Mechanics and statistics of the worm-like chain

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The worm-like chain model is a simple continuum model for the statistical mechanics of a flexible polymer subject to an external force. We offer a tutorial introduction to it using three approaches. First, we use a mesoscopic view, treating a long polymer (in two dimensions) as though it were made of many groups of correlated links or "clinks," allowing us to calculate its average extension as a function of the external force via scaling arguments. We then provide a standard statistical mechanics approach, obtaining the average extension by two different means: the equipartition theorem and the partition function. Finally, we work in a probabilistic framework, taking advantage of the Gaussian properties of the chain in the large-force limit to improve upon the previous calculations of the average extension.
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I. INTRODUCTION

Polymers are critical players in the mechanochemical framework of cellular life; from DNA to the cytoskeletal structures in our cells to the adhesive fibers used in cellular locomotion, these slender molecules are critical to the information storage, structural scaffolding, and dynamical motifs necessary for life. The 1970s and 1980s saw the advent of various advanced biochemical methods for manipulating single molecules—optical tweezers[1–5] and atomic-force microscopy[6–9] in particular—giving scientists unprecedented tools to investigate the mechanical behavior of these important polymers. With these tools, scientists began to pull on strands of DNA,[10–12] proteins,[13,14] and even complicated polymeric complexes[15] in an effort to study their response to mechanical forces. These experimental endeavors showed that DNA strands act like entropic springs under tension, though this behavior was not entirely unexpected; physicists and chemists had earlier observed similar behavior in more industrial applications,[16,17] studying, for example, the long polymer chains in plastics. Their early attempts to understand this restoring force focused on modeling the polymer as a random walk, in which each "link" in the chain represents a single step. The "springiness" of the polymer is then attributed to the larger probability for it to be found in a folded up configuration than a perfectly straight line. This simple model, often referred to as the freely jointed chain (FJC), sufficed to describe the polymer under small forces but failed under larger loads. However, a variant now known as the worm-like chain model (first introduced in 1949 by Kratky and Porod[18]), which incorporates the polymer's bending stiffness, correctly predicts the large-force behavior including the large-force behavior of DNA.[19,20]

This tutorial utilizes a variety of mathematical and physical approaches in an effort to explain the mechanical and probabilistic aspects of the worm-like chain and its mechanochemical predictions. It begins in Sec. II by introducing the statistical and mechanical assumptions that constitute the worm-like chain model. Each of the following sections offers different methods by which to understand the predictions of the model and calculate the average extension of the polymer [Eq. (10)]. Section III offers a pictorial/scaling view in which we treat the polymer as a series of connected "clinks" whose behavior we can describe in the large-force limit.[21,22] By understanding how the size of these clinks scales with the applied force, we are able to deduce the behavior of the polymer at large. Following this heuristic treatment, Sec. IV covers two statistical mechanics approaches to calculating the average extension: by means of the equipartition theorem (Sec. IV A) and through the partition function (Sec. IV B). Finally, Sec. V makes use of the probabilistic framework of Gaussian processes to calculate the average extension and partially extend our calculation beyond the large-force limit.

II. STATISTICS AND MECHANICS OF THE WORM-LIKE CHAIN MODEL

The worm-like chain (WLC) model is fundamentally a continuum description of a chain of length L described (in two dimensions) by the local tangent angle to the chain, $\theta(s)$, where $s \in [0, L]$ denotes the distance along the chain (see Fig. 1). Under the assumption of thermodynamic equilibrium, the probability for the chain to be in any configuration $\theta(s)$ is

$$P[\theta(s)] \propto \exp\left\{-\frac{E[\theta(s)]}{k_B T}\right\}, \tag{1}$$

where T is the temperature of the system, k_B is Boltzmann's constant, and $E[\theta(s)]$ is the energy of the chain in configuration $\theta(s)$. Unless otherwise stated, throughout this tutorial we assume that the ends of the chain are fixed at $\theta(0) = \theta(L) = 0$. We do this in an attempt to model the physical setup in which the ends of the chain are anchored perpendicular to glass beads held in a pair of optical tweezers (Fig. 1).

The energy functional for this polymer chain is of the familiar form $E[\theta(s)] = U[\theta(s)] + W[\theta(s)]$. Here $U[\theta(s)]$ represents the internal energy stored in the bending of the chain and $W[\theta(s)]$ represents the external work done on the chain by an external force of magnitude F pulling on one of its ends. In our 2D setting, the bending energy is given by

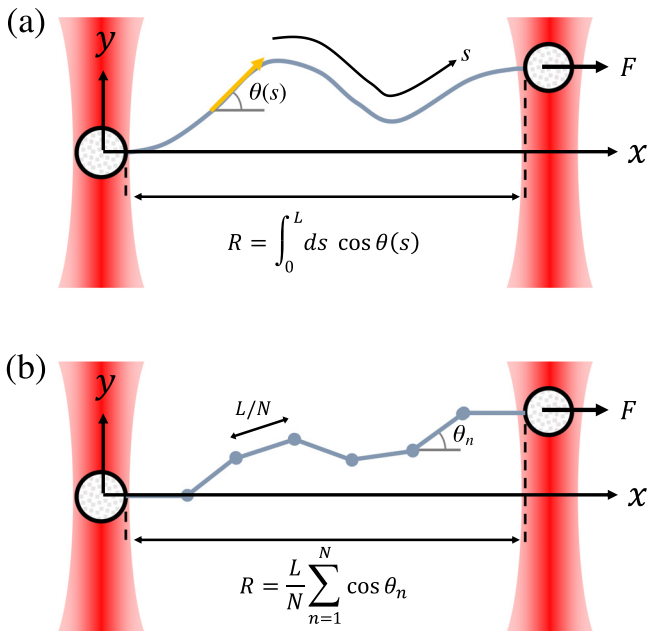

Fig. 1. (Color online) Parameterization of the worm-like chain in two dimensions under (a) the standard continuum description and (b) under a discrete formulation. In (a), we describe the chain by specifying the angle $\theta(s)$ of its tangent vector at every point s on the chain (where s is an arclength parameter running along the length L of the polymer). Each end of the chain is attached perpendicular to a glass bead held by a pair of optical tweezers, keeping $\theta(0) = \theta(L) = 0$. By confining the beads, the tweezers provide an external force of magnitude F on the chain, which we assume to be in the x-direction (we assume no force is applied in the y-direction). The total extension of the polymer is then given by $R = \int ds\, \cos\theta(s)$. In the discrete formulation (b), the chain is modeled by a set of N links of length L/N and $\theta(s)$ is replaced by N angles $\theta_1, \ldots, \theta_N$, where θ_n describes the orientation of the nth link in the chain. The extension is then described by a sum, $R = \frac{L}{N}\sum \cos\theta_n$.

$$U[\theta(s)] = \frac{1}{2}B\int_0^L ds\left(\frac{d\theta}{ds}\right)^2, \tag{2}$$

where B is the bending stiffness (units of energy times length), and the work term (assuming the force is applied along the x-axis) is given by

$$W[\theta(s)] = -F\int_0^L ds\,\cos\theta(s). \tag{3}$$

Combining Eqs. (2) and (3) yields the chain energy

$$E[\theta(s)] = \frac{B}{2}\int_0^L ds\left(\frac{d\theta}{ds}\right)^2 - F\int_0^L ds\,\cos\theta(s). \tag{4}$$

Dividing $E[\theta(s)]$ by k_BT, we can write the normalized energy of the polymer as

$$\frac{E[\theta(s)]}{k_BT} = \frac{l_p}{2}\int_0^L ds\left(\frac{d\theta}{ds}\right)^2 - f\int_0^L ds\,\cos\theta(s), \tag{5}$$

where we define two new parameters

$$f = \frac{F}{k_BT} \quad \text{and} \quad l_p = \frac{B}{k_BT}, \tag{6}$$

with f representing the scaled force (with units of inverse length) and l_p representing the persistence length of the polymer.[23] (N.B. It may be easier to understand the physical consequences of l_p via its effect on the chain's correlation length ξ [Eq. (47)], as the correlation length has a familiar meaning.) The worm-like chain distribution is then

$$P[\theta(s)] \propto \exp\left[-\frac{l_p}{2}\int_0^L ds\left(\frac{d\theta}{ds}\right)^2 + f\int_0^L ds\,\cos\theta(s)\right]. \tag{7}$$

While the statistical mechanical underpinnings of the WLC model may be familiar—assigning probabilities according to the energies of given configurations—the idea of assigning probabilities to *functions* rather than a finite set of variables (like the positions and momenta of a set of particles) may not, and not every intuition from the discrete case carries over to the continuum version. However, the statement $P[\theta(s)] > P[\theta'(s)]$ still means that the model predicts configuration $\theta(s)$ to be more likely than configuration $\theta'(s)$. In any case, our primary interest is in using the WLC to calculate the average value of a single variable, the polymer extension R, given by

$$R = \int_0^L ds\,\cos\theta(s). \tag{8}$$

Nevertheless, the average $\langle R\rangle$ still requires us to average over all chain configurations $\theta(s)$, which we formally denote by an integral over all configurations or a *path integral*

$$\langle R\rangle = \int \mathcal{D}[\theta(s)]\, R[\theta(s)]\, P[\theta(s)], \tag{9}$$

where $\int \mathcal{D}[\theta(s)]$ represents the statement that we are integrating over all configurations or *paths*. We treat this operation in detail in Sec. IV B. For notational convenience, we continue to use the angle bracket notation even in this continuum case so that we may write

$$\langle R\rangle = \int_0^L ds\,\langle\cos\theta(s)\rangle. \tag{10}$$

Since integration is a linear operator, we can exchange the average and the integral.

Alternatively, we can avoid some of the delicate issues relating to the calculation of probabilities for functions and path integration by considering the WLC model as the continuum limit of a discrete-link model. Although there is no unique choice for this discrete description, we can start with the freely jointed chain (FJC) model, which assumes the chain is made of N links of length L/N free to rotate about their joints [Fig. 1(b)], and then add a bending energy. The chain is then described by a set of N angles $\boldsymbol{\theta} = (\theta_1, \ldots, \theta_N)$, the probability for which is governed by another Gibbs distribution

$$P(\boldsymbol{\theta}) \propto \exp\left[-\frac{E_N(\boldsymbol{\theta})}{k_BT}\right], \tag{11}$$

with an associated normalized energy

$$\frac{E_N(\boldsymbol{\theta})}{k_BT} = \frac{l_p}{2}\sum_{n=1}^{N-1}\frac{L}{N}\left(\frac{\theta_{n+1}-\theta_n}{L/N}\right)^2 - f\sum_{n=1}^{N}\frac{L}{N}\cos\theta_n. \tag{12}$$

In the limit as $N \to \infty$, the differences between neighboring angles become curvatures, $\lim_{N\to\infty}(\theta_{n+1} - \theta_n)/(L/N) = d\theta/ds$, the sums turn into integrals, $\lim_{N\to\infty} \sum_{n=1}^{N} L/N \to \int_0^L ds$, and so the discrete system energy $E_N(\boldsymbol{\theta})$ limits to the WLC energy from Eq. (4). As for the chain extension, in this discrete setting R is defined by

$$R = \frac{L}{N}\sum_{n=1}^{N} \cos\theta_n. \tag{13}$$

Since the angles $\theta_1, \ldots, \theta_N$ are ordinary variables, the average extension has the usual meaning. This formulation is useful when it comes to numerically simulating the behavior of worm-like chains. To derive the average extension in the continuum setting, we can first compute $\langle R\rangle$ in this discrete formulation and then take $N \to \infty$ (Sec. V).

Unfortunately, the presence of $\cos\theta(s)$ in both the WLC energy [Eq. (5)] and in the definition of the extension [Eq. (8)] makes it rather difficult to exactly compute $\langle R\rangle$ analytically. However, by making a key approximation in the large-force limit (Sec. II A), we enable the use of a variety of calculational techniques (Secs. III–V).

A. The large-force limit

In the limit of small forces and a length much larger than the persistence length ($L \gg l_p$), the worm-like chain behaves like a Gaussian chain, with the extension being proportional to the force. However, as the extension approaches the full length of the chain, we expect the force to increase nonlinearly and eventually diverge as $\langle R\rangle/L \to 1$. This is a consequence of our not allowing the chain to break or stretch: no amount of force can make $\langle R\rangle > L$. So what approximations can we make in this large-force limit ($f\, l_p \gg 1$)? As we pull harder and harder on our polymer, we expect it to straighten out in the direction of the force (the x-direction). In other words, we expect the local tangent angle $\theta(s)$ to be nearly zero all along the polymer. Thus, in this large-force limit, we can approximate $\cos\theta(s) \approx 1 - \theta^2(s)/2$, allowing us to simplify Eq. (5) to

$$\frac{E[\theta(s)]}{k_B T} \approx \frac{l_p}{2}\int_0^L ds \left(\frac{d\theta}{ds}\right)^2 + \frac{f}{2}\int_0^L ds\, \theta^2(s) - f\,L. \tag{14}$$

The distribution for $\theta(s)$ [Eq. (7)] in the large-force limit then becomes

$$P[\theta(s)] \propto \exp\left[-\frac{l_p}{2}\int_0^L ds \left(\frac{d\theta}{ds}\right)^2 - \frac{f}{2}\int_0^L ds\, \theta^2(s)\right], \tag{15}$$

where we have absorbed the constant $f\,L$ term into the proportionality sign.

Moreover, we can use the small-angle approximation to simplify the cosine term in Eq. (10), giving

$$\langle R\rangle \approx L - \frac{1}{2}\int_0^L ds\, \langle\theta^2(s)\rangle. \tag{16}$$

The benefit of this is that $\langle\theta^2(s)\rangle$ is much easier to calculate than $\langle\cos\theta(s)\rangle$. However, as we show in Sec. V A, it is possible to calculate the average extension using the exact expression [Eq. (10)] under the assumption that the distribution for $\theta(s)$ is still described by the large-force limit [Eq. (15)].

Exercises for Sec. II:

(1) While Eq. (8) defines the extension R of the chain in the direction of the force, we might also consider the extension perpendicular to the direction of the force, $R_\perp$, defined by

$$R_\perp = \int_0^L ds\, \sin\theta(s). \tag{17}$$

Using symmetry arguments, show that $\langle R_\perp\rangle = 0$.

(2) In reality, optical tweezers also confine the beads along the y-axis. Thus, it is more accurate to say that the actual positions of the ends of the chain are fixed. Assuming the beads are fixed at the same y-position, this then places an additional constraint on the chain, namely, that $\int_0^L ds\, \sin\theta(s) = 0$. This *global* constraint is difficult to enforce. How might one change the chain energy [Eq. (4)] in order to *approximately* enforce this constraint?

III. SCALING APPROACH

Having seen that the average extension is a function of the average projection of each link in the chain, we now turn to a simple scaling approach to capture the essence of the result before moving on to increasingly sophisticated methods. When a worm-like chain that is much longer than its persistence length is extended weakly by an external force, it behaves like a Gaussian chain, with a force that is proportional to the end-to-end extension. However, as we increase the force, we expect more and more of the chain to align with the direction of the external force and hence for the average extension to increase. We show this scenario in Fig. 2. On very short length scales, comparable to the persistence length, the polymer is straight but not oriented with the external force; on intermediate length scales, the polymer's bending resistance induces the links of the polymer to group into a series of correlated links, or clinks, each of which is partially straightened out by the external force; and on large length scales, these polymer clinks are approximately oriented with the external force.

To characterize the length of a clink ξ (i.e., the correlation length), we will consider how the external work and the bending energy balance with thermal effects on the order of $k_B T$. The key idea here is that any given clink is able to bow out by some distance h, reducing the effective end-to-end length to $\xi - \Delta$ (Fig. 2).

The bending energy of the clink should depend on the square of the curvature of the clink. Assuming the clink bends into a circular segment and Δ is small, the curvature is approximately $\kappa \sim h/\xi^2$ and so the total bending energy is

$$U_{\text{clink}} = \frac{1}{2}\int_0^\xi ds\, B\,\kappa^2 \sim B\frac{h^2}{\xi^3}. \tag{18}$$

At equilibrium, the average of U_{clink} must be comparable to $k_B T$, which implies that $\langle h^2\rangle \sim \xi^3\, k_B T/B \sim \xi^3/l_p$. Assuming that the WLC is well approximated as an inextensible filament, this deviation from straightness leads to an effective end-to-end shrinkage $\Delta \sim \langle h^2\rangle/\xi \sim \xi^2/l_p$ (which follows from an application of Pythagoras' theorem, see Fig. 2).

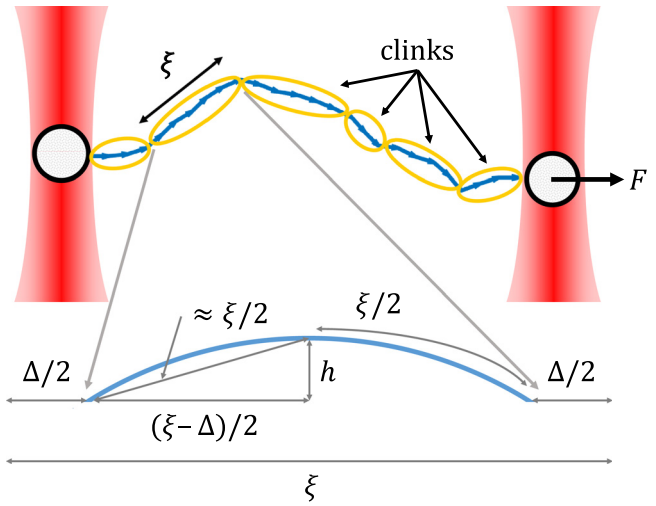

Fig. 2. (Color online) Parameterization of the "clink" used in the scaling approach of Sec. III A clink is a group of correlated links of the polymer over which it is nearly straight. On average, we expect the length of a clink to be given by the correlation length ξ. The slight bending of a clink leads to a deviation of size h from a straight line of length ξ and, since the polymer is inextensible, also reduces the end-to-end length by Δ. Given the statistical nature of the problem, the leading order measure of bending is $\langle h^2 \rangle$, not $\langle h \rangle$, as $\langle h \rangle = 0$ by symmetry.

The work done by the external force serves to iron out this shrinkage of Δ and so the total work scales as $F\Delta$, i.e., the force applied over the distance Δ. Balancing with thermal fluctuations at equilibrium then implies $F\xi^2/l_p \sim k_BT$ and $\xi \sim (k_BTl_p/F)^{1/2}$. Using our definition of the extrinsic inverse length scale $f = F/k_BT$, we see that the characteristic "clink size" $\xi \sim (l_p/f)^{1/2}$ demarcates the transition from random to oriented states; on scales smaller than ξ, the filament is not oriented on average with the external force. Our scaling theory also provides an estimate for the shrinkage per clink $\Delta \sim \xi^2/l_p$. As the force increases the clink size decreases and the filament gets increasingly oriented with the external force.

With these simple results, we can now estimate the average extension of a filament of length L. The number of clinks of size ξ is given by L/ξ with each having shrunk an amount Δ, so that the average end-to-end extension of the WLC is $\langle R \rangle \sim L - \Delta(L/\xi)$, which yields

$$\langle R \rangle \approx L\left(1 - \frac{1}{4\sqrt{f\,l_p}}\right). \tag{19}$$

Note that we have included the factor of 4 to match the more accurate computations in Secs. III–V; the scaling approach does not provide us a way to get it. This expression for the force-extension curve matches what is seen experimentally, for example, in stretching DNA using optical tweezers,[10] as shown in Fig. 3, and was the first direct evidence that the worm-like chain is an excellent model for the mechanical response of DNA.

IV. STATISTICAL MECHANICS APPROACH

There are several ways to use the tools of statistical mechanics to calculate $\langle R \rangle$ in the large-force limit. Here, we discuss two methods: the first applies the equipartition theorem and the second makes use of the partition function.

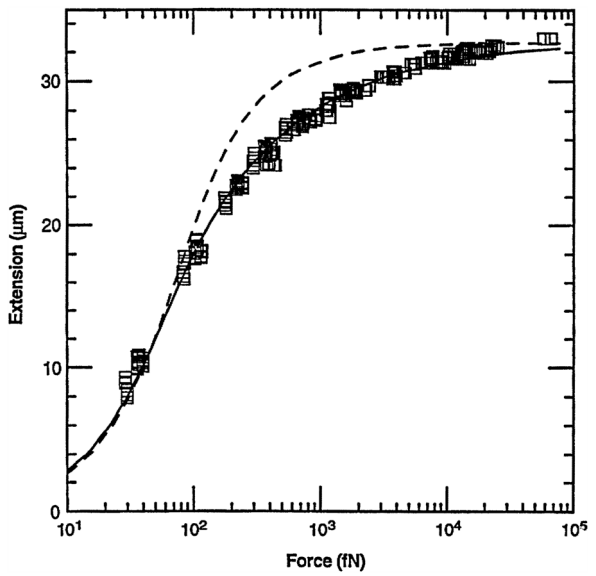

Fig. 3. The squares are experimental force versus extension data for 97 kb λ-DNA dimers from Fig. 3 of Smith *et al*. (Ref. 25), while the solid line is a fit of the entropic force required to extend a worm-like polymer. The fit parameters are the DNA length ($L = 32.80 \pm 0.10\,\mu$m) and the persistence length ($l_p = 53.4 \pm 2.3$ nm). Shown for comparison (dashed curve) is the freely jointed chain model (Ref. 25) with $L = 32.7\,\mu$m and a segment length $b = 100$ nm chosen to fit the small-force data. Reprinted with permission from Bustamante *et al*., Science **265**, 1599–1600 (1994). Copyright 1994, American Association for the Advancement of Science.

The partition function method allows us to derive the average extension, average energy, average bending, and averages of other physical quantities; however, calculating the partition function requires functional (path) integration. The equipartition method, on the other hand, relies only on the validity of the equipartition theorem and allows us to avoid the topic of path integration, but applies more specifically to the average extension.

A. Via the equipartition theorem

Although we have the (approximate) formula for the average extension in Eq. (16), it is not necessarily obvious how to interpret the expected value of an integral over a random function. In this first approach, we sidestep the questions of distributions for *functions* by rewriting the *function* $\theta(s)$ in terms of *variables* that we know how to manipulate. Thus, instead of dealing with $\theta(s)$ itself, we can work with its Fourier coefficients.

In a finite domain ($s \in [0, L]$), we can describe all (square-integrable) functions $\theta(s)$ by a Fourier series. Assuming that both ends of the polymer are fixed at $\theta(0) = \theta(L) = 0$, we can write

$$\theta(s) = \sum_{n=1}^{\infty} a_n \sin\left(\frac{n\pi s}{L}\right), \tag{20}$$

and so by direct integration we can convert the integral in Eq. (16) to a sum

$$\int_0^L ds\,\theta^2(s) = \frac{L}{2}\sum_{n=1}^{\infty} a_n^2. \tag{21}$$

Thus we can write the average extension in terms of the second moments of the Fourier coefficients

$$\langle R\rangle \approx L - \frac{L}{4}\sum_{n=1}^{\infty}\langle a_n^2\rangle, \tag{22}$$

and use statistical mechanics to calculate them.

We begin by rewriting the normalized energy [Eq. (14)] in terms of the Fourier coefficients

$$\frac{E}{k_BT} = \frac{1}{4}\sum_{n=1}^{\infty} a_n^2\left(fL + \frac{l_p}{L}\pi^2 n^2\right). \tag{23}$$

Taking the expectation of Eq. (23) and multiplying through by k_BT, we can write the average energy as the sum of the average energy in each Fourier mode, $\langle E\rangle = \sum_{n=1}^{\infty}\langle E_n\rangle$, where E_n is given by

$$E_n = \left(\frac{1}{2}k_BT\right)\left[\frac{1}{2}\left(fL + \frac{l_p}{L}\pi^2 n^2\right)\right]a_n^2. \tag{24}$$

The mode energy E_n depends quadratically on the nth Fourier coefficient; thus, the equipartition theorem implies that each mode should contribute an average energy

$$\langle E_n\rangle = \frac{1}{2}k_BT, \tag{25}$$

to the overall average $\langle E\rangle$ so that Eq. (24) implies

$$\langle a_n^2\rangle = \frac{2}{fL + (l_p/L)\pi^2 n^2}. \tag{26}$$

Putting Eq. (26) back into our expression for the average extension [Eq. (22)], we find

$$\langle R\rangle \approx L - \frac{1}{2f}\sum_{n=1}^{\infty}\left(1 + \frac{l_p}{fL^2}\pi^2 n^2\right)^{-1}. \tag{27}$$

Recognizing the sum as the Taylor series of the coth function, we find that the average extension is given by

$$\langle R\rangle \approx L\left[1 - \frac{1}{4\sqrt{f\,l_p}}\coth\left(\frac{L}{l_p}\sqrt{f\,l_p}\right) + \frac{1}{4f\,l_p}\frac{l_p}{L}\right]. \tag{28}$$

Note that the average extension only depends on two combinations of parameters: $f\,l_p$, the amount of work done over the persistence length of the polymer relative to the thermal energy, and l_p/L, the ratio of the persistence length to the overall length of the chain.

In the large-force limit, $\coth((L/l_p)\sqrt{f\,l_p}) \to 1$, so to leading order in f (ignoring the term that scales as $1/f\,l_p$) we obtain the same large-force approximation that we found in Sec. III [Eq. (19)].

B. Via the partition function

In this approach, we do not directly compute the average extension $\langle R\rangle$ via Eq. (16); instead, we first calculate a more universal object—the *partition function* $\mathcal{Z}$—which is the normalization constant for Eq. (15)

$$P[\theta(s)] = \frac{1}{\mathcal{Z}}\exp\left\{-\frac{E[\theta(s)]}{k_BT}\right\}, \tag{29}$$

and so we should be able to calculate $\mathcal{Z}$ by integrating over $\theta(s)$. However, $\theta(s)$ is a function, not a simple variable, and so we instead have to integrate over all possible *configurations* of $\theta(s)$

$$\mathcal{Z} = \int \mathcal{D}[\theta(s)]\exp\left\{-\frac{E[\theta(s)]}{k_BT}\right\}. \tag{30}$$

Before delving into the details of path integration, let us first justify the effort by showing how $\mathcal{Z}$ relates to $\langle R\rangle$. First note that we can formally write the expectation in Eq. (16) as an integral over the distribution for $\theta(s)$ [Eq. (29)]

$$\left\langle \frac{1}{2}\int_0^L ds\,\theta^2(s)\right\rangle = \frac{1}{\mathcal{Z}}\int \mathcal{D}[\theta(s)]\left(\frac{1}{2}\int_0^L ds\,\theta^2(s)\right) \times \exp\left\{-\frac{E[\theta(s)]}{k_BT}\right\}. \tag{31}$$

Then, given the form of the normalized energy [Eq. (14)], it follows that taking the derivative of $\exp(-E/k_BT)$ with respect to f yields

$$\frac{\partial}{\partial f}\exp\left\{-\frac{E[\theta(s)]}{k_BT}\right\} = -\left(\frac{1}{2}\int_0^L ds\,\theta^2(s)\right)\exp\left\{-\frac{E[\theta(s)]}{k_BT}\right\}. \tag{32}$$

Hence we can rewrite Eq. (31) in terms of this derivative

$$\left\langle \frac{1}{2}\int_0^L ds\,\theta^2(s)\right\rangle = -\frac{1}{\mathcal{Z}}\frac{\partial}{\partial f}\int \mathcal{D}[\theta(s)]\exp\left\{-\frac{E[\theta(s)]}{k_BT}\right\}, \tag{33}$$

where we also pull the derivative outside the integral. Looking at Eq. (30), we see that the remaining path integral is just $\mathcal{Z}$, and so we can write the expectation as

$$\left\langle \frac{1}{2}\int_0^L ds\,\theta^2(s)\right\rangle = -\frac{1}{\mathcal{Z}}\frac{\partial \mathcal{Z}}{\partial f} = -\frac{\partial \log \mathcal{Z}}{\partial f}. \tag{34}$$

Putting this expression into Eq. (16), it follows that we can calculate the average extension directly from the derivative of the logarithm of the partition function

$$\langle R\rangle \approx L + \frac{\partial \log \mathcal{Z}}{\partial f}. \tag{35}$$

Now in order to evaluate Eq. (30), we have to figure out how to "sum over all paths/configurations." From a computational perspective, in order to do this we first need a way in which to describe all possible functions $\theta(s)$. As we note in Sec. IV A, we can write any $\theta(s)$ in terms of its Fourier representation [Eq. (20)], in which case we can interpret the "summation over all paths" implied by the path integral operator $\int \mathcal{D}[\theta(s)]$ as an integration over all Fourier series coefficients a_n

$$\int \mathcal{D}[\theta(s)] = \prod_{n=1}^{\infty}\left(\int_{-\infty}^{\infty} da_n\right). \tag{36}$$

Having made explicit what we mean by path integration, we use our simplified expression for the normalized energy [Eq. (23)] in our expression for $\mathcal{Z}$ [Eq. (30)], turning the sum over modes in the exponential into a product

$$\mathcal{Z} = \prod_{n=1}^{\infty} \left\{ \int_{-\infty}^{\infty} da_n \, \exp\left[-\frac{1}{4} a_n^2 \left(f L + \frac{l_p}{L} \pi^2 n^2 \right) \right] \right\}, \tag{37}$$

so that the partition function reduces to an infinite product of Gaussian integrals. Integrating over each a_n directly yields

$$\mathcal{Z} = \prod_{n=1}^{\infty} \left[\frac{1}{4\pi} \left(f L + \frac{l_p}{L} \pi^2 n^2 \right) \right]^{-\frac{1}{2}}. \tag{38}$$

Substituting this into Eq. (35) and noting that

$$\frac{\partial \log \mathcal{Z}}{\partial f} = -\frac{1}{2f} \sum_{n=1}^{\infty} \left(1 + \frac{l_p}{f L^2} \pi^2 n^2 \right)^{-1} \tag{39}$$

conveniently converts the infinite product of Eq. (38) into the same infinite sum we encountered in the equipartition approach, so that

$$\frac{\partial \log \mathcal{Z}}{\partial f} = L \left[-\frac{1}{4\sqrt{f\, l_p}} \coth\left(\frac{L}{l_p} \sqrt{f\, l_p} \right) + \frac{1}{4 f\, l_p} \frac{l_p}{L} \right]. \tag{40}$$

Inserting this expression into Eq. (35) yields the same average extension that we found using the equipartition method [Eq. (28)] and thus the same large-force approximation [Eq. (19)].

One might wonder why we went through the trouble of deriving $\langle R \rangle$ via both the equipartition and path integral methods if the answer came out the same. First, the fact that the answer did come out the same serves as a good check that we did our calculations correctly. But more importantly, both methods have their uses in other physical problems and are thus both worth knowing. With that in mind, Sec. V provides yet another useful technique that can reproduce Eq. (28) and even allows us to do better.

Exercises for Sec. IV:

(1) In our treatment of a polymer with fixed ends $[\theta(0) = \theta(L) = 0]$, we claimed that we could write any configuration $\theta(s)$ in a Fourier sine representation [Eq. (20)]. Why were we able to ignore the cosine terms?
(2) Calculate the average extension under the Neumann boundary condition $\theta'(0) = \theta'(L) = 0$.
(3) We had an expression for $\mathcal{Z}$ in terms of an infinite product [Eq. (38)], but we only calculated $\partial \log \mathcal{Z}/\partial f$. Show that this expression for $\mathcal{Z}$ (or $\log \mathcal{Z}$) does not converge. Does it matter that $\mathcal{Z}$ fails to converge so long as $\partial \log \mathcal{Z}/\partial f$ does?

V. GAUSSIAN PROCESS APPROACH

The approximate worm-like chain energy [Eq. (14)] depends only upon quadratic powers of $\theta(s)$ and $d\theta/ds$, and so the worm-like chain distribution [Eq. (15)] resembles a continuum version of a multivariate Gaussian distribution

$$P(\boldsymbol{\theta}) = \frac{1}{\sqrt{\det(2\pi\Sigma)}} \exp\left(-\frac{1}{2} \boldsymbol{\theta}^T \Sigma^{-1} \boldsymbol{\theta} \right), \tag{41}$$

where $\boldsymbol{\theta}$ is a vector of polymer joint angles and Σ is their covariance matrix. We can make this similarity more striking by applying integration by parts to the derivative term and integrating over a Dirac delta function, transforming the argument of the exponential into

$$-\frac{1}{2} \int_0^L ds \int_0^L ds' \, \theta(s) \left[\delta(s - s') \left(f - l_p \frac{d^2}{ds'^2} \right) \right] \theta(s'). \tag{42}$$

In this form, it is clear that the integrals are the continuum analogue of the sums in Eq. (41),

$$\boldsymbol{\theta}^T \Sigma^{-1} \boldsymbol{\theta} = \sum_{m=1}^{N} \sum_{n=1}^{N} \theta_m (\Sigma^{-1})_{mn} \theta_n. \tag{43}$$

Indeed, Eq. (15) is a Gaussian *functional* distribution for $\theta(s)$ and the term between $\theta(s)$ and $\theta(s')$ in Eq. (42) is the inverse correlation function

$$C^{-1}(s, s') = \delta(s - s') \left(f - l_p \frac{d^2}{ds'^2} \right). \tag{44}$$

That our distribution for $\theta(s)$ is Gaussian is a powerful statement with two particularly useful implications:

(1) The distribution for any finite set of N parameters $\boldsymbol{\theta} = (\theta_1, \ldots, \theta_N)$, where $\theta_n = \theta(s_n)$ for some $s_n \in [0, L]$, is multivariate Gaussian with zero mean and covariance matrix Σ [Eq. (41)].
(2) The elements of the covariance matrix Σ are given by the correlation function

$$\Sigma_{m,n} = C(s_m, s_n). \tag{45}$$

These properties of a Gaussian process allow us to not only reproduce the results from Secs. III and IV, but also obtain a better estimate of $\langle R \rangle$ by using the exact definition of R [Eq. (13)] in our calculation. Note, however, that we are still using the large-force approximation to simplify the form of the energy, and so our calculation of $\langle R \rangle$ is only improved, not exact (Fig. 4).

Before continuing with this approach, we must calculate the correlation function $C(s, s')$, i.e., the function satisfying $\int ds'' \, C(s, s'') \, C^{-1}(s'', s') = \delta(s - s')$. We leave it to the reader to derive the result [exercise (2) of Sec. V]

$$C(s, s') = C(|s - s'|) = \frac{1}{2\sqrt{f\, l_p}} \exp\left(-\frac{|s - s'|}{\sqrt{l_p / f}} \right). \tag{46}$$

As we predicted via our clink picture (Sec. III), the correlation length ξ is given by

$$\xi = \sqrt{l_p / f}. \tag{47}$$

The correlation length [Eq. (47)] begins to vanish as we increase f. This seems rather counterintuitive; after all, we

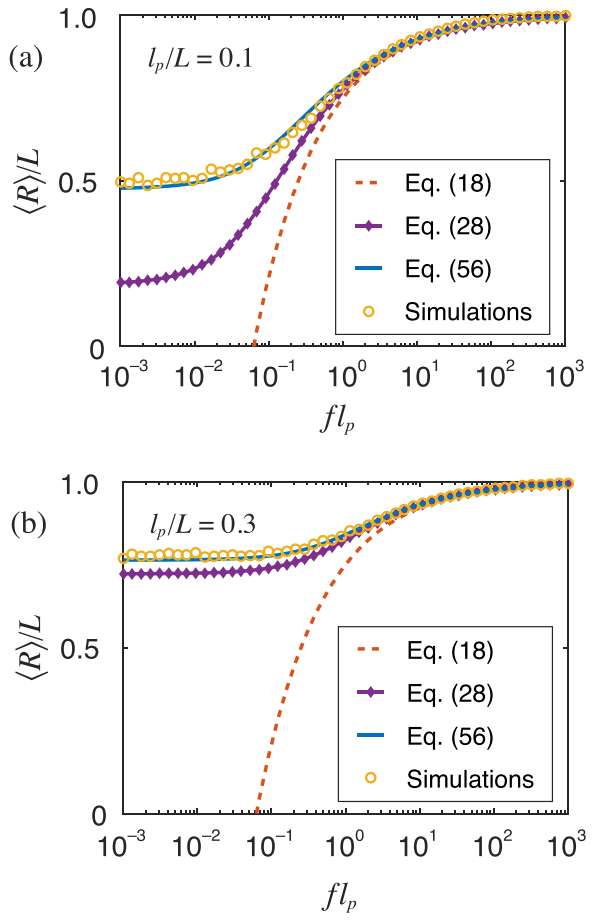

Fig. 4. (Color online) Comparison of theoretical predictions and simulated values of the relative average extension as a function of $f\,l_p$ (the ratio of the unbending energy to the thermal energy) for relative persistence lengths (l_p/L) of (a) 0.1 and (b) 0.3. The dashed (red online) curve representing the large-force approximation [Eq. (19)] is only accurate for $f\,l_p \gg 1$ and exhibits no dependence on the relative persistence length. The diamond-studded (purple online) curve represents the prediction we derive via statistical mechanics [Eq. (28)] by using the large-force approximation of $\langle R \rangle$ [Eq. (16)], while the solid (blue online) curve represents Eq. (56), the prediction we obtain by treating $\theta(s)$ as a Gaussian process and using the exact expression for R [Eq. (13)]. As l_p/L increases, the polymer becomes less likely to bend and thus, in the presence of a force, $\theta(s)$ becomes more likely to be small and the approximation in Eq. (16) improves, which explains the convergence of the exact and approximate extension curves in going from $l_p/L = 0.1$ to $l_p/L = 0.3$. The simulated average extension for each value of $f\,l_p$ represents 1000 samples of 40-link chains, each drawn from a separate instance of a slice sampler (with a 1000-sample burn-in period) working under the exact energy [Eq. (12)].

argued in deriving Eq. (16) that applying a large force should force the links of the polymer to all line up in the direction of the force, which seems to suggest that the angles become highly correlated. On the contrary, the angles end up not being correlated with each other, but with the direction of the force.

A. Calculating the average extension

In the Gaussian process framework, we can work with the exact definition of the extension in the discrete formulation [Eq. (13)]. However, we do have to properly account for the correlations between the given boundary angles and the interior angles. It is then useful to define two vectors, $\boldsymbol{\theta}_{\text{in}}$ and $\boldsymbol{\theta}_{\text{out}}$, the latter of which contains the given boundary angles $\boldsymbol{\theta}_{\text{out}} = (\theta_1, \theta_N)$ and the former contains all the interior angles $\boldsymbol{\theta}_{\text{in}} = (\theta_2, \ldots, \theta_{N-1})$. For our calculations here, we take $\boldsymbol{\theta}_{\text{out}} = (0, 0)$. Our distribution of interest is thus not $P(\boldsymbol{\theta}) = P(\boldsymbol{\theta}_{\text{in}}, \boldsymbol{\theta}_{\text{out}})$, but the conditional distribution $P(\boldsymbol{\theta}_{\text{in}}|\boldsymbol{\theta}_{\text{out}})$. Likewise, we must calculate not $\langle R \rangle$, but $\langle R \,|\, \boldsymbol{\theta}_{\text{out}} \rangle$

$$\langle R \,|\, \boldsymbol{\theta}_{\text{out}} \rangle = \frac{L}{N} \sum_{n=2}^{N-1} \langle \cos\theta_n \,|\, \boldsymbol{\theta}_{\text{out}} \rangle. \tag{48}$$

Because $P(\boldsymbol{\theta}_{\text{in}}, \boldsymbol{\theta}_{\text{out}})$ is a zero-mean multivariate Gaussian distribution and we set $\boldsymbol{\theta}_{\text{out}} = \langle \boldsymbol{\theta}_{\text{out}} \rangle$, it follows that the conditional distribution $P(\boldsymbol{\theta}_{\text{in}}|\boldsymbol{\theta}_{\text{out}})$ is also zero-mean multivariate Gaussian, $P(\boldsymbol{\theta}_{\text{in}}|\boldsymbol{\theta}_{\text{out}}) \sim \mathcal{N}(\mathbf{0}, \Sigma_{\text{in|out}})$. [N.B. $\mathcal{N}(\boldsymbol{\mu}, \Sigma)$ denotes a (multi)variate Gaussian distribution with mean $\boldsymbol{\mu}$ and covariance matrix Σ.] The only tricky part is calculating the conditional covariance matrix $\Sigma_{\text{in|out}}$. To begin, we consider the form of the joint distribution, $P(\boldsymbol{\theta}_{\text{in}}, \boldsymbol{\theta}_{\text{out}}) \sim \mathcal{N}(\mathbf{0}, \Sigma)$, where Σ is determined by Eq. (45). We then write Σ and its inverse in block form

$$\Sigma = \begin{pmatrix} \Sigma_{\text{in,in}} & \Sigma_{\text{in,out}} \\ \Sigma_{\text{in,out}}^T & \Sigma_{\text{out,out}} \end{pmatrix}, \quad \Sigma^{-1} = \begin{pmatrix} \Sigma_{\text{in|out}}^{-1} & P_{12} \\ P_{12}^T & P_{22} \end{pmatrix}, \tag{49}$$

where $\Sigma_{\text{in,in}} = \langle \boldsymbol{\theta}_{\text{in}} \boldsymbol{\theta}_{\text{in}}{}^T \rangle$, $\Sigma_{\text{out,out}} = \langle \boldsymbol{\theta}_{\text{out}} \boldsymbol{\theta}_{\text{out}}{}^T \rangle$, and $\Sigma_{\text{in,out}} = \langle \boldsymbol{\theta}_{\text{in}} \boldsymbol{\theta}_{\text{out}}{}^T \rangle$. The matrices P_{12}, P_{12}^T, and P_{22} will not matter in $P(\boldsymbol{\theta}_{\text{in}}|\boldsymbol{\theta}_{\text{out}})$ as they end up multiplying $\boldsymbol{\theta}_{\text{out}} = 0$. We can thus get an expression for $\Sigma_{\text{in|out}}$ by block-inverting Σ

$$\Sigma_{\text{in|out}} = \Sigma_{\text{in,in}} - \Sigma_{\text{in,out}}\, \Sigma_{\text{out,out}}^{-1}\, \Sigma_{\text{in,out}}^T, \tag{50}$$

which requires us to compute the inverse of the matrix $\Sigma_{\text{out,out}}$, which in this case is only 2×2.

Fortunately, for our purposes here we do not have to compute $\Sigma_{\text{in|out}}$ for all the interior angles all at once. The reason is simple: the expectations appearing in our expression for the average extension [Eq. (48)] each depend on only a single interior angle, and so the Gaussianity of $P(\boldsymbol{\theta}_{\text{in}}|\boldsymbol{\theta}_{\text{out}})$ implies that these expectations reduce to

$$\langle \cos\theta_n \,|\, \boldsymbol{\theta}_{\text{out}} \rangle = \int_{-\infty}^{\infty} d\theta_n \, \cos\theta_n \, P(\theta_n|\boldsymbol{\theta}_{\text{out}}). \tag{51}$$

where $P(\theta_n|\boldsymbol{\theta}_{\text{out}}) \sim \mathcal{N}(0, \sigma_{n|\text{out}}^2)$. This Gaussian distribution for θ_n is simple enough that we can exactly evaluate the integral in Eq. (51)

$$\langle \cos\theta_n \,|\, \boldsymbol{\theta}_{\text{out}} \rangle = \exp\left(-\frac{\sigma_{n|\text{out}}^2}{2} \right). \tag{52}$$

Now we can focus on calculating the conditional covariance $\sigma_{n|\text{out}}^2$. The covariance matrix Σ for the joint distribution $P(\theta_n, \boldsymbol{\theta}_{\text{out}})$ is only a 3×3 matrix

$$\Sigma = \begin{pmatrix} C(0) & C\left(\frac{n}{N}L\right) & C\left(\frac{N-n}{N}L\right) \\ C\left(\frac{n}{N}L\right) & C(0) & C(L) \\ C\left(\frac{N-n}{N}L\right) & C(L) & C(0) \end{pmatrix}, \tag{53}$$

in which $C(x)$ is the correlation function from Eq. (46). (Note that in principle all the n's should be $(n-1)$'s;

however, this will not matter in the large N limit and so we have purposely ignored this for notational convenience.) Evidently, in this case, the block matrices are

$$\Sigma_{\text{in,in}} = C(0),$$
$$\Sigma_{\text{in,out}} = \begin{pmatrix} C\left(\frac{n}{N}L\right) & C\left(\frac{N-n}{N}L\right) \end{pmatrix}, \tag{54}$$
$$\Sigma_{\text{out,out}} = \begin{pmatrix} C(0) & C(L) \\ C(L) & C(0) \end{pmatrix},$$

and so according to Eq. (50) the conditional variance of θ_n, denoted by $\sigma^2_{n|\text{out}} = \Sigma_{\text{in|out}}$, is given by

$$\sigma^2_{n|\text{out}} = \frac{\cosh\left(\frac{L}{l_p}\sqrt{f\,l_p}\right) - \cosh\left[\left(\frac{2n-N}{N}\right)\frac{L}{l_p}\sqrt{f\,l_p}\right]}{2\sqrt{f\,l_p}\sinh\left(\frac{L}{l_p}\sqrt{f\,l_p}\right)}. \tag{55}$$

Substituting Eq. (55) into Eq. (51) and then plugging that result into Eq. (48) leads to a very difficult sum, but by taking the large N limit, we can convert it to an integral expression

$$\frac{\langle R\rangle}{L} = \int_0^1 dz\, \exp\left[\frac{\cosh\left(z\frac{L}{l_p}\sqrt{f\,l_p}\right) - \cosh\left(\frac{L}{l_p}\sqrt{f\,l_p}\right)}{4\sqrt{f\,l_p}\sinh\left(\frac{L}{l_p}\sqrt{f\,l_p}\right)}\right]. \tag{56}$$

Although the resulting integral still resists analytical evaluation, we can evaluate it numerically, as we do in Fig. 4. Indeed, Eq. (56) agrees with simulations over at least four decades of $f\,l_p$, whereas our large-force approximation [Eq. (19)] holds only for $f\,l_p \gg 1$. Moreover, we can obtain our previous expressions for the average extension [Eqs. (19) and (28)] by making the appropriate large-force approximations in Eq. (56), as you are asked to show in exercise (4) of Sec. V.

Exercises for Sec. V:

(1) Show how to write the argument of the exponential in Eq. (15) in the form of Eq. (42).
(2) Starting from the definition of an operator inverse $\int ds''\, C^{-1}(s,s'')\, C(s'',s') = \delta(s-s')$ and the inverse correlation function [Eq. (44)], calculate the correlation function for $\theta(s)$ [Eq. (46)]. For simplicity, assume the range of integration spans the whole real line, $s \in (-\infty, \infty)$, so that Fourier techniques apply.
(3) Calculate the average extension using its exact definition [Eq. (48)] in the case where only one end of the polymer is fixed, $\theta(0) = 0$.
(4) Derive Eqs. (19) and (28) from Eq. (56) by making the appropriate large-force approximations. Alternatively, make a large-force approximation in Eq. (48) and use the Gaussian process formalism to derive Eq. (28).

VI. DISCUSSION

The basic theoretical model of a polymer is the Gaussian (entropic) chain, which is analogous to a connected random walk in space. This model ignores all effects of mechanical rigidity, statistical correlations, and self-avoidance and yet has served as a powerful paradigm within which to study the statics and dynamics of simple polymers.[16,17,24] For many biological applications, the Gaussian chain model is not sufficient to describe the fact that these large macromolecules are relatively stiff on small length scales and thus resist bending deformations enthalpically. The natural extension of the Gaussian chain to account for this effect is the worm-like chain, the paradigm for semi-flexible polymers. In this tutorial, we have provided a variety of complementary approaches to study the mechanical response of a single worm-like chain under the influence of an external force.

Fundamentally, the mechanical response of a worm-like chain arises from a conflict/compromise between two driving forces—an internal orientational order that dominates at short length scales comparable to the persistence length l_p, and an external driver of orientational order that dominates at long length scales of magnitude $f^{-1} = k_BT/F$. Together, these effects yield an effective correlation length that scales as $\xi = (l_p/f)^{1/2}$, the effective size of a clink. As the external force becomes larger this clink becomes smaller so that the external force becomes more and more effective at forcing orientational order even at short length scales. Equivalently, the force diverges as the average end-to-end extension of the polymer approaches its natural length. Using this result, it is possible to derive the mean-field mechanical response of a cross-linked network of worm-like chains,[22] but this is the subject of another tutorial.

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Condensing Vessel

If you want to do an experiment with compressed air today, you probably have available a rapidly-running pressure pump that produces a steady stream of air. In the nineteenth century you turned to a stout metal cylinder that had been previously filled with air from a lever-action air pump. This early example from Cornell University has had a 20th century stopcock fitted to it. (Picture and Notes by Thomas B. Greenslade, Jr., Kenyon College)