitian, $i = 1, 2, 3$) which on reduction to non-relativistic quantum mechanics becomes[65,82,113]

$$H_{pv} = -(\Gamma/2) \sum_a \sum_i Q_a \{\mathbf{p}_i \cdot \sigma_i, \, \delta^3 (\mathbf{r}_i - \mathbf{r}_a)\}_+$$

where the summations are over all electrons i and nuclei a in the molecule, N_a is the neutron number of nucleus a and $\Gamma = 5.732 \times 10^{-17}$ a. u. This elegant expression shows directly that the PVES is a result of the handedness of the electron, since $\mathbf{p}_i \cdot \sigma_i$ represents the projection of the electron spin onto its momentum and is a pseudoscalar as required ($\mathbf{p}_i$ polar, σ_i axial). The delta-function expresses the contact nature of the weak interaction, in this case between electron and neutron at the nucleus. The matrix elements of the operators in the anticommutator $\{\ \}_+$ may themselves be large, but the result becomes very small when multiplied by Γ, which is related to the weak coupling constant G_F.

Having obtained the parity-violating hamiltonian H_{pv}, the PVES should be given by $E_{pv} = \langle \Psi_0 | H_{pv} | \Psi_0 \rangle$, where Ψ_0 is the ground state molecular electronic wavefunction. It would seem natural to separate Ψ into spin and orbital parts. But since the electron momentum operator $\mathbf{p}_i$ is pure imaginary, its expectation value over the real orbital wavefunctions vanishes. This vanishing of E_{pv} is due to the assumed separability of Ψ into spin and orbital parts, and therefore only occurs in the absence of spin-orbit coupling. If

spin-orbit coupling is included[65,81,82,83,113] then in first-order perturbation theory the true ground state wavefunction

$$| \Psi'_0 \rangle = | \Psi_0 \rangle + \sum_T (E_0 - E_T)^{-1} \langle \Psi_T | H_{so} | \Psi_0 \rangle | \Psi_T \rangle$$

includes an admixture of excited states mixed in by the spin-orbit coupling hamiltonian

$$H_{so} = \sum_b \sum_j \xi(b, j) \, \mathbf{l}(b, j) \cdot \mathbf{s}(j)$$

(where summation is over all electrons j and nuclei b). This leads to

$$E_{pv} = 2 \sum_T Re \left\{ \langle \Psi_0 | H_{pv} | \Psi_T \rangle \langle \Psi_T | H_{so} | \Psi_0 \rangle (E_0 - E_T)^{-1} \right\}$$

for the parity-violating energy shift of the singlet electronic ground state Ψ_0 of one enantiomer of a chiral molecule (where summation is over triplet excited states Ψ_T).

Next the multi-electron wavefunctions $| \Psi \rangle$ are expressed as products of one-electron molecular spin-orbitals $| \psi; m_s \rangle$, the total hamiltonians as sums over one-electron hamiltonians, and the spin parts of the wavefunctions are factored out[65,113] to give

$$E_{pv} = \sum_j^0 \sum_k^u P_{jk} (\varepsilon_j - \varepsilon_k)^{-1}$$

where

$$P_{jk} = Re \left\{ \langle \psi_j | \mathbf{V}_{pv} | \psi_k \rangle \cdot \langle \psi_k | \mathbf{V}_{so} | \psi_j \rangle \right\}$$

$$\mathbf{V}_{pv} = -\Gamma \sum_a Q_a \{ \mathbf{p}, \delta^3 (\mathbf{r} - \mathbf{r}_a) \}_+$$

$$\mathbf{V}_{so} = \sum_b \xi(b) \, \mathbf{l}(b)$$

ε_j is the energy of the molecular orbital Ψ_j, and the summation in E_{pv} is over all occupied MOs j and all unoccupied MOs k.

P_{jk} is called the parity-violating strength of the virtual transition connecting MOs Ψ_j and Ψ_k, and is analogous to the rotational strength

$$R_{jk} = Im \left\{ \langle \psi_j | \mu | \psi_k \rangle \cdot \langle \psi_k | \mathbf{m} | \psi_j \rangle \right\}$$

in pure electromagnetic optical activity. $\mathbf{V}_{pv}$ and μ are polar vectors, changing sign under space-inversion, while $\mathbf{V}_{so}$ and $\mathbf{m}$ are axial vectors, making both P_{jk} and R_{jk} pseudoscalars and therefore of opposite sign for enantiomeric molecules.

The LCAO approximation is used to express the molecular orbitals

$$| \psi_j \rangle = \sum_\gamma \sum_c C_{c\gamma}{}^j | c\gamma \rangle$$

in terms of atomic orbitals γ on atom c. The operators $\mathbf{V}_{so}$, and more particularly $\mathbf{V}_{pv}$, which contains the delta function, are most effective in a region close to the nucleus, so overlap is neglected and each matrix element is confined to a single atom, giving

$$P_{jk} = \sum_a \sum_b \sum_\alpha \sum_{\alpha'} \sum_\beta \sum_{\beta'} C_{a\alpha}{}^{j*} C_{a\alpha'}{}^k C_{b\beta}{}^{k*} C_{b\beta'}{}^j Re \left\{ \langle a\alpha | \mathbf{V}_{pv} | a\alpha' \rangle \cdot \langle b\beta | \mathbf{V}_{so} | b\beta' \rangle \right\}$$

for the final expression to be evaluated. Owing to the delta function, the operator V_{pv} only connects s and p orbitals, showing that $s - p$ mixing is responsible for the PVES as well as for the optical activity of atoms described in section 2. The operator V_{so} connects only orbitals with non-zero angular momentum, i. e. the p-orbitals. An interesting feature of the formula for the parity-violating strength is that it contains cross-terms involving the parity-violating matrix element on nucleus a and spin-orbit coupling on nucleus b, without any reference to the distance between these nuclei. Such couplings between distant parts of a large molecule could therefore in principle be quite significant — whether they are or not will depend, through $C^k_{a\alpha'}$, $C^{k*}_{b\beta}$ etc., on whether the molecular orbitals spread throughout the molecule or are localized. The PVES increases in proportion to Z^5 [82,109] and so should be largest for molecules containing heavy atoms.

The method described above is that used by Mason, Tranter and Mac Dermott:[65,113-126] preliminary computations on chiral conformations of H_2O_2 with a range of basis sets suggested STO-6-31G as the optimum,[113] and their subsequent calculations[65,113-126] for a large range of biomolecules were carried out with this basis set using the GAUSSIAN76[127] and GAUSSIAN82[128] computer programs.

An alternative treatment using a relativistic formalism has recently been developed by Wiesenfeld.[129] In the Dirac formalism the ground-state matrix element of the parity-violating hamiltonian does not vanish, so no spin-orbit coupling correction is necessary; ab initio relativistic atomic wavefunctions are used, and the method is suited to compounds containing very heavy atoms. In two series of compounds of C, Si, Ge, Sn, Pb, and O, S, Se, Te, the PVED obtained by the relativistic method was found to increase faster down the group than the non-relativistic Z^5-dependence would predict, the difference becoming significant by the third or fourth row; the largest relativistic effect was for the lead compound, which had a PVED of 10^{-10} kT, about 20 times larger than predicted by Z^5 extrapolation.[129]

5. THE ELECTROWEAK STABILIZATION OF NATURAL BIOMOLECULES

Mason and Tranter have calculated the PVES of some α-amino acids in their common zwitterionic form $^+NH_3CHRCO_2^-$, starting with glycine (R=H) and L-alanine (R=CH₃).[65,113,114] Glycine is not resolvable, but is chiral over most of the conformational range spanned by the rotation of the CO_2^- plane about the bond to C_α. The magnitude and sign of the PVES shows a similar sinusoidal dependence on this angle for both glycine and L-alanine. The angle in L-alanine crystals is on the negative part of the curve, and the preferred angle in solution — which enhances the solvation of the zwitterion — is right at the minimum of the sinusoidal curve. Subsequent calculations for other amino acids dealt only with this preferred solution conformation and gave the following results[115,117] for the PVES, $E_{pv}/10^{-20}$ a. u.: glycine, —1.14; L-alanine, —1.79; L-valine, —2.29; L-serine, —0.84; L-aspartate anion, —1.46. These L-amino acids are therefore stabilized relative to their D-enantiomers by some 10^{-20} a. u., or 10^{-17} kT, just enough for the resulting enantiomeric excess to be amplified to homochirality by the Kondepudi mechanism described earlier.

The total PVES of a molecule can be resolved into contributions from each nucleus. Hydrogen nuclei give a zero contribution, as they have no

neutrons, but their presence does influence the PVES of the other nuclei through its effect on the molecular orbitals. For the amino acids studied, the major contributions to the PVES are from the C_α chiral centre and the electron-rich carboxylate oxygens, and these are consistently negative in all cases. The contribution from the side group R is consistently positive, and increases in magnitude on going from alanine through valine and serine to the aspartate anion, following the approximate order of increasing side-group polarizability. This is because the side groups are achiral in themselves, and are able to contribute only if they acquire a degree of chirality by the rest of the molecule asymmetrically polarizing them. The relatively small positive contribution from the side group does not, however, prevent the overall PVES being negative for all L-amino acids studied. It appears reasonable to assume that this electroweak stabilization of the natural L-enantiomers is a general result for all L-α-amino acids with achiral side-groups of limited polarizability.[115,116]

As well as the solution conformation, the L-polypeptide conformations in the α-helix and β-sheet were also considered:[65,113] a single polypeptide unit, —NH—CHR—CO—, with R = H, gave, coincidentally, a PVES of —0.33×10^{-20} a. u. for both α-helix and β-sheet, corresponding to a PVED of —0.66×10^{-20} a. u. per peptide residue. An L-polypeptide of n residues should therefore be stabilized relative to the D-polypeptide by —0.66 n $\times 10^{-20}$ a. u., but there may be additional contributions from cross-terms between residues, since, as explained earlier, these do not necessarily fall off with increasing residue separation.

As well as the PVES of biomolecules themselves, it is important to consider the variation of the PVES over the pre-biotic reaction paths leading to their production. Tranter[117-119] has examined Miller's mechanism[130] for the pre-biotic formation of the chiral alanine precursor α-amino-propionitrile (APN) by attack of a cyanide ion on the ethylidene-iminium cation, $CH_3CH{=}\overset{+}{N}H_2$. This reaction is important because the reactants are achiral, and production of APN represents the first introduction of chirality into the system. Either L- or D-APN can be produced, depending on which side of the planar ethylidene-iminium ion the CN^- ion approaches from. The PVED of the L-APN reaction was calculated as a function of distance along the reaction coordinate, and rose from zero for the infinitely separated achiral reactants to a maximum of $+0.46 \times 10^{-20}$ a. u. in the transition state, before dropping to —0.40×10^{-20} a. u. for the product L-APN molecule. If the reaction were under kinetic control, then this result shows that D-APN would form faster, and therefore come to predominate, because the activation energy for formation of the L-form is higher by $+0.46 \times 10^{-20}$ a. u. If however, as seems more likely, the reaction is under thermodynamic control, then the reverse reaction must be considered, and D-APN would clearly also decompose faster, because the activation energy for decomposition of the L-form is higher by $+0.86 \times 10^{-20}$ a. u. The excess decomposition rate of the D-form is greater than its excess formation rate, and so the L-form will eventually predominate under conditions of thermodynamic equilibrium.

In conclusion, the work of Mason and Tranter shows that the natural L-α-amino acids are favoured not only by their own electroweak stabilization

relative to their unnatural D-enantiomers, but also by electroweak enantio-selection during their pre-biotic formation. Tranter and MacDermott are now examining whether this success can be repeated for the D-sugars.

The sugars could have been formed pre-biotically by the formose reaction,[131–134] in which successive addition of a formaldehyde molecule, H_2CO, gives rise to the aldoses, $(H_2CO)_n$, where n = 3 corresponds to glyceraldehyde, the smallest sugar with a chiral centre, n = 4 to erythrose and threose, the smallest sugars in which furanose ring formation is possible, and n = 5 to ribose, arabinose and two other stereoisomers. Deoxyribose can presumably be formed by dehydroxylation of ribose or arabinose. Tranter and MacDermott have calculated the PVEDs of all these molecules,[125] but it is difficult to draw a definite conclusion because not all the natural enantiomers are PVED-stablized. Hydrated D-glyceraldehyde has a PVES of -0.41×10^{-20} a. u.,[120] and the resulting enantiomeric excess in this parent of the higher sugars may have led to the selection of D-ribose and D-deoxyribose for RNA and DNA. Chiral conformations of tetrahydrofuran (THF), the basic furanose skeleton of the higher sugars, have also been studied,[121] and the C2-*endo* form found in DNA has a PVES of -1.67×10^{-20} a. u., making it more stable than its C3-*endo* enantiomer by a PVED of -3.34×10^{-20} a. u. Taken together, these two results for the D chiral centre and the chiral ring conformation suggest that D-deoxyribose should be PVED-stabilized, and indeed it is, with a PVES of -0.62×10^{-20} a. u. in its C2-*endo* solution conformation.[125] D-ribose is also PVED-stabilized in C2-*endo* conformations,[122] but the preferentially adopted C3-*endo* solution conformation has a PVES of $+2.92 \times 10^{-20}$ a. u.

D-ribose cannot therefore have been selected by its own PVED, but may have been selected by that of its parent D-glyceraldehyde. Alternatively, the D-sugar series may have been selected by the diastereomeric connection with the PVED-stabilized L-amino acids. Pre-biotic synthesis of ribose, however, presents many problems[134,135] — for example the formose reaction leads to many different stereoisomers, each in low yield — and so it is quite likely that ribose is not prebiotic, but represents a later biological evolution after the first self-replicating system had appeared, in which case its own PVED is irrelevant because the handedness of life would already have been determined.

There is new evidence that duplex formation with base-pairing can occur with a glycerol rather than ribose-based polymer: it differs from polynucleotides in being pyrophosphate-linked and in being without the C2 ring atom, giving an open chain structure.[98,136] The monomer units of this possible primitive replicator are achiral but can form a chiral base-paired double helix. In this respect it is like quartz, with achiral monomers adding to form a helix of either hand, and so the handedness of such a helix could be selected by the Yamagata cumulative amplification mechanism (see section 3). It is normally assumed that the right-handedness of the polynucleotide double helix is fixed by the D-sugars, but it may have been the other way round: if a right-handed helix was selected in the glycerol-based primitive replicator, then steric considerations in any later insertion of C2 to give ribose would result in production of the D form.

6. THE SEARCH FOR LARGER PVEDs

The amino acids and sugars have PVEDs of 10^{-17} kT — only just large enough to be amplified kinetically. But ribose is highly symmetrical: but for the CH_2OH at C4 and OH at C1, it would have a plane of symmetry and be achiral apart from the ring pucker. Would a more asymmetrically substituted THF ring have a larger PVED? Recent preliminary calculations by MacDermott, Tranter and Indoe[137,138] suggested that 1-hydroxy-THF had a PVED of 10^{-15} kT, 100 times larger than »normal«. However, these results have now been shown[125] to be wrong — the PVED is in fact only 10^{-17} kT as before — due to systematically erroneous computer inputs. This error does not affect earlier or subsequent work by Mason, Tranter and MacDermott:[65,113–126] only the work with Indoe[137,138] is involved.

The erroneus results involved a large PVES from the 1-hydroxyl oxygen; in fact the correct O1 PVES is quite large, at $+ 1.30 \times 10^{-20}$ a. u., for a single atom contribution, although nowhere near as large as the erroneous estimate, and the reason given[137] for O1 having a large PVES remains correct. For an atom to give a large PVES contribution, it must be in a chiral environment, and have a large enough electron density for this chirality to be felt, as well as having electron-rich neighbours with large spin-orbit coupling matrix elements.[137] These factors can be assessed from the charges on each atom (obtained from the Mulliken population analysis of the GAUSSIAN82 program). The environment of each atom is created in part by the electrostatic field produced by the surrounding charges on other atoms. In 1-hydroxy and other substituted THFs including ribose, only the oxygen atoms are significantly charged; the 1-hydroxyl oxygen therefore sees the negative charge of the nearby ring oxygen to one side, giving a highly chiral environment; furthermore, its own negative charge corresponds to an elevated electron density which can feel this chirality (large molecular orbital coefficients $C_{a\alpha}^{j*}$ etc. weighting the matrix elements of $\mathbf{V}_{pv}$). The PVES of O3 and O2 is much smaller than that of O1 because O3 and O2 are too far away from the ring oxygen.

The O1 contribution has almost the same value of $+ 1.30 \times 10^{-20}$ a. u. in the C2-*endo* forms of 1-hydroxy-THF, 1,2-dihydroxy-THF, 1,2,3-trihydroxy-THF (erythrose) and ribose; it also varies little between the C2 and C3-*endo* conformations.[125] This suggests that there are two independent and additive contributions to the PVES, that from the ring pucker and that from the very chiral environment of O1: the positive O1 contribution shifts the PVESs of the C2-*endo* and C3-*endo* forms of ribose ($- 0.29$ and $+ 2.92 \times 10^{-20}$ a. u. respectively) relative to the equal and opposite values for the corresponding forms of THF ($- 1.67$ and $+ 1.67 \times 10^{-20}$ a. u.); but the difference in PVES between the C2- and C3-*endo* forms remains almost the same (-3.21 for ribose and $- 3.34$ for THF). This represents the first intimation that PVESs from different parts of a molecule may be additive, making it possible to predict the overall PVES of a molecule — which could be useful in the case of molecules too large to perform calculations on.

This example of ribose demonstrates the sort of molecular features, such as chirally juxtaposed oxygen atoms, which might enhance the PVES. More obvious features likely to produce large PVESs are helicity and heavy atoms, as exemplified[113] by the large PVES of $+ 27.7 \times 10^{-20}$ a. u. obtained by Tranter for the (admittedly hypothetical) right-hand $(O_8)^{2-}$ helix, and the much

larger value of $+374 \times 10^{-20}$ a. u. obtained for the corresponding $(S_6)^{2-}$ helix (which does exist).

MacDermott and Tranter therefore turned their attention next to phosphates,[126] since these contain a second-row heavy atom, phosphorus, and also several juxtaposed oxygen atoms. They considered deoxyribose-type rings without the 1-hydroxyl group but with a phosphate group at either the 3′ position or the 5′ position, or both 3′ and 5′ positions. These molecules represent the building blocks of the sugar-phosphate backbone of DNA, but without the bases. The PVESs obtained were however once again only of the order of 10^{-17} kT. The contributions of the oxygen atoms are small (probably because each O atom sees others on all sides) and tend to cancel, while that of the phosphorus atoms is larger (-1.65×10^{-20} a. u. for a 3′-phosphate and $+2.07 \times \times 10^{-20}$ a. u. for a 5′-phosphate). But the overall PVES is not as large as might have been expected from a molecule with a second-row atom in view of the Z^5-dependence of the PVES: this was found to be because the P atoms are quite electropositive in phosphates, and therefore have a reduced electron density, corresponding to small coefficients $C_{a\alpha}^{j*}$, etc., weighting the matrix elements of $\mathbf{V}_{pv}$ and $\mathbf{V}_{so}$. (Also the PO_4 unit is essentially achiral apart from the perturbing influence of the ring and the helical conformation of the backbone — the torsion angles used were those found in DNA.) Clearly therefore, one must look to more electronegative heavy atoms in more chiral environments for large PVESs.

The results do, however, confirm PVES additivity: the THF ring contribution, at about -1.70×10^{-20} a. u. in the C2-*endo* conformation of all three molecules, differed little from that in ribose and in THF itself; the 3′-phosphate contribution was of the same sign and order of magnitude in 3′- and 3′,5′-substituted THFs (-2.32 and -1.78×10^{-20} a. u. respectively) as was the 5′-phosphate contribution in the 5′- and 3′,5′-substituted THFs ($+1.98$ and $+2.68 \times 10^{-20}$ a. u. respectively). This additivity is due to the fact that cross-terms between completely different parts of these molecules — e. g. the phosphate and the ring — are negligible, reflecting a corresponding localization of the molecular orbitals.

This additivity could be used to determine the PVES of the sugar-phosphate backbone of DNA, and eventually the PVES of DNA itself. We already have the PVES of C2-*endo* THF, and have seen that it is almost unaffected by phosphate linkage. We now need the PVES of a phosphate group between two deoxyribose-type rings, attached to the 3′ position of one and the 5′ position of the other (since we have seen that 3′ and 5′ phosphate groups attached to only one deoxyribose-type ring have oppositely signed PVES), but unfortunately this system has too many atoms for GAUSSIAN82. Instead, a »minimal« helical backbone, with all ring atoms removed except the essential C5, C4 and C3, was considered, using B-DNA torsion angles. This system gave $E_{pv}/^{-20}$ a. u. values of -4.00 for a 3′-end phosphate, $+2.84$ for a 5′-end phosphate (in reasonable agreement with the results using full sugar rings) and -1.67 a. u. for a »middle« phosphate with $-(CH_2)_3-$ carbon chains to either side. These preliminary results suggest that the right-hand helical backbone of DNA may be stabilized — by an $E_{pv}/10^{-20}$ a. u. of about $-(1.70 + 1.67) = = -3.37$ per sugar-phosphate unit — although clearly more work is required, and in particular any additional contribution from the bases must be assessed

(but this may be small as the bases are planar). It would be especially interesting to examine next the glycerol-based achiral replicator[136] mentioned earlier, to see if the right-hand helix (and thence, perhaps, the D-sugars) is favoured in this case too.

7. CHIRAL MINERAL CATALYSTS

An important system which contains both helices and second-row atoms is quartz, which consists, in the 1 (—)-form, of right-hand 3-fold and left-hand 6-fold helices of silica tetrahedra. As a chiral mineral made of achiral units it can undergo cumulative chiral amplification, and indeed a 1.4% excess of 1 (—)-quartz is reported in a total collection of 16807 crystals from all over the world,[139,140] although the statistical interpretation of this has been disputed.[141] Furthermore there has been considerable recent interest in the role of quartz-like minerals as catalysts in the early evolution of life, or even as the first self-replicating systems themselves.[142,143]

MacDermott and Tranter[124] have recently calculated the PVES of Si and O atoms at the centre of small fragments of quartz (atoms at the edges will obviously give atypical PVES). For helices consisting of three silica tetrahedra, values of $E_{pv}/10^{-20}$ a. u. of — 1.27 per Si and — 0.24 per O, giving — 1.75 per SiO_2 unit, were obtained for the right-hand 3-fold helix, and + 0.30 per Si and — 0.13 per O, giving + 0.04 per SiO_2, for the left-hand 6-fold helix. (Helices of five tetrahedra did not give significantly different results as cross-terms with atoms more than two tetrahedra away were negligible.) Taking a more realistic fragment of five tetrahedra, in which the central tetrahedron is surrounded by four others and is simultaneously in two right-hand 3-fold helices and two left-hand 6-fold helices, $E_{pv}/10^{-20}$ a. u. values of — 0.88 per Si and — 0.12 per O were obtained, giving — 1.12 per SiO_2, intermediate between the values for the left and right-hand helices separately.

At — 2.24×10^{-20} a. u. per SiO_2 unit, the PVED, although gratifyingly of the right sign, is again of the order of 10^{-17} kT and thus disappointingly small for a second-row atom: again this is because here the Si is highly electropositive. However, the PVED does not need to be any larger than 10^{-17} kT to acocunt for the 1.4% excess. According to Yamagata's mechanism,[103,104] the enantiomeric excess of an n–unit crystal will be of the order of $n\varepsilon$, where ε is the electroweak advantage ratio of a single unit; so $n\varepsilon = 10^{-2}$ can be obtained easily from $\varepsilon = 10^{-17}$ because the required $n = 10^{15}$ corresponds[104] to a crystal side of about 0.1 mm.

These new PVED results for quartz are therefore tremendously exciting because they predict almost exactly the observed 1% excess of 1 (—)-quartz, so that this excess can now for the first time be regarded as evidence for the global symmetry-breaking effects of the weak interaction. Furthermore, catalysis by quartz-like minerals presents an opportunity for their chiral bias to be transferred to biology, for 1 (—)-quartz has been shown to adsorb L-alanine preferentially from a racemic mixture, for purely diastereomeric reasons, with an enantioselectivity of 1% or more.[144,145] Combining this asymmetry of 10^{-2} in adsorption with the 10^{-2} asymmetry in the quartz crystals themselves gives[104] an overall electroweak enantioselectivity of 10^{-4}, which is much greater than that of 10^{-17} from the PVED of individual molecules.

Such a large enantiomeric excess would require only minor subsequent amplification, and homochirality could be achieved in relatively short times using small reaction volumes.

Quartz crystals themselves are unlikely to have been important prebiotic catalysts, but more significant chiral mineral catalysts may exhibit similar enantiomeric excesses. Some aluminosilicate clay minerals contain heavy cations and so may exhibit a larger chiral bias. Other chiral crystals have been studied to see if heavy atoms produce a chiral bias, e. g. Mason observed a 6.8% enantiomeric excess in sodium uranyl acetate crystals.[84] Laboratory crystallizations have suggested that potassium silico-tungstate crystallizes predominantly in a dextrorotatory habit[146-148] but it is almost impossible to prevent chiral contamination in such studies.[149] This might appear to suggest that an alternative explanation for the excess of l(—)-quartz is that it was laid down in the post-biotic period and was influenced by chiral biomolecular contamination; this is very unlikely, however, in view of the elevated temperatures associated with the hydrothermal crystallization of quartz (amino acids racemize at 160 °C).

8. SPACE OPTICAL ACTIVITY

If the world-wide terrestrial enantiomeric excess of l(—)-quartz is evidence for the weak interaction as a global symmetry breaker, then even better such evidence would come from finding a cosmic chiral bias in the same direction in different extra-terrestrial systems. Furthermore, the Kondepudi amplification mechanism is difficult to test in the laboratory because of the large volumes and timescales and the danger of biochiral contamination. A planet with no life, undergoing purely chemical evolution, would, however, provide an excellent laboratory in which to test the pre-biotic emergence of chiral bias. An ideal candidate is Saturn's moon Titan. Its atmosphere is largely nitrogen, with some argon, methane and ethane, above an ocean of liquid ethane and methane. It has an active photochemistry, and the Voyager mission detected many hydrocarbons and three nitriles (HCN, HC≡C—CN and NC—CN). Brack has pointed out[150] that from these simple starting materials many chiral photoproducts can be formed, e. g. 2,3-dimethylpentane, 3-methyl-1-pentene, 2-amino-butane, and many more, and he has suggested that the forthcoming Cassini mission should carry instruments to test for optical activity. Despite the lack of oxygen there are many polymerization reactions through which chiral amplification could occur, e. g. the formation of polyisoprene (derivatives of which occur on Earth in vitamins, chlorophyll and the lipids of certain bacteria[5]).

9. CONCLUSIONS

Many influences previously thought to be enantioselective are now known to be either falsely chiral or else only locally chiral, being even-handed on a time and space average. The weak interaction appears to be the only consistent universal chiral influence.

In theory, the largest enantioselective effect of the weak interaction is from β-radiolysis, which should give an asymmetry of 10^{-12}, but experiments have not yet adequately demonstrated that enantiodifferential radiolysis occurs, and it is again a local effect. The parity-violating energy differences,

PVED, between enantiomers, give a smaller asymmetry of 10^{-17}, but they are present everywhere and at all times, giving a consistent and uniform background chiral bias which may become amplified over long periods. Amplification mechanisms are typically polymerizations, and the small number of laboratory studies carried out so far are moderately encouraging, but have achieved enrichments of only a few percent starting from initial enantiomeric excesses of a few percent. Amplification from the β-radiolysis excess of 10^{-12} could be demonstrated in a large-scale laboratory experiment over a timescale of about a year, and space optical activity studies could help to confirm the possibility of amplification from the 10^{-17} PVED level, which needs larger volumes and takes about 10^4 years.

Most calculations of the PVED carried out so far do favour the natural enantiomers. The L-α-amino acids are PVED-stabilized, as is D-deoxyribose. D-ribose, however, is not stabilized, but the D-sugars could have been selected either through their PVED-stabilized parent D-glyceraldehyde, or else through diastereomeric interaction with the L-amino acids. However, a molecule's PVED is only relevant if the molecule is truly pre-biotic, and it is quite likely that ribose is not. Early polynucleotide-like replicators may have been built from achiral monomers, and if a right-hand double helix were selected by its PVED, then D-ribose would be diastereomerically selected at a later stage. Preliminary studies of the phosphate links do suggest that right-handedness may be favoured in polynucleotidelike backbones.

The most promising PVED results so far are those predicting the observed 1% excess of l (—)-quartz crystals, although more surveys using larger numbers of crystals are necessary to confirm this excess and extend it to other chiral minerals. The catalytic role of such minerals could increase the electroweak asymmetry from 10^{-17} to 10^{-4}. Future studies will be directed increasingly towards systems containing heavy electronegative atoms, in which the Z^5 PVED dependence could further increase the available enantiomeric excess.

It therefore does appear that electroweak bioenantioselection is in principle possible, and moreover that the observed terrestrial chiral bias is in the direction predicted by the weak interaction.

REFERENCES

1. J. Lederburg, *Nature* **207** (1965) 9.
2. T. L. V. Ulbricht, *Orig. Life* **11** (1981) 55.
3. A. Meister, *Biochemistry of the Amino Acids*, Academic Press, New York, 1965.
4. D. Perlman and M. Bodansky, *Ann. Rev. Biochem.* **40** (1971) 449.
5. G. Spach and A. Brack, *Structure, Dynamics and Evolution of Biological Macromolecules*, C. Helene (Ed.), Reidel 1983, p. 383.
6. T. L. V. Ulbricht, *Comp. Biochem.* **4** (1962) 1.
7. G. F. Joyce, G. M. Visser, C. A. A. van Boeckel, J. H. van Boom, L. E. Orgel, and J. van Westresen, *Nature* **310** (1984) 602.
8. M. Idelson and E. R. Blout, *J. Amer. Chem. Soc.* **80** (1958) 2387.
9. R. D. Lundberg and P. J. Doty, *J. Amer. Chem. Soc.* **79** (1957) 3961.
10. N. E. Blair, F. M. Dirbas, and W. A. Bonner, *Tetrahedron* **37** (1981) 27.
11. E. Fischer, *Chem. Ber.* **27** (1894) 2985, 3189.
12. M. L. Wolfrom, R. U. Lemieux, and S. M. Olin, *J. Amer. Chem. Soc.* **71** (1949) 2870.
13. G. Melcher, *J. Mol. Evol.* **3** (1974) 121.

14. S. L. Miller and L. E. Orgel, *The Origins of Life on the Earth*, Prentice Hall, Englewood Cliffs, 1974, p. 171.
15. A. G. Cairns-Smith, *Chem. Brit.* **22** (1986) 559.
16. L. Pasteur, *Compt. Rend. Acad. Sci. (Paris)* **78** (1874) 1515.
17. L. Pasteur, *Rev. Scientifique* **7** (1884) 2.
18. L. Pasteur, *Bull. Soc. Chim. France* **41** (1884) 215.
19. L. Pasteur, *Compt. Rend. Seances Soc. Biol. Paris* **26** (1848) 535.
20. L. Pasteur, *Oeuvres de Pasteur*, Vol I, *Dissymetrie Moleculaire*, Pasteur Vallery-Radot (Ed.), Masson et Cie, Paris, 1922, p. 369.
21. T. M. Borchkhade and N. G. Kogoshvili, *Astron. Astrophys.* **53** (1976) 431.
22. T. Yamagata, M. Hamabe, and M. Iye, *Tokyo Obs. Annals.* **18** (1981) 164.
23. H. T. MacGillivray and R. J. Dodd, *Astron. Astrophys.* **145** (1985) 269.
24. N. Humphrey and C. McManus, *New Scientist* **59** (1973) 437.
25. L. D. Barron, *Chem. Soc. Rev.* **15** (1986) 189.
26. L. D. Barron, *Chem. Phys. Lett.* **123** (1986) 423.
27. L. D. Barron, *BioSystems* **20** (1987) 7.
28. P. Curie, *J. Phys. (Paris)* **3** (1894) 393.
29. P. Gerike, *Naturwissenschaften* **62** (1975) 38.
30. R. C. Dougherty, *J. Amer. Chem. Soc.* **102** (1980) 380.
31. D. Edwards, K. Cooper, and R. C. Dougherty, *J. Amer. Chem. Soc.* **102** (1980) 381.
32. R. C. Dougherty, *Orig. Life* **11** (1981) 71.
33. W. Rhodes and R. C. Dougherty, *J. Amer. Chem. Soc.* **100** (1978) 6247.
34. L. D. Barron, *Chem. Phys. Lett.* **135** (1987) 1.
35. R. R. Birss, *Symmetry and Magnetism*, North Holland, Amsterdam, 1966.
36. C. A. Mead and A. Moscowitz, *J. Amer. Chem. Soc.* **102** (1980) 7301.
37. A. Peres, *J. Amer. Chem. Soc.* **102** (1980) 7390.
38. G. Wagnière and A. Meier, *Experientia* **39** (1983) 1090.
39. D. Radulescu and J. Moga, *Bull. Soc. Chim. Romania* **1** (1939) 2.
40. H. Pracejus, *Top. Curr. Chem.* **8** (1967) 54.
41. H. Teutsch and W. Thiemann, *Orig. Life* **16** (1986) 420.
42. W. Thiemann, private communication; H. Teutsch, Doctoral thesis, Universität Bremen (1988).
43. S. F. Mason, *Molecular Optical Activity and the Chiral Discriminations*, Cambridge University Press, 1982.
44. Y. Izumi and A. Tai, *Stereo-differentiating Reactions*, Academic Press, New York, 1977.
45. S. F. Mason, *Int. Rev. Phys. Chem.* **3** (1983) 217.
46. J. C. Kemp, R. D. Wolstencroft, and J. B. Swedlund, *Nature* **232** (1971) 165.
47. P. D. Ritchie, *Asymmetric Synthesis and Asymmetric Induction*, Oxford University Press, 1933, p. 44.
48. W. A. Bonner, *Exobiology*, C. Ponnamperuna (Ed.), North Holland, Amsterdam, 1974, p. 205.
49. J. R. P. Angel, R. Illing, and P. G. Martin, *Nature* **238** (1972) 389.
50. R. D. Wolstencroft, *IAU Symposium 112*, Boston, 1984.
51. J. J. Florey, W. A. Bonner, and G. A. Massey, *J. Amer. Chem. Soc.* **99** (1977) 3622.
52. B. Norden, *Nature* **266** (1977) 567.
53. J. C. Kemp, G. D. Henson, C. T. Steiner, and E. R. Powell, *Nature* **326** (1987) 270.
54. I. J. R. Aitchison and A. J. G. Hey, *Gauge Theories in Particle Physics*, Adam Hilger, Bristol, 1982.
55. T. D. Lee and C. N. Yang, *Phys. Rev.* **104** (1956) 254.
56. C. S. Wu, E. Ambler, R. W. Hayward, D. D. Hoppes, and R. P. Hudson, *Phys. Rev.* **105** (1957) 1413.
57. S. Weinberg, *Phys. Rev. Lett.* **19** (1967) 1264.
58. A. Salam, in *Proc. 8th Nobel Symp., Elementary Particle Theory*, N. Svartholm (Ed.), Almquist & Wiksell, Stockholm, 1968.

59. R. Walgate, *Nature* **303** (1983) 473.
60. P. G. H. Sandars, *Fundamental Interactions and Structure of Matter*, K. Crowse, J. Duclos, G. Fiorentini, and G. Torelli (Eds.), Plenum, New York, 1980, p. 57.
61. E. N. Fortson and L. Wilets, *Adv. Atom. Molec. Phys.* **16** (1980) 319.
62. L. D. Barron, *Mol. Phys.* **43** (1981) 1395.
63. A. L. Barra, J. B. Robert, and L. Wiesenfeld, *BioSystems* **20** (1987) 57.
64. T. P. Emmons, J. M. Reeves, and E. N. Fortson, *Phys. Rev. Lett.* **51** (1983) 2089; **52** (1984) 86.
65. S. F. Mason and G. E. Tranter, *Proc. Roy Soc. (London) A* **397** (1985) 45.
66. T. L. V. Ulbricht and F. Vester, *Tetrahedron* **18** (1962) 628.
67. R. A. Hegstrom, *BioSystems* **20** (1987) 49.
68. D. M. Campbell and P. S. Farago, *Nature* **318** (1985) 52.
69. H. P. Noyes, W. A. Bonner, and J. A. Tomlin, *Orig. Life* **8** (1977) 21.
70. W. J. Bernstein, R. M. Lemmon, M. Calvin, in *Molecular Evolution* L. Rohlfing and A. I. Oparin (Eds.), Plenum, New York, 1972.
71. M. Goldhaver, L. Grodzins, and A. W. Sunyar, *Phys. Rev.* **106** (1957) 826.
72. K. W. McVoy, *Phys. Rev.* **106** (1957) 828.
73. K. W. McVoy, *Phys. Rev.* **110** (1958) 1484.
74. H. Schopper and S. Glaster, *Nucl. Phys.* **6** (1958) 125.
75. W. A. Bonner, *Orig. Life* **14** (1984) 383.
76. J. Van House, A. Rich, and P. W. Zitzewitz, *Orig. Life* **14** (1984) 413.
77. R. A. Hegstrom, A. Rich, and J. Van House, *Nature* **313** (1985) 391.
78. R. A. Hegstrom, *BioSystems* **20** (1987) 49.
79. D. W. Rein, *J. Mol. Evol.* **4** (1974) 15.
80. V. S. Letokhov, *Phys. Lett. A* **53** (1975) 275.
81. B. Ya. Zel'dovich, D. B. Saakyan, and I. I. Sobel'man, *JETP Lett.* **25** (1977) 94.
82. R. A. Hegstrom, D. W. Rein, and P. G. H. Sandars, *J. Chem. Phys.* **73** (1980) 2329.
83. R. A. Hegstrom, D. W. Rein, and P. G. H. Sandars, *Phys. Lett. A* **71** (1979) 499.
84. S. F. Mason, *Nouv. J. Chim.* **10** (1986) 739.
85. F. C. Frank, *Biochim. Biophys. Acta* **11** (1953) 459.
86. F. F. Seelig, *J. Theor. Biol.* **31** (1971) 355.
87. F. Decker, *J. Mol. Evol.* **4** (1974) 49.
88. L. Wei-Min, *Orig. Life* **12** (1982) 205.
89. L. L. Morozov, V. V. Kuzmin, and V. I. Gol'danskii, *Sov. Sci. Rev. D Physicochem. Biol.* **5** (1984) 357.
90. K. Tennakone, *Chem. Phys. Lett.* **105** (1984) 444.
91. C. Fasji and J. Czege, *Orig. Life* **11** (1981) 143.
92. D. K. Kondepudi and G. W. Nelson, *Phys. Rev. Lett.* **50** (1983) 1023.
93. D. K. Kondepudi and G. W. Nelson, *Physica* **125A** (1984) 465.
94. D. K. Kondepudi and G. W. Nelson, *Nature* **314** (1985) 438.
95. D. K. Kondepudi, *BioSystems* **20** (1987) 75.
96. R. A. Hegstrom, *Nature* **315** (1985) 749.
97. V. I. Gol'danskii and V. V. Kuzmin, *Z. Phys. Chemie (Leipzig)* **269** (1988) 216.
98. J. L. Bada and S. L. Miller, *BioSystems* **20** (1987) 21.
99. A. Brack and G. Spach, *Nature (Physical Science)* **229** (1971) 124.
100. G. Spach, *Chimia* **28** (1974) 500.
101. A. Brack and G. Spach, *J. Mol. Evol.* **13** (1979) 35, 47.
102. A. Brack and G. Spach, *J. Mol. Evol.* **15** (1980) 231.
103. Y. Yamagata, *J. Theor. Biol.* **11** (1966) 495.
104. G. E. Tranter, *Nature* **318** (1985) 172.
105. L. Keszthelyi, *Phys. Lett. A* **64** (1977) 287.
106. L. Keszthelyi, J. Czege, C. Fajszi, J. Pofai, and V. I. Gol'danski, *Origins of Optical Activity in Nature*, D. C. Walker (Ed.), Elsevier, 1979, p. 229.

107. W. A. Bonner, N. E. Blair, and F. M. Dirbas, *Orig. Life* **11** (1981) 119.
108. J. Jacques, A. Collet, and S. H. Wilen, *Enantiomers, Racemates and Resolutions,* Wiley, New York, 1981, p. 76.
109. C. C. Bouchiat and M. A. Bouchiat, *J. Phys. (Paris)* **35** (1974) 899; **36** (1975) 493.
110. M. A. Bouchiat and C. C. Bouchiat, *Phys. Lett. B* **48** (1974) 111.
111. L. F. Abbott and R. M. Barnett, *Phys. Rev. D* **19** (1979) 3230.
112. J. C. Taylor, *Gauge Theories of Weak Interactions,* Cambridge University Press, 1979.
113. S. F. Mason and G. E. Tranter, *Mol. Phys.* **53** (1984) 1091.
114. S. F. Mason and G. E. Tranter, *J. Chem. Soc. Chem. Commun.* (1983) 117.
115. G. E. Tranter, *Chem. Phys. Lett.* **120** (1985) 93.
116. G. E. Tranter, *Mol. Phys.* **56** (1985) 825.
117. G. E. Tranter, *Chem. Phys. Lett.* **115** (1985) 286.
118. G. E. Tranter, *J. Theor. Biol.* **119** (1986) 467.
119. G. E. Tranter, *BioSystems* **20** (1987) 37.
120. G. E. Tranter, *J. Chem. Soc. Chem. Commun.* (1986) 60.
121. G. E. Tranter and A. J. MacDermott, *Chem. Phys. Lett.* **130** (1986) 120.
122. G. E. Tranter, *Chem. Phys. Lett.* **135** (1987) 279.
123. A. J. MacDermott and G. E. Tranter, submitted to *Chem. Phys. Lett.*
124. A. J. MacDermott and G. E. Tranter, submitted to *Nature.*
125. G. E. Tranter, A. J. MacDermott, R. E. Overill, and P. J. Spears, to be submitted to *Proc. R. Soc. A Lond.*
126. A. J. MacDermott and G. E. Tranter, to be submitted to *Proc. R. Soc. A Lond.*
127. J. S. Binkley, R. A. Whiteside, P. C. Hariharan, R. Seyer, J. A. Pople, W. J. Hehre, and M. D. Newton, *Quant. Chem. Prog. Exch.* **11** (1978) 368.
128. J. S. Binkley, M. J. Frisch, K. Raghavachari, D. DeFrees, H. B. Schlegel, R. A. Whiteside, E. Fluder, R. Seeger, and J. A. Pople, *GAUSSIAN82,* Carnegie-Mellon University, Pittsburgh.
129. L. Wiesenfeld, *Mol. Phys.,* in press.
130. S. L. Miller, *Biochim. Biophys. Acta* **23** (1957) 480.
131. C. Ponnamperuma, in *The Origins of Prebiological Systems and of Their Molecular Matrices,* S. W. Fox (Ed.), Academic, New York, 1965, p. 221—236.
132. J. Oro, *ibid.,* p. 137—162.
133. N. W. Gabel and C. Ponnamperuma, *Nature* **216** (1967) 453.
134. C. Reid and L. E. Orgel, *Nature* **216** (1967) 455.
135. R. Shapiro, *Orig. Life* **16** (1986) 283.
136. A. W. Schwartz and L. E. Orgel, *Science* **228** (1985) 585.
137. A. J. MacDermott, G. E. Tranter, and S. B. Indoe, *Chem. Phys. Lett.* **135** (1987) 159.
138. A. J. MacDermott, G. E. Tranter, and S. B. Indoe, *Proc. 2nd FECS Int. Conf. on Circular Dichroism,* Budapest (1987), p. 145.
139. A. B. Vistelius, *Zapiski Vsyesoyuz. Mineral. Obsh.* **79** (1950) 191.
140. C. Palache, H. Berman, and C. Frondel, *Dana's System of Mineralogy,* 7th ed. Vol. III, Wiley, New York, 1962, p. 16.
141. C. Frondel, *Am. Mineral.* **63** (1978) 17.
142. A. G. Cairns-Smith, *Genetic Takeover and the Mineral Origins of Life,* Cambridge University Press, 1982.
143. A. W. Schwartz and L. E. Orgel, *J. Mol. Evol.* **21** (1985) 299.
144. P. R. Kavasmaneck and W. A. Bonner, *J. Amer. Chem. Soc.* **99** (1977) 44.
145. S. Furuyama, M. Sawada, K. Machiya, and T. Morimoto, *Bull. Chem. Soc. Jap.* **55** (1982) 3394.
146. G. Wyrouboff, *Bull. Soc. Mineral. Fr.* **19** (1896) 219.
147. C. Soret, *Arch. Sci. Phys. Nat.* **7** (1899) 80.
148. H. Copaux, *Bull. Soc. Mineral. Fr.* **33** (1910) 167.
149. A. Amariglio, H. Amariglio, and X. Duval, *Ann. Chim.* **3** (1968) 5.
150. A. Brack and G. Spach, *BioSystems* **20** (1987) 95.

SAŽETAK

Elektroslaba bioenantioselekcija

A. J. MacDermott i G. E. Tranter

Ovaj rad daje pregled dokaza za stav da biomolekulska kiralnost nije odre-đena slučajno nego elektroslabom interakcijom. Ostali utjecaji, kao npr. zemljino magnetsko i gravitacijsko oplje ili cirkularno polarizirano svjetlo, ili su lažno kiralni ili pak spareni (akiralni) u prostornom ili vremenskom prosjeku, ostavlja-jući tako slabe interakcije kao jedini konzistentan i univerzalan kiralni utjecaj.

Elektroslaba bioenantioselekcija može se odvijati ili β-radiolizom ili preko malih energijskih razlika koje povređuju pravilo sparivanja (PVED, parity-violat-ing energy differences) između enantiomera. PVED proizvode električki slabi enantiomerni višak od samo 10^{-17}, ali se ovaj može povećati do homokiralnosti u toku 10^4 godina pomoću snažnog Kondepudijevog mehanizma. Računi PVED po-kazuju da su prirodne L-amino kiseline stabilnije od njihovih »neprirodnih« D-enan-tiomera, a također su PVED-stabilizirani prirodni D-gliceraldehid i D-deoksiriboza. PEVD također objašnjava zapaženi 1% višak 1-(—)-kvarca, koji može pre-biotskom mineralnom katalizom povećati elektroslabi enantiomerni višak do 10^{-4}.