Force-Induced Melting and Thermal Melting of a Double-Stranded Biopolymer

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(July 3, 2000)

As a prototype of systems bearing a localization-delocalization transition, the strand-separation (melting) process in a double-stranded biopolymer is studied by a mapping to a quantum-mechanical problem with short-ranged potentials. Both the bounded and the extensive eigenmodes of the corresponding Schrödinger equation are considered and exact expressions for the configurational partition function and free energy are obtained. The force-induced melting is a first order phase transition process, while the thermal melting is found to be second order. Some scaling exponents governing thermal melting are given.

PACS: 87.15.By, 87.10.+e, 64.60.Cn, 05.70.Jk

DNA melting, the strand-separation of a DNA double-helix, is an issue with both practical biological significance (because it is closely related to DNA replication and gene transcription) and pure academic interest. The first realistic model of DNA melting was proposed by de Gennes in 1969 \[1\] and reintroduced by Peyrard and Bishop twenty years later \[2\]. The essential advance of the de Gennes-Peyrard-Bishop approach, distinguishing it from earlier efforts based on Ising-like models \[3\], is the de Gennes-Peyrard-Bishop approach, distinguishing between the two complementary strands have been explicitly incorporated. The DNA molecule is considered as consisting of two flexible Gaussian chains with short-ranged on-site interactions between them; its statistical property can be studied by a mapping to a weakly-bounded quantum mechanical problem \[4\]. The corresponding Schrödinger equation has a finite number of bounded eigenstates and a continuous series of extensive ones, representing respectively localized and delocalized eigenmodes of structural fluctuations. In fact, it has been well recognized that problems such DNA melting, flux line depinning in superconducting shells \[5\], adsorption of polymeric materials onto a surface \[6\], and some wetting phenomena \[7\], are all governed by the competition between enthalpy-favoring localized states and entropy-favoring delocalized ones.

We study the melting of a double-stranded biopolymer as a prototype of such many phenomena. Earlier studies have focused mainly on thermal melting \[8\]–\[10\], here both the thermal and the force-induced melting processes are discussed; and different some previous efforts \[8\]–\[10\] which considered only the localized ground-state, we explicitly incorporate all the bounded and delocalized eigenmodes of fluctuations (we are grateful to Prof. D. R. Nelson for informing us that in \[3\] a similar treatment has been performed in studying vortex pinning). This makes it possible for us to obtain exact expressions for the partition function and free energy of the system. We rigorously show that the stretch-induced melting is a first order structural phase transition while that induced by heating is of second order. The phase diagram for the double-stranded polymer is exactly obtained, and some scaling laws governing thermal melting are given. The effects of sequence heterogeneity and base-pair stacking are also briefly discussed.

The model double-stranded biopolymer is formed by two Gaussian chains. Each strand contains \(N + 1\) beads, with a harmonic attraction between any two consecutive ones; and between each pair of beads of the two strands with the same index there is a short-ranged interaction potential \(V\). The model energy is

\[
\mathcal{H} = \sum_{n=1}^{N} \left[ k \left( \mathbf{r}_{n}^{(1)} - \mathbf{r}_{n}^{(2)} \right)^{2} + \sum_{n=0}^{N} V \left( \mathbf{r}_{n}^{(1)} - \mathbf{r}_{n}^{(2)} \right) \right] = \sum_{n=1}^{N} \left[ k \left( \mathbf{r}_{n}^{(1)} - \mathbf{r}_{n-1}^{(2)} \right)^{2} + \frac{k}{4} \left( \mathbf{r}_{n}^{(1)} - \mathbf{r}_{n-1}^{(2)} \right)^{2} \right] + \sum_{n=0}^{N} V \left( \mathbf{r}_{n} \right). \tag{1} \]

Here, \(\mathbf{r}_{n}^{(i)}\) denotes the position vector of the \(n\)th bead in the \(i\)th strand; and \(\mathbf{r}_{n} = \mathbf{r}_{n}^{(1)} - \mathbf{r}_{n}^{(2)}\) and \(\mathbf{R}_{n} = \left( \mathbf{r}_{n}^{(1)} + \mathbf{r}_{n}^{(2)} \right)/2\) are, respectively, the distance between a pair of beads of the two strands and the center-of-mass position of these two beads. For computational simplicity, in the following we discuss only the one-dimensional case of model Eq. \(\text{(1)}\). The principal conclusions of this work is independent of dimensionality as well as the particular forms for the short-ranged potential \(V\), since the underlying physics, the competition between enthalpy in the localized states and entropy in the extended states, is reserved. We first discuss the situation of symmetric potentials and assume the short-ranged attraction to be \(\delta\)-form, \(V(r) = -\delta \delta(r)\). At index \(n = 0\) the two strands intersect each other, i.e., \(\mathbf{R}_{0} = \mathbf{r}_{0} = 0\). The statistical weight for the center-of-mass position at the other end to be equal to \(R\) is easily known: \(Z_{R}(R, N) = (\beta k/kN)^{1/2} \exp(-\beta k R^{2}/N)\), where \(\beta = 1/k_{B}T\) with \(T\) being the temperature.

The statistical weight \(Z_{r}(r, N)\) for the relative distance \(r\) between the two strands at index \(N\) is governed by the Schrödinger equation \(\text{(1)}\).

\[\text{arXiv:cond-mat/0007015v2} \quad \text{[cond-mat.soft]} \quad 9 \text{ Aug 2000.} \]
\[
\frac{\partial Z_r(r, N)}{\partial N} = \left[ \frac{2\beta^2}{\beta \kappa \beta^2} - \beta V(r) \right] Z_r(r, N),
\]
with the initial condition \( Z_r(r, 0) = \delta(r) \). Equation (3) corresponds to a weakly-bounded statistical system with only a finite number of localized eigenstates (in the case of \( \delta \)-form attraction used here, this number is unity); the ground eigenfunction of Eq. (2) is \( \phi_0(r) \propto \exp(-\eta |r|/2) \), where \( \eta = \kappa \gamma \beta^2 \). The statistical weight \( Z_r(r, N) \) is expressed as
\[
Z_r(r, N) = \exp(N \eta^2 / 4 \kappa \beta) \phi_b(0) \phi_b(0) + \int d\lambda \exp[-N \epsilon(\lambda)] \phi(\lambda, r) \phi^*(\lambda, 0),
\]
where \( \epsilon(\lambda) \) and \( \phi(\lambda, r) \) are the eigenvalue and the eigenfunction of the extensive eigenstate of Eq. (2) with wave number \( \lambda \). For the force-fixed ensemble with an external stretching \( f \) acting on the \( N \)th bead of the first strand, the partition function is \( \Xi(f, N) = \int dR_N \int d\lambda f \exp(\beta f R_N + (1/2)\beta f R_N^2) Z_R(R_N, N) Z_r(r_N, N) \). Since the first term of \( Z_r(r, N) \) is proportional to \( \exp(-\eta |r|/2) \), it seems that when \( f \geq \eta / \beta \) this integral will turn to be divergent. Earlier studies \([1, 2]\) considered only the ground eigenstate and therefore took such a divergence as signifying the occurrence of force-induced melting process. Actually, however, there is no divergence problem. After taking into account of the second term in Eq. (3), this term is canceled out by a term resulted from the integral. The correct form of the statistical weight is
\[
\Xi(f, N) = \exp(N \beta f^2 / 4 \kappa \beta) \left[ \left( \frac{\eta}{\eta - \beta f} + A_0 \right) \exp\left( \frac{N \eta^2}{4 \kappa \beta} \right) + \frac{\beta f}{\beta f - \eta} \exp\left( \frac{N \beta^2 f^2}{4 \kappa \beta} \right) \right],
\]
where \( A_0 = (2/\sqrt{\pi}) \int_0^\infty dt \exp(-t^2) \int_{\beta f / \eta}^\infty dy \exp[-(y^2 - \beta^2 f^2 y^2 / \eta^2)] \) is a small quantity. Equation (4) shows that in the thermodynamic limit, the free energy linear density is \( g(f) = \lim_{N \to \infty} -k_B T \Xi(f, N)/N = -\kappa \gamma \beta^2 f^3 / 4 - f^2 / 4 \kappa \) for \( f \leq f_c \) and \( -f^2 / 4k \) for \( f > f_c \), with \( f_c = \kappa \gamma \beta \). Therefore a first order phase transition occurs at the threshold force \( f_c \). The inter-beads distance for the first strand is \( f / 2k \) for \( f < f_c \) and \( f / k \) for \( f > f_c \) and a discontinuity appears at \( f_c \). Similarly, the average distance between the end beads of the two strands is approximately zero for \( f < f_c \) and proportional to \( N \) for \( f > f_c \) (\( r_N = N f / k \), see Fig. 1). At \( f_c \), \( r_N = 3/\eta + N \eta / 2k \beta \).

The extension-fixed ensemble may be more directly related with actual experiments [4, 7]: it is much easier for one to fix the total extension of the first strand than to fix the external force. The statistical weight for the end-to-end distance of the first strand to be fixed at \( \sigma N \) is equal to \( \int dR \int d\sigma (r N - R - r/2) Z_R(R, N) Z_r(r, N) \). \( \sigma \) is the inter-beads distance of the first strand. Based on Eq. (4), we find the free energy density to be \( \tilde{g}(\sigma) = \kappa \sigma^2 / N \kappa \beta^2 \) for \( \sigma < \sigma_c \), \( \tilde{g}(\sigma) = \eta \sigma^2 / 2 \kappa \beta - \eta^2 / 2 \kappa \beta \) for \( \sigma_c \leq \sigma \leq 2 \sigma_c \), and \( \tilde{g}(\sigma) = \kappa \sigma^2 / 2 \) for \( \sigma > 2 \sigma_c \), with \( \sigma_c = \eta / \beta \). The free energy function is hence a piecewise smooth function. Correspondingly, the average force is \( \bar{f}(\sigma) = 2 \kappa \sigma \) for \( \sigma < \sigma_c \), \( \bar{f}(\sigma) = \kappa \beta \sigma \) for \( \sigma_c \leq \sigma \leq 2 \sigma_c \), and \( \bar{f}(\sigma) = \kappa \beta \sigma \) for \( \sigma > 2 \sigma_c \) (see Fig. 1). The occurrence of a force platform may be striking [4, 7]. It indicates that as the inter-beads distance in the first strand reaches \( \sigma_c \), melting of the double-stranded polymer originates from the end point (index \( N \)) and progresses along the chain until the whole polymer becomes separated. Stretch-induced melting can be termed as directional melting [4, 7]. The phase diagram of this system is shown in Fig. 1, it includes a double-stranded native region, a single-stranded denatured region, and a coexisting region. This transition is caused by enthalpy-entropy competition, different from that discussed in Ref. [19], which is caused by the appearance of two minima in the ground-state eigenfunction.

The above model with symmetric potential does not exhibit thermal melting behavior. In the following we improve our model by changing the attractive potential in Eq. (4) into the following asymmetric form \( V(x) = \infty \) for \( x \leq 0 \) and \( V(x) = -\gamma \delta(x - a) \) for \( x > 0 \), where \( a \) is a characteristic distance. For such an asymmetric system, when the temperature becomes high enough, the localized eigenstate disappears. Hence it might be possible to qualitatively describe the thermal melting of double-stranded biopolymers.

We focus on how the distance between the two strands changes with external stretching or temperature. It is convenient for us to assume that \( r_0 = a \). For this revised model system, we find that the statistical weight for the relative distance is
In the above expression, \( \tau = \alpha k \gamma \beta^2 \) and \( \zeta \) is the largest solution of \( \zeta = 1 - \exp(-\zeta \tau) \). This equation has a nonzero solution only when \( \tau > \tau_c = 1 \). When \( \tau \leq \tau_c \) the solution is \( \zeta = 0 \). Since \( \tau \) decreases as temperature increases, the polymer’s structure might undergo a transition at temperature \( T = T_m = \sqrt{\gamma \alpha / k_B} \).

When an external force is acting on the first strand, the total partition function is \( \Xi(f, N) = \exp(N \beta^2 f^2 / 4k\beta) \int_0^\infty d\lambda \exp(\beta f r / 2) Z(r, N) \). This integral is always convergent for any value of \( f \), although the first term of Eq. (6) scales as \( \exp(-\zeta \tau r / 2a) \). The integrand in the second term of Eq. (6) has two poles at \( \lambda = \pm \zeta \tau r / 2a \), hence it will generate a term which precisely cancels out the first term in this equation. To obtain the analytical expression for the partition function \( \Xi(f, N) \) is nevertheless a demanding task. We evaluate alternatively its Laplace transform:

\[
\mathcal{L}[\Xi(f, N)](s) = \int_0^\infty dN \exp(-sN)\Xi(f, N) = 8 \sqrt{s(\kappa^3 a^3 \beta^3 a^2 \exp(\beta f a / 2) - \exp(-\sqrt{sk} \beta a)] / [4sk^2 F^2[2\sqrt{k} \beta a - \tau (1 - \exp(-2\sqrt{k} \beta a))}] .
\]

The largest solution of the equation \( 1 / \mathcal{L}[\Xi(f, N)](s) = 0 \) corresponds to the linear free energy density of the polymer system. When the temperature is less than \( T_m \), the free energy density \( g(f) = -2(\zeta \gamma r^2 / 4\kappa^2 \beta^3 a^2 - f^2 / 2\kappa) \) for \( f < f_c \), and \( g(f) = -(f^2 / 2\kappa) \) for \( f > f_c \), where \( f_c = (\zeta / \alpha) \beta \). Thus, the external force will induce a first order phase transition at the threshold force \( f_c \), which decreases as the temperature increases (see Fig. 2). This is similar with what we have attained with the earlier model. At \( T = T_m \), the threshold force decreases to zero. The statistical behavior of the extension-fixed ensemble is also similar with that of the earlier model and the phase diagram is shown in Fig. 2.

When there is no external force, the free energy density is \( g = -2(\zeta \gamma r^2 / 4\kappa^2 \beta^3 a^2 \) for \( T < T_m \) and zero for \( T > T_m \). At \( T_m \), the free energy and its first order derivative with temperature is continuous but the second order derivative is not, indicating that the thermal melting at \( T_m \) is a second order continuous phase transition, with a discontinuity in the specific heat. The order parameter for the thermal melting can chose to be the probability \( P_{loc}(n) \) for the distance of a pair of beads (with index \( n \)) of the double-stranded polymer to be less than the characteristic length \( a \). For the thermal melting process, we can predict based on Eq. (8) that, as the melting temperature \( T_m \) is approached from below, \( P_{loc} \sim (T_m - T)^\beta \), with the critical exponent \( \beta = 1 \). It is also easy to obtain that as the temperature approaches \( T_m \), the correlation “length” in \( P_{loc}(n) \) between different indices \( n \) and \( n' \) scales as \( (T_m - T)^{-\eta} \), with the critical exponent \( \eta = 2 \). At \( T_m \), \( \langle P_{loc}(n)P_{loc}(n') \rangle_c \sim (n - n')^{-1+\eta} \), but the critical exponent \( \eta \) is difficult to be obtained by the present asymmetric model. Nevertheless, we notice that the phase diagram for the symmetric (Fig. 1) and the asymmetric model (Fig. 2) is identical albeit that the symmetric model has \( T_m = \infty \). Therefore, it should be possible for us to obtain a good estimation of \( \eta \) based on the symmetric model by artificially assuming \( \gamma = 0 \) \( (T_m - T)/T_m \) for \( T < T_m \) and \( \gamma = 0 \) otherwise. This treatment reduces the melting temperature from infinity to \( T_m \). For this system we know from Eq. (1) that \( \eta = 1/2 \), and we think it should be the same for the asymmetric model.

Can the present approach be extended to consider the possible random variations in the on-site potential \( V(r) \) (this is caused by the sequence heterogeneity in the case of DNA) \( ? \) This is certainly a challenging problem and beyond the scope of this paper. But we think that inclusion of such an effect will not alter the qualitative behavior of the phase diagram, since in the renormalization sense, near the transition point the details of the interactions will be smoothed out \( \cite{21} \).

It is of interest to ask whether the inclusion of base-stacking effect (by making the parameter \( \kappa \) in Eq. (1) position dependent as done in Ref. \( \cite{8} \)) will change the thermal melting from second order to first order. It seems still be an issue of debate. An recent work done by Peyrard and coworkers \( \cite{21} \) answered it confirmatively, while the numerical work of Cule and Hwa \( \cite{10} \) suggested that the transition behavior is still of second order. We noticed that in Ref. \( \cite{21} \), a force field is first included and at the final stage a limiting procedure is performed to make the field equal to zero. Our present work demonstrates that the property of the double-stranded system depends considerably on the external field, therefore it might be helpful for one to carefully evaluate whether the above mentioned limiting procedure in Ref. \( \cite{21} \) causes a significant effect.

The author benefits from discussions with Xin Zhou and Yong Zhou. He is grateful to Z.-C. Ou-Yang for encouragement and to W.-M. Zheng for bringing Ref. \( \cite{19} \) to his attention.
FIG. 1. Phase diagram for a double-stranded biopolymer with a symmetric potential. The broken line shows a force-extension curve at temperature $T_0$. The phase-coexistence region collapses to a point only when $T \to \infty$, indicating there is no thermal melting. (Inset) The relation between the average distance of the ends of the two strands and the force at temperature $T_0$. We set $\kappa = k_BT_0/b^2$ and $\gamma = k_BT_0 d_0$.

FIG. 2. Phase diagram for a double-stranded biopolymer with a asymmetric potential. This system shows second order thermal melting behavior at $T_m = \sqrt{\kappa \gamma a}/k_B$. Inset shows how the threshold force $f_c$ for melting changes with temperature $T$. 

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