B to Z transition of the DNA

Tapas Kumar Sinha.
Sachinandan Chanda
Computer Centre.
North Eastern Hill University
Shillong-793022

Sachinandan Chanda
Department of Mathematics
Shillong Polytechnic
Shillong-793022

Abstract**—**In this paper we study the transition from B DNA to Z DNA. We find soliton solutions for angular and longitudinal fluctuations in the DNA lattice. However non bonded interactions couple the angular and longitudinal fluctuations. Only when the coupled equations are solved exactly can we identify the mode which leads to the transition from B DNA to Z DNA.

Keywords**—** *B DNA, Z DNA, Solitons, Domain Walls*

*****

I. INTRODUCTION

The right handed helical structure of (B form) DNA was discovered by Watson and Crick [1]. The left handed form of DNA (Z form) was discovered by Rich et.al [2]. Initially the Z form was thought to be an aberration [11]. Later it was found to play a pivotal role in the transcription process [3]. In this paper we suggest that the Z form of DNA induces (or facilitates) Soliton formation which allows transcription to take place.

It has been established [4] that the DNA can switch from the left handed (B) to the right handed (Z) conformation and vice versa. Further there is evidence of synchronous stretching and rotation from the B form to the left handed Z form [5]. This transition is concisely written in the parametric form of the helix. The parametric form of the right handed helix is

$$x_i(t) = a\cos t, y_i(t) = a\sin t, z_i t = bt \qquad (1)$$

The stretching of the DNA lattice may now be written as

$$x_i(t) \to x_{i+N}(t), N = 1, 2, 3, ... \qquad (2)$$

$$y_i(t) \to y_{i+N}(t) \;, N = 1, 2, 3, ... \qquad (3)$$

The stretching is accompanied by rotation:

$$x_{i+N}(t) = -a\cos t = a\cos(t+\pi) \qquad (4)$$

$$y_{i+N}(t) = -a\sin t = a\sin(t+\pi) \qquad (5)$$

This corresponds to a lattice stretching and base flipping as has been confirmed via MD (molecular Dynamics) simulations [5].

The rotation of the bases takes place about the Glycosidic bond. We note that in the Z DNA the base motions (oscillations, twisting and tilting) are slower by about a factor of ½ than the motion in B DNA [5]. Using P NMR and nuclear Overhauser effect Patel et. al. have demonstrated that in the right handed B DNA the guanosine residue is in anti conformation while in the Z DNA This may be accounted for by the stretching which the lattice undergoes in the guanosine residue is in the syn conformation. transformation from B to Z DNA. The phosphate backbone exists in a double well.

The potential for rotation about this bond, for the Z DNA may be written as

$$V = V_0(1-\cos 3\psi) \approx 9V_0\left(\psi^2 - \frac{9}{4}\psi^4\right) \qquad (6)$$

This is the double well potential observed by [5] via Molecular Dynamics simulation. However in reality the potential is modified via non bonded interactions (while still retaining the double well profile). We write this potential as

$$V(\psi) = \frac{A_t}{2}\psi^2 + \frac{B_t}{4}\psi^4 \qquad (7)$$

where the coefficients A_t, B_t as obtained from fig.(5) of [5]

For this potential the solutions are Domain walls (Tanh Solitons, ()) which propagate down the lattice. According to this picture the BZ junction is a propagating Domain wall.

II. MODEL AND DOMAIN WALL SOLUTIONS

We approximate the lattice by a point mass m attached to a base of mass m and moment of Inertia I about the glycosidic bond. The model thus accounts for both longitudinal and angular fluctuations. The Hamiltonian for the system may be written as

$$H = H_t + H_L \qquad (8)$$

$$H_t = \sum_n I\dot{\psi}_n^2 + 9V_0\sum_n\left(\psi_n^2 - \frac{9}{4}\psi_n^4\right) + \frac{Ic_t^2}{2}\psi'' \qquad (9)$$

$$H_L = \sum_n \frac{m\dot{u}_n^2}{2} + \sum_n \left(\frac{A}{2} u_n^2 + \frac{B}{4} u_n^4 \right) + \sum_n \frac{mc_0^2}{2} u_n^{''} \qquad (10)$$

We have neglected any interaction between longitudinal and angular fluctuations. The equations of motion which follow from the above Hamiltonian are

$$I\ddot{\psi}_n + A_t\psi_n + B_t\psi_n^3 - mc_t^2\psi_n^{''} = 0 \qquad (11)$$

$$m\ddot{u}_n + A_L u_n + B_L u_n^3 - mc_L^2 u_n^{''} = 0 \qquad (12)$$

The domain wall solutions of the above system of equations [6] is:

$$\psi_n \approx \tanh\left((\psi_0 - \omega t) / \xi_t \sqrt{2} \right) \qquad (13)$$

$$u_n \approx \tanh\left(\left((x - vt) \right) / \xi_L \sqrt{2} \right) \qquad (14)$$

These solutions describe a longitudinal and an angular Solitons. The longitudinal Soliton produces a compression of the lattice while the angular fluctuation produces a rotation about the glycosidic bond resulting in the left handed DNA. The potential energy of longitudinal and angular Domain wall is ~ $\left(\frac{A_L^2}{2B_L} \right)$ and $\left(\frac{A_T^2}{2B_T} \right)$ or the height of the respective double wells. We note that $\left(\frac{A_T^2}{2B_T} \right)$ ~ 14Kcals/mol, as obtained from Molecular Dynamics simulations. DNA give $\left(\frac{A_L^2}{2B_L} \right)$ ~ 0.3 Kcals/mole.

III. STATISTICAL MECHANICS

The double well model offers a convenient platform to study the inter conversions of energy from the molecular twist (Tw (read ψ) to the axial writhe (Wr (read u)). We note first that the motion of the bases and the lattice fluctuation are on different time scales (Base rotation is of the order of nano seconds and lattice fluctuation is of the order of micro seconds). Hence we consider the partition functions separately. The partition function for the Hamiltonian H_t is

$$Z_u \approx e^{-\left(\frac{L}{l}\right)\beta\varepsilon_{0,s}} + e^{-\left(\frac{L}{l}\right)\beta\varepsilon_{0,a}} \qquad (15)$$

$$\varepsilon_{0,s} = \frac{1}{2}\left(\frac{2A}{m^*}\right)^{1/2} \left\{ 1 - \frac{1}{2}\exp\left(-\phi_0 \left(\frac{A^2}{2B} m^* \right)^{1/2} \right) \right\} \qquad (16)$$

$$\varepsilon_{0,a} = \frac{1}{2}\left(\frac{2A}{m^*}\right)^{1/2} \left\{ 1 + \frac{1}{2}\exp\left(-\phi_0 \left(\frac{A^2}{2B} m^* \right)^{1/2} \right) \right\} \qquad (17)$$

With

$$K_1 = \frac{1}{2}\left(\frac{2A}{m^*}\right)^{1/2}, \text{ and } K_2 = \left(\frac{A^2}{2B} m^*\right)^{1/2} \qquad (18)$$

one obtains for the statistical average value of ϕ_0 (in the linear approximation),

$$\langle \phi_0 \rangle = -\frac{1}{\beta}\frac{\partial}{\partial \phi_0} \ln Z_u =$$

$$\frac{L}{4l}\left(\frac{A^3}{2B}\right)^{1/2} \tanh\left[\frac{L\beta}{2L}\left(\frac{A^3}{2B}\right)^{1/2} \right] \phi_0 \qquad (19)$$

The asymptotic value of $\langle \phi_0 \rangle$ is $\tanh\left[\frac{L\beta}{2L}\left(\frac{A^3}{2B}\right)^{1/2} \right] \phi_0$.

To understand the behavior near $\phi_0 \approx 0$ we neglect the ϕ_0^4 term. The non bonded interactions may be written as

$$\sum_i \sum_v V e^{-\psi_{vi}\psi_{vi+1} + \frac{A}{2}\psi_{vi}^2 \frac{B}{2}\psi_{vi+1}^2} \qquad (20)$$

The first term in the exponential of (22) represents the interactions between positive and negative super coiling [14]. The next term represents the non bonded interactions [15]. Ramachandran plots of Polynucleotides by Olson and Flory [15] have shown that there are only certain regions in the $\left(\psi_{vi}, \psi_{vi+1}\right)$ space contribute to the interaction. We denote these regions by two dimensional gaussians whose half width at half height are given by A$\left(\psi_{vi}\right)$ and B $\left(\psi_{vi+1}\right)$ respectively. Evaluating the partition function now gives

$$\langle \phi_0 \rangle = \exp\left(-\frac{(J\psi)^2}{2} \right) \qquad (21)$$

Since ψ is small expanding the exponential to first order we get

$$\langle \phi_0 \rangle = 1 - \frac{(J\psi)^2}{2} \qquad (22)$$

Near $\phi_0 \approx 0$ we have parabolic behavior as observed by Rich et. al.

IV. DYNAMICS

The results of the last section show that it is important to include the coupling term $J\psi\phi$ when $\phi_0 \approx 0$.

Including this term in the Hamiltonian, we find the coupled equations of motion to be

$$I\ddot{\psi}_n + A_t\psi_n + B_t\psi_n^3 - mc_t^2\psi_n'' + \sum_n V e^{-\frac{A(\psi_n)}{2}\psi_n^2} e^{-\frac{B(u_n)}{2}u_n^2} = 0 \tag{23}$$

$$m\ddot{u}_n + A_L u_n + B_L u_n^3 - mc_L^2 u_n'' + \sum_n V e^{-\frac{A(\psi_n)}{2}\psi_n^2} e^{-\frac{B(u_n)}{2}u_n^2} = 0 \tag{24}$$

Expanding the exponential one obtains

$$I\ddot{\psi}_n + A_t\psi_n + B_t\psi_n^3 - mc_t^2\psi_n'' + V\frac{A(\psi_n)B(u_n)}{2}\psi_n u_n^2 = 0 \tag{25}$$

$$m\ddot{u}_n + A_L u_n + B_L u_n^3 - mc_L^2 u_n'' + V\frac{A(\psi_n)B(u_n)}{2}\psi_n^2 u_n = 0 \tag{26}$$

We look for travelling wave solutions [6] of the form

$$\psi_n = f_1(z - v_1 t), \tag{27}$$

$$u_n = f_2(z - v_2 t) \tag{28}$$

$$\left(Iv_1^2 + mc_t^2\right) f_1'' + A_t f_1 + B_t f_1^3 + V\frac{A(\psi_n)B(u_n)}{2} f_1 f_2^2 = 0 \tag{29}$$

$$\left(mv_2^2 + mc_L^2\right) f_2'' + A_L f_2 + B_L f_2^3 + V\frac{A(\psi_n)B(u_n)}{2} f_2 f_1^2 = 0 \tag{30}$$

We convert the above coupled equations to the dimensionless form

$$A_1 f_1'' + B_1 f_1 + C_1 f_1^3 + D_1 f_1 f_2^2 = 0 \tag{31}$$

Making the substitutions

Let $\frac{A_1}{B_1} = \xi_1^2, \frac{f_1}{u_0} = \eta_1, \frac{f_2}{u_0} = \eta_2, \frac{C_1}{B_1} = \frac{1}{u_0^2}, \frac{D_1}{B_1} = \frac{1}{u_0^3}$ (32)

$$\frac{A_1}{B_1} = \xi_1^2, \frac{f_1}{u_0} = \eta_1, \frac{f_2}{u_0} = \eta_2, \frac{C_1}{B_1} = \frac{1}{u_0^2}, \frac{D_1}{B_1} = \frac{1}{u_0^3} \tag{33}$$

we obtain

$$\frac{d^2\eta_1}{ds^2} + \eta_1 + \eta_1^3 + \eta_1\eta_2^2 = 0 \tag{34}$$

$$\frac{d^2\eta_2}{ds^2} + \eta_2 + \eta_2^3 + \eta_1^2\eta_2 = 0 \tag{35}$$

Adding two equations one obtains

$$\frac{d^2}{ds^2}(\eta_1 + \eta_2) + (\eta_1 + \eta_2) - (\eta_1 + \eta_2)^3 + 4\eta_1\eta_2(\eta_1 + \eta_2) = 0 \tag{36}$$

Let us put

$$\eta_1 + \eta_2 = y, \eta_1 = ke^{i(\pm 2n\pi + \theta)}, \eta_2 = \frac{1}{4k}e^{-i(\pm 2n\pi + \theta)} \tag{37}$$

Where $n = 0, 1, 2, 3.........$

We note here that

$$\frac{d^2y}{ds^2} + y - y^3 + y = 0 \tag{38}$$

$$\frac{d^2y}{ds^2} + 2y = y^3 \tag{39}$$

$$\eta_1 + \eta_2 = \tanh(\sigma) \tag{40}$$

$$\text{or } ke^{i(\pm 2n\pi + \theta)} + \frac{e^{-i(\pm 2n\pi + \theta)}}{4k} = \tanh(\sigma) \tag{41}$$

Taking the real part we obtain

$$k\cos(\pm 2n\pi + \theta) + \frac{\cos(\pm 2n\pi + \theta)}{4k} = \tanh(\sigma) \tag{42}$$

$$\left(4k^2 + 1\right)\cos(\pm 2n\pi + \theta) = \tanh(\sigma) \tag{43}$$

$$\cos(\pm 2n\pi + \theta) = \frac{\tanh(\sigma)}{\left(4k^2 + 1\right)} \tag{44}$$

Since $\pm 2n\pi + \theta \neq 0$, we obtain

$$4k^2 = 1 \tag{45}$$

$$\text{or } k = \pm\frac{1}{2} \tag{46}$$

Hence

$$\cos(\pm 2n\pi + \theta) = \frac{1}{2}\tanh(\sigma) \tag{47}$$

$$\text{or } \pm 2n\pi + \theta = \cos^{-1}\left[\frac{1}{2}\tanh(\sigma)\right] \tag{48}$$

$$\text{This gives } \theta = \cos^{-1}\left[\frac{1}{2}\tanh(\sigma)\right] \mp 2n\pi \tag{49}$$

Here $\pm 2n$ is the winding number []. (The positive (negative) sign of n refers to the positive (negative) super coiling of DNA [].) Note that if $\theta = \pi$ it corresponds to a base flip. This corresponds to the B DNA to Z DNA transformation (see equations (1) – (5)). For

For the DNA, the linking number Lk, can be expressed in terms of the twist Tw and the writhing number Wr [12]

$$Lk = Tw + Wr \qquad (50)$$

We identify θ with the twist Tw and n with linking number Lk. We note that the free energy of the super coiled DNA in terms of the linking number and twist has been derived by [12].

We note that the energy of the Lattice due to the presence of the Soliton is given by

$$\frac{1}{2} M \sum_n \dot{\psi}_n^2 = \frac{M u_0^2 v_s^2}{2 l^2 a^2} \sum_n \sec h^4 \left(\frac{n}{l} \right) \qquad (51)$$

Thus both the axial writhe Solitons and the Molecular twist Solitons have the above energy distribution. In the model developed far there is no scope of energy interchange as we have not built any interaction between the angular and longitudinal fluctuations. As there is coupling between the two forms of energy we are forced to include the coupling term ψu.Further in the limit of t=0 (static case) one obtains the modified Marko-Siggia model. For $t \neq 0$ the equations describe both bending and twisting of the DNA as the Soliton propagates down the lattice.

V. CONCLUSION

We have developed a physical picture of the transition from B DNA to Z DNA. In the process we have made the following approximations:

1) We have neglected the non bonded interactions

2) We have neglected interactions between longitudinal and angular fluctuations

This model yields a picture of coupled domain wall model. A particular solution of the coupled model ($\theta = \pi$) corresponds to the B DNA to Z DNA transition.

REFERENCES

[1] J. D. Watson and F.H.C Crick Nature," A Structure for Deoxyribose Nucleic Acid" 171,pp.737-778(1953).

[2] A. Wang et.al, "Molecular Structure of a left-handed double helical DNA fragment at atomic resolution, Nature, 282 pp.682-686(1979).

[3] H. Drew et.al "High-salt d(CpCpCpG), a left-handed Z DNA double helix", Nature, 286 pp.567-(1980).

[4] F.M.Pohl and T.M.Jovin, "Salt-induced co-operative conformational change of a synthetic DNA:Equilibrium and Kinetic studies with poly(dG-dC)",J.Mol Biol.67 pp.375-(1972)

[5] Oliver K. Strobel, Robert S. Keyes, and Albert M. Bobst " Base Dynamics of Local Z-DNA Conformations As Detected by Electron Paramagnetic Resonance with Spin-Labeled Deoxycytidine Analogues" Bio Chemistry 29, pp.8522-8528 (1990).

[6] Juyong Lee et.al, Journal of Physical Chemistry B, 114(30), 9872(2010).

[7] J.A.Krumhansl and J.R.Schrieffer, "Dynamics and Statistical Mechanics of a one-dimensional model for structural phase transitions" Physical Review B, 9, pp.3535-3545(1975).

[8] Liming Ying, Mark J.Wallace and David Klenerman, "Two State model of conformation fluctuation in a DNA hairpin-loop", Chemical Phyics letters,145 pp

[9] Todd M. Alam, John Orban and Gary P.Drobny, Biochemistry, 30. 9229(1991)

[10] Michael E.Hogan and Oleg Jarditzky, Biophysics, 76. 6341(1979).

[11] M. D. Barkley and B. H. Zimm, J. Chem. Phys. 70, 2991(1970).

[12] J. L. Marx, "Z-DNA: still searching for a function ",230 pp.794-796(1985).

[13] Proc. Natl. Acad. 85, 7069(1988)

[14] R. Daniel Camerini-Otero and Gary Felsenfeld,"A simple model of DNA super helices in solution", Proc. Natl. Acad. Sci., 75 pp1708-1712 (1978).

[15] J. F. Marko and E. D. Siggia "Statistical Mechanics of supercoiled DNA" Physical Review E, 52 pp2912-2938 (1995).

[16] Raymond J. Kelleher III et.al., "Competitive behavior of multiple, discrete B-Z transitions in supercoiled DNA", Proc. Natl. Acad. Sci., 83 pp.6342-6346(1986)

[17] P. Shing Ho, "The non-B-DNA structure of d(CA/TG)does not differ from that of Z DNA" Proc. Natl. Acad. Sci., 91 pp.9549-9553(1994).

[18] Wilma K. Olson, Paul J. Flory, "Polynucleotide spatial configuration I,II,III" Biopolymers

[19] Wilbur Lim "Solitary Excitations in B-Z DNA transition: A theoretical and numerical study", Physical Review E 75 pp.031918-1 031918-9(2007).