Chemically driven traveling waves in DNA

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(Received 17 February 1999; revised manuscript received 11 May 1999)

The nonlinear mechanical model constructed in a previous paper [Nuovo Cimento D **20**, 833 (1998)] is developed in order to study the dynamics of the DNA double helix. It is assumed that the hydrophobic interaction between subsequent base pairs may be influenced by a RNA polymerase. The Lagrangian, constructed on the basis of ''geometrical'' properties of the DNA molecule, depends on time and contains first and second derivatives of the twist angle. The energy dissipation term is added to the dynamical equations resulting from the Lagrange formalism. It is proved that the system has pulselike solitary wave solutions for which the dissipated energy is balanced by the energy pumped by the advancing RNA polymerase. The physical interpretation of our solution is the local untwisting of the DNA molecule during transcription of messenger RNA. [S1063-651X(99)00712-6]

PACS number(s): 87.15.He, 87.10.+e

I. INTRODUCTION

The basic form of DNA is double helix, consisting of two sugar-phosphate backbones and a base pairs chain inside. A schematic drawing of the duplex DNA in an unwound hypothetical state, which one can call a planar ladder state, is shown in Fig. 1 (from Calladine and Drew [1]). The distance B between adjacent sugars or phosphates in the DNA chains is roughly 6 Å , while the thickness of the flat part of the DNA base is $A=3.3$ Å , which implies a gap of 2.7 Å between the bases. Because the four DNA bases guanine, adenine, cytosine, and thymine are hydrophobic substances, these bases tend to stay together, and the surrounding water does not fill gaps between them. If the bases are in contact, the distance between their centers is A, smaller than the distance between the adjacent sugars B. This is because the sugar-phosphate backbones must wrap around the base pair chains in order to preserve their length. Elementary geometric considerations enable one to calculate the angle $\Delta\Theta$ by which each phosphate turns relative to its neighboring phosphate along the helix:

$$\Delta\Theta = 2\arcsin\left(\frac{(B^2-A^2)^{1/2}}{2R}\right) = 32.3^o, \tag{1}$$

where $2R=18$ Å is the distance between the corresponding phosphates from the opposite chains. From Eq. (1) it follows that there are roughly $360/32.3 \approx 11$ phosphates per complete turn of the DNA helix. This result closely agrees with experiment: almost all DNA double helices have between ten and 12 phosphates per turn. The above analysis (following Calladine and Drew [1]) suggests that both right- and left-handed duplex helical structures are expected. Although there are, in fact, known examples of both types of double helices, the right-handed forms A and B with 11 and ten phosphates per helical turn are preferred to the left-handed Z form with 12 phosphates per turn.

The base pair sequence codes the genetic information, but from the mechanical point of view it is a nonperiodic chain. The four bases composing DNA have different masses. This poses a problem for all models. Fortunately, the two base pairs composing DNA consist of one light base and one heavy base, so their masses are almost equal. That is, the adenine-thymine (A-T) pair has mass 259 a.m.u., and the guanine-cytosine (C-T) pair is only slightly heavier with mass 260 a.m.u. The total mass per base pair m (i. e., the mass with adjacent sugars and phosphate groups) is approximately 580 a.m.u. Moreover the H-bond interaction coupling the G-C pair is more than twice as strong as that for the A-T pair. Only in an approximation in which one neglects internal degrees of freedom of the base pairs, and treats each base pair as a rigid body, can DNA be regarded as a periodic structure.

The interest in the nonlinear dynamics of DNA started when Englander *et al.* [2] suggested that the existence of solitons propagating along the DNA molecule may be important in a process called ''RNA transcription.'' In the last decade several models (see Gaeta *et al.* [3] for the review) were proposed in order to substantiate this idea in quantitative terms. The scope of RNA transcription is to copy genetic information for DNA into messenger RNA. During this process two DNA strands have to locally separate (local opening of DNA) to let one of the strands serve as a template for the synthesis of a new RNA strand. There are two important models, the one proposed by Yakushevich [4] and improved

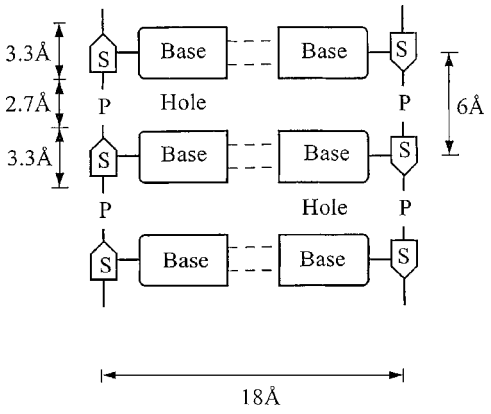

FIG. 1. The scheme of DNA, the hypothetical planar DNA ladder with its key dimensions S (sugar) and P (phosphate).

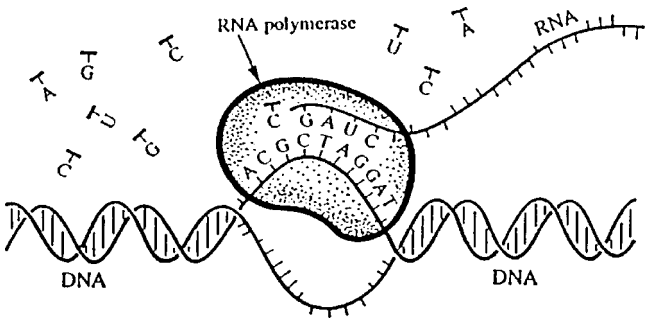

FIG. 2. Transcription of messenger RNA (from Calladine and Drew [1]). The DNA molecule untwists close to RNA polymerase. One of the two DNA strands serves as a template for synthesis of a new RNA strand.

by Gaeta [5], and the second proposed by Peyrard and Bishop [6] which concentrates on transversal openings of base pairs.

In the current paper we propose a different approach to DNA dynamics based on a ''mechanical'' model of DNA dynamics developed by Lipniacki [7]. The constructed model allowed us to describe analytically torsional traveling waves propagating along the DNA molecule. The pulselike solutions described the propagation of an untwisted (or oppositely twisted) region along the molecule. Local untwisting seems necessary for the formation of a transcription bubble (the braided strands cannot separate), and in fact the DNA lost one or two turns in order for the RNA polymerase molecule to function (Fig. 2; also see Calladine and Drew [1]). The untwisted open region, 15-20 base pairs long, together with RNA polymerase, moves along the DNA.

In the previous paper (Lipniacki [7]), the energy dissipation (damping) was not included in the model. However, it seems obvious that the motion of DNA leads to some energy dissipation, due to the nonelasticity of the DNA molecule or to interaction with the solvent. Moreover it is easy to check that when energy dissipation is present, pulse-like solutions cannot exist, unless the energy is somehow added to the system. It was also not explained why the untwisting of the DNA molecule takes place in the vicinity of the RNA polymerase. The present paper will pursue the already proposed model, connecting the mechanism of energy input with the fact that DNA untwists and opens close to the RNA polymerase.

The main idea is the following. In the vicinity of the polymerase the hydrophobic forces between base pairs are weaker than those in the rest of the DNA molecule. This is due to the fact that the RNA polymerase is accompanied by flat oily amino acids such as phenylalanine, tyrosine, and tryptophan, which can insert themselves between the base pairs. Thus, close to polymerase, it is easier to separate base pairs and so untwist the DNA strands. It is known [1] that a hydrophobic substance called ethidium bromide added to the DNA slips between neighboring base pairs, and as the result the DNA untwists. The dependence of the strength of the DNA molecule on the solvent was also confirmed in recent experiments (Smith, Cui, and Bustamante [8]). The hydrophobic forces play a crucial role in stretching DNA up to extensions of 70%, when the separation between bases is 5.8 Å . The motion of the untwisted region is then forced by the motion of the RNA polymerase, which moves along the DNA due to chemical reactions.

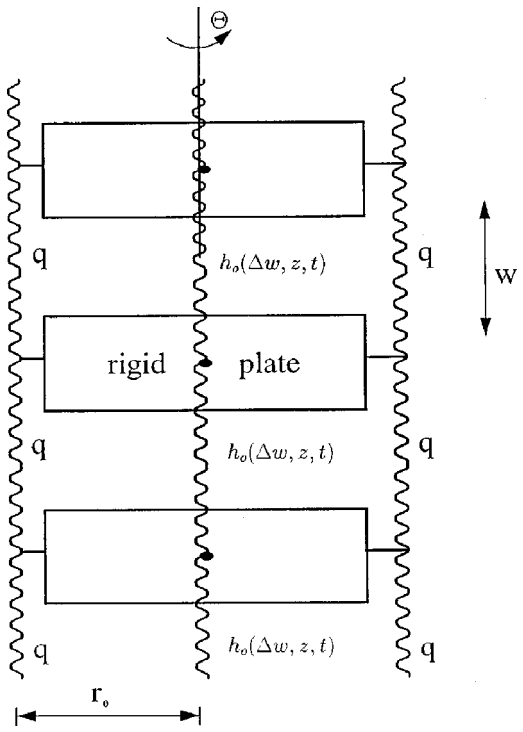

FIG. 3. The schematic picture of the mechanical model. The spring constant of the side spring segments is q, while $h_o(\Delta w,z,t)$ is the energy is the potential energy of hydrophobic interaction between subsequent slabs.

II. DESCRIPTION OF THE MODEL

In the proposed model (Fig. 3) base pairs are represented by rigid plates situated along the z axis. The hydrophobic forces acting between every two subsequent base pairs are represented by springs. The relaxed length of those springs is A; however, it is not assumed that the springs satisfy Hook's law. The sides of slabs are connected by two side springs representing the sugar-phosphate chains. The side spring segments connecting consecutive slabs have a free length B and a spring constant q. The distance between backbone springs and the duplex axis going through the centers of the slabs is r_o . The mass and inertial momentum of each plate is equal to the mass and momentum per base pair, while all the springs are assumed to have no mass. It is assumed that every slab has two degrees of freedom: it can move along and turn around the z axis, and its position is described by a displacement w and a torsional angle θ. When $A<B$, as in real DNA, the system has two natural minima of energy (for which all the springs are in the natural state): a left-hand twisted ladder and a right-hand twisted ladder.

To construct the Lagrangian $L=T-\Phi$ of the system, let us assume that side springs satisfy Hook's law Then the energy of interaction $\Phi_{i,i+1}$ between two adjacent slabs is

$$\Phi_{i,i+1}=h_o(\Delta w-A,z,t)+q(\sqrt{\Delta w^2+4r_o^2\sin^2(\Delta\Theta/2)}-B)^2, \tag{2}$$

where $h_o(\Delta w - A,z,t)$ denotes the potential energy function for the hydrophobic interaction. The h_o dependence on position z and time t is due to the fact that hydrophobic forces depend (as we stated above) on the solvent, and may vary along the DNA molecule. When $\Delta\Theta$ is small, $2\sin(\Delta\Theta/2)$ may be replaced by $\Delta\Theta$ (For $\Delta\Theta = 32^o$ the error is 1.3%).

In the continuum limit,

$$\Delta w = w' A, \quad \Delta\Theta = \Theta' A, \tag{3}$$

the primes denoting differentiation with respect to z. Then the potential energy of the whole chain has the form

$$\Phi = A\int \left[h(w'-1,z,t) + q(\sqrt{w'^2 + r_o^2\Theta'^2} - B/A)^2 + \frac{e_o\Theta''^2}{2}\right] dz, \tag{4}$$

where $h(w'-1,z,t) = h_o(\Delta z - A,z,t)/A$.

The term

$$A\int \frac{e_o\Theta''^2}{2}\, dz \tag{5}$$

has been added to Eq. (4) in order to describe the energy associated with the additional curvature of the side springs when Θ'' differs from zero. This higher order derivative term plays a key role both in the physical interpretation and the mathematical development of the present model. The two zero potential energy states are characterized by

$$w' = \text{const} = 1, \quad \Theta' = \text{const} = \pm\frac{(B^2 - A^2)^{1/2}}{Ar_o}. \tag{6}$$

Without the last term in Eq. (4) the states in which Θ' jumps from

$$+\frac{(B^2 - A^2)^{1/2}}{Ar_o} \quad \text{to} \quad -\frac{(B^2 - A^2)^{1/2}}{Ar_o} \tag{7}$$

will also have a minimum zero energy, which seems unphysical because in those states the side springs (the sugar-phosphate chains) are strongly distorted.

The kinetic energy T is

$$T = \frac{1}{A}\int \left[\frac{m\dot{w}^2}{2} + \frac{J\dot{\Theta}^2}{2}\right] dz, \tag{8}$$

where m and J are the mass and moment of inertia per base pair, and the dot denotes time derivative.

To write the Lagrangian in a simpler form, one may employ units in which $A = 1$; thus let

$$\phi := r_o\Theta, \quad e = e_o/r_o^2, \quad I = J/r_o^2. \tag{9}$$

The potential and kinetic energies of the system are now

$$\Phi = \int \left[h(w'-1,z,t) + q(\sqrt{w'^2 + \phi'^2} - B)^2 + \frac{e\phi''^2}{2}\right] dz, \tag{10}$$

$$T = \int \left[\frac{m\dot{w}^2}{2} + \frac{I\dot{\phi}^2}{2}\right] dz, \tag{11}$$

III. EQUATIONS OF MOTION

In the further analysis we concentrate on the following cases:

(i) In the first case we assume that central springs (like those at the side) satisfy Hook's law [i.e., that the potential function h is quadratic: $h(w'-1,z,t) = k(z,t)(w'-1)^2$] and then we expand the potential energy in power series with respect $(w'-1)$ and ϕ'.

(ii) In the second case we assume that side springs (sugar-phosphate chains) are stretch proof. With that simplification we manage to keep the potential function $h(w'-1,z,t)$ in its general form.

In both cases we introduce a non elastic damping term to the resulting evolution equations.

A. The first case

Let $u' = w' - 1$ and $c = B - 1$. For further analysis we expand the potential energy into a power series with respect to $u' = w' - 1$ and ϕ'. We assume that $u' \sim \epsilon$ with $\epsilon \ll 1$. The order of ϕ' has to be chosen carefully to conserve the main properties of the potential energy function. Let us note that for a fixed $u' < c$ the potential energy is a double well function with respect to ϕ', with the minima at

$$\phi' = \pm\sqrt{2c + c^2 - 2u' - u'^2}, \tag{12}$$

while the global minima of the potential energy as a function of u', ϕ', and ϕ'' are, for $u' = 0$, $\phi'^2 = 2c + c^2$. To conserve this important property one has to expand the potential energy up to fourth order in ϕ'. For small c, typically ϕ' is of order $c^{1/2}$, while u' is of order c. For example, for fixed $\phi' = 0$ the potential energy is minimized for

$$u' = \frac{q}{k+q}c. \tag{13}$$

Moreover, in the second term of Eq. (10), describing the potential energy of the side spring, $u' = w' - 1$ is compared with ϕ'^2. This justifies the assumption

$$u' \sim \epsilon, \quad \phi'^2 \sim \epsilon, \tag{14}$$

where $\epsilon \ll 1$. Hence to within $O(\epsilon^2)$ we have

$$\Phi = \int \left[k(z,t)u'^2 + q((u'-c)^2 + \phi'^2(u'-c) + \phi'^4/4) + \frac{e\phi''^2}{2}\right] dz. \tag{15}$$

One can check that the zero energy state now occurs for $u' = 0$ and $\phi' = \pm\sqrt{2c}$. So here, as in the original case, there are two minimum energy states, and again for any fixed $u' < c$ the potential energy is a double well function of the twist density ϕ'.

The evolution equations for u and ϕ, given by Euler-Lagrange equations with Lagrangian $L = T - \Phi$, are

$$I\ddot{\phi}=q\left(2\phi'(u'-c)+\phi'^3-\frac{e\phi'''}{q}\right)', \tag{16}$$

$$m\ddot{u}=(2(k(z,t)+q)u'+q\phi'^2)'. \tag{17}$$

The dispersive relation for small amplitude oscillations around the relaxed states $u_o=0$ and $\phi=\sqrt{2c}\ z$ in the case $k=$ const can be found in Ref. [7].

Motion of the DNA molecule leads in general to energy dissipation. The mechanical energy can be dissipated due to a friction during the motion through the solvent, or due to nonelasiticity of the DNA molecule. In the first case we may expect that the dissipation term is proportional to the local angular velocity $\dot{\phi}$. There are, however, some fundamental problems going beyond the presented model when including this term; we discuss these when passing to traveling wave solutions.

Now we focus on the second case, and take into account the energy dissipation due to the inelastic torsional motion of DNA molecule. That is, to the right-hand side of Eq. (16) we add the dissipation term $p\dot{\phi}''$ (where $p=$ const >0) proportional to the speed with which the torsion of the sugar-phosphate chains changes. Thus we have

$$I\ddot{\phi}=q\left(2\phi'(u'-c)+\phi'^3-\frac{e\phi'''}{q}\right)'+p\ \dot{\phi}''. \tag{18}$$

We observe that without ''potential energy'' terms, the dynamical equation (18) reads

$$I\ddot{\phi}=p\ \dot{\phi}'', \tag{19}$$

and integrating we obtain

$$I\dot{\phi}=p\phi''+C_o, \tag{20}$$

which is the diffusion equation for the torsional angle ϕ. This suggest that the assumed form $(p\dot{\phi}'')$ of the ''nonelastic'' damping term is resonable.

The role of the dissipation term will become even more clear when we arrive at the final ordinary equation (26) for $X=d\phi/d\tau$, $\tau=(z-vt)$. One may think that the nonelastic dissipation term should be assumed in the form $p\dot{\phi}'$, but in such a case, on the right-hand side one of Eq. (26) one obtains, instead of $-vp\dot{X}$, another term $-vpX$, which is irrelevant since it only modifies the coefficient b. Usually when the order of the original dynamic equation is n, then the order of dissipation term has to be $n-1$.

Now focusing our attention on solitary wave solutions, we transform Eqs. (17) and (18) into ordinary differential equations (ODE's). The solitary waves propagate without changing their form, i.e.,

$$u(z,t)=u(z-vt)=u(\tau),\quad \phi(z,t)=\phi(z-vt)=\phi(\tau), \tag{21}$$

where v is the wave velocity. Furthermore we assume

$$k(z,t)=k(z-vt)=k(\tau). \tag{22}$$

The last assumption reflects the fact that from now on we restrict our considerations to torsional traveling waves forced by advancing RNA polymerase, the presence of which, as stated above, influences the hydrophobic forces between base pairs.

According to assumption (21), $\dot{\phi}=-v\phi'$. We are looking for solutions satisfying $\phi'\to\phi'_o$ for $(z-vt)\to\pm\infty$, where $\phi'_o\neq 0$. This means that $\dot{\phi}\neq 0$ at infinity; in other words, the DNA rotates. This may be a surprising conclusion, but rotation of the DNA probably accompanies the real RNA transcription. Strictly speaking, there are two possibilities: since the RNA polymerase has to follow one of the DNA strands, either the DNA must rotate around its axis, or the RNA polymerase together with the long m-RNA must rotate around the DNA. The latter seems less probable. Of course the rotation of an ''infinitely long'' chain will lead to infinite energy dissipation. Physically, the rotation of the DNA may be due to action of many RNA polymerases which are attached to the DNA and simultaneously make it rotating. The problem is far from being understood. This is why we restrict our considerations to nonelastic damping.

Equations (16)–(21) yield

$$Iv^2\dot{\phi}=q\left(2\dot{\phi}(\dot{u}-c)+\dot{\phi}^3-\frac{e\dot{\phi}}{q}-\frac{vp\ddot{\phi}}{q}\right)+C_1, \tag{23}$$

$$mv^2\dot{u}=2(k(\xi)+q)\dot{u}+q\dot{\phi}^2+C_2', \tag{24}$$

where the dot denotes differentiation with respect to τ. C_1 and $C_2'=C_2-2qc$ are the integration constants, where C_1 and $-C_2$ represent, respectively, the torsional moment and the stretching force applied to the chain at its ends. From Eq. (24) we obtain

$$\dot{u}=\frac{q\dot{\phi}^2-2qc+C_2}{mv^2-2(k(\tau)+q)}, \tag{25}$$

and for $X=\dot{\phi}$ we have

$$e\ddot{X}=-vp\dot{X}+a(\tau)X^3+b(\tau)X+C_1, \tag{26}$$

where

$$a(\tau)=q\left(\frac{2k(\tau)-mv^2}{2(k(\tau)+q)-mv^2}\right), \tag{27}$$

$$b(\tau)=\frac{Iv^4+2qcmv^2-2qC_2-2(k(\tau)+q)Iv^2-4qkc}{2(k(\tau)+q)-mv^2}. \tag{28}$$

For sufficiently small velocity $v^2<2k/m$, the coefficient $a>0$; moreover, $b<0$ when $c(v^2(m-I/c)-2k)-C_2<0$. These two conditions are not very restrictive; the first one is satisfied for any reasonable propagation velocity v (k is of order 10 pN/Å, which implies that our condition is satisfied for velocities as large as 10^9 bases per second). The second condition is satisfied if the strain $(-C_2)$ is not large enough to change the structure of the DNA molecule. Equation (26) can then be rewritten in the form

$$e\ddot{X} = -vp\dot{X} - \frac{\partial U(\tau,X)}{\partial X}, \tag{29}$$

where

$$U(\tau,X) = -\left[\frac{a(\tau)X^4}{4} + \frac{b(\tau)X^2}{2} + C_1 \quad f \quad \right] \tag{30}$$

is a double maximum function with respect to X, provided the torsional moment C_1 is not too large.

To end this section we observe that in the limit $q \to \infty$ (stretch-proof sugar-phosphate chains),

$$a(\tau) = a_o(\tau) = k - mv^2/2, \quad b(\tau) = b_o(\tau) = -2a_o c - Iv^2 - C_2. \tag{31}$$

This means that the assumption that the sugar-phosphate chains are stretch proof does not influence the main properties of the final dynamical equation. In Sec. III B we assume that the side chains maintain their length. Such simplifications allow us to keep the potential function of hydrophobic interaction in its general form.

B. The second case

The potential and kinetic energies are now

$$\Phi = \int \left[h(w'-1,z,t) + \frac{e\phi''^2}{2}\right] dz, \tag{32}$$

$$T = \int \left[\frac{m\dot{w}^2}{2} + \frac{I\dot{\phi}^2}{2}\right] dz. \tag{33}$$

In addition we have the constraint

$$w'^2 + \phi'^2 - B^2 = 0, \tag{34}$$

implying that the side springs maintain their length B.

The evolution equations for w and ϕ given by Euler-Lagrange equations with the Lagrangian

$$L = T - \Phi + \lambda(w'^2 + \phi'^2 - B^2), \tag{35}$$

where λ is the Lagrange multiplier, are

$$I\ddot{\phi} + (e\phi''' + 2\lambda\phi')' - p\dot{\phi}'' = 0, \tag{36}$$

$$m\ddot{w} - \left(\frac{\partial h}{\partial w'} - 2\lambda w'\right)' = 0, \tag{37}$$

$$w'^2 + \phi'^2 - B^2 = 0. \tag{38}$$

As in the first case we included an inelastic friction term $p\dot{\phi}''$ in Eq. (36). Assuming

$$w(z,t) = w(z-vt) = w(\tau), \quad \phi(z,t) = \phi(z-vt) = \phi(\tau), \tag{39}$$

$$h(w'-1,z,t) = h(w'-1,z-vt) = h(w'-1,\tau), \tag{40}$$

we transform the set of equations (36)–(38) into ODE's. After integration we obtain the system of equations

$$Iv^2\dot{\phi} = -e\hat{\phi} - 2\lambda\dot{\phi} - vp\ddot{\phi} + C_2, \tag{41}$$

$$mv^2\dot{w} = \frac{\partial h}{\partial \dot{w}} - 2\lambda\dot{w} + C_1, \tag{42}$$

$$\dot{w}^2 + \dot{\phi}^2 - B^2 = 0, \tag{43}$$

where the dot denotes differentiation with respect to τ. After some simple algebra we obtain the following equation for $X = \dot{\phi}$:

$$e\ddot{X} = X(m-I)v^2 + \left(\frac{\partial h}{\partial \dot{w}} + C_1\right)\frac{\partial \dot{w}}{\partial X} - vp\dot{X} + C_2, \tag{44}$$

with

$$\dot{w} = \sqrt{B^2 - X^2}. \tag{45}$$

Finally,

$$\ddot{X} = -\frac{\partial W(X,\tau)}{\partial X} - \delta\dot{X}, \tag{46}$$

where

$$W(X,\tau) = -\frac{1}{e}\left(\frac{(m-I)v^2X^2}{2} + C_2X + [h(\dot{w}(X),\tau) + C_1\dot{w}]\right) \tag{47}$$

and $\delta = vp/e$.

If $h(\dot{w},\tau)$ is a single minimum function with respect to $\dot{w}$ for any τ (i.e., the potential of the base pair interaction has a single minimum) then $h(X,\tau)$ is a symmetric double well function since $\dot{w}$ is symmetric with respect to X. The potential function $W(X,\tau)$ has precisely two maxima with respect to X (for any τ), satisfying the constraint that the coefficients C_2 and C_1 are not too large. When $C_2 = 0$, $W(X,\tau)$ is symmetric; when $C_2 \neq 0$, $W(X,\tau)$ is not symmetric; and one maximum is higher then the other.

Since the potential function $U(X,\tau)$ appearing in Eq. (29) in Sec. III A is a special case of the potential function $W(X,\tau)$, it is sufficient to examine Eq. (46) only in our further considerations. The homoclinic (heteroclinic) solutions of Eq. (46) correspond to traveling wave pulselike (kinklike) solutions of the initial system of equation (36)–(38) or (17) and (18).

Since the mechanical analogy seems appropriate for the problem [Eq. (46)], we call X the position of the particle, and τ the time. If $W = W(X)$ and $\delta = 0$, Eq. (46) simplifies to

$$\ddot{X} = -\frac{dW(X)}{dX}. \tag{48}$$

This equation can be interpreted as the equation of one-dimensional frictionless motion of a particle in the potential field $W(X)$. If $C_2 = 0$ [see Eq. (47)], then $W(X) = W(-X)$, and Eq. (48) has a heteroclinic solution describing the particle motion from one maximum to the other (starting at τ

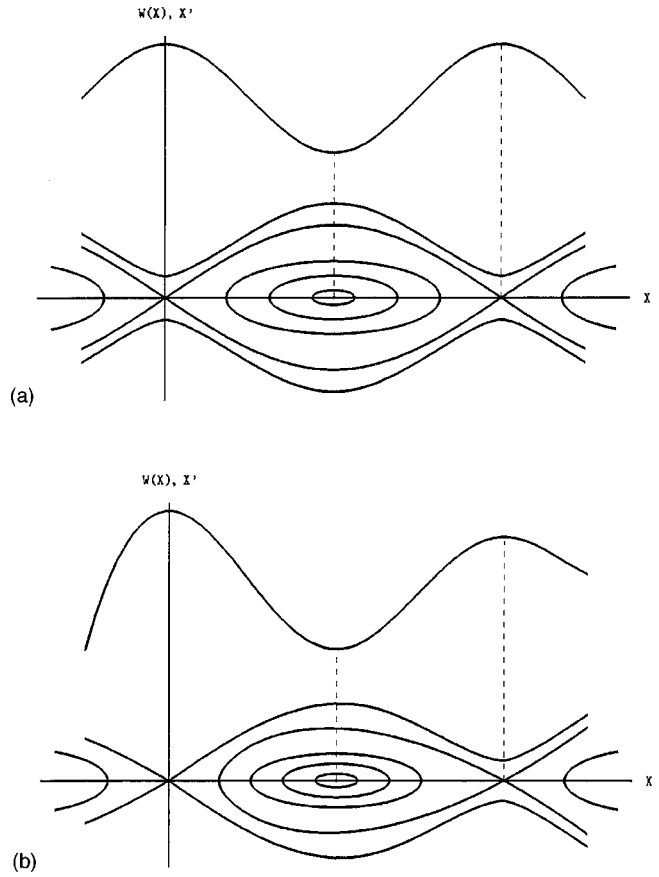

FIG. 4. The potential energy $W(X)$ and phase space $(X,\dot{X})$ diagram of Eq. (48). (a) The maxima have the same height; the heteroclinic orbit spans the two maxima (the two saddle points). (b) The right maximum is lower, and there exists a homoclinic orbit starting and terminating on that maximum.

$=-\infty$ and ending at $\tau=\infty$), [Fig. 4(a)]. If $C_2\neq 0$, then one maximum is lower then the other, and there exists a homoclinic orbit starting and ending on the lower maximum, [Fig. 4(b)].

When $\delta>0$, however, for $W=W(X)$ a homoclinic orbit cannot exist. The term $-\delta\dot{X}$ in Eq. (46) can be interpreted as a friction proportional to the particle velocity. Since the mechanical energy is dissipated, it is obvious that a particle starting from a maximum (with zero kinetic energy) cannot return to this maximum.

If $W_o(X_1)-W_o(X_2)>0$, where X_1 and X_2 are maxima of $W_o(\cdot)$, then, for a properly chosen δ, there exists a heteroclinic orbit ''spanning'' the upper and lower maxima. Recall that $\delta=vp/e$; hence a given δ implies the velocity of the traveling wave. In such a case the velocity of the kinklike traveling wave depends on $W_o(X_1)-W_o(X_2)$, i.e., on the value of the torsional moment C_2 applied to the molecule [see Eq. (45)].

The situation is different when there is a nonzero friction term $\delta\dot{X}$ but the potential $W=W(X,\tau)$ depends on time τ. In this case the dissipated mechanical energy can be balanced by the energy pumped by the varying potential field. In such a case a homoclinic solution may exist. In Sec. IV we show that, under some conditions, Eq. (46) has a homoclinic solution.

IV. EXISTENCE OF THE HOMOCLINIC ORBIT

We confine our considerations to the case when

$$W(X,\tau)=W_o(X)+\epsilon V(X,\tau), \tag{49}$$

and there exists a pair $\tau_1<\tau_2$ such that supp $V(X,\cdot)\in[\tau_1,\tau_2]$ for any X. Let

$$G(X,\tau):=\frac{\partial V(X,\tau)}{\partial X}. \tag{50}$$

We also assume that $W_o(X)$ has precisely two maxima at X_1 and X_2 and $W_o(X_1)\neq W_o(X_2)$ [the last is true if the torsional moment $C_2\neq 0$; see Eq. (47)]. Without loss of generality, we may assume $\Delta E_M:=W_o(X_1)-W_o(X_2)>0$. Equation (46) then takes the form

$$\ddot{X}=\frac{\partial W_o(X)}{\partial X}+\epsilon\ G(X,\tau)-\delta\dot{X}. \tag{51}$$

The last two terms of Eq. (51) will be treated as a perturbation, and the equation

$$\ddot{X}=\frac{\partial W_o(X)}{\partial X} \tag{52}$$

will be called the unperturbed equation.

Let $X_o(\tau)$ be a homoclinic solution of the unperturbed equation such that $X_o(\tau)=X_o(-\tau)$, satisfying

$$\lim_{\tau\to\pm\infty} X(\tau)=X_2. \tag{53}$$

Obviously $X_o(\tau+\tau_o)$ is also the homoclinic solution for any τ_o. Now may state the following theorem.

Theorem: Assume. (1) there exists τ_o such that

$$\int_{\tau_1}^{\tau_2} G(X_o(\tau+\tau_o),\tau)\dot{X}_o(\tau+\tau_o)\ d\tau\neq 0, \tag{54}$$

and (2) $G(\cdot,\cdot)\in C(R^2)$ and $W_o(\cdot,\cdot)\in C^1(R^2)$. Then there exists $\epsilon_o>0$, such that for all $\epsilon\in(0,\epsilon_0)$ there is $\delta_0>0$, such that for all $\delta\in[0,\delta_o]$ there exists a homoclinic solution of Eq. (51) such that $X(-\infty)=X(\infty)=X_2$. Simply put, if the variable part of the potential function $\epsilon\ V(X,\tau)$ is not too large, then for zero or sufficiently small friction term $\delta\ \dot{X}$ there exists a homoclinic solution to Eq. (51). First we prove the following lemma.

Lemma: Under the assumptions of the theorem, we have

$$\sup_{\tau_o}\int_{\tau_1}^{\tau_2} G(X_o(\tau+\tau_o),\tau)\ \dot{X}_o(\tau+\tau_o)d\tau=E^+>0 \tag{55}$$

and

$$\inf_{\tau_o}\int_{\tau_1}^{\tau_2} G(X_o(\tau+\tau_o),\tau)\ \dot{X}_o(\tau+\tau_o)d\tau=E^-<0 \tag{56}$$

We will denote the points τ at which the supremum [Eq. (55)] and infimum [Eq. (56)] occur by τ^+ and τ^-, respectively.

To prove the lemma we note that

$$\int_{-\infty}^{\infty} G(X_o(\tau+\tau_o),\tau)\dot{X}_o(\tau+\tau_o)d\tau_o = \int_{-\infty}^{\infty} G(X_o(t),\tau)\dot{X}_o(t)dt = 0, \tag{57}$$

where $t=\tau+\tau_o$. This is true since $X_o(\cdot)$ is symmetric and $\dot{X}_o(\cdot)$ is antisymmetric. Hence

$$\int_{\tau_1}^{\tau_2}\int_{-\infty}^{\infty} G(X_o(\tau+\tau_o),\tau)\dot{X}_o(\tau+\tau_o)d\tau d\tau_o = 0. \tag{58}$$

Then, if there exists a τ_o for which integral (54) differs from zero, it has to take both positive and negative values; this proves the lemma.

Proof of the theorem: Equation (51) can be rewritten as

$$\dot{X}\ddot{X} + \frac{\partial W_o(X)}{\partial X}\dot{X} = \epsilon G(X,\tau)\dot{X} - \delta\dot{X}^2, \tag{59}$$

and then

$$\frac{dE}{d\tau} = \epsilon G(X,\tau)\dot{X} - \delta\dot{X}^2, \tag{60}$$

where

$$E = \dot{X}^2 + W_o(X) \tag{61}$$

is the mechanical energy of the particle.

The unperturbed Eq. (52) has the form $E=\text{const}$ and the mechanical energy uniquely parametrizes its solutions. First we consider the equation

$$\frac{dE}{d\tau} = \epsilon G(X,\tau)\dot{X}. \tag{62}$$

Let $X_\epsilon^+(\tau)$ denote the solution of the above equation such that $X_\epsilon^+(\tau)=X_o(\tau+\tau^+)$ for $\tau<\tau_1$ (the sense of τ^+ was explained in the lemma). Such a choice is possible since supp $G(X,\cdot)\in[\tau_1,\tau_2]$ for any X. We show that for sufficiently small ϵ there exists finite time τ_3 such that $X_\epsilon^+(\tau_3)=X_2$ (X_2 is the lower maximum). Due to the continuous dependence of solutions on parameters (see Hartman [9]),

$$X_\epsilon^+(\tau) = X_o(\tau+\tau^+) + \epsilon\tilde{X}_\epsilon(\tau) \quad \text{for} \quad \tau\in[\tau_1,\tau_2], \tag{63}$$

where $\tilde{X}_\epsilon(\tau)$ is uniformly bounded for all sufficiently small ϵ.

The mechanical energy E of the particle, whose motion is given by $X_\epsilon^+(\tau)$, remains constant up to time τ_1, and so $E(\tau_1)=E(-\infty)=W(X_1)$. During the time interval $[\tau_1,\tau_2]$ it changes by ΔE_1, where

$$\Delta E_1 = \epsilon\int_{\tau_1}^{\tau_2} G(X_\epsilon^+(\tau),\tau)\dot{X}_\epsilon^+(\tau)d\tau, \tag{64}$$

or, using Eq. (63),

$$\Delta E_1 = \epsilon\int_{\tau_1}^{\tau_2} G(X_o(\tau+\tau^+)+\epsilon\tilde{X}(\tau),\tau)(\dot{X}_o(\tau+\tau^+) + \epsilon\dot{\tilde{X}}(\tau))d\tau. \tag{65}$$

Hence according to the lemma, since $G(\cdot,\cdot)$ is uniformly continuous on $[\tau_1,\tau_2]\times[X_1,X_2]$,

$$\Delta E_1 = \epsilon E^+ + O(\epsilon^2). \tag{66}$$

Hence for sufficiently small ϵ, $\Delta E_1>0$, and moreover $\Delta E_1<E_M$, where we recall that $\Delta E_M=W(X_1)-W(X_2)$. This means that at time τ_2 the particle mechanical energy $E(\tau_2)$ satisfies $X_2<E(\tau_2)<X_1$. Since, starting from time τ_2, the particle will move according to the unperturbed equation $E=\text{const}$, it will pass through the lower maximum X_2 at a finite time (say τ_3).

Let $X_\epsilon^-(\tau)$ denote the solution of Eq. (62) such that $X_\epsilon^-(\tau)=X_o(\tau+\tau^-)$ for $\tau<\tau_1$. In the same manner it can be shown that the mechanical energy of the particle whose motion is described by $X_\epsilon^-(\tau)$ decreases in a time interval $[\tau_1,\tau_2]$, and therefore the particle will remain between the two maxima; i.e., for any $\tau>-\infty$, $X_1<X_\epsilon^-(\tau)<X_2$.

Let $X_{\epsilon,\delta}^+(\tau)$ denote the solution of Eq. (60) such that $X_{\epsilon,\delta}^+(-\infty)=X_2$ and $X_{\epsilon,\delta}^+(\tau_s)=X_\epsilon^+(\tau_s)$, where τ_s is chosen as follows: let τ_{12} be a time, such that $X_\epsilon^+(\tau_{12})=X_{12}$, where X_{12} is the local minimum of $W(X)$ lying between X_1 and X_2. Then $\tau_s=\inf\ (\tau_{12},\tau_1)$. In the same way we define the solution $X_{\epsilon,\delta}^-(\tau)$ corresponding to $X_\epsilon^-(\tau)$.

Again using the theorem for the continuous dependence of the solution on parameters and initial conditions, we can show that, for sufficiently small δ, there exists a finite time (say τ_4) such that $X_{\epsilon,\delta}^+(\tau_4)=X_1$. Obviously for any time $\tau>-\infty$, $X_1<X_{\epsilon,\delta}^-(\tau)<X_2$. If $\delta>0$, then, in addition, $\tau\to\infty$ $X_{\epsilon,\delta}^-(\tau)=X_{12}$, where X_{12} is the minimum between X_1 and X_2.

Thus we have proved the existence of solutions $X_{\epsilon,\delta}^+(\tau)$ and $X_{\epsilon,\delta}^-(\tau)$. The solution $X_{\epsilon,\delta}^+(\tau)$ passes through the lower maximum, while the solution $X_{\epsilon,\delta}^-(\tau)$ does not reach it (Fig. 5). We can regard solutions $X_{\epsilon,\delta}^+(\tau)$ and $X_{\epsilon,\delta}^-(\tau)$ as solutions of Eq. 51, having two different initial condition E_1 and F_1, where

$$E_1 = \begin{bmatrix} X_{\epsilon,\delta}^+(\tau_1) \\ \dot{X}_{\epsilon,\delta}^+(\tau_1)\end{bmatrix} = \begin{bmatrix} X_\delta^+(\tau_1) \\ \dot{X}_\delta^+(\tau_1)\end{bmatrix} \tag{67}$$

and

$$F_1 = \begin{bmatrix} X_{\epsilon,\delta}^-(\tau_1) \\ \dot{X}_{\epsilon,\delta}^-(\tau_1)\end{bmatrix} = \begin{bmatrix} X_\delta^-(\tau_1) \\ \dot{X}_\delta^-(\tau_1)\end{bmatrix}, \tag{68}$$

where X_δ^+ and X_δ^- denote solutions to the equation

$$\ddot{X} = \frac{\partial W_o(X)}{\partial X} - \delta\dot{X}. \tag{69}$$

In Fig. 5 the phase space $(X,\dot{X})$ is shown. The trajectories of Eq. (69) are denoted by continuous lines, while the dashed lines are trajectories of Eq. (51) in the time interval $[\tau_1,\tau_2]$.

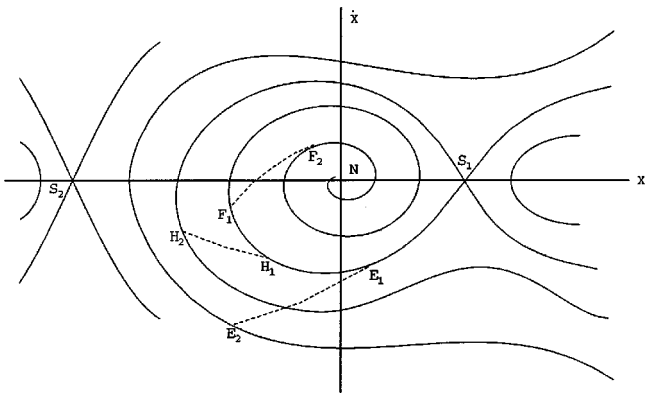

FIG. 5. The phase space diagram. The continuous lines denote the trajectories of Eq. (69). The right maximum S_1 is lower than S_2; due to friction the trajectory starting from the right saddle point S_1 terminates at the node point N. The additional force $\epsilon G(X,\tau)$ during the time interval $[\tau_1,\tau_2]$ prevents the trajectories of the perturbed equation (dashed lines) (51) from following the trajectories of Eq. (69). The trajectory of solution $X^+_{\epsilon,\delta}(\tau)$ (see text) starts at S_1 then passes through E_1 and E_2; the trajectory of $X^-_{\epsilon,\delta}(\tau)$ also starts at S_1 and then passes through F_1 and F_2. The homoclinic orbit starts at S_1, passes through H_1 and H_2, and terminates at S_1.

The trajectories corresponding to solutions $X^+_{\epsilon,\delta}(\tau)$ and $X^-_{\epsilon,\delta}(\tau)$ follow the trajectory of Eq. (69) up to time τ_1, when the force $G(X,\tau)$ starts acting. At τ_1 those trajectories are at two different points E_1 and F_1; then at time τ_2 they are at points E_2 and F_2, respectively. Starting from time τ_2 the trajectories corresponding to solutions $X^+_{\epsilon,\delta}(\tau)$ and $X^-_{\epsilon,\delta}(\tau)$ follow two different trajectories of Eq. (69); one of them passes through the lower maximum, while the other does not reach it.

On the basis of the theorem for the continuous dependence of solutions on initial conditions (see Hartman [9]) we may conclude the following. Any trajectory of Eq. (48) starting at τ_1 at a point on the line connecting E_1 with F_1 has to reach the line connecting F_2 with E_2 at time τ_2; such a line crosses the trajectory of Eq. (69), tending to the saddle point S^1 (see Fig. 5). Hence there exists a point H_1 lying on the trajectory connecting E_1 and F_1, such that trajectory of Eq. (48) starting at time $\tau=\tau_1$ from that point reaches, at time τ_2, a point (say H_2), on the other trajectory of Eq. (69) tending to the saddle point S_1. This means that solution $X^h_{\epsilon,\delta}(\tau)$, such that

$$\begin{bmatrix} X^h_{\epsilon,\delta}(\tau_1) \\ \dot{X}^h_{\epsilon,\delta}(\tau_1) \end{bmatrix} = H_1 \tag{70}$$

is the homoclinic orbit; this proves the theorem.

Remarks on the theorem: (1) Assumption (1) is in fact very weak; probably it is equivalent to the assumption that $G(\cdot,\cdot)\not\equiv 0$ on $(X_1,X_2)\times(-\infty,\infty)$. For the existence of pulselike solutions to the systems of equations (36)–(38) or (17) and (18), it is not important that the presence of the RNA polymerase makes the hydrophobic interactions weaker. It is only necessary that these interactions, in the vicinity of the polymerase, are different than in rest of the DNA molecule.

(2) Probably a homoclinic solution of Eq. (48) also exists (under some additional assumptions) when $G(X_1)=G(X_2)$ i.e., when the torsional moment applied to the chain is zero. However, this case is more delicate since the energy pumped by the varying part of the potential may cause the trajectory to pass over the other (then starting) maximum.

V. CONCLUSION

Based on the proposed model of DNA dynamics, we proved the existence of dissipative traveling (pulselike) waves propagating along the DNA molecule. The existence of these waves, within the limits of the considered model, is due to two main facts.

(i) The potential energy of the DNA chain Φ is a double well function of the twist density Θ'. It follows from the assumed model that Φ is symmetric with respect to Θ', but for existence of solutions it is not necessary. In the relaxed state the chain has a uniform twist densities $\Theta'=\Theta'_o=[(B^2-A^2)^{1/2}/Ar_o]$ [Eq. 6)] or $\Theta'=-\Theta'_o$. Let us focus on the first case. Now, applying the torsional moment at the ends of the chain, one can add some positive twist to the system. This additional twist will spread uniformly over the chain, making the twist density $\Theta>\Theta_o$. On the other hand, applying the opposite torsional moment, one can remove twist from the chain, making the average twist density $\Theta<\Theta_o$. When the average twist density becomes smaller, the energy of the chain grows to some critical point when the system can jump to a state in which a part of the chain has a twist opposite to the rest. If the parameter e_o at Θ'' is small, then it is ''energetically favorable'' to create an oppositely twisted segment of the chain even if the average twist density is close to Θ'_o. The untwisted (or oppositely twisted) segment thus created can then move along the DNA chain. In fact the real DNA is usually underwound, and has a slightly smaller twist density than in the relaxed state. However, the problem is more delicate, since if one underwinds DNA by ten turns, nine turns will be absorbed in supercoiling (writhe), and only one turn will be absorbed in twist (see Calladine and Drew [1], Chap. 6).

(ii) The energy dissipated due to local twisting and untwisting of the DNA molecule is balanced by the energy pumped by the varying hydrophobic potential of the base pair interaction. Without that additional energy, any nonzero dissipation implies that pulselike solutions cannot exist.

The pulselike solutions obtained for the mechanical system correspond to a local untwisting of the DNA molecule during RNA transcription. The scope of this process is to copy the DNA genetic information into the RNA. During the transcription the DNA, must untwist locally to let one strand serve as a template for synthesis of a new RNA strand (Fig. 2 and Ref. [1]). The untwisted open region, 15–20 base pairs long, then moves along the DNA. The transcription process (and so the untwisting of the DNA molecule) takes place in the vicinity of the protein called RNA polymerase. The vicinity of the RNA polymerase probably implies that the hydrophobic forces between the base pairs become weaker. This can be due to the fact that the RNA polymerase is accompanied by flat oily amino acids such as phenylalanine, tyrosine, and tryptophan, which can insert themselves between the base pairs [1]. Within the framework of our model

this effect is interpreted as a variation of the hydrophobic potential. The advancing RNA polymerase forces, by chemical processes, a large scale ''mechanical'' motion (the untwisting) of DNA molecule.

Unfortunately within the limits of our model we cannot describe the opening of the DNA (separation of two DNA strands), because we have assumed that each base pair is a rigid body. To analyze the opening one has to include at least one more degree of freedom to describe the separation of the two bases forming a pair. This goes far beyond our model. Nevertheless one can check that in the short untwisted region, the separation between subsequent base pairs is larger then in the relaxed DNA chain. This means that coupling between subsequent base pairs is weaker. According to the Peyrard-Bishop model [6], the smaller the coupling between base pair the lower the temperature of the thermal denaturation of the DNA molecule. This means that thermal fluctuations which are too small to denaturate DNA at a physiological temperature can lead to the opening of an untwisted DNA region.

ACKNOWLEDGMENTS

The author would like to express his gratitude to Professor H. Zorski, Dr. B. Kazmierczak and Dr. M. Wojciechowski for discussions and corrections of the manuscript. This work was supported by KBN Grant No. 585/T07/97/13.

[1] C. R. Calladine and H. R. Drew, *Understanding DNA* (Academic Press, New York, 1992).
[2] S. W. Englander, N. R. Kallenbach, A. J. Heeger, J. A. Krumhansl, and S. Litwin, Proc. Natl. Acad. Sci. USA **777**, 7222 (1980).
[3] G. Gaeta, C. Reiss, M. Peyrard, and T. Dauxois, Riv. Nuovo Cimento **17**, 1 (1994).
[4] L. V. Yakushevich, Phys. Lett. A **136**, 413 (1989).
[5] G. Gaeta, Phys. Lett. A **190**, 301 (1994).
[6] M. Peyrard and A. R. Bishop, Phys. Rev. Lett. **62**, 2755 (1989).
[7] T. Lipniacki, Nuovo Cimento D **20**, 833 (1998).
[8] S. B. Smith, Y. Cui, and C. Bustamante, Nature (London) **271**, 275 (1996).
[9] P. Hartman, *Ordinary Differential Equations* (unpublished).