DNA Transcription Mechanism with a Moving Enzyme

Julian Juhi-Lian Ting
Institute of Atomic and Molecular Sciences, Academia Sinica, P.O.Box 23-166, Taipei, Taiwan 106, R.O.C.

Received (February 9, 2008)
Revised (revised date)

Previous numerical investigations of an one-dimensional DNA model with an extended modified coupling constant by transcripting enzyme are integrated to longer time and demonstrated explicitly the trapping of breathers by DNA chains with realistic parameters obtained from experiments. Furthermore, collective coordinate method is used to explain a previously observed numerical evidence that breathers placed far from defects are difficult to trap, and the motional effect of RNA-polymerase is investigated.

1. Introduction

The editors of Science, Culotta & Koshland [1994], announced in the last issue of 1994 that ‘the molecule of 1994’ is DNA. One can still find many papers in the physical literature about DNA recently. However, most physicists are concerned about its statistical properties by analyzing some database of DNA sequences, for instance Azbel’ [1995] found DNA sequences have no long-range correlations, instead of dynamical properties analyzed below.

An artistic plot of DNA which appeared on the cover page of that issue of Science and most textbooks of biochemistry is similar to Fig. 1. As one can see, it is a double-helix with hydrogen bonds connecting those two strands. Of course, this is a simplified picture. However, Peyrard & Bishop [1989] untwisted this ladder like DNA, and wrote down its equation of motion.

Biologists told us that transcription of RNA is the first step in a chain of events leading to expression of the genetic information encoded in double-stranded DNA. During this process RNA-polymerase will attached to DNA. Erie et al. [1993] consider the role of RNA-polymerase in transcription is to synthesize, under the DNA template, the nascent RNA chain with high fidelity and at reasonable rates. However, for physicists the enzyme may play an additional role before transcription, i.e. to focus thermal energy so that the double-helix can be opened.

Englander et al. [1980] have proposed the existence of solitons on DNA helices more than 15 years ago. Technical difficulties prevent direct observation of solitons on DNA. However, Urabe & Tominaga [1981] have Raman spectra showing mode softening which might be accounted by the existence of breather traveling. On the

*E-mail address: jlting@gate.sinica.edu.tw
other hand, since DNA is a kind of polymer and solitons have been recognized as important conformational excitations in polymers. Furthermore, numerical and analytical investigations of the Peyrard-Bishop model of DNA, which can be rationally deduced from a real DNA atomic structure, show the existence of breathers traveling on DNA chains. We are now more confident about the existence of breathers on DNA chains today.

Figure 1.: An artistic plot of DNA.

Forinash et al [1991,1994] considered the interaction of enzyme with DNA during transcription as an isolated impurity. In a previous paper, Ting & Peyrard [1996] considered numerically the possibility of breather trapping by a continuous defect and by a multiple scale analysis the necessary condition for trapping to be a reduced coupling constant within the defect area. The conclusion was loose about whether the breather will be trapped by a real DNA. Due to limited computing resources, numerical integrations were only carried out to about 5000 time steps. However, Dauxois & Peyrard [1993] indicated that DNA is a discrete object and the behaviour of a breather at this region of coupling is mainly governed by discrete effect. In that case a stable breather should be thin and move slowly. It is the purpose of this paper to extend those numerical integration to longer time to investigate the long time behaviour of that kind of breather motion. The second purpose of this paper is to extend previous collective coordinate method to show the difficulty of trapping of a far away breather and to consider the effect of moving enzyme, because Erie et al. [1993] told us that RNA-polymerase is actually moving.

2. The Peyrard-Bishop DNA Model

The Peyrard-Bishop model considers a harmonic coupling for neighboring sites and within the same strand, while an anharmonic Morse coupling between strands. A transformation into normal coordinate is made and the longitudinal mode thrown
away, because it is too small. The equations obtained, in dimensionless form, read

\[ \frac{\partial^2 y_n}{\partial t^2} - k_{n+1}(y_{n+1} - y_n) + k_n(y_n - y_{n-1}) - 2e^{-y_n}(e^{-y_n} - 1) = 0, \tag{1} \]

in which \( y_n \) is the relative displacement between strands and \( k_n \) is the coupling constant between \( y_n \) and \( y_{n-1} \). Because we have untwisted the double-helix, there is no difference between A-, B- or Z- types of DNA. Furthermore, the present model does not taken specific DNA sequence into account. Ansari et al. [1995] told us, protein contact DNA at certain sites and bend DNA towards itself as shown in Fig. 2. This will results in a reduced coupling constant for the outside strand. Presumably, enzyme can function as a kind of lens to focus some thermo fluctuation waves present in normal physiological condition, traveling along the strand.

Figure 2.: An artistic plot of a DNA with enzyme, showing the enzyme contact DNA at multiple sites and bend DNA towards itself.

2.1. Long-time numerical integrations

Previous numerical integrations can be summarized as the following: Taller breathers, hence thinner, can be trapped by a defect with reduced coupling constant, while shorter breathers are broader and result in only concentrated energy and pass through. Therefore trapping can be controlled by breather’s amplitude. Furthermore, these two points indicate breathers move collectively as rigid bodies just like bike wheels.

One may wonder whether the results obtained in the previous paper are applicable to more realistic cases. In real DNA one has \( k_n \approx 0.13 \) to 0.15. Two pictures for trapping by realistic DNA are shown in Fig 3. These breathers are so weak,
i.e. move so slowly, so that they are vulnerable to the presence of defect or other breathers. In Fig. 4(a) the defect pattern is reversed in comparison with Fig. 3(a). But we found quite different picture for the breather motion and they were attracted by the region of lowered coupling constant. Fig. 4(b) shows two breathers, the same as in Fig. 3(a) except for their separation, attracting each other.
Figure 3.: Half-tone plots of the energy distribution of breather evolutions, left, and the corresponding amplitudes, right, from direct numerical integration of Eq. (1). In each figure the top insert shows the variation of the coupling constant used for the calculation, while the right inserts show snap-shots of the breather energy or amplitude distributions. Defects positions are shown in the plots axis. The breathers start from $X(0) = 130, 240, K_n = 0.15$ outside the defect, the amplitude of sinusoidal defect is 0.05 and (a) $u_c = 0.14, 0.13, u_e = -0.05, -0.06$. (b) $u_c = 0.13, 0.11, u_e = -0.04, -0.03$. 
DNA Transcription Mechanism
Figure 4.: Both figures are the same as Fig. 3(a), except (a) the defect pattern is reversed. (b) the initial breather position are closer.

2.2. Collective coordinate method for moving defect

Following Remoissenet [1986], a slightly different derivation from the one used before is used below to consider the effect of moving enzyme. Firstly, in the continuum limit with a Taylor expansion in the potential term which assumes small
amplitude excitation Eq. (1) became,

$$\frac{\partial^2 y}{\partial t^2} - \frac{\partial}{\partial x} \left( k_1 \frac{\partial y}{\partial x} \right) + 2(y - \frac{3}{2}y^2 + \frac{7}{6}y^3) = 0 .$$ \hspace{1cm} (2)

Because of the small oscillation assumption, we have $y \approx \epsilon \phi$ and

$$\phi = F_1 e^{i\theta} + F_1^* e^{-i\theta} + \epsilon(F_0 + F_2 e^{2i\theta} + F_2^* e^{-2i\theta}) + O(\epsilon^2) ,$$ \hspace{1cm} (3)

in which $F_1 = F_1(x_1, t_1)$ and $F_2 = F_2(x_1, t_1)$ with $x_1 = \epsilon x$ etc.. This expansion is equivalent to

$$\phi = F_0 + \epsilon F_1 + \epsilon^2 F_2 + O(\epsilon^3)$$ \hspace{1cm} (4)

used before. Furthermore, for low frequency breathers we considered, we have $\theta \approx -\omega t$, and

$$\frac{\partial}{\partial x} = \frac{\partial}{\partial x_0} + \frac{\partial}{\partial x_1} \epsilon + O(\epsilon^2) ,$$ \hspace{1cm} (5)

$$\frac{\partial^2}{\partial x^2} = \frac{\partial^2}{\partial x_0^2} + 2\frac{\partial^2}{\partial x_0 \partial x_1} \epsilon + O(\epsilon^2) .$$ \hspace{1cm} (6)

We also assumed

$$\frac{\partial k_1}{\partial x} \approx \frac{\partial k_1}{\partial x_1} \epsilon ,$$ \hspace{1cm} (7)

for the smooth variation of the defect. Collecting terms of equal powers in $e^{i\omega t}$, with $\omega^2 \approx \omega_0^2 = 2$, we obtain

$$F_0 - 3F_1 F_1^* = 0 ,$$

$$3\epsilon \omega^2 (F_0 F_1 + F_1^* F_2) - \frac{7}{2} \epsilon^2 \omega^2 F_1^2 + k \epsilon \frac{\partial^2 F_1}{\partial x_1^2} + 2i \omega \frac{\partial F_1}{\partial t_1} - \epsilon \frac{\partial^2 F_1}{\partial t_1^2} + \frac{\partial k}{\partial x} \frac{\partial F_1}{\partial x_1} = 0 ,$$

$$F_2 = -\frac{1}{2} F_1^2 .$$

From the above three equations we obtained a perturbed Nonlinear Schrödinger equation (NLS) at order $\epsilon^2$:

$$2i \omega \frac{\partial F_1}{\partial t_2} + \frac{\partial k_1}{\partial x_1} \frac{\partial F_1}{\partial x_1} + k_1 \frac{\partial^2 F_1}{\partial x_1^2} + 8F_1 |F_1|^2 = 0 .$$ \hspace{1cm} (8)

We can rescale it into a standard form,

$$iu_t + \frac{1}{2} u_{xx} + u|u|^2 + \frac{1}{2} \frac{\partial}{\partial x} (\hat k u_x) = 0 ,$$ \hspace{1cm} (9)

and obtain the corresponding Lagrangian density,

$$\Lambda = \frac{i}{2}(u^* u_t - uu_t^*) - \frac{1}{2}(1 + \hat k)|u_x|^2 + \frac{1}{2} |u|^4 .$$ \hspace{1cm} (10)
A collective coordinate ansatz,

\[ u(x, t) = \eta \sech(\eta x - \zeta) e^{i(\phi + \xi x)} , \]

brings the full space integrated Lagrangian density into

\[ L = -2\eta \dot{\phi} - 2\xi \dot{\eta} + \frac{\eta^3}{3} - \xi^2 \eta - \frac{1}{2} \int_{-\infty}^{+\infty} k |u_x|^2 \, dx . \]

For a moving defect

\[ k = \kappa [\Theta(x - vt + l) - \Theta(x - vt - l)] , \]

we have the equation of motion for the collective coordinate variables

\[ \begin{align*}
\dot{\phi} &= \frac{\eta^2}{2} - \frac{\xi^2}{2} - \frac{\kappa}{4} (T_+ + T_-) \xi^2 - \frac{\kappa}{4} (S_+^2 (l - vt) + S_-^2 (l + vt)) \xi^2 \eta \\
&\quad - \frac{\kappa}{4} (S_+^2 T_+^2 (l - vt) + S_-^2 T_-^2 (l + vt)) \eta^3 - \frac{\kappa}{4} (T_+^3 + T_-^3) \eta^2 , \\
\dot{\xi} &= -\frac{\kappa}{4} (S_+^2 T_+^2 - S_-^2 T_-^2) \eta^3 - \frac{\kappa}{4} (S_+^2 - S_-^2) \xi^2 \eta , \\
\dot{\eta} &= \xi \eta + \frac{\kappa}{2} (T_+ + T_-) \xi \eta , \\
\dot{\eta} &= 0 ,
\end{align*} \]

in which

\[ \begin{align*}
T_+ &= -\tanh(\eta vt - \eta l - \zeta) , \\
T_- &= \tanh(\eta vt + \eta l - \zeta) , \\
S_+ &= \sech(\eta vt - \eta l - \zeta) , \\
S_- &= \sech(\eta vt + \eta l - \zeta) .
\end{align*} \]

We find there is nothing essential different from previous stationary defect located at origin, which can be obtained as a special case of present result at \( t = 0 \), except for the variation of \( \phi_t \) and the redefinition of Eqs. (18)-(21). We can still prove that a reduced coupling constant in the defect area is a necessary condition for a breather to be trapped. Since a necessary condition for trapping is \( \zeta_t = 0 \) more than twice, which, according to Eq. (16), is equivalent to

\[ \cosh^2(\eta vt - \zeta) = 1 - \cosh^2(\eta l) - \kappa \sinh(\eta l) \cosh(\eta l) . \]

Because \( \cosh^2 > 1 \) and \( \eta > 0 \), \( \kappa \) has to be negative. Furthermore, we can interpret the above equation as: the greater the separation between the breather and the defect; the larger the left hand side, the smaller \( \kappa \), i.e. the greater \( |\kappa| \), should be in order to balance the left hand side to fulfill the trapping requirement. This point is consistent with our previous numerical experience that if we put the initial breathers farther from origin we require larger breather amplitude for the breather to be trapped. However, the smallest \( \kappa \) is \(-1\).
3. Conclusion

We have demonstrated explicitly the possibility for trapping of realistic DNA. Furthermore, we considered the effect of moving defect. The result shows no special influence on trapping through velocity except through changing the breather-defect separation distance under our collective coordinate model. However, a recent measurement by Yin et al. [1995] on the RNA-polymerase moving force might be taken into account by asymmetrical potentials and stochastic resonance, similar to Jülicher & Prost [1995] for molecular motors.

There are other interesting works on DNA models: For instance, Yakushevich [1989] proposed another DNA model. More models can be found in the references of that paper and Forinash’s [1991]. Within the Peyrard-Bishop model, Hisakado & Wadati [1995] have studied its inhomogeneity effect by considering random mass and random coupling constant. It will also be interesting to take long range volumic interaction into account as Gaididei et al. [1995] considered. Slepyan et al. [1995] considered solitary waves traveling on a three dimensional helicoidal fiber, which might be extendible to a three dimensional DNA model. However, much work remain to be done in the future.

4. Acknowledgment

I thank Professor M. Peyrard for many useful discussions, the organization committee of the NLDC international workshop for making the trip possible, Drs. Victor W.-K. Wu, Gautam Gangopadhyay and Railing Chang for reading the manuscript.

References

[1] Ansari, A. Z., Bradner, J. E. & O’Halloran, T. V. [1995] “DNA bend modulation in a repressor-to-activator switching mechanism,” Nature 374(23), 371-375. However, there are also cases where the protein is on the outside of the bend. See for example: Bor, Y.-C., Bushman, F. D. & Orgel, L. E. [1995] “In vitro integration of human immunodeficiency virus type I cDNA into targets containing protein-induced bends,” Proc. Natl. Acad. Sci. USA 92, 10334-10338.

[2] Azbel, M. Y. [1995] “Universality in a DNA statistical structure,” Phys. Rev. Lett. 75(1), 168-171.

[3] Culotta, E. C. & Koshland, D. E. [1994] “DNA repair works its way to the top,” Science 266, 1926-1929.

[4] Dauxois, T. & Peyrard, M. [1993] “Energy localization in nonlinear lattice,” Phys. Rev. Lett. 70(25), 3935-3938.

[5] Englander, S. W., Kallenbach, N. R., Heeger, A. J., Krumhansl, J. A. & Litwin, S. [1980] “Natural of the opening state in long polynucleotide double helices: possibility of soliton excitations,” Proc. Natl. Acad. Sci. USA, 77(12), 7222-7226.

[6] Erie, D. A., Hajiseyedjavadi, O., Young, M. C. & von Hippel, P. H. [1993] “Multiple RNA polymerase conformations and GreA: control of the fidelity of transcription,” Science, 262(5), 867-873.

[7] Forinash, K., Bishop, A. R. & Lomdahl, P. S. [1991] “Nonlinear dynamics in a double-chain model of DNA,” Phys. Rev. B, 43(13), 10743-10750.
[8] Forinash, K., Peyrard M. & Malomed, B. [1994] “Interaction of discrete breathers with impurity modes,” Phys. Rev. E 49(4), 3400-3411.

[9] Gaididei, Y., Flytzanis, N., Neuper, A. & Mertens, F. G. [1995] “Effect of nonlocal interactions on soliton dynamics in anharmonic lattices,” Phys. Rev. Lett. 74(11), 2240-2243.

[10] Hisakado, M. & Wadati, M. [1995] “Inhomogeneous model for DNA dynamics,” J. Phys. Soc. Jpn. 64(4), 1098-1103.

[11] Jülicher, F & Prost, J. [1995] “Cooperative molecular motors,” Phys. Rev. Lett. 75(13), 2618-2621.

[12] Peyrard, M & Bishop, A. R. [1989] “Statistical mechanics of a nonlinear model for DNA denaturation.” Phys. Rev. Lett., 62(23), 2755-2758.

[13] Remoissenet, M. [1986] “Low-amplitude breather and envelope solitons in quasi-one-dimensional physical models,” Phys. Rev. B 33(4), 2386-2392.

[14] Slepyan, L., Krylov, V. & Parnes, R. [1995] “Solitary waves in an inextensible, flexible, helicoidal fiber,” Phys. Rev. Lett. 74(14), 2725-2728.

[15] Ting, J. J.-L. & Peyrard, M [1996] “Effective breather trapping mechanism for DNA transcription,” Phys. Rev. E 55(1), 1011-1018.

[16] Urabe, H. & Tominaga, Y. [1981] “Low frequency Raman spectra of DNA,” J. Phys. Soc. Jpn., 50(11), 3543-3544.

[17] Yakushevich, L. V. [1995] “Nonlinear DNA dynamics: a new model,” Phys. Lett. A 136(7), 413-417.

[18] Yin, H., Wang, M. D., Svoboda, K., Landick, R., Block, S. M. & Gelles, J. [1995] “Transcription against an applied force” Science 270(5242), 1653-1657.