

Bending elasticity of macromolecules: Analytic predictions from the wormlike chain model

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We present a study of the bend angle distribution of semiflexible polymers of short and intermediate lengths within the wormlike chain model. This enables us to calculate the elastic response of a stiff molecule to a bending moment. Our results go beyond the Hookean regime and explore the nonlinear elastic behavior of a single molecule. We present analytical formulas for the bend angle distribution and for the moment-angle relation. Our analytical study is compared against numerical Monte Carlo simulations. The functional forms derived here can be applied to fluorescence microscopic studies on actin and DNA. Our results are relevant to recent studies of “kinks” and cyclization in short and intermediate length DNA strands.

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I. INTRODUCTION

A classic study in elasticity is the bending of beams or rods subject to forces and moments [1]. At the cellular level there are many macromolecular structures, such as actin and cytoskeletal filaments, which are like beams in giving rigidity and structure to the cell. Unlike the beams studied by civil engineers, these macromolecular beams are subject to thermal fluctuations. The purpose of this study is to look at the role of thermal fluctuations in shaping the elastic properties of macromolecular beams.

We work within the wormlike chain model [2,3], which has been known to describe double stranded DNA [4] as well as actin filaments [5]. For clarity we consider an experiment in which one end of the molecule is fixed at the origin and its tangent vector at the same end is constrained to lie along the \hat{z} direction. We wish to know the number of configurations (counted with Boltzmann weight) that will result in the final tangent vector \hat{t}_f . In this paper we present an approximate analytical study of this statistical mechanical problem.

Some earlier treatments of this problem [6,7] are restricted to small bending angles, so that the polymer is essentially straight. One can then replace the sphere of tangent directions by the tangent plane to this sphere. This gives a good account of small bending angles. However, there is considerable experimental and theoretical interest in large bending angles to understand cyclization of DNA [8–10]. Reference [11] developed a new approximation technique that works even for large bending angles, say of order $\pi/2$. The treatment of [11] is general and includes applied forces and torques. In this paper we apply the general theory to a special case to illustrate its use: we treat the pure bending elasticity of a semiflexible polymer not subject to stretching forces or twisting torques. Two different experimental techniques are possible to probe the elastic properties.

One can tag the ends of the molecule with fluorescent dye [12] to determine the direction of the initial and final tangent vectors. By fluorescence video microscopy, one finds the angular distribution $P(\theta)$ of the bending angle θ , where θ is defined by $\cos \theta = \hat{t}_i \cdot \hat{t}_f$. This experimental technique has been used to study actin in two-dimensional studies in Ref. [12]. The angular distribution of θ gives us the elastic properties of the molecule, and one can compute, for instance,

the probability for a given bending angle θ and compare it with the theoretical expectation.

A more invasive experimental technique is to tether one end of the molecule, attach a magnetic bead to the other, and apply bending moments to the molecule by varying the direction of an applied magnetic field. Note that we do not constrain the final position of the molecule $x(L)$, only its final tangent vector \hat{t}_f . A uniform magnetic field will result in a pure bending moment without applying any stretching force. Plotting the bending moment vs the bending angle gives another experimental probe of the elastic properties. In this paper we derive the predictions of the wormlike chain for both these experimental situations.

We first derive an approximate analytical formula for the free energy, allowing for thermal fluctuations of a wormlike chain polymer. We then plot the expected theoretical distribution of bending angles and the theoretically expected moment-angle relation. We conclude with a discussion.

II. MECHANICS AND FLUCTUATIONS

In the simplest wormlike chain model, we model the polymer by a space curve $\vec{x}(s)$. $\vec{x}(s)$ describes the curve, and $\hat{t}(s) = \frac{d\vec{x}}{ds}$ is its tangent vector. s is the arc length parameter along the curve ranging from 0 to L , the contour length of the curve. $\vec{x}(0) = 0$ since one end is fixed at the origin. The tangent vectors at both ends, $\hat{t}(0)$ and $\hat{t}(L)$, are fixed to \hat{t}_i and \hat{t}_f , respectively.

The mathematical problem we face is to compute the partition function

$$Q(\hat{t}_i, \hat{t}_f) = \sum_{\mathcal{C}} \exp \left[-\frac{\mathcal{E}(\mathcal{C})}{k_B T} \right]. \quad (1)$$

In Eq. (1), the sum is over all allowed configurations of the polymer, those which satisfy the boundary conditions for the tangent vector at the two ends: $\hat{t}_i = \hat{t}(0) = \hat{z}$, $\hat{t}_f = \hat{t}(L)$. The energy functional is given by

$$\mathcal{E}(\mathcal{C}) = \frac{A}{2} \int_0^L \left(\frac{d\hat{t}}{ds} \cdot \frac{d\hat{t}}{ds} \right) ds, \quad (2)$$

where A is an elastic constant with dimensions of energy times length. The quantity $L_p = A/kT$ is the persistence length. For example, actin has a persistence length of about 16 μm and

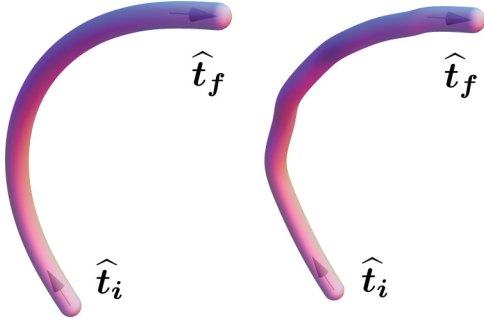


FIG. 1. (Color online) Two configurations of a molecule with fixed end tangent vectors \hat{t}_i and \hat{t}_f . (left) Minimum energy configuration and (right) the same configuration shown slightly perturbed by thermal fluctuations.

an elastic constant of 6.7×10^{-27} in units of N m². Lengths of actin filaments can go up to hundreds of microns, so the molecule is of intermediate flexibility.

We will compute the partition function assuming that near the stiff limit (L not much larger than L_p) the sum over curves is dominated by configurations near the minimum of the energy.

The minimum energy configurations of the polymer are those where the tangent vector $\hat{t}(s)$ describes the shortest geodesic connecting \hat{t}_i to \hat{t}_f (Fig. 1). The minimum energy is easily computed to be

$$E_{\min} = A\theta^2/(2L), \quad (3)$$

which is a purely mechanical contribution to the energy [1,9].

To go beyond mechanics and include the effect of thermal fluctuations (Fig. 1), we use an approximation described in [11]. The approximation consists of using an expansion of the energy about the minimum energy configuration and retaining fluctuation terms about the minimum to quadratic order. This calculation was done in general form in Eq. (53) of Ref. [11] for a single molecule subject to forces and twisting torques. The determinant of the fluctuation operator \mathcal{O} is calculated in [11]. In the present case, this fluctuation determinant can be calculated either by specializing Eq. (53) of [11] to the case of zero force and torque of [11] or by the method described in [13] in the context of Brownian motion on the sphere. As is to be expected, both methods give the same answer:

$$\det \mathcal{O} = L^2 \sin \theta / \theta. \quad (4)$$

Performing the Gaussian integration over the fluctuations, we find the distribution function $1/\sqrt{(\det \mathcal{O})} \exp -\frac{E_{\min}}{kT}$, and we arrive at the approximate formula

$$Q(\theta) = \frac{\mathcal{N}(L)}{L} \sqrt{\frac{\theta}{\sin \theta}} \exp \left[-\frac{A\theta^2}{2LkT} \right] \quad (5)$$

for the partition function as a function of the final angle θ , where \mathcal{N} is a normalization constant to be determined by the

normalization condition

$$\int_0^\pi Q(\theta) \sin \theta d\theta = 1, \quad (6)$$

which includes the measure $\sin \theta$ on the sphere.

The result (5) implies that the number of configurations with a final tangent vector \hat{t}_f making an angle θ defined by $\arccos(\hat{t}_i \cdot \hat{t}_f)$ is given by $P(\theta) = Q(\theta) \sin \theta$, leading to the simple analytic approximate formula for the bend angle distribution

$$P(\theta) = \frac{\mathcal{N}}{L} \sqrt{\theta \sin \theta} \exp \left[-\frac{A\theta^2}{2LkT} \right] \quad (7)$$

for θ . Note that this is a closed analytic form rather than an infinite series [13]. It is thus suitable and convenient for experimental comparison.

In some earlier works [6,7] stiff polymers were considered as perturbations about the straight line. This effectively describes the tangent vector as varying on a plane tangent to the unit sphere. This leads to the planar formula

$$P(\theta) = \frac{A}{LkT} \theta \exp -\frac{A\theta^2}{2LkT} \quad (8)$$

for the distribution of final angles. Such a planar approach neglects the curved geometry of the sphere. One also encounters a hybrid formula [9,14]

$$P(\theta) = \frac{A}{LkT} \sin \theta \exp -\frac{A\theta^2}{2LkT}, \quad (9)$$

in which one computes $Q(\theta)$ using the planar approximation and includes the correct curved measure $\sin \theta d\theta$ on the sphere. The present treatment (unlike the earlier planar ones) deals with geodesics on the sphere of tangents and thus takes into account the curvature of the sphere *both* in the computation of $Q(\theta)$ and in the measure $\sin \theta$. In the limit that the bending angle θ is small, Eq. (7) reduces to the earlier planar and hybrid formulas (8) and (9). Our formula for the bend angle distribution has a wider range of applicability compared to the earlier ones: it is valid for a contour length comparable to the persistence length (stiff and the semiflexible regime) and also correctly describes the rare events involving large bend angles.

III. DISTRIBUTION OF BEND ANGLES

We have performed Monte Carlo simulations using the Kratky-Porod model for comparison with the analytical form (7). We randomly generated 10^6 configurations of the polymer chain, assuming it to be built of N identical short straight segments, each of length l . Given one segment, the direction of the next segment was assumed to be uniformly distributed on a cone of semivertical angle $\Delta\theta = 0.1$ rad around the preceding segment. In the continuum limit when the number of segments goes to infinity $N \rightarrow \infty, l \rightarrow 0, \Delta\theta \rightarrow 0$, keeping $L = Nl$ and $L_p = \frac{2l}{(\Delta\theta)^2}$ fixed, one recovers the wormlike chain model. A frequency distribution of the number of configurations with angle θ between the initial and final tangent vectors was generated.

Figure 2 shows a comparison between our predicted analytical form, the planar formula, and the results of computer simulation. In the stiff regime ($\beta = L/L_p$ less than 1) Eq. (7)

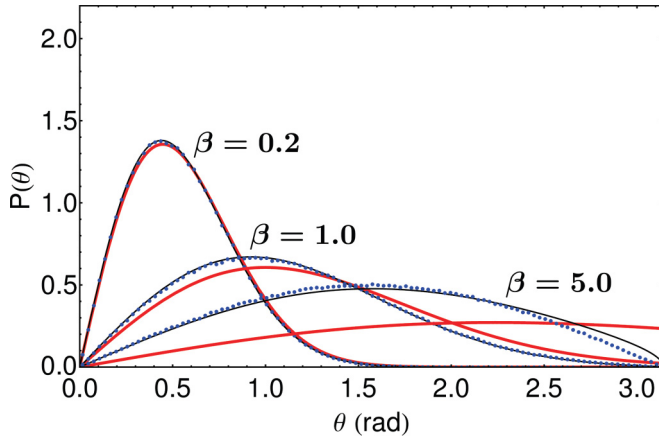


FIG. 2. (Color online) Comparison with simulations of $P(\theta)$ vs θ for a range of flexibilities. Plotted are the simulation data (blue dots), the planar formula (thick red line), and our analytic formula, Eq. (7) (thin black line). Notice that our closed form formula gives a reasonable fit to the simulation data even for $\beta = L/L_p$ as large as 5.

is virtually exact; in the semiflexible regime (β around 5) it remains a reasonable approximation. Thus, in an experiment which takes repeated snapshots of the angle between the final and initial tangent vectors of a molecule, we expect to find a distribution of angles given by Eq. (7). This is a prediction of the wormlike chain model, and it goes beyond earlier studies based on classical elasticity [9].

IV. MOMENT ANGLE RELATIONS

The partition function $Q(\theta)$ can be converted into a free energy by the formula (we drop θ independent terms as they are additive constants in the free energy)

$$\mathcal{F}(\theta) = -kT \ln Q(\theta) = \frac{A\theta^2}{2L} - \frac{kT}{2} \ln \frac{\theta}{\sin \theta} \quad (10)$$

and can be used to calculate the bending moment M needed to bend the final tangent vector through an angle θ . The approximate closed form predicted by our theory is

$$M = \frac{A\theta}{L} - \frac{kT}{2} \left(\frac{1}{\theta} - \cot \theta \right). \quad (11)$$

The first term in (11) represents the mechanical elastic energy, and the second (proportional to kT) is due to thermal fluctuations.

As Fig. 2 shows, the mechanical contribution is Hookean. Within a purely mechanical approach, when the bending angle reaches π , the geodesic connecting \hat{t}_i to \hat{t}_f is no longer the shortest one, and the configuration becomes unstable and buckles to a lower energy configuration. This picture is drastically altered by thermal fluctuations. As shown by the red curve in Fig. 3, the buckling happens at an angle smaller than π . The thermal fluctuations have the effect of “softening” the linear response to external bending.

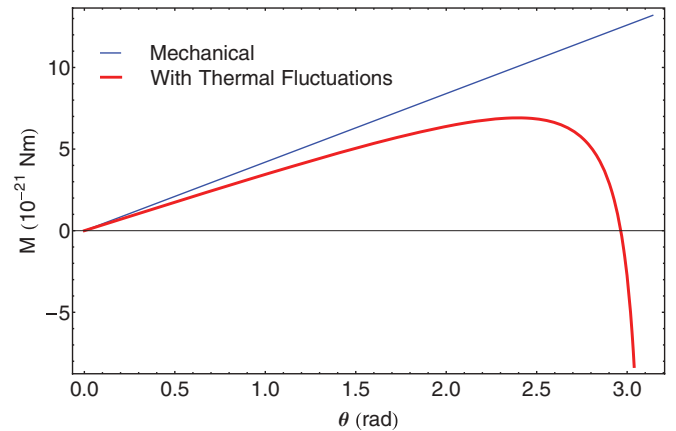


FIG. 3. (Color online) Bending moment vs bending angle theoretically expected. The thin blue line shows the mechanical elastic response, and the thick red line includes the effect of thermal fluctuations. The moment is plotted in units of 10^{-21} N m. The values of A and kT are chosen to reflect actin filaments under physiological conditions.

V. CONCLUSION

We have analyzed the bending mechanics and fluctuations of semiflexible polymers. Our central goal in this paper has been to bridge the gap between mechanics and statistical mechanics by taking into consideration thermal fluctuation effects to quadratic order around mechanically stable configurations. To summarize, our main results are (1) an explicit formula for the bend angle distribution expected from the wormlike chain model and (2) an explicit analytical formula for the moment angle relation.

Our calculational technique assumes that there is a unique shortest geodesic connecting \hat{t}_i and \hat{t}_f . This assumption breaks down at $\theta = \pi$. Our analytical formula (7) should only be used away from the point $\theta = \pi$, where there is a spurious divergence. For a classical elastic rod, such as a poker or a ballpoint pen refill, one sees that if the bending angle exceeds π , the configuration becomes unstable because the tangent vector no longer traces the shortest geodesic. The poker then buckles into a new configuration with lower energy. As shown in Fig. 3, thermal fluctuations cause the buckling to set in at bending angles considerably smaller than π .

For small bending angles θ , one can Taylor expand the free energy (10) and find that the effect of thermal fluctuations is to effectively reduce the bending elastic constant A by $kTL/6$. The fluctuations effectively soften the elastic response of the polymer. For larger bending angles, one can no longer think of the fluctuations as simply renormalizing the bending modulus A since the form of the moment angle relation is non-Hookean.

While we have used actin as a typical example of a semiflexible polymer, our study is also relevant to DNA and efforts to understand the bending elasticity of small segments. Experiments and all atom simulations [8,9,14] are performed to understand the formation of “kinks” and the cyclization of short and intermediate length DNA strands. Our present approach is analytical and computes experimentally relevant

quantities characterizing the bending elasticity of semiflexible polymers within the wormlike chain model. We expect our results to interest researchers studying actin as well as DNA and other biopolymers.

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