Elasticity of semiflexible polymers

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We present a method for solving the wormlike chain model for semiflexible polymers to any desired accuracy over *the entire range of polymer lengths*. Our results are in excellent agreement with recent computer simulations and reproduce important qualitatively interesting features observed in simulations of polymers of intermediate lengths. We also make a number of predictions that can be tested in a variety of concrete experimental realizations. The expected level of finite size fluctuations in force-extension curves is also estimated. This study is relevant to mechanical properties of biological molecules.

Many biologically important molecules such as DNA and Actin, are semiflexible polymers [1]. In recent years there have been experiments [2] that pull and stretch single molecules to measure elastic properties. For instance, one can study the ''equation of state'' of a semiflexible polymer by measuring its extension as a function of applied force. Alternatively, one can tag the ends with fluorescent dye and determine the distribution of end-to-end distances. Such studies reveal a wealth of information about the mechanical properties of semiflexible polymers, which is of clear biological importance.

Till a few years ago, studies of polymer molecules such as DNA were limited to samples containing large numbers of molecules. This made it hard to probe the elastic properties of individual DNA, which are of vital importance to biological processes such as protein-induced DNA bending [2,3]. It is only quite recently, due to advances in technology that studies on single molecules became feasible. In order to correctly interpret single molecular experiments which are now being performed, a good theoretical understanding of semiflexible polymers is essential. Quite apart from the biological interest, semiflexible polymers are of interest to physicists [4,5]. This paper is devoted to understanding the equilibrium statistical mechanics of single semiflexible polymers.

Statistical mechanics of a single polymer molecule is dominated by fluctuations because it is a system of finite size. It is only in the thermodynamic limit of extremely long polymers that these fluctuations about the mean die out. Due to the dominance of fluctuations, the experimentally measured mean values for a semiflexible polymer crucially depend on the precise choice of the ensemble. For instance, one gets qualitatively distinct features in force-extension curves depending on whether the force or the extension is held constant in an experimental setup [6,7].

The most popular theoretical model for understanding semiflexible polymers is the wormlike chain (WLC) [8], which ignores self-avoidance and models the polymer as a framed space curve of fixed total length L with an energy cost for bending and twisting. In order to interpret the experimental data, it would be useful to have a clear and complete understanding of the predictions of the WLC model. Such an understanding would reveal the strengths and deficiencies of the model in describing real polymers and could be used to improve the model. There do exist partial results

[9] on the statistical mechanics of the WLC model: some theoretical studies [1] investigate the flexible limit of very long polymers (long compared to the persistence length; $L \gg L_p$). However experimental interest is *not confined to very long polymers*. For example, experiments on Actin [10] deal with polymers of length $L = 30$ μm, which is only about twice the measured persistence length of $L_p = 16.7$ μm. There is also theoretical work [9] around the rigid limit which works well up to $L = L_p$. There is a clear gap in the present understanding of the WLC model for polymers of intermediate length. Our purpose in this paper is to fill this gap. We present a solution of the WLC model and describe the equilibrium elastic properties expected from the model. Our solution is exact in the sense that the elastic properties can be determined to any desired accuracy. The main results of this paper are contained in the figures which show the force-extension relation and end-to-end distance distributions predicted by the WLC model. These predictions agree well with two independent computer simulations [9,6] (Figs. 3 and 4).

WLC model with pure bend. A configuration $\mathcal{C}$ of the polymer is described by a space curve $\vec{x}(s)$, with s the arc-length parameter ($0 \leq s \leq L$) ranging from 0 to L, the contour length of the polymer. The tangent vector $\hat{t} = d\vec{x}/ds$ to the curve is a unit vector ($\hat{t} \cdot \hat{t} = 1$) and the curvature of the polymer is given by $\kappa = |d\hat{t}/ds|$. We will suppose that one end of the polymer is tethered to the origin [$\vec{x}(0) = 0$] and the other end $\vec{x}(L) = \vec{r}$ is tagged. As the polymer configuration changes with thermal agitation, the location $\vec{r}$ of its tagged end fluctuates. The quantity we wish to compute is $Q(\vec{r})$, which is the probability distribution for the location $\vec{r}$ of the tagged end [6]. If the tagged end is pulled from $\vec{r}$ to $\vec{r} + d\vec{r}$, $Q(\vec{r})$ changes and consequently, the free energy. This implies that a force is needed to stretch the polymer. Thus $Q(\vec{r})$ is directly related to the force-extension relation of the polymer. To compute $Q(\vec{r})$ we need to sum over all polymer configurations $\mathcal{C}$ which end at $\vec{r}$, with a Boltzmann weight: $Z = \Sigma_{\mathcal{C}} \exp(-\mathcal{E}[\mathcal{C}]/k_B T)$, where the energy $\mathcal{E}$ associated with a configuration $\mathcal{C}$ is $\mathcal{E}(\mathcal{C}) = \frac{1}{2}A \int_0^L ds \, \kappa^2$ and A is the *bending modulus*. This is a standard counting problem in statistical mechanics and can be naturally addressed in the language of

path integration [11]. However, not much progress has been made because of the difficulty [12] presented by the inextensibility constraint. The key to circumventing this difficulty is to consider [1,13] Brownian motion in the space of *tangent vectors* ($\hat{t}$) rather than (as is customary for flexible polymers) position vectors $\vec{x}$. The tangent vectors form a unit sphere and the problem reduces to studying Brownian motion on the unit sphere, which can be handled by standard operator techniques familiar from quantum mechanics.

Let us suppose to begin with that the initial ($\hat{t}_A = d\vec{x}/ds|_{s=0}$) and final ($\hat{t}_B = d\vec{x}/ds|_{s=L}$) tangent vectors are held fixed. $Q(\vec{r})$ has the path integral representation

$$\mathcal{N} \int \mathcal{D}[\hat{t}(s)] \exp\left\{ -1 \Big/ k_B T \left[A/2 \int_0^L (d\hat{t}/ds)^2 ds \right] \right\}$$

$$\times \delta^3\left(\vec{r} - \int_0^L \hat{t}\,ds \right), \tag{1}$$

where $\mathcal{N}$ is a normalization constant. Instead of $Q(\vec{r})$ we focus on the quantity $P(z) = \int d\vec{r}\, Q(\vec{r}) \delta(r_3 - z)$, which is $Q(\vec{r})$ integrated over a plane of constant z. Note that $P(z)$ and $Q(\vec{r})$ vanish when the modulus of their arguments exceeds L. The generating function of $P(z)$ is defined as $\tilde{P}(f) = \int_{-L}^{L} dz\, e^{fz/L_p} P(z)$, where $L_p = A/k_B T$. Performing the elementary integrations involving δ functions we find that $\tilde{P}(f)$ can be expressed as $Z(f)/Z(0)$, where $Z(f)$ has the path integral representation

$$Z(f) = \mathcal{N} \int \mathcal{D}[\hat{t}(s)] \exp\left\{ -L_p \Big/ 2 \left[\int_0^L (d\hat{t}/ds)^2 ds \right] \right\}$$

$$\times \exp\left[f/L_p \int_0^L \hat{t}_z\, ds \right]. \tag{2}$$

Making the change of variable $\tau = s/L_p$, we arrive at the expression

$$Z(f) = \mathcal{N} \int \mathcal{D}[\hat{t}(\tau)] \exp\left\{ -\int_0^\beta d\tau [1/2(d\hat{t}/d\tau)^2 - f\hat{t}_z] \right\}, \tag{3}$$

where $\beta = L/L_p$. Equation (3) can be interpreted as the path integral representation for the kernel of a *quantum* particle on the surface of a sphere at inverse temperature β. Thus we can express $Z(f)$ as the quantum amplitude to go from an initial tangent vector $\hat{t}_A$ to a final tangent vector $\hat{t}_B$ in imaginary time β in the presence of an external potential $-f \cos \theta$:

$$Z(f) = \sum_n e^{-[\beta E_n]} \psi_n^*(\hat{t}_A) \psi_n(\hat{t}_B). \tag{4}$$

Here $\{\psi_n(\hat{t})\}$, is a complete set of normalized eigenstates of the Hamiltonian $\hat{H} = -(\nabla^2/2) - f \cos \theta$ and E_n are the corresponding eigenvalues.
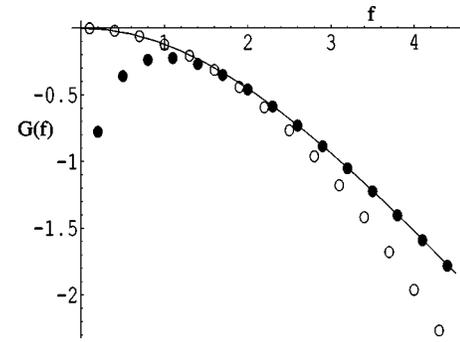
FIG. 1. $G(f)$ as a function of f for $\beta = L/L_p = 1$. Also plotted are approximate analytic forms valid in the small (open circles) and large (filled circles) force regimes.

In this paper, we focus on the situation where the boundary tangent vectors are unconstrained, i.e., they are integrated over with uniform weight. For free boundary conditions the situation is spherically symmetric and Q depends only on $r = |\vec{r}|$ and not on $\vec{r}$ and we can write $Q(r)$. The probability distribution for the end to end distance r is given by $S(r) = 4\pi r^2 Q(r)$, as can be seen by integrating $Q(\vec{r})$ over a sphere of radius r. As we did above, we can integrate $Q(\vec{r})$ over a plane of fixed z: $P(z) = \int d\vec{r}\, Q(\vec{r}) \delta(r_3 - z)$. $P(z)$ is the probability distribution for the z coordinate of the tagged end. Both $S(r)$ and $P(z)$ are experimentally accessible quantities and they are integrals of the spherically symmetric function $Q(\vec{r})$ over two dimensional surfaces. Using tomographic techniques (reconstruction of a function from a knowledge of its integral over two dimensional slices) one can deduce [14] the relation $S(r) = -2r dP(r)/dr$, where $P(r)$ is $P(z)$ with its argument replaced by r.

For free boundary conditions (4) can be written as a "vacuum persistence amplitude"

$$Z(f) = \langle 0 | \exp - \beta H_f | 0 \rangle, \tag{5}$$

where $H_f = -\frac{1}{2}\nabla^2 - f \cos \theta$ is the Hamiltonian of the rigid rotor [1] in a potential and $|0\rangle$ is the ground state of the free Hamiltonian $H_0 = -\frac{1}{2}\nabla^2$. The matrix H_f is an infinite matrix. The key to a numerically efficient evaluation of Eq. (5) is a convenient choice of basis. We choose a basis in which H_0 is diagonal and find that H_f is a symmetric tridiagonal matrix with diagonal elements $H_{ll} = l(l+1)/2$ and superdiagonal elements $H_{ll+1} = f(l+1)\sqrt{1/[(2l+1)(2l+3)]}$. Upto this point the treatment is completely analytical. To evaluate Eq. (5) we need to use numerical methods. We truncate the infinite matrix H_f to $N X N$ size and numerically evaluate Eq. (5) using the MatrixExp function in Mathematica [15]. Equation (5) then emerges as the first diagonal element of $\exp[-\beta H_f]$. We adjust the cutoff N until the answer stabilizes to desired accuracy.

From $Z(f)$ we deduce all the properties of the model, to an accuracy limited only by computational power. The form of $G(f) = -1/\beta \ln Z(f)$ is shown in Fig. 1 along with physically motivated approximate analytical forms valid in the small $[G(f) = C_1(\beta) f^2]$ and large $[G(f) = -f + \sqrt{f}$
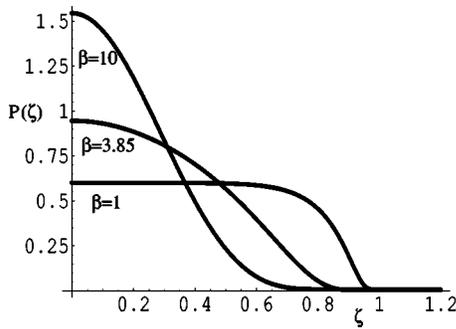
FIG. 2. The distribution $P(\zeta)$ of scaled extension $\zeta = z/\beta$ for $\beta = L/L_p$ equal to 1, 3.85, and 10.

FIG. 4. The function $Q(\rho)$ for $\beta = L/L_p = 1$, 3.85, and 5. Results of a simulation from Ref. [10] are also plotted on the curve for $\beta = 3.85$.

$-\ln f/(2\beta) + C_2(\beta)]$ force regimes. More terms can be computed, but this already gives a fair fit.

From $\tilde{P}(f)$ [which is equal to $Z(f)$ since $Z(0) = 1$], it is possible to compute $P(z)$ by performing the inverse Laplace transform. (Numerically it is more convenient to use the inverse Fourier transform by going to imaginary f). The results are shown in Fig. 2. For convenience, we set $L_p = 1$ so that $\beta = L$ and plot all figures in terms of scaled variables, $\zeta = z/\beta$, $\rho = r/\beta$. From the relation $S(\rho) = -2\rho(d/d\rho)P(\rho)$ we compute the distribution of end-to-end distance. These are displayed in Fig. 3. We have checked that these graphs quantitatively agree (to within the errors of the simulation data) with the published plots of Ref. [9]. Notice that $P(\zeta)$ and $S(\rho)$ both have a single maximum and the corresponding free energies have a single minimum. However, for a range of β near 3.8, $Q(\rho)$ develops a double humped form, reflecting the existence of two stable free energy minima resulting in a "first order transition," where the quotes signify that this is not a true phase transition due to finite size effects. This feature was first noticed [6] in computer simulations of the WLC model. Our theoretical work confirms the results of simulations presented in Ref. [6]. The form of $Q(\rho)$ is plotted in Fig. 4 along with the results of computer simulations from Ref. [6]. A property of direct experimental interest is the force-extension relation (FER). We work in the constant f ensemble and in Fig. 5 plot the scaled mean extension $\bar{\zeta}(f)$ [defined by $\bar{\zeta} = -\partial G(f)/\partial f$].

Since we are dealing with a system of finite size, we expect that the extension ζ will fluctuate about its mean value $\bar{\zeta}$. The theoretically expected root mean square value of these fluctuations $\Delta\zeta = \sqrt{1/\beta \partial \bar{\zeta}/\partial f}$ of ζ is shown in Fig. 5. These fluctuations clearly vanish in the limit of infinitely long polymers [1].

Our work provides predictions of force-extension curves for *all* lengths which can be tested against experiments. All the quantities computed here $[(Q(\rho), P(\zeta), S(\rho), \tilde{P}(f), G(f)$, and FER] are experimentally measurable. Here we briefly go over the pertinent experimental realizations of some of these quantities.

(a) Measurement of $Q(\rho)$: One can measure $Q(\rho)$ by attaching a bead to one end of the molecule and confining the bead in a stiff optical trap and by recording the distribution of location of the other end (tagged with dye) by means of a CCD camera. Using the techniques outlined in this paper one could work out the predictions of the WLC model to any desired accuracy, for example, experimental accuracy. (b) Measurement of $P(\zeta)$: $P(\zeta)$ can be measured by recording the location of the free end of the molecule on a given ζ plane and focussing all the light from the particular ζ plane by using a confocal microscope.

In this paper we have used free boundary conditions for the tangent vectors. Other boundary conditions can also be handled as explained in Ref. [16]. The boundary conditions depend on the particular experimental setup. For example, if the tangent vectors at the ends are held fixed one needs to use δ function weights rather than uniform ones. Choice of the-

FIG. 3. The distribution $S(\rho)$ of scaled end-to-end distances $\rho = r/\beta$ for $\beta = L/L_p$ equal to 1, 3.85, and 10. Dots show simulation data taken from Ref. [9].
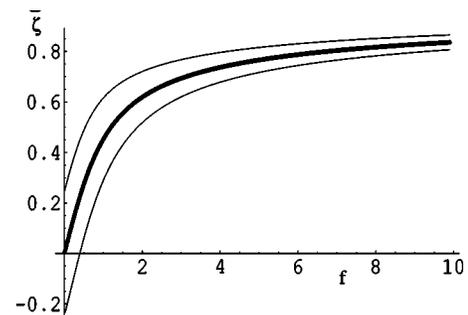
FIG. 5. The mean extension $\bar{\zeta}$ as a function of f (thick line) for $\beta = L/L_p = 10$. Also shown on either side are the root mean square fluctuations (thin lines) of the extension about its mean value.

oretical weights consistent with experimental boundary conditions is particularly crucial in the context of short polymers.

The FERs predicted by the model depend on the ensemble in which the calculation is done. Depending on the experimental situation one should use an ensemble in which one of $z, r, \vec{r}$ or their conjugate forces $f, f_r, \vec{f}$ is held constant. As an example we display in Fig. 5 the FER in the constant f ensemble.

The force extension relations in this ensemble are monotonic for *all* values of β. [In contrast, the FER in the constant ρ ensemble is nonmonotonic [6] in the β range where the function $Q(\rho)$ is double humped.] As mentioned earlier, since we are dealing with a finite system, which is not near the thermodynamic limit, equivalence between conjugate ensembles is not assured [7]. This is due to fluctuations around mean values which are not negligible for short polymers. Our analysis, being exact, correctly takes into account such finite size effects. The pure bend WLC model has a single parameter $\beta = L/L_p$ and predicts not only a force extension relation but also the amount of theoretically expected noise on this curve. In an experiment one can expect to see this noise over and above any instrumental noise that may be present in the system.

Self-avoidance that is present in real polymers is difficult to handle analytically and is one of the important directions for future work. Another important direction is the inclusion of twist [17]. We hope that the results of this paper will stimulate a detailed and quantitative comparison between the predictions of the WLC model and experiments, and lead to an improved understanding of the elasticity of semiflexible polymers.

Note added: Recently we learned of closely related work by Stepanow and Schütz [18].

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