Alternative spring force law for bead-spring chain models of the worm-like chain

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Synopsis

We have developed a new spring force law which can be used in bead-spring chain models of the worm-like chain. The bead-spring chain has no bending potentials between the springs, and so differs from the current models only in the functional form of the force law. This new model can accurately represent a chain that contains many persistence lengths even if each spring represents only a few persistence lengths. We also discuss the assumptions in the model and other sources of possible error. The new force law significantly reduces the error compared with using the Marko-Siggia interpolation formula. © *2006 The Society of Rheology.*
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I. INTRODUCTION

The worm-like chain (WLC) model has been used to represent a wide variety of molecules, ranging from biological macromolecules such as DNA to worm-like micelles [Marko and Siggia (1995); Dalhaimer *et al.* (2003)]. It is important to build accurate but feasible models of these molecules that can be used with experiments to further the understanding of the behavior of the materials. The level of detail included in the model is determined by the physics of the problem of interest. The current models can be roughly grouped into three classes based on the length scale they aim to capture: (1) atom or united-atom level [Schlick *et al.* (2000); Mergell *et al.* (2003); Lu *et al.* (1998)]; (2) continuous worm-like chain, e.g., the limit of the Kratky-Porod model [Kratky and Porod (1949); Yamakawa (1997)]; and (3) bead-spring chain using a force law such as the Marko and Siggia interpolation formula [Marko and Siggia (1995); Underhill and Doyle (2004)].

In this article we will consider groups (2) and (3), in particular how to bridge the gap in models between them. In order for the Kratky-Porod model to represent the continuous worm-like chain, each rod must be smaller than about one-fifth of the persistence length at equilibrium and even smaller when the chain is stretched. At the other end, the bead-spring chains using the Marko and Siggia interpolation formula are only used if each spring represents more than about 20 persistence lengths [Underhill and Doyle (2004)]. This leaves a gap of at least two orders of magnitude. For double-stranded DNA with a persistence length of about 50 nm, this gap corresponds to lengths between 10 nm and

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1 μm. This is exactly the characteristic size when studying polymers in microfluidic and nanofluidic devices [Chen *et al.* (2004); Tegenfeldt *et al.* (2004); Chen *et al.* (2005)], so it is important to have coarse-grained versions of the WLC at that length scale.

There are two basic ways that have been used previously to attempt to close this gap in models. One way is to push the Kratky-Porod model so each rod represents a larger fraction of a persistence length. This has been attempted by using a different bending potential than is typically used in the Kratky-Porod model [Wilhelm and Frey (1996); Farkas *et al.* (2003)]. One of the main disadvantages of this method is that, because rigid rods are used, the response at large forces looks more like the response of a freely jointed chain than the worm-like chain. This is not consistent with trying to represent the continuous WLC or the behavior of double-stranded DNA. The use of finite-size rigid rods with bending potentials has been studied recently [Livadaru *et al.* (2003); Storm and Nelson (2003)]. These researchers were not studying this model as a coarse-grained version of the continuous worm-like chain but as a new *alternative* to the continuous worm-like chain, called the discrete persistent chain. Some polymers such as single-stranded DNA may be better described by the discrete persistent chain than either the freely jointed chain or the continuous worm-like chain [Storm and Nelson (2003)]. However, for double-stranded DNA this difference would only be present at forces larger than about 1 nN [Livadaru *et al.* (2003)]. This is beyond the forces that cause structural changes in the DNA, which are not considered here. Thus, for our purposes, double-stranded DNA is approximately a continuous worm-like chain, and it is this model which we would like to coarse grain.

The other way of bridging the gap is to push the bead-spring chains so each spring represents a smaller number of persistence lengths. This has been attempted by using an effective persistence length in the spring force law which differs from the true persistence length of the continuous worm-like chain to be modeled. We have addressed some of the issues involved in this process previously [Underhill and Doyle (2004)]. Essentially, it is not possible to simultaneously have the correct behavior at small and large extensions. We will quantify in this paper exactly how well it can model the continuous worm-like chain.

Our approach is to use bead-spring chain models, but with a different functional form for the spring force law. We previously applied this idea to the freely jointed chain, an important and common micromechanical model of polymers [Underhill and Doyle (2004), (2005)]. Our focus here is on the worm-like chain which is more complicated to coarse grain because of the coupling along the chain's contour. The goal of this article is to show that we can partially close the gap in models without using bending potentials between the springs. In order to completely close the gap, a more complicated model would need to be used that accounts for the coupling along the contour. We do not attempt that here because there remain complications to overcome, and it may be sufficient for many purposes to use the simple model developed here.

Although we only consider here the spring force law, in many situations hydrodynamic interaction (HI) and excluded volume (EV) interaction play an important role in obtaining accurate predictions from a bead-spring chain model. Our philosophy of building an accurate model is that the spring force law should be chosen such that the model gives the correct response if HI and EV do not affect the response even if included. One such situation is the force-extension behavior at "theta" conditions, so we use that response to determine the spring force law. While theta conditions correspond to the situation where EV can be effectively neglected, HI is always important for long chains. However, HI does not affect the force-extension behavior. Thus, by using the force-

extension behavior in theta conditions to coarse grain the continuous WLC to a bead-spring chain, the spring force law will give the chain the correct configurational distribution function under theta conditions.

If the bead-spring chain developed here is placed in a situation where HI and EV are important, those effects must be included also in the model. Research is ongoing into the "best" way of choosing the parameters governing the strength of HI and EV [Larson (2005); Sunthar and Prakash (2005)]. Separating the development of the spring force law from the choice of HI and EV strength parameters may help in the determination of the "best" HI and EV parameters, particularly when the amount of polymer represented by a spring is being changed.

Even without the inclusion of HI and EV we can still understand some implications of using the new spring force law in terms of rheology and dynamics of single molecules. Previously we have shown how the force-extension behavior at small force is related to the size of the coil at equilibrium and thus to the zero shear rate rheology for a free-draining model in theta conditions [Underhill and Doyle (2004)]. Even though HI is important for all long polymers, free-draining models are still often used, for which analyzing the predictions of a free-draining model is appropriate and useful. For example, λ-phage DNA is generally considered "short" in that the effects of HI on *nonlinear rheology*, such as the start-up of uniaxial extensional flow, can be approximately modeled by using a free-draining model if the drag is rescaled appropriately [Larson (2005)]. The use of these models should be done carefully because a free-draining model fails in predicting some aspects of polymer behavior.

However, our approach here is not limited to this class of molecules. An accurate model will include full fluctuating HI, which is important for all long polymers. Even if HI is included in the model, obviously the size of the coil is critical to model correctly. In fact, in the nondraining limit in theta conditions, any dynamic property is directly related to the radius of gyration R_g through a universal ratio [Sunthar and Prakash (2005)]. Thus, it is crucial for the coarse-grained model to accurately represent the size of the coil, which is directly related to the force-extension behavior at small force. In addition to its impact on rheological properties, the size of the equilibrium coil will have important implications for the behavior in confining geometries in microdevices or in many size-dependent separation techniques. Along these same lines, in non-"theta" conditions EV effects must be included to get the correct coil size. This is particularly important because typical single molecule experiments using DNA are performed in good solvents. Under these conditions it is still important for the spring force law to give the correct theta condition size of the coil, with the solvent quality parameter giving the correct deviation from this size.

The effect of the spring force law on the behavior of the chain far from the coil state seems even easier to understand. In highly stretched states the effects of EV are expected to be small and the influence of HI may be weaker. Even when HI plays a critical role such as in coil-stretch hysteresis, using the correct spring force law may help in determining the appropriate HI strength parameter. Previous work looking at the response of polymers to strong flows or the relaxation after strong flow have illustrated the effect of the spring force law near full extension [Ladoux and Doyle (2000); Shaqfeh *et al.* (2004)]. Our article will show that by simply using a different functional form for the spring force law, the force-extension response of the worm-like chain can be accurately modeled using a bead-spring chain in the coiled state, the extended state, and at intermediate states.

FIG. 1. Illustration of a worm-like chain with vectors connecting positions on the chain. The coarse-grained model would ideally reproduce the average correlation of the vectors. The polymer has persistence length A_p. The contour length represented by the vectors is ℓ. The contour length between the two vectors is ℓc.

II. IMPLICATIONS OF NO BENDING POTENTIALS

Before developing the new spring force law, we must discuss some implications of using a model without bending potentials between the springs as a coarse-grained version of the worm-like chain.

Consider the continuous worm-like chain in Fig. 1. The vectors $\mathbf{r}_1$ and $\mathbf{r}_2$ correspond to segments of polymer which will be modeled by springs. The polymer has a persistence length A_p, and each segment has a contour length of ℓ, so $\nu = \ell / A_p$ represents number of persistence lengths. The segments are separated by an amount of polymer with contour length ℓc. One way of examining the assumptions in the coarse-grained model is to compare $\langle \mathbf{r}_1^2 \rangle$ and $\langle \mathbf{r}_1 \cdot \mathbf{r}_2 \rangle$ between the continuous worm-like chain and the bead-spring model. We can calculate these properties of the continuous WLC by using the average correlation of the tangent vector,

$$\langle \mathbf{t}(s) \cdot \mathbf{t}(p) \rangle = \exp(-|s - p|/A_p), \tag{1}$$

where s and p denote the positions along the contour of the WLC and $\mathbf{t}(s)$ is the unit tangent vector at position s. We will also use that the vector connecting two points on the chain is the sum over all the tangent vectors connecting those points, for example

$$\mathbf{r}_1 = \int_a^{a+\ell} \mathrm{d}s\, \mathbf{t}(s), \tag{2}$$

where a is an arbitrary constant related to the convention of where s and p are defined to be zero. Using these two equations we can show that

$$\langle \mathbf{r}_1 \cdot \mathbf{r}_2 \rangle = A_p^2 (1 - e^{-\nu})^2 e^{-c\nu}, \tag{3}$$

$$\langle \mathbf{r}_1^2 \rangle = 2\,\ell\, A_p + 2A_p^2 (e^{-\nu} - 1). \tag{4}$$

We would like the coarse-grained version of the WLC (the bead-spring chain) to reproduce these two properties. Consider first the behavior of $\langle \mathbf{r}_1 \cdot \mathbf{r}_2 \rangle$. Without bending potentials in the bead-spring chain model, the mean dot product between two spring connector vectors is zero. Note that even if each spring represents a large segment of polymer (i.e., $\nu \rightarrow \infty$), neighboring sections ($c = 0$) would need to have a nonzero mean dot product to exactly model the continuous WLC. Next-nearest neighbors ($c = 1$) in the continuous WLC have an exponentially decaying mean dot product for large ν. As we will see later, it is not possible to use a bead-spring chain without bending potentials to accurately model a WLC with $\nu < 2$ (less than one Kuhn length). For the case $\nu \geq 2$ which we consider here, the correlation between next-nearest neighbors in the continuous WLC is small, and so can be approximately modeled without bending potentials.

Another issue that must be addressed is the matching of the force-extension behavior between the bead-spring chain and the continuous worm-like chain. This turns out to be
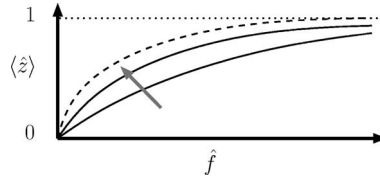
FIG. 2. Sketch of the average fractional extension as a function of the applied force for a continuous worm-like chain model. The arrow denotes increasing $\alpha = L/A_p$, where L is the contour length and A_p is the persistence length. The dashed curve represents $\alpha = \infty$. The z extension is made dimensionless using the contour length, $\hat{z} = z/L$. The externally applied force is made dimensionless using the persistence length, $\hat{f} = (fA_p)/(k_BT)$.

related to $\langle \mathbf{r}_1^2 \rangle$ because the slope of the force-extension behavior at small force is proportional to the second moment of the spring length [Underhill and Doyle (2004)].

Figure 2 shows a sketch of the force-extension behavior of a series of continuous worm-like chains of different contour lengths relative to the persistence length, $\alpha = L/A_p$. This represents the behavior of the exact WLC which we want the bead-spring chain to reproduce. Using the second moment of the squared end-to-end distance for the exact WLC [similar to Eq. (4) but for the entire polymer] and its relation to the zero force slope, one can show that in this sketch, the slope at zero force is

$$\lim_{\hat{f} \to 0} \frac{\partial}{\partial \hat{f}} \langle \hat{z} \rangle = \frac{2}{3} + \frac{2}{3\alpha}(e^{-\alpha} - 1). \tag{5}$$

As α increases, the slope increases until it saturates at $2/3$. The behavior at large force has not been rigorously calculated for finite α. However, approximate calculations for worm-like chains with $\alpha \approx 1$ [Wilhelm and Frey (1996)] suggest that the behavior at large enough force may behave as

$$\langle \hat{z} \rangle \sim 1 - \frac{1}{2\hat{f}^{1/2}} + \mathcal{O}\left(\frac{1}{\alpha \hat{f}}\right) \tag{6}$$

for all values of $\alpha > 0$.

Now, consider two different bead-spring chain models, one with $N_s = 1$ number of springs and $\nu = 4$ number of persistence lengths represented by each spring, and the other model with $N_s = 100$ number of springs and $\nu = 4$ number of persistence lengths represented by each spring. Because there are no bending potentials between the springs and the value of ν is the same, the average fractional extension versus force curves of these bead-spring chains are identical [Underhill and Doyle (2004)]. The total number of persistence lengths in the whole chain is $\alpha = N_s \nu$, so the continuous worm-like chains that are to be modeled contain $\alpha = 4$ and $\alpha = 400$, respectively. Figure 2 shows that these continuous worm-like chains have different force-extension behaviors. This would appear to be an inconsistency in our method of determining the spring force law by matching the force-extension behavior of the bead-spring model with the continuous worm-like chain. This inconsistency results from the absence of bending potentials in the bead-spring chain model.

To proceed with a bead-spring model without bending potentials that is also consistent, we will only attempt to model continuous worm-like chains which are "long" in the sense that $\alpha \gg 1$. However, keep in mind that the systems of interest here, and any real system, will have a finite α no matter how large it is. For example, consider now two bead-spring models, one with $N_s = 25$ number of springs and $\nu = 10$ number of persistence

lengths represented by each spring, and the other model with $N_s=100$ number of springs and $\nu=4$ number of persistence lengths represented by each spring. The continuous worm-like chains to be modeled contain $\alpha=250$ and $\alpha=400$, respectively. While these continuous worm-like chains do not have identical force-extension behaviors, because $\alpha\gg1$, they are very close to each other and also very close to the $\alpha=\infty$ force-extension behavior of the continuous WLC shown in Fig. 2. From Eqs. (5) and (6) we see that the maximum relative error between a curve with finite α and the $\alpha=\infty$ curve is $1/\alpha$ for large α. In this article the spring force law will be constructed so that the force-extension behavior of these bead-spring models with $\nu=10$ and $\nu=4$ will be identical (to within the error discussed later), and that force-extension behavior will be the $\alpha=\infty$ limit in Fig. 2. In other words, the spring force law developed here will be valid even if each spring represents a relatively small amount of polymer (e.g., $\nu=4$) as long as the entire chain contains many persistence lengths ($\alpha=N_s\nu\gg1$). In practice this is not much of a restriction because many worm-like chains of interest contain many persistence lengths, such as the commonly modeled stained λ-phage DNA which contains about $\alpha\approx400$ persistence lengths.

The more subtle point is that we are essentially sacrificing some accuracy at the scale of a single spring (as $\langle\mathbf{r}_1^2\rangle$) or neighboring springs (as $\langle\mathbf{r}_1\cdot\mathbf{r}_2\rangle$ for $c=0$) to obtain the correct behavior at the scale of the entire chain. We can see this sacrifice by comparing $\langle\mathbf{r}_1^2\rangle$ for the bead-spring chain and the WLC. In order for the bead-spring chain to have the $\alpha=\infty$ force-extension behavior at small force without bending potentials, the bead-spring chain will be required to have $\langle\mathbf{r}_1^2\rangle=2\ell A_p$ because of the relation between this moment and the zero-force slope of the force-extension behavior. Comparing this with Eq. (4), we see that the relative error in this second moment decays as $1/\nu$ for large ν and is 76% when a spring represents two persistence lengths.

This is the same type of compromise at equilibrium that is made when the bead-rod chain is used to model $\alpha\gg1$ worm-like chains. In fact, the bead-spring chain models developed here would become the bead-rod chain if each spring represents two persistence lengths. A worm-like chain of two persistence lengths is not a rigid rod and neighboring segments are not freely jointed. The bead-rod chain sacrifices this accuracy to describe the entire $\alpha\gg1$ worm-like chain at equilibrium. The approximation made in this paper is less severe because each spring represents *at least* two persistence lengths and the bead-spring chains developed here also capture the response correctly when external forces are applied.

III. REAL CONTINUOUS WLC

As discussed in the previous section, the spring force law in the new bead-spring chain model will be chosen so that the force-extension behavior of the model matches that of the $\alpha=\infty$ continuous WLC in the limits of large and small force. Recall that the α of any system considered here is finite, but we are only considering systems with $\alpha\gg1$ such that the force-extension behavior is very close to the $\alpha=\infty$ force-extension behavior. To gauge the accuracy of this bead-spring chain we will calculate the error in the force-extension behavior relative to the $\alpha=\infty$ behavior over the entire force range. The force-extension behavior for an $\alpha=\infty$ worm-like chain cannot be written exactly as a simple analytic function, but the response can be calculated numerically. In this article we use the *numerical* calculation by Bouchiat *et al.* (1999) as the "true" worm-like chain.

The asymptotic expansions for both large and small forces are

$$\langle \hat{z} \rangle \sim 1 - \frac{1}{2\hat{f}^{1/2}} - \frac{1}{128\hat{f}^{3/2}} + \mathcal{O}\left(\frac{1}{\hat{f}^2}\right), \tag{7}$$

$$\langle \hat{z} \rangle \sim \frac{2}{3}\hat{f} - \frac{44}{135}\hat{f}^3 + \mathcal{O}(\hat{f}^5), \tag{8}$$

where $\langle \hat{z} \rangle$ is the average fractional extension and $\hat{f}$ is the externally applied force made dimensionless using $k_B T$ divided by the persistence length, A_p. The numerical data from Bouchiat *et al.* have these asymptotic behaviors. Bouchiat *et al.* also developed a simple formula to approximate the numerical evaluation. While this formula only introduces a small error, because of the functional form chosen, it does not have exactly the expansions above. Thus, in the main body of this article we only use the numerical data from Bouchiat *et al.* See the Appendix for a discussion of the simple functions to approximate the behavior.

IV. ACCURACY OF MARKO-SIGGIA SPRING

Before discussing the new spring force law, we will address the accuracy of using the Marko and Siggia interpolation formula as the spring force law at different levels of discretization. This analysis is related to that done previously [Underhill and Doyle (2004)], though it differs in one very important aspect. Previously, we were concerned with understanding how the different ensembles and corresponding fluctuations affect the response. Therefore, when analyzing the behavior of bead-spring chains using the Marko-Siggia force law, we compared the force-extension behavior of the bead-spring chain with a hypothetical polymer which has the Marko-Siggia formula as its true behavior. This is because we did not want the fact that the Marko-Siggia form is not the same as the real WLC to complicate our understanding of the different ensembles and fluctuations.

However, our concern here is to analyze how well a bead-spring chain models the real continuous WLC, so we compare the behavior of Marko-Siggia chain to the real WLC [using the numerical data from Bouchiat *et al.* (1999)]. Note that because the hypothetical Marko-Siggia polymer is the same as the real WLC at small and large force, the error will be the same as the previous analysis in those two limits. It is at intermediate forces where there is a difference.

The Marko and Siggia spring force law takes the form

$$f_{\text{spring}}(r) = \left(\frac{k_B T}{A_{\text{eff}}}\right)\left\{\left(\frac{r}{\ell}\right) - \frac{1}{4} + \frac{1}{4(1 - r/\ell)^2}\right\}, \tag{9}$$

where A_{eff} is an effective persistence length which can be different from the true persistence length of the WLC being modeled, A_{true} (previously denoted A_p). The effective persistence length is a fudge factor used to improve the behavior of the bead-spring chain. An extensive analysis of different choices for this effective persistence length was performed previously [Underhill and Doyle (2004)] in terms of the ratio $\lambda = A_{\text{eff}}/A_{\text{true}}$. The result is that a single choice of λ is not capable of correcting the force-extension behavior at both small and large forces. In this section we will see further evidence of this fact. The value of λ is a function of the number of persistence lengths represented by each spring ν. Here, we will use the low-force criterion for λ, which chooses the function $\lambda(\nu)$ such that the force-extension behavior of the bead-spring chain matches the force-extension behavior of the $\alpha = \infty$ continuous WLC at zero force.
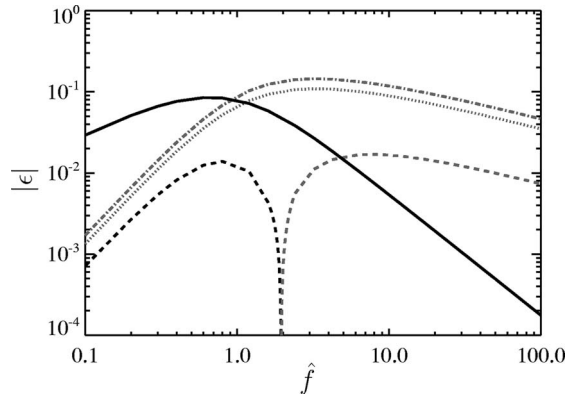
FIG. 3. Relative error in the fractional extension versus force for the Marko-Siggia spring using the low-force criterion for the effective persistence length. The gray lines signify that $\epsilon < 0$, while the black lines signify that $\epsilon > 0$. The curves correspond to $\nu=4$ (dotted), $\nu=20$ (dashed), and $\nu=\infty$ (solid). As $\nu \rightarrow 10/3$ the curves approach the bead-string chain (dash-dot).

Figure 3 shows the relative error in the fractional extension versus force between using the Marko-Siggia spring force law and the $\alpha=\infty$ continuous WLC. The curves correspond to $\nu=4, 20, \infty$, and the low-force criterion was used for λ. To avoid ambiguity in the sign of the relative error, we define it as

$$\epsilon \equiv \frac{\text{true value} - \text{calculated value}}{\text{true value}}. \tag{10}$$

The key point is that the error appears to not be the smallest at $\nu=\infty$. At intermediate ν (like $\nu=20$) the maximum error can be smaller than when $\nu=\infty$. This is because the error discussed previously [Underhill and Doyle (2004)] counteracts the error because the Marko-Siggia formula does not match the real WLC.

The general response can be understood by examining the limiting behaviors of the bead-spring chain and the real WLC. At large force the average fractional extension using the Marko-Siggia force law is

$$\langle \hat{z} \rangle \sim 1 - \frac{1}{2\lambda^{1/2}\hat{f}^{1/2}} + \mathcal{O}\left(\frac{1}{\hat{f}}\right), \tag{11}$$

where the external force $\hat{f}$ is made dimensionless using the true persistence length, denoted A_{true}. Recall that in Fig. 3, $\lambda(\nu)$ was determined using the low-force criterion. This means that for any $10/3 < \nu < \infty$, the relative error eventually decays as $\hat{f}^{-1/2}$ with a coefficient that is negative, and the error gets worse as λ grows (i.e., ν decreases for the low-force criterion).

The form of the Marko-Siggia formula makes the behavior at small force slightly more subtle. For any $10/3 < \nu < \infty$, the relative error at small enough force decays as $\hat{f}^2$. This is because $\langle \hat{z} \rangle$ is an odd analytic function of $\hat{f}$ around small force, and the low-force criterion for the effective persistence length makes the order $\hat{f}$ term match the real WLC. The coefficient to this decay in relative error is determined from the order $\hat{f}^3$ contribution to $\langle \hat{z} \rangle$, which is related to the second and fourth moments of the spring length, $\langle \hat{r}^2 \rangle$ and $\langle \hat{r}^4 \rangle$ [Underhill and Doyle (2004)]. The subtlety arises because as $\nu \rightarrow \infty$, the coefficient to $\hat{f}^2$ in the relative error diverges as $\nu^{1/2}$. Higher order terms in force also have diverging

coefficients. This large number of terms, each with diverging coefficients, combines and cancels perfectly to give a relative error that decays as $\hat{f}$. The actual curve in the $\nu \to \infty$ limit is found by comparing the inverse of the Marko-Siggia force law with the behavior of the real WLC. The inverse of the Marko-Siggia force law is not an odd function, and so has all terms in the expansion for small force.

It may appear that the Marko-Siggia spring force law with an effective persistence length has sufficiently small error at intermediate levels of discretization such as $\nu = 20$. However, in many cases it is not sufficient to simply have the relative error approach zero at large force. Any bead-spring model with a finite fully extended length will have a fractional extension that approaches 1 as the force approaches infinity; thus, the relative error in the fractional extension will approach zero as the force approaches infinity. It is also important for an accurate model to have the correct approach to full extension. As shown in Eq. (11), the approach to full extension is affected by the effective persistence length. The approach to full extension has been used to analyze the behavior in strong flows and the relaxation after cessation of elongational flow [Ladoux and Doyle (2000); Shaqfeh *et al.* (2004)] and is therefore important to capture with the coarse-grained model.

It is useful to pause at this point and recall how far the low-force criterion can be pushed. It was shown previously [Underhill and Doyle (2004)] that the low-force criterion for the Marko-Siggia force law cannot be pushed past $\nu = 10/3$. At that point, the effective persistence length becomes infinite. What that means is the spring force is zero for all extensions less than the fully extended length. This type of model is also called the bead-string chain [Bird *et al.* (1987)]. The fractional extension as a function of the force for the bead-string chain is

$$\langle \hat{z} \rangle = \frac{-3k_{\mathrm{B}}T}{f\ell} + \frac{1}{\mathcal{L}[f\ell/(k_{\mathrm{B}}T)]}, \tag{12}$$

where $\mathcal{L}$ is the Langevin function [Underhill and Doyle (2004)]. We show this curve in Fig. 3, which is the limiting behavior of the Marko-Siggia system with low-force criterion when $\nu \to 10/3$. Note that the $\hat{f}^{-1/2}$ approach to full extension has totally vanished. In fact, the response is not all that different from using the freely jointed chain to model the worm-like chain (with each rod representing two persistence lengths).

V. ALTERNATIVE TO MARKO-SIGGIA

The main goal of this paper is to systematically build a new spring force law which can be used in bead-spring chain models and perform better than the Marko-Siggia formula. We now develop that new spring force law in this section. We proceed as for the freely jointed chain previously [Underhill and Doyle (2005)]. We start by assuming a form of the spring force law

$$\hat{f}_{\mathrm{s}} = \frac{C\hat{r}}{(1 - \hat{r}^2)^2} + \frac{G\hat{r}}{\nu(1 - \hat{r}^2)} + D\hat{r} + B\hat{r}(1 - \hat{r}^2). \tag{13}$$

We choose the values (functions of ν) for C, G, D, B such that the force-extension behavior of the bead-spring chain is the same (in the limits of small and large force) as the $\alpha = \infty$ continuous WLC.

For the similar analysis for the freely jointed chain we knew the way the spring force must approach full extension to have the desired force-extension behavior from the ran-

dom walk spring (RWS) model. For the worm-like chain we must instead directly calculate the force-extension behavior of a bead-spring chain using the postulated form as the spring force law. For large force the fractional extension is

$$\langle \hat{z} \rangle \sim 1 - \frac{C^{1/2}}{2\hat{f}^{1/2}} - \frac{G+7}{4\nu\hat{f}} + \frac{1}{\hat{f}^{3/2}} \left(\frac{C^{1/2}(C-16D)}{64} + \frac{C^{1/2}(G+4)}{16\nu} - \frac{(G+1)(G+3)}{16\nu^2 C^{1/2}} \right) + \mathcal{O}\left(\frac{1}{\hat{f}^2}\right).$$

(14)

To match with the behavior of the $\alpha=\infty$ WLC [Eq. (7)], we choose $C=1$, $G=-7$, and

$$D = \frac{3}{32} - \frac{3}{4\nu} - \frac{6}{\nu^2}.$$

(15)

With these choices the average fractional extension expansion is

$$\langle \hat{z} \rangle \sim 1 - \frac{1}{2\hat{f}^{1/2}} - \frac{1}{128\hat{f}^{3/2}} + \mathcal{O}\left(\frac{1}{\hat{f}^2}\right).$$

(16)

The remaining parameter, B, is chosen to match the behavior at small force (at equilibrium). We will first proceed in the same way as for the freely jointed chain, using the large ν expansion of the second moment of the spring length, $\langle \hat{r}^2 \rangle$. Because this second moment is proportional to the slope of the force-extension behavior at small force, matching the second moment between the spring and the WLC means that the force-extension behavior is correct at small force.

Provided $\hat{r}=0$ is the global minimum of the spring potential energy, the behavior of the second moment for large ν is obtained by expanding the energy for small $\hat{r}$ [Underhill and Doyle (2004), (2005)]. Recall that for our bead-spring chain to match the equilibrium behavior of the $\alpha=\infty$ WLC, each spring must have by construction $\langle \mathbf{r}_1^2 \rangle = 2\ell A_p$. In dimensionless form, this is equivalent to $\langle \hat{r}^2 \rangle = 2/\nu$. If we choose

$$B_{h\nu} = \frac{13}{32} + \frac{39}{16\nu} - \frac{323}{192\nu^2},$$

(17)

then the expansion of the second moment for the spring with our new force law is

$$\langle \hat{r}^2 \rangle \sim \frac{2}{\nu} + \mathcal{O}\left(\frac{1}{\nu^4}\right).$$

(18)

We have denoted this $B_{h\nu}$ because the value comes from examining the expansion at high ν. For the freely jointed chain we found that using the high ν expansion allowed us to get a very small error even at smaller ν. Figure 4 shows the relative error in the second moment of the spring length as a function of ν. While the error does decay as ν^{-3} as we expect, the prefactor is large enough that the relative error at $\nu=4$ is about 15%. This is larger than we want. While one way to reduce the error is to continue the expansion to higher order in $1/\nu$, making the error decay as ν^{-4} or even higher, this will have most of its impact at large ν where the error is already small enough and will barely change the error at small ν.

An alternative is to determine numerically the function $B(\nu)$ such that the error is exactly zero. This is similar to how the effective persistence length is determined numerically as a function of ν when using the Marko-Siggia force law and low-force criterion. In fact, the low-force criterion function for the Marko-Siggia force law $\lambda(\nu)$ is the function such that $\langle \hat{r}^2 \rangle = 2/\nu$. It would be more useful to have an approximate formula for $B(\nu)$ that still has a small error. One such formula is
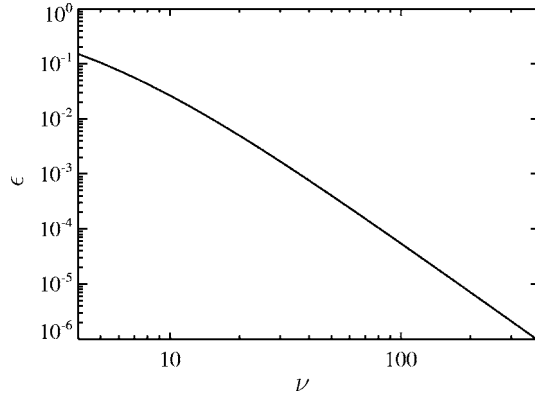
FIG. 4. Relative error in the second moment of the spring length, $\langle \hat{r}^2 \rangle$, using the new spring force law and the function $B_{h\nu}$.

$$B = \frac{(13/32) + (0.8172/\nu) - (14.79/\nu^2)}{1 - (4.225/\nu) + (4.87/\nu^2)}. \tag{19}$$

Using this formula, the error in the second moment of the spring length vanishes at ν $=4,5,9,30,\infty$ by construction and has a maximum relative error of 0.07% for $\nu \geq 4$.

Using this function for the parameter B, we obtain our new spring force law

$$\hat{f}_s = \frac{\hat{r}}{(1-\hat{r}^2)^2} - \frac{7\hat{r}}{\nu(1-\hat{r}^2)} + \left(\frac{3}{32} - \frac{3}{4\nu} - \frac{6}{\nu^2} \right) \hat{r}$$

$$+ \left(\frac{(13/32) + (0.8172/\nu) - (14.79/\nu^2)}{1 - (4.225/\nu) + (4.87/\nu^2)} \right) \hat{r}(1-\hat{r}^2). \tag{20}$$

Figure 5 shows the relative error in the fractional extension versus force using this new spring force law. We see that the maximum error is approximately 1% even for $\nu=4$. The response also has the correct approach to full extension, which can be seen from the steeper power law near large force than was seen for the Marko-Siggia force law.
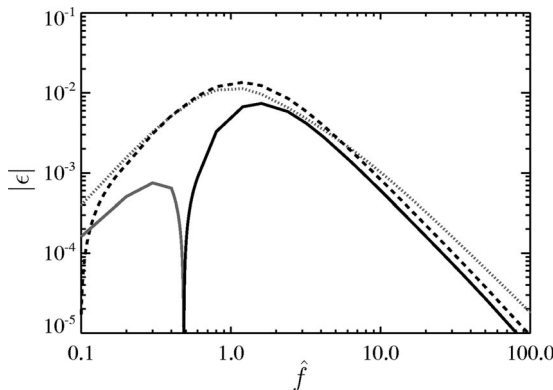

FIG. 5. Relative error in the average fractional extension $\langle \hat{z} \rangle$ using the new spring force law [Eq. (20)]. The gray lines signify that $\epsilon < 0$, while the black lines signify that $\epsilon > 0$. The curves correspond to $\nu=4$ (dotted), $\nu=20$ (dashed), and $\nu=\infty$ (solid).
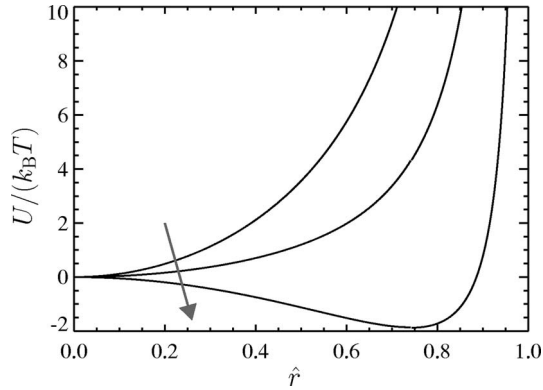
FIG. 6. Spring potential energy versus fractional extension for the new spring force law [Eq. (20)]. The curves correspond to $\nu=20, 10, 4$, with the arrow denoting decreasing ν. The arbitrary additive constant has been chosen so the potential energy vanishes at zero extension.

We can use the expansions of the fractional extensions to examine the limiting behavior of the relative error. At large force our new spring force law captures correctly up to order $\hat{f}^{-3/2}$ so the relative error decays as $\hat{f}^{-2}$. For $\nu=4, 5, 9, 30, \infty$ the parameter B makes the error vanish at small force, so the relative error decays as $\hat{f}^2$. For other values of ν, there is a small but nonzero relative error at zero force, so the relative error behaves as a small constant plus a term of order $\hat{f}^2$.

We will again pause to discuss how far this force law can be pushed. Recall that the force law uses the B parameter to make $\langle \hat{r}^2 \rangle = 2/\nu$. This is only possible if $\nu \geq 2$ because the spring cannot be larger than the fully extended length. If each spring represents two persistence lengths, then the B value would need to make $\langle \hat{r}^2 \rangle = 1$. In other words, the spring will have to look more and more like a rigid rod because the average equilibrium length and fully extended length become equal. To make this true it would be necessary to have $B = -\infty$. In this limit, the bead-spring chain becomes a freely jointed chain. This is best illustrated by examining the spring potential energy directly.

Figure 6 shows the spring potential energy calculated from our new spring force law [Eq. (20)] for a few values of ν. Initially, as ν gets smaller, the potential energy weakens, allowing for fluctuations to larger extensions. As ν gets even smaller, the minimum in the potential appears at nonzero extension. This allows the spring to correctly model both the low and high force behaviors. The minimum is at nonzero extension because the spring is becoming more like a rigid rod. As ν decreases, this minimum moves towards full extension and gets deeper. For $B = -\infty$ (which is necessary to get the correct $\langle \hat{r}^2 \rangle = 1$ for $\nu=2$), the potential is infinitely deep at $\hat{r}=1$. In other words, one way of simulating a freely jointed chain using stiff springs would be to set $\nu=2$ and $B \rightarrow -\infty$ in our spring force law.

The subtle point has to do with the behavior at large force. From the high force behavior in Eq. (14) and our choice of C, G, and D, one might think the behavior at high force is retained even in the limit $\nu=2$ and $B \rightarrow -\infty$. This is not true because one of the neglected terms in Eq. (14) goes as $B/\hat{f}^2$. This means that, for any finite B, there exists a force large enough that the term is negligible. However, at any finite force, as $B \rightarrow -\infty$ these higher order terms become important, so the response approaches that of the freely jointed chain.

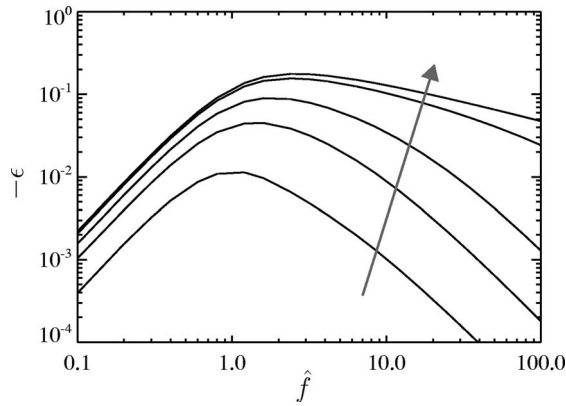We illustrate this approach by showing in Fig. 7 the error in the fractional extension

FIG. 7. Relative error in the average fractional extension $\langle \hat{z} \rangle$ using the new type of spring force law as $\nu \to 2$. The value of B was determined numerically to make the error vanish at zero force. The curves correspond to $\nu = 4, 3, 2.5, 2.1, 2$ with the arrow denoting decreasing ν. The $\nu = 2$ curve is the response of the freely jointed chain.

for $\nu \to 2$, where in this plot B is determined numerically such that $\langle \hat{r}^2 \rangle = 2/\nu$. The curves shown are for $\nu = 4, 3, 2.5, 2.1, 2$ with corresponding $B = -1.265, -9.836, -70.68, -8185.9, -\infty$. For the $\nu = 2$, $B = -\infty$ curve, we have plotted the behavior of the freely jointed chain. Note that each curve eventually decays like $\hat{f}^{-2}$ for large force, but the transition to that behavior is delayed as $\nu \to 2$. When $\nu = 2$, the transition never occurs. For each force, as $\nu \to 2$, the response approaches the freely jointed chain response.

VI. CONCLUSION

We have examined the coarse graining of the continuous worm-like chain polymer into a bead-spring chain model. We have restricted the discussion to very long polymers ($\alpha \gg 1$) so that we can consistently develop a model without bending potentials between the springs. A key point is that, even though the entire chain is very long, each spring does not represent a large number of persistence lengths (ν can be small). We illustrated the deficiencies of using the Marko-Siggia force law even with the use of an effective persistence length. This is related to our previous work analyzing the behavior of the Marko-Siggia force law [Underhill and Doyle (2004)].

We then developed a new spring force law [Eq. (20)] in a systematic way that significantly outperforms the Marko-Siggia spring force law. The new spring force law still has a simple functional form, so it can be easily used in dynamical simulations. The maximum error in the force-extension behavior is about 1% even if each spring represents only four persistence lengths. This naturally raises the questions beyond force-extension behavior: Will all these results be swamped by HI and EV in rheological predictions, and how would previous simulations using the Marko-Siggia force law be affected by using this new force law?

As mentioned in the Introduction, even when including HI and EV in the model, it is important to correctly capture the size of the coil under theta conditions. The solvent quality parameter will cause the chain to swell from theta conditions to the correct size. Inclusion of HI will cause the dynamic properties to have the correct values because of accurate predictions of universal ratios and the correct prediction of the radius of gyration [Sunthar and Prakash (2005)]. Since this size of the coil is related to the force-extension response at small force, correctly modeling the force-extension behavior, as well as

including HI and EV correctly, will result in accurate predictions. Alternatively, if the force-extension behavior or size of the coil is not modeled correctly, the predictions will correspondingly change to incorrect values. The rheological predictions at large forces or extensions seem easier to understand. In this limit, the EV effects should be small and the influence from HI should be smaller, so the spring contribution which comes from the force-extension behavior should be the dominant factor. Our new spring force law correctly models the response in both of the extremes, at small forces (equilibrium) and large forces.

However, using this new force law in place of the Marko-Siggia form in previous simulations will probably only produce a small change in the response. This is because previous simulations have only been performed when each spring represented a fairly large number of persistence lengths (e.g., $\nu \gtrsim 20$). This is in part because the error which occurs if ν became smaller was recognized, but also because the physics of the problems did not necessitate performing simulations for smaller ν. Simulating the behavior of polymers in increasingly smaller microdevices will require a model which can be used for smaller ν. We believe that in this area, a more substantial difference will emerge between our new spring force law and the Marko-Siggia formula. Even for $\nu \gtrsim 20$, where the difference in behavior may be slight, there are advantages to using the new force law. The new force law has a more systematic development which includes the fluctuations in configuration space. Our analysis resulted in a simple formula [Eq. (20)] which eliminates the need to calculate an effective persistence length which must be calculated based on some criteria which balance the response at small and large forces. Using this new force law should also help in the determination of the "best" HI and EV strength parameters to use. Different researchers use different fitting procedures to determine the model parameters and thus simulate using a range of model parameters [Larson (2005); Somasi *et al.* (2002); Jendrejack *et al.* (2002)]. If an incorrect spring force law is used, then the parameters such as the persistence length and EV strength parameter must be changed to compensate for the incorrect force law. Using our new force law should help reduce this variation among researchers and isolate coarse-graining issues associated with springs from that with HI and EV.

However, our new bead-spring chain model does have some assumptions intrinsic to it because there are no bending potentials between the springs. The errors from these assumptions are not as easy to quantify. Keep in mind, though, that these are the same type of assumptions made using the current spring force laws and when the freely jointed chain is used to approximate the worm-like chain. In fact, using the method presented here, a bead-spring chain trying to represent two persistence lengths per spring becomes equivalent to the freely jointed chain.

The results presented here should be considered a step forward towards filling the gap in coarse-grained models discussed in the Introduction. We have been able to reduce the size of this gap without introducing any further assumptions. This has pushed bead-spring chain models without bending potentials as far as possible. In order to eliminate the gap completely and account for the finite length of the worm-like chain ($\alpha \sim 1$), there must be correlation between segments in the coarse-grained model. We think this may be best accomplished using bending potentials between the springs or a generalized bead-spring chain discussed previously [Underhill and Doyle (2005)]. However, if each spring represents more than a few persistence lengths (which also means the whole chain contains more than a few persistence lengths), it seems sufficient to use the simpler model without bending potentials.
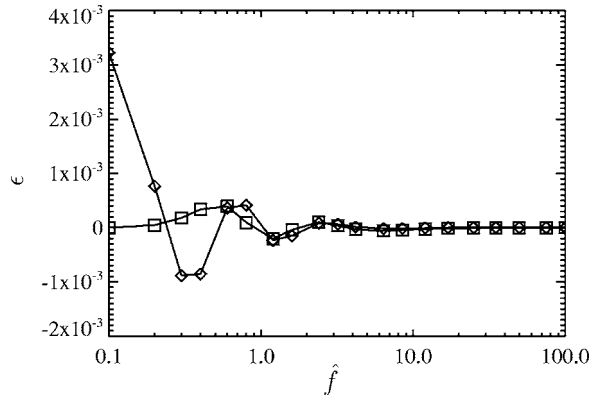
FIG. 8. Relative error in extension between the real infinitely long WLC [numerical data from Bouchiat *et al.* (1999)] and approximate formulas. The approximation from Bouchiat *et al.* [our Eq. (A1)] is shown by diamonds, while our Eq. (A6) is shown by squares.

ACKNOWLEDGMENTS

APPENDIX

1. Alternative to Exact Worm-like Chain

As mentioned previously, the force-extension behavior for the infinitely long WLC is not known analytically. It is convenient to have a simple analytic form which is a good approximation. The Marko-Siggia formula is such a function which is correct asymptotically for small and large forces. However, it can deviate by up to 10% at intermediate forces. Bouchiat *et al.* (1999) developed a new approximate formula by adding terms to the Marko-Siggia form. This formula is

$$\hat{f} = \frac{1}{4(1-\hat{r})^2} - \frac{1}{4} + \hat{r} + [-0.516\,422\,8\hat{r}^2 - 2.737\,418\hat{r}^3 + 16.074\,97\hat{r}^4 - 38.876\,07\hat{r}^5$$

$$+ 39.499\,44\hat{r}^6 - 14.177\,18\hat{r}^7]. \tag{A1}$$

They used this new formula to analyze force-extension experiments with double-stranded DNA to determine if a continuous WLC model is appropriate and determine the persistence length. Figure 8 shows how accurately Eq. (A1) represents the infinitely long WLC. The maximum relative error is 0.3% at a dimensionless force of about 0.1 (about 8 fN for double-stranded DNA), with a much smaller error at higher forces. Certainly for any numerical calculation or comparison to experiments this is sufficiently accurate.

The one drawback of this formula is that it only has the first term correct in a series expansion at small and full extension. This does not dramatically impact the overall error because the coefficients have been determined by fitting. This means that the series converges slowly, making a series expansion of the approximate function not very useful.

It would be nice if the approximate function had many correct terms in the series expansion. We can do this by using a function that is a sum of terms of the form $\hat{r}^{2n+1}(1-\hat{r}^2)^m$ inspired by Flyvbjerg (2001). It is possible to have the same limiting be-

havior as the real WLC with terms for integers $n \geq 0$ and $m \geq -2$. Not all these terms are necessary though because the three terms $(n,m)=(i,j),(i+1,j),(i,j+1)$ are linearly dependent. We have chosen the form

$$\hat{f} = \frac{C\hat{r}}{(1-\hat{r}^2)^2} + \frac{G\hat{r}}{(1-\hat{r}^2)} + D\hat{r} + B\hat{r}(1-\hat{r}^2) + J\hat{r}(1-\hat{r}^2)^2[1 + k_2 r^2 + k_4 r^4 + \cdots]. \quad \text{(A2)}$$

Note that the formulas in this section are not spring force laws, but are approximations to the force-extension behavior of the infinitely long WLC. For the infinitely long system it is not necessary to distinguish between the constant force or constant extension ensembles. We can therefore drop the averaging notation and use simply $\hat{f}$ and $\hat{r}$.

The advantage of the new form is that it correctly captures the odd parity of the WLC. This allows us to match successive terms in the expansions near $\hat{r}=0$ and $\hat{r}=1$ between our approximate form and the infinitely long WLC. We have chosen $C=1, G=0, D=3/32, B=5/64, J=21/64, k_2=41/35$, which gives expansions of

$$\hat{f} \sim \frac{1}{4(1-\hat{r})^2} + \frac{1}{32} + \mathcal{O}((1-\hat{r})^2), \quad \text{(A3)}$$

$$\hat{f} \sim \frac{3}{2}\hat{r} + \frac{33}{20}\hat{r}^3 + \mathcal{O}(\hat{r}^5). \quad \text{(A4)}$$

Our choice of functional form means that performing a fit with the other parameters does not affect the expansions above. We have chosen

$$k_4 = 0.627, \quad k_6 = -11.71, \quad k_8 = 10.26, \quad \text{(A5)}$$

and all higher k's are zero. This gives an approximation to the WLC behavior of

$$\hat{f} = \frac{\hat{r}}{(1-\hat{r}^2)^2} + \frac{3}{32}\hat{r} + \frac{5}{64}\hat{r}(1-\hat{r}^2) + \frac{21}{64}\hat{r}(1-\hat{r}^2)^2\left[1 + \frac{41}{35}r^2 + 0.627r^4 - 11.71r^6 + 10.26r^8\right].$$

$$\text{(A6)}$$

Figure 8 shows how well this new formula approximates the infinitely long worm-like chain. The maximum error is 0.04%, with much smaller error at small and large forces. The main difference between this new form and that developed by Bouchiat *et al.* occurs at small forces where, because the new formula has the correct series expansion, it has a smaller error.

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