

# Chirality as a Fundamental Basis of Macroscopic Helicity

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**Abstract**—Using molecular modeling we have shown that low-molecular-weight gelator molecules, which are able to form long and thin strings in dilute isotropic solutions, do not have any notable shape features. They have neither preferred axes nor visual asymmetry. Thus we confirm a crucial role of chirality itself as molecule asymmetry in the formation of macroscopic helicity.

**Keywords:** chirality, helicity, complexity formation, hierarchy of structures, molecular modeling.

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## INTRODUCTION

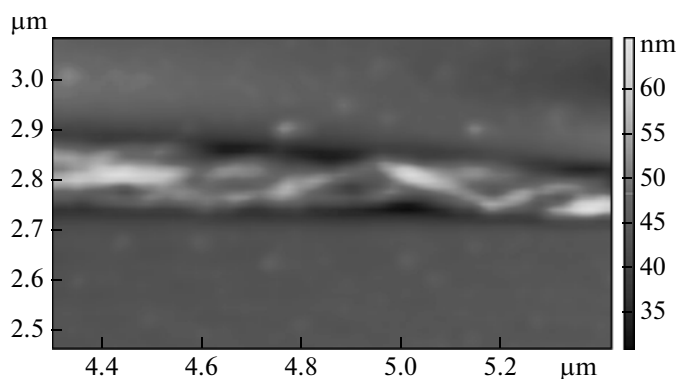
Recently, Professor V.A. Tverdislov from Moscow State University suggested a new fundamental synergetic principle for the formation of complex hierarchical systems, including living ones [1]. An evolving system can repeatedly change its type of symmetry within one level of organization by consistently increasing its complexity and the transition to a higher level of organization can change the sign of the chirality. In other words, during the transition to increasingly large and complex systems we can observe a consistent alternation of the chirality sign. This phenomenon is common in living systems. For example, naturally-occurring amino acids are “left-handed” (L), their folded and twisted  $\alpha$ -helices are “right-handed” (D), while supercoils (coiled coils) formed from coiled together  $\alpha$ -helices are left-handed (L) again. There are many examples that confirm this trend [1]. However, there are exceptions among complex biological systems. This trend has a common physico-chemical and biological meaning and apparently is a general principle of the formation of complex and heterogeneous systems in a more homogeneous and simpler environment.

The transition to the next level of the organization associated with the change of the chirality sign is obviously accompanied by the change in direction of the spiralization (twisting) of the structural elements of the system. As well, the very presence of helicity in the system means the emergence of a preferred direction and often the presence of elongation along this direction of anisometric formation. There are well-known processes in biology during which helical structures spontaneously appear in initially isotropic solution that do not contain any extended structures. For example, the polymerization of actin or formation of microtubules from tubulin subunits have this property

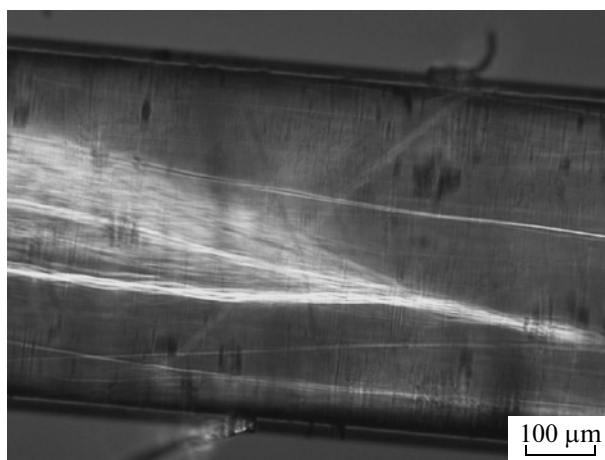
[2]. Moreover, the spontaneous formation of spiral structures, the increase in complexity of which is associated with a change of the chirality sign, is possible in systems with substances of low molecular weight, for example, in solutions of trifluoroacetylated amino alcohols (TFAAA). These chiral molecules chemically mimic amino acids and can serve as their physico-chemical analogues (biomimetics), which reproduce the hierarchy of biomacromolecular structures according to their metrics, scale and symmetry [3].

The spontaneous formation of spiral strings is observed experimentally in TFAAA solutions. In particular, the formation of left-handed spirals in solutions of D-enantiomers is observed with an increase in the concentration of one of these molecules. They then twist into right-handed supercoils. [3] Using the example of this biomimetic system, a rule of the multiple signs of chirality during supercoiling (Figs. 1, 2) was experimentally confirmed, which is equivalent to the emergence of a new level of organization. However, if the heuristic source of the rule formulated by Tverdislov [1, 2] is the molecular source to a large extent, then what are speculative or hypothetical basic premises associated with manifestation of macroscopic helicity in a simple model system at scales ranging from  $\sim 1$  nm to about 100  $\mu\text{m}$ ?

The most obvious cause of the manifestation of anisometry and helicity could be the presence of the preferred axes or form features of TFAAA molecules, which result in their anisotropic condensation. Therefore, during this study the shape and degree of anisometry of TFAAA molecules has been characterized by methods of molecular modeling.



**Fig. 1.** Spiral string coiled from three thinner strings. Xerogel of the TFAAA-5 solution in heptane, 1 mg/mL. AFM (atomic force microscope), semi-contact mode. Horizontal and vertical scale,  $\mu\text{m}$ , subsidiary, nm. Substrate, mica [12]



**Fig. 2.** Supercoiling of strings in a solution. Liquid solution of TFAAA-4 in heptane, 0.4 mg/mL. KOC, line 100  $\mu\text{m}$  [12]

## MATERIALS AND METHODS

Models of TFAAA molecules were designed on the basis of the standard types of atoms for the OPLS-AA force field. [4] Each type of atom corresponds to a certain mass of the atom, its van der Waals radius, and electric charge. Furthermore, parameters of valence interactions with other types of atoms were determined for each atom type. The partial atomic charges of the constant part of the molecule have been adjusted according to the RESP procedure [5] on the basis of quantum-chemical calculations carried out using the FireFly software package [6] in the basis set 6311 by DFT (B3LYP5). The GROMACS 4.5.3 software package was used for simulation of molecular dynamics [7].

For each of the molecules, a 1 ns molecular-dynamics calculation in heptane was performed. To accomplish this, single TFAAA molecules were placed in cubic boxes with edges of 3 nm filled with solvent and pre-relaxed during 100 ns. All calculations were performed using periodic boundary conditions.

The molecular anisometric coefficient was calculated as an average ratio of the maximum size of the molecule to its maximum size in the perpendicular projection. The distance between the centers of atoms without their van der Waals radii was used as the molecular size.

The coefficients of anisometry of TFAAA molecules. Standard deviations are used as the error

Molecule	Anisometry	Molecule	Anisometry
TFAAA-1	$2.95 \pm 1.25$	TFAAA-5	$1.77 \pm 0.29$
TFAAA-2	$1.66 \pm 0.89$	TFAAA-6	$1.51 \pm 0.57$
TFAAA-3	$1.41 \pm 0.14$	TFAAA-7	$1.38 \pm 0.27$
TFAAA-4	$2.07 \pm 1.54$	TFAAA-8	$1.48 \pm 0.22$

## RESULTS AND DISCUSSION

Figure 3 shows three-dimensional models of TFAAA molecules created with consideration of the van der Waals radii of the atoms. These models are almost isodiametric, which is also confirmed by direct calculation of anisometric coefficients (Table 1). The ratio of the maximum size of the molecule to the maximum transverse dimension varies from one and a half to three, which indicates their isodiametricity. It should be noted that despite the presence of a chiral center in the TFAAA molecule (the TFAAA-4 molecule has two chiral carbon atoms), a visual analysis of the 3D-images of the molecules does not reveal any obvious physical and geometrical features in the form of molecules imposed by their chirality. All studied molecules look like isometric bodies that are devoid of both preferred axes and pronounced asymmetry.

This observation may be the key, because every single model of compact media somehow uses the concept “shape of the molecules,” which is needed for an explanation of the properties of the medium. This is a characteristic of both molecular-biological models and of physical models [2, 8, 9]. It is almost paradoxical: macroscopic helicity occurs, but there are no visually detectable features of the molecular form. To overcome this contradiction, it is necessary to use the concept of the ongoing accumulation of helicity in the system of a large number of chiral elements, which leads to the visible manifestations of helicity (Figs. 1 and 2).

The mechanism of such accumulation is based on the symmetry of chiral and achiral molecules. Any achiral molecule by definition contains a mirror rotary axis of the second order in its structure. This means that these molecules have at least two alternative means of interaction with any other molecules or objects. Therefore, if there are no other significant structural features, achiral molecules will equally con-

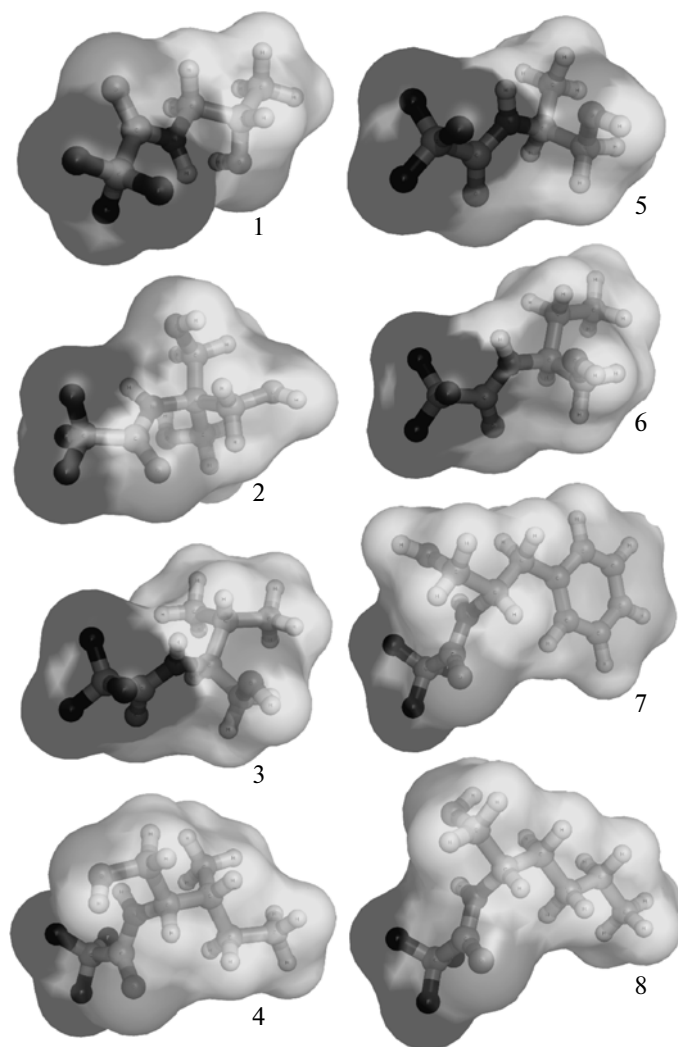


Fig. 3. Molecular models of TFAAA. Covalent bonds and the van der Waals surface of the molecule are shown.

nect with each other on both sites, which may lead to the formation of isotropic structures. In contrast, in the case of chiral molecules, each epitope on the surface of the molecule is structurally unique and may cause asymmetric adhesion of molecules, which leads to one-dimensional helical structures and the accumulation of chiral properties of individual molecules; this leads to helicity.

The change of the helicity sign is apparently due to an increase in the physical size of a compact helical structure during its increase in complexity within the same hierarchical level (Tverdislov [1]), when there is smaller space for each consequent element. As each element joins a structure with a pronounced helicity, it inevitably tightens it. The cause for this is the geometric limitation of possible merging with the next item, which is imposed by spiral motif. Finally, at some point, another element cannot be included in the

structure and its further growth is only possible when an alternative path with opposite symmetry is realized, which is perceived as a transition to the next level of the hierarchy. In fact, this assumption means that the molecular chirality of any molecular object, when it is spontaneously and compactly packed, in statistical systems will inevitably lead to the observed helicity and to the change of its sign at the transition to the next level of the hierarchy, despite its implicit manifestation in the individual structural element.

## CONCLUSIONS

It seems to be quite likely that the discussed manifestation of helicity, which has been proposed as a synergetic pattern [1], is currently the most proven and established criterion (and possibly the only criterion) or even an invariant from prebiotic systems. The presence of this criterion allows one to explain the emergence of homochirality at the stage of chemical evolution in the form of the most abstract formal physical interpretation [10, 11]. It should also be noted that unlike crystals, the conceptions of spontaneous formation of helicity in non-solid media, and especially natural systems, are not trivial. Nevertheless, this is an experimentally observed fact. This fact probably reflects the most common and fundamental features of the medium in which spontaneous development of self-evolved structures is fundamentally possible, which led to the emergence of life on Earth. [1]

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