PART II

BIOSYSTEMS AND MOLECULAR SYSTEMS

DYNAMICS OF BREATHER MODES IN A NONLINEAR "HELICOIDAL" MODEL OF DNA

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ABSTRACT: Via a recent model with an additional helicoidal coupling, the dynamics of breathers modes in DNA are studied analytically and with the use of numerical simulations. It is shown that these excitations are longlived and can match experimentally observed fluctuational openings.

1. INTRODUCTION

Biological macromolecules undergo a complex dynamics and the knowledge of their motions provides insights into biological phenomena. Recently, attention was focused on dynamics of large amplitude localized excitations in DNA [1–4], in which the double helix fluctuates between an open state and its equilibrium structure. These oscillatory states, also called breathing modes [5] or fluctuational openings, are expected to be precursor states for the local denaturation observed during DNA transcription or thermal denaturation. In these studies, the molecule is modeled by two parallel chains of nucleotides, linked by nearest neighbor harmonic interactions along the chains and the strands are coupled to each other by Morse potentials which represent the bonding inside one base pair. Such a model does not include the helical geometry of the molecule.

But, one of the consequences of the helical structure is that nucleotides which are far apart in the one-dimensional model can be close enough in the three-dimensional structure to be connected by hydrogen-bonded water filaments. These strong water filaments has been suggested by indirect experiments [6] and results of Monte Carlo simulations [7]. They connect a phosphate group P_n at one side of the major groove with an another phosphate group $P_{n\pm4}$ at the opposite side. Therefore, in order to take into account the presence of this dynamically stable filament, the model must include a coupling between the nth nucleotide on one strand and the $n+h$ one on the other ($h=4$ according to the experiments). Such an extension was carried out by Gaeta [8], but he considered only

its consequences on the dispersion curves of the small amplitude excitations of the molecule. We consider here the nonlinear excitations in the extended model and show how the additional coupling increases the ability of the molecule to bear rather broad and sufficiently large amplitude breatherlike modes, which propagate easily along the molecule.

2. MODEL

In our model we consider a simplified geometry for the DNA chain in which, we have neglected the assymetry of the molecule and we represent each strand by a set of point masses wich correspond to the nucleotides. The characteristics of the model are the following:

(i) Like Peyrard et al [1], we only take into account transversal motions. The displacement from equilibrium of the nth nucleotide is denoted u_n (respectively v_n) for the chain C_1 (resp. C_2).

(ii) Two neighboring nucleotides of the same strand are connected by harmonic potential because we assume that the displacements due to the bubbles change only gradually from one site to the next. On the contrary, the bonds connecting the two bases belonging to different strands are extremely stretched when the double helix open locally: their nonlinearity must not be ignored. We use a Morse potential to represent not only the hydrogen bonds, but the repulsive interactions of the phosphate, and the surrounding solvent action.

(iii) Finally, we add to the model introduced by Peyrard and Bishop, a harmonic coupling which takes account of the helical geometry discussed above. It connects the nth mass on the chain C_1 to both the $(n+h)$th and $(n-h)$th masses on chain C_2.

Therefore the Hamiltonian is written as

$$H = \sum_n \Big[\tfrac{1}{2}m(\dot{u}_n^2 + \dot{v}_n^2) \quad + \tfrac{1}{2}k\Big[(u_n - u_{n-1})^2 + (v_n - v_{n-1})^2\Big] \\ + D\Big[e^{-a(u_n - v_n)} - 1\Big]^2 \quad + \tfrac{1}{2}K\Big[(u_n - v_{n+h})^2 + (u_n - v_{n-h})^2\Big]\Big] \quad (1)$$

where the four terms are respectively the kinetic energy of transverse vibrations, the potential energy of the longitudinal, transverse (analog to a substrate potential) and helicoidal connections. Here k (respectively K) is the harmonic constant of the longitudinal (resp. helicoidal) spring, m the nucleotide mass and D (resp. a) the depth (resp. width) of the Morse potential.

Using the variables $x_n = (u_n + v_n)/\sqrt{2}$ and $y_n = (u_n - v_n)/\sqrt{2}$, which represent the in-phase and out-of-phase motions respectively, the dynamical equations are then:

$$\begin{cases} m\ddot{x}_n = k(x_{n+1} + x_{n-1} - 2x_n) & +K(x_{n+h} + x_{n-h} - 2x_n) \quad (2) \\ m\ddot{y}_n = k(y_{n+1} + y_{n-1} - 2y_n) & -K(y_{n+h} + y_{n-h} + 2y_n) \\ & +2\sqrt{2}aD(e^{-a\sqrt{2}y_n} - 1)e^{-a\sqrt{2}y_n} \quad (3) \end{cases}$$

The two equations decouple exactly and we find two linear dispersion relations (an acoustical and an optical branch). The introduction of the new coupling affects the spectrum [9], by increasing the frequencies and introducing oscillations in agreement with Gaeta's results [8].

3. BREATHER IN THE SEMI-DISCRETE APPROXIMATION

Let us focus our attention on the nonlinear equation (3), which includes the only degree of freedom interesting for the local denaturation: the stretching y_n between two nucleotides of different strands.

We are interested in collective oscillations which are large enough to be strongly anharmonic, but still much smaller than the motions which result in permanently open states, where the nucleotides reach the plateau of the Morse potential. In this hypothesis, the atoms oscillates near the bottom of the potential well, so that we assume $y = \varepsilon\phi$ (where $\varepsilon \ll 1$) and expand the substrate potential to fourth order terms in $\varepsilon\phi$. The equation of motion is then:

$$\ddot{\phi}_n = \frac{k}{m}(\phi_{n+1} + \phi_{n-1} - 2\phi_n) \quad -\frac{K}{m}(\phi_{n+h} + \phi_{n-h} + 2\phi_n) \\ -\omega_g^2(\phi_n + \alpha\phi_n^2\varepsilon + \beta\phi_n^3\varepsilon^2) \quad (4)$$

by setting $\omega_g^2 = 4a^2D/m$, $\alpha = -3a/\sqrt{2}$ and $\beta = 7a^2/3$.

According to the experimental results, the problem implies two times-scale: one corresponds to the vibration of the particle around its equilibrium position and the second, much larger, to the propagation of a collective coherent stucture along the chain.

So we will use the reductive perturbation method in which we expand in the small parameter ε and, using $\theta_n = qn\ell - \omega t$ (where ω is the optical frequency of the linear approximation and ℓ the distance between adjacent nucleotides on the same strand), we substitute

$$\phi_n(t) = \left[\varepsilon\left[F_1(\varepsilon n\ell, \varepsilon t)e^{i\theta_n} + \varepsilon^2\left(F_0(\varepsilon n\ell, \varepsilon t) + F_2(\varepsilon n\ell, \varepsilon t)e^{i2\theta_n}\right)\right] + cc + O(\varepsilon^3)\right. \tag{5}$$

in (4) by using the semi-discrete approximation [10] (the complete continuum limit would be too restrictive for DNA, where discreteness effects may be important).
Indeed, as we limit ourselves to large enough width excitations, we can determine the envelope in the continuum limit, as function of the slow variables $Z = \varepsilon z$ et $T = \varepsilon t$, while the fast oscillations of the quasiharmonic carrier, inside the envelope, are treated exactly. Equating the coefficients of ε for each harmonic, we get $F_0 = \mu\ |F_1|^2$ and $F_2 = \delta\ F_1^2$, and finally obtain the Nonlinear Schrödinger (NLS) equation for the envelope function F_1:

$$i\frac{\partial F_1}{\partial \tau} + P\frac{\partial^2 F_1}{\partial S^2} + Q|F_1|^2 F_1 = 0 \tag{6}$$

where we have made the transformation $\tau = \varepsilon T$ and $S = Z - V_g T$,
with the linear group velocity $V_g = \ell\left[k\sin(q\ell) - Kh\sin(qh\ell)\right]/m\omega$,
the dispersion coefficient $P = \left[\ell^2\left(k\cos(q\ell) - Kh^2\cos(qh\ell)\right)/m - V_g^2\right]/2\omega$
and the nonlinear one $Q = -\omega_g^2[2\alpha(\mu + \delta) + 3\beta]/2\omega$.

We will briefly discuss the stability of analytic solutions of NLS, which depends on the signs of PQ. However, to simplify this study, we expand these quantities to first order terms in q (a numerical study shows that the results of the stability discussion are almost unaffected by this expansion), since in next section we limit ourselves to large width bubbles, ie $q \ll 1$.

In this limit, P has the sign of $(k - Kh^2)$ and Q of $(1 - 7K/8a^2D)$. Therefore the solutions changes qualitatively, depending on the value of K. PQ is negative for $k/h^2 \leq K \leq 8a^2D/7$; in this case, the solution of (6) is a finite amplitude plane wave with a dip near $S - u_e\tau \simeq 0$, called a dark-soliton (or a enveloppe hole), which does not correspond to the small amplitude limit of breather modes. For $0 \leq K \leq k/h^2$ (this case includes the usual model without helicoidal coupling) and $8a^2D/7 \leq K$, PQ is positive; we have plane waves solutions, unstable because of modulational (or Benjamin-Feir) instability, and a localised envelope solution, with a vanishing amplitude at $|z| \to \infty$: such a solution has the appropriate shape to represent breathing modes in DNA.

Therefore, the solution of (6) is then:

$$F_1(S,\tau) = A\,\mathrm{sech}[\frac{1}{L_e}(S-u_e\tau)]\exp[i\frac{u_e}{2P}(S-u_c\tau)] \qquad (7)$$

with u_e and u_c the velocities of the envelope and carrier waves, the amplitude
$A=\sqrt{(u_e^2-2u_eu_c)/2PQ}$ and the width $L_e = 2P/\sqrt{u_e^2-2u_eu_c}$. The envelope soliton, solution of (4), is a plane wave with a frequency corrected for the nonlinearity, an amplitude modulated by a sech-type envelope modified by the second harmonic and the non-oscillating components. By setting $V_e = V_g+\varepsilon u_e$, $\Theta = q+\varepsilon u_e/2P$ and $\Omega = \omega+(V_g+u_c\varepsilon)\varepsilon u_e/2P$, it reads:

$$y_n(t) = 2\varepsilon A\,\mathrm{sech}[\varepsilon(n\ell-V_et)/L_e]\Big[\cos(\Theta n\ell-\Omega t)$$

$$+\varepsilon A\,\mathrm{sech}[\varepsilon(n\ell-V_et)/L_e]\times\Big(\mu/2+\delta\cos[2(\Theta n\ell-\Omega t)]\Big)\Big] \quad +O(\varepsilon^3)$$

When $K < k/h^2$, we obtain a very narrow pulse, almost identical to those found in the model without helicoidal interactions[4] (because K approaches 0). On the contrary, when $K > 8a^2D/7$, the solution is much broader and has a larger amplitude so that it could provide a better representation of the fluctuational openings of DNA. We have investigated its stability numerically.

4. NUMERICAL RESULTS

The lifetime of the solutions determined above is an important parameter, because only long-lived excitations can be detected experimentally. First we discuss briefly the numerical technique, and then we compare the numerical and theoretical results.

Basically, we perform the simulation by using a continuum breather as an initial condition in the discrete lattice, with the complete Morse potential. Then, we simulate the ensuing propagation of the pulse, solving the Newtonian equations of motion with a fourth-order Runge-Kutta method. The timestep Δt is chosen so that the total energy of the system is conserved to a relative accuracy better than 10^{-3}.

The question of the choice of parameters for this model is still a controversial topic, as shown by the debate over these values in the literature[11]. We have chosen a dissociation energy $D = 0.1\ eV$, $a = 2\ \mathring{A}^{-1}$, coupling constants $k = 1.5\ eV/\mathring{A}^2$ and $K = 0.5\ eV/\mathring{A}^2$, a

distance between base pairs $\ell = 3.4$ $\AA$ and a mass of 300 m.u. for each nucleotide. To generate the bubbles, we choose a small value for the wave vector ($q = 0.01$ $\AA^{-1}$) and therefore th wavelength of the carrier wave is in the range of the envelope width: the solution is similar then to a local opening which oscillates.

As long as the amplitude remains in the region where the Taylor's development is justified (typically where y is lower than the Morse potential inflection point), our approximations are valid so that the solution can be expected to be stable. In order to describe the large amplitude fluctuational openings observed in DNA, we must however consider initial conditions with a larger amplitude.

The figure 1 shows the motion of a breather with an initial amplitude of 1 $\AA$ and a half-width of 18 nucleotides. We can see that, when the motion begins, the amplitude adapts to the real substrate potential. The figure exhibits an amplitude modulation not explained by the calculations performed in the limit of small displacements, ie in the bottom of the Morse well.

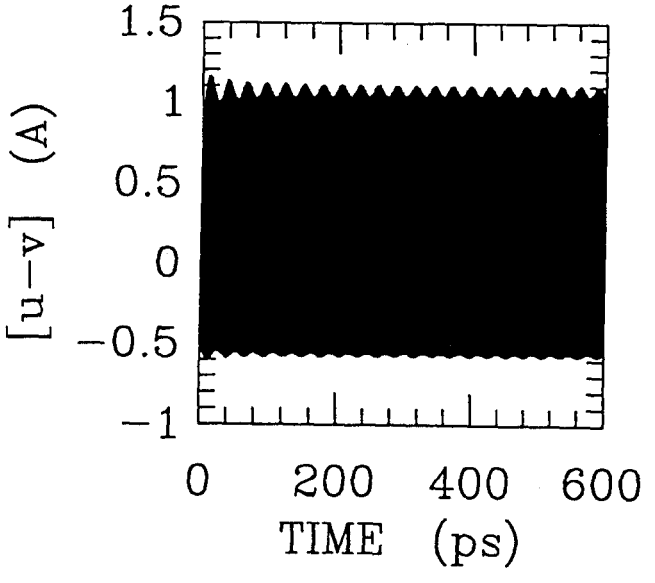

Fig 1: $(u - v)$ vs time for the center of the breather ($\varepsilon = 0.007$, $u_e = 10^3$ $\AA/ps$ and $u_c = 0$ $\AA/ps$). The figure contains about 1000 oscillations of the breather.

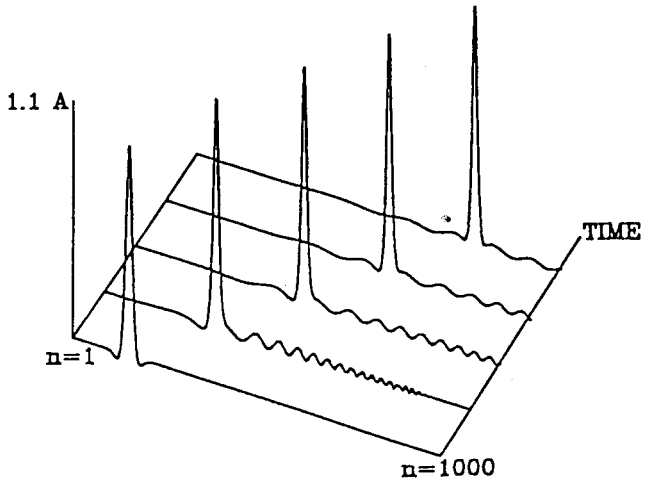

Fig 2: Propagation of the breather along the chain (only 1000 nucleotides are represented). The transverse stretchings are shown every 250 oscillations, when the position of the breather center is at its maximun. Note the assymetry of the backward and forward radiation patterns.

Figure 2 shows these excitations to be very long-lived, although some radiation is emitted by the breather. In spite of this radiation, it should be noticed that the decrease in amplitude is only very weak.

In order to analyse the emitted waves, we have studied the amplitude of the stretching at a distance of 100 particles away from the center of the breather. After the first burst due to adaptation, the radiative rate decreases, and finally corresponds to a permanent emission of resonant phonons. Indeed, a temporal Fourier transform of the same simulation data, started at $t \simeq 400\ ps$, shows that the frequency of the breathing oscillation $\omega_B = 11.20\ ps^{-1}$ is about 1 % higher than the analytical value; the frequency of the radiated phonons is $\omega_P = 10.97\ ps^{-1}$, which coincides with ω within 0.2 % and attests the coupling mechanism of the breatherlike motion to phonons radiation.

The position of the frequency in the bottom of the dispersion relation ($V_g \simeq 0$), explains the slow speed of the radiations packets, compaired to the speed of the burst due to adaptation. Besides, the propagation speed of the breather $V_e = 3.7\ \mathring{A}/ps$, is about 20% less than the theoretical value, because of the discreteness effects which usually tends to slow down the motion.

5. CONCLUSION

Our primary aim was to construct a new extended model for the coherent dynamics of bubbles in DNA. We considered, on one hand, first-neighbour harmonic longitudinal and nonlinear transverse interaction and, on the other hand, an harmonic helicoidal coupling, due to transgroove hydrogenbonded water filaments. Then envelope solitons, solutions of the NLS equation were obtained using a perturbation approach and simulation results were used to show the coupling mechanism between the motion of the breather and phonons radiation. Note that the addition of the helicoidal term, introducing modifications in P and Q, has created a special zone without breather modes. We emphasize that this model can have large amplitude broad oscillations which better correspond to the fluctuational openings of DNA, whereas the previous model with similar parameters cannot.

Nevertheless, it is obvious that before obtaining a suitable description of DNA, we have to take into account the local assymetry of the two helices, as well as the second principal source of nonlinearity which appears as DNA chains unwind: the bistability of the sugar ring, which allows sugar puckering modes.

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