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We develop a simple model to study the effects of the applied force on the melting of a double stranded DNA (dsDNA). Using this model, we could study the stretching, unzipping, rupture and slippagelike transition in a dsDNA. We show that in absence of an applied force, the melting temperature and the melting profile of dsDNA strongly depend on the constrained imposed on the ends of dsDNA. The nature of the phase boundary of the force-temperature diagram, which separates the zipped and the open state for the shearinglike transition is remarkably different than the DNA unzipping. © *2010 American Institute of Physics*. [doi:10.1063/1.3427587]

I. INTRODUCTION

Properties related to structure, functions, stability, etc. of the biomolecule are the results of inter- and intramolecular forces present in the system.[1,2] So far, our understanding of these forces was possible through the indirect physical and thermodynamical measurements such as crystallography, light scattering, and nuclear magnetic resonance spectroscopy, etc.[3] For the direct measurement of these forces, it is essential that the state of the system be monitored while an independent force is applied.[4–7] In recent years, single molecule force spectroscopy (SMFS) techniques such as optical tweezers, magnetic tweezers, atomic force microscope (AFM), etc. have measured these forces directly and many important information about the biomolecules have been inferred.[8–11] Now it has also been realized that the measurement of these forces not only depend on the molecular interactions present in the system but also on the loading rate, direction of the applied force,[6,12–14] etc. Moreover, these experiments also provide a platform, where various theoretical models and their predictions can be verified.[15–18]

In this context, considerable efforts have been made to study the separation of a double stranded DNA (dsDNA) into two single stranded DNA (ssDNA). Understanding the mechanism involved in separation of dsDNA may shed light on the processes such as transcription and replication of DNA.[1] At equilibrium, DNA will be separated when the free energy of the separated ssDNA is lower than that of the dsDNA.[19] In most of the biochemical studies related to DNA separation, the strands separate upon increasing the temperature (T) of the sample until the DNA melts (DNA melting or thermal denaturation). However, *in vivo*, DNA separation is not thermally driven, rather mediated by enzymes and other proteins.[1,20] Mechanical separation of dsDNA using SMFS techniques (DNA unzipping) at temperatures where dsDNAs are stable, have recently been performed. The force (f) required to break a base pair is about 15 pN.[20,21] A large number of theoretical and numerical efforts[15–18] have been made to gain further insight into the mechanism of DNA opening. One of the major result from these studies was the prediction of reentrance in the low temperature region.[17,18,22,23]

Experimental studies conducted by Smith *et al.*[4] and Cluzel *et al.*[5] have revealed unusual elastic properties of DNA. It was found that dsDNA is a semiflexible macromolecule, while ssDNA behaves like a flexible polymer chain. Due to intrastrand electrostatic repulsions, the chain is stiff over short length scales (the persistence length). In the low force regime (<10 pN), the elasticity of dsDNA is entropy dominated. At small forces (10–60 pN), dsDNA obeys Hooke's law and the WLC model can describe the experimentally observed force extension curves. In the high force regime (65 pN) it was found that the dsDNA molecule can be overstretched about 1.7 times the B-form contour length.[5] An explanation of this regime is attributed to the short range nature of base pair stacking interactions. At high forces, the stacking potential cannot stabilize the B-form configuration of dsDNA and the state is termed as S-form. This transition

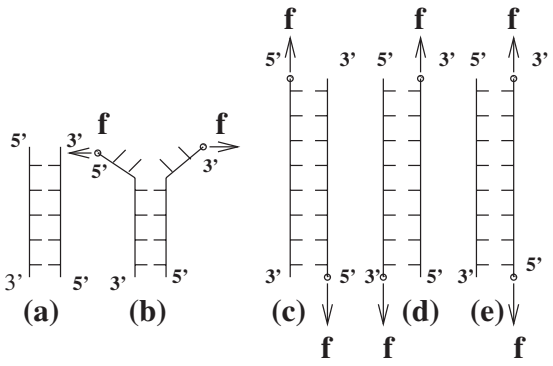

FIG. 1. Schematic representation of dsDNA. (a) dsDNA in zipped form. (b) Unzipping of dsDNA by the force (f) applied at one end (5′-3′). [(c) and (d)] Shearing by the force along the chain applied at the opposite ends (5′-5′ or 3′-3′) of the dsDNA. (e) represents the case where the force has been applied at 5′-3′ end of the same strand of the dsDNA.

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is referred as B-S transition.[4,5,24–26] It may be noted that above 65 pN force the dsDNA and ssDNA have similar response to the applied force.

If the applied stretching force increases above a critical force f_c, there will be force-induced separation of the DNA into two complete separated strands ("melting") and hence the term DNA unzipping will be no more appropriate for such cases. Because instead of pulling a chain of opposite strands at 5′ and 3′ [Fig. 1(b)], which results DNA unzipping, in this case chains have been pulled at 5′ and 5′ end [Fig. 1(c)] or 3′ and 3′ ends [Fig. 1(d)] of the opposite strands or 5′ and 3′ ends of the same strand [Fig. 1(e)]. It is found that in these cases [Figs. 1(c) and 1(d)], transition is akin to shearinglike. The unbinding force strongly depends on the pulling end and lies in between 50 and 150 pN,[6,12] which is much larger than the unzipping force. Moreover, the force-extension curve when a dsDNA is pulled from 3′-3′ ends differs significantly from that which results from when it is pulled from the 5′-5′ ends.[13]

It was pointed out by deGennes[27] that in case of shearinglike transition there is an important length scale κ^{-1} for the DNA over which strain relaxes to both ends implying that the effect of shear stress are local covering less than half a helical turn, while the remainder of the base pairs experience almost no shear force. Here, κ^{-1} is defined as $\sqrt{Q/2R}$ where Q is the spring constant characteristic of stretching of the backbone, and R is the spring constant characteristic of stretching of hydrogen bonds between base pairs. At low temperature, the chain ruptures when the force exceeds a threshold value $f=f_oL$ for short chains and $f=2f_o/(\kappa a)$ for long ones, f_o being the rupture force of a single base pair, L, the chain size, and a, the equilibrium nucleotide spacing. It was experimentally verified for small chains rupture force increases linearly with length for the small sequence of the bases (12–32 bp).[6,26,28,29] Above 32 bases sequence, the rupture force starts saturating in accordance with deGennes prediction.[27,30] However, this theory ignored the effect of temperature as a result effect of formation of bubble has been ignored.

Experimental setups for the unzipping and shearing impose different kinds of constrain on the ends of the dsDNA. Hence the resultant force-temperature diagram may differ accordingly. The first experimentally measured force-temperature diagram of DNA unzipping shows a very rich behavior.[31] However, there is a very little agreement with theoretical predictions.[17,18,22,23] Interestingly, the force-temperature diagram for shearinglike transition remain elusive in the literature. The aim of this paper is to understand the effect of pulling force on the DNA melting under the various constrains imposed on the ends of dsDNA. In Sec. II, we develop a model and discuss two approaches namely the thermodynamic analysis and exact enumeration technique to study the force induced melting of dsDNA. The nature of the phase boundary near $T=0$ and the limitation of the analysis for unzipping and shearinglike transition will also be discussed in this section. Section III comprises results obtained for DNA unzipping, dissociation of dsDNA and the effects of bulge movement in dsDNA. The paper ends with a brief discussion in Sec. IV.

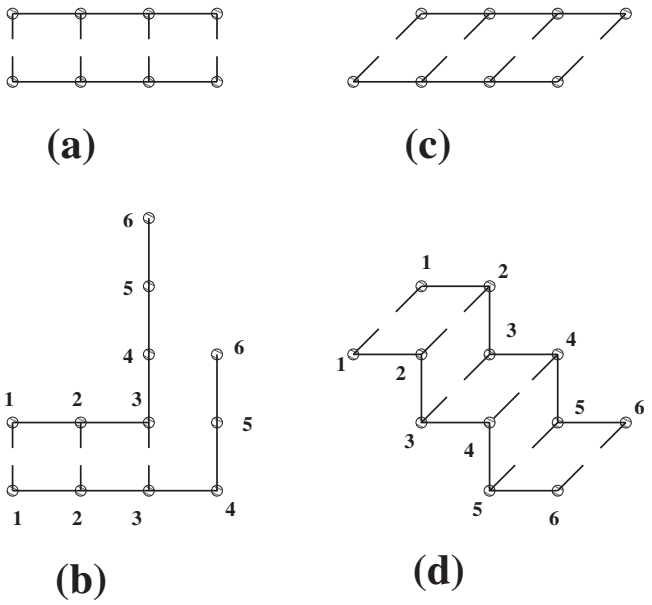

FIG. 2. (a and b) are the schematic representations of some of the conformations of the model introduced in Refs. 17 and 18. In this model, we have only one ground state conformation [Fig. 1(a)]. Because of the lattice restriction, other conformations of zipped state are not possible. [(c) and (d)] are schematic representation of dsDNA conformations with diagonal interaction which leads to the large number of conformations of the zipped state.

II. MODEL AND METHODS

We consider two linear polymer chains which are mutually attracting-self-avoiding walks (MASAWs), as shown in Fig. 2. This is the simplest model of dsDNA where ith monomer of one strand can interact with the ith monomer of other strand only.[17,18,32] This kind of base pairing interaction is similar to the one studied in Poland–Scheraga (PS) model or Peyrard–Bishop (PB) model.[33–35] However, in the present model configurational entropy of the system has been taken explicitly, which was ignored in these (PS or PB) models. The model proposed here is general enough to be defined in any d-dimension, though for computer limitation, we consider it on two dimensional square lattice only.

In order to study the response of an applied force on melting, we consider following cases as discussed above: (I) a pulling force may be applied on the chain at the 5′-3′ end [Fig. 1(b)]. This will correspond to DNA unzipping. (II) For shearinglike transitions, a force may be applied along the chain at two opposite ends of the dsDNA, e.g., 5′-5′ end [Fig. 1(c)] or 3′-3′ end [Fig. 1(d)]. Two interesting scenario may arise for shearing: (a) if pulling is fast, at some critical force f_c, the rupture occurs and the dsDNA dissociates in to the two single strands of DNA [Fig. 3(b)].[6,12] In this case, the system has a larger energy barrier for the complete unbinding. The other possibility involves the slow pulling, where a small bulge loop can form in the chain and propagate to the pulling end [Figs. 3(c)–3(e)]. This process requires spontaneous binding and unbinding of few bases and through the process of diffusion, a bulge slides over the other chain with a small energetic barrier.[14,36,37] This is identified as DNA slippage, which play a key role in the evolution of microsatellites (short repetitive sequence). The existence of such microsatellites have been seen in the genome sequence.[14,37–39]

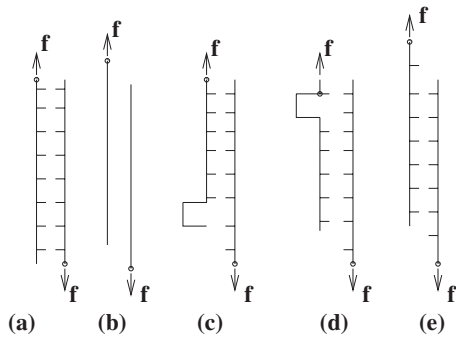

FIG. 3. Schematic representation of slippage of DNA. (a) dsDNA in complete stretched form under the application of force. (b) Dissociation of dsDNA in two ssDNAs at a some critical force f_c without any base pairing. [(c)–(e)] show the schematic representations of bulge movement along the chain. Even if one of the chain slides over the other, the base pairing between ith nucleotide of one strand with $(i+1)$th nucleotide of the other strand is possible.

Neher and Gerland theoretically studied the dynamics of force-induced DNA slippage[37] for the homosequence (bulge movement) and hetero-sequence (dissociation of two strands) and found the expression for the critical force. It was also suggested that the mechanism involved in relative strand motion of DNA is caused by the creation, diffusion, and absorption of bulge movement is analogous to the defect propagation in crystal lattices.[14] However, the model used is basically one dimensional which consists the approximate form of the loop entropy.[40] Inclusion of exact form of configurational entropy, which consists of entropy associated with zipped state, bubble, stretched conformations, and unzipped chains, is beyond the scope of the model.

A. Thermodynamics of force induced melting

The thermodynamics of DNA melting can be obtained from the following relation[41]

$$\Delta G = \Delta H - T\Delta S, \tag{1}$$

Where G, H, S and x are the free energy, enthalpy, and entropy of the system, respectively. To determine the phase boundary for force induced melting, we put $\Delta G=0$ and balance the energy by $-fx$, i.e.

$$-fx = \Delta H - T\Delta S, \tag{2}$$

where x is the reaction coordinate (end-to-end distance in this case) of the dsDNA. The entropy defined in Eq. (1) has contributions from the configurational entropy of the zipped DNA (S_z), entropy associated with the loop (S_o), and entropy associated with unzipped chains (S_u), etc. In unzipping, the applied force acts on the one end and does not influence the configurational entropy of the zipped segments and the entropy associated with the single strands (bubble) as it extends between the zipped segments of dsDNA. For the unzipping, we can write

$$fx = -\epsilon N' + N'TS_z - 2(N-N')TS_o, \tag{3}$$

where ϵ is the effective base pairing energy. At low temperature, i.e., near $T=0$, all bases will be intact $(N'=N)$ and hence there will be no contribution from the loop. Moreover, the second term in Eq. (3) stabilizes the zipped state. Equation (3) may be written as

$$2fN = -\epsilon N + NTS_z. \tag{4}$$

The factor of 2 comes from the fact that chain is in unzipped state and the distance between the extreme ends is equal to $2N$. We substitute the value of $\epsilon=-1$ in Eq. (4) which gives

$$f = 0.5 + \tfrac{1}{2}TS_z. \tag{5}$$

This is in accordance with earlier studies[15,17,18] that the applied force increases with the temperature near $T=0$, which is a signature of reentrance. At higher T, the chain will start opening and the third term of Eq. (3) associated with the loop will start cooperating with the applied force. Therefore, the applied force starts decreasing after a certain value of temperature.

Unlike unzipping, in case of shearing (rupture or slippage), the applied force competes with the entropy associated with the zipped configurations. As a result, the dsDNA acquires first the stretched state before opening. In such a situation entropic contribution of zipped chain [second term of Eq. (3)] at the phase boundary will be absent. However, for the rupture, there will be an additional contribution of entropy associated with the unzipped chain. At low temperature for the rupture $(x=1)$, we can write

$$f = -\epsilon N' - 2NTS_u + 2(N-N')TS_o. \tag{6}$$

At $T=0$, Eq. (6) gives the force required for rupture that is equal to N. Up to certain temperature when the intact bases remain equal to N the entropy associated with the loop will be zero and hence the expression for the applied force (rupture) can be written as

$$f = N - 2NTS_u. \tag{7}$$

Above this temperature, N' decreases with temperature and hence bubble forms, therefore, more force is needed to keep system in the stretched state. Therefore, the phase boundary between zipped and open states should bend. For shearinglike transition, $x=N$ and hence, the required force is equal to 1 and should have similar behavior.

The precise value of entropic contribution near the phase boundary is difficult to obtain analytically. Therefore, it is not possible to get the entire phase boundary from Eqs. (3) and (6). Using the exact enumeration technique,[42] contribution of S_z and S_o can be found for the finite-size chain and an estimate of the phase boundary may be obtained.

B. Exact enumeration analysis

The unzipping case for the model proposed above has been studied in detail,[17,18] where one end of the dsDNA is kept fixed and a force is applied on the other strands, as shown in Fig. 1(b). It was shown that the force-temperature diagram demarcates the zipped and unzipped state and the unzipping force decreases with temperature without any reentrance.[17,18] The absence of reentrance in the force-temperature plane is due to the ground state entropy of the zipped state which has been suppressed because of the im-

posed lattice restriction on the base pairing interaction [Fig. 2(b)]. However, instead of base pairing interaction taken in Refs. 17 and 18, if one considers the diagonal interaction shown in Figs. 2(c) and 2(d), one may observe the reentrance in the lattice models as well. The choice of diagonal interaction introduced here results model more closer to the real system and is analogous to the walks on the oriented square lattice.[22]

In order to study the shearinglike transitions, we apply a force at opposite ends (5′-5′ or 3′-3′) of the strands. We model the fast pulling (i.e., dissociation of two strands), by not allowing the formation of base pair in the model after the chain slides over the other strand. However, for the diffusion of bulge in homosequence (slow pulling),[36,37,43] a force is applied on the opposite strands (5′-5′) so that chain acquires the stretched state. If the force exceeds further, the chain moves one unit toward the applied force direction [Figs. 3(c)–3(e)]. Since the spontaneous binding and unbinding is possible, now we allow the formation of base pairing of $(i+1)$th base of one chain to ith base of other chain [Fig. 3(e)] and calculate the partition function $(Z^{(1)})$ of the reannealed chain. For the next unit of displacement, we allow $(i+2)$th base to interact with the ith base and calculate the partition function $(Z^{(2)})$ and so on. In this way, we can construct a series of partition functions $(Z^{(i)})$ for the slippage. It may be noted that for the unzipping case we monitor the displacement x along the force direction while for the slippage case, we monitor the displacement y along the force direction.

We enumerate all conformations of MASAWs whose one end is fixed and other end is attached with the pulling device (e.g., tip of the AFM). We specifically monitor the reaction coordinate, i.e., end-to-end distance or distance between the fixed end and tip of the AFM. The partition function of the system under consideration can be written as a sum over all possible conformations of dsDNA

$$Z_N = \sum_{\text{all walks}}^{N} x_1^N x_2^N \omega^m u^x = \sum_{m,x} C(m,x) x_1^N x_2^N \omega^m u^x, \qquad (8)$$

where N is the chain length of each strand consisting of N bases. x_1 and x_2 are the fugacities associated with each step of the two self-avoiding walks representing the two strands, respectively. For simplicity we assign $x_1=x_2=1$. $\omega(=\exp(-\beta\epsilon)$ is the Boltzmann weight associated with the binding energy (ϵ) of each diagonal nearest neighbor pair and m is the total number of such pairs in the chain. $u(=\exp[\beta(\vec{f}.\hat{x})])$ ($\hat{x}$=unit vector along x-axis) is the Boltzmann weight associated with the force. $C(m,x)$ is the number of distinct walks[15,17,18] of length $2N$ having m number of pairs whose end points are at a distance x apart. We have obtained $C(m,x)$ for $N \leq 15$ bases and analyzed the partition functions.

Quantities of interest such as reaction coordinate (x or y) and fraction of base pairs can be calculated from the following expressions:

$$\langle x \rangle = \frac{\Sigma_{m,x} x C(m,x) \omega^m u^x}{\Sigma_{m,x} C(m,x) \omega^m u^x}, \qquad (9)$$

$$\langle m \rangle = \frac{\Sigma_{m,x} m C(m,x) \omega^m u^x}{\Sigma_{m,x} C(m,x) \omega^m u^x}. \qquad (10)$$

Dissociation and bulge movement are dynamic phenomena and can be described in quasistatic equilibrium. Since we monitor the distance of the end points of the dsDNA where the force has been applied, we also do our analysis in constant distance ensemble (CDE) at fixed temperature. The partition function in CDE may be defined as $Z_N(x,T) = \Sigma_m C(m,x)\exp(\beta m \epsilon)$. The two ensembles are related by $Z_N(T,f) = \Sigma_x Z_N(x,T)\exp(\beta f x)$. The free energy is given by the relation $F_N(x,T) = -T \ln Z_N(x,T)$ and the average force $\langle f \rangle$ is thus dF/dx. It is pertinent to mention here that in CFE the average separation $(\langle x \rangle)$ fluctuates, while in CDE one measures the average force to keep the separation constant at a fixed temperature.

It may be noted that single molecule experiments are generally performed on finite-size-chain and hence, no true phase transition can occur in the system. Therefore, we calculate the "state diagram" associated with finite chain. The boundary of state diagram (f-T diagram) has been obtained from the peak value in fluctuation of m at the fixed force. The peak height increases with the length. It was shown that f-T diagram obtained through fluctuation is in very good agreement with the exact phase diagram for the force-induced-unfolding of biopolymers.[44] Experimentally, the melting temperature (T_m) use to be obtained from melting profiles by monitoring the change in the UV absorbance with temperature. This provides the information about the fraction of open base pairs, and the melting temperature is defined when half of the total base pairs get open.[3,19] Here, we can also get the melting profile from Eq. (10) that gives the melting temperature close to one obtained from fluctuation of m. In the following, we shall confine ourselves to canonical ensemble and set $\epsilon=-1$ and $k_B=1$ in calculating all the relevant quantities.

III. RESULTS

For a chain of finite length, the melting profile of dsDNA strongly depends on the imposed constrain. For example, if we fix one end of both strands and keep other ends free [Fig. 4(a)], the melting temperature is found to be 0.86 (Fig. 5). However, if one end of both strands of the dsDNA is kept fixed and other ends are tied together [Fig. 4(b)], in such a case dsDNA melts at $T=1.11$. The other possibility is to tie one end of the dsDNA together and keep only one strand of the other side of dsDNA fixed [Fig. 4(c)]. In this case, melting takes place at $T=0.86$. Lastly we can fix one end (5′-end) of the first strand and opposite ends (5′-end) of the other strand [Fig. 4(d)], the melting occurs at $T=0.53$. It is expected that because of reduction in entropy arising due to the imposed restriction on the ends of a dsDNA, melting temperature will change. In the following, we shall discuss the effect of confinement shown by Figs. 4(a) and 4(c) for DNA unzipping and shearing (rupture and slippage), respectively.

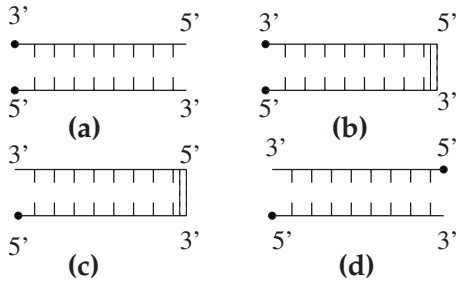

FIG. 4. Schematic representation of the various confinements imposed on the end of dsDNA in the absence of force. (a) One end (5′-3′) of both strands is fixed while other ends are free. (b) One end (5′-3′) of both strands is kept fixed and other ends (3′-5′) of both strands are tied together. In this case, chain opens from the middle. (c) Same as (b), but here only one end (5′) of one strand of dsDNA is kept fixed. (d) It represents the complete zipped-stretched state where 5′-5′ ends are kept fixed while 3′-3′ end are free. For all these cases, melting profile depends on the constrains imposed on the end of the strands shown by black circles.

A. Pulling at 5′-3′ end of opposite strands: DNA unzipping

Pulling at one end of dsDNA (5′-3′ end) results DNA unzipping. We keep one end of the dsDNA fixed [Fig. 4(a)] and apply a force f on the other end, as shown in Fig. 1(b). The force-temperature diagrams shown in Fig. 6 are obtained from the maxima of fluctuation of m with T at a given force f.For the sake of comparison, we also provide the result in Fig. 6(a) for the model studied in Refs. 17 and 18, where base pairing interaction is carried out along the bond, as shown in Figs. 2(a) and 2(b). The fluctuation curve [Fig. 6(b)] at low T shows only one peak indicating that there is no reentrance.[17,18] Since diagonal base pairing interaction gives rise the ground state entropy of the zipped conformations [Fig. 2(c) and 2(d)], we obtain two peaks in the fluctuation of m [Fig. 6(d)]. As a result, the force-temperature diagram for this case shows a reentrance [Fig. 6(c)] at low temperature. The melting temperature ($f=0$) for the diagonal interaction is much higher because of the large contribution arising due to the ground state entropy of the zipped state.

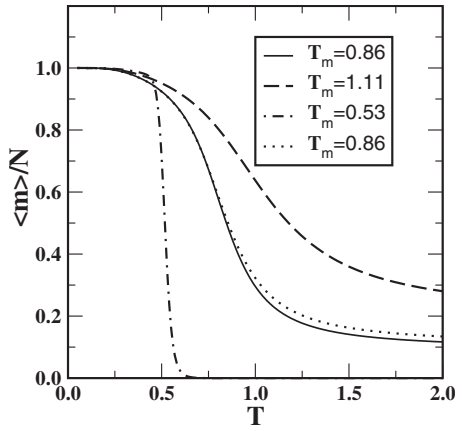

FIG. 5. Melting profiles of dsDNA under different constrain imposed on the ends of the chain. The solid line corresponds to the Fig. 4(a). The dashed line represents the case illustrated in Fig. 4(b). The dotted line is for the situation shown in Fig. 4(c) and the dotted-dashed line is for Fig. 4(d). For all these cases, T_m is found from the fluctuation of m which is close to the temperature (melting temperature) where half of the base pairs are opened.

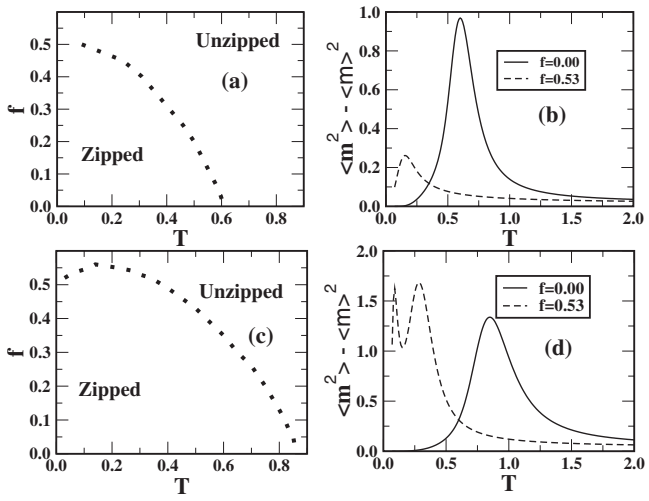

FIG. 6. The force-temperature diagram of DNA unzipping. (a) For the model introduced in Refs. 17 and 18. (b) At low temperature, there is only one peak in the fluctuation curve, which shows the absence of reentrance in the model studied in Refs. 17 and 18. (c) f-T diagram for the model studied here shows the reentrance at low temperature. (d) The existence of two peaks is evident in the fluctuation curve.

B. Pulling at 5′-5′ end or 3′-3′ end of opposite strand

1. Dissociation of two strands

If pulling is fast enough or the chain is heterogeneous, the two strands separate completely without any overlap. In short span of time, rebinding of bases are not possible and rupture takes place at some critical force f_c where two strands dissociate completely. In order to model such process, we consider all conformations of two MASAWs, as shown in Fig. 4(c) along with the conformations where the second chain has shifted one unit [Fig. 3(b)] toward the force direction. Since pulling is fast, there is no contribution of base pairing in the displaced partition function. As a result, two walks will be noninteracting and will only impose the confinement arising due to mutual exclusion on each other. The combined partition function can be written as

$$Z_N = Z^0 + Z^1, \tag{11}$$

where Z^0 is the partition function of the model system in which one end of the strand is attached with the AFM tip which may vary in between $x=0$ to $x=N$, while other end of one strand [Fig. 4(c)] is kept fixed. Here, formation of base pairing is possible in between ith base of one strand with the ith base of other strand only. The ground state consists all conformations of the zipped chain. The partition function Z^1 corresponds to the situation, when one end of the second strand has displaced a unit distance toward the force direction after acquiring complete zipped stretched state (i.e., $m=N$ and $x=N$).

The force-temperature diagram for the rupture is shown in the Fig. 7. It is evident from the plot that the nature of phase boundary is significantly different than the DNA unzipping shown in Figs. 6(a) and 6(c). This is because in case of unzipping, the applied force does not affect the entropy associated with conformations of bubble and zipped segments while in case of rupture, because of stretching, the contribution of entropy approaches to zero. It can be seen

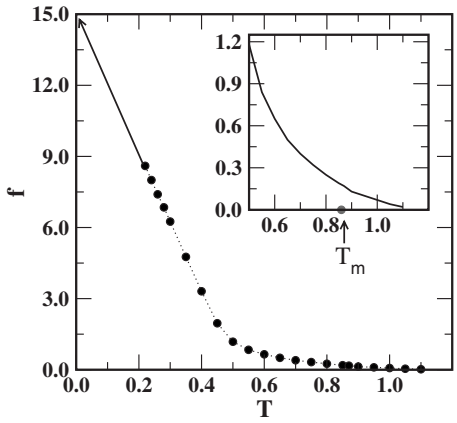

FIG. 7. The force-temperature diagram for the DNA dissociation. At low temperature force decreases linearly with the temperature. At $T=0$, it intercepts y-axis at 15 which is the required force for the rupture. It is clear from the Fig. 5 that above the temperature $T=0.4$, the dsDNA melts and because of entropic contribution the phase boundary bends. Above the melting temperature ($T_m=0.86$), there are still some bases are in contact and hence a small force is required for the complete unbinding, as shown in the inset.

from the melting profile (Fig. 5) that above the melting temperature at $f=0$, there are significant number of intact base pairs. In order to have complete unbinding (i.e., no base is in contact), one requires still some (vanishingly small) force near the melting temperature, as shown in the inset of Fig. 7.

The force extension curve obtained in CDE is shown in the Fig. 8. At low temperature, when the dsDNA is in the zipped state, the applied force brings the dsDNA from coil state to the stretched state. Depending on the temperature, at a certain value of the force, rupture takes place and then the force becomes zero. The qualitative nature of the force-extension curve is similar to the one seen in recent experiments.[6,12]

2. Bulge movement

Due to the formation of a bulge and application of shearing force at opposite ends of the dsDNA,[36,37] one strand slowly moves over the other strand along the force direction. Since pulling is quite slow, there is enough time for unbinding and rebinding of the bases. In order to study the effect of bulge on the force-temperature diagram, we consider the following partition function:

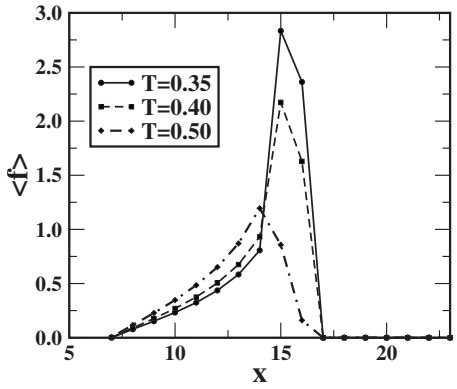

FIG. 8. The force-extension curve in CDE for the dissociation of dsDNA. With the rise of temperature, the force required for rupture decreases. The applied force brings system first from the coil state to the stretched state and at a certain force rupture takes place and force approaches to zero in accordance with the experiments.

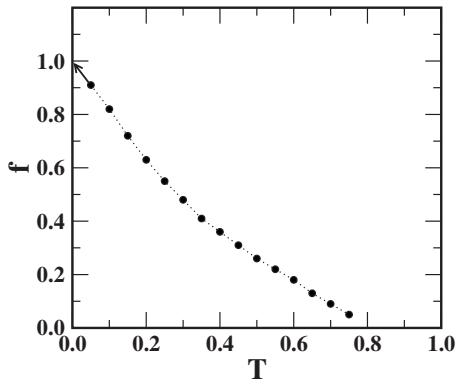

FIG. 9. The force-temperature diagram for the DNA slippage. In this case, the dsDNA separates at much lower force compare to the rupture, as shown in Fig. 7. The other features remain same as of Fig. 7.

$$Z_N = \sum_{i=0}^{N} Z^i. \tag{12}$$

Unlike the model for the rupture, we calculate the partition function Z^1, where the formation of the base pairs is allowed in between ith base of one strand with the $(i+1)$th base of the other strand when the chain slides one unit distance along the force direction. Similarly, Z^2 corresponds to the situation when the chain slides two units along the force direction. In this case, the base pairing is allowed to take place in between ith base of one strand with $(i+2)$th base of the other strand and so on. In quasi static equilibrium, this represents the bulge movement along the chain.

The force-temperature diagram is shown in the Fig. 9. The nature of phase boundary between zipped state and open state is different than the one obtained for the DNA unzipping [Fig. 6(c)], but similar to the rupture (Fig. 7). Moreover, the magnitude of the required force is much less than the rupture. At low temperature, the entropy contribution is negligible and hence the force required to break a base pair is nearly equal to 1. However, at higher temperature, contribution arises due to entropy and hence the applied force decreases with the temperature. This is in accordance with the thermodynamic analysis presented in Sec. II A.

The force-extension curve obtained in CDE has been plotted in the Fig. 10. With the rise of force, the dsDNA acquires the stretched state. Because of the formation of bulge and applied force, chain slides over the other chain along the force direction. This can be seen from the Fig. 10, where extension increases without increasing the applied force. It may be noted here that the force required to bring chain from coiled state to the stretched state for both cases (rupture and slippage) is the same. In order to have a rupture, large force is required to overcome the energy barrier, while for the slippage, comparatively a less force is required.

IV. CONCLUSIONS

The simple model presented here shows that the melting profile as well as the melting temperature of dsDNA depend

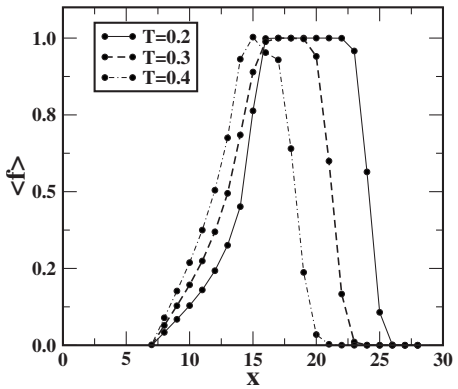

FIG. 10. The force-extension curve in CDE for DNA slippage. At low temperature, there is a significant overlaps of the bases. Therefore, strand slides over the other strand. As temperature increases, the number of base pairs decreases and hence the width also decreases. The two strands get separated above a certain temperature.

on the constrain imposed on the ends of the strands. The results presented here are relevant in context of single molecule force experiments of finite-size chain, where experimental setups for unzipping and shearing usually imposed such constrains on dsDNA. Moreover, with proper modification in the model, we could describe the phenomena such as unzipping, stretching, rupture and slippage of DNA. We have shown here that the force required for the slippage is much less than the rupture or dissociation at any temperature. This is because of the possibility of bulge propagation which requires less force to overcome the energy barrier. The qualitative nature of the force-extension curve for the rupture of dsDNA (Fig. 8) is similar to the one observed in experiments.[6,12] Our model studies also provide unequivocal support for the reannealing of two strands in the form of plateau seen in case of slippage (Fig. 10).

Because of the lattice restrictions, the ground state entropy of the zipped conformation in Refs. 17 and 18 was found to be zero. Inclusion of diagonal interaction gives rise to the ground state degeneracy of the zipped conformations. It is surprising to observe that the nature of force-temperature diagrams for rupture and slippage (Figs. 7 and 9) are significantly different than the DNA unzipping [Fig. 6(c)]. For DNA unzipping, the unzipped segment because of the applied force remains in the stretched state and hence entropy associated with it is zero. The phase boundary (Fig. 6) is determined by the balance of the net force propagated through ssDNA (in the stretched state) and the unzipping potential at center point of the Y-fork [Fig. 1(b)]. The applied force does not influence the entropy associated with the zipped segments. As a result, the force-temperature diagram [Fig. 6(c)] shows the existence of reentrance at low temperature.

In case of slippage and rupture, the applied force brings chain in the stretched state with almost zero entropy and competes with enthalpy only at low temperature. At $T \sim 0$, Eq. (6) gives the force required for rupture, which is equal to N. This is evident from the Fig. 7 as well. Up to $T \approx 0.45$, the number of intact bases (N') remains equal to N and hence entropy associated with the loop is zero. The value found from Eq. (7) matches exactly with the one shown in Fig. 7 up to $T \approx 0.45$ obtain from exact enumeration. In this region, decrease in force with temperature is due to the entropy [second term of Eq. (6)] associated with unzipped chains.

The force-extension curve presented here reflects only the entropic response of stretching below f_c. The overstretching of DNA (B-S transition) and pulling DNA at 3′-3′ end (or 5′-5′ end) as seen in case of DNA stretching is beyond the scope of the present model. It is because of the helical information which has not been incorporated in the model. Hence, the model presented here only reproduce coil to S transition. This is similar to the case when force is applied at 3′-3′ end which results the S-state of the dsDNA.[45] Moreover, on the lattice κ^{-1} is not properly defined and hence saturation of force for longer sequence may not be possible in the framework of exact enumeration. Therefore, our results are better suited for chains of smaller sequence.

It is important to mention here that at high temperature (below the melting temperature) there is a possibility of the formation of bubble, where a dsDNA transforms to two ssDNAs. The persistent length of ssDNA is much smaller than the dsDNA. Neher and Gerland[37] proposed a simple form of rupture force at intermediate force $f_c = \epsilon_b/(2l_s - l_d)$, where l_s and l_d are the effective lengths of ssDNA and dsDNA, respectively, along the direction of the applied force and ϵ_b is the base pairing energy. Since, in the lattice model, different length scales associated with ssDNA and dsDNA are not possible to incorporate and hence quantitative aspect of rupture force may change at high temperature or for longer sequence. At this stage of time, a long chain off-lattice simulation along with orientation of bases along the phosphate bond is needed to understand the role of κ on force induced slippage and dissociation.

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