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A new interpolation formula for semiflexible polymers

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Abstract

A new formula for the force vs. extension relation is derived from the discrete version of the so-called Worm-like chain model. This formula correctly fits some recent experimental data on polymer stretching. Moreover, we have compared our formula with a Monte Carlo simulation of a semiflexible polymer.

Keywords: Single-molecule experiments; Semiflexible polymers; Worm-like chain model; Monte Carlo methods

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1. Introduction

The behaviour of a single polymeric molecule under stretching has become a popular subject among experimental physicists (see, e.g., [1], for a review) and has attracted the attention of theoreticians who have introduced several models to explain these results.

Usually, the models adopted describe the polymer as an elastic (ideal) chain, where self-avoidance is not taken into account. Typically, freely jointed (FJC) or Worm-like chain (WLC) are studied [2].

The former describes a chain of beads connected by links of constant distance, whereas the latter, which has received considerably great attention in the recent past [3–7], introduces an intrinsic stiffness between two consecutive bonds and, in particular, is shown to correctly describe a wide range of experimental results on double-stranded (ds) DNA, single plasmid and lambda phage DNA [8–10]. In this case, the large force behaviour $1 - z/L_c \sim 1/\sqrt{F}$ is found, where z is the elongation along the direction of the force, L_c is the contour length of the polymer and F is the applied force [8]. Let us note that in these cases the continuous version of the WLC model is always used, where the persistence length [8] L_p is very large, compared to the base separation (roughly one persistence length is 150 base pairs).

Here, we focus on the discrete version of the WLC model, that satisfactorily describes the pulling behaviour of a polymer in good solvent [11]. We broadly identify three regimes in the force vs. extension curves obtained in our analytical and numerical calculations. The low force (or low stretch) regime is highly affected by the details of the interactions between the beads (which in nature are, e.g., caused by the different concentration of ions in solution). This regime is discussed only marginally here, as, though it is potentially very interesting, experimental data in this range of forces are quite rare and not precise enough to allow a comparison with theoretical predictions. There is then a second regime, of intermediate stretches or forces, in which the force versus extension characteristic curves obey approximately the laws predicted a few years ago in Ref. [8] by means of a continuum theory of the WLC. Finally, for very large forces (beyond a polymer dependent crossover value), we get a universal, model-independent, freely-jointed-chain like behaviour. In Section 2, we introduce the discrete WLC model and show how it can be related to the well known continuous version. In Section 3, we show a

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comparison between our theory and some recent experiments. Then, in Section 4, we compare our formula with a Monte Carlo calculation for a semiflexible polymer. Finally, Section 5 is left for conclusions.

2. The model

Our model describes a chain of beads, where the distance between the nearest neighbours is kept fixed (we can put it equal to b) and a suitable stiffness K is introduced. Then, the corresponding Boltzmann weight reads [12–14]:

$$e^{-\beta\mathcal{H}} = \prod_{i=1}^{N} \delta(|\vec{t}_i| - b) e^{\beta K \sum_{i=1}^{N-1} \vec{t}_i \cdot \vec{t}_{i+1} + \beta\vec{F} \cdot \sum_{i=1}^{N} \vec{t}_i}, \tag{1}$$

where $\beta=1/T$, T being the temperature in units of Boltzmann constant, $\vec{t}_i \equiv \vec{r}_i - \vec{r}_{i-1}$ ($\vec{r}_i$ being the position vector for the i-th bead, $i=1,\ldots, N$ and N is the total number of bonds), $\hat{t}_i = \vec{t}_i/b$ and $\vec{F} = F\hat{z}$ is the applied force which defines the z-direction. The partition function for the model described by [1] is $\mathcal{Z}_N = \int \prod_{i=1}^{N} \mathrm{d}t_i e^{-\beta\mathcal{H}}$ and the average elongation $\langle z \rangle_N$ along the stretching direction is $\langle z \rangle_N = T \frac{\partial}{\partial F} \log \mathcal{Z}_N$.

Let us now consider the large force behaviour. Due to the δ-function in Eq. (1), the term $\beta K \hat{t}_{i,z} \hat{t}i_{+1,z}$ can be re-written with the substitution $\hat{t}_{i,z} \simeq 1 - t_{i,\perp}^2/2b^2$ and, analogously, the force term in the exponential becomes $\beta\vec{F} \cdot \vec{t}_i = \beta F t_{i,z} = \beta F b\left(1 - t_{i,\perp}^2/2b^2\right)$, where $\vec{t}_i, \perp = \left(t_{i,x}, t_{i,y}\right)$ [8]. Keeping only quadratic terms in the $t_{i,\perp}$'s, we get:

$$\zeta \equiv \lim_{N\to\infty} \frac{\langle z \rangle_N}{Nb} = 1 - \frac{T}{\sqrt{(bF)^2 + 4bKF}}. \tag{2}$$

The continuum approximation of Eq. (2) is obtained with the substitution [15]:

$$\beta K \to L_{\mathrm{p}}/b, \tag{3}$$

in the formal limit $b \to 0$, where L_{p} is the persistence length. The final result $\zeta = 1 - 1/2\sqrt{\beta L_{\mathrm{p}} F}$ does agree with the celebrated result of Marko and Siggia [8]. However, our result is more general, since it predicts a crossover force $F_{\mathrm{c}}=4L_{\mathrm{p}}/\beta b^2$:

$$\begin{array}{ll} \text{WLC}-\text{like behaviour}: 1-\zeta \sim 1/\sqrt{F}, & F \ll F_{\mathrm{c}} \\ \text{FJC}-\text{like behaviour}: 1-\zeta \sim 1/F, & F \gg F_{\mathrm{c}} \end{array} \tag{4}$$

Let us notice that the validity of the continuum approximation proposed in [8] is not simply related to the value of the dimensionless ratio b/L_{p} but rather to F/F_{c}.

A naive derivation of F_{c} is given in the following: from the Hamiltonian defined in Eq. (1), we can see that the stiffness and the force terms are of the same order at $F_{\mathrm{c}} \sim K/b = L_{\mathrm{p}}/\beta b^2$, where Eq. (3) has been used. So the meaning of F_{c} is the one where the bending energy competes with the external force.

From Eq. (2) with the substitution [3], we deduce that:

$$\beta b F = \frac{2L_{\mathrm{p}}}{b}\left[\sqrt{1 + \left(\frac{b}{2L_{\mathrm{p}}}\right)^2 \frac{1}{(1-\zeta)^2}} - 1\right]. \tag{5}$$

The low force behaviour of the average elongation is

$$\zeta = \frac{\beta b F}{3} \frac{1 + y\left(L_{\mathrm{p}}/b\right)}{1 - y\left(L_{\mathrm{p}}/b\right)}, \tag{6}$$

where $y(x)=\coth(x) - 1/x$ [24]. Again, in the limit $b \to 0$, Eq. (6) agrees with the result of Marko and Siggia [8].

Following [8], we give an interpolation formula starting from Eqs. (5) and (6). We calculate the $\lim_{\zeta\to 0}$ of Eq. (5) and compare to Eq. (6). Matching the two results gives the following approximate equation:

$$\beta b F = \frac{2L_{\mathrm{p}}}{b}\left[\sqrt{1 + \left(\frac{b}{2L_{\mathrm{p}}}\right)^2 \frac{1}{(1-\zeta)^2}} - \sqrt{1 + \left(\frac{b}{2L_{\mathrm{p}}}\right)^2}\right] + \left(3\frac{1 - y\left(L_{\mathrm{p}}/b\right)}{1 + y\left(L_{\mathrm{p}}/b\right)} - \frac{b/2L_{\mathrm{p}}}{\sqrt{1 + \left(b/2L_{\mathrm{p}}\right)^2}}\right)\zeta. \tag{7}$$

It is easy to verify that Eq. (7) correctly reproduces the right large and small force behaviours, Eqs. (5) and (6) and that in the continuum limit $b \to 0$ we obtain the well known interpolation formula [8]:

$$\beta L_{\mathrm{p}} F = \frac{1}{4(1-\zeta)^2} - \frac{1}{4} + \zeta. \tag{8}$$

In next section, we shall apply our formula, Eq. (7), to two recent experiments. The first discusses the stretching of a single plasmid DNA molecules, to which the formula (8) was previously applied with success [9]. Nevertheless, our formula predicts a non trivial value for the parameter b, that gives an estimate for the intra bead distance. Then, the second experiment [16,17] demonstrates that Eq. (7) gives the right large force behaviour.

In the following, we shall define $\zeta = z/L_{\mathrm{c}}$, where z is the elongation along the direction of the force and $L_{\mathrm{c}} = Nb$ is the contour length of the polymer (see also Eq. (2)).

3. Comparison with two recent experiments

Let us consider the experimental data reported in the plot at the top of Fig. 3 of [9], that is the case of uncondensed molecules of a single plasmid of DNA molecules, whose stretching pattern is reproduced in Fig. 1.

As described in the caption, the contour and persistence lengths obtained with our formula, Eq. (7), and with Eq. (8) are perfectly compatible. Nevertheless Eq. (7) predicts a non trivial value for the intra bead effective distance b=2.5 nm, that corresponds to 7–8 base pairs. Let us notice that this matches the DNA hydration thickness (here, we have used

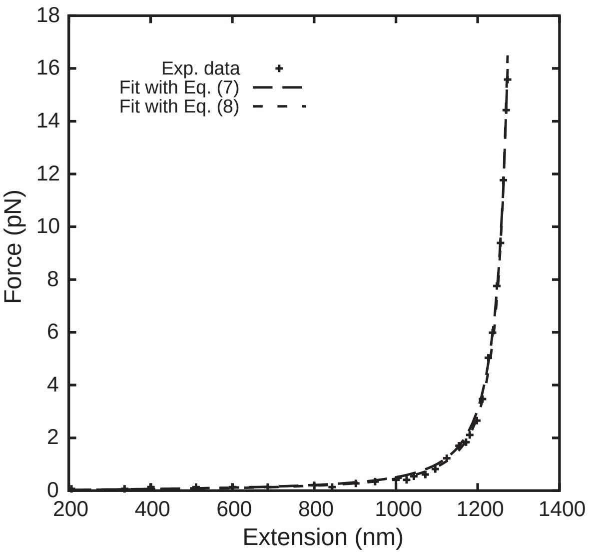

Fig. 1. (+): Experimental data on a single plasmid of DNA molecules, taken from [9]. Long dashed line: fit with the curve, Eq. (7), yielding L_c=1324 nm, L_p=38 nm and b=2.5 nm. Short dashed line: fit with the curve, Eq. (8), yielding L_c=1324 nm and L_p=38 nm, see [9].

~0.34 nm as the distance between two consecutive base pairs [9]).

If we take T=300 K, the crossover force F_c~100 pN and $F/F_c \leq 0.16$ for the data of [9], thus justifying the use of the interpolation formula, Eq. (8). However, as pointed out in Eq. (4), the discrete nature of the chain does emerge, when $F \geq F_c$. Notice also that for forces considerably smaller than F_c double-stranded DNA would undergo an overstretching transition [18,19], where a more sophisticated theory is needed [2].

An interesting question is how this treatment may be applied to single-stranded DNA (ssDNA). On one hand, if we keep as physical parameters the persistence length of ssDNA ~1 nm, and as the equivalent of b the separation between two phosphates, i.e., 0.5 nm roughly, we would end up with a crossover force again of the order of 70 pN. Data in this regime do exist [16,17], and suggest that the WLC grossly fails to fit the data [17,20]. In fact (see Fig. 4, [17]), the authors pointed out that the corresponding fit with Eq. (8) gives good results in the large force regime, but with a calculated persistence length ($\simeq 0.21$ nm) which is clearly not physical. Our equation does not do much better for low and intermediate force, in which case, as shown in Ref. [17], evidently the self-interactions dominate the behaviour. Still a large force fit, even if a bit dependent on the contour length which we choose, suggests that the large force exponent in the [$\log(1-\zeta)$, $\log(F)$] plane is -1 as predicted by our model (see Fig. 2). The calculated fitting parameters L_p and b (see the caption of Fig. 2) give $F_c \simeq 300$ pN. However, it can be seen that the fit is good already for $F \simeq 100$ pN, in order-of-magnitude agreement with the naive guess proposed above.

Let us notice that in this case $b/L_p \simeq 0.46$, an order of magnitude larger than the dsDNA value $b/L_p \simeq 0.07$. This is a clear indication of the fact that ssDNA is more flexible than dsDNA and that our formula predicts the correct high force behaviour.

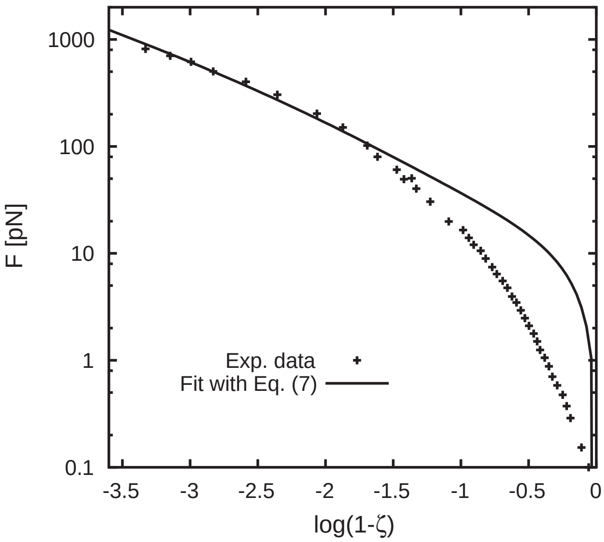

Fig. 2. (+): Experimental data on ssDNA, taken from [17]. Continuous line: fit with the curve, Eq. (7), yielding L_c=2.31 (in units of the contour length l^0_{ds} of the equivalent dsDNA molecule observed in 10 mM PB [17]), L_p=0.26 nm and b=0.12 nm.

In next section we introduce a Monte Carlo calculation and compare it to Eqs. (7) and (8).

4. Monte Carlo calculations

As already said, our model is a *stiff* chain described by the Boltzmann weight, Eq. (1), where the *intra* bead distance b is now kept fixed to 1.

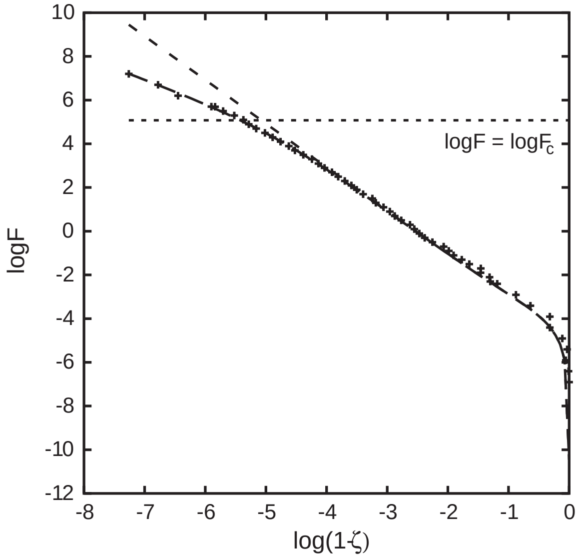

Fig. 3. (+): Monte Carlo data for a stiff chain of N=100 beads and stiffness K=40, for β=1. Long dashed line: Eq. (7) with L_p=40 and b=1. Short dashed line: Eq. (8) with L_p=40. The crossover force F_c, see Eq. (4), is also shown.

We have considered the case when K=40 and β=1. In Fig. 3 we have plotted the Monte Carlo data (+) and the curves given by Eqs. (7) and (8) (long and short dashed line, respectively), for L_p=40 and β=1.

As observed, the agreement is perfect only for Eq. (7). In fact, the discrete nature of the chain emerges around F=F_c~160 (in the chosen units) and the WLC approximation is no more valid.

5. Remarks and conclusions

Let us remark that the range of applicability of our formula, Eq. (7), is more general than the one described here.

In [21] we have reported the results concerning some Monte Carlo simulations of semiflexible polymer with different kinds of intra bead potentials. For a short range repulsive potential we have correctly found that our formula is in good agreement with the numerical data, predicting a renormalized stiffness [22,23]. For a more realistic Lennard–Jones potential the situation is more complicated. For temperatures above the θ point [11,24], Eq. (7) gives a good fit. The main result is that, now, both the persistence length and the intra bead distance b are renormalized by the potential. For temperatures below the θ point, our formula agrees with the numerical data only at large forces.

Moreover, we have performed also simulations to examine the validity of our new formula for the pulling of flexible polymers under quasi-fixed stretch conditions. This kind of simulations has been done by using Molecular Dynamics methods. Like in Monte Carlo simulations we considered chains with repulsive and attractive Lennard–Jones potentials but now the chains have no intrinsic stiffness. It is found that for both types of interaction our new formula works very well at high extension and it correctly predicts the intra bead distance. The case of attraction is even more interesting since when the temperature is above the θ point both the high and low extension stretching data can be fitted reasonably well to Eq. (7). It is shown that the Marko and Siggia formula does not fit the numerical data for the chains considered. The reason for this is that the modest stiffness induced by the Lennard–Jones potentials is not sufficiently large to yield the continuous WLC behaviour as described by Eq. (8). The results indicate that Eq. (7) can be used to characterize elastic behaviours of a much wider range of biomolecules.

In conclusion, here we have revised the well-known WLC model that correctly describes the behaviour under pulling of a stiff polymer. We have pointed out that its discrete version has a different large force behaviour respect to the continuous version by Marko and Siggia [8], Eq. (4). We predict a crossover force between these two different regimes. It should be noticed that two recent papers [19,25] report a similar result. However, here we have given a simpler formula, Eq. (7), which can be tested on real polymers as well as on numerical simulations, where self-interactions are present.

References

[1] C. Bustamante, J.C. Macosko, G.J.L. Wuite, Grabbing the cat by the tail: manipulating molecules one by one, Nat. Rev., Mol. Cell Biol. 1 (2000) 130.

[2] M.D. Wang, H. Yin, R. Landick, J. Gelles, S.M. Block, Stretching DNA with optical tweezers, Biophys. J. 72 (1997) 1335.

[3] J. Wilhelm, E. Frey, Radial distribution function of semiflexible polymers, Phys. Rev. Lett. 77 (1996) 2581.

[4] J. Samuel, S. Sinha, Elasticity of semiflexible polymers, Phys. Rev. E 66 (2002) 050801.

[5] J. Samuel, S. Sinha, Molecular elasticity and the geometric phase, Phys. Rev. Lett. 90 (2003) 098305.

[6] A. Dhar, D. Chaudhuri, Triple minima in the free energy of semiflexible polymers, Phys. Rev. Lett. 89 (2002) 065502.

[7] A. Lamura, T.W. Burkhardt, G. Gompper, Semiflexible polymer in a uniform force field in two dimensions, Phys. Rev. E 64 (2001) 061801.

[8] J.F. Marko, E.D. Siggia, Stretching DNA, Macromolecules 28 (1995) 8759.

[9] C.G. Baumann, V.A. Bloomfield, S.B. Smith, C. Bustamante, M.D. Wang, Stretching of single collapsed DNA molecules, Biophys. J. 78 (2000) 1965.

[10] R. Podgornik, P.L. Hansen, V.A. Parsegian, Elastic moduli renormalization in self-interacting stretchable polyelectrolytes, J. Chem. Phys. 113 (2000) 9343.

[11] P.-G. De Gennes, Scaling Concepts in Polymer Physics, Cornell University Press, Ithaca, 1979.

[12] M. Fixman, J. Kovac, Polymer conformational statistics: 3. Modified Gaussian models of stiff chains, J. Chem. Phys. 58 (1973) 1564.

[13] S. Cocco, R. Monasson, J.F. Marko, Unzipping dynamics of long DNAs, Phys. Rev. E 66 (2002) 051914.

[14] S. Cocco, J.F. Marko, R. Monasson, Theoretical models for single-molecule DNA and RNA experiments: from elasticity to unzipping, Cr. Phys. 3 (2002) 569.

[15] D. Bensimon, D. Dohmi, M. Mezard, Stretching a heteropolymer, Europhys. Lett. 42 (1998) 97.

[16] M. Rief, H. Clausen-Schaumann, H.E. Gaub, Sequence-dependent mechanics of single DNA molecules, Nat. Struct. Biol. 6 (1999) 346.

[17] M.-N. Dessinges, B. Maier, Y. Zhang, M. Peliti, D. Bensimon, V. Croquette, Stretching single stranded DNA, a model polyelectrolyte, Phys. Rev. Lett. 89 (2002) 248102.

[18] S.B. Smith, Y. Cui, C. Bustamante, Overstretching B-DNA: the elastic response of individual double-stranded and single-stranded DNA molecules, Science 271 (1996) 795.

[19] C. Storm, P.C. Nelson, Theory of high-force DNA stretching and overstretching, Phys. Rev. E 67 (2003) 051906.

[20] A. Montanari, M. Mézard, Hairpin formation and elongation of biomolecules, Phys. Rev. Lett. 86 (2001) 2178.

[21] A. Rosa, T.X. Hoang, D. Marenduzzo, A. Maritan, Elasticity of semiflexible polymers with and without self-interactions, Macromolecules 36 (2003) 10095.

[22] N. Lee, D. Thirumalai, Stretching DNA: role of electrostatic interactions, Eur. Phys. J., B Cond. Matter Phys. 12 (1999) 599.

[23] P.L. Hansen, R. Podgornik, Wormlike chains in the large-d limit, J. Chem. Phys. 114 (2001) 8637.

[24] M. Doi, S.F. Edwards, The Theory of Polymer Dynamics, Clarendon Press, Oxford, 1988.

[25] L. Livadaru, R.R. Netz, H.J. Kreuzer, Stretching response of discrete semiflexible polymers, Macromolecules 36 (2003) 3732.