Elasticity of stiff biopolymers

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(Received 25 June 2007; published 6 December 2007)

We present a statistical mechanical study of stiff polymers, motivated by experiments on actin filaments and the considerable current interest in polymer networks. We obtain simple, approximate analytical forms for the force-extension relations and compare these with numerical treatments. We note the important role of boundary conditions in determining force-extension relations. The theoretical predictions presented here can be tested against single molecule experiments on neurofilaments and cytoskeletal filaments like actin and microtubules. Our work is motivated by the buckling of the cytoskeleton of a cell under compression, a phenomenon of interest to biology.

DOI: 10.1103/PhysRevE.76.061801 PACS number(s): 82.35.Lr, 87.15.La, 82.37.Rs

In recent years, statistical mechanics of semiflexible polymers has emerged as an active area of research. This has been triggered by single molecule experiments designed to understand the role of elasticity of these polymers. Elastic properties of polymers are of importance in biology as in the structure of the cytoskeleton, a biopolymer network which controls cell mechanics [1,2]. The parameter which determines the stiffness of a polymer is β, the ratio of its contour length L to the persistence length L_P. While the entire range of β is of biological interest, in this paper we focus our attention on rigid filaments such as actin filaments and microtubules which constitute the cytoskeletal structure and serve as tracks for motor proteins like myosin and kinesin [2,3]. Recently, filaments of intermediate rigidity like neurofilaments have also been studied in some detail [4]. It has been shown that some remarkable features of single stiff filament bending response are relevant to cross-linked biofilament networks [2]. A good understanding of the elastic properties of biopolymers at the single molecule level is essential to a study of polymer networks.

There are two classes of experiments which probe the elasticity of single biopolymers. In one class of experiments [5] a semiflexible polymer molecule is pulled and stretched to study its "equation of state" by measuring its extension as a function of applied force. In the other class of experiments, one tags the ends with fluorescent dye [6,7] to determine the distribution of end-to-end distances. Such experimental studies provide valuable insight into the mechanical properties of semiflexible polymers. A good theoretical model is needed to correctly interpret these experiments. A simple and popular model which captures much of the physics is the worm like chain model [8].

In this paper we analyze the bending degrees of freedom of a stiff polymer where at least one end of the polymer is *clamped*. By this it is meant that the tangent vector at this end is kept in a fixed direction. Just as in the case of a stretched polymer [9], the tangent vector of a stiff polymer executes small wanderings around this fixed direction. The theoretical analysis for the statistical mechanics of a stiff polymer, clamped at least at one end is similar to that of a polymer in the high stretch limit. We refer to this approximation as the paraxial approximation. This approximation has been previously used to study the elasticity of twist storing flexible stretched polymers [10–13] in the paraxial worm like chain model (PWLC model). In an earlier paper [9] we had an "exact" numerical scheme for a semiflexible polymer with free boundary conditions for the end tangent vectors. The main difference in the numerical scheme presented here is that we impose boundary conditions on the tangent vectors at the ends. As a general rule, in the stiff regime the convergence of the numerical scheme is poorer and therefore one needs to use larger matrix sizes. The search for simple analytic forms to describe the elastic properties of stiff polymers is therefore well-motivated.

For stiff polymers, the experimentally measured mean values crucially depend [14] on the precise choice of the ensemble. This is due to finite size fluctuation effects, which are entirely absent in the elasticity of a classical rod. 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 [15–17]. This is an aspect of stiff polymer statistical mechanics which is both theoretically challenging and experimentally significant. In this paper, we remain throughout in the Gibbs ensemble, where the applied force is held fixed and we measure the mean extension.

The organization of this paper is as follows. We first present results based on an "exact" numerical scheme for stiff polymers for two different boundary conditions, one in which both ends are clamped and the other in which one end is clamped and the other end is free. We then present simple analytical forms for these two cases. Our main results are displayed in Figs. 1–3 comparing the numerical scheme with the analytic formulas for force-extension relations. Finally, we end the paper with a concluding discussion of the buckling of stiff polymers and the consequent breakdown of the paraxial approximation.

Our starting point is the worm like chain (WLC) model in which the 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

$$\hat{t} \cdot \hat{t} = 1, \tag{1}$$

and the curvature of the polymer is given by $\kappa=|d\hat{t}/ds|$.

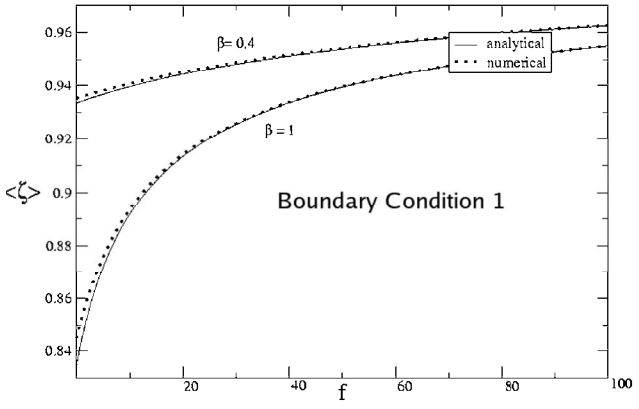

FIG. 1. The mean extension is plotted against the force f for β=0.4, 1 for a setup with both ends clamped.

One can study the case of stiff polymers using a combination of analytical and numerical techniques [9]. Let one end of the polymer be fixed at the origin and a stretching force F be applied in the $\hat{z}$ direction, which we refer to as the north pole of the sphere of directions. Introducing a dimensionless force variable $f=\frac{FL_p}{k_BT}$, where k_BT is the thermal energy we can express the partition function $Z(f)$ as

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

where $\beta=L/L_p$. Equation (2) 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 $-f\cos\theta$:

$$Z(f,\hat{t}_A,\hat{t}_B) = \langle \hat{t}_A|\exp[-\beta\hat{H}_f]|\hat{t}_B\rangle. \tag{3}$$

The Hamiltonian $\hat{H}_f=-\frac{\nabla^2}{2}-f\cos\theta$ is that of a rigid rotor [18] in a potential. In the absence of a force, the free Hamiltonian is $H_0=-\frac{1}{2}\nabla^2$. By choosing a standard basis in which H_0 is diagonal we find that H is a symmetric tridiagonal matrix with diagonal elements $H_{l,l}=l(l+1)/2$ and superdiagonal elements $H_{l,l+1}=f(l+1)\sqrt{1/[(2l+1)(2l+3)]}$. Inserting a complete set of eigenstates of the free Hamiltonian into Eq. (3), we find

$$Z(f,\hat{t}_A,\hat{t}_B) = \sum_{m,n}\langle \hat{t}_A|\psi_n\rangle\langle\psi_n|\exp[-\beta\hat{H}_f]|\psi_m\rangle\langle\psi_m|\hat{t}_B\rangle, \tag{4}$$

where $\hat{M}^f=\exp[-\beta\hat{H}_f]$. From this general form, we can compute the partition function in the present cases of interest.

In Ref. [9] we had studied the elastic properties of polymers with free boundary conditions: the directions of the tangent vectors at both ends were integrated over. In the present paper, we will fix the tangent vector at the ends (one or both) to lie along the $\hat{z}$ direction. To implement this numerically, we have to evaluate the eigenfunctions in Eq. (4) at this value of $\hat{t}$.

(i) Both ends clamped. $\hat{t}_A=\hat{t}_B=\hat{z}$. While a complete set of eigenstates are labeled by (l,m), only the $m=0$ terms contribute here because of azimuthal symmetry and we have

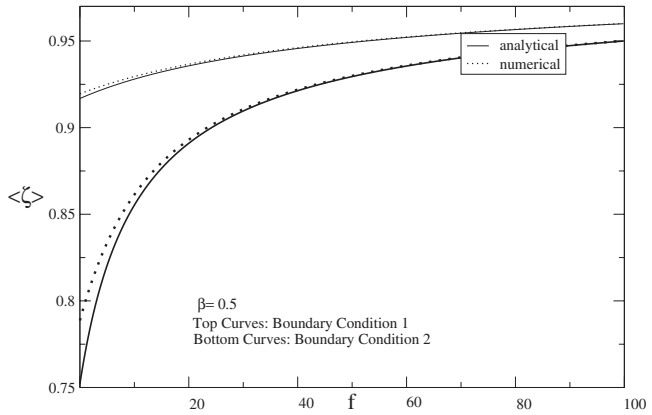

FIG. 2. The figure demonstrates that force-extension relations depend on the boundary conditions. Note that as expected, for a given force, the extension is greater for the case where *both* ends are clamped in the $\hat{z}$ direction.

$$Z(f,\hat{z},\hat{z}) = \sum_{l,l'} U_l M^f_{l,l'} U_{l'} = U\cdot M\cdot U, \tag{5}$$

where $U_l=\sqrt{\frac{2l+1}{4\pi}}$.

(ii) One end clamped. Integrating Eq. (4) over $\hat{t}_B$, we find that

$$Z(f,\hat{t}_A) = \sum_l U_l M^f_{l0} = (U\cdot M^f)_0. \tag{6}$$

Both Eqs. (5) and (6) are suitable for numerical implementation. H_f is an infinite symmetric matrix. We truncate it to finite order N and choose N large enough to attain the desired accuracy [19].

While this numerical method is effective, it has a limitation in describing stiff polymers due to the poor convergence of statistical sums in Eq. (4). For stiff polymers a convenient and accurate analytical approximation scheme can be developed as shown below.

For a stiff polymer with one end clamped along the $\hat{z}$

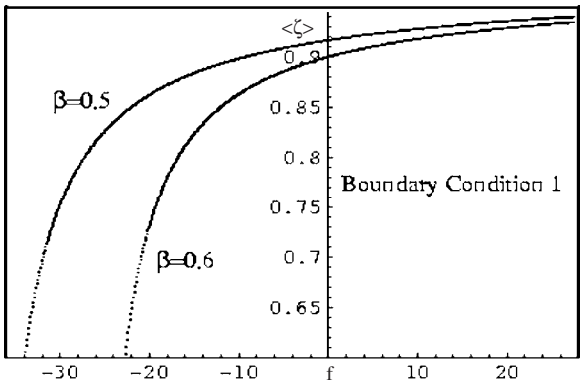

FIG. 3. Figure shows buckling, i.e., spontaneous decrease in extension under a compressive force for a stiff polymer with end tangent vectors clamped for β=0.5 and 0.6. Note that buckling takes place at a smaller magnitude of the compressive force f for a larger β.

direction, we can approximate the sphere of directions by a tangent plane at the north pole of the sphere as the angular coordinate θ always remains small. Introducing Cartesian coordinates $\xi_1=\theta\cos\phi$ and $\xi_2=\theta\sin\phi$ on the tangent plane R^2 at the north pole one can express the small θ Hamiltonian H as $H=H_P-f$ where H_P is

$$H_P=\frac{1}{2}p_{\xi_1}^2+\frac{1}{2}p_{\xi_2}^2+\frac{f}{2}(\xi_1^2+\xi_2^2). \tag{7}$$

Notice that H_P is the Hamiltonian of a two-dimensional harmonic oscillator with a frequency $\omega=\sqrt{f}$. For a single oscillator in real time the propagator is given by [20]

$$K(\xi_i,\xi_f,T)=F(T)\exp\frac{i\omega}{2\sin\omega T}[(\xi_i^2+\xi_f^2)\cos\omega T-2\xi_i\xi_f], \tag{8}$$

where $F(T)=\sqrt{\frac{\omega}{2\pi i\sin(\omega T)}}$.

For the sake of convenience we set $L_P=1$ so that $\beta=L$.

Case (i). Both end tangent vectors clamped along the $\hat{z}$-direction. Setting $\xi_i=\xi_f=0$ in Eq. (8) and continuing the expression to imaginary time results in the trigonometric functions being replaced by hyperbolic ones. We can express the partition function $Z(f)$ as $\exp(\beta f)$ times the product of the propagators of two independent harmonic oscillators:

$$Z(f)=\sqrt{f}\exp(\beta f)/[2\pi\sinh(\beta\sqrt{f})], \tag{9}$$

"in Euclidean time" β; the free energy is

$$G(f)=-\log Z(f)/\beta=\left[\frac{-1}{2\beta}\log f-f+\frac{1}{\beta}\log(2\pi)+\frac{1}{\beta}\log[\sinh(\beta\sqrt{f})]\right]. \tag{10}$$

The mean extension $\langle\zeta\rangle=\langle z\rangle/L=-\partial G(f)/\partial f$ is given by (see Fig. 1)

$$\langle\zeta\rangle=1+1/(2\beta f)-\coth(\beta\sqrt{f})/(2\sqrt{f}), \tag{11}$$

where $\langle\zeta\rangle$ is the $\hat{z}$ component of the extension (or the end-to-end distance vector). Note in Fig. 1 that the analytical form agrees with the numerical scheme to an accuracy of about 1%.

Case (ii). A stiff polymer with one end tangent vector pointing along the $\hat{z}$-direction and the other end free. In this case the propagator for the harmonic oscillator has to be integrated over the final coordinates ξ_f and evaluated at $\xi_i=0$. The partition function in this case turns out to be

$$Z(f)=\exp(\beta f)/\cosh(\beta\sqrt{f}). \tag{12}$$

From the expression of the partition function, we get the free energy

$$G(f)=-f+\frac{1}{\beta}\log[\cosh(\beta\sqrt{f})] \tag{13}$$

and differentiate it with respect to f to get the force—extension relation—

$$\langle\zeta\rangle=1-\tanh(\beta\sqrt{f})/(2\sqrt{f}). \tag{14}$$

Note that even at zero force, there is a nonzero extension because of the boundary condition and the stiffness of the polymer. Figure 2 shows a comparison of the force extension curves for the two boundary conditions. We find, as expected, that for the same force, the extension is larger for the more constrained boundary condition [case (i)] compared to a less constrained one [case (ii)]. For positive forces the paraxial approximation is very good and the forms are displayed in Eqs. (11) and (14). For large positive forces they become $\langle\zeta\rangle=1-\frac{1}{2\sqrt{f}}$ [9,18] as expected.

For negative forces, the hyperbolic functions appearing in Eqs. (9) and (12) go over to circular functions. For instance, for the case in which both end tangent vectors are clamped along the $\hat{z}$ direction, for negative f, our simple analytical form for the partition function reads

$$Z(f)=\frac{\sqrt{-f}e^{\beta f}}{2\pi\sin(\beta\sqrt{-f})} \tag{15}$$

and varies continuously with f as f ranges from positive to negative values. As the compressive force is increased, we find that at a critical value of the force f the extension $\langle\zeta\rangle$ spontaneously decreases. This is the analog here of the classical Euler buckling instability which occurs for rods.

Consider the mean extension versus force relation [Eq. (11)] for negative forces (i.e., for compressive forces). For negative values of forces Eq. (11) reduces to

$$\langle\zeta\rangle=1+1/(2\beta f)-\cot(\beta\sqrt{-f})/(2\sqrt{-f}), \tag{16}$$

which can be rewritten in the form

$$\langle\zeta\rangle=1+\beta u(x), \tag{17}$$

where $x=\beta\sqrt{-f}$ and

$$u(x)=\frac{\cot(x)}{2x}-\frac{1}{2x^2}.$$

The criterion for the onset of the buckling instability is the divergence of $\partial\langle\zeta\rangle/\partial f$. From Eq. (17) this is equivalent to the divergence of $\partial u/\partial x$, which takes place at a value of $x_c=\pi$. This gives us the following expression for the critical force for buckling [21]:

$$f_c=-\left(\frac{\pi}{\beta}\right)^2.$$

Because of the quadratic dependence, the compressive force needed to buckle a polymer rises sharply with stiffness. The mean extension versus force curves displayed in Fig. 3 demonstrate the phenomenon of buckling. As expected, we notice that as β goes up, the magnitude of the critical force f_c needed to buckle the polymer goes down.

A stiff polymer is energy dominated and its buckling is very similar to that of a classical rod subject to identical boundary conditions and a compressive force. The effect of thermal fluctuations is to slightly "round off" the transition from the straight to the buckled configuration. This is due to thermally activated processes that permit the polymer to

overcome the elastic energy barrier. As a result the buckling force for a stiff polymer is slightly smaller in magnitude than the f_c given above.

There is a long history of the use of path integrals in the study of polymers [22,23]. Such methods have been used in the study of elasticity of semiflexible polymers [9,24–26]. This connection between path integrals in quantum mechanics and statistical mechanics of polymers enables us to import ideas back and forth between these two distinct domains. The main point of this paper is that standard results in path integrals give us new results for stiff biopolymers. Our main results are contained in the analytic forms displayed in Eqs. (9)–(14) and Figs. 1–3.

In this paper we have theoretically studied the elasticity of stiff biopolymers. We have studied some cases with boundary conditions realizable in single molecule experiments. By attaching a magnetic bead to an end of the polymer, one can apply forces using magnetic field gradients and torques using magnetic fields. By such techniques one can impose a variety of boundary conditions on the polymer including the ones discussed here. Recent studies have shown [2] that the elastic behavior of such a biopolymer at the single molecular level affects the elastic properties of a biopolymer network. This is much like the way the structural stability of a roof is determined by the rigidity of its rafters. In a cytoskeletal structure the end tangent vectors of the stiff biopolymers that make up the structure are pinned. A cytoskeleton can be viewed as a replica of a large number N of semiflexible polymers. By studying the elastic properties of a single polymer constituting such a network, we can draw conclusions regarding the stability of the N polymer cytoskeletal structure. Here we have presented closed form simple analytical expressions for force-extension relations for a single stiff filament which can be tested against single molecule experiments. These analytical results are expected to shed light on the structural stability of the N polymer cytoskeletal structure.

We have also considered the case in which one end of a stiff polymer is clamped and the other end is free. This is a boundary condition that is more natural to an experimental setup for measuring the end-to-end distance distribution $P(\zeta)$ of a polymer via imaging of a polymer tagged with fluorescent dye. In fact one can construct a force-extension curve from the experimental data of $P(\zeta)$ versus ζ. We have theoretically analyzed this case and made predictions for experiments in this case as well. As in the earlier case, in this case also we have a simple analytic form.

In the future, we would like to investigate buckling of stiff filaments like actin in greater detail. This is an issue that is of relevance at the single molecular level as well as at the level of a biopolymer network like the cytoskeletal structure and is expected to shed light on its structural stability [2,27] and collapse under stress. The stiffness and collapse of the cytoskeletal structure of a red blood cell [27] has a direct connection to its functional aspects and is used, for instance, as a diagnostic for detection of sickle cell anemia. In studying the cytoskeletal structure it would be most useful to have a good understanding of the individual polymers that make up the structure. Simple analytic forms give valuable insight into a problem and we expect the analytic results presented here to provide some fresh impetus to this rapidly growing field of semiflexible polymers.

Note added in proof. Recently, we became aware of a closely related work by Emanuel *et al.*, entitled "Buckling of stiff polymers: Influence of thermal fluctuations," which is to appear in *Physical Review E*.

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