Conformations of Linear DNA

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We examine the conformations of a model for under- and overwound DNA. The molecule is represented as a cylindrically symmetric elastic string subjected to a stretching force and to constraints corresponding to a specification of the link number. We derive a fundamental relation between the Euler angles that describe the curve and the topological linking number. Analytical expressions for the spatial configurations of the molecule in the infinite length limit are obtained. A unique configuration minimizes the energy for a given set of physical conditions. An elastic model incorporating thermal fluctuations provides excellent agreement with experimental results on the plectonemic transition.

I. HISTORY AND INTRODUCTION

Conformations of a slender elastic rod were originally viewed as an interesting problem in classical elasticity theory. Kirchhoff [1] was the first to make significant headway towards a complete solution. Almost a century later, as polymers became the subject of intense study, interest in the problem picked up once again [3]. After the discovery of biological polymers—nucleic acids and proteins—researchers recognized the importance of predicting the elastic shape of linear molecules. The shape (“tertiary structure”) of DNA and RNA plays an important role in the processes of replication and transcription. Because of this a number of authors have analyzed various aspects of elastic DNA conformation [12] for both closed (circular) and open (linear) configurations. The approaches taken include Lagrangian mechanics [12], (numerical) molecular dynamics [6] and statistical mechanics [9,11,2]. Despite significant progress [2], the equilibrium configurations of infinitely long open DNA have not been analytically described. Our main aims are to set up a formalism for obtaining equilibrium configurations; to find one such configuration for stretched twisted DNA, and to set up a model of plectonemic transition to compare with experimental results [11].

The work reported here is based on two major results obtained over a century apart. Kirchhoff [1] provided the basic framework of elasticity theory. He observed that the equations of equilibrium that describe an elastic rod are formally identical to the equations of motion of a heavy symmetric top with one point fixed (see figure 1). The rod Hamiltonian is identical to the top Lagrangian, with arclength mapping onto time. This duality provides an added insight into the nature of the solutions. White’s Theorem [4] provides another crucial analytical tool. This important theorem relates the linking number—a natural topological invariant of strings and ribbons—to two manageable components, each calculable in terms of locally defined quantities. According to White’s theorem, \( Lk = Tw + Wr \), \( Lk \) is the linking number, while \( Tw \), the twist, monitors the twist of the molecule about its axis, and \( Wr \), the writhe, records the contortions of the axis. This theorem greatly simplifies the problem of formulating a constraint on the linking number. In addition we make use of the results of Fixman and Kovac [20] and Marko and Sigcia [11,24] to develop thermal effects of the plectonemic transition.

II. THE MODEL

The elastic model of DNA represents the molecule as a slender cylindrical elastic rod. To model external forces and torques the rod is stretched (in the \( z \) direction) by a force \( F \) and is required to have a fixed \( Lk \) (see figure 2 top). The rod is parametrized by arclength, \( s \). At each point \( s \) we describe the rod by relating the local coordinate frame \( \mathcal{L} \) to the frame \( \mathcal{L}_0 \) rigidly embedded in the curve in its relaxed configuration. The relationship between the stressed and unstressed local frames is specified by Euler angles \( \theta(s), \phi(s), \psi(s) \) needed to rotate \( \mathcal{L}_0 \) into \( \mathcal{L} \) (see figure 2 bottom). The shape of the backbone \( \mathbf{r}(s) \) is traced out by the unit tangent \( \mathbf{t}(s) \), \( \mathbf{n}(s) \), a unit normal, keeps track of the twist, \( T \omega \). In this paper we will often omit \( s \)-dependence for brevity. We also make use of the notation \( \dot{x} \equiv \frac{dx}{ds} \).

\[
\mathbf{r}(s) = \int_0^s \mathbf{t}(s') \, ds' \tag{1}
\]
\[
\mathbf{t}(s) = (\sin \theta \sin \phi, \sin \theta \cos \phi, \cos \theta) \tag{2}
\]
\[
\mathbf{n}(s) = (\cos \phi \cos \psi - \cos \theta \sin \phi \sin \psi, -\cos \phi \sin \psi - \cos \theta \cos \phi \sin \psi, \sin \theta \sin \psi) \tag{3}
\]

Let the elastic constants of bending and torsional stiffness be denoted, respectively, by \( A \) and \( C \), and let \( L \) be
the length of the rod. The energy of the twisted, stressed rod is the sum of bending and twisting energies and the potential energy produced by the stretching force $F$. Using (4) and (3):

$$E_{\text{tot}} = E_{\text{el}} - F \cos \theta = E_{\text{bend}} + E_{\text{twist}} - F \cos \theta =$$

$$= \frac{A}{2} \int_0^L \left( \dot{t} \right)^2 ds + \frac{C}{2} \int_0^L (\mathbf{n} \times \dot{\mathbf{n}}) \cdot \mathbf{t} \right)^2 ds +$$

$$- F \cos \theta$$

(4)

Using (2) and (3) in (4) we obtain

$$E_{\text{tot}} = \int_0^L ds \left( \frac{A}{2} \left( \dot{\theta}^2 \sin^2 \theta + \dot{\phi}^2 \right) + \right.$$

$$\left. \frac{C}{2} \left( \dot{\phi} \cos \theta + \dot{\psi} \right) \right)^2 - F \cos \theta.$$  

(5)

The feature that sets this work apart from previous attempts and allows us to unambiguously determine a unique configuration for a given set of initial conditions is the constraint of maintaining a fixed linking number, $Lk$. Although linking number is usually associated with closed curves, the bound ends of our string allow us to define a fractional linking number for it. A caveat is that the local expressions we derive are only valid for the configuration (extended) we consider. White’s theorem (3) allows us to express $Lk$ in terms of its components, $Tw$ and $Wr$. Using (3) and (2):

$$Tw = \frac{1}{2\pi} \int_0^L (\mathbf{n} \times \dot{\mathbf{n}}) \cdot \mathbf{t} \ ds = \frac{1}{2\pi} \int_0^L \dot{\phi} \cos \theta + \dot{\psi} \ ds$$  

(6)

$$Wr = \frac{1}{4\pi} \int_0^L ds \int_0^L ds' \frac{(\mathbf{r} - \mathbf{r}') \cdot (\mathbf{t} \times \mathbf{t}')}{|\mathbf{r} - \mathbf{r}'|^3}.$$  

(7)

A local expression for twist follows straightforwardly, as evidenced by the far right hand side of Eq. (9). The writhe, however, is not yet suitable for use as a Lagrange multiplier. To express it as an integral of a local quantity we use a theorem by Fuller (4). The theorem allows us to define $Wr$ locally using a diffeomorphism onto a reference curve, $C_r$. (Once again, we must stress that a different configuration, e.g. a circular plasmid, would require a different reference curve, producing slightly modified local expressions). The writhe is expressed as

$$Wr = Wr_r + \frac{1}{2\pi} \int_0^L t_r \times t_r \cdot \frac{d}{ds} \left( t_r + t \right) ds,$$  

(8)

where $Wr_r$ is the writhe of the reference curve. Finding a suitable reference curve proves crucial. The best choice is also the simplest - a straight line $C_r = (0, 0, s)$. This gives $t_r = (0, 0, 1)$ and $Wr_r = 0$. Substituting (2) into (8) we obtain

$$Wr = \frac{1}{2\pi} \int_0^L \dot{\phi} (\cos \theta - 1) \ ds.$$  

(9)

Combining (8) and (9) we are led to the simple expression for $Lk$:

$$Lk = -\frac{1}{2\pi} \int_0^L \left( \dot{\phi} + \dot{\psi} \right) ds.$$  

(10)

Thus we have derived a simple conservation law that expresses the invariance of $Lk$. Inserting $p dLk$ into the right hand side of Eq. (9), with $p$ a Lagrange multiplier, the expression to be minimized becomes

$$H = \int_0^L \frac{A}{2} \left( \dot{\phi}^2 \sin^2 \theta + \dot{\psi}^2 \right)$$

$$+ \frac{C}{2} \left( \dot{\phi} \cos \theta + \dot{\psi} \right)^2 - F \cos \theta - p \left( \dot{\phi} + \dot{\psi} \right) ds.$$  

(11)

DNA conformations of minimum energy are found among the extrema of $H$.

### III. SOLUTIONS

We find the extrema of $H$ by applying standard variational techniques to (11). The resulting Euler-Lagrange equations for $\theta(s)$, $\phi(s)$ and $\psi(s)$ are:

$$\ddot{\phi} = \frac{p (1 - \cos \theta)}{A \sin^2 \theta}$$

$$\ddot{\psi} = \frac{p (1 - \cos \theta) \cos \theta}{A \sin^2 \theta}$$

$$\ddot{\theta} = - \frac{p^2}{A (1 + \cos \theta)} - F \cos \theta + E_0.$$  

(12)

(13)

A central goal is to find a unique configuration of the rod given a set of externally imposed constraints, $F$ and $Lk/L$, where $L$ is the length of the rod. We find that equations (12) and (13) support two types of solutions. The first is a family of twisted vertical lines:

$$\theta = 0; \quad \phi = 0; \quad \psi(s) = (2\pi Lk/L) s$$  

(14)

The energy of the straight line follows directly from (3):

$$E_{\text{line}} = \frac{2CT}{2} \left( \pi Lk/L \right)^2.$$  

(15)

The second family of solutions can be extracted from (13). Multiplying Eq. (13) by $\sin^2 \theta$ and integrating once we can rewrite (13) in the following form ($u \equiv \cos \theta$):

$$ds = \frac{du}{\sqrt{\frac{2p^2}{A^2} (1 - u) + \frac{p^2}{A^2} (E_0 - Fu) (1 - u^2)}}$$

$$\equiv \frac{du}{\sqrt{\frac{2p^2}{A^2} (u - a) (u - b) (u - c)}}$$  

(16)

These “writhing” solutions are characterized by the roots $(a, b, c)$ of the cubic polynomial in the denominator of (16) (see figure 3). One of the roots, either $a$ or $b$, is 1. If $u = 1$ is a single root, then the configurations form
“superhelices.” If $u = 1$ is a double root $(a = b = 1)$ the molecule supports a soliton-like excitation (See figure 3). The quantity $u = \cos \theta$ takes on values between $c$ and $b$, the quadrature turning points. The expressions for $\phi$, $\psi$ and other quantities of interest follow by quadratures. The integrals are easily evaluated in terms of elliptic functions.

We have investigated the properties of solutions to \((12)\) and \((13)\), with the bending and torsional stiffness, $A$ and $C$, appropriate to DNA \([3]\). Using both numerical and analytical methods we find that, given a particular $Lk/L$, the member of the writhing family with the lowest energy is the soliton configuration $(a = b = 1)$ (see figures 3 and 4). The shape of this solution is defined by the following relationship between the arclength $s$ and $u \equiv \cos \theta$:

$$\begin{align*}
  s(u) &= \sqrt{\frac{2F}{A(1-c)}} \ln \left( \frac{1 + \sqrt{\frac{u - c}{1-c}}}{1 - \sqrt{\frac{u - c}{1-c}}} \right) \\
  \text{where the lower root, } c, \text{ is given by} \\
  c &= \frac{2(\pi C Lk/L)^2}{4AF} - 1 \\
  &= \frac{p^2}{4AF} - 1, \quad (17)
\end{align*}$$

and $\phi$ and $\psi$ are similarly determined. A very interesting quantity is the energy of the soliton and its relationship to the twist of the twisted line solution (which are both infinite in the limit $L \to \infty$):

$$E_{\text{soliton}} = E_{\text{line}} + \Delta E \quad \text{with } \Delta E = \frac{4F}{L} \sqrt{\frac{1-c}{1+c}} \left[ \frac{1-c}{1+c} - \arctan \left( \sqrt{\frac{1-c}{1+c}} \right) \right] \geq 0 \quad (19)$$

It’s clear from \((14)\) that the $E_{\text{soliton}}$, while smaller than the energies of the other members of the “writhing” family, is always greater (by a finite amount) than the energy of the twisted line configuration satisfying the same conditions.

**IV. PLECTONEMIC TRANSITION**

Thus we find that an extended solution that minimizes energy and has a specified $Lk/L$ it is always a twisted straight line. To check stability we perturb the straight line solution $\theta(s) = 0 + \delta \theta(s)$. The perturbation calculation shows that the non-trivial zero-energy mode satisfies

$$\left( A \frac{d^2}{ds^2} - \left( F - \frac{p^2}{4A} \right) \right) \delta \theta(s) = 0 \quad (20)$$

Thus for $Lk/L \leq \frac{4\pi \sqrt{F}}{L}$ the straight line $\theta = 0$ is stable to small fluctuations. What happens to the molecule when the $Lk/L$ approaches the critical value? Our results strongly indicate that the molecule attempts to loop over and pass through itself to shed a unit of $Lk/L$ and thus starts to form a plectonemic bubble. In this sense the twisted rod is in a metastable state. The plectoneme plays the role of the “bounce” via which a system tunnels out of the false vacuum. Beyond the transition to local instability the plectonemes ought to proliferate. To explore this scenario we formulate a very simple model of the plectonemic transition of stretched twisted DNA and compare its predictions with recent beautiful experiments by Strick et al. \([4]\).

**A. plectonemic transition model**

The model is diagrammed in fig. \([5]\). In the following all quantities are normalized by the length $L$. DNA researchers prefer to use $\sigma \equiv \Delta Lk_{tot}/Lk_0$ to measure topological properties of DNA. Here $Lk_0$ is the natural link of the unstressed DNA molecule; B-DNA has one right-handed twist every $h = 3.4nm$. We will follow this notation.

The molecule is constrained to have a total Link $Lk_{tot} = \sigma_{tot}/h$. The plectonemic fraction takes up $X$ leaving $1 - X$ straight. The plectoneme has a radius $R$ and a pitch $P$. The straight portion is twisted to its critical value $dTw = h\sqrt{AF}/(2\pi C) = \sigma/h$. The actual twist is slightly below critical \([22]\), but numerical results indicate that the precise value (which depends weakly on $L$) is adequately approximated by that of an infinite string \([22]\). Guided by “twist conservation” implied by eqns. \((12)\) we assign the same rate of $dTw$ to the plectoneme. The remaining link, $Lk_{tot} - (Tw_{pl} + Lk_l)$, is absorbed by the plectoneme’s $WR_p$. Let us account the link distribution:

$$Lk_l = Tw_k = \frac{\sigma_l}{h} X \quad \text{and } Lk_p = Lk_{tot} - Lk_l = \frac{\sigma_{tot} - \sigma_l}{h} + \frac{\sigma_l}{h} X = WR_p + Tw_p \quad (21)$$

Because the plectoneme has the same rate of twist as the line, we can read off its writhe from eqn. \((21)\). At the same time the writhe of a plectoneme can be expressed as a function of $P$ and $R$ \([21][22]\). This gives us a constraint:

$$\frac{\sigma_{tot} - \sigma_l}{h} = WR_p = \frac{XP}{2\pi (R^2 + P^2)} \quad (22)$$

Up to now we have not considered any thermal effects or corrections. Our aim is to build a formalism of obtaining equilibrium zero-temperature solutions about which a thermodynamic theory can be obtained (e.g. by considering fluctuations) \([1]\). However, because the experiments we are examining contain a regime in which thermal effects play a significant role \([19]\) we must consider them.
Marko and Siggia [11,12] have derived the free energy of a plectoneme in their examination of fluctuations about helical structures. To within order unity constants

$$E_{pl} = \frac{A}{2} \left( \frac{R}{(R^2 + P^2)^{3/2}} \right)^2 + \frac{C}{2} \left( \frac{2\pi \sigma_0}{h} \right)^2 +$$

$$\left( (R/r_0)^{-12} + (\pi P/r_0)^{-12} \right)/r_0 +$$

$$A^{-1/3} \left( R^{-2/3} + (\pi P)^{-2/3} \right)$$

(23)

The first two terms in (23) are elastic contributions from curvature and twist, respectively. The next line is the hard core interaction ($r_0 \approx 1.75$nm [14]). The last term is the entropic penalty incurred for winding too tightly [11]. (It is interesting to note that although we include the last term in our model, its value is always negligible.) Setting the plectonemic fraction $X$ we use (22) and (23) to minimize $E_{pl}$ with respect to $R$ and $P$.

Next let us determine the thermal behavior of the straight-line segment. Such behavior for the untwisted rod has been examined in some detail by Fixman and Kovak [20]. Eqn. 21 allows us to make use of their results provided we replace $F$ with $F' \equiv F - \frac{\pi}{4}$. Siggia provided a valuable summary of their results in an approximate interpolation formula [24,11]. We employ the above substitution in Siggia’s result to solve for the thermal shortening of the straight portion of the molecule. $Z$ is the actual observed extension:

$$\frac{(F - \frac{\pi}{4}) A}{k_b T} = \left( 1 - \frac{Z}{X} \right)^{-2} - 1 + \frac{Z}{X}$$

(24)

In the final analysis we compute the optimum plectonemic fraction $X$ and the extension $Z$ for a given $Lk$ and $F$. The results are plotted in fig. 3 as a solid line and as a dashed line with experimental results [13]. Because our model is a very simple one, and we have made no attempts to compute exact parameters (i.e., ‘critical winding’, etc.) we cannot claim perfect agreement. Nonetheless the resemblance is striking. Our model shows the shift from purely thermal behavior for very small $\sigma$ to a transition completely driven by elastic considerations for larger $\sigma$’s and forces.

FIG. 2. The elastic strand is described by a local coordinate frame, $L$. At each point $L$ is related to an unstressed frame, $L_0$, by Euler angles. The molecule is stretched by $F$ and is required to have a constant $Lk$.

FIG. 3. The behavior of the solutions is determined by the polynomial $f(u) = 2F/A (u_a) (u - b) (u - c)$. The solid curve shows $f(u)$ for a typical set of parameters. Motion is defined where $f(u) \geq 0$ in the range $u_- \leq u \leq u_+$. The shaded curve shows a case where $u_+ > 1$. The dotted curve ($u_+ = 1$) shows the set of parameters that minimize the energy given a fixed $Lk$. This is the soliton configuration discussed toward the end of the paper.

FIG. 4. The writhing family of solutions. The solution with the lowest energy is the soliton. In the infinite-length limit the soliton and the twisted line have the same energy.

FIG. 5. The extended and plectonemic phase coexist in the molecule. The plectonemic phase takes up a portion $X$.

FIG. 6. A comparison of our predictions and the data of Strick et al. The families of curves are $\sigma = 0.102, 0.043, 0.031, 0.001$ and 0 from top to bottom. The stretching of the untwisted ($\sigma = 0$) line is purely entropic; $\sigma = 0.102$ transition is dominated by elastic energy. No attempts have been made to fit the data.

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FIG. 1. A mapping of arclength onto time renders the equations governing symmetric elastic rods and spinning tops identical. The top left figure represents our elastic model of DNA (see figure 3). The lower right figure is the conventional way of representing the motion of the top. The locus of the angles of inclination of the axis is represented as a curve on the unit sphere.
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\[ f(u) = \cos(\theta) \]
