II. MOLECULAR DIPOLES AND CHIRALS

A. ELECTRIC DIPOLE MOMENTS

According to Debye (1912) if the two gravity centers of opposite charges in a molecule coincide in the absence of an external electric field, it is electrically symmetrical; its electric moment, namely the product of the charge by the distance of the charges to gravity centers is null. Oppositely, in the case of a permanent existence of a "dipole", the molecule is asymmetrical. There is a shift between the gravity centers of the negative charges (electrons) and the positive charges (nuclei); such centers constitute, in the molecule, the two poles of opposite charges which together are called the "electric dipole". The molecule itself and the bonding uniting its two atoms are called "polar".

In the lack of a field, the thermic agitation (in gazes and liquids) confers to the vectors (electric moments of the dipoles) all possible directions in the space.

In a field, two phenomena occur:

1) charges are displaced in the molecule and this becomes polarized (if it was not already);

2) dipoles, formed or modified, tend to orient themselves parallely to the direction of the field when thermic agitation allows it.

In the case of a very quick oscillation of the field, as in a light ray, this polarization of orientation cannot occur because the molecular movement is too slow compared to the frequency of the radiation.

In electricity, the dipole generates a *dipolar electric moment* or molecular movement represented by a vector with important orientation and largeness. The dipolar electric moment is the vector $M = Ql$ in which two equivalent punctual Q charges and of contrary sense are separated by a fixed distance l. In an electrical field E, the dipole is submitted to the couple $C = M \times E$ which tends to orient it in the direction of the field. It is the case of molecules of which negative and positive charges have a gravity center which does not coincide. More complicated charge distributions correspond to multipolar moment.

Polar molecules are able to orient themselves under the many external actions. This phenomenon is known as *polarization,* a term which expresses the idea of the disequilibrium of a phenomenon (electric, magnetic, chemical, vibratory) which is not equally distributed in the space but oriented, eventually around poles. For instance, in dielectricals, the term of polarization expresses the modifications of an insulator submitted to the effects of an electric field.

In *spontaneous* polarization, as in the case of ferro-electrical crystals, all dipolar moments are oriented in the same direction. The dipolar electric moment in their molecules results from dissymmetry of their positive and negative charge distribu-

tions. In other materials whose molecules are permanently polarized by chemical forces, polarization can be caused by molecules induced to rotate into the same alignment under the influence of the electric field (see water molecules, II.B1).

In geophysics, the study of disposition of electric charges at the interface of sand and electrolyte has provided *induced* polarization models (Loeb, 1970). Electric current paths were shown to be altered due to polarization of an ore grain. At the beginning of the charging process, the current passes through the electrolyte and the sphere if it is conductive. Then a polarization builds up and, at the end, the electrolyte shell acts as the dielectric of a condenser; the charging current cannot cross it any more, the grain is by-passed, and the particle of polarizable material acts as an elementary electric dipole. By contrast, in absence of polarizing field, the spherical core is surrounded by an electric field which has a spherical symmetry, and the particle does not act as an elementary electric dipole (Bertin and Loeb, 1976).

B. MINERAL DIPOLES

1) *Dipolar water*

Water has many unusual properties (Franks and Mathias, 1982), among which polarity and self-association which have biological consequences in macromolecule hydration and in cell membranes where the polarity of the molecular components is a major factor in determining how they are arranged. No doubt then that "the chemistry of life is water chemistry" as pointed out by Sheeler and Bianchi (1987).

In the cell, water exists in two forms: free and bound. Free water represents 95 per cent of the total cellular water and is the principal part used as a solvent for solutes and as a dispersion medium of the colloid system of protoplasm. Bound water, which represents only 4 to 5 per cent of the total cellular water, is loosely held to the proteins by hydrogen bonds and other forces. It includes the so-called unmobilized water contained within the fibrous structure of macromolecules. Because of its polarity (see below), water can bind electrostatically to both positively and negatively charged groups in the protein. Thus, each amino group in a protein molecule is capable of binding 2.6 molecules of water (De Robertis *et al.*, 1979).

Macromolecules in aqueous solutions may be "vicinally (interface) hydrated" while small solutes (small ions; small non-electrolyte molecules) do not have such type of hydration but have ion-hydration or "hydrophobic hydration". Thus if one accepts that macromolecules are vicinally hydrated while small solutes are not, the following question must be answered "is there a critical size of molecules above which vicinal hydration occurs?" (Drost-Hansen, 1982).

The hydrogen bonds between water molecules "loose" in water freezing to ice (below 4°C) which then increases its volume while decreasing in density (floating icebergs). "Solid water" or ice may occur with a large number of different structures,

such as the high-pressure ice polymorphs and the clathrate hydrates forming a lattice network. Despite its rigid structure, ice has about the same electrical conductivity as liquid water. This would be due to the possibility of proton jumping or tunnelling effect (see p. 38) along immobilized water molecules in the crystal lattice of ice (Lehninger, 1975).

Considering the many different crystalline ices known, and the nature of their structures, Rice (1975) has suggested that a modest arrangement of the positions of a group of water molecules can (and does) generate new minima in the potential energy surface, and that these new minima correspond to qualitatively different connectivities of the hydrogen-bond network. Only such an infinite hydrogen-bond network (Stanley *et al.*, 1981) could be invoked to explain the "memory" of water when tested as a template for antibody molecules (Davenas *et al.*, 1988).

In a water molecule the hydrogen atoms approximate naked protons on the surface of the oxygen atom. The net charge for the molecules as a whole is neutral (same number of electrons and protons). From spectroscopic and X-ray analyses the precise H-O-H bond angle is 104° 45' (Pauling, 1960). It is not absolutely stable but represents an average sharing of electrons and distribution of charges (Salisbury and Ross, 1985). The protons, thus distributed apart on the surface of the oxygen atom, provide a slight positive charge on one side of the molecule. This is balanced by an equal negative charge on the other side of the molecule. Such a polar molecule in which the electrons are asymmetrically distributed has a dipole moment. Thus, although the water molecule is electrically neutral, its partial positive and partial negative charges are separated, with the result that the molecule is an *electric dipole* (Fig. 3A).

Dipolar molecules of H_2O are attracted to each other to give associated clusters of definite structure (Fig. 3A), but of a size which remains undefined as long as the "surfaces" of the associated entities display a polar distribution of positive and negative charges. However, the oxygen atoms which carry the negative charge are very much larger than the hydrogen atoms. One hydrogen atom is situated between two oxygens, and is bonded on one side covalently to one O atom; in a covalent bond, valency electron pairs are shared between two atoms; since the valency electrons of two atoms are involved, the electron doublet is called a shared pair. On the opposite side it is attracted electrostatically by the negative charge of the other O atom and such electrostatic linkage is known as a hydrogen bond (Pimentel and McClellan, 1960). The fact that the hydrogen bond is considerably weaker than the covalent bond is conventionally denoted by O-H--O. As a result of the asymmetric arrangement of the two covalent bonds, the distribution of electric charges within the neutral molecule of water is such that the hydrogen nuclei appear to be positive with respect to the oxygen which has taken up two electrons. Such dipolar structure of H_2O leaves weakly negative regions near the central oxygen atom at the other two corners of an imaginary tetrahedron. Consequently, when molecules of water
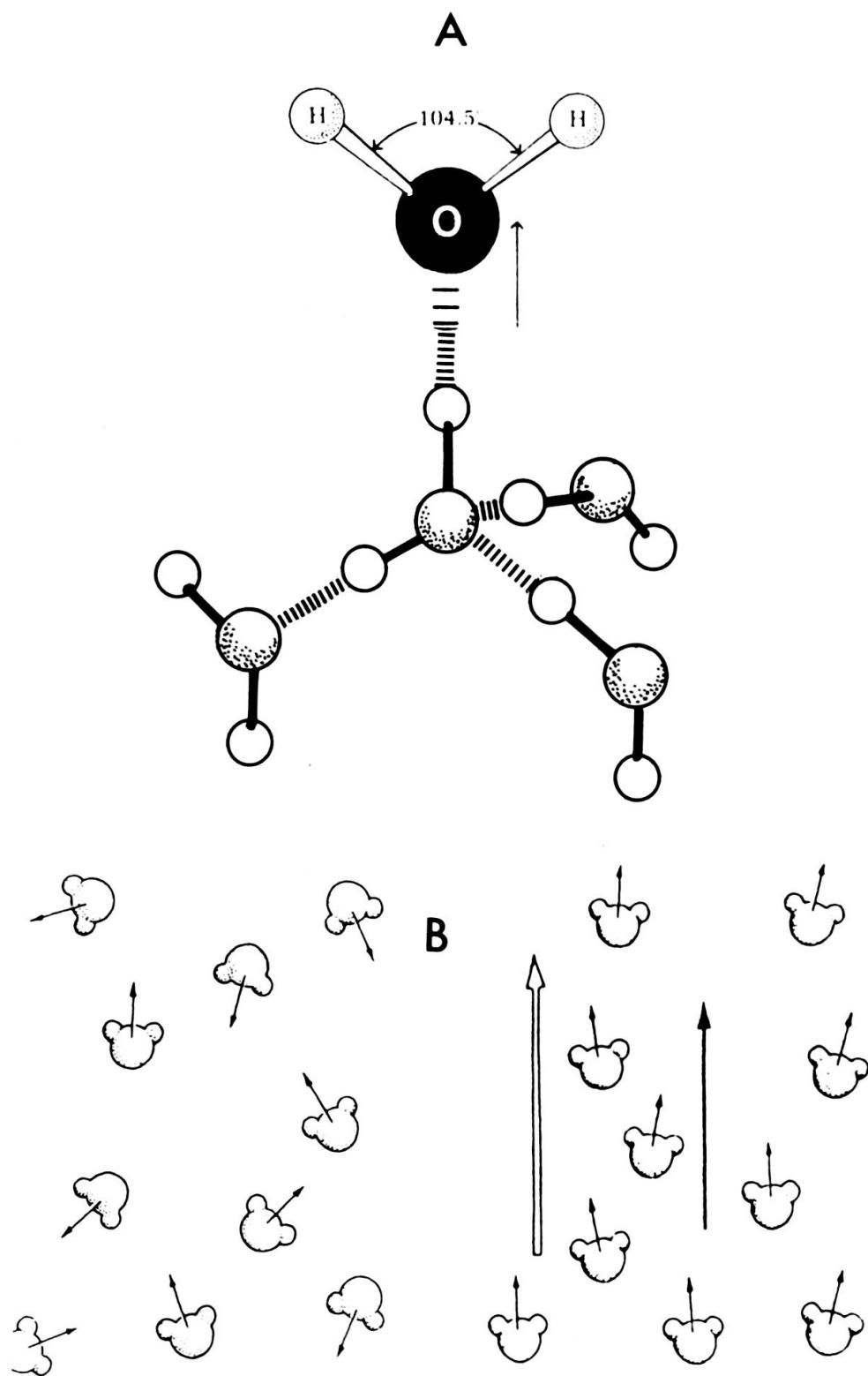
FIG. 3.

Electric dipolar nature of the H₂O molecule.

(A) One water molecule transiently joined to four others in a hydrogen-bonded lattice (''flickering cluster''). Redrawn from ''water structure'' in Alberts *et al.,* 1983.

(B) Multidirectionally-oriented torques of H₂O dipoles *(left)*. Torques of dipolar molecules all oriented in an electric field *(right)*. Adapted from Walker, 1987.

join together transiently in a hydrogen-bond lattice, one molecule becomes the center of four-components clusters. These small clusters can then join to other water molecules to constitute short-lived assemblies known as "flickering clusters" (Alberts *et al.*, 1983). Liquid water can thus be considered as "a fluid network of transiently hydrogen-bonded molecules eventhough its precise structure is still not known with certainty" (Darnell *et al.*, 1986).

The polarity of water and its hydrogen-bonding property make it a potent polar solvent for many ionic compounds and other polar molecules. Water also disperses amphipathic molecules, such as soaps, to form micelles with hydrophobic groups inside and charged, hydrophilic groups on the external surface. Crystalline salts, e.g. NaCl, readily dissolve in this polar liquid. The Na^+ and Cl^- ions are rapidly hydrated by the dipolar molecules and pulled away from the crystal lattice (Lehninger, 1982).

Among both polar (hydrophilic) and non polar (hydrophobic) types of molecules there can occur a so-called Van der Waals interaction which is considered as a non specific weak attractive force created when two atoms or two molecules such as O_2 approach one another closely. Such weak interaction would result from the formation of transient dipoles because, in any atom, momentary random interaction between transiently forming dipoles results in a net weak attraction (Darnell *et al.*, 1986).

The polarization of the water is expressed as the net dipole moment per unit of volume. It is zero when the dipole moments are randomly oriented, because for every moment pointing in one direction another moment points in the opposite direction. When an electric field begins to align the dipole moments, polarization increases. It would be at the maximum if all the dipoles were in alignment. Random molecular motion or Brownian motion, however, continuously knocks dipoles out of alignment, keeping the polarization below the maximum level. Early in this century the eminent Dutch physicist Peter J. W. Debye demonstrated mathematically why microwave energy is strongly absorbed by water. The key fact is that water molecules cannot rotate instantaneously into alignment with electric field. Since they have a mass spread over a certain volume, it takes time for torque to make them rotate (Fig. 3B). The retarding forces from surrounding molecules also affect rotation. This is the theoretical basis for one of the hypotheses proposed to explain "the secret of microwave oven's rapid cooking action" as being that water in the food rapidly absorbs the energy of the waves (Walker, 1987).

Water has only a very sligth tendency to ionize but the products H^+ and OH^- (10^{-7} M of each at 25°C and pH 7.0) have very profound biological effects. The extent of this reversible dissociation is quantitatively expressed by an equilibrium constant (K'_{eq}, see Lehninger, 1982). However, protons do not exist "bare" in water to any significant extent; they occur only in hydrated form of the so-called hydronium cation H_3O^+ [$= H^+(H_2O)$], which is itself further hydrated through

additional hydrogen bonding with water to form the $H_9O_4^+$ ion, as well as more highly hydrated forms (Fig. 2-6 in Lehninger, 1975).

A proton can jump very rapidly from an hydronium ion to a neighboring H_2O molecule to which it is hydrogen-bonded. Such *tunnelling* has the effect of translocating protons at a rate that is much higher than the rate of diffusive or bulk movement of H_3O^+ ions per se (Lehninger, 1975).

Proton tunnelling may be an important phenomenon in polarized biological systems. It has been proposed that H^+ could jump along the lattice of H_2O molecules hydrating the filaments of actin (Tirosh *et al.* 1980). Hydrated filaments of this contractile protein could thus function as electric "cables" in the polar conduction of protons implied in the internal electric circuitry of apically growing cells (Turian *et al.*, 1985; see VI.A2b).

2) *Other mineral dipoles*

Following H_2O as maximal dipole with a permanent electric moment or Debye unit μ of 1.8, there are SO_2 ($\mu = 1.7$), NH_3 ($\mu = 1.5$), HCl ($\mu = 1.03$) and SH_2 ($\mu = 1.0$). Oppositely, CCl_4 and CO_2 have no electric moment ($\mu = 0$) (Eggert and Hock, 1947). Polar molecules can be associated either in series or as parallel dipoles and quadrupoles. Among the six dimeric species that may be formed from the first row hydrides, HF, H_2O and NH_3 monomers, all the predicted structures illustrated by the Van der Waals stereochemistry were in essential agreement with experimental data obtained by high-resolution spectroscopy, except for the NH_3 dimer.

New results lead to revise the traditional view that the condensed-phase interaction of NH_3 (NH_3 dimers, etc.) are dominated by hydrogen bonding and that NH_3 can be viewed as an amphoteric substance that can donate a proton through bonding (Nelson *et al.*, 1987). Nevertheless, and in agreement with the traditional view, NH_3 has been confirmed as a nearly universal proton acceptor. As dipole it can combine with H^+ to form the cation $(HNH_3)^+$ or NH_4^+. Electrostatically, the cations H_3O^+ and NH_4^+ are thus comparable as the nucleus H^+ is fixed in the same way on both H_2O and NH_3 molecules acting as dipoles.

C. ORGANIC DIPOLES

In the more complex polar molecules, dissymmetry of the electronic "cloud" occurs in the same way as in diatomic molecules. The several attractive moments of the atoms for the electrons combine themselves and create a single dipole globally attributed to the whole molecule.

Methane (CH_4) as the primordial molecule of the so-called organic, carbon chemistry is structurally *isometric* and *apolar*: its single C atom shares four electrons

with four H atoms and the shared electron pairs form four covalent single bonds isometrically spaced in tetrahedral arrangement.

Oxidative steps can lead, through the hydrophilic methanol (CH_3OH), to the first negative "monopole" formic acid ($HCOO^-$) while the reductively produced methylamine ($CH_3NH_3^+$) features a primitive positive "monopole".

It is the biologically very significant ability of C atoms to share electron pairs with each other to form very stable carbon-carbon single bonds which has led to *anisometric* molecules, with ethane (CH_3CH_3) as prototype of the hydrocarbon series of homologues. This neutral and hydrophobic molecule has evolved to the primordial biogenic molecules through the hydrophilic ethanol (CH_3CH_2OH) and the electrically *mono*polar molecules (acetic-glycolic-glyoxylic acids) either to the most oxidized, *homo*bipolar oxalic acid ($^-OOC\text{-}COO^-$) or to the primordial amino acid, the electrically *hetero*bipolar glycine as prototypic organic dipole:

$$\overset{\displaystyle H}{\underset{\displaystyle H}{H_3N^+\text{-}\overset{|}{\underset{|}{C}}\text{-}COO^-}}$$
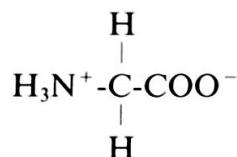
1) Single molecules

a) *Small molecules*

Molecules such as CH_4 (methane) and CCl_4 (carbon tetrachloride) are electrically symmetrical and their permanent electric moment or Debye unit is therefore $\mu = 0$. It is in CH_3Cl (chloroform) in which the gravity centers of positive and negative charges are the most distant that the μ ($= 1.89$) is the highest among chloride derivatives of methane (Eggert and Hock, 1947, Tabl. 35). Nitromethane ($\mu = 3.8$), acetonitrile ($\mu = 3.5$) and acetone ($\mu = 2.83$) have the highest electric moments among organic compounds.

Non polar molecules are those with no effective dipole moments. Their bonds are covalent, electrons binding atoms being equally shared as for C-C bonds. The molecules of non polar liquids, like benzene or hexane, show relatively little tendency to attract each other electrostatically. In CH_4 (methane), for example, the carbon and hydrogen atoms have a similar affinity for their shared electron pairs, and so neither the carbon nor the hydrogen atom is noticeably charged.

b) *Fatty acids*

Fatty acid molecules contain both polar or hydrophilic and non polar or hydrophobic parts. In their dissociated states the carboxyl ends of the molecules are mildly soluble in water, whereas the long hydrocarbon chains repel water (Sheeler and Bianchi, 1987).

Like free fatty acids, their salts or soaps, and glycerophosphatides which also contain both polar and nonpolar groups do not dissolve in water, but they do form micelles. A micellar arrangement is not a true solution but a suspension or dispersion. Soap molecules consist of a long, nonpolar hydrocarbon chain terminating in a polar carboxyl group that is ionically bonded to a metal ion such as K^+ or Na^+. When dispersed in water, the soap molecules aggregate to form spherical micelles, in which the polar carboxyl groups of the soap molecules are arranged at the surface of the sphere, where they form weak bonds with the surrounding water, and the nonpolar hydrocarbon chains project inward.

The more complex molecules of glycerophosphatides are characterized as amphipathic, that is, one end of the molecule is strongly hydrophobic (i.e., the end containing the hydrocarbon chains) while the other end is hydrophilic due to the charged nature of the dissociated phosphate group and other substituents (Sheeler and Bianchi, 1987).

c) *Amino acids and amines*

With its simple H- as residue (R) group, glycine is the only α-amino acid having no asymmetrical carbon atom. In the classification of the 20 amino acids according to the polarity of their R groups, glycine belongs to the "polar but uncharged R group" (see below). The high degree of polarity of its α-amino and α-carboxyl groups is not influenced by either a hydroxyl (serine, etc.), amide (asparagine, etc.) or thiol (cysteine, etc.) groups.

Some of the other amino acids are also polar molecules: although they are electrically neutral overall, they have localized concentrations of positive and negative charges. The polarization results from the presence of oxygen or nitrogen atoms, which have a strong affinity for electrons. A few of the amino acids not only are polar but also carry a net electric charge; in other words, they are ionized under physiological conditions. When a polar or charged side chain projects into the aqueous environment, the strongly polar H_2O molecules assume an orderly arrangement.

An approximate classification of amino acids in five groups is based on the degree to which the amino acid's side chain is polarized at pH 7 (Doolittle, 1985): amino acids can be separated into *non-polar* side chains molecules (alanine, valine, leucine, isoleucine); uncharged, *polar* chains molecules (glycine, serine, threonine, cysteine); basic, *positively* charged side chains molecules (lysine, arginine, histidine); acidic, *negatively* charged side chains molecules (aspartic and glutamic acids); other side chains (generally those made up exclusively of carbon and hydrogen) are non polar.

The dipolar nature of amino acids was first suggested by the fact that crystalline amino acids have melting points that are much higher than those of organic molecules of similar size. The crystal lattice of amino acids is held together by strong electro-

negative forces between positively and negatively charged functional groups of neighboring molecules. When a crystalline polar amino acid such as alanine is dissolved in water, it occurs as a dipolar ion which can act either as an acid (proton donor) or as a base (proton acceptor). Amino acids having this two-way property are *amphoteric* or ampholytes (from "amphoteric electrolytes"). Simple monoamino monocarboxylic α-amino acids such as glycine and alanine are considered as *diprotic* acids when they are fully protonated (see Lehninger, 1982); in this bipolar form they have two groups that can ionize to yield protons (see glycine, p. 39).

Those α-amino acids having a single amino group and a single carboxyl group crystallize from neutral aqueous solutions in a fully ionized species and are called a dipolar ion or zwitterion (German for "hybrid ion"). The characteristic pH at which the amino acid is present as its fully ionized but electrically neutral dipolar form is called the isoelectric pH or isoelectric point (pH_i or P_I). Although such dipolar ions are electrically neutral and do not move in an electric field, they have opposite, equal electric charges at their two "poles".

Bipolarity also occurs in quaternary amines such as the N,N,N,-trimethylglycine or betaine. This molecule is metabolically inert and because of its dipolar nature, no counterions need to be accumulated to maintain electroneutrality when it functions as an important osmoprotective molecule as reported in several groups of Gram negative eubacteria, including halotolerant bacteria, extreme and moderate halophiles, and nonhalophilic bacteria (Hutkins *et al.*, 1987).

2) *Multiple molecules (polar chains)*

Polar molecules can evidently — because of their bipolar fields — associate into multiple molecules that can be described by stoechiometry. There results the formation of polar chains, with a decrease or with an increase of the bipolar state. These associations influence the curve expressing as a function of the concentration, the variations of the orientation polarization of solutions of polar compounds. As prototypic polar chain, the molecule cystine, formed by linkage of two molecules of cysteine via a disulfide bond, is a sort of heterobipolar molecular twin:

$$
\begin{array}{ccc}
& H & \\
& | & \\
H_3N^+ - C - COO^- \\
& | & \\
H_2C \quad\text{---}\quad S
\end{array}
\qquad
\begin{array}{ccc}
& H & \\
& | & \\
H_3N^+ - C - COO^- \\
& | & \\
S \quad\text{---}\quad CH_2
\end{array}
$$
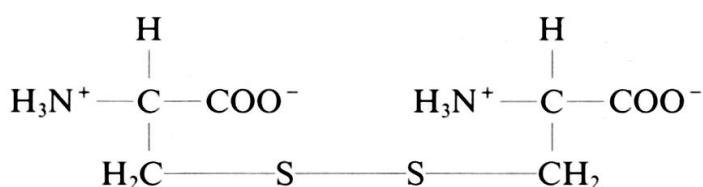
By contrast, the molecules involved in primary electrons transfer steps seem to be rather widely separated, by distances of approximately 10 Å. There is no evidence that they are connected by molecular "wires" for electrons to flow through. The active components are rigidly embedded in a non-polar region of the transmembrane protein

matrix. Charge separation, therefore, must occur by electron tunnelling between the components. Quantum-mechanical tunnelling enables electrons to move across relatively large, atomic distances without ever being in between. To elucidate this electron-tunnelling process, compounds are synthesized with barriers to electron transfer deliberately built in — an approach that could be described as molecular engineering. In this spirit, the compound thus synthesized is considered as a device fulfilling a physicochemical function: that of a rectifier for converting electromagnetic waves into a d.c. voltage. The basic design involves a donor group with a low ionization potential, an acceptor with an affinity for electrons, and a hydrocarbon spacer or bridging unit that is (in the first instance) electrically insulating — an inert separator of the donor and acceptor (Fig. 4). The synthesis of such donor-insulator-acceptor devices (DIADs) is now being performed in many laboratories. The most renowned of these compounds are the three-components TRIAD assemblies of Moore *et al.* (1984) composed of carotene, porphyrin and quinone residues.
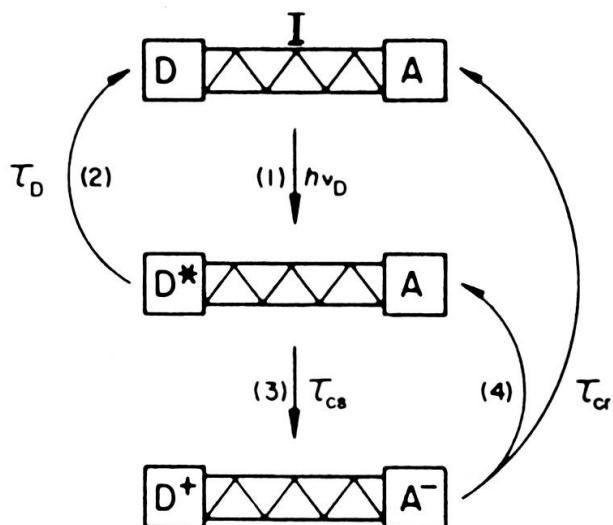

FIG. 4.

Reversible photolytic production of the giant dipole state (D^+-A^-) from a rigid donor (D) − insulator (I) − acceptor (A) molecular device; $h\nu_D$ = photoexcitation of the donor moiety; T_{CS} = charge separation; T_{CR} = charge recombination; T_D = lifetime of local-excited-donor to ground-state relaxation. Schemated from Warman *et al., Nature* 320: 615 (1986) and *Nature* 327: 462 (1987).

Joran *et al.* (1987) reported the fluorescence lifetimes of a homologous series of seven porphyrin-quinone molecules, each with differently substituted benzoquinones separated by an identical rigid phenylbicyclo[2.2.2]octane spacer (10 Å, edge-to-edge) which vary with respect to driving force for electron transfer from the first excited single state of the porphyrin. The key features of these series of molecules lie in the fact that the edge-to-edge distance is fixed and exothermicity ($\triangle$G) is tunable.

Thus, the effect of $\triangle G$ on electron transfer can be measured while avoiding major perturbations of the electronic structure.

Many parameters need to be investigated for long-distance electron transfer to be understood and controlled. The role of the driving force for charge separation is clearly of prime importance. Without a driving force, electron transfer could not compete with deactivating processes after excitation by light. However, the energy used in charge separation is lost, unavailable for further chemical or physical work. So it is important to know the minimum driving force necessary to compete efficiently with deactivation. It is significant that for a given compound the rate of charge separation is almost independent of the solvent, be it non-polar benzene or highly polar acetonitrile. This has also been found for the forward electron transfer step of Paddon-Row *et al.* (1986) compounds. The eventual stabilization energy gained from specific ion-polar-solvent interactions in the giant dipole state apparently has little influence on the forward kinetics.

The intensity of charge-separation kinetics to solvent polarity is in sharp contrast with the very strong solvent influence on charge recombination (Wasielewski *et al.,* 1985; Warman, 1987). The rate of long-distance charge recombination increases by two orders of magnitude when the solvent medium is changed from a non-polar saturated hydrocarbon to the more highly solvating ether dioxane (Paddon-Row *et al.,* 1986). This contradicts the intuitive feeling that ionic species are more stable in more polar media, but evidently is highly favourable for photosynthetic compounds working in a non-polar environment. Terms such as "superexchange" and "through-band interactions" have been used in an attempt to describe this non-classical behaviour which may be of particular relevance to the mechanism of photosynthesis. Structural analysis (Deisenhofer *et al.,* 1984) showed that an extra bacterio-chlorophyll and two non-conjugated phytyl side-chains lie along the path followed in the primary electron-transfer steps. This may not be just a coincidence.

Polarization of orientation of the dipole depends upon concentration and provides information about the behaviour of the associated polar molecules. This is examplified by solutions of nitrobenzene in the benzene (non-polar molecules) which present a constantly decreasing polarization of orientation (when concentration increases) while when it is dissolved in ethanol, such decrease is only produced after having passed by a maximum. The study of specific medium effect on the highly exothermic recombination of giant dipoles should be extremely interesting.

D. Chiral molecules

The name of chirality is derived from the Greek word for hand and the chiral symmetry has to do with handedness, the property defined in nuclear physics by a particle's spin (see I.D.4) and direction of motion.

Like other symmetries of nature, chiral symmetry has a conservation law associated with it. This law states that the total number of right-handed particles and the total number of left-handed ones can never change. In the ordinary world of protons, electrons and similar particles handedness or chirality clearly is *not* conserved and there is violation of the conservation law. The symmetry-breaking mechanism implies that the weak charge, and the associated handedness of particles, should only be conserved at extremely high energy, where a particle mass is a negligeable fraction of its kinetic energy (Harari, 1983).

"A deeper truly chiral influence comes from the weak interactions, mediated by the recently discovered $W^{\pm}$ and Z^0 bosons. The weak force gives an intrinsic left-handedness, or helicity, to the electron: radioactive β-decay produces an excess of electrons with anti-parallel (left-handed) momentum and spin vectors over the alternative parallel (right-handed) combination, which increases in proportion to v/c, the velocity of light. Similarly positrons emitted in β-decay have an intrinsic right-handedness. Left and right-handed molecules are therefore not true enantiomers, because the weak interaction can distinguish them. The true enantiomer of an L-amino acid is the D-amino acid made of anti-matter. This parity-violating effect of the weak interaction is detectable in a very slight optical activity of atoms" (MacDermott, 1986).

In 1884, Louis Pasteur has conjectured that a dissymmetric force pervades the physical world, extending even to the crystallization dish used for the separation of tartrate enantiomers. He was the first to identify the class of handed or enantio-morphous molecules, which are characterized by structures that are not superposable by translation and rotation alone upon the corresponding mirror-image form. Such structures were first termed "dissymmetric" by Pasteur and, subsequently, "chiral" by Kelvin (1904) from the familiar analogy of the morphological relationship between the left and the right hand. Fischer (1891) then introduced a convention to distinguish between the two mirror-image molecular forms, one being termed the D-isomer *(dextro)* and the other the L-enantiomer *(laevo)*. Although still used for the α-amino acids and the sugars, the Fischer convention accumulated ambiguities of nomenclature and was superceded. In the generally adopted system of Cahn *et al.* (1966), based on the relative mass of the atoms bonded to an asymmetric carbon atom or other chiral centre, the absolute structure of a given chiral molecule is unambiguously specified as that of the R configuration *(rectus)* or the S configuration *(sinister)*.

A stereochemical feat has challenged the general principle originally enunciated by Louis Pasteur. In the so-called *la coupe du roi,* each apple yields a pair of homochiral segments, the two being identical in the ideal case of the sphere (Horeau, 1937). The particular handedness of the two segments depends on the pair of opposite equatorial quadrants chosen for the horizontal cuts. A left-handed segment, given by one of the choices, and a right-handed segment, provided by the other, cannot

be reassembled to form an apple. According to Pasteur (1884), a chemist without dissymmetric agents is able to synthesize only an equimolecular mixture of R and S isomers, a racemic mixture, or an internally compensative single product, with bonded R and S moieties, the so-termed *meso-substances*. Similarly, the chemical degradation of a large achiral molecule would produce, at most, a racemic mixture of chiral fragments (achiral *meso*-2,3-dimethyltartaric acid R- + S- lactic acid). The homochirality of the two halves produced by *la coupe du roi* has as chemical analog the reductive cleavage of an achiral diether which contains *meso*-bridges. "The thought-experiment of Horeau does not violate Pasteur's principle, since a dissymmetric agent is involved, the chiral stereospecific catalyst" (Mason, 1983).

The left-right handedness or chirality is one of the strangest things about the universe. It ranged from the preponderance among spiral galaxies of rotation to the left with respect to the direction of recession to the fundamental question of why life is based on DNA made itself of D-sugar and proteins made of L-amino acids, rather than the enantiomeric (mirror-image) L-sugar/D-amino-acid system. The fact that the L-amino acids and the L-polypeptides are more stable than their D-enantiomers might be a first answer. This could take into account quantifiable disordering effects, such as the known rates of spontaneous racemization of amino-acid enantiomers, and the minor enantiomeric photodiscrimination of solar radiation at twilight, when there is a small net circular polarization, oppositely handed at dawn and dusk (Kondepudi and Nelson, 1985). The slight circular polarization of sunlight around sunrise is balanced by an equal and opposite polarization around sunset, "so this mechanism would only be viable if life evolved in a lake bounded to the east or west by a large mountain" (MacDermott, 1986). Circularly polarized photons would thus cause a similar chiral selection, but without the need for a nearby radio-active source.

The discovery, in 1956, of the non-conservation of mirror-image symmetry in the weak nuclear interaction supported Pasteur's surmise. "The parity-violating weak neutral current interaction gives rise to an energy difference between a chiral molecule and its mirror-image isomer, resulting in a small stabilization of the L-amino acids and the L-peptides in the α-helix and the β-sheet conformation relative to the corresponding enantiomer" (Mason, 1985). The subsequent unification with electro-magnetism has allowed the characterization of both the sign and the magnitude of the universal chiral electroweak interaction. The sign is in accord with the observed products of natural selection of enantiomers of one hand from the heterochiral mixture of a racemic substrate, and for the propagation of optically pure homochiral products. In 1953, Frank was surprised to learn, that the origin of biomolecular handedness still appeared to be problematic. He then proposed a homogeneous chemical kinetic mechanism for an open flow-reactor system with a continuous input of achiral substrate from which both enantiomers, L and D, are formed. Each of

the optical isomers autocatalyses its own production and competitively inhibits propagation of its enantiomer.

Life processes on a molecular scale take place between chiral molecules in a chiral environment; presumably, this has been so since primordial biotic times. How did the selection (or production) of one enantiomer of a chiral pair of molecules take place in a prebiotic world where presumably ordinary chemical processes had no statistical preference for selecting (or producing) one isomer over the other? Ordinarily, chemical reactions are indifferent to chirality. However, a reaction such as the formose reaction (formaldehyde polycondensation into monoses) that produces chiral molecules is expected to make racemic mixtures with "left-handed" and "right-handed" forms of the products equally represented. If biochemistry is different in this respect, and if cells can treat enantiomers differently, then this is because the molecules in cells, especially the enzymes, are already chiral. In the evolutionary process, RNA has been suggested as the original genetic material. Since, RNA has been found to function as an enzyme, a new principle which throws light on early evolution (Cech, 1986). The substrates for oligomerization of the first informational RNA molecules could have been prochiral. Thus they gained a chiral centre on oligomerization and molecular-dynamics simulations led to predict a flexible (pyrophosphate) backbone permitting incorporation of monomers in either syn-L-like or anti-D-like conformations without chain termination.

Bernal (1951) suggested that quartz crystals in the primitive environment might have biased a mixture of molecules locally. Quartz crystals come in "left-handed" and "right-handed" versions which are self-seeding; so quite extensive regions might well have contained only one of the kinds of quartz, and hence tended to accumulate or destroy enantiomers preferentially. The units out of which quartz crystals are built — silicic acid — are achiral, so in making a quartz crystal chirality is literally being generated. Presumably in any particular case this is from an initial chance that might have gone either way: "an initial seed happened to start, say left-handed quartz and it simply went on that way" (Cairns-Smith, 1982).

Bonner (1972) has reviewed the long history of this fundamental question of origin. In terms of the doctrine of chemical evolution there are two sorts of explanations that have been given: an external "abiotic" explanation and an internal "biotic" explanation, that is:

1. The environment created an asymmetric bias: in particular, at least somewhere, it provided especially L-amino acids and D-sugars.

2. The environment always produced racemic mixtures of chiral molecules, but at some stage in their evolution organisms came to select molecules of uniform chirality from these mixtures.

Asymmetric synthesis by the use of asymmetric catalysts must also be deliberately considered along with other available methods as a practical strategy for the synthesis of only one of two possible stereoisomers (Mosher and Morrison, 1983). In laboratory

experiments circularly polarized light can show small discriminations in the photochemical decomposition of chiral organic molecules. But it is doubtful if there was much circular polarisation of light in primordial skies: the effect in any case could only have been very feeble.

Other asymmetric influences have been considered. Circulatory polarized photons such as "Bremsstrahlung" γ-rays are generated when longitudinally polarized β-decay electrons interact with matter. Thus, it has been suggested that a fundamental asymmetry of matter — expressed in the non conservation of parity — might have left its mark at the chemical level: "Bremsstrahlung" photons are always polarized the same way. It has been further shown (Bonner *et al.*, 1975) that longitudinally polarized electrons can have a different effect on enantiomers. But again the effect found was small — a 1% enantiomeric bias in the destruction of D,L-leucine.

According to Cairns-Smith (1982), the most radical cause that has been suggested for a possible asymmetry in the early environment is that enantiomers are not, after all, chemically equivalent, only very nearly so (Yamagata, 1966). The idea here is that the fundamental asymmetry between matter and antimatter might show up directly, creating differences in the energies of enantiomers (the true enantiomer of, say, L-alanine being D-alanine made of antimatter). For example, reaction rates, melting points and solubilities might be slightly different.

So where does this lead us: supposing that there was a primordial soup, was it chirally biased? "I don't know" is clearly the best answer, according to Cairns-Smith (1982).

Recently, attention has been called by Rubenstein *et al.* (1983) to synchrotron radiation emanating from supernovae as source of circularly polarized light capable of inducing asymmetric photochemical reactions of prebiotic molecules. This light is predominantly polarized in the plane of motion of fast electrons orbiting around supernovae and when viewed off-axis the polarization is elliptical or circular. Chiral molecules in the interstellar medium or on planetary surfaces would undergo preferential photosynthesis or photolysis when irradiated by such a source. Domains on opposite sides of the plane of predominant polarization would be exposed to light of opposite helicity so that overall symmetry would be preserved. But in a single location, one enantiomer would predominate.

Molecular chirality can be approached either as an expression of random fluctuation or as the result of a specific mechanism. Mann and Primakoff (1983) point out that statistical fluctuation as the basis of chiral dominance is highly unlikely because it would require the assumption of a very small number of terrestrial polymerization sites. The physical processes that have been invoked include the interaction of a racemic mixture with electrons of specific helicity emitted by a nuclear β-decay process, and the apparently more effective interaction of circularly polarized light (CPL) with molecular orbitals. Photosynthetic and photodestructive reactions with

CPL have been described in a number of reviews, and a 2.50% optical enrichment of a racemic mixture of the amino acid leucine has been achieved by photolysis with 212.8-nm CPL. The sources of CPL previously considered include sunlight reflected at the Earth's surface, and by the Earth's magnetic field (Flores *et al.,* 1977). Alignment of interstellar grains has also been identified as a source of linear polarization, and a phase shift can lead to circular polarization (Savage and Mathis, 1979).

It has also been thought that polarized X-rays produced from β-particles could have a role in the origin of homochirality and primeval life processes. Asymmetric decomposition of racemic mixtures of biomolecules by longitudinally polarized β-rays has been described as a possible mechanism. However, the exceptional prebiotic conditions required "do.not favour asymmetric β-radiolysis as a selector of the exclusive signature of optical activity in nature" (Meiring, 1987). For life to arise from chiral building-block molecules modified by synchrotron light, it would be necessary for these either to survive intact during the heating process of planet formation or to be ferried on incoming grains as the planet periodically traverses clouds of interstellar material or to be assembled on tepid planetary surfaces illuminated by residual supernova synchrotron radiation.

As already described above, the slight circular polarization of sunlight around sunrise is balanced by an equal and opposite polarization around sunset. Recently, measurements of a net circular optical polarization in sun's light have led Kemp *et al.* (1987) to wonder whether a quite small circular polarization might have influenced the chirality (average handedness) of the Earth's biomolecules: "if biogenesis began not slowly but in a burst of photochemistry, over a period of months perhaps, then a net circular polarity in sunlight might have promoted chirality".