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EVALUATION OF THE FORCE CONSTANTS OF A DNA MOLECULE USING ITS MODEL IN THE FORM OF COIL SPRINGS

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An analysis of the force coupling constants used in the models of a DNA macromolecule is made. Expressions for evaluation of the flexural and torsional rigidity of the macromolecule skeleton which are based on one mole and on a pair of bases are provided. For the first time, analytical formulas to calculate the force coupling constants are given.

The structure and functioning of living organisms are determined by the structural information, whose self-reproducing carrier is a DNA molecule. The latter accumulates various mutation changes, which lead to the mutability of organisms and are subject to natural selection. The information encoded in DNA is transferred to an RNA intermediary and then is embodied in the structure of proteins, which are the carriers of all vital functions.

In connection with the particular role of DNA in a cell, of great interest is the determination of its conformational mobility, which is implemented in various displacements of structural elements of a double-stranded chain (nucleic acid bases, sugars, phosphates). As long as these displacements are small, they represent oscillations in relation to the equilibrium conformation of a macromolecule. These oscillations, named conformational ones, characterize the double-stranded state of DNA and are the precursors of significant rearrangements of the macromolecule, such as transitions to another form of a double spiral.

Numerous works are devoted to the dynamics of conformational mobility of a DNA macromolecule [1–8]. However, despite the significant body of results obtained, no unique interpretation of the low-frequency ($\nu < 200$ cm^{-1}) Raman spectra of DNA has been given yet. Calculations performed using the valence-optical method give a number of vibrational bands for the low-frequency spectrum of DNA that is an order of magnitude larger than that of the observed ones [1, 2]. Moreover, because of the ambiguity of choice of the force constants [2] it is difficult to correlate the results with experimental data. On the other hand, the simplified dynamic DNA models developed in [3, 4] do not allow one to reach a level sufficient for interpretation of experimental data.

In [5–8], Volkov et al. suggest an approach to describe the low-frequency mobility of a DNA macromolecule in the context of the dynamics of a crystal lattice. This approach is most adequate for investigation of the conformational oscillations of macromolecules. The difficulties encountered in interpretation of the experimental data in these works are related, first of all, to the ambiguity of determination of the force constants.

To compare theory with experiment, it is necessary to calculate the frequencies of macromolecular oscillations. In the general case, their calculation requires knowledge of the force coupling constants used in the dynamic models (α_0, β_0, ε_0, c, f, g_1, g_2, g_3, τ).

Evaluation of the Force Constants α_0, β_0, and ε_0. We believe that the low-frequency quasicontinuous model of a DNA macromolecule based on the phenomenological theory developed by Volkov and

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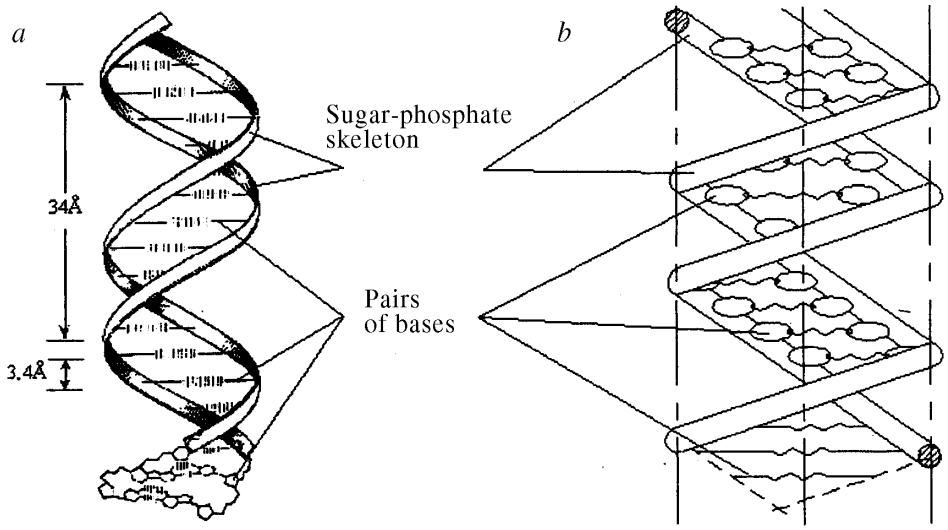

Fig. 1. Double spiral of DNA (a) and the DNA model in the form of two coil springs (b).

Kosevich [5] is up to date. The force constants α_0, β_0, and ε_0 obtained in [6, 7] with the use of independent calculations of the conformational energy have the following values: $\alpha_0 \approx 55.557$ N/m; $\beta_0 \approx 2.778 \cdot 10^{-19}$ N/m; $\varepsilon_0 \approx 29.862$ N/m.

The inaccuracy of calculation of the constants is related to the heterogeneity of the composition of a DNA macromolecule. In the calculation, the following parameters of the model of a DNA macromolecule have been used: $l_0 \approx 0.49$ nm; $\theta_0 \approx 28^o$; $m \approx 199$ amu; $m \approx 109$ amu; $M_0 = m_0 + m \approx 308$ amu.

At present, we know of a modified model [8] which is capable of giving good quantitative agreement with experiment for the frequencies of the internal oscillations of a DNA molecule in the low-frequency range [9]. For this model the following refined values of the macromolecule parameters are used: m = 289 amu, m_0 = 224 amu, M_0 = 513 amu, $\theta_0 = 34^o$; l_0 = 0.885 nm. As a result, the force constants α_0, β_0, and ε_0 have the values $\alpha_0 \approx 54.168$ N/m, $\beta_0 \approx 116.669 \cdot 10^{-19}$ N·m, and $\varepsilon_0 \approx 95.141$ N/m.

The values of the force constants β_0 and ε_0 in [8], for which good agreement with experiment is attained, are too large as compared to the results of [6, 7]. Such a discrepancy in determination of the force constants is related, first of all, to the presence of more than one mode in the frequency spectrum [9]. To refine the values of these constants, it is necessary to carry out new experimental studies.

Although theory [8] is in good agreement with experiment [9], the interpretation of the low-frequency modes of DNA oscillations still encounters certain difficulties (for instance, it is impossible to draw a concrete conclusion about the 25-cm^{-1} mode). To resolve the existing contradictions, not only new experimental data in the low-frequency range ($\nu < 40$ cm^{-1}) are required but also knowledge of the force constants f, g_1, g_2, g_3, and τ, which have not been evaluated yet.

Evaluation of the Force Constants f, g_1, g_2, g_3, c, and τ. To evaluate these coupling constants, we have suggested an elastic model of a DNA macromolecule in the form of two coil springs (Fig. 1). Such a model is possible, since by virtue of its macroscopicity a biopolymer model is characterized by flexural and torsional elasticity as well as by other macroscopic properties [10]. According to this representation, in our work a DNA molecule is considered as a double cylindrical coil spring in which the coils represent a sugar-phosphate skeleton. The structural elements (nitrogen bases) are rigidly connected to the skeleton; they are perpendicular to the axis of the double spiral, around which they rotate as they move along the axis, and are mutually connected by elastic elements (hydrogen bonds).

Leaning upon the statics of cylindrical coil springs (it is studied fairly well [11–13]) and allowing for the geometric parameters of a DNA molecule, we have been able to evaluate the constants f, g_1, g_2, g_3, c,

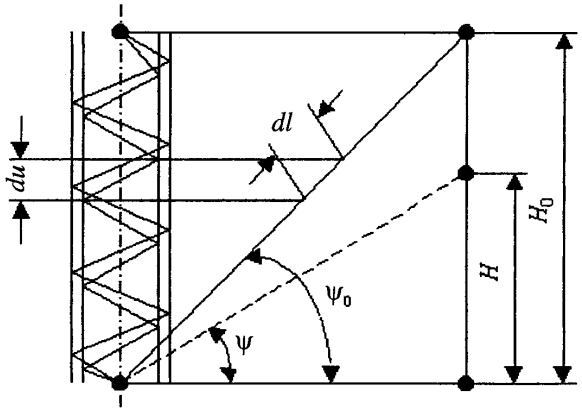

Fig. 2. Calculational scheme of the DNA-molecule model.

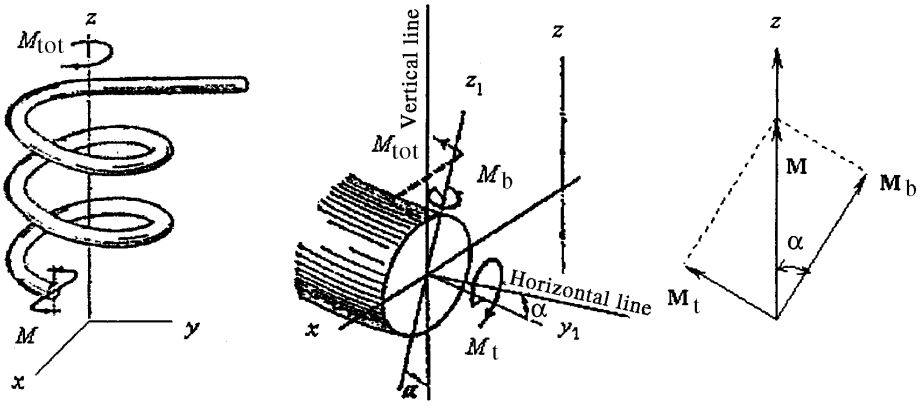

Fig. 3. Schematic of the axial torsion of the spring.

and τ using the Mohr integrals. The calculational scheme for the DNA model mentioned above is presented in Fig. 2.

Evaluation of the Force Constant f. It should be noted that in calculating the torsion of the coils it is of greatest interest to determine the angular displacement of one end relative to the other Δφ. In torsion, in the cross sections of a spring coil the total moment $\mathbf{M}_{tot} = \mathbf{M}$ develops. Decomposing it with respect to the axes, we obtain expressions for the bending moment and for the torque: $\mathbf{M}_b = \mathbf{M}\cdot\cos\alpha$; $\mathbf{M}_t = \mathbf{M}\cdot\sin\alpha$ (Fig. 3). After applying unit moments to the spring ends, we obtain $\mathbf{M}_{b1} = \text{cons}\ \alpha$ and $\mathbf{M}_{t1} = \sin\alpha$. Then, for determination of the displacement sought, we write the Mohr integrals

$$\Delta\varphi = \int_0^l \left(\frac{M\cos^2\alpha}{EI} + \frac{M\sin^2\alpha}{GI_p} \right) dl ,$$

whence we obtain

$$\Delta\varphi = \frac{MH}{\sin\alpha} \left(\frac{\cos^2\alpha}{x'_b} + \frac{\sin^2\alpha}{x'_t} \right).$$

We determine the relative angular displacement

$$\varepsilon_\varphi = \frac{\Delta\varphi}{H} = \frac{\partial\varphi}{\partial z} = \frac{M}{\sin\alpha} \left(\frac{\cos^2\alpha}{x'_b} + \frac{\sin^2\alpha}{x'_t} \right).$$

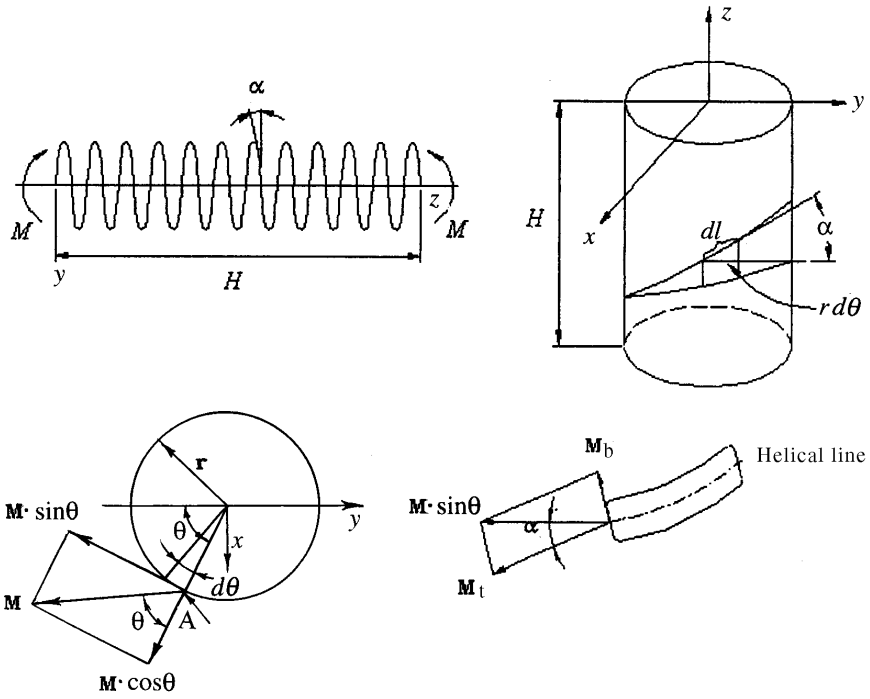

Fig. 4. Scheme of the pure bending of the coil spring in its longitudinal plane.

Then the effective rigidity in torsion based on unit length can be written as follows:

$$c_\varphi = \frac{M}{\varepsilon_\varphi} = \frac{\sin\alpha}{\dfrac{\cos^2\alpha}{x'_b} + \dfrac{\sin^2\alpha}{x'_t}}. \qquad (1)$$

We transform the results obtained for the case of torsion of a spring to a DNA macromolecule. Here, the torsional rigidity based on a pair of bases will represent the force constant *f*. With allowance for the peculiar features of the suggested model (two coil springs) the expression for the force constant acquires the form

$$f = \frac{2\sin\psi}{\left(\dfrac{\cos^2\psi}{x_b} + \dfrac{\sin^2\psi}{x_t}\right)}. \qquad (2)$$

Evaluation of the Force Constants g_1, g_2, and g_3. Let us determine the effective rigidity of the spring in bending of the central axis (the axis of the DNA spiral) with the example of pure bending of a coil spring (Fig. 4).

Considering the element *ds* of the spring at point *A* determined by the angle θ, we decompose the vector **M** into two components: **M**·cos θ and **M**·sin θ. The former represents a couple of forces in the plane tangential to the cylindrical surface of radius *r* and causes the bending of the wire in this plane. The latter represents a couple acting in the longitudinal plane of the spring and can be decomposed into the torque $\mathbf{M}_t$ = **M**·sin θ cos α and the bending moment in the coil plane $\mathbf{M}_b$ = **M**·sin θ sin α. After applying the unit moments, we obtain $\mathbf{M}_{b1}$ = sin θ sin α, $\mathbf{M}_{t1}$ = sin θ cos α, and $\mathbf{M}_1$ = cos θ. We substitute the quantities

obtained into the Mohr integrals to determine the angular displacement of one end of the spring relative to the other:

$$\Delta\varphi = \int_l \left(\frac{M\cos^2\theta}{EI} + \frac{M\sin^2\theta\sin^2\alpha}{EI} + \frac{M\sin^2\theta\cos^2\alpha}{GI_p} \right) dl .$$

From Fig. 4, $dl = rd\theta/\cos\alpha$; then

$$\Delta\varphi = \frac{nr}{\cos\alpha} \int_0^{2\pi n} \left(\frac{\cos^2\theta + \sin^2\theta\sin^2\alpha}{x_b'} + \frac{\sin^2\theta\cos^2\alpha}{x_t'} \right) d\theta .$$

With allowance for the fact that $\int_0^{2\pi n} \cos^2\theta d\theta = \pi n$ and $\int_0^{2\pi n} \sin^2\theta d\theta = 0$, we obtain

$$\Delta\varphi = \frac{Mr\pi n}{\cos\alpha} \left(\frac{1+\sin^2\alpha}{x_b'} + \frac{\cos^2\alpha}{x_t'} \right).$$

Taking into account the relationship between the parameters of the model $\frac{1}{\rho} = \frac{\Delta\varphi}{H}$, $H = l\sin\alpha = \frac{2\pi rn}{\cos\alpha}$, we can write the expression for the bending moment in the form

$$M = \frac{2\sin\alpha}{\left(\frac{1+\sin^2\alpha}{x_b'} + \frac{\cos^2\alpha}{x_t'} \right)} \frac{1}{\rho} = G_b \frac{1}{\rho} .$$

We transform the results obtained for the case of bending of the helical line of a spring to the bending of the spiral of DNA. Let us pass to the force constant in the known manner with allowance for the fact that the DNA molecule is double-stranded. Moreover, assuming that the bending is isotropic in both planes, we write an expression for the constants g_1 and g_2, which characterize the change in the free energy of the polynucleotide chain upon the shift of the bases and the skeleton along the *OX*- and *OY*-axes, respectively:

$$g_1 \approx g_2 = g = \frac{4\sin\psi}{\frac{1+\sin^2\psi}{x_b} + \frac{\cos^2\psi}{x_t}} . \qquad (3)$$

In connection with the particular difficulty encountered in evaluation of the force constant g_3, we will assume temporarily that the nucleoside is absolutely rigid.

Evaluation of the Force Constant c. Let us determine the effective rigidity of the coil spring upon its tension by the longitudinal force **P** (Fig. 5).

We consider the spring as a two-dimensional beam. In each cross section of the coil of the extended spring, the torque $\mathbf{M}_t = Pr\cos\alpha$ and the bending moment $\mathbf{M}_b = Pr\sin\alpha$ develop. The values of the bending moment and of the torque developed due to the unit forces applied instead of the forces **P** are $\mathbf{M}_{b1} = r\sin\alpha$ and $\mathbf{M}_{t1} = r\cos\alpha$, respectively.

We determine in advance the increase in the spring height Δu:

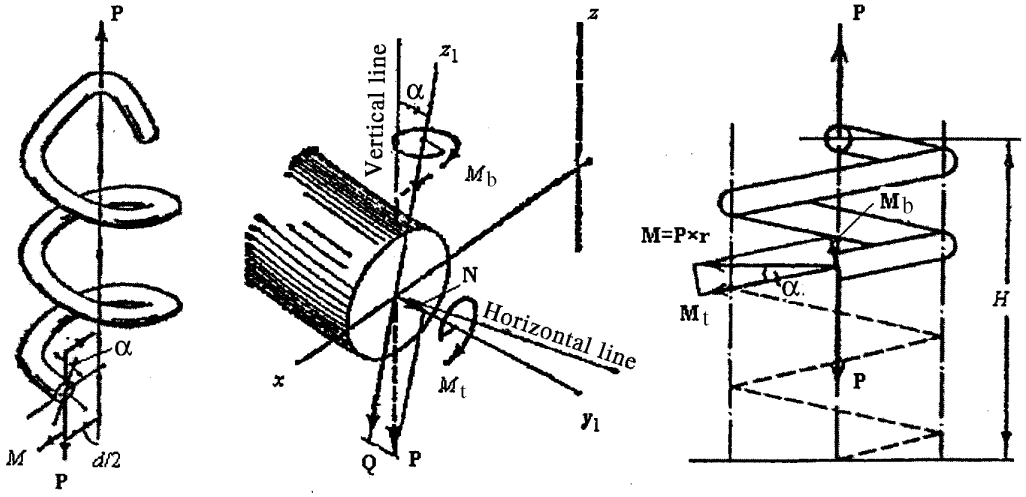

Fig. 5. Scheme of the longitudinal torsion of the spring.

$$\Delta u = Pr^2 l \left(\frac{\sin^2 \alpha}{EI} + \frac{\cos^2 \alpha}{GI_p} \right).$$

With allowance for ($l = H/\sin \alpha$) we obtain

$$\Delta u = \frac{Pr^2 H}{\sin \alpha} \left(\frac{\sin^2 \alpha}{EI} + \frac{\cos^2 \alpha}{GI_p} \right).$$

Then the expression for the relative linear deformation acquires the form

$$\varepsilon_u = \frac{\Delta u}{H} = \frac{\partial u}{\partial z} = \frac{Pr^2}{\sin \alpha} \left(\frac{\sin^2 \alpha}{x'_b} + \frac{\cos^2 \alpha}{x'_t} \right).$$

The tensile force P with allowance for the foregoing can be written as follows:

$$P = c_{tr} \varepsilon_u = \frac{\sin \alpha}{r^2 \left(\frac{\sin^2 \alpha}{x'_b} + \frac{\cos^2 \alpha}{x'_t} \right)} \varepsilon_u .$$

For two springs we obtain

$$c_{tr} = \frac{2 \sin \alpha}{r^2 \left(\frac{\sin^2 \alpha}{x'_b} + \frac{\cos^2 \alpha}{x'_t} \right)}.$$

Now we pass to the force constant c that describes the change in the free energy of the polynucleotide chain upon the shift of the bases and the skeleton along the OZ-axis:

$$c = \frac{2 \sin \psi}{r^2 \left(\frac{\sin^2 \psi}{x_b} + \frac{\cos^2 \psi}{x_t} \right)}. \qquad (4)$$

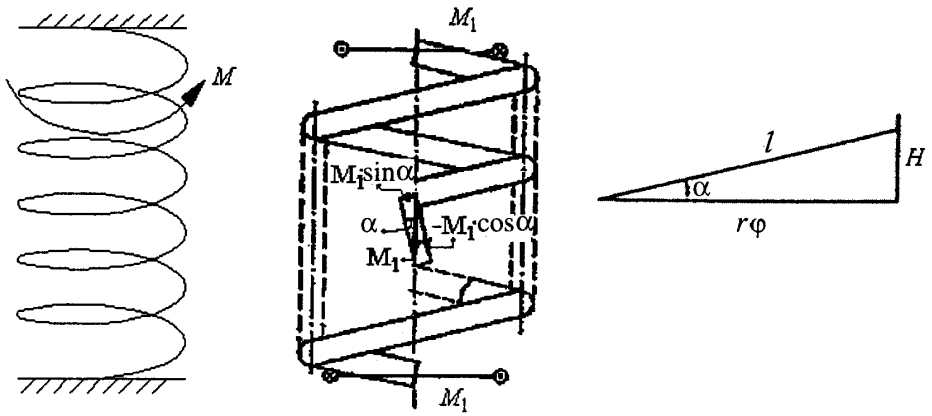

Fig. 6. Scheme of the interrelation between the longitudinal displacement and the turn of spring coils.

Evaluation of the Force Constant τ. We investigate the longitudinal shift under the action of a torque (Fig. 6).

We decompose the acting torque **M** into $\mathbf{M}_b = -\mathbf{M}\cdot\cos\alpha$ and $\mathbf{M}_t = \mathbf{M}\cdot\sin\alpha$. Upon the action of the tensile force of unit value, we obtain $\mathbf{M}_b = \mathbf{r}\cdot\sin\alpha$ and $\mathbf{M}_t = \mathbf{r}\cdot\cos\alpha$.

The increase in the spring height under the action of force factors is

$$\Delta u = Mr\int_0^l\left(\frac{-\cos\alpha\sin\alpha}{EI}+\frac{\sin\alpha\cos\alpha}{GI_p}\right)dl$$

or after integration

$$\Delta u = MrH\cos\alpha\left(\frac{1}{x_t'}-\frac{1}{x_b'}\right).$$

It is also easy to obtain an expression for the relative linear elongation:

$$\varepsilon_u = \frac{\Delta u}{H}=\frac{\partial u}{\partial z}=Mr\cos\alpha\left(\frac{1}{x_t'}-\frac{1}{x_b'}\right).$$

Then the torque can be determined as

$$M=\frac{\varepsilon_u}{r\cos\alpha\left(\frac{1}{x_t'}-\frac{1}{x_b'}\right)}=c_{r,tr}\varepsilon_u\,. \tag{5}$$

Now we determine the angle by which the upper end of the spring rotates in the horizontal plane relative to its lower end upon the tension of the spring:

$$\Delta\varphi = Prl\left(\frac{1}{GI_p}-\frac{1}{EI}\right)\sin\alpha\cos\alpha \quad \text{or} \quad \Delta\varphi = PrH\cos\alpha\left(\frac{1}{x_t'}-\frac{1}{x_b'}\right).$$

The relative angular displacement can be written as

$$\varepsilon_\varphi=\frac{\Delta\varphi}{H}=\frac{\partial\varphi}{\partial z}=Pr\left(\frac{1}{x_t'}-\frac{1}{x_b'}\right)\cos\alpha\,.$$

Then the expression for the tensile force acquires the form

$$P = \frac{\varepsilon_\varphi}{r\cos\alpha\left(\frac{1}{x_t'} - \frac{1}{x_b'}\right)} = c_{tr,r}\varepsilon_\varphi . \quad (6)$$

Comparing expressions (5) and (6), we have obtained the relationship between the tension and the rotation. As a result, the force constant τ can be evaluated as follows:

$$\tau = \frac{2}{r\cos\psi\left(\frac{1}{x_t} - \frac{1}{x_b}\right)} . \quad (7)$$

Analysis of the Results Obtained. We evaluate the flexural and torsional rigidities of the skeleton based on one mole and a pair of bases. With this aim in view, we write expressions (2) and (3) in the form

$$\frac{\cos^2\alpha}{x_b} + \frac{\sin^2\alpha}{x_t} = \frac{2\sin\alpha}{f}, \quad \frac{1+\sin^2\alpha}{x_b} + \frac{\cos^2\alpha}{x_t} = \frac{4\sin\alpha}{g} .$$

If we multiply the first equality by $\cos^2\alpha$ and the second equality by $\sin^2\alpha$ and then subtract the second equality from the first one, we arrive at

$$x_b = \frac{3\cos^2\alpha - 2}{2\sin\alpha\left(\frac{\cos^2\alpha}{f} - \frac{2\sin^2\alpha}{g}\right)} . \quad (8)$$

In the case where the first and second expressions are added and not subtracted, we can obtain

$$x_t = \frac{3\cos^2\alpha - 2}{2\sin\alpha\left(\frac{\cos^2\alpha - 2}{f} + \frac{2\cos^2\alpha}{g}\right)} . \quad (9)$$

We take into account the geometric parameters of a DNA molecule [14] ($\tan\psi = H/\pi d$; H = 34 Å; r = 10 Å; d = 20 Å) and the expressions for f and g by allowing for the persistent mechanism of flexibility, which is inherent in all spiral molecules according to [15]: $f = 185RT$ and $g = 150RT$.

With consideration for the foregoing, we have been able to evaluate by formulas (8) and (9) the rigidity in bending and in torsion based on one mole and a pair of bases ($x_b = 290RT$; $x_t = 91.41RT$) and, by formulas (4) and (7), the force constants $\tau = 3.0354\cdot10^{11}RT$ and $c = 1.0298\cdot10^{20}RT$.

The calculation of the force constants by formulas (2), (3), (4), and (7) has yielded $f = 7.659\cdot10^{-19}$ N·m, c = 0.426 N/m, g = 5.372 N/m, and $\tau = 12.566\cdot10^{-10}$ N.

Thus, for the first time we have evaluated numerically the constants c, f, g_1, g_2, g_3, and τ. The force constants obtained can be used for solving the dispersion equations derived for the corresponding dynamic models with the aim of interpreting experimental results in the low-frequency range of oscillations of DNA macromolecules.

NOTATION

Force constants: α_0, describes the interaction in hydrogen-bonded pairs, β_0, accounts for oscillations of nucleosides around the skeleton chains, ε_0, describes the intranucleoside mobility, f, accounts for the turn

of one pair of bases relative to the other, $g_1 \approx g_2 = g$, take into account the shifts of nucleotides along the *OX*- and *OY*-axes, respectively, g_3, accounts for the change in the reduced nucleoside length, *c*, describes the interactions along the macromolecular chain, τ, accounts for the relationship between torsion and bending; ν, oscillation frequency; l_0, reduced nucleoside length, which is equilibrium for the present conformation of the double spiral; θ_0, angle accounting for nucleoside oscillations around the skeleton chains; *m*, nucleoside mass; m_0, skeleton mass; $M_0 = m_0 + m$, nucleotide mass; **M**, moment of a force couple; $\mathbf{M}_1$, unit moment; $\mathbf{M}_{tot}$, total moment; $\mathbf{M}_b$, bending moment; $\mathbf{M}_t$, torque; $\mathbf{M}_{b1}$, unit bending moment; $\mathbf{M}_{t1}$, unit torque; *E*, modulus of elasticity of the first kind; *G*, modulus of elasticity of the second kind; *I*, centroidal moment of inertia; I_p, polar moment of inertia; **P**, longitudinal force; *r*, radius of the helical line; *d*, diameter of the spring coil; ρ, radius of curvature of the elastic curve of the spring axis; ds, elementary section of the helical line between two adjacent cross sections; ε_u and ε_φ, relative linear and angular displacements; Δu and $\Delta\varphi$, linear and angular displacements; *l*, length of the spring coils; α, helix angle of the helical line; ψ_0 and ψ, helix angles of the double spiral of a DNA macromolecule at the initial and arbitrary instants; θ, angle determining the point of application of the bending moment in the *YOZ*-plane; H_0 and *H*, spring height at the initial and arbitrary instants, respectively; *h*, distance between the neighboring pairs of bases; x_b' and x_t', flexural (rigidity in bending) and torsional rigidity of the spring coil, respectively ($x_b' = EI$; $x_t' = GI_p$); $x_b = x_b'/k$; $x_t = x_t'/h$, flexural and torsional rigidity based on one mole and a pair of bases, respectively; *n*, number of spring coils; G_b, effective flexural rigidity of the coil spring based on unit length; c_φ, effective rigidity of the helical line in its torsion; $c_{tr,r}$, effective rigidity in tension of the spring with allowance for its rotation; c_{tr}, effective rigidity of the coil spring in its tension; $c_{r,tr}$, effective rigidity in rotation of the spring with allowance for its longitudinal displacement; *R*, universal gas constant; *T*, absolute temperature. Subscripts: b, bending; t, torsional, torque; b1, unit bending; t1, unit torsion; p, polar; tot, total; r,tr, rotation and displacement (translation); tr,r, displacement and rotation.

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