Writhe distribution of stretched polymers

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Motivated by experiments in which single deoxyribose nucleic acid molecules are stretched and twisted we consider a perturbative approach around very high forces, where we determine the writhe distribution in a simple, analytically tractable model. Our results are in agreement with recent simulations and experiments.

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In recent years, there has been much interest in the area of statistical mechanics of semiflexible polymers. These studies have been motivated by experiments [1] on biopolymers in which single molecules are stretched and twisted to measure elastic properties. These experiments are designed to understand the role of semiflexible polymer elasticity in, for instance, the packaging of these polymers in a cell nucleus. Twist elasticity plays an important role in several biological functions. The first step in packaging deoxyribose nucleic acid (DNA) in a cell nucleus a few microns across involves DNA-histone association which makes use of supercoiling in an essential way. The process of DNA transcription can generate and be regulated by supercoiling [2]. Here we focus on a particular class of experiments which probes the twist elasticity of DNA.

In the experiments of Strick *et al.* [2] the ends of a single molecule of double stranded DNA are attached to a glass plate and a magnetic bead. Magnetic fields are used to rotate the bead and magnetic field gradients to apply forces on the bead. By such techniques the molecule is stretched and twisted and the extension of the molecule is monitored by the location of the bead. One thus gets the extension of the molecule as a result of the applied twist and force.

The simplest theoretical model used to interpret the experiments makes use of the fact that the molecule is under such high tension that it is essentially straight. We call this limit the *paraxial limit* of the elasticity of a semiflexible polymer keeping the optical analogy in mind [3,4]. In this situation, the molecule, being straight and taut, cannot intersect itself and so one does not expect self-avoidance effects to be important. In computing the partition function one simply sums over all configurations without regard to self-avoidance. This model is instructive because it is analytically tractable and enables us to derive a simple explicit analytic expression for the writhe distribution. This is the central result of our analysis.

Before discussing the schematics of the derivation of the writhe distribution let us define a few pertinent quantities: link, twist, and writhe numbers. For an open polymer of the kind that is used in the twist-stretch experiments one can define the link number (Lk), an arbitrary real number, as the externally imposed twist given by $2\pi n$ where n is the number of applied turns on the bead. The twist number (Tw) corresponds to the integrated rotation of the polymer around its backbone and the writhe number (Wr) pertains to the twist of the polymer backbone and is captured by the rotation of the tangent vector. In computing the writhe distribution we make use of the fact that the link number Lk is related to twist and writhe numbers via $\mathrm{Lk}=\mathrm{Tw}+\mathrm{Wr}$ [5–7]. It is convenient to go to the conjugate space and work with the variable B, the generator of link Lk. In this space the partition function $Z(B,f)$ neatly factors into writhe $Z_W(B,f)$ and twist $Z_T(B,f)$ [8]. The distribution $\tilde{Z}(\mathrm{Lk},f)$ is a convolution of the writhe distribution and the twist distribution. We compute the link distribution in the $\alpha=L_{\mathrm{BP}}/L_{\mathrm{TP}}$ (the ratio of the bend and the twist persistence lengths) $\to 0$ limit. In this limit the writhe distribution coincides with the link distribution. This is simply because in the $\alpha\to 0$ limit it is very expensive to twist the polymer around a straight backbone and the polymer goes into a bending mode resulting in a twisting of the polymer backbone [5]. From the writhe distribution computed in this manner, one can recover the link distribution by convolving it with the distribution of "dynamical twist."

Our starting point is the wormlike chain (WLC) model in which the polymer is modeled as a framed space curve $\mathcal{C}=\{\mathbf{x}(s),\hat{e}_i(s)\}, i=1,2,3$, where $0\leqslant s\leqslant L$ is the arclength parameter along the curve. The unit tangent vector $\hat{e}_3=d\mathbf{x}/ds$ to the curve describes the bending of the polymer while the twisting is captured by a unit vector $\hat{e}_1$ normal to $\hat{e}_3$. In keeping with the optics analogy [3,4], we refer to $\hat{e}_1$ as the polarization vector. $\hat{e}_2$ is then fixed by $\hat{e}_2=\hat{e}_3\times\hat{e}_1$ to complete the right handed moving frame $\hat{e}_i(s)$, $i=1,2,3$. The energy $\mathcal{E}[\mathcal{C}]$ of a configuration of the polymer is a sum of contributions coming from its bending and twisting modes.

In the presence of large forces $|\mathbf{F}|\to\infty$, the molecule is stretched taut and there is an energy barrier for the polymer to pass through itself. In fact, the molecule is constrained to lie in nearly a straight line between its ends with small deviations. As mentioned earlier, in this regime the polymer being essentially straight cannot cross itself and thus self-avoidance effects present in a real polymer are automatically taken into consideration. Under these conditions the tangent vector only makes small deviations from the $\hat{z}$ direction. We can approximate the sphere of directions [5] by a tangent plane at the north pole of the sphere. We call this limiting model of the WLC the paraxial wormlike chain (PWLC) model.

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In this straight taut limit the polymer Hamiltonian [5,8–10] reduces to

$$H_{\mathrm{PWLC}} = \frac{p_\theta^2}{2} + \frac{(p_\phi - A_\phi)^2}{2\theta^2} + \frac{B^2\alpha}{2} - f\left(1 - \frac{\theta^2}{2}\right) = H_P - f + \frac{B^2\alpha}{2},$$

where H_P is the Hamiltonian of interest in the paraxial limit after we take out a constant piece. α is the ratio of the bend persistence length L_{BP} and the twist persistence length L_{TP}. The constant B corresponds to the conserved momentum conjugate to the Euler angle ψ. $f = FL_{\mathrm{BP}}/k_BT$ where F is the stretching force and k_BT is the thermal energy. The "vector potential" $A_\phi = B(\theta^2/2)$. Thus, the PWLC maps on to the problem of a particle moving on a plane in the presence of a magnetic field B and an oscillator confining potential which arises from making a small θ expansion for the stretching force $-f\cos\theta$ ($-f\cos\theta \approx -f(1-\theta^2/2) = -f + f\,\theta^2/2$) [8,10]. Notice that, in contrast to the regime of low tension [5], in this high tension regime the polymer cannot release an imposed twist by passing through itself because of the condition of suppression of configurations in which the polymer folds back onto itself. This implies that in contrast to the WLC model [5], in the PWLC model the free energy, torque-twist relation and other related distributions are *not* periodic functions of the imposed twist.

Introducing Cartesian coordinates $\xi_1 = \theta\cos\phi$ and $\xi_2 = \theta\sin\phi$ on the tangent plane R^2 at the north pole of the sphere of directions one can express the small θ Hamiltonian H_P as follows:

$$H_P = \frac{1}{2}(p_{\xi_1} - A_{\xi_1})^2 + \frac{1}{2}(p_{\xi_2} - A_{\xi_2})^2 + \frac{f}{2}(\xi_1^2 + \xi_2^2), \qquad (1)$$

where $A_{\xi_1} = -B\xi_2/2$, $A_{\xi_2} = B\xi_1/2$. The corresponding partition function Z can be written in terms of the eigenvalues E_n and eigenfunctions $\{u_n\}$ of H_{PWLC} as follows:

$$Z(B, f, \boldsymbol{\xi}_0, \boldsymbol{\xi}_L) = \sum_n e^{-\beta E_n(B,f)} u_n^*(\boldsymbol{\xi}_0) u_n(\boldsymbol{\xi}_L),$$

where $\boldsymbol{\xi}_0 = (\xi_1(0), \xi_2(0))$ and $\boldsymbol{\xi}_L = (\xi_1(L), \xi_2(L))$ are the initial and final tangent vectors at the two ends of the polymer. In order to simplify our analysis further we confine ourselves to the limit of very long polymers. Many of the experiments involving biopolymers such as DNA explore this limit of very long polymers which is also theoretically more tractable. For long polymers ($\beta = L/L_{\mathrm{BP}} \to \infty$) only the lowest eigenvalue $E_0(B,f) = \sqrt{f + B^2/4} - f + B^2\alpha/2$ [10,11] of H_{PWLC} dominates the expression for the partition function. Thus, the partition function can be written as

$$Z(B,f)_{\beta\to\infty} = e^{-\beta E_0(B,f)}. \qquad (2)$$

Determination of the writhe distribution. Let us consider the link distribution $\tilde{Z}(\mathrm{Lk}, f)$:

$$\tilde{Z}(\mathrm{Lk}, f) = \int e^{-\beta E_0(B,f) - iB\mathrm{Lk}} dB = \int e^{i\phi(B,\mathrm{Lk},f)} dB, \qquad (3)$$

where the phase $\phi(B, \mathrm{Lk}, f)$ is given by $\phi(B, \mathrm{Lk}, f) = i\beta E_0(B,f) - \beta B(\mathrm{Lk}/\beta)$. Since we are working in the limit of long polymers we can compute this partition function using the stationary phase or saddle point method [8] where only the stationary value $\phi(B_{\mathrm{st}}, \mathrm{Lk}, f)$ of the phase dominates. $\phi(B_{\mathrm{st}}, \mathrm{Lk}, f)$ is the *central quantity of interest* from which all the relevant elastic properties of the taut polymer can be derived. A similar perturbative analysis was done by Moroz and Nelson [10], who in fact carry the analysis out to higher orders in perturbation theory. What is new in our treatment is an *explicit analytical expression* for the writhe distribution in the straight taut limit.

Here we outline the derivation for the writhe distribution. The condition for stationarity ($\partial\phi/\partial B = 0$) satisfied by the stationary value B_{st} of B is

$$\frac{(i\widetilde{\mathrm{Lk}} - \alpha B_{\mathrm{st}})}{B_{\mathrm{st}}/4} = \frac{1}{\sqrt{f + B_{\mathrm{st}}^2/4}}, \qquad (4)$$

where $\widetilde{\mathrm{Lk}} = \mathrm{Lk}/\beta$. We restrict to the case of $\alpha = 0$. In this case the equation simplifies and we get the following stationary value of B_{st}:

$$B_{\mathrm{st}} = \pm i\frac{4\sqrt{f}\widetilde{\mathrm{Lk}}}{\sqrt{(1 + 4\mathrm{Lk}^2)}}.$$

Of the two roots, only the positive root is the physically relevant one consistent with the saddle point approximation. Setting $iB_{\mathrm{st}} = \tau$, where τ has the interpretation of torque, we get the following torque-link relation:

$$\tau = \frac{4\sqrt{f}\widetilde{\mathrm{Lk}}}{\sqrt{(1 + 4\widetilde{\mathrm{Lk}}^2)}}. \qquad (5)$$

Notice that for small $\widetilde{\mathrm{Lk}}$ we get a linear torque-link number (τ-$\widetilde{\mathrm{Lk}}$) relation which goes over to a torque-link relation independent of $\widetilde{\mathrm{Lk}}$ in the limit of large $\widetilde{\mathrm{Lk}}$. This is consistent with recent experiments [12] and numerically generated plots [8]. Inserting the expression for the stationary value B_{st} of B into the partition function $\tilde{Z}(\mathrm{Lk}, f)$ we get the pertinent writhe distribution $P(W, f)$. To compute this distribution we have made use of the fact that for $\alpha \to 0$, twist is extremely expensive and the applied twist goes completely into the bending mode. Thus, the link distribution in this limit corresponds to the distribution $P(W, f)$ of writhe. Given the writhe distribution $P(W, f)$ obtained in this manner the link distribution $P(\mathrm{Lk}, f)$ can be constructed for *all* values of α by convolving it with the twist distribution. In the generating function space one simply needs to multiply the writhe partition function $Z_W(B, f)$ by a simple Gaussian factor $Z_T(B, f) = e(-\alpha B^2/2)$ pertaining to the pure twist distribution at finite α.

The analytic form of the scaled distribution $P(W) = P(W, f)/P(0, f)$ of the writhe number W and stretching force in the high-tension regime (see Fig. 1) is

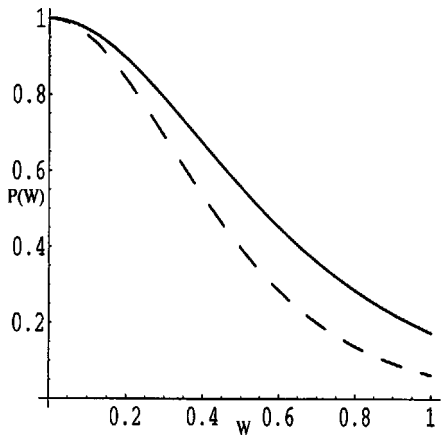

FIG. 1. The writhe distribution $P(W)$ for $f=2$ and $f=5$ (dashed curve) for $L/L_{\mathrm{BP}}=10$.

$$P(W) = \exp[-\beta\sqrt{f}\{\sqrt{1+4W^2}-1\}]. \tag{6}$$

Here $f=FL_{\mathrm{BP}}/k_BT$ with F the applied stretching force. This analytic form of the writhe distribution is the central result of this paper. Plots of this distribution are displayed in Fig. 1. The form reduces to a Gaussian form $\{P(W) \approx \exp[-2\beta f W2]\}$ for small values of writhe W and goes over to $P(W)\approx\exp[-2\beta\sqrt{f}|W|]$ for very large values of writhe W. The writhe distribution [Eq. (6)] represented in Fig. 1 has all the expected features—it peaks near smaller values and dies off for larger values of the writhe number. This writhe number gets suppressed with increasing strength of the stretching force. These qualitative features are in agreement with recent simulations [13] of the writhe number as a function of the stretching force. The explicit expression for the writhe distribution presented here is exact in the high tension limit and we expect quantitative agreement between the predicted distribution and future experiments probing the writhe distribution in this regime.

To summarize, we have obtained an explicit analytical expression for the writhe distribution of a semiflexible polymer in the high tension regime. The expression for the writhe distribution is simple and transparent and the qualitative features agree well with available computer simulations [13]. For very large forces a DNA molecule undergoes force induced denaturation [2] and therefore the distribution predicted here may not be directly applicable to DNA experiments at very high tension. However, one can test the predictions against experiments with other semiflexible polymers. We therefore, expect this work to generate interest amongst experimentalists to measure the writhe distribution of stretched polymers. The distribution computed here is also relevant to depolarized light scattering in turbid media in the limit of small angle scattering [3,4,14]. We also have an explicit analytic form for the torque-twist relation which is in agreement with recent experimental data [12]. In this model the mean-squared writhe fluctuation which corresponds to the second derivative of the conjugate distribution $\tilde{Z}(\mathrm{Lk}, f)$, diverges at $\tau=2\sqrt{f}$, the point at which a "buckling instability" sets in for the polymer. More explicitly, the divergence of the second moment of the writhe distribution at the buckling instability point $\tau=2\sqrt{f}$ has the following form which can be tested against future experiments:

$$\langle W^2\rangle = \frac{f}{4\left(f-\frac{\tau^2}{4}\right)^{3/2}}.$$

The second moment of the distribution is consistent with earlier predictions for the mean squared writhing angle for long tense molecules [15]. At the buckling instability there is a divergence of the writhe fluctuations. Since such a divergence makes the polymer backbone fluctuate violently one expects it to lead to a corresponding divergence in the mean squared extensional fluctuations $\langle\xi^2\rangle$. This has, in fact been probed in some recent experiments [16]. In the "paraxial" limit we find that $\langle\xi^2\rangle/\langle W^2\rangle=1/f$.

The paraxial approximation breaks down for large values of the applied twist more precisely for $\tau>2\sqrt{f}$ [see Eq. (4)] in which case the polymer explores configurations which deviate considerably from the straight taut limit. In the future we would like to explore the low tension nonlinear regime for the writhe distribution where phenomena like plectoneme formation would play an important role and nontrivial self-avoidance effects [3,15,17,18] need to be taken into consideration. The present work will provide a limiting check on calculations done in the nonlinear regime. As we mentioned earlier, the writhe distribution has important implications in the context of transcription and gene regulation. Therefore, a complete understanding of writhing of a biopolymer backbone and its stabilization is of relevance to current research.

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