Chirality and Homochirality of Lipids is Necessary to Form LD-Supramolecular Structures of Cell-Cell Communications

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The processes of cell-cell commutations via anisometric supramolecular structures (strings) *in vitro* and in physicochemical models of lipids (trifluoroacetylated amino alcohols) were studied. It was shown that biological commutation through strings is more efficient than the diffusion mechanism of transfer of bioactive molecules at distances typical of populations. Strings kinetics was constructed and the signal turnover rate in these systems was evaluated. It was demonstrated that the condition of chirality of lipids forming the cell biomembrane stems from experimentally observed cell commutation through anisometric supramolecular structures.

Key Words: *strings, commutation, chirality, lipids, supramolecular structures*

There is a long-range intercellular communication mechanism with anisometric structures 10-100 μ in length and diameter of 0.1 μ. They presumably consist of membrane lipids and have an axial cavity for molecular transport [6,7,8].

We demonstrated commutation of mesenchymal cells *in vitro* through extremely anisometric structures or strings formed from molecular components of the membrane (experimental data [3], Fig. 1). Numerous cytonemes 170-200 nm thick, in some cases branching, up to 100 μ length connecting the lamellar regions of cells (Fig. 1) obviously could be classified as strings. As follows from the condition the condensed phase continuity, the strings consist of membrane material (Fig. 1). This in turn suggests dynamic nature of string formation and the existence of efficient molecular mechanisms underlying reversible processes of generation and disintegration of these structures.

However, it remains unclear whether low-molecular lipid fractions are sufficient to form these ld-supramolecular communication structures or additional high-molecular compounds (*e.g.*, proteins) are necessary. This question is of special interest in regard with the fundamental problems of prebiological evolution under conditions of shortage of high-molecular material.

The role of low-molecular-weight lipids in the formation of strings was experimentally evaluated by molecular modeling of the main elements or domains of physicochemical lipid design. In physical and supramolecular chemistry, weak intermolecular interactions are usually described classically, so this approach should enable us to assess properly the main features of cooperative processes [1,5]. Thus, our experimental model represents all physical and chemical domains corresponding to the majority of the weak interactions (polar, hydrophobic, hydrophilic, *etc.*) involving lipid molecules. The reliability of this simulation is much higher than in any theoretical and calculated molecular model. Variations in the molecular design of the model allows us not only to take into account the amphiphilicity of lipids and variety of weak interactions but, more importantly, to identify the role of chirality in the formation of ld-anisometric structures. Figure 2 shows structural formulas of trifluoroacetylated amino alcohols (TFAA) used as molecular models. Molecular isometry related to low molecular weight of TFAA (200 Da) provided model versatility relative to these

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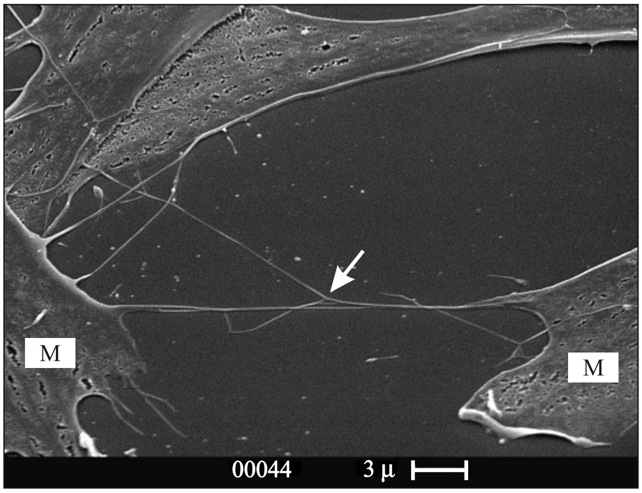

Fig. 1. Strings between mesenchymal cells (M). Scanning electron microscopy.

physical and chemical characteristics of the original (lipid) and excluded the effect of possible structure-forming steric factors not related to chirality. Figures 3 and 4 show anisometric structures for xerogels of low-concentration (10^{-3} M) solutions of compounds (I-III). Thus, strings are formed from the chiral compound I with self-assembly in solution concentration of 10 M with anisometry $l/d \sim 10^4$ (where l is the length of the string and d is its diameter), while the dendrite-like structures were fairly shaped from the achiral compounds II and the racemate (III), having significantly different values of anisometry. In case of compound II, this phenomenon is associated with poor stereospecificity of molecules, from which the isotropic nature of the condensation inevitably follows. In case of racemate (III), isometry during condensation is due to efficient association of enantiomers of opposite signs in achiral dimer with lower stereospecificity. Therefore, formation of extremely anisometric ld-structures requires not only chirality, but also homochirality of constituent molecules.

The following relationship was previously established for the growth rate (V) of string with continuous thickness in the solution, which occurs through diffusion of the dissolved substance to the end of the string: $V=4(D/r_0)[(n_0-n^*)N]$, where r_0 is the radius of the string end, n_0 is real concentration of the solution, n^* is equilibrium concentration of the solution corresponding to the zero rate of string growth, and N is the concentration of molecules in the condensed phase of the string [2]. Physically, this means that growth rate of the string of a smaller diameter is significantly higher than that of thick string, or the growth rate significantly (linearly) decreases with decreasing anisotropy. At the same time, obviously more material needed to form a condensed phase of such a topology. Naturally, the preferred option of living systems is the lower consumption of substances and a greater rate of string formation (as a switching or communication element). Therefore, the molecular chirality as a factor increasing the regularity of the supramolecular self-assembly is a necessary condition for the formation of extremely anisometric structures when modeling cell-cell communications.

The experimental data suggest that the presence of a single chiral carbon atom is sufficient for the formation of strings even for small isometric lipid molecules at sufficiently trivial spectrum of weak bonds (polar

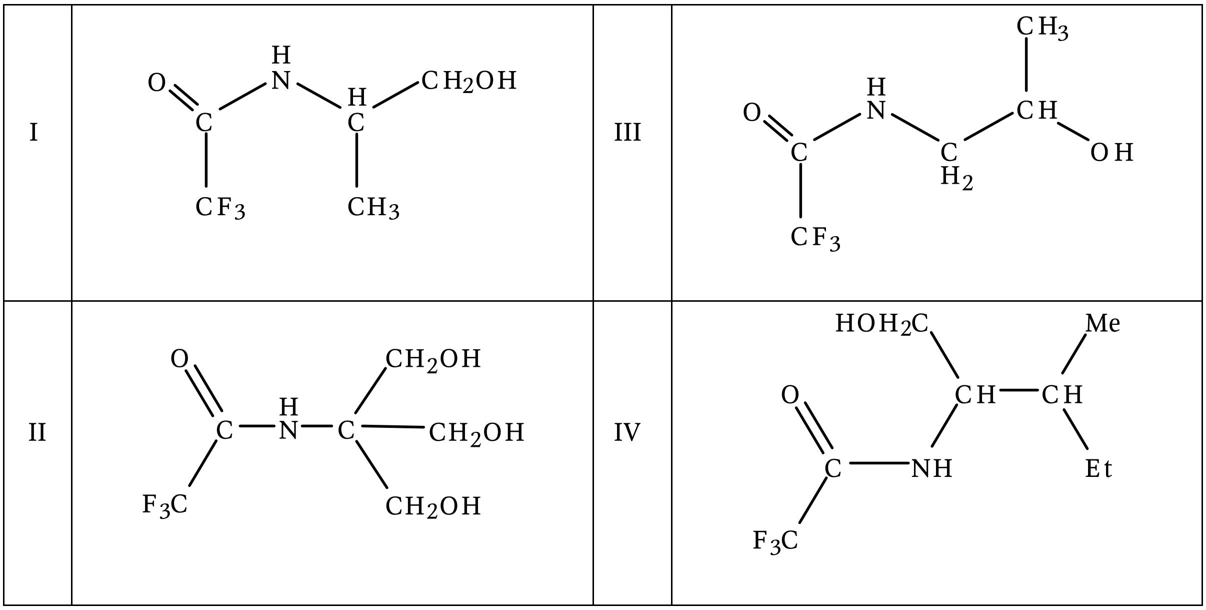

Fig. 2. Structural formulas of model TFAA compounds.

Fig. 3. Supramolecular strings in a model system.

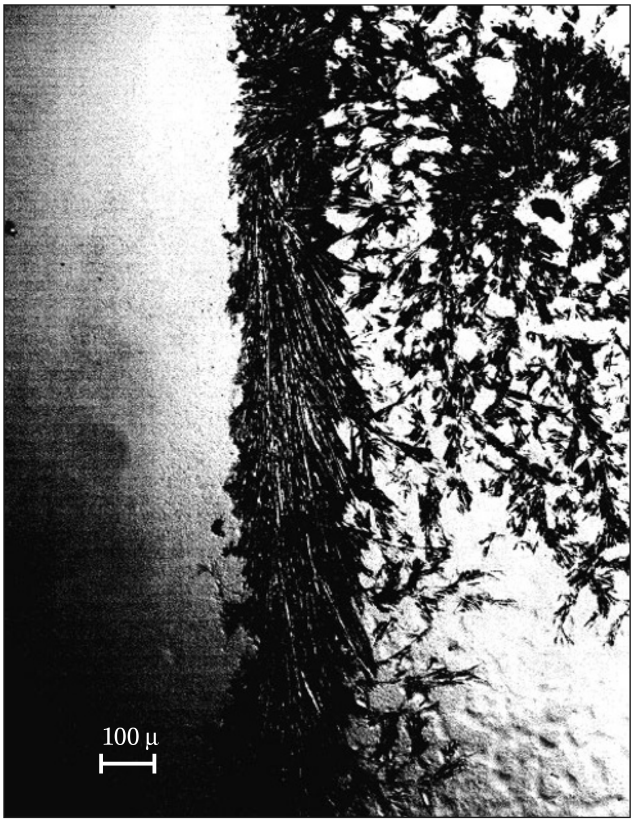

Fig. 4. Dendrite-like structures in a model system.

and hydrogen), in which they participate. Our experiments have shown that introduction of an extra chiral carbon atom (compound IV) reduced the threshold concentrations of string formation by almost 1.5 times. This reflects general physical principles of long-range order supramolecular self-assembly with increasing stereospecificity or complementarity of the molecules determined by their chirality [1]. The above-mentioned reversibility of string formation is provided by weak intermolecular interactions. Thus, activation energy for reversible string formation was found to be 0.5 eV and the melting temperature in the solution is above the range of physiological temperatures (50-60°C); to melt or dissolve the string, local heating, increase in the polarity, or change in medium pH are sufficient [2]. This process can be provided by physicochemical fluctuations of local extracellular environment, which can take place under physiological conditions.

Thus, it is shown that the condition of lipid homochirality may result from the necessity of cell-cell communications via extremely anisometric supramolecular structures (strings). In this case, the factors determining the formation of these structures in low-concentrated solutions are chirality and homochirality.

The new phenomenon of formation of strings as elements of commutation (communication) in low-concentration solutions (10^{-3} M) as well as the necessary and sufficient condition of lipid chirality and homochirality provide new insight into the processes of prebiological evolution. Indeed, if string-mediated communication is the preference of natural selection, the choice of lipid homochirality and its sign, *i.e.* chiral asymmetry should occur at the stage of lipid vesicles in low-concentration solutions of prebiological evolution [4].

REFERENCES

1. J. W. Steed and J. L. Atwood, *Supramolecular Chemistry*, Eds. A. Tsivadze, V. V. Arslanov, A. D. Garnovsky [in Russian], Moscow (2007).
2. S. V. Stovbun, *Chemical Physics,* Moscow (2011), Vol. 5, pp. 57-64.
3. S. V. Stovbun, A. I. Mikhailov, A. A. Skoblin, *et al.*, *Khim. Fizika*, **6**, 73-82 (2011).
4. V. A. Tverdislov, L. V. Yakovenko, and A. A. Zhavoronkov, *Ros. Khim. Zh.,* **51**, No. 1, 13-22 (2007).
5. P. Atkins, *Physical Chemistry*, New York (1994).
6. A. Rustom, R. Saffrich, I. Markovic, *et al.*, *Science*, **303**, 1007-1010 (2004).
7. A. O. Tarakanov and L. B. Concharova, *Commun. Integr. Biol.*, **2**, No. 4, 359-361 (2009).
8. B. G. Zani and E. R. Edelman, *Commun. Integr. Biol.*, **3**, No. 3, 215-220 (2010).