BIOPHYSICS AND BIOCHEMISTRY

Biological Fluids as Chiral Anisometric Media

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Molecules of dissolved substance in many homochiral solutions are arranged in linear associations forming chiral strings (with length to diameter proportion of 10^1-10^5), which leads to solidification of the solution into anisometric gel. This paper describes the formation of the string system in aqueous solution of amino acid phenylalanine, formation of individual strings, weaving of thin strings into thick ones, successive alteration of the solution chirality sign with transition to new levels of the association organization. It seems that biological media are anisometric fluids containing chiral molecular associations and strings, or anisometric gels.

Key Words: *association; anisometry; strings; chirality; biological fluid*

Biological fluids are chiral by certain classes of molecules and homochiral by identifiable biochemical components (proteins, amino acids, carbohydrates, lipids, *etc*.) [10]. We studied the formation of anisometric structures in model homochiral fluids in order to detect the corresponding effects in biological media.

MATERIALS AND METHODS

The following methods were used: light microscopy of liquid solutions and xerogels formed after evaporation of the solvent from solution; measurements of absorption IR spectra of solutions; measurement of polarization plane rotation angle in chiral solutions.

RESULTS

We shall discuss the results and compare them with previously known facts.

Experimental studies of polarization plane rotation, circular dichroism, IR spectroscopy, and fluorescence indicate that in many homochiral solutions of low concentrations [$(10^{-2}$-$10^{-3})$M and lower] chiral molecules are spontaneously united into associations, subsequently transferred into anisometric macroscopic objects, strings [6-8]. The fluid filled with strings should be regarded as not homogeneous, but dispersed medium, for which the term "anisometric fluid" is suggested. As the concentration increases (or the temperature is reduced), the concentration and thickness of the strings increase. The solution is eventually solidified, as a chaotic framework of rather rigid strings forms in it. It is suggested to call this substance "anisometric gel".

Previously the strings were observed in nonpolar solvents; here we describe the formation of strings in aqueous solution of phenylalanine and in model solutions of trifluoroacetylated amino alcohols (TFAAA). A droplet of phenylalanine solution in a concentration of 10^{-1} M was applied onto a slide, which was placed on ice. Microscopy after drying showed a well-developed system of strings in the sample (Fig. 1). This model system presumably indicated that strings of this kind could form in typical biological fluids, after the formation of associations. Hence, biological fluid by certain components could be regarded as a homochiral solution containing associations of these

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chiral molecules, which transformed (as its concentration increased) into a string-containing anisometric fluid and in some cases into anisometric gel.

The possibility of molecule assembly in associations in a homochiral solution of homogeneous composition was confirmed by rearrangement of IR absorption spectrum (Table 1). The stereospecificity of multicenter interaction of molecules at the expense of weak bonds (complementarity) determined by their chiral nature led to geometrical linearity of associations (*i.e.*, for these associations the parameter analogous to Kuhn segment was much larger than its molecular size). In other words, the multicenter connection between the molecules is significantly less hinged than in usual macromolecule.

The formation of short associations has been described [5]. Multi-particle associations, forming Bethe lattice and hence, isometric, have been discussed previously [2].

The time (t*) of chiral molecules joining in an association was evaluated in a cell model of solution [1]. A molecule jumps from cell to cell to a distance I during time t, where I and t are the model parameters. Let us calculate by the standard mode the time between successive collisions, assuming that the chiral molecules as a rule form an association during collision: $t^* \sim I/6Dna^2$, where $D=I^2/6t$ is diffusion coefficient and a is the characteristic size of the molecule. Under conditions of the above experiments $a \sim 5\times10^{-8}$ cm, $I \sim 10^{-8}$ cm, $D \sim 10^{-5}$ cm^2/sec, $n \sim 10^{20}$ cm^{-3}, and hence, $t^* \sim 10^{-9}$ sec.

The formation of linear associations leads to their further combination into macroscopic objects, strings. We recorded the formation of a solitary string in a capillary with the inner diameter of 300 μ (Fig. 2).

Let us evaluate the velocity (V) of string formation by elementary spiral geneatrix with a radius (r) of ~5 angstrom and step (*h*) ~r, so that the spiral consists of one coiled pile of molecules and the molecules' transport to the string end is determined by the diffusion mechanism. We found that $V \sim Da^2hn/r$, where n is the number of dissolved substance molecules in a volume unit [6], that is, V~1 cm/sec, which coincides by the order of magnitude with the experimental value of 2 cm/sec obtained by microvideorecording as the below value. This coincidence indicates that the forming string is practically monomeric. Let us call the string of this kind elementary.

TABLE 1. IR Absorption Coefficient for Solution of a Chiral TFAAA Compound in Cyclohexane as a Function of Concentration n. Bands 1736 cm^{-1} and 1700 cm^{-1}

1736 cm^{-1}	0.2	1.2	1.9	1.3
1700 cm^{-1}	0	0	2.1	6.2
n, mg/10 ml	0.42	1.67	3.5	7

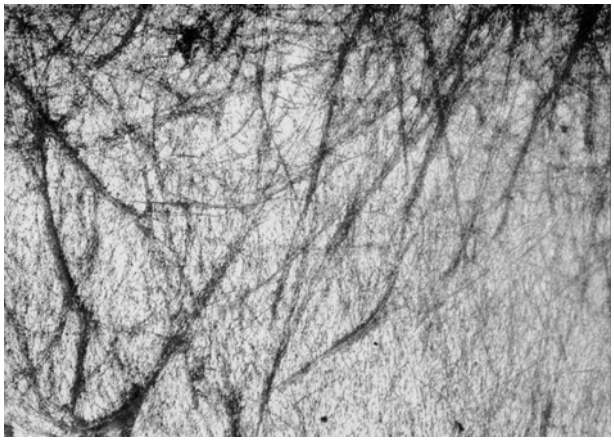

Fig. 1. Strings formed in aqueous solution of phenylalanine, ×100.

On the other hand, if $nd^2/kT \sim 1$ (d~ea – the molecule dipole moment, e electron charge, k Bolzman constant, and T temperature), the solution can experience cooperative effects, augmenting significantly if the time of cooperative processes is short in comparison with association life spans. In order to minimize free energy, the molecules dipole elements are to be oriented and directed differently in the string and the adjacent mesophase, which is shown by common analysis of complete energy of a standard dipole-dipole interaction [3]. This leads to the radial mechanism of string assembly for strings of virtually any length (up to centimeter fractions) in diffuse times $t_D \sim h^2/6D \sim 10^{-8}$ sec, where $h \sim 10^{-6}$ cm is cross-section area, from which molecules diffuse during radial assembly of a string.

This interaction implies high sensitivity to the external electric field near the point of phase transition to the string system and string orientation along the force lines, which we have presumably observed (growth of strings from crystallites, numerous double strings, and many other effects).

These evaluations indicate that transition from associations to string takes place in solution during the time ~(10^{-9}-10^{-7}) during which an association is assembled from ~(10^1-10^2) molecules (in case of purely diffuse mechanism of assembly; it is easy to show that an association of ~20 molecules meets the macroscopicity criterion [9]) to macroscopically high number thereof (in case of radial assembly in a cooperative field). Hence, in fact associations and strings can form simultaneously during time of ~(10^1-10^2) under experimental conditions.

The strings strongly interact with each other under certain conditions. Thick strings are woven from thinner ones (Fig. 3). Presumably, these interactions are due to dipole moment periodically distributed along the strings. The above processes determine the structure of the strings and solution in general.

Change in the polarization plane rotation angle φ in TFAAA solutions is caused by changes in the homochiral solution structure. In our experiment at a concentration below 6 mg/10 ml, φ linearly increased with the concentration in accordance with Bio law [4], this indicating a statistical independence of individual TFAAA molecules. The velocity of φ alteration then changed the direction, this indicating the emergence of associations and chirality alteration in the system of molecules newly added into solution. At a concentration of 10 mg/10 ml the φ alteration velocity changed the sign once more, which indicated the formation of a new level of association organization — the strings.

Successive alteration of the chirality sign in transition to subsequnt levels of molecular association formation should be regarded as a half-empirical rule resulting from the thermodynamic systems inclination to the free energy minimum. This seems to be the common rule of macroscopically chiral phases formation in molecular systems with mixed weak interactions (polar, hydrogen, *etc.*), which due to the universal molecular design of TFAAA were in fact simulated in [6-8]. Hence, the left chiral structural motive was to lead to the emergence of the right chiral motive in the suprastructure (for example, in transition from monomer to macromolecule) and vice versa, which should be taken into considerationwhen discussing the biomacromolecules complementarity.

Let us offer a persuasive example of the universal nature of this assumption. A previous study [11] showed by means of Bruster laser microscopy the formation of chiral dimeric domains on the surface of aqueous solution of N-stearoylserine methyl ester L- or D-enanthiomeres. Surface-active molecules of this substance form a condensed phase in the form of spirals. Macrostructures observed in the monolayer domains from pure L-enanthiomeres are mirror-symmetrical to the macrostructures in the domains of monolayers isolated from pure D-enanthiomeres. The L-enanthiomeres form right spirals, D-enanthiomeres left ones.

Let us note that by the present time it is hardly possible to find the precise minimum of free energy with consideration for the full spectrum of molecule-molecule interactions in so intricate systems and to calculate from the first principles the thermodynamic characteristics of the system, including the chirality sign.

Hence, at a certain concentration of dissolved substance (~(10^{-2}-10^{-3}) M for TFAAA solutions in weakly polar solvents) the solution is solidified because of formation of a chaotic carcass of rather rigid strings in it [6-8]. We suggest calling this dispersed system, macroscopically homogeneous at the millimeter level and more, anisometric gel.

Fig. 2. Solitary string in a capillary, ×200.

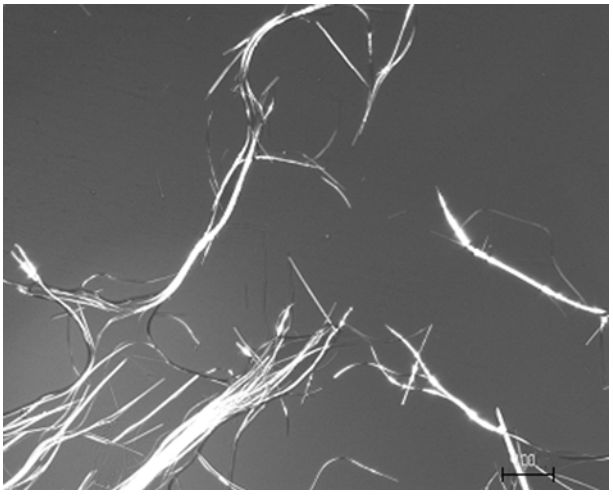

Fig 3. Weaving of thick strings from thin ones, ×200.

The results indicate that biological fluids are most likely anisometric fluids containing associations and strings of many chiral molecules. In some cases they can be anisometric gels formed by a carcass of chiral strings. We may hypothesize that the formation of these anisotropic supramolecular chiral structures served the base for the initial pre-biological morphogenesis in living cell precursors and determined their subsequent architecture and choreography.

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