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Method for determining the chirality sign of peptide nanotubes using the dipole moments vectors calculations

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ABSTRACT

In this work the method for calculating the index and sign of chirality using the values of the dipole moments of each individual dipeptides forming a helix structure of a peptide nanotube is proposed.

Calculations of the individual dipeptide dipole moments using semi-empirical quantum method PM3 and force field method Amber are preformed in the frame of HyperChem software package.

Results obtained for diphenylalnine (FF) peptide nanotube (PNT) with two different initial chirality L-FF and D-FF shows correct results of the chirality changes on D and L for helical PNT, corresponding to the law of the change in the sign of chirality, when the hierarchical structure of the molecular system becomes more complex.

The results obtained give us a new opportunity to see the physical basis for the formation of the type and sign of chirality and open up new possibilities for a quantitative study of this phenomenon. This approach can be applied to other similar structures and peptide nanotubes based on other amino acids and dipeptides.

1. INTRODUCTION

Amino acids form the basis of many complex biomolecular structures and systems in biology, medicine and modern nanotechnology. They form spiral (helix) self-organizing structures of different levels of hierarchical organization [1]. Among them, the simplest and most energetically favorable are α-helices - in biology, this is a common type of regular secondary structure of proteins [1-3]. Moreover, in biology, these helical polypeptide structures of proteins are composed mainly of amino acid residues of left chirality - L-aminoacids [2]. This homochirality of biological systems has developed here, apparently, evolutionary and its reasons are still not clear, although there are a number of hypotheses [4].

But it is important that for natural proteins from these L-aminoacids the regular alternation of the sign (or type) of chirality from the left type “L” to the right type “D” begins in structures of different levels of hierarchical organization: L-D-L-D [5-8]. Accordingly, a biological reproduction system based on DNA has a parallel sequence of changes in the chirality of D-L-D-L with increasing complexity of their level of organization. Research by V.A. Tverdislov’s group from Moscow State University [5-8] showed that this property of chirality is a key point in the hierarchy and self-organization of biological systems.

It should be noted that the very concept of chirality is a general property of an object - not to overlap with its mirror image; so the left and right hand do not match in the mirror. This universal property of matter can be observed at various hierarchical levels from subatomic, molecular and supramolecular scales [9-11]. And not only in living biological systems, but also in many related structures based on the same initial amino acids, artificial and self-organizing molecular structures with various bionanotechnological applications. And here, in principle, left L and right D amino acids can be present on equal terms, while providing a difference in the physical and chemical properties of the structures formed on their basis. This also turns out to be very important for pharmacology and the like.

One of the examples of such self-organizing macromolecular systems are peptide nanotubes (PNT) based on the amino acid phenylalanine (Phe or F) and its dipeptide, diphenylalanine (FF, or in its usual aqueous zwitterionic form H-FF-OH) [11–20]. Possessing a wide range of useful properties, these structures are promising for various applications in nanotechnology, nanoelectronics, and biomedicine [14-16]. Self-assembly of such PNTs occurs in aqueous media rather quickly and under certain conditions affecting the rate of their growth, the shape of self-organizing structures (their thickness and length), and their physical properties [21].

Despite the increasingly widespread use of the concept of chirality in various fields, the assessment of the sign of chirality has so far been mainly qualitative. There is an urgent need for a quantitative assessment of the magnitude and sign of chirality.

Just recently, in the works of a group of the Department of Biophysics, Moscow State University, a simple and clear method for calculating chirality was proposed, based on a strict quantitative calculation of the mixed vector product of three consecutive vectors connecting the central carbon atoms of Ca of neighbouring amino acids of the polypeptide helical structures [22-24]. This approach has already been tested by authors of these works on a wide variety of proteins taken from the Protein Data Bank [25]. These approaches are described in detail in the mentioned works.

In this work, we propose a similar approach, but based on other vectors, namely, on the vectors of the dipole moments of individual amino acids that form the peptide sequence of such α-helix. Here, as an example, we use the structures of peptide nanotubes (PNT) forming α-helices of different types of chirality D and L based on self-assembly from solutions of di-phenylananine (FF) dipeptides of different initial chiralities L-FF and D-FF.

These PNTs were recently investigated in detail experimentally and by methods of computer simulation and calculations, using various approaches - quantum chemical and density functional theory methods [26, 27], including using the VASP program [28]. These studies made it possible to identify sets of sequential vectors of individual dipole moments on the turn of each helix of different types of chirality. To calculate the dipole moments, we used the HyperChem software package [29], which includes an extensive set of different methods: molecular mechanics, molecular dynamics, and various quantum mechanical methods, including semi-empirical quantum methods of various parametrization (AM1, PM3, RM1, etc.) in the Hartree-Fock approximation (restricted and unrestricted). Using these results, in this work, the chirality index is calculated using a technique similar to that proposed and developed in [22-24], but for vectors of dipole moments.

It should be noted that these nanotubes (as well as many similar self-organizing peptide molecular nanostructures in general, based on ordered periodic molecular-crystal structures), well experimentally recorded by modern X-ray methods, and accumulated in the well-known crystallographic Cambridge database CDCC [30], in somewhat similar to the protein database [25]. However, they are not formed on the basis of individual single amino acid residues, but their dipeptides, that is, pairs of amino acids. Depending on the conditions of self-assembly (the type of solution and other factors), they can form both α-helices and β-sheet [16, 17], the latter being characteristic of Anzheimer's disease. In this case, the right D-FF dipeptides obtained in the experiment have the initial α-helix structure (a-helix) and form a left type α-helix - “L”, while the initially left L-FF dipeptides have the structure named as “left-handed helix” [11] and form a right-type α-helix - “D”.

Our task is to carry out calculations using the known dipole moments of each individual dipeptide, arranged sequentially along a turn in the structure of nanotubes with their own different chiralities (for one turn, one turn in a helix (spiral) - 6 such dipeptides is put here).

It is important here to choose the right basis and orientation of the coordinate axes - for left and right nanotubes.

2. COMPUTATIONAL METHODS AND MODEL DETAILS

In this work the models of the diphelylalanine (FF) peptide nanotubes (PNT) with different chirality D-FF and L-FF were constructed using the experimental X-ray data obtained from the Cambridge Crystallographic Data Centre (CCDC) crystallographic database [30] and transformed to the workspace of the HyperChem software [29]. The full details of the FF PNT α-helix constriction on the HyperChem workspace is described in our work [19]. These using data correspond to L-FF was taken from Görbitz work [13] (placed at the No. CCDC 16337 on [30]); and for D-FF was taken from recently reported in the paper [20] (deposited in the CCDC [30], at the No. CCDC 1853771).

For calculation of dipole moment of each FF dipeptides as well as the total dipole moment of both L-FF and D-FF PNT α-helix the semi-empirical quantum-mechanical (QM) method PM3 in the restricted Hartree-Fock approximation (RHF) and molecular mechanical (MM) force field method Amber from HyperChem package [29] were used in this work similarly as in works [18-20].

In these studies were shown that main features of the other methods used (such as AM1 and BIO CHARM) give in these cases approximately the same results of the dipole moments and energy calculations. Therefore, now in this work we use only PM3 and Amber. All calculated dipole moment data are presented in Debye units in this HyperChem software.

To evaluate and calculate the index and sign of chirality, in this work is proposed to use a *mixed (or vector-scalar) product* of three successive vectors of dipole moments $\boldsymbol{D}_i$ produced by individual FF dipeptides constituting the α-helix PNT coil. This approach is similar to the method for evaluating the sign and measure of chirality of the protein helical structures recently developed in [22-24]. The essence of this method is as follows. A model of a polypeptide chain consisting of *n* amino acid residues and having, respectively, *n* C_α atoms - reference points in the method is considered. Vectors v_i are built between each two adjacent reference points, and then for each three consecutive vectors their mixed (scalar vector) product is calculated (taking into account their coordinates):

$$([v_1, v_2], v_3) = (y_1 z_2 - y_2 z_1)x_3 + (z_1 x_2 - z_2 x_1)y_3 + (x_1 y_2 - x_2 y_1)z_3 \,, \quad (1)$$

The sum of all mixed products allows us to estimate the sign of chirality

$$\chi_{total} = \sum_{i=1}^{n-3}([v_i, v_{i+1}], v_{i+2}), \quad (2)$$

If the structure is right-handed, then the mixed products will be positive and the chirality value will also be positive, and for left-handed structures - negative. The mixed product was normalized to a certain degree of the average length of the vectors used (a cylindrical helical line with evenly spaced points was taken as a standard). This made it possible to obtain a quantitative characteristic of the normalized value of chirality:

$$\chi_{norm} = \sum_{i=1}^{n-3} \frac{([v_i, v_{i+1}], v_{i+2})}{C_i} \quad (3)$$

where C_i is the normalization factor.

The method is implemented as a computer program in Python 3.7 and has been validated for over 700 proteins.

In this work we provide the calculation of the sign of the chirality for diphenylalanine (FF) PNT based on dipeptides of different initial chirality (L-FF and D-FF). Using the approach similar [24], and applying it to the vectors of dipole moments of the each individual dipeptides $\boldsymbol{D}_{t,i}$ with its module of total dipole momentum

$$\boldsymbol{D}_{t,i} \; (D_{t,i} = \sqrt{D_{x,i}^2 + D_{y,i}^2 + D_{z,i}^2},$$

where $D_{t,\,i}$ is the total dipole moment of the *i*-th dipeptide vector in the α-helix structure of the PNT; $D_{x,\,i}$, $D_{y,\,i}$, $D_{z,\,i}$ are the components of the *i*-th vector

$D_{t,\,i}$ in the Cartesian coordinates; we can write down the chirality index of the helical structures c_{total} ; and for the normalized chirality - c_{norm}:

$$c_{total} = \sum_{i=1}^{n-2}\left(\left[D_{t,i}, D_{t,i+1}\right], D_{t,i+2}\right),$$
$$c_{norm} = \frac{c_{totaL}}{\left(D_{t,i}^{av}\right)^3} \quad (4)$$

To calculate these data of the chirality index we must to compute data for all individual FF dipole moment and obtain a full set of these dipoles momentum data.

3. MAIN RESULTS AND DISCUSSIONS

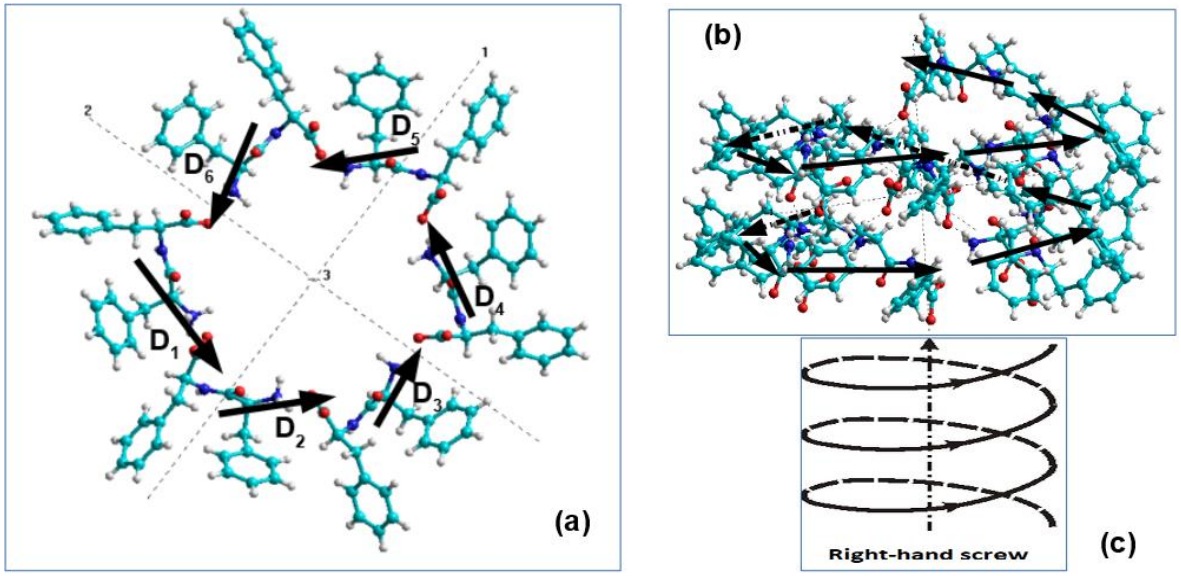

Figure 1. Schematic representation of the spatial distribution of FF individual dipole moments D_i ($D_{t,i}$ in (4)) for two coils of the PNT α-helix of L-FF chirality conformation structure forming right-hand screw D.

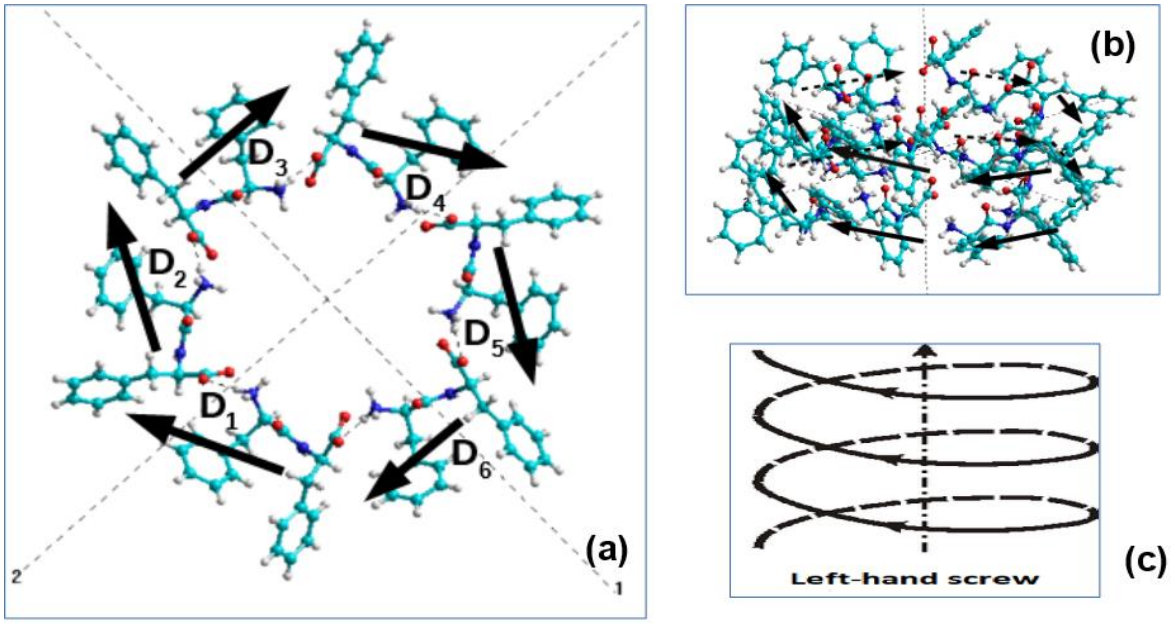

Figure 2. Schematic representation of the spatial distribution of FF individual dipole moments D_i ($D_{t,i}$ in (4)) for two coils of the PNT α-helix of D-FF chirality conformation structure forming left-hand screw L.

Table 1. Dipole moments data for **L-FF PNT,** computed using QM **PM3 RHF** and MM **Amber** methods for 2-turns (coils) model structure of L-FF PNT, obtained on the experimental structural X-ray data. All values of dipole moments are given here in **Debye** units.

(Data presented are for one upper turn, containing 6 FF molecules, from 2 turns of α-helix L-FF PNT model, stacked in one period of PNT structure along the c axis).

#	**PM3 RHF**				**Amber (BIO CHARM) after PM3**			
i	Dt	Dx	Dy	Dz	Dt	Dx	Dy	Dz
1	24.02219	X1= 14.5761	Y1= -15.42046	Z1= -11.26109	23.458	X1= 14.90109	Y1= - 15.2501	Z1= - 9.78108
2	22.54937	X2= - 6.31283	Y2= -18.92332	Z2= -10.51334	21.73396	X2= - 6.27949	Y2= -18.8788	Z2= - 8.74779
3	22.38913	X3= -18.64552	Y3= -3.63554	Z3= -11.84906	21.54498	X3= -18.69828	Y3= - 3.62846	Z3= -10.06949
4	22.38099	X4= -11.56362	Y4= 14.46055	Z4= -12.57315	21.53041	X4= -11.69506	Y4= 14.49542	Z4= -10.80125
5	22.44077	X5= 7.55462	Y5= 17.30774	Z5= -12.12264	21.57784	X5= 7.39696	Y5= 17.40837	Z5= -10.38445
6	22.58646	X6= 18.76678	Y6= 2.56837	Z6= -12.30284	21.63747	X6= 18.5810	Y6= 2.74461	Z6= -10.74216
Sum /n	136.36891 / 6	4.37553	-3.64266	-70.62212 / 6	131.48266 / 6			- 60.52622 / 6
mean	22.72815			-11.770353	21.913777			- 10.0877

Computed data of the individual dipole momentum of FF dipeptides obtained using PM3 RHF and Amber (after PM3) methods are presented in Table 1 (L-FF) and Table 2 (D-FF).

Schematic representation of the spatial arrangement of FF individual dipole moments $\boldsymbol{D_i}$ for two coils of the PNT α-helix (corresponding to the period of the FF structures along the main axis c) are shown in Fig. 1 for L-FF and in Fig. 2 for D-FF chiral conformations.

From our previous studies [19, 20] it is known that dipeptides L-FF form a helix structure with a right screw (D), while D-FF dipeptides create a helix with a left screw (L). These two conformations of the different FF PNT chirality is shown on these Fig. 1 and Fig. 2 with schematically selected and highlighted individual dipole moments $\boldsymbol{D_i}$ for each cases.

The calculations of chirality value (and corresponding sign obtained) were done in according with formulae (1). For greater clarity, here we give a more detailed record of this expression of the mixed vector-scalar product of three successive vectors $D_{t,i} = \{D_{x,i}; D_{y,i}; D_{z,i}\}$ for i = 1, 2, 3 in the following form:

$$\left([D_{t,1}, D_{t,2}], D_{t,3}\right) = \left(D_{t,1} \times D_{t,2}\right) \cdot D_{t,3} = \begin{vmatrix} D_{x,1} D_{y,1} D_{z,1} \\ D_{x,2} D_{y,2} D_{z,2} \\ D_{x,3} D_{y,3} D_{z,3} \end{vmatrix} =$$

$$= D_{x,1}\left(D_{y,2}D_{z,3} - D_{y,2}D_{z,2}\right) - D_{x,2}\left(D_{y,1}D_{z,3} - D_{y,3}D_{z,1}\right) + D_{x,3}\left(D_{y,1}D_{z,2} - D_{y,2}D_{z,1}\right) =$$

$$= \left(D_{y,1}D_{z,2} - D_{y,2}D_{z,1}\right)D_{x,3} - \left(D_{x,1}D_{z,2} - D_{x,2}D_{z,1}\right)D_{y,3} + \left(D_{x,1}D_{y,2} - D_{y,1}D_{x,2}\right)D_{z,3} =$$

$$= D_{t,1} \cdot \left(D_{t,2} \times D_{t,3}\right). \quad (5)$$

Table 2. Dipole moments data for **D-FF PNT,** computed using QM **PM3 RHF** and MM **Amber** methods for 2-turns (coils) model structure of L-FF PNT, obtained on the experimental structural X-ray data. All values of dipole moments are given here in **Debye** units.

(Data presented are for one upper turn, containing 6 FF molecules, from 2 turns of α-helix D-FF PNT model, stacked in one period of PNT structure along the c axis).

#	**PM3 RHF**				**Amber (BIO CHARM) after PM3**			
	Dt	Dx	Dy	Dz	Dt	Dx	Dy	Dz
1	22.52289	X1= -12.2278	Y1= - 15.26662	Z1= -11.16655	21.70719	X1= -12.29934	Y1= -15.17052	Z1= -9.47542
2	22.36979	X2 = 7.30246	Y2= -18.01367	Z2= -11.07199	21.52719	X2= 7.21028	Y2= - 17.99544	Z2= - 9.35929
3	22.37242	X3= 19.23444	Y3= -2.59708	Z3= -11.12526	21.52045	X3= 19.16798	Y3= - 2.65611	Z3= - 9.41612
4	22.47472	X4= 11.90525	Y4= 15.90525	Z4= -11.2899	21.62461	X4= 11.91393	Y4= 15.27363	Z4= - 9.61239
5	22.62851	X5= -6.61276	Y5= 17.47797	Z5= -12.76093	21.70319	X5= - 6.4868	Y5= 17.38568	Z5= -11.25557
6	23.85476	X6= -19.81989	Y6= 4.38208	Z6= -12.53070	23.27134	X6= - 19.89297	Y6= 4.72746	Z6= -11.11199
Sum /n	136.2231 / 6	-0.2183	1.88793	-69.94533/6	131.35397 / 6			- 60.23078 / 6
mean	22.70385			-11.657555	21.892328			- 10.038463

Calculations are carried out sequentially for each three vectors 1-3, 2-4, 3-5 and 4-6 and with n = 6 we get the final sum of n - 2 = 4 members in the total sum in formulae (4).

This calculation can also be carried out using a program in the language Python 3.7., written in the work of [24] for the appropriate calculation of the chirality index by the vectors connecting the Ca atoms in each α-helix. In this case, as the normalization, one can take the approach and the corresponding expression for its calculations, developed and applied in the work [24]. It is also possible to normalize to the value of the square of the mean dipole moment.

However, it should be noted that the mixed vector-dot product is the volume of the prism built on the three vectors used. In this case, it is logical to propose a normalization to the cube of the average dipole moment for each case, as is point out in relation (4) above.

Ultimately, for comparison, Table 3 shows the calculation results for all species-normalizations, as well as the data without normalization.

The main conclusion to which we come - and this can be seen from all the calculations performed unambiguously and reliably show - that there is a change in the sign of chirality during the transition from the initial chirality of dipeptides to their helical structure in the nanotube.

The results obtained show that the ongoing change in the sign of chirality during the transition from the initial single dipeptides to the spiral structure of the nanotube, which is the next in complexity in the hierarchy of these structures, fully corresponds to the law of the change in chirality [5-8]. This can also be a confirmation of the adequacy of the proposed quantitative method for calculating the sign of chirality from the value of individual dipole moments of individual dipeptides forming a spiral structure of a nanotube.

4. CONCLUSIONS

The proposed method for calculating the index and sign of chirality using the values of the dipole moments of each individual dipeptides forming a helix structure of a peptide nanotube shows correct results corresponding to the law of the change in the sign of chirality, when the hierarchical structure of the molecular system becomes more complex.

This method makes it possible to numerically determine the sign of chirality in a helix structure based on the knowledge of the dipole moment of the initial dipeptides, forming the helical peptide nanotube structure.

The results obtained give us a new opportunity to see the physical basis for the formation of the type and sign of chirality and open up new possibilities for a quantitative study of this phenomenon. This approach can be applied to other similar structures and peptide nanotubes based on other amino acids and dipeptides.

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REFERENCES

[1] A. L. Lehninger, Biochemistry. The Molecular Basis of Cell Structure and Function. New York: Worth Publishers, Inc. (1972).

[2] A.V. Finkelstein, O. B. Ptitsyn. Protein Physics: a course of lectures with color and stereoscopic illustrations and tasks. 3rd ed., rev. and suppl. Moscow: KDU, (2012). (In Russian).

[3] A. C. Mendes, E. T. Baran, R. L. Reis, H. S. Azevedo. Self-assembly in nature: using the principles of nature to create complex nanobiomaterials. *Wiley Interdiscip. Rev. Nanomed. Nanobiotechnol.* **5(6),** 582–612 (2013).

[4] Chirality and Biological Activity. Eds. Holmstedt B., Frank H., Testa B. New York: Liss, (1990).

[5] V. A. Tverdislov. Chirality as a primary switch of hierarchical levels in molecular biological systems. *Biophysics* **58** (1), 128–132 (2013).

[6] E. V. Malyshko, V. A. Tverdislov. *IOP. J. Phys. Conf. Series* **741**, 012065 (2016).

[7] V. A. Tverdislov, E. V. Malyshko, S. A. Il'chenko, O. A. Zhulyabina, L. V. Yakovenko. A periodic system of chiral structures in molecular biology. *Biophysics* **62** (3), 331–341 (2017).

[8] V. A. Tverdislov, E. V. Malyshko. On regularities in the spontaneous formation of structural hierarchies in chiral systems of nonliving and living matter. *Physics-Uspekhi* **62**, 354-363 (2019).

[9] S. F. Mason. Origins of biomolecular handedness. *Nature* **311**, 19–23 (1984).

[10] S. R. Blanke. Expanding Functionality within the Looking-Glass Universe. *Science* **325**, 1505–1506 (2009).

[11] V. S. Bystrov, P. S. Zelenovskiy, A. S. Nuraeva, S. Kopyl, O. A. Zhulyabina, V. A. Tverdislov. Chiral peculiar properties of self-organization of diphenylalanine peptide nanotubes: modeling of structure and properties. *Mathematical Biology and Bioinformatics* **14** (1), 94-124 (2019).

[12] M. R. Ghadiri, Juan R. Granja, Ronald A. Milligan, Duncan E. McRee, Nina Khazanovich. Self assembling organic nanotubes based on cyclic peptide architecture. *Nature* **366**, 324–327 (1993).

[13] C. H. Görbitz. Nanotube formation by hydrophobic dipeptides. *Chem. Eur. J.* **7**, 5153–5159 (2001).

[14] S. Scanlon, A. Aggeli. Self-assembling peptide nanotubes. *Nano Today* **3**, 22–30 (2008).

[15] V. S. Bystrov, I. Bdikin, A. Heredia, R. C. Pullar, E. Mishina, A. Sigov, A. L. Kholkin. Piezoelectricity and Ferroelectricity in biomaterials from proteins to self-assembled peptide nanotubes. In: G. Ciofani and A. Menciassi, eds. Piezoelectric nanomaterials for biomedical applications., Berlin Heidelberg, Springer-Verlag. 187-212 (2012).

[16] V. S. Bystrov. Computer Simulation Nanostructures: Bioferroelectric Peptide Nanotubes. Bioferroelectricity: Peptide Nanotubes. Saarbruecken: LAP Lambert Academic Publishing. OmniScriptum GmbH & Co. KG. (2016).

[17] V. S. Bystrov, E. Paramonova, I. Bdikin, S. Kopyl, A. Heredia, R.Pullar, A.Kholkin. BioFerroelectricity: Diphenylalanine Peptide Nanotubes Computational Modeling and Ferroelectric Properties at the Nanoscale. *Ferroelectrics* **440 (01)**, 3 – 24 (2012).

[18] V. S. Bystrov, S. A. Kopyl, P. Zelenovskiy, O. A. Zhulyabina, V. A. Tverdislov, F. Salehli, N. E. Ghermani, V. Ya. Shur & A. L. Kholkin. Investigation of physical properties of diphenylalanine peptide nanotubes having different chiralities and embedded water molecules. *Ferroelectrics* **525**, 168–177 (2018).

[19] V. S. Bystrov, P. S. Zelenovskiy, A. S. Nuraeva, S. Kopyl, O. A. Zhulyabina, V. A. Tverdislov. Molecular modeling and computational study of the chiral-dependent structures and properties of the self-assembling diphenylalanine peptide nanotubes. *J. Mol. Mod.* **25,** 199 (2019).

[20] P. S. Zelenovskiy, A. S. Nuraeva, S. Kopyl, S. G. Arkhipov, S. G. Vasilev, V. S. Bystrov, D. A. Gruzdev, M.Waliczek, V.Svitlyk, V. Ya. Shur, L. Mafra, and A.

L. Kholkin. Chirality-dependent growth of self-assembled diphenylalanine microtubes. *Cryst. Growth Des.* **19,** 6414−6421 (2019).
[21] A. Nuraeva, et al. Evaporation-Driven Crystallization of Diphenylalanine Microtubes for Microelectronic Applications. *Cryst. Growth Des.* **16**, 1472–1479 (2016).
[22] A. E. Sidorova, E. V. Malyshko, A. R. Kotov, V. A. Tverdislov, M. N. Ustinin. Quantitative Criteria of Chirality in Hierarchical Protein Structures. *Biophysics* **64** (2), 155-166 (2019).
[23] A. E. Sidorova, N. T. Levashova, E. V. Malyshko, V. A. Tverdislov. Autowave Self-Organization in the Folding of Proteins. *Moscow University Physics Bulletin* **74**(3), 213-226 (2019).
[24] A. E. Sidorova, A. O. Lutsenko, D. K. Shpigun, E. V. Malyshko, V. A. Tverdislov. Methods for Determining the Chirality sign of the Helical and Superhelical Protein Structures. *Biophysics,* (Russian Federation) **66**, 421 (2021).
[25]. RCSB PDB. Available online: http://www.rcsb.org (accessed on 15 December 2020).
[26] V. S. Bystrov, J. Coutinho, P. Zelenovskiy, A. Nuraeva, S. Kopyl, O. Zhulyabina, V. Tverdislov. Structures and properties of the self-assembling diphenylalanine peptide nanotubes containing water molecules: modeling and data analysis. *Nanomaterials* **10** (10), 1999 (2020).
[27] V.S. Bystrov, J. Coutinho, O.A. Zhulyabina, S.A. Kopyl, P.S. Zelenovskiy, A.S. Nuraeva, V.A. Tverdislov, S.V. Filippov, A.L. Kholkin, V.Ya. Shur. Modelling and physical properties of diphenylalanine peptide nanotubes containing water molecules. *Ferroelectrics* (2021). (in press).
[28] VASP (Vienna Ab initio Simulation Package). Available online: https://www.vasp.at/ (accessed on 27 December 2020).
[29] Hypercube Inc. HyperChem, versions 7.51 and 8.0; Hypercube Inc.: Gainesville, FL, USA, 2002. Available online: http://www.hyper.com/?tabid=360 (accessed on 27 December 2020).
[30] The Cambridge Crystallographic Data Centre (CCDC). Available online: https://www.ccdc.cam.ac.uk/ (accessed on 27 December 2020).