Elastic and Proton Dynamics of the DNA

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The subject of this report is the dynamics of elastic system in conjunction with hydrogen bonds of the DNA. We draw attention to the draw-back of the familiar rod model of the DNA, and make a case of constructing models that could accommodate the intrinsic structure of the DNA. In this respect studying the interplay among the elastic system and the protons of the DNA, is of interest, for it could accommodate the inter-strand as well as the tunneling modes of protons. Following this direction, we come to the conclusion that the elastic-proton dynamics may have a bearing on biophysics of the DNA. The phenomenon of point mutations is discussed within this framework.

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I. INTRODUCTION

A molecule of the DNA can attain several hundred \( \mu \text{m} \) in length. If we neglect details that have a size of one thousand \( \text{Å} \), or less, we can visualize it as a soft shapeless line and conclude that on this scale it behaves like an ordinary polymer. In contrast, looking at its smaller segments, of one hundred \( \text{Å} \) or less, we observe that it tends to be straight. Thus, borrowing a comparison from everyday life, we may say that a molecule of the DNA looks like a piece of steel wire whose long segments are flexible and the short ones are stiff. The elastic properties of the DNA are intimately related to its being a double helix. The latter imposes severe constraints on deformations which can be effected without destroying the molecule and to a large extent determines its mechanical properties. In fact, the two strands comprising the molecule of DNA have just small bending rigidities, just as usual polymers. But the formation of the two-stranded structure drastically changes the DNA by making it both stiff and capable of forming
sophisticated spatial shapes. Similarly, the dynamics of the DNA is largely determined by the relative motion of its strands. The functioning of the DNA also involves the charge transport in the molecule. The latter may be related either to the motion of electrons along the strands, or to the tunneling of protons inside the hydrogen bonds connecting the bases. The problem that still waits its answer is whether there is any interaction between the elastic dynamics of the double helix and the tunneling dynamics of charge.

The diameter of the DNA is about 20 Å, and taking into account its enormous length we may consider it both a microscopical and macroscopical object. Thus, the DNA requires a special means for analysis of its physical properties. Important, the approach from 'first principles' aimed at conformational dynamics, for example using the methods of quantum chemistry, often comes across very serious difficulties, which do not have just technical character, but correspond to the need for a physical picture to rely upon. Therefore, the theoretical study of the DNA is to utilize models, which are necessarily based on extremely crude simplifications. Their connection with the microscopical structure of the DNA, is a matter of intuition rather than of rigorous demonstration. Yet it would not be quite appropriate to accept only rigorously demonstrated facts and to ignore ideas that could motivate the development of the DNA theory and provide a stimulus to further experimentation.

Owing to the large stiffness of the molecule of DNA, described by the persistence length of about 500 Å at which it strongly resists strains caused by heat fluctuations, one may try to visualize it as an elastic rod. The above model serves the basis for a number of theoretical approaches, but even though it has turned out to be successful, for example for the topological analysis of the DNA conformations, there are situations in which it does not work properly; specifically, when external charges are to be taken into account. It is also important that it does not allow for the internal degrees of freedom due to the two-stranded helical structure. The latter imposes stringent constraints on possible strains of a molecule of the DNA, which result in the specific structure of its vibrational modes, very important for understanding its functioning. Therefore, we shall consider consequences that may be inferred from the basic properties of the DNA, aiming at a qualitative approach that uses simple theoretical models that may accommodate the internal degrees of freedom. At this point we should like to note that since different problems require the use of appropriate approximations and specific choice of dynamical variables, there is no unique form of the energy functional, even though the object of our study remains a molecular of the DNA. Indeed, we shall choose various forms of the energy owing to the necessity to accommodate conformations of the DNA under consideration and external conditions in action.

Let us recall that the double helix of DNA consists of long chains, or strands, which have the backbones composed of sugar and phosphate residues, and special chemicals, bases, keeping the two strands together. The fundamental building blocks of the strands are nucleotides, joined to each other in polynucleotide chains. The nucleotide consists of a phosphate joined to a sugar (2'-deoxyribose), to which a base is attached. The sugar and base alone are called a nucleoside. The chains, or strands, of the DNA wind round each other in a spiral forming a double helix, the bases being arranged in pairs: adenine - thymine (AT), guanine - cytosine (GC), so that the sequence of bases in one strand determines the complimentary sequence of bases in the other and constitutes the genetic code stored by the molecule of DNA. There are several forms of the DNA, denoted by A,B, and Z. The most common one in nature, is the so-called B-form. One turn of the helix of the B-form, corresponds approximately to 10.5 base-pairs, and the distance between adjacent pairs of bases is approximately 3.4 Å. In real life there are considerable deviations from the canonical B-form of the DNA. Therefore, there is a need for a special nomenclature for describing its conformations (see [1] for the details). In fact, it is easy to see that generally a considerable set of parameters are required to this end. For example, even if we assume a simple picture of base pairs as flat plates, we still need to use vector quantities for describing their distance from each other and angles for mutual orientation, that is on the whole nine parameters. The most common one, Roll and Tilt, shall describe the planes of successive base pairs not being parallel, as is prescribed for the B-form. In fact, it is necessary to introduce the so-called propeller angle for defining the measure for deviations of the normals to the bases inside a base-pair. It is worth noting that the deviations from the canonical form are by no means small, and may have a size of tens of degrees.

In contrast to the sugar-phosphate backbone of a single strand of DNA, which is formed by strong covalent forces, the double helix of the DNA is due to the interplay of weak chemical forces. In fact, the two chains of the DNA are held together by the hydrogen bonds between complementary bases and the stacking interactions between adjacent bases attached to the same sugar-phosphate strand above each other in neighbouring pairs, so that on the whole it requires the energy of order $10K cal/mol$ or several
The theoretical treatment of the inter-strand modes. Raman scattering, [13], [12], indicate that the attenuation of the modes is substantial, see also [14] for the motion of the bases, or inter-strand modes, are assumed to be less sensitive to the viscosity of the dynamical modes of the bases and the sugar-phosphate backbone by considering the coupling between them. The helical structure supposes the existence of motions; (3) the relative position of the strands verify the helical symmetry. But, the DNA is not totally symmetrical structure due to the choice of base-pairs, which is generally random. This circumstance results in considerable theoretical complications. Important, the helical structure supposes the existence of the preferred local system of coordinates for every base-pair, and these coordinate systems should change with external charges by allowing the graphic representation of their distribution on the surface of a molecule of DNA. It should be noted as well that a molecule of the DNA is itself negatively charged. Therefore, the emerging picture of the DNA conformation due to elastic and electrostatic forces is generally very complicated, and should be treated within the framework of electro-elasticity theory. But the available experimental values of elastic stretch constants and the dependence of persistence lengths on the ionic strength of aqueous solution, indicate that, strictly speaking, a molecule of the DNA does not behave like an elastic rod. The effect could be due to the backbones of the two DNA strands, which contain phosphoric groups carrying negative charge that may cause the strands to repel each other, facilitate the separation of the strands, and make for the double-helix being less stable, at low ionic strength. The overall picture strongly depends on the specific arrangement of the constituent base pairs, because the forces keeping a base-pair together depend on the choice of constituent nucleotides, the number of the hydrogen bonds involved being different, e.g. 2 for adenine-thymine and 3 for guanine-cytosine. The important point about it is that the competition makes for the increase of entropy, and thus the stability of the DNA. The stacking interaction is due to the bases being flat water-insoluble molecules, lying above each other roughly perpendicular to the direction of the helical axis so as to enable electron clouds between bases to contribute to the helical stability. This is again only a plausible hypothesis, or even simply an intuitive picture that needs careful investigating. The energy of the interaction between complementary base pairs has been estimated by various means which rely on experimental data and computer calculations within the framework of the quantum chemistry, [3]. It is generally falls within 10Kcal/mol (see [3] for more recent results).

The large persistence length of the DNA, ≈ 500Å, which is more than 20 times larger its diameter, serves the main, and essentially intuitive, argument for considering it as an elastic rod and employing the methods of continuum mechanics for its study. Strictly speaking, this is not correct, for the cross section of this 'rod' corresponding just to a base-pair comprises only several tens of atoms. The main argument in favour of such approach is generally the pragmatic one, "the truth is useful" . In fact, as follows from numerical simulation within the framework of this approach, the above model appears to be acceptable for many regimes that involve functioning of the DNA, [4], [5]. It needs some modifications so as to take into account the important effects of the anisotropy due to unsymmetrical positions of constituent nucleoside, and thus requires the use of anisotropic elastic moduli. Equally important, there is also a geometrical asymmetry generated by the relative positions of nucleosides inside a base pair. The asymmetry can be visualized as two grooves on the surface of the rod. The grooves are helpful in describing the interactions of the DNA with external charges by allowing the graphic representation of their distribution on the surface of a molecule of DNA. It should be noted as well that a molecule of the DNA is itself negatively charged. Therefore, the emerging picture of the DNA conformation due to elastic and electrostatic forces is generally very complicated, and should be treated within the framework of electro-elasticity theory. But the available experimental values of elastic stretch constants and the dependence of persistence lengths on the ionic strength of aqueous solution, indicate that, strictly speaking, a molecule of the DNA does not behave like an elastic rod. The effect could be due to the backbones of the two DNA strands, which contain phosphoric groups carrying negative charge that may cause the strands to repel each other, facilitate the separation of the strands, and make for the double-helix being less stable, at low ionic strength. The overall picture strongly depends on the specific arrangement of the constituent base pairs, because the forces keeping a base-pair together depend on the choice of constituent nucleotides, the number of the hydrogen bonds involved being different, e.g. 2 for adenine-thymine and 3 for guanine-cytosine. It is also important, that the relative positions of bases change from pair to pair. Obviously, we are very far from the simple elastic rod model. Therefore, there is a need for a semi-microscopic theory that could accommodate the elasticity of the DNA and take into account its micro-structure.

The current approach to the problem relies on the hypothesis that it is possible to separate the dynamical modes of the bases and the sugar-phosphate backbone by considering the coupling between them as perturbation. The backbone modes are suggested to be strongly overdamped, whereas the modes due to the motion of the bases, or inter-strand modes, are assumed to be less sensitive to the viscosity of ambient liquid. The theoretical calculations of paper [5] support the statement, whereas the experiments on Raman scattering, [13], [12], indicate that the attenuation of the modes is substantial, see also [14] for the theoretical treatment of the inter-strand modes.

The approaches commonly used to manufacture qualitative models that could give an adequate picture of the dynamics of the DNA, are generally based on the concept of lattice (see paper [9], [10], [11] in which a coarse-grained model is considered), that is one considers the molecule of DNA as a regular structure similar to a one-dimensional crystal. It is necessary to take into account that: (1) the DNA comprises the two strands; (2) the strands are bound together by certain forces determining inter-strand motions; (3) the relative position of the strands verify the helical symmetry. But, the DNA is not totally symmetrical structure due to the choice of base-pairs, which is generally random. This circumstance results in considerable theoretical complications. Important, the helical structure supposes the existence of the preferred local system of coordinates for every base-pair, and these coordinate systems should change.
from one base-pair to another, the neighboring one. Constructions accommodating the phenomenon utilize the concept of gauge field, following its current use in field theory and condensed matter physics. In the case of the DNA dynamics, it allows for at least qualitative description of its elastic modes.

Using the lattice has also the advantage of allowing for tautomeric forms of the base pairs. There are of two classes of the DNA bases, purine (adenine, guanine) and pyrimidine (cytosine, thymine). Under the ordinary circumstances adenine and cytosine are in amino form, and only rarely in the imino one, whereas guanine and thymine prefer the keto form, and rarely the enol one. Inside the base-pairs the transformation of the tautomeric forms correspond to the tunneling transitions of protons in the hydrogen bonds keeping the bases together. It is alleged that the transitions may result in mutations, \[15\], \[16\], \[17\], \[18\]. The intriguing question is whether there is an interplay among the elastic properties of the DNA and the tautomeric transitions.

II. THE ELASTIC ROD MODEL

In this section we shall consider more fully the rod model and its possible modifications. One may advance the hypothesis that the conformation of the molecule of DNA could be qualitatively described by visualizing the latter as an elastic thread that has the elasticity constant, \(\gamma\), of such a size that heat fluctuations due to surrounding solvent be small on a scale called the persistence length. In order to make a rough estimate to the effect, we may assume that the elastic energy of a molecule be given by the equation

\[ E_{\text{elastic}} \approx \int_0^L \gamma \left( \frac{d\phi}{ds} \right)^2 ds \]

in which \(L\) is the length of the molecule, \(\phi\) is the deviation angle of the vector tangent to its central line. Then the condition for the persistence length, \(L_p\), reads

\[ E_{\text{elastic}} \geq k_B T \]

If we take \(L \approx 500 \text{ Å}, \quad T \approx 300\) and \(\phi \approx 1\) radian, we obtain \(\gamma \approx 10^{-19} \text{ erg} \cdot \text{cm}\), that is the value which is in reasonable agreement with the experimental data, \[8\], \[9\]. Thus, on the spatial scale between one coil of the double helix and 500 \(\div\) 1000Å, that is 10 \(\div\) 150 base pairs a molecule of the DNA may preserve its straight form and has the appearance of an elastic rod. This model of the DNA allows to calculate, at least qualitatively, interwound structures called plectonemic supercoils formed by DNA molecules (first found by electron microscopy, \[19\]).

Within the framework of this model, the double helix of DNA is characterized by three spatial scales: (1) the microscale of order 3.4 Å, that is the distance between adjacent base pairs along the chain; (2) the mesoscale of order 10\(^3\) Å, or several persistent lengths; (3) the macroscale of the size of a molecule of DNA, that is up to several \(\mu\)m or more. On the microscale, the molecule of DNA is formed by the base pairs of purines and pyrimidines linked by hydrogen bonds between the bases; the whole constitutes a double stranded structure. The DNA helix considered on the mesoscale, is suggested to have the properties of an elastic rod with the torsional and the bending rigidities of about \(10^{-19}\)\ erg \cdot cm, \[10\]. The stretching of the rod is assumed to be small compared with the bending and twisting, and in many cases may be neglected. On the macroscale, a molecule of DNA is flexible, its rigidity does not influence its shape, and one can consider it as usual polymer. The whole picture constitutes the so-called worm-like-chain model, \[4\].

The picture of the DNA considered on the mesoscale can be cast in a quantitative form using the classic theory of elastic rod worked out by G. Kirchhoff, \[20\]. It should be noted that the use of the Kirchhoff theory for the needs of the DNA involves certain approximations. First, there is a problem of taking into account the finite diameter of the molecule, for strictly speaking the Kirchhoff equations are written down for the elastic line. Second, the use of continuum mechanics for objects with spatial scales of several tens of Å may raise some doubts; in fact, there is no continuous medium at hand. Third, Kirchhoff’s model does not allow for the possible extension of a molecule of the DNA, and the internal degrees of
freedom, for example the relative motion of the the strands. Nonetheless, the cautious employment of the Kirchhoff theory gives reasonable qualitative results and appears to be justifiable in certain regimes, \[4\].

The static of a system of this kind can be described by means of the effective energy, which constitutes the core of Kirchhoff’s model. It is given by the equation

\[ F = \int_0^L ds \frac{1}{2} \sum_{ij} a_{ij} \omega_i \omega_j \]  

(1)
in which \( L \) being the total length of rod, \( s \) the length parameter, \( a_{ij} \) its elastic moduli, and \( \omega_i \) coordinates of a vector that describes the strain of the rod corresponding to the molecule. The vector \( \vec{\omega} \) is constructed as follows. Consider a local frame defined at a point of the central line of the rod; its first vector \( \vec{v}_1 \) being the unit tangent vector at the point, and the second and the third, \( \vec{v}_2, \vec{v}_3 \) unit vectors along the principle directions of the strain. The three vectors are considered as columns of the rotation matrix \( R = R(s) \) describing the change of the local frame. The matrix

\[ \omega = R^{-1} \frac{d}{ds} R \]  

(2)
can be visualized as an angular velocity of the local frame, the length parameter \( s \) playing the part of time, or in the vector form

\[ \omega = \sum_i f^i \omega_i, \quad (f^i)_{jk} = -\epsilon_{ijk} \]  

(3)
The minimization equations for the Kirchhoff energy have the same form as the equations of motion for the top (the so-called Kirchhoff analogy)

\[ \frac{d}{dt} \vec{\omega} = \vec{\omega} \times \vec{\mu}, \quad \vec{\mu} = \frac{\partial F}{\partial \vec{\omega}} \]

The rich analytical and topological structure of solutions to the top, or Kirchhoff equations has provided the necessary framework for their application to conformational problems of the DNA, and the most important one has been the theory of supercoiling, \[4\]. The Kirchhoff model allows for the twist-bend coupling, \[5\], which corresponds to the chiral character of the DNA. In paper \[21\] the model is further extended by taking into account the stretch of a molecule of DNA, and considering the bend-stretch coupling. In the notations of papers \[21, 22, 23, 24\], this means that the elastic energy of the molecule reads

\[ E = \frac{1}{L} \int_0^L ds \left[ A' \Omega_1^2 + A \Omega_2^2 + C(\Omega_3 - \omega_0)^2 + B \omega_0^2 \alpha^2 \right. \]

\[ + 2D(\omega_3 - \omega_0)\alpha + 2G(\Omega_3 - \omega_0)\Omega_2 + 2K(\Omega_3 - \omega_0)\Omega_2 \alpha \]  

(4)
where the vector \( \Omega_1, \Omega_2, \Omega_3 \) defined by Eqs.\((2 - 3)\) determines the bend and twist of the molecule, the constant \( \omega_0 \), in fact the vector \( \omega_1 = 0, \omega_2 = 0, \omega_3 = \omega_0 \), accommodates the helix twist, and \( \alpha \) accounts for the stretch. Thus, \( C \) is the twist-bending coupling constant of paper \[5\], and \( K \) the bend-stretch one. The conformations of the rod is finally determined by the minimum of the functional given by the equation

\[ \mathcal{M} = \frac{E}{k_B T} - fZ - 2\pi \tau Lk \]  

(5)
in which \( f \) is an applied tension and \( Lk \) is the topological invariant, the so-called linking number, that defines the linking between a closed path and its image obtained by a small translation in space without self-intersections. The Lagrange multiplier \( \tau \) serves a kind of chemical potential for the linking. In paper \[22\] the authors put forward arguments that there are twist-stretch terms in the elastic energy if the molecule of DNA is modelled on a stack of thin, rigid plates that are not permitted to deform. They obtain an equation for the elastic energy of the form given by Eq.\((4)\). The problem is related to that of small fluctuations of bend in the helical backbone that are important for understanding the mechanism of
the torsional stress accompanying the transcription. As is shown in paper [23], the drag could correspond to a torque of $19^{-13}$ dyn cm, which rather surpasses the actual torque involved during transcription. In contrast, if the bend fluctuations are not taken into account, the torque is negligible, which contradicts the experimental facts. These results are in qualitative agreement with the value $4.5 \times 10^{-19}$ for the twist rigidity (see also [26]).

In spite of the successes of the elastic rod model, there has been a considerable criticism levelled at it. Baumann et al. [6], have studied the elastic properties of the DNA as a function of ionic strength and in the presence of multivalent cations. They measured the extension of the DNA caused by an external force applied to it. It should be noted that there are three regimes in the elastic response of DNA molecules, [30]:

1. $0.01 \div 10 \text{pN}$ the molecule behaves as an entropic spring, the worm-like chain model (WLC), [27];

2. $10 \div 65 \text{pN}$ deviations from the WLC, enthalpic elasticity;

3. at about $65 \text{pN}$ the molecule suddenly yields in a highly cooperative fashion and overstretches $\approx 1.7$ times, [30].

In the region where the WLC model is valid, a molecule of the DNA is a kind of hybrid of a rigid rod and a flexible coil, and is usually visualized as a homogeneous elastic rod. But the assumption is in contradiction with the elasticity theory according to which the persistence length $P$ and the stretch modulus, $S$, given by the equation $S = EA$, in which $E$ is the Young modulus and $A$ is the cross-sectional area of the rod, should vary in the same way with the ionic strength whereas the results of [6] indicate that they change in opposite directions. Another discrepancy comes while considering the Poisson ratio $\sigma$ defined by the equation

$$B/C = 1 + \sigma$$

in which $B$ and $C$ are the bending and the torsional rigidity, respectively. The thermodynamical stability requires, [20], $-1 < \sigma < 1/2$, while $\sigma < 0$ corresponds to the thickening of the rod as it is stretched. The values of $B$ are alleged to be $2 \cdot 10^{-19}$ erg cm, and $C$ in the range $2 \cdot 10^{-19}$ to $3.4 \cdot 10^{-19}$ erg cm. These values correspond to $-0.4 < \sigma < 0.$, and therefore the DNA rod should thicken while it is stretched. Thus, we should either accept that the DNA is an elastic rod of quite unusual nature, or admit that there is a need for a model that could accommodate its double-stranded structure, helical symmetry, and internal stacked base pairs.

Besides the drawbacks mentioned above the rod model fails to accommodate the process of denaturation when a molecule of the DNA splits up into separate strands. But, the breaking of the hydrogen bonds between the base pairs and the formation of bubbles comprising segments in which the two strands are separated, may happen under other circumstances. Equally important, there may exists relative motions of the strands which do not result in breaking the hydrogen bonds. In fact, the dynamics of these inter-strand modes is accessible to experimental studying, (see for example [12], [13], [31], [32]). It may tell a lot about the physics of the DNA.

One may try to mimic the partition of a single double-stranded molecule into two strands within the framework of the rod model, by employing an additional quantity $\mathbf{q}(s)$ that indicates a relative displacement of the strands from the equilibrium conformation. The procedure is similar to that discussed above in connection with the coupling between the stretch and the twist-bend modes of the DNA. What’s more, we shall see that thermal fluctuations of the field $\mathbf{q}(s)$ result in a contribution to the twist-bend momentum and thus turn out to be similar to the stretch term introduced in [21], [22].

The field $\mathbf{q}(s)$ gives displacements of points coinciding in the initial equilibrium conformation of the rod, and possible going apart because of the deformation and breaking on the microscopical scale, of bonds between base pairs of the molecule. On the mesoscale, which we use to describe the molecule, the vectors $\mathbf{q}(s)$ are determined at points of the rod by the parameter of arc length, $s$. Thus, outside the region of states where the breaking up takes place, we visualize the molecule of DNA as comprised of two elastic wires attached to each other; the whole being an elastic rod that one can bend, twist, and stretch.
It is worth noting that on allowing the partition of the strands we at the same admit that the molecule can be stretched. In fact, the sugar-phosphate backbones of the strands are formed by strong covalent bonds and are hard to be stretched, so that the partitioning of the strands should result in changing the total length of the total molecular. Whether it will be diminishing or increasing, depends on the deformation of helix that should accompany it.

The static of a system of this kind can be described within the framework of Kirchhoff’s model of the elastic line with the help of its extension with the vector $\vec{q}$. It is determined by the energy given by the equation, \[F = \int_0^L ds \left( \frac{1}{2} \sum_{ij} a_{ij} \omega_i \omega_j + \sum_i b_i \omega_i + \frac{1}{2} A \left[ \partial_s \vec{q} + \vec{\omega} \times \vec{q} \right]^2 + U(\vec{q}) \right)\] (6)
in which $L$ is the total length of rod, $a_{ij}$ are its elastic modulii, and $\omega_i$ coordinates of the vector of deformations described above for the Kirchhoff model. The potential $U(\vec{q})$ accommodates forces that keep the two strands hanging together. The vector $(b_1, b_2, b_3)$ is analogous to $\omega_0$ of paper [21], and describes the molecule’s winding determined by certain external conditions, for example, a histone.

We have used the vector $\vec{q}$ in the fourth term of equation (6) so as to accommodate deformation and breaking of bonds between base pairs, and as well as the separation of strands. But here, again, it is worthwhile to note that the term is similar to the fourth term in Eq.(4), see paper [21], Eq.(3); besides the mathematical similarity we should like to draw attention to the fact that the reason for this lies in the relation of $\vec{q}$ to stretching the molecule.

The third term in equation (6) is the covariant derivative

$$\nabla_s \vec{q} = \partial_s \vec{q} + \vec{\omega} \times \vec{q}$$

The covariant derivative is in order because we have to consider the displacements of the strands with respect to the local coordinates determined by the helical structure and the strain described by the vector $\vec{q}$. The procedure is quite common in the theory of gauge fields.

The state of equilibrium corresponds to the minimum of $F$ and gives the equations

$$\nabla_s^2 \vec{q} = \frac{\partial U}{\partial \vec{q}}, \quad \nabla_s (\vec{m} + A\vec{q} \times \nabla_s \vec{q}) = 0$$
in which $\nabla_s$ is the covariant derivative

$$\nabla_s \vec{X} = \partial_s \vec{X} + \vec{\omega} \times \vec{X}$$

and $\vec{m}$ reads

$$m_i = \sum_{j=1}^3 a_{ij} \omega_j$$

Now let us neglect nonlinear, that is greater than second order terms, in the potential $U$, and consider the effect of thermal fluctuations of the field $\vec{q}(s)$, that is inter-strand motion, or in the context of paper [21] the stretching, on the total configuration of the molecule. To that end we need to average the field $\vec{q}$ out, and find the effective energy

$$e^{-\beta F_{\text{eff}}} = \int D\vec{q} e^{-\beta F}, \quad \beta = 1/kT$$

We aim at a specific, but very important, configuration in which the vector $\vec{\omega}$ is equal to the constant

$$\vec{\omega}_0 = -a^{-1} \vec{b}$$

that provides the absolute minimum for the density of Kirchhoff’s energy given by Eq.(1), and the conformation of the regular coil for the molecule. Here $a$ is the matrix of Kirchhoff’s modulii $a_{ij}$. 
To evaluate the functional integral in Eq. (7), we shall employ Feynman’s variational principal, and to that end resolve the expression for the energy in the form

\[ F = F_0 + F_1 \]

with

\[ F_0 = \int_0^L ds \left( \frac{1}{2} \sum_{ij} a_{ij} \omega_i \omega_j + \sum_i b_i \omega_i \right) + \frac{1}{2} A \sum_i \left[ \frac{d}{ds} q_i \right]^2 + \frac{1}{2} \sum_i \left[ B + A \left[ \omega^2 - \omega_0^2 \right] \right] q_i^2 \]

and \( F_1 \) by the equation

\[ F_1 = A \int_0^L ds \left( \sum_{ijk} \epsilon_{ijk} \omega_i q_j \frac{d}{ds} q_k - \sum_{i \neq j} \omega_i \omega_j q_i q_j \right) \]

According to Feynman’s variational principal, there is the estimate for free energy

\[ F \leq F_0 + \langle F_1 \rangle_0 \]

with

\[ F = \int D\vec{q} e^{-\beta F_0} \]

\[ \langle F_1 \rangle_0 = \int D\vec{q} F_1 e^{-\beta F_0} \]

The average \( \langle F_1 \rangle_0 \) gives zero contribution owing to the Gaussian nature of the integration. Hence, within the limits of accuracy provided by Feynman’s principle, we have

\[ F_{\text{eff}} = F_0 + \langle F_1 \rangle_0 \]

with \( z_i \) being given by

\[ z_i = \frac{1}{2} L \sqrt{\frac{B}{A} + \omega_0^2 - \omega_{0i}^2}, \quad i = 1, 2, 3 \]

Here \( B/A \) evaluates the coupling between the strands of a molecule, and \( \omega_{0i} \) are coordinates of the vector given by Eq. (8) determining the configuration without fluctuation corrections.

Let us consider the small coiling and coupling of strands, that is \( \omega \ll 1 \) and \( B/A \ll 1 \), or \( z_i \ll 1, i = 1, 2, 3 \). Assuming \( \omega \) to be constant, we may cast the equation for the effective energy in the form

\[ F_{\text{eff}} = L \left( \frac{1}{2} \sum_{ij} a_{ij} \omega_i \omega_j + \sum_i b_i \omega_i \right) - kT \sum_i \ln \frac{z_i}{s h(z_i)} \]

By minimizing \( F_{\text{eff}} \) with respect to \( \vec{\omega} \), we obtain the correction of the value of \( \omega_0 \) effecting the equilibrium conformation. Since the contribution of fluctuations is assumed to be small, we may write down the corrections to \( \omega_0 \) given by Eq. (8)

\[ \omega_0^{\text{fluct}} = \omega_0 + \delta \omega_0 \quad \text{and} \quad \delta \omega_0 = -\frac{1}{3} kTL \omega_0^2 \cdot \vec{b} \]

From the last equation, we infer that fluctuations of the field \( \vec{q} \) make for an increase in the coiling of a molecule. It is easy to estimate a spatial scale on which the arguments given above are valid; the fluctuation energy should be smaller than the elastic one, that is counting by orders of magnitudes \( L a \omega^2 \gg L^2 kT \omega^2 \), which amounts to \( a/L \gg kT \). For the rigidity of order \( 10^{-19} \text{ erg cm} \) and room temperatures, one obtains the scale of order \( 5 \times 10^{-3} \text{ cm} \), that is the persistence length. To understand the estimates given above, let us notice that in the opposite regime, far from equilibrium, we may set...
\(B \gg 1\), and \(B/A \gg \omega^2\). It is easy to see that in this case there are no corrections of the values of \(\vec{\omega}\), and consequently no additional increase in the supercoiling of molecule.

Working within the framework of paper [21], Moroz and Nelson found the renormalization of twist stiffness by bend fluctuations; they averaged the partition function corresponding to the functional given by Eq. (4), obtained the Schrödinger-like equation for the correlator of the tangent vector to the molecular axis, [24], [25], and found the torque, \(\tau(f, \sigma)\), as a function of applied stress \(f\) and external twist \(\sigma = \Delta L k\)

\[
\tau(f, \sigma) = \frac{\omega_0 \sigma}{C^{-1} + \left(4A\sqrt{Af/k_BT}\right)^{-1}}
\]

(10)

Since the setting of the two problems is not identical, we are not in a position to compare Eqs. (9) and (10); qualitatively, they are related to the same phenomenon of renormalization of stiffness by bend fluctuations.

It is worth noticing that the hydrogen bonds of DNA can be deformed and even broken due to the local action of an external agent, for example enzyme. We may try to describe the process by an energy term that be included in Eq. (1)

\[
F_{int} = \int_0^L ds \left( \vec{\beta} \cdot \vec{q} + \vec{q} \hat{\gamma} \vec{q} \right) \delta (s - s_0)
\]

(11)

with \(\vec{\beta}\) and \(\hat{\gamma}\) being a constant vector and a matrix, respectively. The \(\delta\)-function factor is used for describing point-like action of the external disturbance. Consider the case of the initial value for \(\vec{b}\) equal to zero before the breaking up of a molecule. For small \(\vec{q}\), using the linear approximation, we have the following equation for \(\vec{q}\)

\[
\frac{\partial^2}{\partial s^2} \vec{q} - \Omega^2 \vec{q} = \frac{\vec{\beta}}{A} \delta (s - s_0) + \frac{1}{A} \hat{\gamma} \vec{q} \delta (s - s_0)
\]

(12)

with \(\Omega^2 = B/A\). Up to the second order terms the minimization equation for \(\vec{\omega}\) reads

\[
a \nabla \vec{\omega} - A \nabla \left( \frac{d}{ds} \vec{q} \times \vec{q} \right) = 0
\]

From the last equation one can infer that the external action due to Eq. (11) results in the formation of an effective rotating moment \(\vec{b}_{ext}\) that reads

\[
\vec{b}_{ext} = -\frac{G^2(s, s_0)}{A^2} \frac{d}{ds} G(s, s_0) \left( \vec{\beta} \times \hat{\gamma} \vec{\beta} \right)
\]

with \(G(s, s_0)\) being the Green function of Eq. (12).

From the equation for \(G(s, s_0)\) it is easy to see that the size of the defect changes from \(L\), or the mesoscopic scale, for small \(\Omega\), to \(1/\Omega\) for large \(\Omega\).

\[
G(s, s_0) = \frac{1}{\Omega sh(\Omega L)} \left( \theta(s_0 - s) sh(\Omega s) sh \left( (L - s_0) \Omega \right) \right)
\]

with \(\vec{\beta}\) and \(\hat{\gamma}\) being a constant vector and a matrix, respectively.

The local influence due to a chemical-biological agent may result in the strands of a molecule being split up on a scale of order \(1/\Omega\) determined by the potential describing the hydrogen bonds, so there is a kind of Lindemann’s criterion: the breaking up of a molecule takes place if \(\sqrt{\frac{B}{A}} \propto 1/L\). The magnitude of the splitting is determined by the properties of the agent. A drawback of the model which is based on a quadratic Lagrangian, is that it does not allow for a threshold effect, which might be taken into account
by considering high order terms. In the region of conformations far from the splitting of a molecule the fluctuations of the field $\vec{q}(s)$ are suppressed by the bond due to $U(q)$, and there is no enhancing the supercoiling, in contrast to the region close to the splitting, where the potential $U(q)$ is effectively small. Since the minimization of energy makes sense only on the mesoscale of several persistence lengths, the conformation of a molecule being determined by entropy on the macroscale, different segments of a molecule should be broken up independently from each other so as to give a blurred character to the transition corresponding to the splitting up of the molecule.

There are various arguments to the effect that the double-stranded DNA should suffer local denaturation and open up locally so that hydrogen bonds between base pairs be broken. Besides physiological processes that involve the 'unzipping', it can take place spontaneously due to fluctuations owing to the small energy required, less than $3k_B T$ [3]. Therefore, the breathing of DNA is a phenomena that could happen in many situations.

It was G.S. Manning, [36], who suggested that the real flexibility in the DNA molecule could be due to opening of base pairs and the breathing fluctuations be related to elastic properties of the DNA. The solution to the problem requires the knowledge of the rate of the breathing fluctuation, and at this point there is some controversy.

By now there are two methods for studying the breathing fluctuations: the NMR and the fluorescence correlation spectroscopy.

The NMR measures the exchange of protons from imino groups with water, which are suggested only to occur from open base pairs, [37]. According to paper [38], the opening of base pairs may require prior unwinding or bending of the DNA double helix, which does not necessarily lead to imino proton exchange. The life times of base pairs and open states depend on temperature and bases involved. In the B-DNA at $15^\circ C$ typical lifetimes range 0.5 through 7 ms for $A\cdot T$ pairs and 7 through 40 ms for $G\cdot C$. The open state life time is $10\sim 100 ms$, [35]. Leroy et al, [38], estimate the activation enthalpy for $C\cdot G5$ opening to within $45\pm 56 kJ/mol$, or $10.7 \pm 13.3 Kcal/mol$. It is important that the NMR of imino proton exchange measures the lifetime of a single base pair, [39].

The fluorescence spectroscopy relies on the translation of base pair fluctuations in fluorescence fluctuations. Altan-Bonnet et al, [40], use synthetic DNA samples containing modified bases tagged with a fluorophore and a quencher. When the DNA structure is closed, the fluorophore and the quencher are in close proximity and the fluorescence is quenched, it is again restored if the structure opens so that the fluorophore and the quencher are pulled apart. Thus, the fluorescence spectroscopy detects the local denaturation of the DNA, or bubbles of 2 to 10 base pairs with lifetimes in the $50\mu s$ range at $37^\circ C$.

The divergence between the NMR and the fluorescence spectroscopy measurements could be explained by several reasons. First, the NMR picks up very fast modes owing to the imino proton exchange being very sensitive to the conformation of a base pair, whereas the fluorescence spectroscopy picks up large scale deformations of the DNA. Second, the NMR measures the life time of a formed base pair; the fluorescence spectroscopy measures the life time of the open state. Third, the range of temperatures and the composition of the strands in the two experimental settings is different. For these arguments I am indebted to G. Altan-Bonnet.

Thus, the available experimental data indicates that partial denaturation of the DNA is a common phenomenon, and it should be taken into account while using the elastic rod model. The latter requires, generally, serious modifications when the internal motions of the double helix need accommodating.

There are arguments of qualitative nature in favour of the fact that the fluctuations of open hydrogen bonds result in an effective interaction between the strands of the double helix (cf. p[38] about the bonds between base pairs and those with water). We shall describe a hydrogen bond as two-level system, $|0\rangle$ and $|1\rangle$, with the energy difference $\epsilon = E_0 - E_1$, and the Hamiltonian $\epsilon \sigma_3$ where $\sigma_3$ is the third Pauli matrix

$$\sigma_3 = \frac{1}{2} \begin{bmatrix} 1 & 0 \\ 0 & -1 \end{bmatrix}$$

To describe the coupling between the Pauli operators of hydrogen bonds between base pairs and the classical system due to the elasticity of the molecule, we shall employ the field $\vec{q}$ (see p[10]). We suggest that
the interaction between the elastic forces and a single hydrogen bond is small, and therefore perturbation theory could be employed, that is a kind of Born-Oppenheimer approximation in the sense that one part of the system is considered to be classical, whereas the other one quantum. We cast the equation for energy in the form

\[ E = F(\omega, \vec{q}) + E_{\text{int}}(\vec{q}, \vec{\sigma}) + E_{\text{exc}} \]

where \( F \) is the energy of elastic rod given by Eq. (13), and \( E_{\text{exc}} \) is the energy of hydrogen bonds,

\[ E_{\text{exc}} = -\epsilon \sum_{n=0}^{N-1} \sigma_n^3 + \beta \sum_{n=0}^{N-1} \left[ \sigma_n^+ \sigma_{n+1}^+ \sigma_n^- \sigma_{n+1}^- + \sigma_n^- \sigma_{n+1}^- \sigma_n^+ \sigma_{n+1}^+ \right] \]

with \( \sigma_n^\pm \) being the matrices

\[ \sigma_n^\pm = \frac{1}{2}(\sigma_n^1 \pm i \sigma_n^2) \]

The second sum in the above equation accommodates the possible propagation of opened base pairs. The third term in Eq. (13) is the interaction between the classical elastic system and the quantum one given by the hydrogen bonds. The field \( \vec{q} \) has the sense of a mean field describing the partition of the strands and its characteristic spatial scale is hundreds of \( \text{Å} \). The spatial scale of the Pauli operators is a few \( \text{Å} \).

It is important that the operators \( \sigma_n^3, \sigma_n^+, \sigma_n^- \) are intimately related to the conformation of the molecule.

In fact, the breakdown of a hydrogen bond follows a certain direction in space. At each site \( n \) corresponding to a base pair of the molecule, there is a local frame formed by unit orthogonal vectors \( \vec{w}_1, \vec{w}_2, \vec{w}_3 \), for which the vector \( \vec{w}_1 \) is tangent to the axis of the double helix, \( \vec{w}_2 \) is normal to the axis, and \( \vec{w}_3 \) indicates the direction of the bond’s breakdown. The operators \( \sigma_n^3, \sigma_n^+, \sigma_n^- \) indicated above are chosen in accord with the frame \( \vec{w}_1, \vec{w}_2, \vec{w}_3 \). Thus, the term \( \sigma_n^3 \sigma_{n+1}^- \) in the energy \( E_{\text{exc}} \) involves the operators that act in spaces \((|0\rangle_n, |1\rangle_n)\) and \((|0\rangle_{n+1}, |1\rangle_{n+1})\). To form the interaction term we need to cast \( \vec{q} \) and the Pauli operators in the same co-ordinate system. By using the unitary transformation

\[ s_n^i = U^{-1} \sigma_n^i U \]

we may find the operators \( s_n^i \), and specifically \( s_n^3 \), that correspond to \( \sigma_n^i \) in the laboratory co-ordinate system and describe the state of the hydrogen bond at site \( n \) from the point of view of an external observer. In fact, there is the equation

\[ U^{-1} \sigma_n^i U = \sum_{k=1}^{3} R_{ik} \sigma_n^k \]

in which the matrix \( R_{ik} \) corresponds to the rotation that brings the frame \( \vec{w}_1, \vec{w}_2, \vec{w}_3 \) in the standard laboratory one. Therefore, we choose the interaction energy in the “minimal” form

\[ E_{\text{int}}(\vec{q}, \vec{\sigma}) = \gamma \sum_{n=0}^{N-1} \vec{q}_n \cdot R_n \vec{\sigma}_n \]

We shall confine ourself to the circular conformation of the molecule for which the matrices \( R_n \) have the form

\[ R_n = \begin{pmatrix} 1 & 0 & 0 \\ 0 & \cos \phi_n & -\sin \phi_n \\ 0 & \sin \phi_n & \cos \phi_n \end{pmatrix} \]

Therefore the interaction terms read

\[ \vec{q}_n \cdot R \vec{\sigma}_n = (\cos \phi_n q_n^2 + \sin \phi_n q_n^3) \sigma_n^2 + (-\sin \phi_n q_n^2 + \cos \phi_n q_n^3) \]

and we have

\[ E_I + E_{\text{exc}} = \gamma \sum_{n=0}^{N-1} \left[ (\cos \phi_n q_n^2 + \sin \phi_n q_n^3) \sigma_n^2 + (-\sin \phi_n q_n^2 + \cos \phi_n q_n^3) \right] + \sum_{n=0}^{N-1} (\sigma_n^+ \sigma_{n+1}^- + \sigma_n^- \sigma_{n+1}^+) \]
Since we are considering the molecule of DNA at temperature far from denaturation, and therefore in accord with the results of papers [37, 38, 39] the number of excitations, that is of broken hydrogen bonds, is small. Consequently, we may utilize the method of approximate secondary quantization, [28], familiar in the theory of spin systems. Let us consider the Bose operators \( b_k, b_k^+ \)

\[
[b_k, b_m] = 0, \quad [b_k^+, b_m^+] = 0, \quad [b_k, b_m^+] = \delta_{km}
\]

By using the substitution

\[
\sigma^3_k = \frac{1}{2} - b_k^+ b_k, \quad \sigma^-_k = b_k^+, \quad \sigma^+_k b_k = b_k
\]

we may cast the energy \( E_{\text{int}} + E_{\text{exc}} \) in the form

\[
E_{\text{int}} + E_{\text{exc}} = \frac{\epsilon N}{2} + \gamma \sum_{n=0}^{N-1} \left( -\sin \phi_n q_n^2 + \cos \phi_n q_n^3 \right) + N \sum_{n=0}^{N-1} \left( b_n b_{n+1} + b_n^+ b_{n+1}^+ \right) - \frac{i \gamma}{2} \sum_{n=0}^{N-1} \left( \cos \phi_n q_n^2 + \sin \phi_n q_n^3 \right) (b_n^+ - b_n)
\]

The first line in the above equation corresponds to the ‘vacuum’ fluctuations, which may be of interest as regards the conformation of the double helix given by the matrices \( R_n \) and the field \( \vec{q} \). The above equation is quadratic with respect to the Pauli operators \( b_k, b_k^+ \) and we can cast it into the diagonal form by employing Fourier transform

\[
B_n = \frac{1}{\sqrt{N}} \sum_{n=0}^{N-1} e^{\frac{2i\pi nk}{N}} b_k
\]

\[
B_n^+ = \frac{1}{\sqrt{N}} \sum_{n=0}^{N-1} e^{-\frac{2i\pi nk}{N}} b_k^+
\]

so that the energy \( E_{\text{int}} + E_{\text{exc}} \) be given by the equation

\[
E_{\text{int}} + E_{\text{exc}} = \text{const} + \frac{\gamma}{2} \sum_{n=0}^{N-1} \left( -\sin \phi_n q_n^2 + \cos \phi_n q_n^3 \right) + \sum_{k_1 k_2} \epsilon_{k_1 k_2} B_{k_1}^+ B_{k_2} + \sum_{n=0}^{N-1} (A_n B_n^+ + A_n^* B_n)
\]

in which \( \epsilon_{k_1 k_2} \) and \( A_n \) read

\[
\epsilon_{k_1 k_2} = \delta_{k_1 k_2} \left( \epsilon + 2\beta \cos \frac{2\pi k_1}{N} \right) - \frac{\gamma}{N} \sum_{n=0}^{N-1} \left( -\sin \phi_n q_n^2 + \cos \phi_n q_n^3 \right) e^{\frac{2i\pi (k_2 - k_1) n}{N}}
\]

\[
A_n = \frac{1}{2} \frac{i \gamma}{\sqrt{N}} \sum_{n=0}^{N-1} e^{-\frac{2i\pi (k_2 - k_1) n}{N}} (\cos \phi_n q_n^2 + \sin \phi_n q_n^3)
\]

We may eliminate the linear terms in \( B_n, B_n^+ \) using the canonical transformation

\[
B_n \rightarrow S^{-1} B_n S, \quad B_n^+ \rightarrow S^{-1} B_n^+ S
\]
We obtain the equation

$$E_I + E_{exc} = \text{const} + E_{conf} + \sum_{k_1k_2} \epsilon_{k_1k_2} C_{k_1}^+ C_{k_2}$$

in which the conformation energy $E_{conf}$ reads

$$E_{conf} = \frac{\gamma}{2} N \sum_{n=0}^{N-1} \left( -\sin \phi_n q_n^2 + \cos \phi_n q_n^3 \right) + 3 \sum_{k_1k_2} (\epsilon^{-1})_{k_1k_2} A_{k_1}^* A_{k_2}^*$$ (16)

According to the results of Leroy et al [37, 38, 39] the effective temperature of the excitations due to the opening of hydrogen bonds is very low, and therefore the energy of the system is given by $E_{conf}$. As was assumed the interaction between the elastic part of the total energy and that due to the breakdown of the hydrogen bonds is also small, so that we may use the approximation of Born-Oppenheimer. Therefore, it is possible to consider the operators $B_n, B_n^+$ assuming that $\vec{q}$ and $\vec{\omega}$ are constant. At the same we shall assume that $\gamma$ is small and make all calculations up to the order $\gamma^2$. In fact, we are considering the interaction energy given by the term $\gamma \vec{q}_n \cdot R \vec{\sigma}_n$, which is smaller than $\epsilon$. Since $A_n \propto \gamma$, we shall neglect terms of order $\gamma^2$ in $(\epsilon^{-1})_{k_1k_2}$ and obtain

$$(\epsilon^{-1})_{k_1k_2} = -\frac{\delta_{k_1k_2}}{\epsilon - 2\beta \cos \frac{2\pi k}{N}}$$

On setting $q_n = q_n^2 + i q_n^3$ we cast the conformational energy in the form

$$E_{conf} = \frac{\gamma}{4} \sum_{n=0}^{N-1} \left( e^{i\phi_n q_n} + e^{-i\phi_n q_n^*} \right) - \frac{3\gamma^2}{16} \sum_{n=0}^{N-1} \frac{|D(k)|^2}{\alpha - 2\beta \cos \frac{2\pi k}{N}}$$

where

$$D(k) = \frac{1}{2} \frac{1}{\sqrt{N}} \sum_{m=0}^{N-1} e \frac{2\pi i m k}{N} [\cos \phi_m q_m^2 + \sin \phi_m q_m^3]$$

On integrating out the phases $\phi_n$, we find the effective potential

$$U(\vec{q}) = E_{conf} = \frac{3\epsilon^2}{32\epsilon} \sum_{n=0}^{N-1} |q_n|^2$$

or using the integral form

$$U(\vec{q}) = E_{conf} = \frac{3\gamma^2}{32\epsilon d} \int |q_n|^2 ds$$ (17)

Within the framework of the model considered above the excitation of the hydrogen bonds, i.e their breakdown, is visualized as an ideal gas, similar to that of magnons. It is applied only to regimes far enough from the denaturation, when the number of the broken hydrogen bonds is small. Nonetheless, it sheds some light on the formation of locally denatured regions, or bubbles, of the DNA. It is worthwhile to recall that G.Manning had suggested that there are two types of excitations of the DNA; the modes of bending and those of breathing, [36]. By now it is generally accepted that the bending modes are of high frequency, and could be related to nonlinear phenomena in the DNA. The breathing modes according to [37] are in GHz-region, which is at the edge of the elastic modes of the DNA. If we direct our attention primarily to bubbles formed by opened base pairs, characteristic time appear to be by orders of magnitude larger, [40]. It is also worthwhile to note that the model of elastic chain of the Pauli operators, has some bearing on the opening of base pairs and the breakdown of hydrogen bonds, mentioned on p[3].
III. THE EXTENDED LATTICE MODEL

As was discussed above, the elastic rod model is not generally sufficient for describing the conformational dynamics of the DNA. Important, it does not allow for its intrinsic degrees of freedom corresponding to the structure of the double helix. To build an adequate model to the effect, is a difficult problem, and an attempt to manufacture it ‘from first principles’ is doomed to failure. Thus, there is a need for drastic simplifications, and it is necessary to take into account: (1) the DNA having the two strands; (2) the base-pairs being linked by the hydrogen bonds; (3) the helical symmetry of the DNA. The problem still waits its general solution, but specific cases are nonetheless tractable. In this section we are going to see what could happen if elastic modes that can be expected within the rod model, may interact with internal motions of the double helix.

We consider short pieces of the DNA, of several persistence lengths, so that the spatial conformation of the molecule on the mesoscale, is not of primary importance. We focus on the internal dynamics, trying to accommodate the above requirements through a one-dimensional lattice model of the DNA. The key point in this respect is the wise choice of dynamical variables that could give a picture of the DNA dynamics, both simple and adequate. El Hasan and Calladine, [1], give the framework for such analysis by setting up the scheme for the internal geometry of the double helix of the DNA. They describe the relative position of one base with respect to the other in a Watson-Crick base-pair, and also the positions of two base-pairs, by introducing local frames for the bases and the base-pairs, and translation-slides along their long axes.

We follow the guidelines of paper [1], but aiming at a qualitative description of the DNA dynamics use a simplified set of variables. We shall describe the relative position of the bases of a base-pair by means of the vector \( \vec{Y} \) directed along the axis of orientation for complimentary bases inside the base pair; \( \vec{Y} \) being equal to zero when the base-pair is at equilibrium. The relative position of the base-pairs is described by the torsional angles \( \phi \), which give deviations from the standard equilibrium twist of the double helix. Thus a twist of the DNA molecule, which does not involve inter-strand motion or mutual displacements of the bases inside the pairs, is determined by the torsional angles \( \phi \) that are the angles of rotation of the base-pairs about the axis of the double-helix. The twist energy of the molecule is given by the equation

\[
\sum_n \left[ \frac{I}{2} \dot{\phi}_n^2 + \frac{\tau}{2a^2} (\phi_{n+1} - \phi_n)^2 \right]
\]

in which \( I \) is the moment of inertia, and \( \tau \) is the twist coefficient, which for the sake of simplicity and taking into account the qualitative picture at which we aim, are assumed the same for all the base-pairs. Inter-strand motions should correspond to the relative motion of the bases inside the base-pairs, therefore the kinetic energy due to this degree of freedom may be cast in the form

\[
\sum_n \frac{M}{2} \dot{Y}_n^2
\]

where \( M \) is the effective mass of a couple.

For each base-pair we have the reference frame in which z-axis corresponds to the axis of the double helix, y-axis to the long axis of the base-pair, x-axis perpendicular to z- and y- axes. At equilibrium the change in position of adjacent base-pairs is determined only by the twist angle \( \Omega \) of the double helix. We shall assume \( \Omega = 2\pi/10 \). To determine the energy due to the inter-strand displacements we need to find the strain taking into account the constraint imposed by the helical structure of our system. For this end one may utilize the method employed by G.Kirchhoff for the twisted rod, that is the covariant derivative, as was done in paper [41] for the DNA molecule. But a more simple and straightforward approach is possible.

Let us confine ourself only to the torsional degrees of freedom of the double lattice and assume the vectors \( \vec{Y}_n \) being parallel to x-y plane, or two-dimensional. Consider the displacements \( \vec{Y}_n, \vec{Y}_{n+1} \) determined within the frames of the two consecutive base-pairs, \( n, n+1 \). Since we must compare the two vectors in the same frame, we shall rotate the vector \( \vec{Y}_{n+1} \) to the frame of the n-th base pair,

\[
\vec{Y}_{n+1}^{\text{back}} = R^{-1}(\phi) \vec{Y}_{n+1}
\]
Here $R^{-1}(\phi)$ is the inverse matrix of the rotation of the n-th frame to the (n+1)-one given by the equation

$$R(\phi) = \begin{bmatrix} \cos \phi & -\sin \phi \\ \sin \phi & \cos \phi \end{bmatrix}$$  (18)

The matrix $R$ is 2 by 2 since the vectors $\vec{Y}_n$ are effectively two-dimensional. Then the strain caused by the displacements of the base-pairs is determined by the difference

$$\vec{Y}_{n+1}^{\text{back}} - \vec{Y}_n$$

For this argument I am indebted to D.I. Tchertov.

It is important that the angle $\phi$ is given by the twist angle, $\Omega$, describing the double helix, in conjunction with the torsional angles $\phi_n$, so that

$$\phi = \Omega + \phi_{n+1} - \phi_n$$

Therefore, the energy due to the inter-strand stress reads

$$\sum_n \left\{ \frac{M}{2} \ddot{\vec{Y}}_n^2 + \frac{K}{2a^2} \left[ R^{-1}(\Omega + \phi_{n+1} - \phi_n) \vec{Y}_{n+1} - \vec{Y}_n \right]^2 \right\}$$

It corresponds with the fact that the equilibrium position of the double helix is the twisted one determined by $\Omega$ and all $\phi_n$ being equal to zero. We suppose that the size of DNA molecule is small enough that it can be visualized as a straight double helix, that is not larger than the persistence length. Hence the number of base-pairs, $N \leq 150$, approximately. Combining the formulas given above we may write down the total energy of the DNA molecule in the form

$$H = \sum_n \left[ \frac{I}{2} \dot{\phi}_n^2 + \frac{\tau}{2a^2} (\phi_{n+1} - \phi_n)^2 \right] + \sum_n \left\{ \frac{M}{2} \dot{\vec{Y}}_n^2 + \frac{K}{2a^2} \left[ R^{-1}(\Omega + \phi_{n+1} - \phi_n) \vec{Y}_{n+1} - \vec{Y}_n \right]^2 + \frac{\epsilon}{2} \vec{Y}_n^2 \right\}$$  (19)

in which $K$ and $a$ are the torsional elastic constant and the inter-pairs distance, correspondingly. In summations given above $n$ is the number of a site corresponding to the n-th base-pair, and $n = 1, 2, \ldots, N$, $N$ being the number of pairs in the segment of the DNA under consideration. The last term, $\epsilon/2 \vec{Y}_n^2$ accommodates the energy of the inter-strand separation due to the slides of the bases inside the base-pairs.

It should be noted that the dynamical variables $\phi_n$ and $\vec{Y}_n$ are of the same order of magnitude, that is the first. Consequently, preserving only terms up to the third order, we may transform Eq. (19), so that it takes on the form

$$H = \sum_n \left[ \frac{I}{2} \dot{\phi}_n^2 + \frac{\tau}{2a^2} (\phi_{n+1} - \phi_n)^2 \right] + \sum_n \left\{ \frac{M}{2} \dot{\vec{Y}}_n^2 + \frac{K}{2a^2} \left[ R^{-1}(\Omega) \vec{Y}_{n+1} - \vec{Y}_n \right]^2 + \frac{\epsilon}{2} \vec{Y}_n^2 \right\} + \frac{K}{a^2} \sum_n (\phi_{n+1} - \phi_n) \left[ R^{-1}(\Omega) \vec{Y}_{n+1} \times \vec{Y}_n \right]_3$$  (20)

We have used the fact that the axis of the double-helix is directed along Oz-axis.

Let us simplify Eq. (20) by diagonalizing it with the help of the unitary transformation

$$\vec{Y}_n = S \vec{u}_n; \quad S = \begin{bmatrix} \frac{1}{\sqrt{2}} & \frac{1}{\sqrt{2}} & \frac{1}{\sqrt{2}} \\ \frac{1}{\sqrt{2}} & -\frac{1}{\sqrt{2}} & \frac{1}{\sqrt{2}} \end{bmatrix}$$
which is a two by two matrix, for the vectors $\vec{Y}_n$ and $\vec{u}_n$ are effectively two-dimensional, their third coordinates being equal to zero. The equation for the energy (20) takes on the form

$$\mathcal{H} = \sum_n \left[ \frac{I}{2} \dot{\phi}_n^2 + \frac{\tau}{2a^2} (\phi_{n+1} - \phi_n)^2 \right]$$

$$+ \sum_n \left[ \frac{M}{2} \ddot{u}_n \cdot \dot{\vec{u}}_n^* + \frac{\epsilon}{2} \ddot{u}_n \cdot \dot{\vec{u}}_n^* + \frac{K}{2a^2} \left( | e^{i\Omega} u_{n+1}^1 - u_n^1 |^2 + | e^{-i\Omega} u_{n+1}^2 - u_n^2 |^2 \right) \right]$$

$$- \frac{K}{a^2} \sum_n (\phi_{n+1} - \phi_n) \left[ -ie^{i\Omega} u_{n+1}^1 \dot{u}_n^1 + ie^{-i\Omega} u_{n+1}^2 \dot{u}_n^2 \right]$$

The star * signifies complex conjugation.

We can further simplify the equation for the energy by applying the Fourier transform given by the equations

$$f_n = \frac{1}{\sqrt{N}} \sum_q e^{-inq} f_q$$

$$f_q = \frac{1}{\sqrt{N}} \sum_{n=-N/2}^{N/2} e^{inq} f_n \quad q = \frac{2\pi}{Na} m; \quad m = 0, \pm 1, \pm 2, \ldots, \pm N/2$$

It is important that after the Fourier transform the variables $\vec{u}_n$ verify the following equations for their complex conjugates

$$\dot{u}_q^1 = iu_{-q}^2, \quad \dot{u}_q^2 = iu_{-q}^1$$

The equation for the energy can be cast in the form

$$\mathcal{H} = \sum_q \left[ \frac{I}{2} \dot{\phi}_q \dot{\phi}_q^* + \frac{\tau}{2a^2} \sin^2 \frac{aq}{2} \dot{\phi}_q \dot{\phi}_q^* \right]$$

$$+ \sum_q \left[ \frac{M}{2} \ddot{u}_q \cdot \dot{\vec{u}}_q^* + \frac{\epsilon}{2} \ddot{u}_q \cdot \dot{\vec{u}}_q^* + \frac{2K}{a^2} \left( \sin^2 \frac{\Omega - aq}{2} u_q^1 \dot{u}_q^1 \dot{u}_q^1 \sin^2 \frac{\Omega + aq}{2} u_q^2 \dot{u}_q^2 \right) \right]$$

$$+ \frac{K}{a^2} \sum_{q'q''} \frac{e^{-i\Omega}}{\sqrt{N}} \dot{\phi}_{q'} \left[ -e^{i\Omega} u_{q'}^1 \dot{u}_{q'+q''}^1 + e^{-i\Omega} u_{q'}^2 \dot{u}_{q'+q''}^2 \right]$$

in which

$$q_* = \Omega/a$$

The above equation serves as well a Hamiltonian that describes the dynamics of a molecule of the DNA, within the framework of the present model, up to terms of the third order. It is worth noting that the latter is based on the assumptions given above concerning the basic structural properties of the DNA, that is it takes into account its two-strand structure, the lattice formed by the base pairs, and the helical symmetry. The specific feature of the Hamiltonian is the presence of the interaction term that describes three-wave interaction, $[42]$, and may result in resonance. We shall utilize the fact for deriving the parametric maintenance of the $u_q$ modes, i.e. the HBS (hydrogen-bond-stretch) modes, (see below).

One can obtain, in the usual way, the equations of motion for $u_q^\alpha, \alpha = 1, 2$ and $\phi_q$, from the equation for the energy indicated above. The essential point is the effects of dissipation, which are due to ions in the close neighborhood of the molecule and water effects, see $[43]$. The dissipation could be accommodated
by writing down terms linear in $\dot{u}_q^\alpha$, $\dot{\phi}_q$. We shall take into account external force, or torque $T_q$, only in the equation for $\phi_q$, for it corresponds to external degrees of freedom of our model. Thus, the equations of motion can be cast in the form

$$
\ddot{u}_q^\alpha + \omega_{\alpha q}^2 u_q^\alpha + \gamma_u \dot{u}_q^\alpha + \frac{4K \sin \Omega}{Ma^2 \sqrt{N}} \sum_{q'} e^{-i\alpha q'} \phi_{q'} u_{q'-q}^\alpha = 0,
$$

$$
\ddot{\phi}_q + \omega_q^2 \phi_q + \gamma_\phi \dot{\phi}_q + \frac{i4K \sin \Omega e^{i\alpha q}}{Ia^2 \sqrt{N}} \sum_{q'} u_{q'}^1 u_{q'-q}^2 = T_q
$$

Here

$$
\omega_{\alpha q}^2 = \frac{4K}{Ma^2} \sin^2 \frac{\Omega}{2} + \frac{\epsilon}{M} \omega_q^2 = \frac{4\tau}{Ia^2} \sin^2 \frac{aq}{2}
$$

are the dispersion laws for the fields $u_q^\alpha$, $\alpha = 1, 2$, and $\phi_q$. We see that the spectrum of $\phi_q$ has a typical acoustic character, whereas that for $u_q^\alpha$ has a local minimum determined by the helical twist, $\Omega$. Thus, the spectrum of our model is in qualitative agreement with conclusions of [14]. The specific nature of the torque is to be specified elsewhere, for the moment, we shall consider general dynamical phenomena to which the torque may be conducive.

Let us suppose that for one thing the amplitudes of the HBS-modes given by $u_q^\alpha$ be so small that the quadratic term in Eq. (24) can be neglected, and for another the external torque $T_q$ be appreciable enough to maintain the vibration of the torsional mode $\phi_q$. Thus, we can visualize the latter as a pump mode that interacts with the HBS-mode $u_q^\alpha$ through the non-linearity in Eq. (23). We shall confine ourself to the case of the torque $T_q$ being non-zero only at $q = q_*$ and having a frequency $2\omega$. Therefore, the forced wave, or the pump wave for the HBS-mode, has the form

$$
\phi_{q*} = e^{i2\omega t} \Phi \delta_{qq*}, \quad \phi_{-q*} = e^{-i2\omega t} \Phi^* \delta_{-qq*}
$$

To obtain larger values for the pump wave, $\phi_{q*}$, the resonance condition

$$
\omega_{q*} = 2\omega
$$

should be verified, even though the resonance behavior of the torsional $\phi_q$-mode itself could be attenuated by dissipation, i.e. it may be a mode of small amplitude.

The equations of motion for $u_q^\alpha$ in the pumping regime read

$$
\ddot{u}_q^\alpha + \omega_{\alpha q}^2 u_q^\alpha + \gamma_u \dot{u}_q^\alpha + \frac{2K \sin \Omega}{Ma^2 \sqrt{N}} \left( A e^{i2\omega t} u_{q-q*}^\alpha + A^* e^{-i2\omega t} u_{q+q*}^\alpha \right) = 0
$$

here

$$
A = e^{-i\Omega} \Phi
$$

Note that the momentum conservation in the $q$-values is preserved, as required by the three-wave interaction. The equations indicated above can be cast in the matrix form

$$
\ddot{\bar{u}}_\alpha + \omega_\alpha^2 \bar{u}_\alpha + \gamma_u \dot{\bar{u}}_\alpha = \left( e^{i2\omega t} \mathcal{K} + e^{-i2\omega t} \mathcal{K}^+ \right) \bar{u}_\alpha
$$

where $\mathcal{K}$ and $\mathcal{K}^+$ are hermitian conjugate, and

$$
\mathcal{K}^+ \mathcal{K} = \mathcal{I} \left( \frac{2K \sin \Omega}{Ma^2 \sqrt{N}} \right)^2 |A|^2, \quad \mathcal{I}_{ij} = \delta_{ij}
$$
It is worth noting that Eq. (27) is a kind of matrix Mathieu equation. In fact, we can apply to it Rayleigh’s method for studying parametric resonance. For this end let us look for the solution to Eq. (27) in the form of a series

\[ \vec{u}(t) = \vec{A}_1 e^{i\omega t} + \vec{B}_1 e^{-i\omega t} + \vec{A}_3 e^{3i\omega t} + \vec{B}_3 e^{-3i\omega t} + \ldots \]

On substituting the expression given above into Eq. (27) and preserving only the terms corresponding to \( e^{\pm i\omega t} \), we obtain the equations

\[
\begin{align*}
\left[ (-\omega^2 + i\gamma_u \omega) I + \hat{\omega}_0^2 \right] \vec{A}_1 + \mathcal{K} \vec{B}_1 &= 0 \\
\left[ (-\omega^2 - i\gamma_u \omega) I + \hat{\omega}_0^2 \right] \vec{B}_1 + \mathcal{K}^+ \vec{A}_1 &= 0
\end{align*}
\]

The compatibility condition of the equations indicated above can be cast in the form of determinant for the block matrix

\[
\det \begin{bmatrix} \hat{\omega}_0^2 - \omega^2 + i\gamma_u \omega & \mathcal{K} \\ \mathcal{K}^+ \hat{\omega}_0^2 - \omega^2 - i\gamma_u \omega & \mathcal{K}^+ \end{bmatrix} = 0
\tag{28}
\]

Here \( \hat{\omega}^2 \) is the matrix of frequencies given by Eq. (25), and \( \omega^2 \) and \( \gamma_u \omega \) are the scalar ones. We can transform Eq. (28) into a more amenable form. Let us notice that it is equivalent to the equation

\[
\det \left\{ \begin{bmatrix} \hat{\omega}_0^2 - \omega^2 + i\gamma_u \omega & \mathcal{K} \\ \mathcal{K}^+ & \hat{\omega}_0^2 - \omega^2 - i\gamma_u \omega \end{bmatrix} \begin{bmatrix} I & -(\hat{\omega}_0^2 - \omega^2 + i\gamma_u \omega)^{-1} \rho^2 \mathcal{K}^+ \\ 0 & 1 \end{bmatrix} \right\} = 0
\]

in which

\[
\rho = \frac{Ma^2 \sqrt{N}}{2K \sin \Omega}
\tag{29}
\]

and the matrices \( \mathcal{K}^+ \) and \( \mathcal{K} \) verify the equation

\[-I + \rho^2 K \mathcal{K}^+ = 0
\]

We have used the fact that for the range of frequencies we are considering, the matrix

\[ \hat{\omega}_0^2 - \omega^2 + i\gamma_u \omega \]

is not degenerate. Therefore, the equation given above is equivalent to the following one

\[
\det \left\{ -I + \rho^2 (\hat{\omega}_0^2 - \omega^2 + i\gamma_u \omega) \mathcal{J} (\hat{\omega}_0^2 - \omega^2 - i\gamma_u \omega) \mathcal{J}^+ \right\} = 0
\]

in which the matrix \( \mathcal{J} \) is given by

\[ \mathcal{J}_{qq'} = \delta_{qq'} \]

We may cast the last equation into the form

\[
(\omega_{\alpha q}^2 - \omega^2 - i\gamma_u \omega)(\omega_{\alpha q}^2 - \omega^2 + i\gamma_u \omega) - \left( \frac{2K \sin \Omega}{Ma^2 \sqrt{N}} \right)^2 |A|^2 = 0
\tag{30}
\]

which is quite similar to the usual condition for parametric resonance. Solutions to Eq. (30) are generally complex and therefore correspond to attenuated regimes. But there is a specific wave number, \( q_{\text{res}} \), for which the solution gives the real frequency \( \omega \), and it is easy to see that it should satisfy the constraint

\[ \omega_{\alpha q_{\text{res}}}^2 = \omega_{\alpha q}^2, \quad \text{at} \quad q = q_{\text{res}} \tag{31} \]
Thus, we may cast the condition for parametric resonance in the familiar form, \([44]\),

\[
\left( \omega^2 - \omega_{\alpha q e}^2 \right)^2 + \gamma^2 \omega^2 - \left( \frac{2K}{Ma^2} \frac{\sin \Omega}{\sqrt{N}} \right)^2 |A|^2 = 0 \tag{32}
\]

The existence of the parametric resonance discussed above presupposes that the bands of the torsional acoustic (TA), the \(\phi_q\) modes of the present paper, and the hydrogen-bond-stretch (HBS) modes, that is the \(u_\alpha^q\) modes, of the DNA interpenetrate each other. So far, the knowledge of the spectra of the DNA vibrations relies mainly on the computer analysis within the framework of quantum chemistry, \([14]\). According to these results, it is accepted that the conformational dynamics of the DNA is confined to elastic vibrations of the DNA molecule in the range of \(10^9 \pm 10^{12} \text{ Hz} \), \([48]\). Kim and Prohofsky, \([14]\), claim that the region comprises two domains, which correspond with different degrees of freedom of the molecule: (1) acoustic modes, which do not involve the hydrogen bonds; (2) modes that stretch the hydrogen bonds between the base-pairs (the HBS modes). Local minimum of the frequency is characteristic of the HBS-modes, \([14]\); its position depending on the choice of the band. The vibrations of the DNA, which are ascribed to the inter-strand modes, were observed in the low-frequency Raman scattering, \([12], [13]\), and the Fourier-transform infra-red absorption experiments, \([45]\). Globus et al, \([46]\), report the existence of internal modes generated by the interaction of artificial DNA-type molecules with electromagnetic radiation in sub-millimetre range. It should be noted that the type of modes observed depends on the kind of DNA samples, i.e. in aqueous solutions, or films and filaments, \([46]\). The experimental data, \([48]\), is not conclusive as to the relative positions of the acoustic and the HBS modes. The inter-strand and the acoustic modes of the DNA are alleged to be overdamped, \([14]\). But the opinion of scientific community in this respect is not unanimous. First of all, they are observed and measured, fairly well, in experiment, \([49], [12], [13], [49]\). Second, according to paper \([8]\) it is the modes related to motion of the sugar-phosphate backbone that are overdamped, that is the \(\phi_q\) modes discussed above, whereas the inter-strand modes, or the above \(u_\alpha^q\) are not. Third, Davis and VanZandt, \([43]\), had shown that the dissipative effects suffered by the modes are greatly diminished in case the GHz-frequency range is taken into account; in the region it is necessary to employ the so-called Maxwell model of hydrodynamics, or the Leontovich theory, \([47]\). Thus, we see that there are serious arguments against the inter-strand modes being overdamped and absent.

We are in a position to assess the action of mw-radiation on the molecule of the DNA. The question which has aroused controversy during the last fifteen years. We wish to make it clear that there is no “scare-mongering”, but merely a suggestion to employ microwave radiation for studying the biophysics of the DNA. In fact, we feel that the technic of Raman scattering, which had been successfully used for detecting the inter-strand modes, in conjunction with the microwave radiation could be instrumental in studying intrinsic motions of the DNA.

The key point of the theoretical analysis of the interaction of electromagnetic radiation with the DNA is accommodating the fact that the wavelength of radiation is by many orders of magnitudes larger than the characteristic size of the region of the molecule involved in the process. It was Chun-Ting Zhang, \([50]\), who suggested a mechanism to overcome this difficulty. The main point of Zhang’s argument is that the helical configuration of the electric dipoles corresponding with the base-pairs makes the interaction of the dipole \(\vec{P}\) and the field \(\vec{E}\)

\[
U = -\vec{P} \cdot \vec{E}
\]

dependent on angle. Therefore, different torsional momenta are applied at the base-pairs. The equation for the energy of interaction between the dipoles of DNA and an incident micro-wave reads

\[
- \sum_n \vec{E} \cdot R(n\Omega + \phi_n) \vec{P}_o
\]

Here \(R(n\Omega + \phi_n)\) is the rotation matrix given by Eq.\([18]\), and \(\vec{P}_o\) is the dipole at site \(n = 0\). Consequently, even though on the molecular scale the radiation has a plane wave configuration, it still twists the DNA molecule about the axis of the double-helix. Since the momenta changes periodically in time with the incident wave, the irradiation results in a periodic stress that may produce elastic vibrations in the DNA molecule. Zhang suggested that the force may generate resonance vibrations, resulting in a cross-over
mechanism which takes up initial torsion excitations and transforms them into longitudinal acoustic vibrations.

In the present paper we will try to combine Zhang's mechanism, and the excitations of the double-helix studied by Prohofsky and Kim, with the view of generating inter-strand waves in the DNA by mw-irradiation. In contrast to the original idea by Zhang, we do not utilize a cross-over into longitudinal acoustic vibrations, but employ the interaction between torsional oscillations and the inter-strand ones, i.e. the three-wave, given by Eq.(22).

The main point is that by expanding the rotation matrix \( R(n\Omega + \phi_n) \) in the angles \( \phi_n \) and keeping only the first order terms, we may cast Zhang's interaction in the form

\[
\mathcal{H}_Z = -\sum_n \phi_n (\vec{E} \times \vec{P}_n)_3 + \text{const}, \quad \vec{P}_n = R(n\Omega) \vec{P}_0
\]

in which \( \vec{P}_0 \) is the dipole vector at site \( n = 0 \). Next, by using Eq.(18) for the matrix \( R(n\Omega) \) and neglecting the constant term we may cast Eq.(33) in the form

\[
\mathcal{H}_Z = \frac{1}{2} \sum_n \phi_n \left\{ e^{i\Omega n} ((\vec{E} \times \vec{P}_n)_3 - i(\vec{E} \cdot \vec{P}_n)) + e^{-i\Omega n} ((\vec{E} \times \vec{P}_n)_3 + i(\vec{E} \cdot \vec{P}_n)) \right\}
\]

On applying the Fourier transform for the \( \phi_n \), and utilizing the equation

\[
\frac{1}{N} \sum_n e^{i(\Omega \pm \omega)n} = \delta_{\Omega, \pm \omega}
\]

we obtain the following expression for Zhang's interaction

\[
\mathcal{H}_Z = \frac{N}{2} \left\{ \phi_{\omega = \frac{\Omega}{a}} ((\vec{E} \times \vec{P}_n)_3 - i(\vec{E} \cdot \vec{P}_n)) + \phi_{\omega = -\frac{\Omega}{a}} ((\vec{E} \times \vec{P}_n)_3 + i(\vec{E} \cdot \vec{P}_n)) \right\}
\]

Hence, the torque \( T_q \) in Eq.(24) corresponding to \( \mathcal{H}_Z \) is given by the equation

\[
T = \frac{Z}{I} \delta_{q,-q} + \frac{Z^*}{I} \delta_{q,q} \quad q = \Omega/a
\]

in which

\[
Z = \frac{N}{2} \left[ (\vec{E} \times \vec{P}_n)_3 + i(\vec{E} \cdot \vec{P}_n) \right]
\]

It should be noted that \( \pm q_\ast \) are the local minima of the HBS-modes. From Eq.(34) we infer that \( q \) verifies the constraint given by Eq.(31) reads

\[
q_{res} = \frac{3}{2} q_\ast
\]

It is worth noting that the wave numbers \( q_\ast \) and \( q_{res} \) correspond to the wavelengths of one and \( \frac{2}{3} \) turns of the double-helix.

Equations given above provide an opportunity for making numerical, order of magnitude, estimates, which enable us to assess the effect of mw-radiation on the HBS-modes. From Eq.(34) we infer that the torque \( T \) has the size

\[
T \propto e^{2i\omega t} E P
\]

where \( E \) and \( P \) are the external field and the dipole moment of the base-pair, respectfully. Next, suppose that the resonance condition

\[
\omega_q = 2\omega, \quad q = q_\ast = \frac{\Omega}{a}
\]
be true, so that the action of the radiation on the torsional modes should be the largest possible. Then
the amplitude of the pumping wave, $\phi_q$, according to Eq. (24), is of the order

$$\Phi \propto \sqrt{N \frac{E_P}{2\omega_\gamma}}$$  \hspace{1cm} (36)$$

Next, we turn to Rayleigh’s condition for the parametric resonance of the HBS-mode given by Eq. (32).
For the pumping wave corresponding to Eq. (36), it gives

$$(\omega^2 - \omega_{\alpha q}^2)^2 + \gamma^2 \omega^2 \approx 4 \left( \frac{K \sin \Omega \ E_P}{Ma^2 \ I \gamma_\phi} \right)^2$$

Hence we have the threshold

$$\gamma_u \gamma_\phi \leq \frac{2K \sin \Omega \ E_P}{Ma^2 \ I}$$  \hspace{1cm} (37)$$

which is the condition that the energy supplied to a DNA molecule is greater than that dissipated, so that
the maintaining of the HBS-mode can take place. We suppose that the frequency of the HBS-modes, as
given by Eq. (25), is generally determined by the gap term $\epsilon/M$ in the equation for $u_{aq}$ and the first factor
in Eq. (37) does not differ much from unity. It signifies that the energies of the inter-strand separation
per base-pair and the twist of the relative positions of the two adjacent base-pairs, should be comparable.
At any rate, the hypothesis appears not to contradict the data reproduced in paper \[14\]. If so, we could
have the estimate for the dissipative constants, at least by orders of magnitude,

$$\gamma_u \gamma_\phi \leq \frac{E_P}{I}$$  \hspace{1cm} (38)$$

On utilizing the relation

$$E \propto 2 \sqrt{\frac{\pi S}{c}}$$

which follows from the expression for Pointing’s vector

$$\vec{S} = \frac{c}{4\pi} \vec{E} \times \vec{H},$$

in which $c$ is the velocity of light, we cast the estimate given by Eq. (38) in the form

$$\gamma_u \gamma_\phi \leq \frac{2P}{I} \sqrt{\frac{\pi S}{c}}$$  \hspace{1cm} (39)$$

in which $S$ is the power density of the interaction. If we assume

$$P \propto 1 \text{ Debye} \quad \text{or} \quad 10^{-18} \text{ CGS}$$

and the inertia coefficient $I \propto 10^{-36} \text{ gr cm}^2$, corresponding to the mass of the base-pair $\propto 10^{-22} \text{ gr}$, and
the size $\propto 10 \AA$, then for the power density $S \propto 100 \text{ mW/cm}^2$, we have

$$\gamma_u \gamma_\phi \leq 10^{16} \text{ Hz} \quad \text{or} \quad \gamma_u, \gamma_\phi \leq 10^8 \text{ Hz}$$

The estimate suggests that the effect produced by mw-radiation is to be looked for at the edge of the
GHz zone, for in this case the requirement on the line-width is less stringent. It should be noted that the
crucial point in assessing the feasibility of experiments on mw-irradiation of the DNA, and its possible
influence, is the part played by ambient solvent and ions contained in it. In fact, the irradiation may result
in just heating the solvent, so that the dissipation due to the ions takes up all effects on the molecules
of DNA. Generally, the thin boundary layer of water and ions close to the DNA-molecule may have an
important bearing on the dynamics initiated by the incident mw-radiation and result in the overdamping
of the molecule’s torsional oscillations.
Davis and VanZandt, [43], put forward arguments that the ions contained in a layer close to the DNA molecule should have an influence small enough to allow the survival of the effect due to mw-irradiation. The part played by the dissipation caused by water is more subtle.

The current arguments, [51], about the overdamping of the DNA elastic modes, rely on the Stokes law for frictional force, \( F = 6\pi\eta R v \), for a sphere of radius \( R \) moving in a fluid of viscosity \( \eta \) at speed \( v \). It is important that for the specific case of the DNA it should involve the GHz region of frequencies. But, the classical hydrodynamics, that is the Navier-Stokes theory, breaks down in the region, as can be inferred from the phenomenon of light-scattering in liquids, which is characterized by the triplet structure: the central Rayleigh line, \( \nu \), due to the elastic scattering, and the Mandelstam-Brillouin doublet, \( \nu \pm f \), of the inelastic one; \( f \) being the frequency of elastic waves in liquid. The classical hydrodynamics gives the width of a line in the Mandelstam-Brillouin doublet larger than the distance between this line and the maximum of the central line of the triplet, so that the discrete triplet structure should not be observable; in fact, it is, [47]. Mandelstam and Leontovich, [47], brought about the solution to this problem by using the relaxational theory of hydrodynamics in which liquid is considered as a viscous elastic medium characterized by a coefficient \( \eta \) of viscosity and a shear modulus \( G \), the so-called Maxwell model. In fact, the theory also takes into account effects of anisotropy, [47]. It predicts that in the region of hypersound, a few GHz or more, the attenuation coefficient for sound waves, \( \alpha \), ceases to depend on frequency \( \omega \), whereas in the low frequency classical region, in which the Stokes law is valid, the dependence reads \( \alpha \sim \omega^2 \). Davis and VanZandt, [43], used the approach of the Maxwell theory to find estimates for the damping of the DNA elastic modes, taking into account the first and the second hydration layers, and the quasi-crystalline structure of water in a neighborhood of the DNA. They found the attenuation to be two orders of magnitude smaller than that given by the Stokes law.

In fact, there is a further reason for rejecting the approach based on the Stokes law. The water molecules form hydration shells of DNA, [31], [32]. The primary hydration shell comprises the water molecules immediately adjacent to the DNA, about 20 molecules per nucleotide pair, which constitute a medium different from bulk water. The secondary hydration shell is generally considered to be similar to bulk water. But, at the spatial scale of the diameter of the DNA-molecule, that is several tens \( \AA \), the water in the second hydration shell, is hardly a condensed medium. Indeed, in this case one should have accommodated its local quasi-crystalline structure, described by the icosahedral model, [52], [53], which is to result in sophisticated dynamical equations. The conclusion is that, presently, it is difficult, if possible at all, to construct accurate theoretical estimates for the attenuation of DNA-modes.

From the experimental point of view the situation is more advanced. The DNA helical modes were observed in the experiments on the Raman, [12], [13], [31], and the far-infrared, [45], scattering. Therefore, one may suggest that the attenuation effects due to viscosity should not preclude elastic modes of the DNA. At the same time small relaxation times for damping between the DNA and the first hydration layer, of order of several tens ps, (see [32]) should result in the double helix of DNA concerted motion with surrounding layer of water. The circumstance could be accommodated within the framework of the semi-phenomenological model of the present paper. In fact, the DNA molecule and its first hydration layer still form a helix structure, and the mutual motion of constituent bases of a pair together with hydration water molecules could be described with the field \( Y \). Of course, the values of the model’s constants, \( K, \tau \), should be changed, and for the time being there is lack of information as to their size.

It is also worth noting that the effects of dissipation in aqueous solutions, where a certain form of the Stokes law could be possible, and in films, or fibers, should be quite different. So far there has been no comprehensive theoretical analysis of the dissipation, which would allow for comparing the DNA dynamics in solutions and in films. Nonetheless, the interplay of internal vibration modes and sub-millimeter electromagnetic irradiation was registered in paper [46], using Fourier transform spectroscopy and films of the double-stranded homopolymers poly[A]-poly[U] and poly[C]-poly[G] . Employing the concept of normal modes, or oscillators, of macromolecules, developed earlier for proteins, [54], and used later for DNA, [55], Globus et al, [46], made a numerical simulation of their experimental results, and thus obtained an estimate for the relaxational parameter \( \gamma \), which has the meaning of oscillators dissipation. It turned out that in the range of frequencies several 10 cm\(^{-1}\), the best fit for \( \gamma \) is less than 1 cm\(^{-1}\), depending on the conformation of an external electric field and a sample. This value of \( \gamma \) is too large for Eq.(39), but the region of frequencies studied in [46] is far from the edge of GHz region, so that one may consider the question of acceptable rate of dissipation as still open, and suggest that studying the effects of mw-radiation on the DNA modes may be instrumental for understanding the phenomenon.
We see that the elastic dynamics of the double helix could have enough structure for providing a means for stretching the hydrogen bonds of the base-pairs of DNA, or generating the HBS-modes. If the vibrational modes of the DNA are not overdamped by the ambient solvent, and the balance between energies supplied and dissipated is favourable, the maintenance of the HBS-modes could be expected at the edge of the HBS-zone. The best technique for studying the H-bond stretching still remains the Raman spectroscopy on which certain improvements have been made (see \cite{58} and references therein). Thus, the HBS-modes, and also the breathing modes, are well accessible from the experimental point of view.

The choice of specific means for generating torsional excitations of the DNA is important and interesting. In this paper we have envisaged mw-irradiation of the DNA. In case the interpenetration of the acoustic and the HBS-modes takes place, mw-radiation could maintain the HBS-modes, if the power density is sufficiently large, $100 \text{mW/cm}^2$ or more. It is important that there is no need for long exposures of the sample to the radiation. If the effect be sufficiently pronounced, it may result in the formation of the bubbles of broken H-bonds. At this point it is worth noting that our estimate for the critical power density, $100 \text{mW/cm}^2$, is by orders of magnitude larger than that officially prescribed, i.e. $0.2 - 0.1 \text{mW/cm}^2$.

IV. PROTON TUNNELING INSIDE THE HYDROGEN BONDS OF THE DNA

In the previous sections we have just considered a few specific situations which, nonetheless, indicate that the use of simple models and rough approximations is not sufficient for the study of conformations accessible for the DNA. The main conclusion is that a molecule of the DNA has an intrinsic structure that should be accounted for. Similar situations happen in continuum mechanics when it is necessary to consider a medium having an internal structure. But, the problem of the DNA is more sophisticated since the system under investigation is not a continuum medium, in fact, it is a macromolecule. Looking at the problem squarely, we have to acquiesce that we should work within the framework of nonlinear elasticity theory, if we wish to follow in this way. But the situation is still even more difficult owing to the necessity to allow for the intrinsic structure of 'the material'. Thus, at first sight the problem does not look tractable.

It is reasonable to diminish the scope of regimes under the investigation and confine ourselves mainly to problems that could be treated within the framework of the internal, or inter-strand, dynamics while assuming that deformations of the molecule of DNA are small on the mesoscale, that is a few persistence length. The assumption does not exclude the presence of external influences, as can be inferred from results of Section \[\text{II}\]. There is another point we have to take into account: the dynamics of proton inside the hydrogen bonds between the base pairs. In contrast to the inter-strand modes of the DNA, they are essentially quantum modes. Therefore, we need a model that combines classical elasticity of the double helix and quantum dynamics of the protons.

The model of this kind had been worked out by Davydov, \cite{75}, for the needs of protein dynamics. It has been used for the dynamics of protons in the DNA in papers \cite{85}, \cite{41}. It is important that the Davydov model has enough structure to accommodate both the inter-strand modes and the proton tunneling. The interaction between the two dynamics is a subject of great controversy, and whether it really takes place, or is merely speculative, depends on values of the elastic constants of the DNA, which are by no means precisely known. But if the numerical values are favourable, we may expect an interesting interplay between these forces. In what follows, we shall try to see what consequences could be inferred in this case.

By changing both positions and mutual orientations of the base pairs, the inter-strand dynamics of the DNA should deform the hydrogen bonds between them, and thus have some bearing upon the protons. It should be noted that a proton effecting a hydrogen bond between two bases of the DNA, do not have a unique position of equilibrium. Under ordinary circumstances it occupies a position that corresponds to the bases being in the amino, or keto, forms for adenine-guanine, and cytosine-thymine, respectively. The change in position of the proton result in the transition amino/keto $\rightarrow$ imino/enol of the DNA base pairs. Does the transition influence elastic properties of the molecule of the DNA ? At this point we again come across the interplay between the microscopical and macroscopical dynamics of the DNA, and
its significance for the proton transport. The latter is of primary importance for the DNA, for among other things it could be a cause of spontaneous mutations. It also raises a question of whether irradiation with electromagnetic waves could result in generating the inter-strand modes, deforming the dynamics of proton tunneling, and causing genetic effects.

Recall that according to the Watson-Crick hypothesis, the double helix of the DNA molecule comprises the two strands linked together by purine-pyrimidine base-pairs of adenine-thymine (AT) and guanine-cytosine (GC), the four chemicals A,T,G,C existing in various isomeric forms, or tautomers, that may change into one another (see FIG. 1, for example). Under ordinary conditions the equilibrium shifts towards the amino-form for adenine and guanine, and the keto-form for thymine and cytosine. But the imino-form for the adenine and cytosine, and the enol-form for guanine and thymine are also possible, even though rare; in fact, they correspond to concentrations of $10^{-4}$ to $10^{-5}$ moles/liter. The implications wrought by the tautomeric transitions are important in that the sequence of base-pairs constitutes the genetic information of cell, so that exact copies of the DNA should be produced during the replication. In fact, the complementarity between the bases may change if a tautomeric transition takes place, and other combinations become possible,

$$A_{\text{imino}} \leftrightarrow C, \quad A \leftrightarrow C_{\text{imino}}$$

(40)
in contrast to the usual and stable ones

\[ A \leftrightarrow T, \quad G \leftrightarrow T \]

An opportunity for generating "unnatural" pairs arises also from the tunneling of protons in hydrogen bonds (see FIG. 1), which results in the formation of the pairs

\[ (A \leftrightarrow T) \quad \Rightarrow \quad (A_{\text{imino}} \leftrightarrow T) \]
\[ (G \leftrightarrow C) \quad \Rightarrow \quad (G_{\text{enol}} \leftrightarrow C) \]

During the replication, tautomeric transition driven by the proton tunneling in conjunction with the complimentarity according to (41) may lead to the change of base-pairs

\[ (A \leftrightarrow T) \quad \Rightarrow \quad (G \leftrightarrow C) \]
\[ (G \leftrightarrow C) \quad \Rightarrow \quad (A \leftrightarrow T) \]

and result in loss, or corruption, of genetic information, i.e. mutations. The specific case given by the diagram (42) is called transition mutations; it has the property of being reversible, i.e. able to go back to the wildlife type.

The arguments given above constitute the main points of the theory of spontaneous mutations suggested by Crick and Watson. It is based on the assumption that the transitory tautomeric shifts of base-pairs may occur during the replication, i.e. when two molecules of DNA are formed from a paired molecule, so that the double-stranded molecule is split into two single strands, each of which controls the synthesis of a new strand complimentary to itself with the help of the special enzyme called DNA polymerase. It has been realized that the latter plays an active role in the selection of bases at replication, so that it may affect the mutation rates. Thus, tautomeric transitions are not a unique cause of mutation; the situation is more subtle, and many questions, of quite a classical nature, wait their solutions. Nonetheless, the original idea of Watson and Crick still conserves its appeal, and even more so as its new links with other phenomena related to the mutagenesis are brought to light. So, Robinson et al, report that the enol tautomer of iG, that is 2'-deoxyisogine, may form at physiological temperature (37°C) and pair with thymine in a Watson-Crick geometry; thus, iG being present as the nucleoside, results in the formation of incorrect base-pairs during in vitro replication. Robinson et al, suggests that iG · T pairing may have a bearing on mutagenesis in vivo involving tautomers of the common nucleobases. On the other hand, Fresco et al, have found that the imino tautomer HO5dCyt may serve as an example of an unfavored base tautomer making for substituting mutagenesis.

Mutations within the framework of the Crick-Watson model of DNA and in conjunction with the concept of tautomeric transition, have been drawing attention, beginning from the early fifties, to the present time, and involved the use of condensed matter theory. So, one of the first papers in this direction was published by Geracitano and Persico, who suggested that there should be expected a collective behavior of codons, resembling that taking place in hydrogen-bonded ferroelectric crystals.

In this paper we intend to look after the interplay between tautomeric transitions caused by the proton tunneling in base-pairs (see FIG. 1) and elastic properties of the double helix.

We feel that quantum effects caused by the proton tunneling may have an appreciable bearing on mutagenesis. In this respect we would like to draw attention to the fact that mutations could be generated by irradiation with electromagnetic waves in infra-red region corresponding to the energies of tautomeric shifts in the base pairs of DNA. In fact, as was pointed out by Sukhorukov et al, the available data on the absorption spectra at \( \nu = 1697 \text{ cm}^{-1} \), for the synthetic polynucleotide (PolyU)-(PolyA) forming a two-stranded structure, may indicate the transfer of protons between purine and pyrimidine bases. In papers there is reported an absorption band at \( \nu = 1712 \text{ cm}^{-1} \), for DNA at certain values of pH; the authors claim that the effect could be due to the proton tunnelling in hydrogen bonds of base pairs. Similar results are obtained in for two-stranded (PolyC) in LB-films.

It is worth noting that the interplay among the proton tunneling and the elastic properties of DNA may manifest itself in the dynamical properties of mutagenesis. To be specific, it could result in the...
phenomenon that the action imposed upon a set of base pairs of DNA may finally cause a substitution mutation in a different region of base pairs. One could expect the effect similar to the freak waves of nonlinear theory, when a low intensity initial perturbation for which the probability of mutation per base pair is low, could focus on a few base pairs and result in a mutation, (see FIG. 2).

The main point about our hypothesis is that, since the \( \pi \)-electrons of the tautomeric rings of the nucleotides have direct bearing on the interaction of the plates of adjacent base-pairs, a tautomeric transition of base-pairs should substantially influence the distribution of delocalized electrons of the nucleotides, i.e. the \( \pi \)-electrons, and result in deformation of the elastic system of DNA. The hypothesis is in accordance with the conclusions of paper. It is worth noting that tautomeric transitions may occur in several base pairs, not necessary adjacent, at a time, and their dynamics is determined by the proton tunneling. In fact, for one thing the latter is due to electrostatic interaction, i.e. the dipole forces, between the protons belonging to adjacent base-pairs, and for another the elastic system of the DNA molecule, which plays a role like that of the crystalline lattice of the polaron theory. According to D. Landau’s original idea, a charge moving in the crystalline lattice, deforms the latter so that an effective field \( U_{eff} \) is generated, and within the framework of a self-consisted picture its motion is determined by \( U_{eff} \). This argument can be also applied to the propagation of excitations of molecules constituting the lattice, that is the exciton theory. An important specific case is the regime in which the lattice relaxes to an equilibrium state fast enough so that we could neglect its motion and consider only the motion of the exciton, or charge. Then we may write down an effective hamiltonian that allows for the deformation of the lattice caused by the exciton, or charge, and next using an appropriate trial function derive an equation for its motion. Davydov, used the idea for the theory of \( \alpha \)-helix in proteins, the molecule of protein playing the part of the crystalline lattice, and Volkenstein, for his conformon theory.

The essential point about the possible interplay among the proton tunneling and the conformation of the DNA is the values of its elastic constants. In fact, as far as the transport of torsional stress (torque) along DNA is concerned, its estimates obtained by various means diverge widely. The numerical values derived with the help of the theory of continuous media, are of the order \( \tau \propto 10^{-17} \text{dyne} \cdot \text{cm} \), whereas the experimental evidence, indicates that it can attain the value of \( \tau \propto 10^{-13} \text{dyne} \cdot \text{cm} \). Philip Nelson, suggested that these deviations could be due to small bends in the helix backbone, so that one may assume

\[
\tau \propto 10^{-17} \div 10^{-13} \text{ dyne} \cdot \text{cm}
\]

For describing the elastic properties of the double-helix we may use the approach worked out in \[82\], \[83\], \[85\]. Thus, the double helix is considered as a one-dimensional lattice of vectors \( \vec{y}_n \) describing the mutual position of the two strands at sites corresponding to the base-pair of index \( n \). It is important that the system has a twisted ground state characterized by the twist vector \( \Omega \), so that the elastic energy of the molecule can be cast, at least for sufficiently small \( \vec{y}_n \), in the form

\[
H_{tor} = \sum_{i=1}^{N} \left[ \frac{1}{2} M (\partial_t \vec{y}_i)^2 + \frac{1}{2} K (\nabla \vec{y}_i)^2 + \frac{1}{2} \epsilon \vec{y}_i^2 \right]
\]

(43)

where the first term is the kinetic energy, the second one the elastic torsional energy and the last one corresponds to the separation of the two strands. The covariant derivative that accommodates the torsion of the molecule, reads

\[
\nabla \vec{y}_i = \frac{1}{a} \left( \vec{y}_{i+1} - \vec{y}_i + \vec{\Omega} \times \vec{y}_i \right)
\]
Here \( a \) is the spacing between the adjacent nucleotides, \( M \) is the mass of base-pair. For the sake of simplicity, we shall assume that the torsion vector \( \vec{\Omega} \) is always parallel to the axis \( Oz \), that is

\[
\vec{\Omega} = (0, 0, \Omega)
\]

and the vectors \( \vec{y}_n \) describe only transversal motions, that is \( y^3_n = 0 \). It should be noted that we consider a very simplified model, use the harmonic approximation for its elastic energy, and assume that all sites, corresponding to base-pairs are identical. The subtle question is the value of the elastic constant \( K \); obviously enough it has a direct bearing on the torque \( \tau \) mentioned above, and therefore, as was discussed above, its estimate may read

\[
K \propto 10^{-17} \div 10^{-13} \text{ erg}
\]

It should be noted that the calculations within the framework of molecular dynamics, (see paper[26] and references therein), give the upper value for \( K \), i.e. close to \( 10^{-12} \div 10^{-13} \text{ erg} \).

The interplay between the torsional stress due to the relative motion of the base-pairs and the proton tunneling is very important. As was mentioned above the tautomeric transitions are driven by the proton tunneling, and therefore we shall describe them quantum mechanically, that is the stable amino/keto form corresponding to the ground state of proton, and the unstable imino/enol one to the excited state.[84] In accord with the qualitative character of our approach we neglect the fact that the tautomeric transitions in question, involve the tunneling of more than one proton, and assign only one proton to each site of the lattice. There are few hydrogen bonds in which the protons are transferred towards the imino/keto groups, or if one uses the concept of the two-level system, excited states. Therefore, one can consider the system as being close to equilibrium, or only weakly excited. This suggestion is very important for what follows.

We shall describe the states of a base-pair at site \( n \) with the Bose operators \( b^+_n, b_n \) that verify the usual conditions

\[
[b_n, b^+_m] = \delta_{nm}, \quad [b_n, b_m] = [b^+_n, b^+_m] = 0,
\]

and accommodate the assumption that the tunneling states of protons be described as two level systems by considering only their ground states and the first excited state. The energy of the protons, neglecting the interaction with the elastic degrees of freedom, reads[84]

\[
H_P = \sum_n E_o b^+_n b_n + \kappa \sum_n (b^+_n b_{n+1} + b^+_{n+1} b_n)
\]

Here \( E_o \) is the energy of the tautomeric shift; its estimates depend on the choice of nucleotide and according to quantum chemistry calculations vary within the range of \( 2 \div 10 \text{ Kcal} \), (see[2] and references therein). The constant \( \kappa \) could be ascribed to dipole interactions between adjacent sites, similarly to Davydov's theory.[12] Presently, there are no reliable estimates of its value (see below); by analogy with the Davydov theory one may assume that it should correspond to the characteristic frequency of tautomeric excitation due to the proton tunneling, that is of the order \( 10^{11} \text{ Hz} \), or less. This estimate is generally accepted (see below).

The central point of the model introduced in[84] is the interaction between the elastic degrees of freedom of DNA and the tautomeric transitions, or the proton tunneling in nucleotides; it reads

\[
H_I = -\lambda \sum_n \left( \nabla \vec{y}_n \cdot \vec{h}_n \right) b^+_n b_n
\]

Here the vectors \( \vec{h}_n \) give the spatial orientation for the hydrogen bonds of base-pairs

\[
\vec{h}_n = (\cos n\alpha, \sin n\alpha, 0)
\]

It is important that the angle \( \alpha \) is the rotation angle of the double-helix, and thus close to the angle \( \Omega \), in accord with the fact that the covariant derivative term in the elastic energy provides only a qualitative description for the DNA-helix.
An argument in favor of the choice for the interaction $H_I$ is that it takes into account the deformation of positions of adjacent base-pairs and its influence on the $\pi$-electrons of the bases, and therefore, the tautomeric transitions, or the related excitations of protons. According to the theory of [72], the interaction could be appreciable. Thus, one may suggest that the interaction term could be larger than the tunneling term in the equation for $H_P$ given above.

Concluding we write the total energy within the framework of the model introduced in [84] in the form

$$H_{total} = H_{tor} + H_P + H_I$$

To find weakly excited states we shall use the Davydov approximation [75, 86], that is we shall look for the state vector of the system using the trial function

$$|D> = \sum_n A_n(t) \cdot b_n^+ |0>$$

where $|0>$ is the ground state of the system, for which all the base-pairs, or the protons in the hydrogen bonds, are in the ground state, the amplitudes $A_n(t)$ being subject to the constraint

$$\sum_n |A_n(t)|^2 = 1$$

The adiabatic approximation, which is important for the implementation of the Davydov theory, holds for the following reasons. The vectors $\vec{y}_n$ describe the dynamics of base-pairs, that is relatively massive objects, and therefore one may consider them as classical fields. We can derive the size of characteristic frequencies for $\vec{y}_n$ from expression (43) of the elastic energy. In fact, the mass $M$ is that of the base-pair, that is of the order 500 Dalton, and $K$ is of the same order of magnitude as the torque $\tau$ discussed above. Hence, we get the characteristic velocity $v$ for the $\vec{y}$ modes

$$v \propto \sqrt{\frac{K}{M}}$$

Interesting numerical values for the velocity $v$ follow from the equation indicated above and the rough estimates for $\tau$ or $K$ we have mentioned. Indeed, for $K \propto 10^{-17} \text{dyn} \cdot \text{cm}$ or less we obtain

$$v \propto 10^2 \text{cm/sec}$$

For wavelengths of a few tens of Å it gives the characteristic torsion or phonon frequencies of the order

$$\nu_y \propto 10^8 \div 10^9 \text{Hz}$$

On the other hand, if we use the values for $K$ provided by the molecular dynamics simulations [26], we get the velocity of excitations of the order $1000 \text{m/sec}$, and $\nu_y \propto 10^{11} \div 10^{12} \text{Hz}$, as for ordinary condensed media.

The elasticity of the DNA strongly depends on nucleotide sequence, and therefore the arguments given above are only of qualitative nature. Coleman et al. [88], put forward a lattice model of the DNA in which they try to accommodate the sequence dependence of elastic properties. At each side the deformation of the lattice is described by six kinematical variables: the three angular variables $\theta^n_i$ (tilt, roll, twist) and the three displacement variables $\rho^n_i$ (shift, slide, rise). The elastic energy $\Psi$ of a DNA segment is assumed to be the sum

$$\Psi = \sum_n \psi^n$$

of the interaction energies of adjacent base pairs $\psi^n$, which are functions of the above kinematic variables. In the notations of paper [88] energy $\psi^n$ reads

$$\psi^n = \frac{1}{2} F^n_{ij}(\Delta \theta^n_i)(\Delta \theta^n_j) + G^n_{ij}(\Delta \theta^n_i)(\Delta \rho^n_j) + \frac{1}{2} H^n_{ij}(\Delta \rho^n_i)(\Delta \rho^n_j)$$
where $F_{ij}^n$, $G_{ij}^n$, $H_{ij}^n$ are constants with $F_{ij}^n = F_{ji}^n$, $H_{ij}^n = H_{ji}^n$, $i,j = 1,2,3$. Coleman et al. [88], estimate

$$F_{11} = F_{22} = 4.27 \times 10^{-2} \frac{k_B T}{\deg^2}$$

For $T = 300$ the above estimate gives $1.76 \times 10^{-14}$ erg, and the velocity of 'angular' waves corresponding to the above expression for the energy, several hundred m/sec. If the corresponding excitations of the double helix are of wavelength comparable with the distance between adjacent base pairs, we get the GHz-frequency range. It should be noted that inter-strand modes, which are likely to correspond to the angular waves in the double helix, have been detected and measured in the region of tens - hundreds GHz, [12, 13, 31, 32]. Consequently, their propagation velocity could be well within a few hundred m/sec.

It is instructive to compare the values of $\nu_y$ with the transition frequencies for tautomeric reactions inside the nucleotides,

$$\nu_p = \frac{\kappa}{2\pi \hbar}$$

The estimates for the latter differ considerably, [87],

$$\nu_p \propto 10^6 \div 10^{11} \text{ Hz}$$

The lowest estimate, $10^6$ Hz appears to be not unreasonable (V. Benderskii, and J.L.Leroy, personal communications).

The relative sizes of $\nu_p$ and $\nu_y$ are important for choosing the right approximation for the model. In fact, if we are at the lowest end of the spectra $\nu_p$, then according to the estimate for $\nu_y$ obtained above the characteristic times for the acoustic modes are at least by an order of magnitude smaller than for the protons. In this case, we may suggest that the elastic system should follow the motion of the protons in hydrogen bonds, adjusting itself to it, so that a kind of adiabatic approximation can be employed. In this paper we shall follow this conjecture.

Thus, we assume, as in paper [84], that the adiabatic approximation is valid, and therefore neglect the kinetic energy of the elastic system and take into account only its potential energy generated by the field $\vec{y}_n$. Then we are in a position to apply the self-consisted method of the exciton theory, in the form suggested by Davydov [75], that is to calculate the mean value

$$U_{\text{eff}} = < D | H_{\text{tor}} + H_I | D >$$

find the minimum, $y_{n}^{(o)}$ of $U_{\text{eff}}$ with respect to $\vec{y}_n$, substitute it into the equation for the total energy $H_{\text{total}}$ so as to get the effective Davydov hamiltonian $H_D$, which depends only on the operator variables $b_n^+, b_n$, the classical variables $\vec{y}_n$ having disappeared through the minimization. To make this paper as self consistent as possible we reproduce the necessary calculations of paper [84]. Thus, we obtain an equation that has the form of the Schrödinger one

$$i\hbar \frac{\partial}{\partial t} | D > = H_D | D >$$

and in which the wave function $| D >$ should be of the form prescribed above. The assumption that the excited states correspond to the set of two-level systems is accommodated by the requirement that the operators $b_n^+$ are allowed only in the first power. It results in a system of equations, called the Davydov equations, for the amplitudes $A_n$, which one obtains on equating the coefficients at $b_n^+$ on both sides of (45) (see [75] for the details). In this paper we consider the case of the stretching energy for the DNA strands being smaller than the torsional one, that is we assume

$$\frac{\kappa a^2}{K\Omega^2}$$

being small enough.
The Davydov Hamiltonian for our problem reads

$$H_D = \sum_n E_0 b_n^+ b_n - \sum_n \kappa (b_{n+1}^+ b_n + b_n^+ b_{n+1})$$

$$- \frac{\lambda^2}{K} \sum_n |A_n|^4 \frac{\lambda^2}{K} \sum_n |A_n|^2 b_n^+ b_n$$

$$+ \frac{\lambda^2}{2K} \epsilon a^2 \sum_{m,n} \cos|m-n| \phi \cdot \cos [(m-n)(\phi - \alpha)] |A_m|^2 |A_n|^2$$

$$+ \frac{\lambda^2}{2K} \epsilon a^2 \sum_{m,n} \cos|m-n| \phi \cdot \cos [(m-n)(\phi - \alpha)] |A_n|^2 b_n^+ b_n$$

and the equation for the amplitudes $A_n$

$$i \hbar \frac{\partial}{\partial t} A_n = E_0 A_n - \kappa (A_{n+1} + A_{n-1}) - \frac{\lambda^2}{K} |A_n|^2 A_n - \frac{\lambda^2}{K} \sum_m |A_m|^4 A_n$$

$$+ \frac{\lambda^2}{K} \epsilon a^2 \sum_{m_1, m_2} \cos|m_1 - m_2| \phi \cdot \cos [(m_1 - m_2)(\phi - \alpha)] |A_{m_1}|^2 |A_{m_2}|^2 A_n$$

$$+ \frac{\lambda^2}{K} \epsilon a^2 \sum_m \cos|m-n| \phi \cdot \cos [(m-n)(\phi - \alpha)] |A_m|^2 A_n$$

which has the form of a nonlinear discrete Schrödinger equation for the amplitudes $A_n$. The terms given by the third and the fourth lines of the equation written above, describe an interaction that has a very long range, so that one may claim Eq. (47) is essentially nonlocal in character.

We shall make an important approximation that agrees with the general qualitative setting of our work, and set

$$\alpha = \phi$$

where $\phi = \arctan \Omega$. Thus, the oscillating factors in Eq. (47) are cancelled out. With the help of the reduced variables $B_n$

$$A_n = \exp(-\frac{i}{\hbar} E_0 t) B_n(t)$$

we cast the equation for $A_n$ in the form

$$i \hbar \frac{\partial}{\partial t} B_n = -\kappa (B_{n+1} + B_{n-1}) - \frac{\lambda^2}{K} |B_n|^2 B_n$$

$$- \frac{\lambda^2}{K} \sum_m |B_m|^4 B_n$$

$$+ \frac{\lambda^2}{K} \epsilon a^2 \sum_{m_1, m_2} \cos|m_1 - m_2| \phi |B_{m_1}|^2 |B_{m_2}|^2 B_n$$

$$+ \frac{\lambda^2}{K} \epsilon a^2 \sum_m \cos|m-n| \phi |B_m|^2 B_n$$

Introduce the characteristic frequencies

$$\nu_P = \frac{\kappa}{2 \pi \hbar}, \; \nu_T = \frac{\lambda}{2 \pi \hbar}, \; \nu_{tor} = \frac{K}{2 \pi \hbar}$$
and the dimensionless time

$$\Upsilon = t \cdot \nu_p$$

It should be noted that the frequencies $\nu_y$ and $\nu_{\text{tor}}$ are not identical, $\nu_y \neq \nu_{\text{tor}}$. Then the Davydov equation takes the form

$$i \frac{\partial}{\partial \Upsilon} B_n = -(B_{n+1} + B_{n-1}) - W|B_n|^2 B_n$$

$$- W(\sum_m |B_m|^4) B_n$$

$$+ W\Lambda\left( \sum_{m_1,m_2} \cos|m_1-m_2|\phi|B_{m_1}|^2|B_{m_2}|^2 \right) B_n$$

$$+ W\Lambda\left( \sum_m \cos|m-n|\phi|B_m|^2 \right) B_n$$

in which

$$W = \frac{\nu_y^2}{\nu_p \cdot \nu_{\text{tor}}}$$

$$\Lambda = \frac{ca^2}{K \cdot \Omega^2}$$

Now we aim at making the numerical simulation of Eq.(50) for various values of the parameters $W$, $\Lambda$, looking for solutions of the soliton type. We use the term soliton in a sense close to that used by applied scientists, i.e. a solution different from zero in a finite region of space, whose size we shall call the size of soliton, and preserving its shape for very long periods of time. For some values of $W$, $\Lambda$ it has the form identical to the usual one, i.e. corresponding to the non-linear Schrödinger equation, but generally our solitons are different. The standard definition suggests that it be of the form

$$Y(x,t) = e^{i(qx - \nu t)} \psi(x - vt)$$

in which $\psi$ is a real function. It is by no means clear that our solitons always have the form given by Eq.(53).

The parameter $\Lambda$ is a quantitative characteristic that enables us to take into account the structure of the double helix, and also the relative size of the torsional and deformation energies. In fact, $\Lambda$ determines the magnitude of the nonlocal terms in Eq.(50), and in this respect it is worthwhile to note that for certain values of $\Lambda$ and $W$ we have not been able to find soliton solutions, e.g. $\Lambda = 0.2$ and $W = 2$, at least for physically reasonable sizes of solitons, i.e. less than 150 base pairs. The last constraint is due to the fact that we consider straight segments of DNA, parallel to Oz-axis, and therefore they should be of a size less than the persistence length, that is about 150 base pairs. But it is important that generally the condition $\Lambda \neq 0$ does not forbid the existence of solitons, and its influence only results in the size of soliton becoming larger, which is quite natural, for $\Lambda$ represents non-local terms in Eq.(50). The general case of soliton with $\Lambda$ not equal to zero, even though small, is illustrated in FIG. 3. To understand the general situation let us consider the two special cases.

1. Stationary solutions in the sense that the absolute value, $|B_n(t)|$ does not depend on time. For the usual solitons given by Eq. (53) this requirement means that the velocity $v = 0$. The typical case is illustrated in FIG. 4 (a), for $W = 10$ and $\Lambda = 0.5$. The half-width of soliton equals to one spacing between base-pairs, that is the solution is extremely narrow, and according to our main hypothesis it must correspond to the tautomeric transition of a base-pair. The very interesting case is illustrated in FIG. 4 (b), $W = 5$ and $\Lambda = 0.5$. There is a central peak of half-width 1.5 $\cdot a$ which stands still, and two symmetrical wave packets, moving in opposite outward directions. The distance traveled by these wave packets during 0.018 msec is equal to 33 base pairs. The value of $\nu_p$ was taken $10^6 \text{ Hz}$.

2. The usual solitons given by Eq.(53). The half-width of these solitons may be several tens of base-pair spacings, and thus they could correspond to tautomeric transitions taking place in adjacent base-pairs.
FIG. 3: Typical moving solitons. Solid line: $|A_n|$. Thin line: the real and the imaginary part of the amplitude $A_n$, $\nu_P = 10^6 \text{ Hz}$. (a) for $W = 0.75$, $\Lambda = 0.001$, velocity 1330 base pairs per msec, the period of time spent 0.533 msec. (b) Moving soliton for $W = 0.75$, $\Lambda = 0.075$, velocity 1340 base pairs per msec, the period of time spent 0.530 msec, distance travelled 707 base pairs. (c) Moving soliton for $W = 2$, $\Lambda = 0.1$, velocity 850 base pairs per msec, the period of time spent 0.577 msec, distance travelled 491 base pairs. The values of $W, \Lambda$ are close to the borderline [see FIG. 5 (b)], dividing the region of stable solitons from the unstable ones.

The typical cases are illustrated in FIG. 3. It is interesting to note that these solitons move, even though slowly. Their velocity is given by the asymptotic formula

$$v \approx 2\nu_P \sin(aq)$$

Hence, one might suggest the picture of tautomeric transitions moving along the DNA-molecule.

Both types of solutions indicated above are stable with respect to perturbation of $W$ and $\Lambda$. 

FIG. 4: Typical breathers. Solid line: $|A_n|$. Thin lines indicate the real and the imaginary part of the amplitude $A_n$, $\nu_P = 10^6$ Hz. (a) Breather, or still soliton. $W = 10$, $\Lambda = 0.5$. The period of time spent 0.501 msec. (b) Radiation emitted from the motionless central peak during the period of time 0.018, for $W = 5$ and $\Lambda = 0.5$; the velocity of side waves 1830 base pairs/msec, distance traveled 33 base pairs.

Perhaps, the most characteristic feature of discrete non-linear Schrödinger equation is solutions that periodically oscillate in time and decay exponentially in space, or breathers. From a purely qualitative point of view the existence of breathers can be inferred from a truncated version of Eq.(50). Let us neglect all the terms on its RHS except the first two, that is consider

$$i\hbar \frac{\partial B_n}{\partial t} = -(B_{n+1} + B_{n-1}) - W|B_n|^2 B_n$$

and look for $B_n$ such that

$$B_n = e^{i\nu t} a_n$$

$a_n$ being real. Next, cast the equation for $a_n$ in the form
Suppose that the soliton we are looking for is large enough so that we may change the expression $a_{n+1} - 2a_n + a_{n-1}$ for the second derivative. Thus we obtain the equation

$$a'' + [Wa^3 + (2 - \epsilon)]a = 0$$

or the conservation law for one dimensional motion with the effective potential

$$V = \frac{2 - \epsilon}{2}a^2 + \frac{W}{4}a^4$$

The soliton solution exists for $\epsilon \geq 2$, and its size tends to infinity as $\epsilon \to 2$. On the other hand for large $W$ we may expect thin solitons.

The key point is that the nonlocal terms generated by the double helix bring serious modifications to the picture given above. Thus, we may infer that the dimensionless constants $W$ and $\Lambda$ play a crucial role in determining the form of solitons for Eq.(50). The general situation to the effect is illustrated in FIG. 5 in which the horizontal axis corresponds to values of $\nu$, that is the soliton frequency measured in units of $\nu_P$. It should be noted that $\nu$ defines only the main Fourier component both for solitons and for breathers, so that $\nu$ turns out to be only a rough characteristic. The breathers are represented by the solid line, that serves also as a right-handed border for the region of moving solitons. This line continues up to infinity with both $W$ and $\nu$ rising. It’s lower end was not clearly found. The lower left-handed border of the soliton region is not strictly defined, owing to the fact that there are solitons for values of $W$ and $\nu$ lower than the borders but of sizes greater than 100 base pairs, that is beyond the physical context of our problem. The upper left-handed part of the border is determined by solitons turning out to be unstable for values of $W$ and $\nu$ beyond the boundary, and thus is not defined clearly. We see that the soliton region is decreasing as $\Lambda$ grows (see FIG. 5), and for $\Lambda = 0.2$, FIG. 5 (d), there are only breathers, at least under the constraint of their size being less than 100 base pairs. It is worth noting that Eq.(50) derived in [84] is valid only for small $\Lambda$.

We would like to draw attention to a class of solutions that correspond to the nomenclature of "freak waves" [89, 90], and which may have a bearing upon the dynamics of tautomeric transitions. A solution of the type is illustrated in FIG. 6. It is characterized by an initial set of amplitudes $B_n(t)$ which is a broad distribution of the size of 80 base-pair spacings; after the period of time 0.017 msec, the characteristic frequency $\nu_P$ being taken $10^6$ Hz, it focuses itself on a narrow peak of half-width of one spacing. The peak exists for the brief period of time 0.002 msec, and next breaks down into a broad distribution again, i.e. a kind of partial self focusing is taking place. Thus, there may exist low probability tautomeric transitions distributed over wide areas of the molecule, and which may collapse into a small region of the molecule, and stay there for a period of time, brief but perhaps sufficient to cause mutation. For finding the initial configurations producing the peaks indicated above we used the method of numerical integration backward in time, similar to that used in papers [89, 90].

It is instructive to see the conformation of the field $\vec{y}_n$ accompanying the dynamics of solitons. The typical configuration of $\vec{y}_n$ corresponding to the soliton solution of Eq.(50) is shown in FIG. 7.

We see that the formation and the dynamics of solitons corresponding to the tunneling of protons is accompanied by conformational changes. Thus, we may infer that the tautomeric transitions studied in this paper are to a large extent similar to conformons [77]. In fact, the concept of conformon was suggested for describing the dynamics of charge transfer in macromolecules, especially proteins, similarly to the situation we are considering.

It is also interesting to invert the picture discussed above, and suggest that there is a deformation of the double helix described by a distribution of $\vec{y}_n$, like that shown in FIG. 7, then there should be a
FIG. 5: Sets of $W$ and $\nu$ that allow for soliton solutions. Solid line represents still solitons, or breathers. Shaded area represents moving solitons. Points are trial solutions. The transition from solitons to breathers goes smoothly as the soliton speed decreases to zero. We take into account only solutions of size less than 100 base pairs. (a) $\Lambda = 0$. (b) $\Lambda = 0.1$. (c) $\Lambda = 0.15$. (d) $\Lambda = 0.2$.

distribution of the soliton amplitude, that is a proton tunneling generated by the conformational change. Thus, we may suggest that the conformational transitions may result in the proton tunneling, or the tautomeric shifts.

As was shown above, the dynamics of tautomeric transitions in DNA depend on elastic properties of the latter and proton tunneling in base pairs; $W$ and $\Lambda$ serving as indicators for possible regimes. Our numerical simulation suggests that the interesting tautomeric dynamics may happen for $W \geq 1$. This allows for sufficiently wide range of material constants of DNA so that the phenomenon could occur. The second constant, $\Lambda$, provides a quantitative characteristic for the part played by the double helix; it can totally modify the structure of solitons corresponding to tautomeric transitions.

Depending on the value of $W$ one may expect the existence of two quite different dynamics: (1) solitons that move at velocities smaller by orders of magnitude compared with that of elastic excitations in DNA, and have a size of several tens of base-pairs, and (2) stationary solutions, or breathers, that have a form of peaks over a few base-pairs. We may suggest that the second type of solutions correspond to point mutations, whereas the first one may describe tautomeric transition moving along the chain of double helix, and therefore there may happen mutations related to the transition. Thus, one may suggest that an action imposed on a set of nucleotide in a region of the molecule might generate mutations in a different region owing to the motion of excitations corresponding to the proton tunneling.

It is alleged to be known that by substituting the "artificial" nucleotides instead of the natural ones, e.g. brom-uracil for thymine, one can increase dramatically the rate of mutations; this could be due to the increase of tautomeric transitions inside base-pairs. At any rate, it is worthwhile to study the interplay
FIG. 6: Partial self-focusing of an initial low amplitude distribution on a peak for a period of time 0.002 msec, for \( W = 1 \), \( \Lambda = 0.5 \), \( \nu_P = 10^6 \) Hz.

FIG. 7: Moving soliton for \( W = 2 \), \( \Lambda = 0.1 \), velocity 880 base pairs per msec, \( \nu_P = 10^6 \) Hz. Maximum \( |\vec{y}_n| = 0.52 \mathring{A} \). (a) The amplitude \( A_n \). Solid line: \(|A_n|\). Thin line: the real and the imaginary part of the amplitude \( A_n \). (b) \( \vec{y}_n \) distribution. Solid line: \(|\vec{y}_n|\). Thin line: the first and second coordinates of the \( \vec{y}_n \).

between the rate of such transitions and mutations. Within the context of the present paper, artificial DNA of this kind could ease the stringent constraints imposed on \( W \), as was indicated above.

It is worth noting that the "focusing" of solutions (see FIG. 6), similar to the freak waves which take place in the theory of non-linear waves [89, 90], may have a very important bearing on mutations. In fact, it amounts to the possibility of a weak external influence generating a low amplitude distribution of mutation sites that would focus itself later on a high amplitude distribution concentrated in a different...
region of the molecule. Thus, one may expect generating mutations by low intensity agents distributed in a region of the molecule, or to put it the other way round, acting on a set of codons different from those that suffer the actual mutation.

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