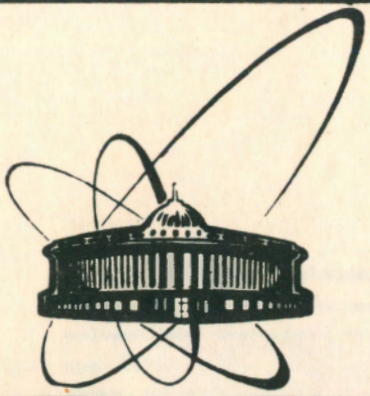

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ON THE DYNAMIC PLANE BASE-ROTATOR MODELS OF DNA: BASE-BASE INTERACTION AND DISSIPATION

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1. Introduction

In the work by Englander et al (1980) intensive hydrogen-deuterium exchange between the Watson-Crick base pairs and a solvent was explained by using two hypotheses. According to the first one, the so-called open states arise in the DNA double helix as a consequence of thermal fluctuations. These states are segments consisting of open pairs of complementary bases and moving along the helix with constant velocity and energy. The second hypothesis identifies these states with soliton excitations (kinks of the sine-Gordon (SG) equation). The cited paper stimulated the study of solitons in DNA by many authors. On the one hand, a possible role of solitons in the properties of DNA is discussed (providing a mechanism for long-range energy transfer and a mechanism of the DNA duplication and the transcription of mRNA, protein production in cells, conformational transitions, etc.). Discussions on this theme still continue and have a contradictory character (Baverstock and Cundall 1988, Maddox 1987, Frank-Kamenetskii 1988). Even the observations of Englander et al (1980) have since been questioned. On the other hand, various models have been proposed to describe the nonlinear DNA dynamics and to substantiate the possibility that soliton-like excitations exist in DNA (Yomosa 1983 and 1984, Takeno and Homma 1983, Homma and Takeno 1984, Fedyanin and Yakushevich 1984, Fedyanin et al 1986, Fedyanin and Lisy 1986 and 1987, Zhang 1987, Xiao et al 1987). Common features of these (essentially mechanical) models are as follows. The bases are modelled by physical pendula performing rotational vibrations in the plane perpendicular to the helix axis. Along the axis the pendula are coupled together by a nonextensible strand (however, an attempt has already been made to take into account the longitudinal motion (Xiao et al 1987)). The strands of the double helix are elastic with

respect to torsion. The above-mentioned models highly idealize the realistic picture of the internal DNA dynamics. However, they can be considered as a possible step towards the description of great fluctuational rebuildings in DNA. One of the central points in the models discussed is the modelling of interactions between the complementary bases in pairs. The potential energy of this interaction, $V(\phi_n,\phi'_n)$, is considered to depend only on ϕ_n and ϕ'_n, being the angles of rotation of the bases in the n pair. Various expressions for V have been used in the literature, however, without any serious substantiation. In the following section a brief review of $V(\phi_n,\phi'_n)$ will be given and one of the variants will be substantiated. There is one more point not taken into account in the discussed theories, namely, the problem of friction that always takes place in real biopolymers. The effects of dissipation caused by the viscosity of a solvent have already been considered (Yakushevich 1987) in connection with nonlinear models of the internal DNA dynamics. However, in that work the consideration was carried out in the frame of Yomosa's model (Yomosa 1983) of the dynamics of only one strand of the double helix. Moreover, as it has been shown later (see, e.g., Yomosa 1984, Fedyanin and Lisy 1986) this model contains some unphysical features. In the corresponding section, we consider the account of dissipation (both the external and internal one) in the above-cited more general models. We will proceed with the introduction of model dissipative functions.

2. Base-base interaction

In the original model of mechanical plane rotators in DNA (Yomosa 1983) the following expression has been suggested for the potential energy of interaction between the complementary bases in pairs:

$$V(\phi,\phi') = \text{const}\,[1-\cos(\phi-\phi')]. \qquad (1)$$

In the subsequent paper (Yomosa 1984) this expression has been considered to be too much simplified to contain an unphysical feature and the new variant of the H-bonding energy, V, has been presented:

$$V(\phi,\phi') = 2A+B-A(\cos\phi+\cos\phi')-B\cos\phi\cos\phi'. \qquad (2)$$

However, this energy is symmetric with respect to ϕ and ϕ'. There are no physical reasons for such a strong demand. Takeno and Homma (1983) have suggested $V(\phi,\phi')$ of the form

$$V(\phi,\phi') = 2-C-\cos\phi-\cos\phi'+C\cos(\phi-\phi'). \qquad (3)$$

This potential gives a correct ground state of the molecule (the correct minimum state is given by $\phi_n=\phi'_n=0$ or $2\pi n$) but no more reasons have been given there for such a choice. From our point of view, the most reasonable choice of V in this class of models is of the form V=V(l), with l being the distance between the complementary bases (Fedyanin et al 1986, Fedyanin and Lisy 1986). In these papers, dynamical equations of the model with this type of the potential (including the break of the H-bonding) have been obtained. In the next work (Zhang 1987), the potential (1) has been supplemented with the dipole-dipole interaction using, however, the condition l=const. The potential of the kind V=V(l) has also been used in the recent paper by Yakushevich (1989). This model differs from the previous ones as follows. The pendula are replaced by rotating discs which are coupled to each other by elastic springs (both along the axis and in complementary bases). But we note that there is no longitudinal motion along the strands in Yakushevich's model so that the springs should be replaced by nonextensible strands. Moreover, the discs have no distinguishable points (one cannot determine whether the disc is turned out from the ground state or not). Hence, it

is also not clear how to specify the ground state of the helix. For the same reason the definition of l is uncertain. The function V(l) is taken in the harmonic form $(\sim(l-l_0)^2$, where l_0 is the equilibrium distance). This seems to be true only for small deviations $l-l_0$.

In general, the potential energy $V(\phi_n,\phi'_n)$ in the n pair of bases can be expressed using the Fourier expansion:

$$V(\phi_n,\phi'_n)=\sum_{l,k} C^n_{k,l}\exp(ik\phi_n)\exp(il\phi'_n). \qquad (4)$$

The minimum of V corresponds to the finite quantity $V(0,0)=\sum C^n_{k,l}$, therefore, beginning from some k and l the expansion coefficients $C^n_{k,l}$ decrease. The condition $V(\phi,\phi')=V(-\phi,-\phi')$ implies $C^n_{k,l}=C^n_{-k,-l}$. Assuming the bases in pairs being approximately identical, we obtain $C_{0,1}=C_{1,0}$, etc. If only the terms of the lowest order of k and l are kept in the sum (k,l=0,1), we find

$$V(\phi,\phi') = C-A(\cos\phi+\cos\phi')-B\cos(\phi+\phi'). \qquad (5)$$

For V(0,0) corresponding to the minimum of V, the conditions A>0 and B>-A/2 must be satisfied. If $A/2|B|<1$, we have also B>0. In this case $V_{max}= C+A^2/2B+B$. For $A/2|B|\geq 1$ $V_{max}=C+2A-B$. Note that the harmonical potential (Fedyanin and Lisy 1986, Yakushevich 1989) with $l_0=0$ is a particular case of Eq.(5).

Now, consider the stacking and torsional (intra-strand) interaction. Following Yomosa's paper (1983), the expression $-\sum_n[2-\cos(\phi_n-\phi_{n-1})-\cos(\phi'_n-\phi'_{n-1})]$ is usually used. In the frame of the continuum approximation, the model intra-strand potential can be assumed to be of the form $\sum_n[K(\phi_n-\phi_{n-1})+K(\phi'_n-\phi'_{n-1})]$, with only the additional condition $K(\Delta\phi\to 0)\approx K_0(\Delta\phi)^2/2$ for the function K (K_0 is a constant).

It is also necessary to take into account the energy of interaction between the bases and the surrounding solvent. One can assume that a) the influence of this interaction

appears only in the change of the coefficients in V (Yomosa 1984); b) this energy W contains a potential of the Brownian forces; c) W includes a potential of vector forces, e.g., such as the electric ones (the bases are electric dipoles). In what follows, we shall dwell on the most simple case a).

Finally, the kinetic energy of rotational motion of the bases is necessary to construct the model Hamiltonian. It has the following form:

$$T=(1/2)\sum_n[I_n\dot{\phi}_n^2+I'_n\dot{\phi}'^2_n]. \qquad (6)$$

The moments of inertia of the bases, I_n, will be replaced, for simplicity, by some effective moment, I (the bases are close in masses).

Thus, the Hamiltonian of the model system can be written as follows:

$$H=\sum_n[(I/2)(\dot{\phi}_n^2+\dot{\phi}'^2_n)+K(\phi_n-\phi_{n-1})+K(\phi'_n-\phi'_{n-1})+V(\phi_n,\phi'_n)]. \qquad (7)$$

3. Dissipative function

We introduce the model dissipative function with the help of the following expression:

$$R = (1/2)\sum_n(\zeta_n\dot{\phi}_n^2+\zeta'_n\dot{\phi}'^2_n)+\sum_n[Z(\dot{\phi}_n-\dot{\phi}_{n-1})+Z(\dot{\phi}'_n-\dot{\phi}'_{n-1})]. \qquad (8)$$

The first term in Eq.(8) has an ordinary form and it describes the external friction for the bases moving in a solvent. For simplicity, the approximate equality of the friction coefficients for different bases will be assumed: $\zeta_n\approx\zeta'_n=\zeta$. The second term in Eq.(8) is a model dissipative function describing the internal friction between the nearest-neighbour bases. The most simple form of Z is

$$Z = (1/2)\zeta_{in}(\dot{\phi}_n-\dot{\phi}_{n-1})^2, \qquad (9)$$

with ζ_{in} being the coefficient of the internal rotational friction. Within the continuum (long-wave) approximation,

that is usually used in the considered models, it is unnecessary to know Z for all values $\Delta\phi_n$. It is enough to assume that for small $\Delta\phi_n$ the function Z is approximately given by Eq.(9).

Using the Hamiltonian (7) and dissipative function (8), we obtain the following system of coupled differential equations for the angles ϕ and ϕ':

$$IX_{tt}+\zeta X_t+\zeta_{1n}a^2X_{tzz}-K_0a^2X_{zz}+\partial V/\partial X = 0, \qquad X=\begin{pmatrix}\phi\\ \phi'\end{pmatrix}. \tag{10}$$

Here z is the co-ordinate along the helix axis, a is the nearest-neighbour distance of bases in the same strand and the continuum approximation has been used: $X_n(t)\to X(z,t)$, $X_{n\pm1}(t)\to X(z,t)\pm a^2X_{zz}/2$.

4. Particle-like solutions of the model without dissipation

It is difficult to obtain exact solutions of the coupled nonlinear equations (10) with arbitrary V. The system can easily be solved in the linearized case (for example, optical and acoustic modes can be found). However, nonlinear solutions, which are of particular interest, can be found only in a few special cases. So for the potential (5) the system (10) takes the form

$$\left.\begin{matrix}\phi_{zz}-c_0^{-2}\phi_{tt}\\ \phi'_{zz}-c_0^{-2}\phi_{tt}\end{matrix}\right\}=[A\sin\phi+B\sin(\phi+\phi')]/K_0a^2, c_0^2=K_0a^2/I \tag{11}$$

and, if $\phi=-\phi'$, it reduces to the SG equation. If $\phi=\phi'$, we come to the so-called double SG equation that is also integrable (Condat et al 1983). One can easily find the exact first integral of Eq.(10) for wave solutions depending only on the combination (z-vt) (Homma and Takeno 1984, Fedyanin et al 1986). In the case when the ratio A/|B| is small or large, Eq.(10) can be solved using perturbation methods. Consider, for example, the wave solution of Eq.(11)

for small $\varepsilon=B/A$. "Nonperturbed" solution (for $\varepsilon=0$) are kinks ($\eta_1=1$, i=1,2) or antikinks ($\eta_1=-1$):

$$\phi_0 = 4\tan^{-1}\exp(\eta_1 x), \quad \phi_0' = 4\tan^{-1}\exp(\eta_2 x), \qquad (12)$$
$$x=\gamma(A/K_0a^2)^{1/2}(z-vt-z_0), \quad \gamma=(1-v^2/c_0^2)^{-1/2}.$$

Here, z_0 is the initial position of a soliton (with no restriction of consideration we can take $z_0=0$). We represent the solution of the system at $\varepsilon\neq0$ but $|\varepsilon|\ll1$ as follows:

$$\phi = \phi_0 + \phi_1 + \ldots, \qquad \phi' = \phi_0 + \phi_1' + \ldots, \qquad (13)$$

that is, we use the standard perturbation theory. Substituting Eqs.(12) and (13) into (11) and keeping only the terms of the first order of small quantities ε, ϕ_1 and ϕ_1', we obtain

$$\begin{pmatrix} \phi_1 \\ \phi_1' \end{pmatrix} = (1-2/\cosh^2 x)[\phi_1 - 2\varepsilon(\eta_1+\eta_2)\sinh x/\cosh^2 x]. \qquad (14)$$

For $\eta_1\neq\eta_2$, we have two homogeneous equations with the common general solution $C_1/\cosh x + C_2(\sinh x + x/\cosh x)$. Using the requirements that the solution must be finite as $|x|\to\infty$ and vanish at $\varepsilon=0$, we obtain $C_1=C_2=0$. Thus, in the lowest approximation, ϕ_1 and ϕ_1' are nonzero only if $\eta_1=\eta_2=\eta$. Then, the solution of Eqs.(14) is

$$\phi_1 = \phi_1' = 2\varepsilon\eta(x-\tanh x)/\cosh x. \qquad (15)$$

One can see from Eqs.(13) and (15) that the full wave solutions of Eqs.(11) for $|\varepsilon|\ll1$ have the form of a kink (antikink) slightly deformed in a region of about its width but with a nondisplaced centre. Analogously, the opposite case of "strong coupling" ($|\varepsilon|\gg1$) can easily be considered. In this limit, we obtain corrections to the π-kink excitations.

5. Effects of dissipation

The account of dissipation effects will be demonstrated by using as an example the system (11) when it reduces (at $\phi=-\phi'$) to the sine-Gordon equation. In this case, soliton solutions of the nonperturbed equations (without dissipation) are as follows:

$$\phi_0 = 4\tan^{-1}\exp(\eta\xi) = -\phi_0', \qquad (16)$$

$$\xi=\gamma(z-vt)/d, \quad \eta=\pm1, \quad d=c_0/\omega_0=a(K_0/A)^{1/2}, \quad \omega_0=\sqrt{A/I}.$$

We expand the solutions as in Eqs.(13) and substitute them into Eqs.(10). After linearizing these equations in ϕ_1,ϕ_1' and in the dissipative terms that are assumed to be small perturbations, we come to the following equations:

$$\Psi_{\tau\tau}-\Psi_{\xi\xi}+[2B/A+1-2/\cosh^2\xi]\,\Psi = 0$$
$$\Phi_{\tau\tau}-\Phi_{\xi\xi}+[1-2/\cosh^2\xi]\,\Phi = \beta(\xi), \qquad (17)$$

where $\Psi=(\phi_1+\phi_1')/2$, $\Phi=(\phi_1-\phi_1')/2$ and the substitution $\tau=\omega_0\gamma(t-vzc_0^{-2})$ has been made. The function $\beta(\xi)$ is given by the formulae

$$\beta(\xi) = 4p/\cosh^3\xi-4q/\cosh\xi, \qquad (18)$$

$$-Ap = 2\eta\zeta_{1n}a^2v(\gamma/d)^3, \quad -Aq = \eta\zeta v\gamma/d+\eta\zeta_{1n}a^2v(\gamma/d)^3.$$

We search for the solution expanding Ψ and Φ on the basis of the orthogonal system of functions $f(\xi)=1/\sqrt{2}\cosh\xi$ and $f_k(\xi)=(k+i\tanh\xi)\exp(ik\xi)/\sqrt{2\pi}w_k$, where $w_k^2=1+k^2$ and $-\infty<k<\infty$ (Fogel et al 1977):

$$\Phi(\tau,\xi) = A(\tau)f(\xi)+\int_{-\infty}^{+\infty}dk\; f_k(\xi)B_k(\tau) \qquad (19)$$

$$\Psi(\tau,\xi) = C(\tau)f(\xi)+\int_{-\infty}^{+\infty}dk\; f_k(\xi)D_k(\tau).$$

Substituting Eqs.(19) into (17), we find equations for the

determination of the functions $A(\tau)$, $B_k(\tau)$, $C(\tau)$ and $D_k(\tau)$:

$$C_{\tau\tau}(\tau)+(2B/A)C_{\tau}(\tau)=0, \quad D_{k\tau\tau}(\tau)+(2B/A+w_k^2)D_k(\tau)=0, \quad (20)$$
$$A_{\tau\tau}(\tau)=a, \quad B_{k\tau\tau}(\tau)+w_k^2B_k(\tau)=b_k,$$

with

$$a=8p\sqrt{2}/3-4q\sqrt{2}, \quad b_k=(4/3)(\pi/2)^{1/2}pkw_k/\cosh(\pi k/2).$$

The equations are solved with the initial conditions corresponding to ϕ_1, ϕ_1' and their first derivatives being zero at t=0 (the soliton is supposed to create at t=0). Then, we have $\Psi=\Phi=\Psi_{\tau}=\Phi_{\tau}=0$ at t=0. Using, e.g. for $C(\tau)$, the representation $C(\tau)=\int d\xi\Psi(\tau)f(\xi)$, we obtain $C(\bar{\tau})=(dC/d\tau)_{\tau=\bar{\tau}}=0$, where $\bar{\tau}=-\omega_0\gamma vzc_0^{-2}$. Hence, C=0. In the same way we find $D_k=0$, $A(\tau)=a(\omega_0\gamma t)^2/2$ and $B_k=b_k[1-\cos w_k(\tau-\bar{\tau})]/w_k^2$. After substitution of these results into Eqs.(19) and integration, we obtain

$$\Psi(\tau,\xi) = 0 \quad (\phi_1=-\phi_1'), \quad (21)$$
$$\Phi(\tau,\xi) = \phi_1 = a(\tau-\bar{\tau})^2f(\xi)/2 + \int dk w_k^{-2}b_kf_k(\xi)[1-\cos w_k(\tau-\bar{\tau})].$$

It is evident that the method used is correct only for not very large $\tau-\bar{\tau}\sim t$. Keeping in Eq.(21) only the terms to the second order of t, we have

$$\phi_1(z,t) \approx -2(\omega_0\gamma t)^2(q/\cosh\xi+p/\cosh^3\xi), \quad \phi \approx \phi_0+\phi_1 \approx -\phi'. \quad (22)$$

This function is of the same sign as v for a kink and of the opposite sign for an antikink. It slightly changes the soliton form in the region of its centre (in all cases it leads to a deceleration of the soliton). If ξ increases, ϕ_1 rapidly decreases.

Let us calculate the ratio of the energy E of the obtained wave solution to the kink (antikink) energy E_k:

$$E/E_k = (8\omega_0c_0\gamma)^{-1}\int_{-\infty}^{\infty}dz[(\phi_t^2+c_0^2\phi_z^2)/2+\omega_0^2(1-\cos\phi)]. \quad (23)$$

Using ϕ from Eq.(22), we find with the above-used degree of precision

$$E/E_k \approx 1+2\eta\gamma vtd^{-1}\int_0^\infty dx(q/\cosh^2 x+p/\cosh^4 x)$$

$$\approx 1-2(\zeta t/A)(\gamma v/d)^2[1+7\zeta_{1,n}(a\gamma/d)^2/3\zeta]. \qquad (24)$$

For velocities not very close to $\pm c_0$ the decrease of the soliton energy is determined essentially by external friction. It is due to the continuum approximation condition $a/d \ll 1$. Then, the solution can be written as follows:

$$\phi(z,t) \approx 4\tan^{-1}\exp(\eta\xi)+(\omega_0\gamma t)^2\frac{2\eta\gamma v\zeta}{Ad\cosh\xi} \approx \phi_0[\xi+\frac{\gamma v\zeta}{dA}(\omega_0\gamma t)^2]. \qquad (25)$$

This is true including the second order of small quantities (we have also used $\phi_{0\xi}=2\eta/\cosh\xi$). The expression (25) describes the kink (antikink) with velocity decreasing according to the rule

$$V = v\,[1-2(\omega_0\gamma)^2\zeta t/A]. \qquad (26)$$

Note that the results of this section are equally applicable to Yomosa's potential, if $A \to A+B$ is substituted in Eq.(2). In this case the obtained solution takes into account the effects of dissipation for the so-called uncoupled 2π-solitons (Yomosa 1984). In such a way the dissipation effects can be considered in all the above-discussed models.

7. Conclusion

We made here an attempt to present today's status of one trend in modelling DNA: the mechanical plane base-rotator models. These models are called to describe large fluctuational rebuildings in DNA, namely, the opening of base pairs. At present, such attempts are of very oversimplified character but they can be considered as a possible step towards some more realistic description. For the first time, we consistently took into account effects of

dissipation. The perturbation theory scheme we have used is also applicable in considering spatial inhomogeneity that arises from small deviations in the effective moments of inertia of the bases. In the continuum models it is displayed in a spatial dependence of the "frequency" ω_0. Perturbation methods can also be used if the model system acquires an energy from the surroundings. This will be the subject of our next investigation.

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