Elasticity Theory of the B-DNA to S-DNA Transition

Amir Ahsan, Joseph Rudnick, and Robijn Bruinsma
Department of Physics, University of California at Los Angeles, Los Angeles, California 90024 USA

ABSTRACT We propose in this note a simple model—the two-state Worm Like Chain—to describe the elasticity of the recently discovered stress-induced transformation from B-DNA to S-DNA. The model reduces for low tractions to the well-known Worm Like chain theory, which is used to describe the elastic properties of B-DNA, while in the limit of high chain-bending moduli it reduces to the two-state Ising model proposed by Cluzel et al. for the B-S transition [Cluzel, P., A. Lebrun, C. Heller, R. Lavery, J-L. Viovy, D. Chatenay, and F. Caron. 1996. DNA: an extensible molecule. *Science*. 271:792–794]. Our model can be treated analytically to produce an explicit form of the force-extension relationship which agrees reasonably with the observations. We use the model to show that conformational fluctuations of the chain play a role also for the B to S transformation.

INTRODUCTION

Advances in the manipulation of individual macromolecules now allow measurement of the elastic properties of individual DNA molecules under external traction (Bustamante et al., 1994). It would appear, at first sight, as if these elastic properties could only be understood on the basis of detailed molecular models of DNA; models which should depend on the basepair sequence. Surprisingly, the elastic properties of the standard B form of DNA actually can be modeled very well by a simple one-parameter theory known as the *Worm Like Chain* (WLC), borrowed from studies of stiff polymers (Grosberg and Khoklov, 1994). This single parameter is the elastic bending modulus κ. Suppose we fix the end-to-end distance of a WLC of chain length L to have the value x. After allowing the chain to thermally equilibrate, we can measure the (thermally averaged) tension $T(x)$ required to maintain the end-to-end-distance at the fixed value x. The free energy $F_{\mathrm{el}}(x,L)$ of the chain is then related to the tension by $\partial F_{\mathrm{el}}(x,L)/\partial x = T(x)$. For a WLC it can be shown (Bustamante et al., 1994) that for L large compared to ξ:

$$T(x) \cong \frac{k_{\mathrm{B}}T}{\xi}\left[\frac{1}{4}\left(1-\frac{x}{L}\right)^{-2}-\frac{1}{4}+\frac{x}{L}\right] \tag{1}$$

with $\xi = \kappa/k_{\mathrm{B}}T$ the so-called "persistence length" (for the case of DNA, ξ is known to be ~50 nm under physiological conditions). The restoring force described by Eq. 1 is entropic in nature. Measured force-extension curves for B-DNA agree well with Eq. 1 at lower force levels (Bustamante et al., 1994). Note that for tensions small compared to $k_{\mathrm{B}}T/\xi$, $T(x) \cong 3k_{\mathrm{B}}Tx/2\xi L$ so the chain obeys Hooke's law for small x. If the tension is large enough for the chain to be fully stretched out, deviations between Eq. 1 and experimental values appear due to intrinsic, nonentropic stretching of the chain, but this can be included in the model (Odijk, 1995).

Recent studies (Cluzel et al., 1996; Smith et al., 1996) of the properties of DNA under large tractions reveal that a DNA molecule abruptly increases its length by a factor between 1.5 and 2 when the tension T exceeds a threshold in the range of 50–100 pN. Molecular modeling (Cluzel et al., 1996; Lebrun and Lavery, 1996) indicates that under such conditions, the standard B form of DNA transforms reversibly to new molecular architecture called "S-DNA." If the ends of the molecule are allowed to rotate freely under traction, then the structure of S-DNA is ladderlike, and can be considered as an unwound double helix. This unwinding leads to an elongation of S-DNA compared to B-DNA. It is speculated that S-DNA may be significant biologically, since it allows easier access to the basepairs for transcription purposes.

An interesting question is now whether a simple and general elastic model can be found for biopolymers like DNA, which are subject to tensions sufficient to induce an internal structural transition from a low tension state (which we will denote by "B") to a new elongated state (which we will denote by "S"), which under applied tension has a lower free energy. Because of the complex internal structure of biopolymers, stress-induced phase changes should in fact be a common feature for biopolymers under traction. Cluzel et al. (1996) proposed a *two-state model* (or Ising model) coupled to the external traction, which produced a good fit to their force-extension curves in the region of the B to S transformation. In this model, a section of the biopolymer is either in the B or in the S state. The B and S sections are separated by narrow borders ("junctions"), which are energetically unfavorable. The higher the junction energy, the more the B to S phase transformation becomes cooperative. It should be noted here that because of the one-dimensional nature of the chain, the B to S transition is not a true phase transition.

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Address reprint requests to Dr. Robijn Bruinsma, Dept. of Physics, University of California at Los Angeles, 405 Hilgard Ave., Los Angeles, CA 90024-1547. Tel.: 310-825-8539; Fax: 310-206-5668; E-mail:bruinsma@physics.ucla.edu.

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A defect of the pure two-state model is that it does not include the effects of chain flexibility and thus must fail in the regime of lower tensions where the WLC expression Eq. 1 should hold. In this paper we will compute analytically the force-extension curve of a WLC which allows for an internal B to S transformation of the two-state type, a model we can call the *two-state WLC*. The pure WLC and the pure Ising model are limiting cases of this two-state WLC and the new force extension relation reduces to Eq. 1 in the limiting case of small T. The aim of the model is, on the one hand, to provide a useful expression for fitting measured force-extension curves over an increased range of tensions and, on the other hand, to provide a tool to study the effect of thermal fluctuations of the shape of a chain on the B to S transition.

Stress-induced transformations of flexible chains under traction have actually been previously studied for two-state models in the context of the temperature-driven helix-coil transition of DNA [Vedenov et al. (1971)]. The physical difference between the temperature driven helix-coil transition and the tension driven B to S phase transition resides in the nature of the coupling between the internal structural degrees of freedom and the shape of the chain. For the helix-coil transition the coupling is only provided by the increased bending stiffness of double-stranded coiled DNA compared with uncoiled DNA. There thus exists only a *local* coupling between the internal order parameter and the shape of the chain. For the tension-driven B to S transformation, coupling is provided by the fact that the S state is elongated. The increase in length alters the conformational energy of the chain, but in a *global* way (Cluzel et al., 1996; Kubo, 1967). If the B and S states have different bending energies, then there of course also may be a local coupling as well, as discussed below.

To define the two-state model more precisely, divide the DNA chain into a sequence of short segments of length a_o such that every segment can be said to be either in the B or in the S state (the choice of a_o will be discussed below). The zero-tension free energy cost, ΔE, of transforming a B segment into an S segment will depend on the state of the neighboring two segments. If we denote the state of a segment by an arrow which is up ($\uparrow$) for B and down ($\downarrow$) for S, then there is an energy spectrum that takes on four different values: $\Delta E(\uparrow\uparrow)$, $\Delta E(\downarrow\downarrow)$, $\Delta E(\uparrow\downarrow)$, or $\Delta E(\downarrow\uparrow)$, depending on the state of the two neighbors. By symmetry, $\Delta E(\uparrow\downarrow) = \Delta E(\downarrow\uparrow)$. The simplest case corresponds to a symmetric spectrum around the middle level $\Delta E(\uparrow\downarrow) = \Delta E(\downarrow\uparrow)$. This spectrum can be parametrized by two quantities, H and J:

$$\Delta E(\uparrow\uparrow) = 2H + 4J \tag{2a}$$

$$\Delta E(\uparrow\downarrow) = \Delta E(\downarrow\uparrow) = 2H \tag{2b}$$

$$\Delta E(\downarrow\downarrow) = 2H - 4J \tag{2c}$$

The quantities H and J must be determined either by molecular modeling or, as done below, treated as fitting parameters to be determined by comparison with experiment. Physically, we can identify $2H$ as the (zero-tension) free-energy difference per segment between the B and S states. If we denote by ϵ the fractional elongation of the S state over the B state, then the critical tension T_c for B to S conversion is of order $H/(a_o\epsilon)$. The parameter J measures the correlation energy between adjacent segments. By analogy with the helix-coil transition, we will interpret $\sigma \equiv \exp(-4J/k_BT)$ as a measure of the cooperative nature of the transition. For $\sigma \ll 1$, the transition can be considered as highly cooperative (for the helix-coil transition $\sigma \approx 10^{-3} - 10^{-4}$). We will assume that the bending energies of S and B states are the same. Finally, the global coupling between internal structure and chain conformation is provided by the constraint:

$$L(\{S_i\}) = L_0\left(1 - \frac{\epsilon}{2N}\sum_{i=1}^{N}(S_i - 1)\right) \tag{3}$$

with L_0 the length of the chain in the B phase, $N \gg 1$ the number of segments, and $S_i = \pm 1$ a variable which is equal to one in the B state and minus one in the S state. The chain length L has thus become a statistical variable whose thermal average $\langle L\rangle$ must be determined, like any other thermodynamic variable, by taking a suitable derivative of the free energy.

By using this simple description of the tension-induced B-to-S conversion, it is possible to analytically obtain a new force-extension relationship. The required mathematical steps are given in the Appendix with the result:

$$\frac{x(t)}{L_0} = y(t)\left(1 + \frac{\epsilon}{2}\left(1 - \frac{e^{\beta J}\sinh\beta\tilde{H} + \tfrac{1}{2}e^{2\beta J}\sinh 2\beta\tilde{H}\left(e^{2\beta J}\cosh^2(\beta\tilde{H}) - 2\sinh(2\beta J)\right)^{-1/2}}{e^{\beta J}\cosh(\beta\tilde{H}) + \sqrt{e^{2\beta J}\cosh^2(\beta\tilde{H}) - 2\sinh(2\beta J)}}\right)\right) \tag{4}$$

with

$$y(t) = 1 - \frac{1}{[2 + \sqrt{4 - (\tfrac{4}{3}t - 1)^3}]^{1/3} + \dfrac{\tfrac{4}{3}t - 1}{[2 + \sqrt{4 - (\tfrac{4}{3}t - 1)^3}]^{1/3}}} \tag{5}$$

and with

$$\tilde{H}(T) = H + \frac{\epsilon a_0}{2\xi k_B T}\left(\frac{1}{4}\frac{1}{(1 - y(t))} - 4(1 + y(t)) + \tfrac{1}{2}y(t)^2 - ty(t)\right) \tag{6}$$

a renormalized H parameter. The tension is expressed in dimensionless units as $t = T\xi/k_BT$ and $\beta = 1/k_BT$.

To fit Eq. 4 to measured force-extension curves, we first must specify the proper segment length a_o. Molecular modeling of the S-B transition by Lebrun and Lavery (1996) suggests that an S-B domain wall is ~5 bp wide, indicating that a_o should not be much less than 5 bp (since shorter a_o values would produce segments that cannot be clearly assigned to the B or S state). Large values of a_o, on the other hand, lead to loss of internal structural degrees of freedom. We have performed fits for a_o equal to both 1 bp and to 10 bp. The quality of the two fits were comparable for the two cases. The fitted J value of the 10 bp case was considerably smaller than for the 1 bp case: increasing the segmental length indeed imposes local coherence and hence requires smaller values for J to fit to the data. The physical interpretation of the J parameter is thus somewhat ambiguous as it depends on the choice of a_o.

The fitted force-extension curve is shown in Fig. 1 *A*, together with data points of Cluzel et al. (1996) (for clarity, only a limited number of data points are shown). The best fit (*solid curve J, H*) was obtained for $J = 1.25\ k_BT$, $H = 1.64\ k_BT$ per basepair, and $\epsilon = 0.78$, using a standard value for ξ under physiological conditions (53.4 nm). The cooperativity parameter σ is of order 10^{-3}, which is comparable to the helix-coil transition. The agreement between theory and experiment is good except for relative extensions of ~1. These deviations are due to the internal stretch which, as noted earlier, is not included in the model. As shown in Fig. 1 *B*, for force levels <10 pN, our results are indistinguishable from the pure WLC (*dotted curve*). Thermal fluctuations of the two-state type thus have a negligible effect for low force levels. The flat section for relative extensions greater than one and force levels of ~70 pN indicates coexistence of large B and large S sections on the same chain. In this region B transforms rapidly to S with increasing tension. For very large tensions, the force-extension curve rises rapidly: the chain has (nearly) reached its maximum extension for the S form.

We now apply the model to examine the effect of thermal fluctuations of the chain shape on the B to S transformation, a question which would be difficult to address by detailed numerical modeling of short sections of DNA under traction. We will address this problem by recomputing the force extension curve for the same J and H values as found above fitting to the Cluzel et al. (1996) data, but now increasing the bending energy by a factor of 10. This leads, as expected, to large changes in the force extension curve for forces <10 pN (*dashed curve J, H* in Fig. 1 *B*) since we are there in pure WLC regime where $T(x)$ is inversely proportional to the bending energy (see Eq. 1). It would seem natural to assume that at the higher force levels of the B-S transition, where the chain is stretched out, bending fluctuations are quite irrelevant. However, *noticeable changes are present as well at higher force levels* (Fig. 1 *A*): the whole force extension curve appears to be shifted somewhat to the right for the stiffer chain. The physical reason for this shift can be traced to the fact that the increase in stiffness suppresses thermal fluctuations in the shape of the chain. This reduction increases the effective length of the chain, which increases the effective maximum extensions of both the B and S states by a certain amount. Note that in the coexistence regime, chain flexibility has no effect.

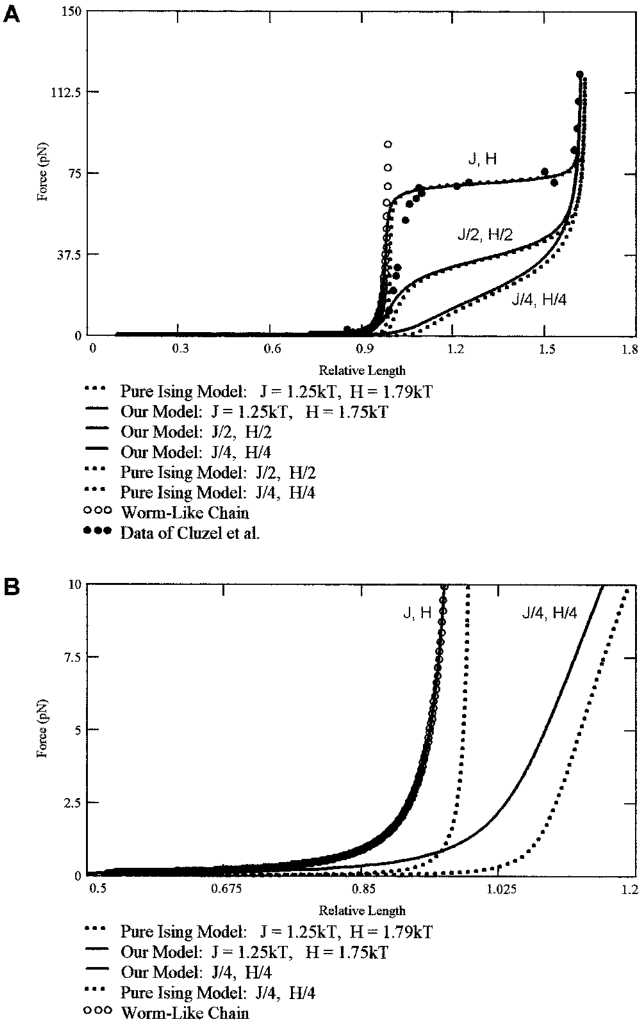

FIGURE 1(*A*) Comparison between the measured force-extension curve of the B to S transition of DNA by Cluzel et al. (1996) (*solid circles*), and the force-extension curve of Eqs. 4–6. For clarity, only a limited number of data points are shown. Solid curve (*J*, *H*) represents our best fit. We used the fitting parameters $J = 1.25\ k_BT$, $H = 1.64\ k_BT$ per basepair, $\epsilon = 0.78$, and $\xi = 53.4$ nm. The segmental length was 1 bp. Dashed curve (*J, H*): chain stiffness increased by a factor of 10 (i.e., $\xi = 534$ nm). Solid and dashed curves (*J*/2, *H*/2) and (*J*/4, *H*/4) have *J* and *H* reduced by a factor of, respectively, two and four. The dashed curve has again a 10-fold increased stiffness. The dotted curve represents the pure WLC (see Eq. 1). (*B*) Expanded version of (*A*) for low force levels. The pair of curves (*J*/2, *H*/2) is not shown for clarity.

The effect of chain flexibility on the B to S transition is further enhanced if the J and H parameters are reduced below the fitted values. In Fig. 1 *A* we show the force extension curves for the parameter values (*J*/2, *H*/2) and for (*J*/4, *H*/4), both for the original and for the enhanced chain stiffness (*solid*, respectively *dashed curves*). The deviations are increasingly serious and now also affect the coexistence regime. Note that in all cases increased stiffness produces larger extension for the same force level, as is intuitively reasonable. Fluctuations in the chain conformation are thus important not only in the regime of low force levels but also at higher force levels, indicating that models including both the internal degrees of freedom and the geometrical shape (such as curvature) are required to fit the full force extension measurements.

It is important to note, however, that the fact that even though the computed force extension curves agree reasonably with the measurements, away from relative extensions of order one, this does not constitute a proof of the validity of the two-state WLC model. The two-state WLC model incorporates a number of simplifying assumptions: 1) a symmetric spectrum for the transformation energy, 2) neglect of next-nearest-neighbor segmental correlation, 3) equal bending energies of S and B states, 4) neglect of heterogeneity of the chain (e.g., due to the basepair sequence of DNA), and 5) no "nicks" or other defects that could produce detachment of the two strands or trigger local "melting" of the DNA. To improve the fit for relative extensions of order one, it also would be necessary to include the intrinsic elasticity of the chain (Odijk, 1995). It can be shown that local coupling between the order parameter and the bending stiffness essentially can be absorbed into a simple redefinition of the *J* parameter, but the other assumptions require experimental testing or numerical modeling. A useful test would be to remeasure the force-extension curves at lower salt concentrations. This could reduce the *J* and *H* values (because of the extra electrostatic repulsion between the strands). Deviations from the pure two-state model should be more serious in this regime according to Fig. 1 *A*. Finally, Smith et al. (1996) report significant hysteresis in their study of the B to S transition. The kinetics of our two-state WLC is not expected to show significant hysteresis, so if the hysteresis is intrinsic (and not due to nicking of the DNA chains or adsorption of small molecules on highly stretched DNA) then this would constitute a serious problem for the applicability of the model.

In summary, we can compute the force extension curves analytically for a two-state WLC model that produces force-extension curves appearing to be in reasonable agreement with measured data on DNA force-extension curves. Chain flexibility affects the force extension curve also at higher force levels in the regime of the B-S transition. It is hoped that the model will be useful as well for the analysis of force-extension measurements on other linear macromolecules whose internal structure allows a "flip" between a B and an S state with different elongation.

APPENDIX

The model described in the text for the internal structure of the chain is mathematically identical to the one-dimensional Ising model [for a discussion of global coupling for a two-state model of an *inflexible* chain with $J = 0$ see Kubo (1967)]. To see this, we introduce the segmental variable S_i, with $i = 1, 2, \ldots, N$. For a B segment, $S_i = 1$, while for an S segment, $S_i = -1$. The subscript i runs over the *N* segments of the chain. In terms of these variables, the internal energy of the chain H_{int} takes on the following form:

$$H_{int} = -J \sum_{i=1}^{N} S_i S_{i+1} - H \sum_{i=1}^{N} S_i \tag{A1}$$

It is easy to check that if one assumes that the internal energy of the chain is given by Eq. A1, then the rules specified in Eq. 2 of the text for the transformation energy indeed hold.

We must add to H_{int} the elastic bending energy H_{el} of a WLC. By assumption, both B and S segments have the same bending energy κ, so we will adopt the usual expression for H_{el} for a WLC of length *L*:

$$H_{el} = \frac{1}{2} \kappa \int_0^L ds \left(\frac{1}{R(s)} \right)^2 \tag{A2}$$

Here, $R(s)$ is the curvature radius of the chain at a position *s* along the chain. The connection between the internal structure and the bending energy is provided by the dependence of the chain length *L* on the structural variable S_i:

$$L = L_0 \left(1 - \frac{\epsilon}{2N} \sum_{i=1}^{N} (S_i - 1) \right) \tag{A3}$$

with L_0 the chain length if DNA is completely in the B state and $L_0(1 + \epsilon)$ the chain length if it is in the S state.

The partition function *Z* is the configurational average of the Boltzmann factor over all internal configurations $\{S_i\}$ and over all geometrical configurations $\vec{r}$ of the chain. Performing the second average first, we define

$$F_{el}(L, x) = -\beta^{-1} \ln \left(\int D[\vec{r}(s)] e^{-\beta H_{el}} \right) \tag{A4}$$

with *x* the end-to-end distance, which is held fixed when computing the average and with $\beta = 1/k_B T$ (to avoid confusion between tension and temperature, we will below reserve "T" for tension). Note that F_{el} still depends on the particular configuration $\{S_i\}$ through *L*. This is just the elastic free energy of an ordinary WLC. From general considerations, we know that this free energy has the form:

$$F_{el}(x, L) = Lf(x/L) \tag{A5}$$

The function $f(y)$ is determined from the condition of mechanical equilibrium. Let $T(x)$ be the tension required to keep *x* fixed. Then, $\partial F_{el}(x, L)/\partial x = T(x)$ so

$$f'(x/L) = T(x) \tag{A6}$$

This must agree with Eq. 1 in the text so:

$$f'(y) = \frac{\beta^{-1}}{\xi} \left[\frac{1}{4}(1 - y)^{-2} - \frac{1}{4} + y \right] \tag{A7}$$

from which we can find $f(y)$ (up to a constant independent of *y*).

It is now convenient to switch from a "fixed *x*" to a "fixed T" thermodynamic ensemble. It follows from Eq. A6 that the ratio $y(t) = x/L$ is just a function of $t = \beta T \xi$, and *independent of the internal configuration*. The appropriate variational energy for fixed T is H_{WLC} with

$$H_{WLC} = Lf(x/L) - Tx \tag{A8}$$

It follows from Eqs. A6 and A8 that H_{WLC} is proportional to *L*: $H_{WLC} = Lg(T)$ with

$$g(T) = f(f'^{-1}(T)) - Tf'^{-1}(T) \tag{A9}$$

Note that the unknown constant in $f(y)$ contributes a T-independent constant to $g(T)$

We now perform the remaining configurational sum over the internal states over the effective internal energy $H_{\mathrm{eff}} = H_{\mathrm{int}} + H_{\mathrm{WLC}}$ at fixed external tension:

$$H_{\mathrm{eff}} = -J\sum_{i=1}^{N} S_i S_{i+1} - \tilde{H}(T)\sum_{i=1}^{N} S_i + L_0(1+\epsilon/2)g(T) \qquad \text{(A10)}$$

with

$$\tilde{H}(T) = H + \frac{\epsilon a_0}{2} g(T) \qquad \text{(A11)}$$

The total free energy F in the fixed T ensemble is found by performing the configurational sum over the internal states:

$$F = -\beta^{-1}\ln\left(\sum_{\{S_i\}} e^{-\beta H_{\mathrm{eff}}}\right) \qquad \text{(A12)}$$

This is just the free energy of the one-dimensional Ising model with a "magnetic field" $\tilde{H}(T)$ applied to the Ising variables S_i. The expression for the Ising free energy is well known (Kubo, 1967):

$$F = L_0(1+\epsilon/2)g(T) - \beta^{-1}N\ln Z \qquad \text{(A13)}$$

with

$$Z(J,\tilde{H}) = e^{\beta J}\cosh(\beta\tilde{H}) + \sqrt{e^{2\beta J}\cosh^2(\beta\tilde{H}) - 2\sinh(2\beta J)} \qquad \text{(A14)}$$

The new force-extension relation follows from the condition of mechanical equilibrium in the fixed T ensemble:

$$x = -\left.\frac{\partial F}{\partial T}\right|_{\beta} \qquad \text{(A15)}$$

with x still the end-to-end length. Using Eqs. A11–A15, together with the fact that $g'(\mathrm{T}) = -f'^{-1}(\mathrm{T})$ (see Eq. A9), we find that:

$$\frac{x}{L_0} = f'^{-1}(T)\left(1 + \frac{\epsilon}{2}(1 - \langle S\rangle)\right) \qquad \text{(A16)}$$

Here,

$$\langle S\rangle = \frac{1}{N}\left.\frac{\partial F}{\partial \tilde{H}}\right|_{\beta} \qquad \text{(A17)}$$

is the expectation value of the state variable S_i (which thus varies between 1 and -1). Eq. A16 has a simple interpretation. We can write it as:

$$f'\left(\frac{x}{\langle L\rangle}\right) = T \qquad \text{(A18)}$$

with

$$\langle L\rangle = L_0\left(1 + \frac{\epsilon}{2}(1 - \langle S\rangle)\right) \qquad \text{(A19)}$$

the thermodynamic expectation value for the chain length. We have, in Eq. A18, recovered the WLC force-extension relation (see Eq. 1), provided we replace the chain length by $\langle L\rangle$.

To obtain an explicit form for the force-extension relation Eq. A16, we first specify $\langle S\rangle$:

$$\langle S\rangle = \frac{e^{\beta J}\sinh\beta\tilde{H} + \tfrac{1}{2}e^{2\beta J}\sinh 2\beta\tilde{H}\left(e^{2\beta J}\cosh^2(\beta\tilde{H}) - 2\sinh(2\beta J)\right)^{-1/2}}{Z(J,\tilde{H})} \qquad \text{(A20)}$$

To determine $\tilde{H}(T) = H + \epsilon a_0/2g(T)$ in Eq. A20, we also must specify $g(\mathrm{T})$. Using Eqs. A6 and A9, it follows that

$$g(T) = f(y(t)) - Ty(t) \qquad \text{(A21)}$$

The function $f(y)$ follows from a straightforward integral of Eq. A7:

$$f(y) = \frac{\beta^{-1}}{\xi}\left(\frac{1}{4}\frac{1}{(1-y)} - \frac{1}{4}(1+y) + \frac{1}{2}y^2 - ty\right) \qquad \text{(A22)}$$

The additive constant in $f(y)$ can be absorbed in a redefinition of the fitting parameter H. We have required in Eq. A22 that $f(0) = 0$. Our result for $g(\mathrm{T})$ is now:

$$g(T) = \frac{\beta^{-1}}{\xi}\left(\frac{1}{4}\frac{1}{(1-y(t))} - 4(1+y(t)) + \frac{1}{2}y(t)^2 - ty(t)\right) \qquad \text{(A23)}$$

which depends on tension through the dimensionless parameter $t = T\xi/k_BT$. To find $y(t)$, first invert Eq. A7 in the form:

$$t = \left[\frac{1}{4}(1-y)^{-2} - \frac{1}{4} + y\right] \qquad \text{(A24)}$$

which yields:

$$y(t) = 1 - \cfrac{1}{\left[2 + \sqrt{4 - (\tfrac{4}{3}t - 1)^3}\right]^{1/3} + \cfrac{(\tfrac{4}{3})t - 1}{\left[2 + \sqrt{4 - (\tfrac{4}{3}t - 1)^3}\right]^{1/3}}} \qquad \text{(A25)}$$

For practical purposes, the dimensionless parameter t is normally large compared to one (for the B-S transition, it is ~800). For $t >$ ~0.4, a good approximation for $y(t)$ is

$$y(t) \cong 1 - \frac{1}{2\sqrt{t}} \qquad \text{(A26)}$$

With $y(t)$ in hand, $g(\mathrm{T})$ follows from Eq. A23, while the "order-parameter" $\langle S\rangle$ now follows from Eqs. A14 and A20. The force-extension relation in the form

$$\frac{x}{L_0} = y(t)\left(1 + \frac{\epsilon}{2}(1 - \langle S\rangle)\right) \qquad \text{(A27)}$$

then gives Eqs. 4–6 of the text.

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