Pulling strings at finite temperature:
Another force-extension formula for the Worm-Like Chain Model

Henrik Flyvbjerg
Condensed Matter Physics and Chemistry Department, Risø National Laboratory, DK-1000 Roskilde, Denmark
and
The Niels Bohr Institute, Blegdamsvej 17, DK-2100 Copenhagen Ø, Denmark
(August 1, 2000)

The derivation of Marko and Siggia’s interpolation formula for the force-extension relation of the Worm-Like Chain Model (C. Bustamante, J. F. Marko, E. D. Siggia, and S. Smith, Science 265, 1599 (1994); J. F. Marko and E. D. Siggia, Macromolecules 28, 8759 (1995)) is retraced. Isotropy of space, resulting in rotational invariance of the free energy, is invoked together with analyticity. A new interpolation formula results for the force-extension relationship. It is as simple as the old one, but twice as close to the exact force-extension relationship. Application of the same reasoning to the second-order perturbative result obtained at strong force (J. D. Moroz and P. Nelson, Proc. Natl. Acad. Sci. USA 94, 14418 (1997)) results in yet a new interpolation formula, good to 1% at all forces.

Introduction. The worm-like chain (WLC) model is the quintessential model of entropic elasticity from a flexible, but unstretchable fiber, string, or thread. The model is conceptually simple, mathematically minimalist, and widely used to interpret experiments that involve pulling at strings at finite temperature. Thus recent single-molecule experiments in biological physics cause new interest in this old model from polymer physics. It was successfully employed to model the experimental force-extension relationship of double-stranded DNA some years ago. Also, the force-extension relations for the giant muscle protein titin, the polysaccharide dextran, and single molecules of xanthan were explained with the WLC model. A refined analysis of DNA’s force-extension relationship, in terms of the WLC model was recently presented in [9]. The relaxation dynamics of extended DNA molecules, measured with millisecond resolution and femtonewton force spectroscopy, was interpreted using the WLC model in [14]. In [15], the WLC model was used to interpret stretching of single collapsed DNA molecules. Furthermore, the WLC model was extended with stretch and twist, and references therein] to model also these properties of double stranded DNA.

The WLC model. The WLC-models describes a string of vanishing cross section, unstretchable, but flexible. As it cannot stretch, the string can only bend, and it resists even that with a force (per unit length) proportional to its curvature. The constant of proportionality, $A$, is called the bending modulus, and has dimension energy per unit length of string, per unit curvature squared. Thus the bending energy of the string is

$$E[\tilde{t}] = \frac{A}{2} \int_0^{L_0} ds \left( \frac{d\tilde{t}}{ds}(s) \right)^2,$$

where $L_0$ is the length of the string; $s$ parametrizes points on the string by their distance from one end, as measured along the string, $s \in [0, L_0]$; $\tilde{t}(s)$ is the tangent vector to the string at its point at $s$. This energy is evidently minimal for a straight string, since a straight string has constant tangent vector.

When the string is submerged in a heat bath, a bending energy of order $k_B T$ is available to each of its degrees of freedom. The string consequently bends in a random manner obeying Boltzmann statistics, and an attempt to pull apart its ends is resisted with a force $\vec{F}$ which depends on the string’s end-to-end separation $\vec{R}$, $\vec{F} = \vec{F}(\vec{R})$. Because of the isotropy of space and the rotational invariance of the bending energy in Eq. (1), $\vec{F}(\vec{R})$ is anti-parallel to $\vec{R}$, and $|\vec{F}|$ depends only on $R = |\vec{R}|$. Because the string is unstretchable, the largest possible end-to-end separation is $R = L_0$. So a natural dimensionless measure of the end-to-end separation is $r = R/L_0 \in [0, 1]$.

Despite its simplicity, the WLC model cannot be solved analytically in general. When its ends are left free, a small calculation based on the Boltzmann weight factor $\exp(-E[\tilde{t}]/k_B T)$, results in the correlation function $\langle \tilde{t}(s_1) \cdot \tilde{t}(s_2) \rangle = \exp(-|s_1 - s_2|/L_0)$, where the persistence length $L_p$ is inversely proportional to the temperature: $L_p = A/k_B T$. In the limit $L_p/L_0 \to \infty$ where the string is much longer than its persistence length, $L_p F(r)/k_B T$ is a dimensionless function of the dimensionless variable $r$. But not even in this convenient limit is an exact analytical solution possible. A numerical solution for the force-extension relationship is not difficult to obtain, and is given in a useful form in [15, 16].

The Marko-Siggia interpolation formula. It is sometimes convenient, however, to have a simple analytical expression for the force-extension relationship, even if only an approximate one. Marko and Siggia presented such a relationship in [15]:

$$F(r) = F_0 \left(\frac{r}{R}\right)^p \exp\left(-\frac{1}{2} \frac{r}{R} \left(\frac{r}{R}\right)^p\right),$$

where $F_0$ is the maximum force the string can resist, $R$ is the natural critical separation of the ends, $p$ is an adjustable parameter that determines the overall shape of the force-extension curve.
\[
\frac{L_p F_{\text{MS}}(r)}{k_B T} = \frac{1}{4(1-r)^2} - \frac{1}{4} + r .
\]

This formula was derived by calculating the force-extension relationship analytically to leading order in the limit of very large force, where the string is nearly fully stretched, \( r \approx 1 \). That yielded
\[
\frac{L_p F_{\text{exact}}(r)}{k_B T} = \frac{1}{4(1-r)^2} + \text{unknown subdominant terms}.
\]

An attempt to use the known part of this result for all \( r \in [0,1] \) fails at small forces/small \( r \), where a calculation shows that
\[
\frac{L_p F_{\text{exact}}(r)}{k_B T} \sim \frac{3}{2} r \quad \text{for} \quad r \sim 0.
\]

The explicit term in Eq. (3) does not satisfy Eq. (4). The last two terms on the right-hand-side of Eq. (2) were added to ensure Eq. (4) is satisfied. We note that this procedure does not compromise the validity of the result, Eq. (2), at \( r \rightarrow 1 \), because the two added remain finite in that limit. The result is accurate to 17% when at its worst—see Fig. 1—and is by construction asymptotically correct for \( r \rightarrow 0 \) and for \( r \rightarrow 1 \).

Another interpolation formula. Now consider the exact force-extension relationship. Suppose we could calculate the string’s free energy, \( F \), analytically at given temperature and end-to-end separation \( \vec{R} \). Then we could calculate its force-extension relationship as
\[
\vec{F}(\vec{R}) = -\frac{\partial F}{\partial \vec{R}}.
\]

We cannot do this, but we know that the free energy is independent of the direction of \( \vec{R} \). It depends only on \( R \equiv |\vec{R}| \). Furthermore, we expect the free energy to be an analytical function of \( \vec{R} \) for \( |\vec{R}| < L_0 \), hence analytical in \( R = 0 \). Arguments for analyticity may be given, or one may regard analyticity as a conjecture or postulate. Or one may simply disregard the issue; the interpolation formulas given below have the precision demonstrated in Fig. 1 no matter how we arrive at the formulas. Faulty logic works fine here.

Analyticity of \( F(\vec{R}) \) in \( R = 0 \) implies that \( F(\vec{R}) \) has a Taylor series expansion in powers of \( \vec{R} \)'s components. Rotational invariance consequently implies that \( \vec{R} \)'s components only occur in the combination \( \vec{R}^2 \) in this Taylor series. Consequently, \( F \) is an analytical function of \( \vec{R}^2 \), \( F = F(\vec{R}^2) \). Thus \( F \) is an even analytical function of \( \vec{R} \). From Eq. (3) then follows that \( \vec{F}(\vec{R}) \) must be an odd analytical function of \( \vec{R} \).

Marko and Siggia’s interpolation formula, Eq. (3), is not an odd analytical function of \( r \). But if we retrace its derivation from Eq. (3), we note that this expression already contains what it takes to mend it: we extrapolate Eq. (3) from the limit \( r \rightarrow 1 \) to lower values of \( r \) in an odd manner by realizing that the factor 1 in the numerator really is \( r \), while the factor 4 in the denominator is \((1 + r)^2 \). Thus we arrive at a new analytical interpolation formula for the force-extension relationship of the WLC model:
\[
\frac{L_p F_{\text{MS}}(r)}{k_B T} = \frac{r}{(1-r)^2} + \frac{1}{2} r^2 .
\]

The last term on the right-hand-side has been added to ensure that Eq. (4) is satisfied, entirely in the spirit of Marko and Siggia’s derivation of their formula.

\( F_{\text{MS}}(r) \) should be a better approximation than \( F_{\text{MS}}(r) \), because it respects rotational symmetry and correctly captures all odd terms in the Taylor series for the exact result. They vanish in the exact result, and they vanish in \( F_{\text{MS}}(r) \). Figure 1 illustrates this improvement: \( F_{\text{MS}}(r) \) is much closer to the exact result than \( F_{\text{MS}}(r) \). It differs less than 8%, at most, while \( F_{\text{MS}}(r) \) differs up to 17%. At low values of \( r \), \( F_{\text{MS}}(r) \) represents an improvement by much more than a factor two. For larger values of \( r \), the improvement is approximately a factor two. Note that \( F_{\text{MS}} \) achieves this doubled precision with half as much “patching” at \( r \sim 0 \): only one correcting term was added.

Yet another interpolation formula. Moroz and Nelson have calculated the first correction term to Eq. (3) [17,18,24]:
\[
F_{\text{MN}}(r) = \frac{1}{4(1-r)^2} + \frac{1}{32} + O(1-r) .
\]

This result also is not an odd function of \( r \). But again this is easily remedied. The first term on the right-hand-side was treated above, and the next two terms are treated similarly, yielding
\[
\frac{L_p F_{\text{MN}}(r)}{k_B T} = \frac{r}{(1-r^2)^2} + \frac{r}{32} + O(r(1-r^2)) .
\]

This last expression is an odd analytical function of \( r \), but it does not satisfy Eq. (4), and we cannot mend that simply by adding terms which remain finite for \( r = 1 \), as Marko and Siggia did. But we can proceed entirely in their spirit, and add terms of same order as the neglected terms, in the present case \( O(r(1-r^2)) \). Doing that, we arrive at
\[
\frac{L_p F_{\text{F}}(r)}{k_B T} = \frac{r}{(1-r^2)^2} + \frac{r}{32} + \frac{15}{32} r(1-r^2) .
\]

Figure 1 shows that \( F_{\text{F}}(r) \) reproduces \( F_{\text{exact}} \) to within 1.5%.

Discussion. It is clear from the procedure we have used that one may continue it systematically by calculating more terms in the two series for \( F_{\text{exact}}(r) \)'s asymptotic behavior at \( r = 0 \) and \( r = 1 \), respectively. This exact asymptotic information can then be incorporated in
an increasingly complex result, by including an increasing number of terms of the general form \( r^{2n+1}(1-r^2)^m \), with suitable coefficients and exponents \( n \) and \( m \). In view of the accuracy already achieved with Eq. (1), this is hardly worthwhile for most purposes.

For one purpose, however, it looks promising: as a way to present a high-precision analytical interpolation formula meant for numerical evaluation \[25\]. At weak and strong force (small and large end-to-end separations) where numerical methods typically fail unless special care is taken, such a result is exact to a chosen order in perturbation theory. And chosen properly, this order renders the result uniformly good to a desired precision, for all forces/end-to-end separations. Bouchiet al.’s numerical interpolation formula \[13,20\] is of this nature, being exact to leading order at small and large force, and uniformly good to 1% \[28\].

The improved force-extension formulas presented here remain valid when the WLC model is extended to describe a somewhat stretchable string as done in \[8\]. This because the extension consists in allowing \( L_0 \) to stretch in a simple manner depending on \( R \), while \( F(r) = F(R/L_0) \) is left unchanged.

It may be of interest to apply the approach used here to the WLC model extended with twist. This model is analyzed with strong-force perturbation theory in \[17,18,19\]. So the results obtained there might have their range of validity for a given precision extended down to lower force.

**Acknowledgments.** This work was prompted by work with the Optical Tweezer Group at the Niels Bohr Institute and by Workshop on Models of Biological Motion at Collegium Budapest, June 19–22, 2000. Thanks to T. Vicsek for the invitation, and to F. Jülicher, J. Prost, and M. D. Wang for discussions.

[1] Also known as the Kratky-Porod model.
[2] O. Kratky and G. Porod, Rec. Trav. Chim. **68**, 1106 (1949).
[3] M. Fixman and J. Kovac, J. Chem. Phys. **58**, 1564 (1973).
[4] J. Kovac and C. C. Crabb, Macromolecules **15**, 537 (1982).
[5] M. Doi and S. F. Edwards, *The Theory of Polymer Dynamics* (Clarendon Press, Oxford, 1986).
[6] C. Bustamante, J. F. Marko, E. D. Siggia, and S. Smith, Science **265**, 1599 (1994).
[7] J. F. Marko and E. D. Siggia, Macromolecules **28**, 8759 (1995).
[8] M. D. Wang, H. Yin, R. Landick, J. Gelies, and S. M. Block, Biophys. J. **72**, 1335 (1997).
[9] M. Rief, M. Gautel, F. Oesterhelt, J. M. Fernandez, H. E. Gaub, Science **276**, 1109 (1997).
[10] M. Rief, J. M. Fernandez, and H. E. Gaub, Phys. Rev. Lett. **81**, 4764 (1998).
[11] M. Rief, F. Oesterhelt, B. Heymann, and H. E. Gaub Science **275**, 1295 (1997).
[12] H. Li, M. Rief, F. Oesterhelt, and H. E. Gaub, Appl. Phys. A **68**, 407 (1999).
[13] C. Bouchiat, M. D. Wang, J.-F. Allemand, T. Strick, S. M. Block, and V. Croquette, Biophys. J. **76**, 409 (1999).
[14] J.-C. Meiners and S. R. Quake, Phys. Rev. Lett. **84**, 5014 (2000).
[15] C. G. Baumann, V. A. Bloomfield, S. B. Smith, C. Bustamante, M. D. Wang, and S. M. Block, Biophys. J. **78**, 1965 (2000).
[16] J. F. Marko and E. D. Siggia, Macromolecules **27**, 981 (1994); Errata: Macromolecules **29**, 4820 (1996).
[17] J. D. Moroz and P. Nelson, Proc. Natl. Acad. Sci. USA **94**, 14418 (1997).
[18] J. D. Moroz and P. Nelson, Macromolecules **31**, 6333 (1998).
[19] C. Bouchiat and M. Mezard, Phys. Rev. Lett. **80**, 1556 (1998).
[20] In \[13\] Eq. (11)], a numerical solution for the exact force-extension relationship in the limit \( L_0/L_0 \to 0 \) is approximated with

\[
\frac{L_0 F_{\text{numeric}}(r)}{k_B T} = \frac{1}{4(1-r)^2} - \frac{1}{4} + r + \sum_{n=2}^{7} a_n r^n,
\]

where \( a_2 = -0.5164228, a_3 = -2.737418, a_4 = 16.07497, a_5 = -38.87607, a_6 = 39.49944, a_7 = -14.17718 \). This re-

![FIG. 1. \( F_{\text{MS}}/F_{\text{exact}} \) (upper curve), \( F_{\text{MS}}/F_{\text{exact}} \) (middle curve), and \( F_{\text{MS}}/F_{\text{exact}} \) (bottom curve) plotted against \( r \). The maximum of \( F_{\text{MS}}/F_{\text{exact}} \) is 1.17, and occurs at \( r = 0.56 \). The maximum of \( F_{\text{MS}}/F_{\text{exact}} \) is 1.08, and occurs at \( r = 0.64 \). The ratios plotted here are identical to the inverse of the effective persistence length suggested in \[13\] Eq. (14)] for this kind of comparisons.
sult is accurate to 0.01% “over the useful extension range” [13], and renders obsolete an older, less precise, formula by Vologodskii [21] based on Monte Carlo simulation results, good to 5% for $0 < R/L_0 < 0.97$. The precision of Eq. (10) is not compromised by the fact that the finite part of $L_0F_{\text{numeric}}(r)/k_BT$, $-1/4 + r + \sum_{n=2}^{\infty} a_n r^n$, equals 0.0173192 for $r = 1$, hence differs from the exact result of 1/32 known from second order perturbation theory (see next-to-last section of present article), by almost a factor 2. The diverging part of $L_0F_{\text{numeric}}(r)/k_BT$, $1/(4(1-r)^2)$, diverges for $r \to 1$, so the relative error on $F_{\text{numeric}}$ actually vanishes in that limit. The precision of Eq. (10) is, however, compromised for $r \to 0$, where it gives $F_{\text{numeric}}(r)/k_BT = \frac{3}{4} r + \left(\frac{3}{4} - a_2\right) r^2 + O(r^3)$. The coefficient to $r^2$ is $\frac{3}{4} - a_2 = 0.23\ldots$ while it should vanish. This causes a 1% error near $r = 0.05$. So to achieve sufficient precision in Fig. 1 above, another numerical evaluation of $F_{\text{exact}}(r)$ was done.

[21] A. Vologodskii, Macromolecules 27, 5623 (1994).

We sketch what might be developed into a proof of analyticity of the free energy of the WLC: Instead of the free energy for fixed end-to-end separation $\vec{R}$, consider the free energy in the case where a constant force $\vec{F}$ pulls at one end of the string, with the other end attached to a fixed point. When the system has equilibrated in the heat bath, the string pulls back with an opposing force of the same size. This problem is, in the limit $L_0/L_p \to \infty$, equivalent to that of finding the ground state energy $E(\vec{F})$ of a quantum rotator with a vector product interaction with $F$. The end-to-end separation $\vec{R}$ as a function of force $\vec{F}$ is then found as $\vec{R} = -\partial E/\partial \vec{F}$. The eigenvalue equation determining $E(\vec{F})$ renders it rotationally invariant and analytical as a function of $\vec{F}$ at $F = 0$. Consequently, $E(\vec{F})$’s Legendre transform, $F(\vec{R})$, is an analytical function of $\vec{R}^2$, as claimed.

[23] H. Yamakawa, Pure Appl. Chem. 46, 135 (1976).

Actually, what Moroz and Nelson calculated perturbatively and give in [17,18] is $r$ as a series in $1/K$, where $K \equiv \sqrt{L_0F_{\text{exact}}/k_BT}$: $r = 1 - 1/(2K) - 1/(128K^3) + O(1/K^4)$. They did this for a version of the WLC model extended to describe twist, as well. Ignoring twist and inverting the series, one arrives at Eq. (7) above.

[25] H. Flyvbjerg, in preparation.

The formula, Eq. (10), is much more precise than 1% in the range where the authors actually used it!