Shape fluctuations in DNA-type molecules

V. L. Golo

Department of Mechanics and Mathematics, Moscow State University, 119899 Moscow, Russia

E. I. Kats

L. D. Landau Institute of Theoretical Physics, Russian Academy of Sciences, 142432 Chernogolovka, Moscow Region, Russia

(Submitted 7 July 1995)
Zh. Éksp. Teor. Fiz. **108**, 1860–1874 (November 1995)

Fluctuations in the shape of DNA-type molecules are described by expanding the elastic energy of the molecule in powers of the gradients of the components of a moving Frenet reference frame. A Fokker–Planck functional equation describing diffusion in conformation space (trajectories in the dynamical analogy) is derived. The correlation functions of the components of the moving Frenet reference frame are calculated. According to the fluctuation–dissipation theorem, the correlation function is equal (to within a coefficient) to the response function of the conformation of the molecule with respect to an external force. In the special case in which the equilibrium configuration of the molecule is a helix, we calculate the fluctuation contribution to the energy, which leads to an angular momentum that depends on the length and pitch of the helix (Casimir momentum, whose physical origin in this case is the fluctuations in the shape of a helix of finite length). © *1995 American Institute of Physics.*

1. INTRODUCTION

It is well known that the DNA molecule, on the one hand, is a very complicated object that stores and transfers biological information and, on the other, is structurally fairly simple: it consists of two polynucleotide strands twisted into a double helix. The diameter of the double helix is 20 Å, the distance between the neighboring pairs of bases along the helix is 3.4 Å, and the double helix makes a complete revolution every ten pairs (i.e., the pitch of the helix is 34 Å). The length of the molecule depends on the organism to which the DNA belongs, varying from 10^4 to 10^9 links. The parameters of the helix also depend on the chemical environment and the external conditions. The objective of many biophysical investigations is to determine these parameters. One such investigation is the impressive experiment of Ref. 1, in which the stretching of the molecule induced by an external force was measured directly. The elasticity of the molecule yields another characteristic dimension, the so-called persistence length, which describes the stiffness of the molecule with respect to bending. Under normal conditions this length is of the order of 10^3 Å.

The relatively simple mechanical structure of the DNA molecule makes it possible to neglect, to a first approximation, small scales (of the order of the thickness or pitch of the helix) and to model the molecule as an elastic strand. The existence of the double-helix structure can be described by introducing an anisotropy of the elastic moduli (the characteristic bending modulus must correspond in magnitude to a persistent length of the order of 10^3 Å). The anisotropic elastic strand model has been studied by Marko and Siggia,[2] and a model that allows for the spontaneous torque that gives rise to superhelicity was studied in Ref. 3. These papers were concerned with the ground state, i.e., the equilibrium or quasiequilibrium conformations, of the molecules.

In the present paper we investigate theoretically the fluctuations in the shape of a DNA-type molecule modeled as an anisotropic elastic curve. For simplicity and focus, we consider the important special case in which the equilibrium configuration of the molecule is described by a helix (here and below, when we speak of the conformation of a molecule, we have in mind the shape of an anisotropic elastic curve which in the approximation described above models a real DNA molecule).

In the next section, we present the method of the moving Frenet reference frame. This method has a number of advantages over the more traditional application of Euler angles (see Ref. 2). In our method, the problem of finding stationary solutions reduces to the classical Kirchhoff problem of the equilibrium of an elastic strand. The latter problem is a Hamiltonian problem (the form of the problem is identical to Euler's equations of motion for a top); this makes it possible to use the well-developed methods of the theory of Hamiltonian systems.

In Sec. 3, we introduce the Fokker–Planck functional equation, which describes diffusion in the space of molecular conformations (or trajectories, in the mechanical analogy). This equation is used to calculate the equal-time correlation functions of the components of the moving Frenet reference frame (Sec. 4). In static fluctuations in the shape of the molecules (the problem addressed in the present work), the parameter that characterizes the distance along the equilibrium shape of the curve plays the role of time, but there is no causality principle for that coordinate. A perturbation of the shape at some point influences all points on the curve (rather than solely affecting later times, as happens in true dynamical problems). In the present case, therefore, the fluctuation–dissipation theorem reduces to an equality (to within a mul-

1063-7761/95/111018-07$10.00

tiplicative factor) between the correlation function and the response function.

In Sec. 5, the fluctuation contribution to the free energy of a DNA type of molecule of finite length is determined. The part of this contribution that depends on the length and pitch of the helix leads to the appearance of a specific fluctuation angular momentum. Physically, this phenomenon is similar to the Casimir effect, which is well known in physics.[4] The classical Casimir effect is associated with a modification of the electromagnetic zero-point energy fluctuations in systems of finite size. In the present problem, we are concerned with fluctuations in the shape of a DNA-type molecule, and the finiteness of the system is manifested both in the finite length of the molecule and in the fact that the shape fluctuations are limited to fluctuations about the equilibrium helical conformation. In the situations studied here (helix consisting of an incompressible strand), the fluctuations can only change the pitch of the helix or, under conditions in which the equilibrium pitch is fixed, they can only lead to the appearance of a fluctuating angular momentum (Casimir momentum).

2. DESCRIPTION OF MOLECULAR CONFORMATIONS

We study a DNA-type molecule whose equilibrium configuration is superhelical, i.e., we treat the base structure of the double helix as a linear rod whose deformed state is superhelical (the conditions under which this assumption is justified were discussed in Refs. 2 and 3). The equilibrium configuration can therefore be described by the parametric equations of a helix:

$$x=Ar\cos\frac{s}{r},\quad y=Ar\sin\frac{s}{r},\quad z=Bs, \tag{1}$$

where A and B are constants that characterize the helix, $A^2+B^2=1$, $\rho=Ar$ is the radius of the cylinder about which the helix is wound, and the coordinate s along the helix itself parameterizes its length. Instead of the constants A and B, we can also use the curvature K and the torsion W of the helix:[5]

$$K=\frac{A}{r},\quad W=\frac{B}{r}.$$

The energy and other physical properties of such a linear DNA-type molecule are most naturally formulated in terms of a local Frenet reference frame[5] $\mathbf{v}_1$, $\mathbf{v}_2$, and $\mathbf{v}_3$, where $\mathbf{v}_1$ is the tangent vector of the curve $\mathbf{r}(s)$, which specifies the configuration of the axis of the molecule, and $\mathbf{v}_2$ and $\mathbf{v}_3$ are vectors directed along the principal deformation axes of an elastic rod, such that

$$\mathbf{v}_1=\frac{\partial\mathbf{r}}{\partial s},\quad \mathbf{v}_i\mathbf{v}_j=\delta_{ij}.$$

For a helix, for example,

$$\mathbf{v}_1^0=(-A\sin(s/r);\ A\cos(s/r);B),$$

$$\mathbf{v}_2^0=(-\cos(s/r);-\sin(s/r);0),$$

$$\mathbf{v}_3^0=(B\sin(s/r);-B\cos(s/r);A),$$

where the superscript zero indicates the equilibrium configuration.

Fluctuations in the shape of the molecule are described by the matrix δv_{ij}, where the first index refers to the vector of the local Frenet reference frame, and the second refers to the projection on the coordinate axis. To characterize shape fluctuations quantitatively, however, it is necessary to have an expression for the energy required to produce a given fluctuation δv_{ij}. Indeed, we are dealing here with the description of deformations of a spontaneously twisted, anisotropic elastic rod. In classical mechanics, the deformation energy of such a rod is given in a natural manner by the vector $\boldsymbol{\omega}$ that describes rotation of the coordinate axes along the rod.[6] The elastic energy of an anisotropic rod can be represented as a series expansion in $\boldsymbol{\omega}$, the leading terms of which take the form[6]

$$E=\frac{1}{2}\sum_{ij=1}^{3}a_{ij}\omega_i\omega_j+\sum_{i=1}^{3}b_i\omega_i. \tag{2}$$

The total elastic energy is

$$F=\int_0^L E\,ds,$$

where L is the length of the rod. The matrix a_{ik} is the symmetric matrix of the elastic moduli of the rod, and the vector $\mathbf{b}$ describes the spontaneous deformation of the stationary configuration of the molecule. Physically, spontaneous deformation can result, for example, from the adsorption of a DNA molecule on the nucleosomes (usually modeled by a cylindrical surface).

To find the relationship between the vector $\boldsymbol{\omega}$ and the molecular shape-fluctuation matrix δv_{ij}, Note that the variation in the local reference frame along a strand (rod) is given by[6,7]

$$\frac{d}{ds}\mathbf{v}_j=[\omega\mathbf{v}_j],\quad j=1,2,3. \tag{3}$$

Moreover, we can set up the equation describing the variation in the local reference frame as a chiral field theory (see Ref. 7, Chap. 8), as we did for a membrane.[8]

We introduce the matrix X_{ij}

$$X_{ij}=(\mathbf{v}_j)_i.$$

The chiral current constructed according to this matrix has the form

$$J=\frac{d}{dt}XX^{-1}.$$

The matrix J must have the structure

$$J_{kj}=-\sum_{i=1}^{3}\omega_i\epsilon_{ijk},$$

where ϵ_{ijk} is the Levi–Civita antisymmetric tensor.

An arbitrary infinitesimal variation of the reference frame is given by the transformation (for a non-stretchable curve, the only admissable transformations of the Frenet reference frame are rotations):

$$X \to RX, \quad R = I + \delta v,$$

where

$$(\delta v)_{ij} = -\sum_{k=1}^{3} \delta v_k \epsilon_{ijk},$$

δv is a matrix describing the infinitesimal rotation specified by the vector $\delta \mathbf{v}$. Accordingly, variations take the form

$$\delta J = \frac{d}{ds}\,\delta v + [J, \delta v] = \nabla \delta v,$$

$$\delta \omega = \frac{d}{ds}\,\delta \mathbf{v} + [\omega \delta \mathbf{v}] = \nabla \delta \mathbf{v}, \tag{4}$$

where $[\ldots,\ldots]$ is a commutator and ∇ is the covariant derivative operator (compare the analogous procedure for membranes in Ref. 8).

Using Eqs. (4), we can express the variation $\delta \boldsymbol{\omega}$ in terms of the covariant derivative $\delta \mathbf{v}$ and write the energy associated with the fluctuation $\delta \mathbf{v}$ in the form

$$\delta^2 E = \frac{1}{2} \int_0^L ds\; a_{ij} (\nabla \delta \mathbf{v}_i)(\nabla \delta \mathbf{v}_j), \tag{5}$$

where a_{ij} is the matrix of elastic moduli. For the helix (1), the covariant differentiation operator has the form

$$\nabla(\ldots) = \frac{d}{ds} + [\omega(\ldots)],$$

where $\omega^2 = W^2 + K^2$. Recall that we also assume that the elastic strand making up the helix cannot be stretched, i.e., L is constant.

Thus, we have the following situation. The elastic energy of the molecule can be most naturally and simply expressed in the form of an expansion in the components of the "angular velocities" $\boldsymbol{\omega}$. However, these components are not independent, since under arbitrary transformations, the Frenet reference frame must revert to a Frenet reference frame. To allow for this condition, we must express the angular velocities $\boldsymbol{\omega}$ explicitly in terms of the components v of the Frenet reference frame. For a non-stretchable strand (which is a good approximation to a real DNA molecule), the matrix J can be expressed in terms of the rotation matrix

$$J = \frac{d}{ds} R R^{-1},$$

which can in turn be parametrized by admissable variations of the components of the Frenet reference frame (rotations, for a non-stretchable strand).

3. FOKKER–PLANCK EQUATION

We consider fluctuations in the shape of a curve to be Brownian motion in the function space of configurations. Physically, this picture corresponds to the assumption that the total interaction of a molecule with the ambient medium leads to purely relaxational dynamics of the fluctuations in the shape of the molecule (with some effective kinetic coefficient), and the role of the environment itself is played by a source of stochastic Langevin noise. Since we consider a continuous curve, mathematically this means that the Brownian motion occurs in function space. In a similar manner, we study in the same space the vector of random forces $y_s^i(t)$ which we assume to be Gaussian:

$$\langle y^i_{s'}(t') y^j_{s''}(t'') \rangle = D \delta^{ij} \delta_{s',s''} \delta(t' - t''). \tag{6}$$

Here t is the time and D is the diffusion coefficient. Here we have made the simplifying assumption that the correlation function of the random forces is a delta function of the coordinate ($\delta_{s',s''} \equiv \delta(s - s')$ in the continuous notation). The existence of a finite correlation length can alter quantitative results, but the derivation of the Fokker–Planck equation itself is still valid.

As usual, we introduce the conditional probability

$$W[\mathbf{v}'_s, t'; \mathbf{v}''_s, t''],$$

which is the probability density that the curve at time t'' is characterized by the vector field $\mathbf{v}''_s$, which specifies the variation of the Frenet reference frame under the condition that at time t', the corresponding vector was $\mathbf{v}'_s$. Note that W is a functional. The function W satisfies the standard composition law[9]

$$W[\mathbf{v}_{s'}, t'; \mathbf{v}_{s'''}, t'''] = \int W[\mathbf{v}_{s'}, t'; \mathbf{v}_{s''}, t''] \times D\mathbf{v}_{s''} W[\mathbf{v}_{s''}, t''; \mathbf{v}_{s'''}, t'''].$$

We derive the Fokker–Planck equation for the probability distribution W by Kolmogorov's method (see Ref. 10). This method entails introducing two characteristic averages over the noise: the first is associated with the regular displacement

$$\lim_{\tau \to 0} \langle \mathbf{v}_s(t + \tau) \rangle \equiv \mathbf{A}[\mathbf{v}_s; s, t] \equiv \mathbf{A}_{ts}[\mathbf{v}_s], \tag{7}$$

and the second is associated with the noise

$$\lim_{\tau \to 0} \langle (v^i_{s'}(t + \tau) - v^i_s(t))(v^j_{s'}(t) - v^j_s(t)) \rangle \equiv B^{ij}[\mathbf{v}_s; s, s', t]. \tag{8}$$

The right-hand sides of these identities are given along the curve by functionals that are time-dependent as well. The functional $\mathbf{A}$ specifies the regular part of the motion, and B^{ij} specific the stochastic part.

Using the definitions (7) and (8) and the composition law, we can obtain the standard form of the Fokker–Planck equation, which for the present case of shape fluctuations takes the form

$$\partial_t W[\mathbf{v}_s^0, t_0; \mathbf{v}_s, t] + \sum_{i=1}^{L} \int_0^L ds_1 \frac{\delta}{\delta v^i_{s_i}} (A^i[\mathbf{v}_s; t, s_1] W[\mathbf{v}_s^0, t_0; \mathbf{v}_s, t]) - \frac{1}{2} \sum_{i,j=1}^{3} \int_0^L \int_0^L ds_1 ds_2 - \frac{\delta^2}{\delta v^i_{s_i} \delta v^j_{s_2}} (B^{ij}[\mathbf{v}_s; t, s_1, s'_2] W[\mathbf{v}_s^0, t_0; \mathbf{v}_s, t]) = 0. \tag{9}$$

This form of Eq. (9), which in physical terms is essentially transparent, is quite complicated. It can be simplified somewhat by representing B^{ij} in the form:

$$B^{ij}_{s,s_1}=D\delta^{ij}\delta(s_1-s_2),$$

where D is the constant conformational diffusion coefficient, which appears in the correlation function of the random forces. For the special case of the functional B^{ij} given above, the Fokker–Planck equation (9) can be cast in the form

$$\frac{\partial}{\partial t}W=D\sum_{i=1}^{3}\int_0^L ds\,\frac{\delta}{\delta v_s^i}\left(Z\frac{\delta}{\delta v_s^i}(Z^{-1}W)\right) \tag{10}$$

if we find a functional Z satisfying the equation

$$\frac{\delta Z}{\delta v_s^i}=Z\frac{1}{D}A_i[\mathbf{v}_s;t,s]. \tag{11}$$

We now find the explicit form of the functional Z for the elastic curve problem. Consider the functional $Z=\exp(-E/T)$, where T is the temperature. According to the meaning of the functional $A^i_{ts}[\mathbf{v}_s]$ as being associated with the regular part of a Langevin motion (in the conformation space) we have

$$A^i_{ts}[\mathbf{v}_s]=-\frac{1}{\gamma}\frac{\delta E}{\delta v_s^i}, \tag{12}$$

where γ is the effective transport coefficient in the Langevin equation for $\mathbf{v}_s$, and describes the relaxation of fluctuations in the shape of the molecule as a result of interactions with the ambient medium.

By definition of the functional Z we obtain, taking into account Eqs. (11) and (12), the following equation for Z:

$$\frac{\delta Z}{\delta v_s^i}=\frac{\gamma}{T}A^i_{ts}[\mathbf{v}_s]Z=\frac{1}{D}A^i_{ts}[\mathbf{v}_s]Z, \tag{13}$$

where in writing down the last equality we made use of the Einstein relation

$$\frac{\gamma}{T}=D^{-1}.$$

Equation (13) has the steady-state solution

$$W=\mathrm{const}\cdot Z,$$

and for configurations close to the steady-state configuration,

$$\frac{\delta A^i_{ts}[\mathbf{v}]}{\delta v^j_u}=-\frac{1}{\gamma}\frac{\delta^2E[\omega_0]}{\delta v^i_s\,\delta v^j_u}.$$

4. CORRELATION FUNCTIONS AND RESPONSE FUNCTIONS

To find the response function we must apply a weak external force to the system (in the case at hand, the external torque $\mathbf{m}$ plays the role of such a force, coupled to $\mathbf{v}$). According to Eq. (11), adding the interaction with the external torque to the system energy results in the following modification of the functional $A^i_{ts}[\mathbf{v}]$ in the Fokker–Planck equation:

$$A^i_{ts}[\mathbf{v}]=-\frac{1}{\gamma}\frac{\delta E}{\delta v^i_s}+\frac{1}{\gamma}m^i.$$

As a result of this substitution, the Fokker–Planck equation (10) acquires the form

$$\frac{\partial}{\partial t}W+\frac{1}{\gamma}\sum_{i=1}^{3}\int_0^L ds\,m^i(s)\frac{\delta W}{\delta v^i_s}=D\sum_{i=1}^{3}\int_0^L ds\,\frac{\delta}{\delta v^i_s}\left(Z\frac{\delta}{\delta v^i_s}(Z^{-1}W)\right). \tag{14}$$

Recall that in the static regime

$$Z=\mathrm{const}\cdot\exp(-E/T)\equiv f_0.$$

We seek a solution of Eq. (14) in the form

$$W=f_0+f,$$

where the small correction f is associated with the action of the external torque $\mathbf{m}$. From Eq. (14) we have

$$f=\frac{f_0}{T}\sum_{i=1}^{3}\int_0^L ds\,m^i(s)v_i(s).$$

On the other hand, the presence of an external torque $\mathbf{m}$ results in a nonvanishing response $\langle\mathbf{v}\rangle$, even in the steady state ($\partial w/\partial t=0$). Using the fact that the mean value of $\mathbf{v}$ is zero in the steady state, we obtain

$$\langle v_j(s)\rangle=\int_L Dv(s)v_j(s)W=\int Dv(s)v_j(s)f$$
$$=\frac{1}{T}\sum_{i=1}^{3}\int_0^L ds'm^i(s')\int Dv(s)v_j(s)v_i(s')\times\exp\left(-\frac{E[\mathbf{v}]}{T}\right).$$

The last equality is the fluctuation–dissipation theorem

$$b_{ij}(s,s')=\frac{1}{T}G_{ij}(s,s'), \tag{15}$$

which relates the response function

$$b_{ij}(s,s')=\frac{\delta\langle v_j(s)\rangle}{\delta m^i(s')}$$

to the correlation function

$$G_{ij}(s_1,s_2)=\langle v_j(s_1)v_i(s_2)\rangle. \tag{16}$$

It is helpful to note the symmetry relation

$$G_{ij}(s_1,s_2)=G_{ji}(s_2,s_1).$$

The identity (15) is the analog of the fluctuation–dissipation theorem in our case. Since in the Kirchhoff problem the spatial coordinate plays the role of time without being constrained by causality (a torque applied at the point s will affect a point s' on either side of s), the fluctuation–dissipation theorem establishes the identity (up to the factor $1/T$) of the response and correlation functions.

Our next problem, then, is to calculate the correlation function $G_{ij}(s,s')$, which according to Eq. (15) also determines the change in the conformation of the molecule induced by the externally applied torque **m**. Interestingly enough, the nonvanishing off-diagonal elements b_{ij} are responsible for the important biological significance (Ref. 11, see also Ref. 2) of superhelicity effects (i.e., twisting of the curve on the basis of our model) as it bends (i.e., accompanying a change in the curvature). In our case of arbitrary anisotropy a_{ij} and twisting ω_0 of the original helix, the expressions obtained for G_{ij} are very complicated. Accordingly, we concentrate our efforts on a very important special case.

We assume that the conformation of the molecule considered on some scale L is such that $\boldsymbol{\omega}$ has the form

$$\omega=\omega_0+\delta\omega,$$

where the vector $\delta\boldsymbol{\omega}$ is small, and $\boldsymbol{\omega}_0$ is the global minimum for the energy density E given by Eq. (2):

$$\omega_0=-a^{-1}\mathbf{b}, \tag{17}$$

where a^{-1} is the inverse of the matrix $a=[a_{ij}]$. The vector $\delta\boldsymbol{\omega}$ is the variation of $\boldsymbol{\omega}$ near $\boldsymbol{\omega}_0$, which according to Eq. (4) can be expressed in terms of the vector $\mathbf{v}$:

$$\delta\omega=\nabla\mathbf{v}=\frac{d\mathbf{v}}{ds}+[\omega_0\mathbf{v}].$$

We can write the expansion of the elastic energy of the rod in terms of $\mathbf{v}$ as

$$F=F[\omega_0]+\delta^1F+\delta^2F+\dots .$$

The first variation δ^1F vanishes, since $\boldsymbol{\omega}_0$ corresponds to a minimum. It can easily be shown by direct calculation that the second variation takes the form

$$\delta^2F=\int_0^L ds\nabla\mathbf{v}_i a_{ij}(\nabla\mathbf{v})_j. \tag{18}$$

Neglecting third- and higher-order terms, and assuming boundary conditions $\mathbf{v}(s=0)=\mathbf{v}(s=L)=0$, we obtain the elastic energy of the rod (molecule):

$$F=F[\omega_0]-\int_0^L ds(\mathbf{v}\nabla[a\nabla\mathbf{v}]). \tag{19}$$

The calculation of the correlation function $\langle v_i(s_1)v_j(s_2)\rangle$ has thus been reduced to a calculation of the Gaussian functional integral

$$G_{ij}(s_1,s_2)=\langle v_i(s_1)v_j(s_2)\rangle=\text{const}\times\int Dv(s)v_i(s_1)v_j(s_2)\exp\left(-\frac{\delta^2F}{T}\right), \tag{20}$$

where the second variation of the energy is given by Eq. (18). According to the standard rules, this reduces to solving the equation

$$\nabla(a\nabla)G(s_1,s_2)=\delta(s_1-s_2) \tag{21}$$

with vanishing boundary conditions. The latter problem can be solved with the aid of the Fock–Schwinger proper time (see Ref. 10, Chap. 2), but the exact formulas so obtained are very complicated, and we therefore restrict our attention here to perturbation theory.

To simplify the calculations, we consider an isotropic rod:

$$a_{ij}=a\delta_{ij}.$$

Then Eq. (21) assumes the form

$$\left(\frac{d}{ds}-\omega_0\right)^2 G(s_1,s_2)=\delta(s_1-s_2), \tag{22}$$

or

$$\frac{d^2}{ds^2}G(s_1,s_2)-2\omega_0\frac{d}{ds}G(s_1,s_2)+\omega_0^2G(s_1,s_2)=\delta(s_1-s_2),$$

where ω_0 is the matrix corresponding to the vector $\boldsymbol{\omega}_0$:

$$[\omega_0]_{ij}=-\epsilon_{ijk}\omega_k.$$

We have dropped the scalar factor a, so that the correlation function is now related to the Green's function by

$$\langle v_i(s_1)v_j(s_2)\rangle=\frac{1}{a}G_{ij}(s_1,s_2).$$

We now assume that $|\boldsymbol{\omega}_0|$ is small, and we take as the zeroth-order approximation the Green's function

$$G_0^{ij}=\delta_{ij}G_0(s_1,s_2),$$

which satisfies the equation

$$\frac{d^2}{ds^2}G_0(s_1,s_2)=\delta(s_1-s_2)$$

with vanishing boundary conditions. The Green's function $G_0(s_1,s_2)$ satisfies the explicit formula[10]

$$G_0(s_2,s_1)=-\frac{1}{L}[(L-s_2)s_1\theta(s_2-s_1)+(L-s_1)s_2\theta(s_1-s_2)], \tag{23}$$

where

$$\theta(x)=\begin{cases}1, & x\geqslant 0,\\ 0, & x<0,\end{cases}$$

is the Heaviside unit step function.

The equation (22) can be rewritten in integral form,

$$G(s_2,s_1)=IG_0(s_2,s_1)-\int_0^L ds\left(2\omega_0\frac{d}{ds}G_0(s,s_2)+\omega_0^2G_0(s,s_2)\right)G(s,s_1),$$

where $I=\delta_{ij}$ is the unit matrix. The above equation for the Green's function $G(s_2,s_1)$ can be solved iteratively. As a result, we obtain to first order in ω

$$G(s_2,s_1)=IG_0(s_2,s_1)+\omega_0\frac{s_1-s_2}{2L}[-s_1s_2+L\min(s_1,s_2)]. \tag{24}$$

Equations (15) and (24) constitute the fluctuation–dissipation theorem for our system in the approximation of small $\boldsymbol{\omega}$, i.e., small twisting and bending of the molecule.

5. CASIMIR TORQUE

In this section we calculate the contribution of fluctuations in the shape of a single molecule in the superhelical configuration to the free energy. This is reminiscent of the classical Casimir effect[4] associated with fluctuations of the electromagnetic field (or zero-point fluctuations). The energy of zero-point fluctuations in the melting of inert-gas crystals seems to have first been studied by Bennewitz and Simon.[12] Simon[13] subsequently clarified the important role of zero-point fluctuations in the equation of state of helium: the importance of the zero-point energy of the helium atoms means that helium solidifies only under pressure, even at very low temperatures. A similar situation occurs in two-dimensional systems, in helium films adsorbed on graphite, where the zero-point energy is important for the formation of two-dimensional phases.[14] In all of the cases enumerated above, the zero-point energy depends strongly on the geometric characteristics of the system; for example, the volume of the system, as in the case of helium, or boundaries, as in the case of the classical Casimir effect. The symmetry of the medium may also be important, as in films of adsorbed atoms[14] (see Ref. 15, which deals with the interplay between crystal surface reconstruction and zero-point energy).

The Casimir effect is now regarded as resulting from the interdependence of the zero-point energy and the widely understood topological structure of a system,[16] and it is precisely the fluctuating nature of the oscillations, which can behave like thermal fluctuations at a temperature far above $T=0$, that is important. As shown in Ref. 17 (see also Refs. 18 and 19), fluctuations in the polarizability of macroscopic bodies lead to interactions among those bodies. The same idea was applied in Refs. 20 and 21 to investigate the melting of ice. A similar approach was employed to study forces in liquid crystals and membranes.[22,23]

As we show below, the energy of the vibrations of a DNA-type molecule depends on its dimensions, which are specified by its scale L and geometry—in the present case a superhelix given by the vector $\boldsymbol{\omega}$. The Casimir effect thus occurs in the sense indicated above, and the torque

$$-\frac{\partial F_{\text{fluct}}}{\partial L},$$

which is dictated by fluctuations in the shape of the helix, plays the role of the Casimir force.

We now consider fluctuations in the shape of a molecule near its configuration given by the vector $\boldsymbol{\omega}=\boldsymbol{\omega}_0$ (17). The energy of the molecule in this case is given to second order by Eq. (18). We now assume that the elastic modulus tensor is isotropic, $a_{ij}=a\delta_{ij}$. Hence, the energy of the fluctuations is given by

$$\delta^2 F=a\int_0^L ds(\nabla\mathbf{v}\nabla\mathbf{v}).$$

We represent it in the form

$$\delta^2 F=S_0+(\delta^2 F-S_0),$$

where

$$S_0=a\int_0^L ds\left[\left(\frac{d}{ds}\mathbf{v}\,\frac{d}{ds}\mathbf{v}\right)-\omega^2(\mathbf{v}\mathbf{v})\right]$$

and

$$\delta^2 F-S_0=-2a\int_0^L ds\left[\frac{d}{ds}\mathbf{v}\mathbf{v}\right]\omega.$$

To estimate the contribution to the free energy, which is given by

$$\exp\left(-\frac{F_{\text{fluct}}}{T}\right)=\int Dv(s)\exp\left(-\frac{\delta^2 F}{T}\right),$$

we employ Feynman's inequality,[24] which in our notation takes the form

$$F_{\text{fluct}}\leqslant\langle S_0\rangle_0+\langle S-S_0\rangle_0,$$

where the mean $\langle S_0\rangle_0$ is defined as

$$\langle S_0\rangle_0=\text{const}\int Dv(s)\exp(-S_0/T)$$

and

$$\langle\delta^2 F-S_0\rangle_0=\frac{\int Dv(s)[\delta^2 F-S_0]\exp(-S_0/T)}{\int Dv(s)\exp(-S_0/T)}.$$

To calculate these means we take Fourier transforms

$$\mathbf{v}=\sum_{n=-\infty}^{+\infty}e^{i\nu_n s}\mathbf{w}_n,\quad \nu_n=\frac{2\pi}{L},$$

where $\mathbf{w}_n=\mathbf{a}_n+i\mathbf{b}_n$ and since $\mathbf{v}$ is real, we have $\mathbf{w}_n=\mathbf{w}^*_{-n}$. The Fourier representation for S_0 has the form

$$S_0=\sum_{n=-\infty}^{+\infty}\mathbf{w}_n(\nu_n^2-\omega_0^2)\mathbf{w}_n^*.$$

Having carried out the rotational transformation with the constant matrix R, the vector $\boldsymbol{\omega}_0$ can be put in the form

$$|\omega_0|f_1,\quad (f_3)_{ij}=-\epsilon_{ijk},$$

and in the new coordinates the expression for S_0 takes the form

$$S_0=\sum_{n=-\infty}^{+\infty}(\nu_n^2+|\omega_0|^2)\mathbf{w}_n\mathbf{w}_n^*$$

$$=\sum_{n=-\infty}^{+\infty}(\nu_n^2+|\omega_0|^2)(\mathbf{a}_n^2+\mathbf{b}_n^2).$$

Hence,

$$\langle S_0\rangle=\text{const}\cdot\int Da_n\,Db_n\,\exp(-S_0/T).$$

To calculate $\langle S_0\rangle$ explicitly we can use the formula

$$\prod_{n=1}^{\infty}\left[1+\frac{z^2}{\pi^2 n^2}\right]=\frac{z}{\sinh z}.$$

Finally, Note that the calculation of $\langle \delta^2 F - S_0 \rangle_0$ in the Fourier representation considered here reduces to a Gaussian integral of the type

$$\int_{-\infty}^{\infty} da \int_{-\infty}^{\infty} dbab \exp[-k(a^2+b^2)]$$

which vanishes. We therefore obtain for the energy of the fluctuations

$$F_{\text{fluct}} \leqslant \langle S_0 \rangle_0 .$$

For small energy fluctuations, Feynman's inequality[24] gives very good estimates; we therefore set

$$F_{\text{fluct}} = \langle S_0 \rangle_0 = -2T \ln \frac{L|\omega_0|/2}{\sinh(L|\omega_0|/2)}$$

and for large L we have

$$F_{\text{fluct}} \propto TL|\omega_0| .$$

For the Casimir torque we obtain

$$M_{\text{fluct}} \propto T|\omega_0| .$$

In the present case, of course, the formula presented above holds if the fluctuation (Casimir) contribution to the energy does not exceed the elastic (Kirchhoff) contribution:

$$aL|\omega_0|^2 \geqslant T|\omega_0| ,$$

or

$$|\omega_0| \geqslant \frac{T}{a} . \qquad (25)$$

Significantly, one of the physical mechanisms of superhelicity (i.e., $|\boldsymbol{\omega}_0| \neq 0$) is adsorption of a DNA molecule on nucleosomes, which on the basis of our model is described by the vector **b**. Using Eq. (17) for $\boldsymbol{\omega}_0$, we obtain from Eq. (25)

$$|\mathbf{b}| \geqslant T . \qquad (26)$$

Equation (26) takes a perfectly natural form, demonstrating that when the torque **b** is large enough (i.e., in the limit of strong adsorption), our results hold over arbitrarily large scales.

6. CONCLUSIONS

Our problem has been to analyze the physical consequences of the model discussed (which, in turn, might be compared with experimental data for real systems), and to develop a method for studying such models theoretically. We have shown how classical mechanics and statistical physics "work" in the proposed model of a DNA-type molecule. From the standpoint of mechanics, a DNA molecule is a new, heretofore unstudied object with anisotropic elasticity [the tensor a_{ik} in the expression for the energy (2) or (5)] that is subject to a spontaneous distributed torque [the vector **b** in Eq. (2)]. The mechanics of such objects were constructed in Sec. 2.

Statistical physics applied to one DNA-type molecule describes the distribution of the possible conformations of a single molecule. This differs from traditional problems in the statistical physics of polymers in the existence of no more than a few stationary configurations of the molecule, with all possible conformations being small fluctuations near this stationary configuration. Thus, Brownian motion in the function space of conformations provides a natural description of the statistical behavior of such systems, and the Fokker–Planck equation is the natural mathematical apparatus (Sec. 3).

Of course, the two approaches (mechanical and statistical) complement and agree with one another. This was demonstrated in Sec. 4, where we derived the analog of the fluctuation–dissipation theorem, relating the mechanical response function b_{ij} to the static correlation function G_{ij}.

Finally, the aforementioned characteristic feature of the statistical behavior (small fluctuations in shape about a steady conformation) leads to a natural constraint on the spectrum of fluctuations as a result of the geometric characteristics of the steady conformation. In the case of a helical steady shape, this geometric factor is the skew-symmetric matrix (or the vector $\boldsymbol{\omega}$), introduced above, which describes the rotation of the Frenet reference frame during motion along a curve. This size effect is physically similar to the classical Casimir effect, and leads to a fluctuating torque that tends to twist the equilibrium helical configuration of the molecules (Sec. 5).

This work was supported by INTAS (grant No. 94-4078) and the Russian Fund for Fundamental Research (projects 94-02-06306 and 95-02-05343).

[1] S. B. Smith, L. Finzi, and C. Bustamante, Science **258**, 793 (1992).

[2] J. F. Marko and E. D. Siggia, Macromolecules **27**, 891 (1994); Preprint, Lab. Atomic and Solid State Physics, Cornell University (1994).

[3] V. L. Golo and E. I. Kats, JETP Lett. **60**, 679 (1994).

[4] H. B. Casimir, Proc. Kon. Ned. Akad. **51**, 793 (1948).

[5] L. D. Landau and E. M. Lifshitz, *Theory of Elasticity*, Pergamon Press, New York (1986).

[6] B. A. Dubrovin, S. P. Novikov, and A. T. Fomenko, *Modern Geometry* [in Russian], Nauka, Moscow (1979).

[7] V. L. Golo and E. I. Kats, Zh. Éksp. Teor. Fiz. **105**, 898 (1994) [JETP **78**, 482 (1994)].

[8] E. M. Lifshitz and L. P. Pitaevskiĭ, *Physical Kinetics*, Pergamon Press, New York (1981).

[9] A. N. Kolmogorov, *Collected Works. Theory of Probability and Mathematical Statistics* [in Russian], Nauka, Moscow (1986).

[10] K. Itzykson and J.-B. Zuber, *Quantum Field Theory*, McGraw-Hill, New York (1980).

[11] A. D. Bates and A. Maxwell, *DNA Topology*, Oxford University Press, Oxford (1993).

[12] K. Bennewitz and F. Simon, Z. Phys. **16**, 183 (1927).

[13] F. Simon, Nature **133**, 529 (1934).

[14] H. Wiechert, Physica B **169**, 144 (1991).

[15] V. Golo, J. Phys.: Condens. Matter **2**, 9025 (1990).

[16] G. Plunien, B. Müller, and W. Greiner, Phys. Rep. **134**, 89 (1986).

[17] I. E. Dzyaloshinskiĭ, E. M. Lifshitz, and L. P. Pitaevskiĭ, Usp. Fiz. Nauk **73**, 381 (1961) [Sov. Phys. Usp. **4**, 153 (1961)].

[18] Yu. S. Barash, *Van der Waals Forces* [in Russian], Nauka, Moscow (1988).

[19] L. D. Landau and E. M. Lifshitz, *Statistical Physics*, Pergamon Press, New York (1980).

[20] M. Elbaum and M. Schik, Phys. Rev. Lett. **66**, 1713 (1991).

[21] M. Elbaum and M. Schik, J. de Phys. 1 **1**, 1665 (1991).

[22] H. Li and M. Kardar, Phys. Rev. A **46**, 6490 (1992).

[23] A. Ajdari, L. Peliti, and J. Prot, Phys. Rev. Lett. **66**, 1481 (1991).

[24] R. Feynman, *Statistical Physics*, Benjamin, New York (1972).

Translated by M. E. Alferieff