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# PROPAGATION OF ELASTIC WAVES IN DNA

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ABSTRACT. The mathematical analyses of longitudinal and torsional elastic waves transmitted along DNA molecule undergoing Brownian motion in solution are presented. Longitudinal vibrations in DNA are shown to be responsible for drug intercalation and breathing. The near neighbor exclusion mode of drug intercalation is explained. Torsional oscillations in DNA are shown to be responsible for conformation transitions from a right handed to a left handed form, depending on sequence specificity in high salt concentration.

*KEY WORDS AND PHRASES. Stochastic differential equations, drug intercalation within DNA molecule, DNA breathing, handedness of DNA.*

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## 1. INTRODUCTION.

This paper is directed to specialists in mathematical biophysics and in applied mathematics. However, familiarity with references [1-4] would be useful for non-specialists interested in the paper.

X-ray diffraction of DNA has shown that DNA molecules can usually assume a wide range of secondary structures with either right handed or left handed helical

conformations [5,6]. This polymorphic character of complementary base-paired polynucleotide duplexes is not surprising if one considers six single bond angles of the deoxyribose-phosphate backbone and numerous possible conformational angles of the furanose ring making DNA molecules flexible. This indicates that the DNA molecule has considerable internal freedom. When the DNA molecule is kept in solution, it constantly exchanges energy and motion with solvent molecules; thus, internal motions within the structure are set up. These are evidenced from spectroscopic probes: fluorescence depolarization measurements of DNA - bound drug molecules [7], changes of NMR spectral line widths [8], light scattering studies of DNA [9], and hydrogen ion-exchange reaction of DNA bases with solvent molecules [10]. These are sufficient to show that the DNA double helix possesses a dynamic structure. Exploitation of this dynamic nature may allow conformational transitions between various structural forms of DNA which have been experimentally monitored by CD spectroscopy. Investigations by infrared spectroscopy [11] have shown that external conditions of salt content and humidity highly affect the orientations of the phosphate groups and planes of the base pairs with respect to the helix axis of the DNA.

Barkley and Zimm [12] have developed an elastic model of a semiflexible chain like macromolecule in order to treat the internal rotary Brownian motion of the DNA helix which is, in effect, responsible for the decay of emission anisotropy of the fluorescent probe embedded in the chain. Their model predicts average fluctuations in the twist angle between the bases by about 5° and the same for bending of the helix axis between the bases by roughly 4°. Hogan et al [8] have measured the $^{31}P$ and the $^{1}H$ NMR parameters of double-stranded DNA fragments of length 150-600 base-pairs. From NMR analysis, they conclude that internal motions must exist between individual nucleotide components which give rise to large fluctuations in ribose and phosphate backbone geometry while, at the same time, small bending or twisting motion of the duplex should also be present. Lin and Schurr [9] have studied intramolecular dynamics from light scattering studies of DNA. They have shown how internal motions of large and flexible macromolecules due to hydrodynamic interactions are manifested in the intensity auto-correlation functions of polarized Rayleigh scattered light. Studies of measurements of the translational diffusion coefficient and observation of chain relaxation for DNA of bacteriophage N1 have also been reported [13], using the same light-scattering method.

In this paper, we show the possibility of acquiring the conformational flexibility of DNA due to the transmission of the longitudinal waves along the polymeric length. Elasticity of the macromolecule arises through the stacking interaction between the adjoining bases and covalent linkages of the sugar phosphate backbone. The elastic deformation produced by the wave is associated with the Brownian nature of motion of the DNA which is always generated because of the thermal environmental contact. Local stretching of bases giving rise to kinks within the structure and consequent drug intercalation, local compression generating premelted regions of DNA have been studied. Consideration of torsional oscillation within the body of the DNA has led to the study of the transformation of a right handed helix to a left handed one. Existence of such a left handed structure in the presence of high salt concentration or alcohol has been demonstrated by Pohl et al [14]. Other internal motions like transverse wave propagation, bending motions, motions due to shear and couples, etc., have not been considered to avoid complexity and to find the essential simple features of disturbances carried through the elasticity of the macromolecule. This elimination is justified if equations of motion are considered for DNA whose persistence length is of the order of $\lambda = 650$ Å. DNA molecules longer than this length will lack in rigidity, resulting in the production of bending and other flexural motions.

## 2. PROPAGATION OF LONGITUDINAL WAVES.

From discrete layer lines observed in X-ray diffraction of DNA, it is evident that the DNA structure can be thought to be made up of discrete repeating units. So a linear one dimensional discrete lattice model is quite plausible for DNA. If we consider the chain built up from N beads (monomer units) of mass m connected by (N - 1) massless rods of length b, the simple Lagrangian L for harmonic oscillation can be represented as

$$L = \frac{m}{2} \sum_{j=1}^{N} \dot{u}_j^2 - \frac{\alpha}{2} \sum_{j=1}^{N} (u_{j+1} + u_{j-1} - 2u_j)^2 \tag{2.1}$$

where $u_j$ is the displacement of the jth bead and $\alpha$ is the spring constant. If each bead suffers a frictional force $-f\dot{u}_j$ and is subjected to a Brownian force $A_j(t)$, then the resulting force $Q_j$ becomes

$$Q_j = -f\dot{u}_j + A(t) \tag{2.2}$$

Applying principles of least action, one gets the equation of motion of each bead [15] as

$$m\ddot{u}_j + f\dot{u}_j + \alpha(u_{j+2} - 4u_{j+1} + 6u_j - 4u_{j-1} + u_{j-2}) - 2\beta_{j+1}(u_{j+1} - u_j) + 2\beta_j(u_j - u_{j-1}) = A(t) \qquad (2.3)$$

where $\beta_j$ are Lagrangian undetermined multipliers and $\alpha$ is a bending force constant. In the limit of the wormlike chain, given by $N \to \infty$ and $b \to 0$ [where the chain length $\ell = (N - 1)b$, the mass density per unit length $\rho = m/b$, the friction per unit length $\eta = f/b$, the bending force constant $\epsilon = \alpha b^3$, the axial length $x = jb$, the displacement of jth segment $u_j(t) = u(x,t)$, the Brownian force per unit length $A_j(t)/b = A'(x,t)$, and the elastic constant $E(x) = 2\beta_j$], Equation (2.3) transforms into Equation (2.4).

$$\rho\ddot{u} + \eta\dot{u} + \epsilon \frac{\partial^4 u}{\partial x^4} - \frac{\partial}{\partial x}\left[E(x) \frac{\partial u}{\partial x}\right] = A'(x,t) \qquad (2.4)$$

Considering the longitudinal vibrations only and no bending ($\epsilon \to 0$) and for a DNA duplex (say homoduplex) where Young's modulus E is constant throughout the coil length $\ell$, Equation (2.4) is simplified to

$$\ddot{u} = c^2 \frac{\partial^2 u}{\partial x^2} - 2\gamma\dot{u} + A(x,t) \qquad (2.5)$$

where $c^2 = E/\rho$, $2\gamma = \eta/\rho$, and $A(x,t) = A'(x,t)/\rho$. To solve the stochastic differential equation (2.5), we consider $u(x,t) = u_1(x)\, u_2(t)$ and impose the following initial conditions on the system:

$$u(x,0) = 0 \quad \text{and} \quad \frac{\partial u(x,0)}{\partial t} = \frac{P}{\rho}\phi(x) \qquad (2.6)$$

where P = the impact amplitude from solvent molecules and $\phi(x)$ represents the axial variation of the initial impact. The boundary conditions are

$$u(0,t) = 0 \quad \text{and} \quad u(\ell,t) = 0 \qquad (2.7)$$

Then

$$u(x,t) = \sum_{n=1}^{\infty} u_n(x,t) = \sum_{n=1}^{\infty} u_1^n(x)\, u_2^n(t)$$

$$= \sum_{n=1}^{\infty} \{C_{1n}(t) \exp(\mu_{1n}t) + C_{2n}(t) \exp(\mu_{2n}t)\} \sin\left(\frac{n\pi x}{\ell}\right) \qquad (2.8)$$

where

$$\mu_{1n} = -\gamma + (\gamma^2 - K_n^2)^{1/2}, \quad \mu_{2n} = -\gamma - (\gamma^2 - K_n^2)^{1/2} \qquad (2.9)$$

and

$$K_n = n\pi C/\ell \quad \text{with} \quad n = 1,2,3,4, \cdots$$

Here $C_{1n}$ and $C_{2n}$ are time dependent amplitudes, restricted to satisfy Equation (2.10) (see [16])

$$\exp(\mu_{1n}t)\,\frac{dC_{1n}}{dt} + \exp(\mu_{2n}t)\,\frac{dC_{2n}}{dt} = 0 \tag{2.10}$$

Assuming $A(x,t) = \sum_{n=1}^{\infty} A_n(t)\sin(n\pi x/\ell)$, we get with the help of the initial and boundary conditions

$$\sum_{n=1}^{\infty} A_n(t) = \sum_{n=1}^{\infty} (\mu_{1n} - \mu_{2n})\,\frac{dC_{1n}}{dt}\exp(\mu_{1n}t)$$

$$= -\sum_{n=1}^{\infty} (\mu_{1n} - \mu_{2n})\,\frac{dC_{2n}}{dt}\exp(\mu_{2n}t) \tag{2.11}$$

This gives

$$C_{1n}(t) = \frac{1}{(\mu_{1n} - \mu_{2n})}\int_0^t A_n(\xi)\exp(-\mu_{1n}\xi)\,d\xi + C_{1n}(0) \tag{2.12}$$

and

$$C_{2n}(t) = \frac{-1}{(\mu_{1n} - \mu_{2n})}\int_0^t A_n(\xi)\exp(-\mu_{2n}\xi)\,d\xi + C_{2n}(0), \tag{2.13}$$

where

$$C_{1n}(0) = -C_{2n}(0) = \frac{2P\phi_{1n}}{\ell\rho(\mu_{1n} - \mu_{2n})} \tag{2.14}$$

and

$$\phi_{1n} = \int_0^{\ell} \phi(x)\,\sin\left(\frac{n\pi x}{\ell}\right)\,dx \tag{2.15}$$

The wave will propagate if $K_n^2 > \gamma^2$. Now we can write

$$\mu_{1n} = -\gamma + i\omega_n \quad \text{and} \quad \mu_{2n} = -\gamma - i\omega_n \tag{2.16}$$

where

$$\omega_n = (K_n^2 - \gamma^2)^{\frac{1}{2}} \tag{2.17}$$

Then, from Equation (2.18), we get for the nth harmonic

$$u_2^n(t) = \frac{2P\phi_{1n}}{\ell\rho(\mu_{1n} - \mu_{2n})}\{\exp(\mu_{1n}t) - \exp(\mu_{2n}t)\} + \int_0^t A_n(\xi)\,\psi_n(\xi)\,d\xi \tag{2.18}$$

and

$$\frac{du_2^n}{dt} = \frac{2P\phi_{1n}}{\ell\rho(\mu_{1n} - \mu_{2n})}\{\mu_{1n}\exp(\mu_{1n}t) - \mu_{2n}\exp(\mu_{2n}t)\} + \int_0^t A_n(\xi)\,\lambda_n(\xi)\,d\xi \tag{2.19}$$

where

$$\int_0^t \psi_n^2(\xi)\,d\xi = \frac{1 - S_1\exp(-2\gamma t)}{4\gamma(\gamma^2 + \omega_n^2)}, \tag{2.20}$$

$$\int_0^t \lambda_n^2(\xi)\,d\xi = \frac{1 - S_2\exp(-2\gamma t)}{4\gamma}, \tag{2.21}$$

with

$$S_1 = 1 + \frac{2\gamma^2}{\omega_n^2}\sin^2\omega_n t + \frac{\gamma}{\omega_n}\sin(2\omega_n t) \tag{2.22}$$

and

$$S_2 = 1 + \frac{2\gamma^2}{\omega_n^2} \sin^2\omega_n t - \frac{\gamma}{\omega_n} \sin(2\omega_n t). \tag{2.23}$$

Thermal fluctuations are carried out through coefficients like $A_n(\xi)$. To obtain the averages $\langle u \rangle$, $\langle du/dt \rangle$, $\langle (du/dt)^2 \rangle$, etc., one has to find the respective distribution functions using Chandrasekhar's Lemma [16]. Let $W(u_2^n,t,0,0)$ and $W(\dot{u}_2^n,t,\dot{u}_{2|0}^n,0)$ be the distribution functions of $u_2^n(t)$ and $\dot{u}_2^n(t)$ respectively.

Then

$$W(u_2^n,t,0,0) = \frac{1}{\sqrt{\frac{2\pi KT}{\rho(\omega_n^2 + \gamma^2)} \{1 - S_1 \exp(-2\gamma t)\}}} \times$$

$$\exp - \frac{\{u_2^n - \frac{2P\phi_{1n}}{\ell\rho} \exp(-\gamma t) \frac{\sin \omega_n t}{\omega_n}\}^2}{\frac{2KT}{\rho(\omega_n^2 + \gamma^2)} \{1 - S_1 \exp(-2\gamma t)\}} \tag{2.24}$$

and

$$W(\dot{u}_2^n,t,\dot{u}_{2|0}^n,0) = \frac{1}{\sqrt{\frac{2\pi KT}{\rho} \{1 - S_2 \exp(-2\gamma t)\}}} \times$$

$$\exp\left[ - \frac{\{\dot{u}_2^n - \frac{2P\phi_{1n}}{\ell\rho} \exp(-\gamma t)(\cos \omega_n t - \frac{\gamma}{\omega_n} \sin \omega_n t)\}^2}{\frac{2KT}{\rho} \{1 - S_2 \exp(-2\gamma t)\}} \right] \tag{2.25}$$

Now, with the help of (2.24) and (2.25),

$$\langle u \rangle = \frac{2P}{\ell\rho} \sum_{n=1}^{\infty} \phi_{1n} \sin(\frac{n\pi x}{\ell}) \exp(-\gamma t) \frac{\sin \omega_n t}{\omega_n} \tag{2.26}$$

$$\left\langle \frac{du}{dt} \right\rangle = \frac{2P}{\ell\rho} \sum_{n=1}^{\infty} \phi_{1n} \sin(\frac{n\pi x}{\ell}) \exp(-\gamma t)\{\cos \omega_n t - \frac{\gamma}{\omega_n} \sin \omega_n t\} \tag{2.27}$$

$$\left\langle \frac{du}{dx} \right\rangle = \frac{2P}{\ell^2\rho} \sum_{n=1}^{\infty} n\pi\phi_{1n} \cos(\frac{n\pi x}{\ell}) \exp(-\gamma t) \frac{\sin \omega_n t}{\omega_n} \tag{2.28}$$

$$\langle u^2 \rangle = \langle u \rangle^2 + \sum_{n=1}^{\infty} \frac{KT}{\rho K_n^2} \sin^2(\frac{n\pi x}{\ell}) \times$$

$$\left[1 - \exp(-2\gamma t)\{\frac{2\gamma^2}{\omega_n^2} \sin^2 \omega_n t + \frac{\gamma}{\omega_n} \sin(2\omega_n t) + 1\}\right] \tag{2.29}$$

$$\left\langle \left( \frac{du}{dt} \right)^2 \right\rangle = \left\langle \frac{du}{dt} \right\rangle^2 + \sum_{n=1}^{\infty} \frac{KT}{\rho} \sin^2 \left( \frac{n\pi x}{\ell} \right) \times$$

$$\left[ 1 - \exp(-2\gamma t) \left\{ \frac{2\gamma^2}{\omega_n^2} \sin^2 \omega_n t - \frac{\gamma}{\omega_n} \sin(2\omega_n t) + 1 \right\} \right] \qquad (2.30)$$

$$\text{Thus, } \left\langle \text{Kinetic energy of the rod} \right\rangle = \frac{1}{2}\rho \int_0^{\ell} \left\langle (du/dt)^2 \right\rangle dx$$

$$= \frac{2P^2}{\ell\rho} \sum_{n=1}^{\infty} \phi_{1n}^2 \exp(-2\gamma t) \left\{ \cos \omega_n t - \frac{\gamma}{\omega_n} \sin \omega_n t \right\}^2$$

$$+ \sum_{n=1}^{\infty} \frac{KT\ell}{4} \left[ 1 - \exp(-2\gamma t) \left\{ \frac{2\gamma^2}{\omega_n^2} \sin^2 \omega_n t - \frac{\gamma}{\omega_n} \sin(2\omega_n t) + 1 \right\} \right] \qquad (2.31)$$

Thus, for $t \to 0$, we get $\rho \left\langle (du/dt)^2 \right\rangle = \rho \left\langle du/dt \right\rangle^2$ and, for $t \to \infty$, we get $\rho \left\langle (du/dt)^2 \right\rangle = KT$.

$$\text{Hence, } \left\langle \text{Potential energy of the rod} \right\rangle = \frac{E}{2} \int_0^{\ell} \left\langle (du/dx)^2 \right\rangle dx$$

$$= \frac{E\pi^2}{2\ell} \left[ \sum_{n=1}^{\infty} \frac{4P^2 n^2 \phi_{1n}^2}{\ell^2 \rho^2} \exp(-2\gamma t) \frac{\sin^2 \omega_n t}{\omega_n^2} \right.$$

$$\left. + \frac{KTn^2}{\rho K_n^2} \left\{ 1 - \exp(-2\gamma t) \frac{2\gamma^2}{\omega_n^2} \sin^2 \omega_n t + \frac{\gamma}{\omega_n} \sin(2\omega_n t) + 1 \right\} \right] \qquad (2.32)$$

Though these expressions have been derived for homopolymer DNA, they can, in general, be applicable to heteropolymer DNA, assuming that averaging of the elastic constant is possible for the entire rod in view of the small variations in the stacking interaction between different bases of the DNA.

3. KINK FORMATION.

The standing waves along the length of the DNA polymer cause local zones of strectching and compression. At the stretched zones, conformational changes occur in the DNA structure which we define as kinks. In order that a kink should occur, the average energy density must be sufficient to unstack the bases and partially unwind the DNA molecule. Unstacking requires $\Delta E \simeq 2K$ cal/mol [17] and formation of one full super helical turn in the DNA molecule needs a change of free energy [18] $\Delta E = 0.88$ KT. Equations (2.31) and (2.32) show that the average deformation energy density depends on $P^2$, KT, etc. and P itself depends on the temperature T of the solvent. At T = 300°K, KT = 0.6 K cal/mol. So, it is quite possible that the strain energy density developed locally in the DNA molecule may be relieved through

unstacking of base pairs together with some amount of additional untwisting between them. Structural considerations (not within the mathematical treatment) show that, at the kinked position, unstacking should involve the change of sugar puckering from C2'-endo configuration in B-DNA to C3'-endo (3'-5') C2'-endo mixed puckering form [19].

Drug intercalation: If waves produced in the DNA molecule can cause stretching of base pairs by 3.4 Å or more, drugs present near those stretched places insert their chromophoric groups within the gap thus produced. Technically, this phenomenon is represented by drug intercalation. Structurally, this stretching is also associated with left handed unwinding between adjacent base pairs. This unwinding will produce right handed superhelicity and will gradually titrate out negative superhelix density in the covalently closed DNA [20]. Bresloff et.al., [17], have observed that the maximum number of drugs that can intercalate is one drug per two base pairs, a phenomenon known as near neighbor exclusion of dye intercalation.

Since theoretically there should be an upper cut-off in the excited frequency within the polymer as explained below, the total number of kinks formed will also show an upper limit and thus there will always remain occluded sites for the drugs to intercalate. To understand this feature, let us go back to the one dimensional discrete lattice structure.of DNA. In order to generate the maximum number of kinks, i.e., the maximum possible frequency and the shortest wave for the longitudinal motion, let us ignore the dissipative and fluctuation terms; i.e., put $Q_j$ of Equation (2.2) as $Q_j = 0$. Then, we apply Lagrange's equation of motion with L as given in Equation (2.1), where $\alpha$ now stands for the spring constant, and we get

$$m \ddot{u}_j = \alpha(u_{j+1} + u_{j-1} - 2u_j) \tag{3.1}$$

Solving (3.1) in the form

$$u_j = \Psi \exp[i(Kx - \omega t)], \tag{3.2}$$

one gets the frequency dispersion relation as

$$\omega = (4\alpha/m)^{1/2} \sin(Kb/2) \tag{3.3}$$

for the positive branch. From (3.3), it follows that the maximum frequency $\omega_{max}$ is possible at $Kb/2 = \pi/2$; i.e., at $\lambda = 2\pi/K = 2b$.

Figure 1(a) shows the propagation of the shortest wave ($\lambda = 2b$) causing longitudinal displacements in monomer units of a DNA molecule. Figure 1(b) shows the zones of stretching (intercalated sites) and compression (excluded sites). Thus,

we can easily comprehend the basic principle leading to the near neighbor exclusion phenomenon of drug intercalation. Miller [19] has shown, from structural considerations, that disruption of the first intercalation will occur if the second intercalation happens just at the adjacent site, violating the exclusion law. He has also shown how sugar puckering changes alternately from base pair to base pair at maximum drug intercalation condition. This is illustrated in Figure 1(c). Thus, the opposite sense of displacements between two adjacent base pairs Figure 1(b) will always be associated with alternate rhythms of sugar puckering changes.

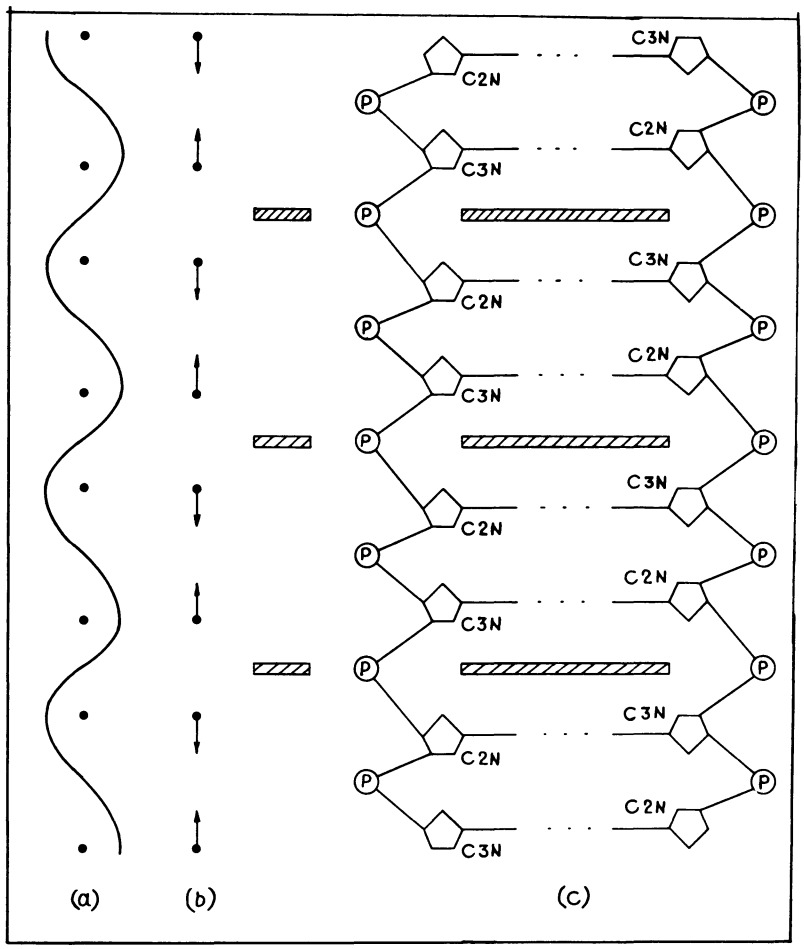


Fig. 1. Schematic representation of neighbour exclusion phenomena. (a) Propagation of shortest longitudinal sinusoidal wave ($\lambda$ = 2b) along the nonomer units. (b) Zones of stretching (intercalated sites) and compression (occluded sites) due to wave transmission. (c) Details of sugar puckering conformation accompanying maximum drug intercalation into the DNA molecule. Dashed blocks represent the intercalated drugs and C2N or C3N stands for C2'-endo or C3'-endo configuration of pentose ring.

DNA breathing: Evidences like exchanges of deuterium and tritium of solvent molecules with protons of DNA, normally engaged in Watson-Crick (W-C) base pairing [22] and irreversible melting of duplex strands [23] and the consequent lowering of the melting temperature ($T_m$) with application of formaldehyde, suggest that within the duplex, bubbles of open strands are always produced. These conformational fluctuations of helix opening and reclosing can also be explained by the thermal waves generated within the duplex. Groups of waves of different normal modes superpose with each other. As a result, localized regions may be produced where deformation energy may be sufficient to snap hydrogen bonds between bases. Lateral tensions produced at the compressional regions of longitudinal waves will be liable to such separating effects. Moreover, realistic boundary conditions may give rise to waves having small differences in frequencies. Superposition of such waves may also produce beats of frequencies of occurrences several times smaller than those of parental waves. Local melting phenomena produced by beats will show, therefore, time constants of magnitudes several orders higher. Mandal et al [10] have found experimentally that processes of duplex opening are innately slow, being of the order of 2 per second at 25°C. However, considerations of bending modes, of rotation of glycosidic bonds etc. which are beyond the present treatment can more easily explain the presence of premelted zones and their closing and also the associated frequencies.

The total average density A from Equations (2.31) and (2.32) due to wave propagation through the rod will be related to the total amount of breathing present within the DNA. Expanding the series and retaining the first order terms in time t, the average energy A can be expressed as

$$A \simeq \frac{\alpha_1}{\ell} + \frac{\alpha_2 t}{\ell} + \alpha_3 \ell t \tag{3.4}$$

where $\alpha_1$, $\alpha_2$, and $\alpha_3$ are proper constants derived from Equations (2.31) and (2.32). Since $\ell t$ is a second order term,

$$A \simeq \frac{\alpha_1}{\ell} + \frac{\alpha_2 t}{\ell} \tag{3.5}$$

Since this is related to the amount of breathing, the instantenous fraction of closed double helical region can be expressed as

$$D(t) \simeq 1 - \left( \frac{C_1}{\ell} + \frac{C_2 t}{\ell} \right) \tag{3.6}$$

This expression can be contrasted with equation (3.7) obtained experimentally [24]

as

$$O_N(t) = 1 - 2(K_f - K_b)t/N \tag{3.7}$$

where $O_N(t)$ is the fraction of closed double helical content (N base pairs long at $t = 0$) at any subsequent time t and $K_f$ and $K_b$ are reaction constants.

It has been experimentally found [25] that breathing becomes more extensive as the superhelical density within the DNA is increased. One of the possible mechanical effects of introducing superhelicity is to reduce the effective length of the DNA. Equation (3.5) and also (2.31) and (2.32) show that deformation energy is increased on making the rod smaller. Hence, with smaller length of DNA, deformation i.e. consequent breathing may get enhanced.

4. TORSIONAL MOTION IN DNA.

It has been found that DNA duplex in high salt concentration can exist either in a left handed conformation or in an overwound right handed C form of DNA depending on the sequence of nucleotide bases. It is well known that in high salt concentration DNA with alternating poly (dG - dC) assumes left handed conformation[10,22] whereas, DNA with no preferred sequences assumes an overwound right handed C form[27]. This salt induced helix - helix transition can be explained at least qualitatively, by assuming the following: the torsional strain generated in the body of B-DNA molecule due to random torque impacts of the solvent molecules, pass through the DNA molecule in the form of waves with more undamped amplitudes at high salt concentration. During optimal torsional oscillation the sequence specificity of the structure engages in suitable high salt environmental interaction so that either the left-handed structure as in poly(dG-dC) or a right-handed overwound structure of C-DNA held stabilized. These transitions can be accounted for if one considers the torsionally stressed DNA molecule under rotary Brownian motion in solution. The equation for torsional oscillation in DNA molecule is given by

$$\ddot{\theta} + 2\gamma\dot{\theta} - c^2 \frac{\partial^2\theta}{\partial x^2} = A(x,t) \tag{4.1}$$

where $\theta$ is the angular displacement at x, $\gamma$ is the damping coefficient, c is the wave velocity and A is the effective Brownian torque. The conditions for the system are

$$\theta(x,0) = 0 \ , \quad \frac{\partial\theta(x,0)}{\partial t} = \frac{\tau}{\rho}\,\phi(x) \tag{4.2a}$$

$$\theta(0,t) = 0 \ , \quad \frac{\partial\theta(\ell,t)}{\partial x} = 0 \ . \tag{4.2b}$$

Assuming that $\theta(x,t) = \theta_1(x)\,\theta_2(t)$, the solution of equation (4.1) becomes

$$\langle\theta\rangle = \frac{2\tau}{\ell\rho}\sum_{n=0}^{\infty}\phi_{1n}\sin\frac{\pi x}{2\ell}(2n+1)\exp(-\gamma t)\frac{\sin\omega_n t}{\omega_n} \tag{4.3}$$

The expression for the average energy density for the polymer is

$$\langle E\rangle = \sum\left\{\left(\frac{\rho}{2} - \frac{KT}{A^2}\right)\ell\gamma^2\langle\theta_2\rangle^2 - \frac{A\rho}{2}\ell\gamma\langle\theta_2\rangle + \frac{A^2\rho\ell}{4}\right\} \tag{4.4}$$

where

$$\langle\theta_2\rangle = A\exp(-\gamma t)\frac{\sin\omega_n t}{\omega_n} \quad \text{and} \quad A = \frac{2\tau}{\ell\rho}\phi_{1n} \tag{4.5}$$

For attaining a stable conformation, the polymer has to twist by a suitable angle to make the average energy minimum, i.e., $\frac{\partial E}{\partial \theta_2} = 0$ which gives

$$\langle\theta_2\rangle = \frac{A}{2\gamma\left[1 - \frac{2KT}{\rho A^2}\right]} \tag{4.6}$$

Since the average deforming twist $\langle\theta\rangle = \langle\theta_1\rangle\langle\theta_2\rangle$ at any place depends on $\langle\theta_2\rangle$, the relative sign of the quantities $\tau\phi_{1n}$ and $(1 - 2KT/\rho A^2)$ actually govern the state of overwinding or underwinding developed in DNA molecule. To have left handed conformation, the deforming negative twist must overcompensate the original twist of the right handed B-DNA. At high salt concentration the damping coefficient $\gamma$ decreases very much and $\langle\theta_2\rangle$ becomes correspondingly large allowing undamped wave of high amplitude. $\langle\theta_2\rangle$ can assume negative sign depending on $\tau\phi_{1n}$ is negative and $\rho A^2 > KT$ or $\tau\phi_{1n}$ is positive and $\rho A^2 < KT$. With negative value of $\langle\theta_2\rangle$, right handed DNA segment will not only swing over to left handed form, but will also be stabilized to remain in the left handed conformation in high salt concentration. From structual consideration, Drew et al. [28] have shown that in the left handed conformation, $N_2$ of guanosine of poly (dG - dC) will be more exposed to form a hydrogen bond with water molecule which is itself hydrogen bonded to the phosphate oxygen at the edge of the groove and thus left handed structure is stabilized. $\langle\theta_2\rangle$ can assume a positive value if $\tau\phi_{1n}$ at the boundary condition is positive and $\rho A^2 > KT$ or $\tau\phi_{1n}$ is negative and $\rho A^2 < KT$. When $\langle\theta_2\rangle$ assumes a positive value, then the DNA segment passes over to an overwound right handed DNA. This overwound form of DNA is stabilized in C form.

## 5. CONCLUDING REMARKS.

DNA molecules in solution continuously suffer from Brownian agitations, and as a result excited internal degrees of freedom render to the helices a very flexi-

ble conformation. Our analyses have shown how longitudinal and torsional elastic vibrations of DNA molecule can be generated resulting in drug intercalation, breathing, or conformational transition. The analysis of longitudinal vibrations helps in understanding one of the various modes of protein-DNA interaction. Drugs having chromophoric planar groups with polypeptide interspersion like actinomycin D[25], Echinomycin[30] etc. bind with DNA. Our model does explain how chromophoric groups intercalate with DNA. And this suggests that DNA binding proteins can also have a similar binding mode provided intercalating planar chromophoric rings (tyrosin, tryptophan residues) are present within them. In both pfl virion and gene-V-protein-DNA complex, there is evidence for stacking of tyrosine residues with nucleic acid base [31]. Furthermore, it has been experimentally demonstrated that the tripeptide namely lysyltryptophyl- -lysine (Lys-Trp-Lys) binds with apurinated DNA through stacking of the Tryptophan residue at the apurinic sites [32].

Our analysis has remained simplistic in several respects. Exact geometry and intertwined double helical shape of the molecule was not taken into account and thus some restrictions in excitations could not be found. The analysis of torsional vibrations in DNA molecule shows that in high salt concentration, DNA duplex can oscillate between left handed and right handed helical conformations depending on sequences of nucleic acid bases. Other classes of thermally generated motions like bending, twisting, rocking, sliding, etc. have not been considered in isolation. Thus explanations of the phenomena that we have discussed above, have been rather qualitative and the optical properties of DNA could not be touched at all. Only a unified theory capable of generating all the internal motions together would be able to describe all the dynamic phenomena with exact quantitative details.

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