Z_2 Symmetry in the Melting Transition of the DNA Helix

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The denaturation transition of DNA molecules is numerically investigated with a focus on the Z_2 symmetry related with the two opposite directions of the winding: the left-handed (Z-type) and the right-handed (B-type) windings. We extend the previous DNA model Hamiltonian to include a term that phenomenologically describes the tangential interaction, making the same twist direction favored by adjacent base pairs. Evoking the large strength of the tangential interaction, we reveal the Z_2 symmetry nature of twist directions associated with the opening of DNA strands. We also observe that the boundary between the B-domain and the Z-domain is point-like, in accordance with a recent experimental result.

I. INTRODUCTION

Spontaneous symmetry breaking is one of the most fascinating phenomena in physics. For a system with spontaneously broken symmetry, although the Hamiltonian of the system is invariant under a given symmetry operation, the actual realization of the system does not possess the symmetry. To mention a few examples in physics, the ferromagnetic phase of the Ising model in statistical physics at low temperatures is a phase with spontaneously broken up-down spin-reversal symmetry (called Z_2 symmetry). Superconductivity has also broken $U(1)$ symmetry related with the rotation of phase variables of the superconducting order parameter. Biological examples are abundant: Most human beings have their hearts in their left chests although there is no physical law prohibiting the opposite. The handedness of the DNA double helix is another popular example of spontaneous symmetry breaking [1,2]. The right-handed structure can be found in the B-DNA, the most common form in physiological conditions. The B-form adopts several helical conformations, for instance, the A-DNA under dehydration, which is also right-handed. There also exists an unusual left-handed form called Z-DNA. It is known that a structural transition between the B-form and the Z-form can be induced, and even more interestingly, the Z-DNA can exist in close vicinity of the B-DNA within

the same duplex, forming a B-Z junction whose length is about three base pairs [3,4].

Among the great diversity in causes for the formation of Z-DNA, a common belief is that the Z-form occupies higher energy states of the DNA morphology. Also, observations by using X-ray crystallography have revealed that the B-Z junction contains base pair breaking [4]. It would be then natural to question the thermodynamic nature of the Z-form in relation to DNA denaturation at high temperatures. The primary goal of the present work is to incorporate the B-Z symmetry as the discrete Ising Z_2 symmetry into a statistical mechanical model for describing the structural dynamics of DNA molecules. To this aim, we introduce a potential offering a preference for the helical twist, either the right-handed or the other, so as to impose the Z_2 symmetry. Implementing a Monte Carlo simulation, we evaluate the fraction of open base pairs and a *magnetization* that measures the net helicity. The magnetization reaches its maximum amplitude when all the bases have twists of the same handedness. We observe that an upturn of the opening fraction occurs at the temperature $T \approx 350$ K, in good agreement with previous results [5]. Further, around that temperature, the magnetization is shown to start to decrease, signifying the Z_2 symmetry engaged in the melting process. Finally, we examine the spatial distribution of the twist angle of bases around at the on-set temperature for the mixture of the either handedness and show that two domains retaining their respective handedness exist to form a point-like boundary. However, our results for

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the point-like B-Z junction need to be taken with caution: No sudden base pair breaking at the junction in real experiments [4] is seen within our model.

II. MODEL

The model for the structural transition of denaturation of DNA of the total number of base pairs N has been proposed by Peyrard and Bishop (PB) [6] with the potential energy function

$$V^{(PB)} = \sum_{n=1}^{N} [D(e^{-ay_n} - 1)^2 + E e^{-b(y_n + y_{n+1})} \\ \times (y_n - y_{n-1})^2], \quad (1)$$

where $y_n \equiv r_n - r$, with $2r_n$ being the distance between the nth complementary bases and $2r$ being their equilibrium separation ($r \approx 10$ Å). Here, the first term with the strength $D = 0.15$eV and the cutoff scale $a = 6.3$ Å^{-1} is called the Morse potential, which describes the hydrogen bonds of base pairs. The second term, which represents the stacking potential with the strength $E = 0.005$ eV/Å^2, has a limited range of interaction $b = 0.5$ Å^{-1}. In the PB model, the DNA double helical structure has been simplified as a flat ladder whose dynamics is governed solely by one-dimensional variables, r_n's. There is an important variant of the PB model proposed by Cocco and Monasson (CM) [7]:

$$V^{(CM)} = V^{(PB)} + K \sum_n (h_n - h)^2, \quad (2)$$

where the elastic potential energy with $K = 0.014$ eV/Å^2 describes the energy cost related to the deformation in the direction along the DNA double helix (the z-direction in the present work). Most importantly, in the CM model, different from the PB model, the helical structure of DNA is taken into account, and, accordingly, the position of each base pair is written as $\mathbf{x}_n = (r_n, \phi_n, z_n)$ in the cylindrical coordinate system. The vertical distance h_n (with the equilibrium value $h = 3$ Å) between two adjacent base pairs is defined as $h_n \equiv z_n - z_{n-1}$, and the twist angle is defined as $\theta_n \equiv \phi_n - \phi_{n-1}$ with the equilibrium value $\theta = 0.638$. In the CM model, the length $L = 6.95$ Å of the sugar phosphate backbone is assumed to be fixed and is given by

$$L^2 = h_n^2 + r_{n-1}^2 + r_n^2 - 2r_{n-1}r_n \cos\theta_n = \text{const.}, \quad (3)$$

which reduces the number of degrees freedom to $2N$. Although the DNA denaturation transition is very well known to occur in model systems, the nature of the phase transition, if it is continuous or discontinuous, has been under strong debate [8].

For the purpose of the present work, neither the PB nor the CM model is adequate to investigate the handedness of a DNA double helix: The PB model lacks the twist angle degree of freedom to start with, and the CM model does not possess the Z_2 symmetry in a proper way. In the latter, the twist angle degree of freedom θ_n enters only through the constraint of fixed L in Eq. (3); thus, the total Hamiltonian is invariant under the local transformation $\theta_n \rightarrow -\theta_n$ for a given n. In contrast, the proper symmetry property one requires for the present work is that the system be invariant under the global symmetry operation, i.e., $\theta_n \rightarrow -\theta_n$ for all n, not the symmetry in the local transformation. To put it in a simpler way, the CM model cannot distinguish the energies of two configurations $\{\theta_1, \theta_2, \cdots, \theta_n\}$ and $\{-\theta_1, \theta_2, \cdots, \theta_n\}$ even though they are very different in terms of the handedness of DNA.

In order to remedy the above-mentioned drawback in the CM model or to have the proper helical rigidity observed in experiments, we include an interaction potential V_t between tangential vectors [9]:

$$V = V^{(CM)} + V_t, \quad (4)$$

$$V_t = \kappa \sum_n (\mathbf{t}_{n+1} \cdot \mathbf{t}_n - J)^2, \quad (5)$$

with $\mathbf{t}_n \equiv (\mathbf{x}_n - \mathbf{x}_{n-1})/|\mathbf{x}_n - \mathbf{x}_{n-1}|$ and $J \equiv \mathbf{t}_{n+1}^{(o)} \cdot \mathbf{t}_n^{(o)}$, where $\mathbf{t}^{(o)}$ is defined similarly to $\mathbf{t}_n$, but with $\mathbf{x}_n^{(o)} = (r\cos n\theta, r\sin n\theta, nh)$. Although there exists a structural difference between B- and Z-DNA, for simplicity, we take $J = 0.84$ from $r = 10$ Å, $h = 3.8$ Å and $\theta = 0.638$ of B-DNA. The potential V_t is introduced to account for the energy cost of deviations of the tangential variations from their equilibrium configurations up to a harmonic order, but yet nonlinear in terms of the angle variables. When a geometry is curved, it has a bending energy $V_b \sim \int ds |\mathbf{c}(s)|^2$, where the curvature $\mathbf{c}$ is related to the rate of change of the tangent such that $\mathbf{c}(s) = d\mathbf{t}/ds$ with the quantities defined along the curve, $\mathbf{t}$ and s, denoting the unit tangent vector and arc length, respectively [10]. For the helical duplex having intrinsic curvature $\mathbf{c}_I(s)$, writing $V_b \sim \int ds |\mathbf{c}(s) - \mathbf{c}_I(s)|^2$ and using a discrete notation ($s = nL$), we have written $V_b = (\ell k_B T_R / 2L) \sum_n |\Delta \mathbf{t}_n - \Delta \mathbf{t}_n^{(0)}|^2$ at room temperature T_R, where ℓ is the persistence length associated only with the helical winding, $\Delta \mathbf{t}_n \equiv \mathbf{t}_{n+1} - \mathbf{t}_n$ and similarly for $\Delta \mathbf{t}^{(0)}$. V_b can be expanded in terms of the tangential deviations from the standard helical structure as $V_b / \kappa \approx \sum_n (\mathbf{t}_{n+1} \cdot \mathbf{t}_n - J)^2 + 4(1-J)^2 \psi_n^2$ with ψ_n being the angle between $\Delta \mathbf{t}_n$ and $\Delta \mathbf{t}_n^{(0)}$. Here, the strength of the tangential interaction κ is given by $\kappa \approx \ell k_B T_R / 4L(1-J)$. Using $(1-J)^2 \ll 1$ and dropping the ψ-term, we have V_t in Eq. (5). Noting that V_t is a three-body interaction, whose invariance under the angle inversion ($\theta_n \rightarrow -\theta_n$) can be acquired only by the global operation, one easily sees that Z_2 symmetry is properly embedded. In fact, there was an attempt to take account of the helicoidal curvature by including a three-body potential $V_b \equiv \kappa_b \sum_n (\theta_n - \theta_{n-1})^2$ [11]. Although V_b, indeed, supports the system tendency to have either hand-
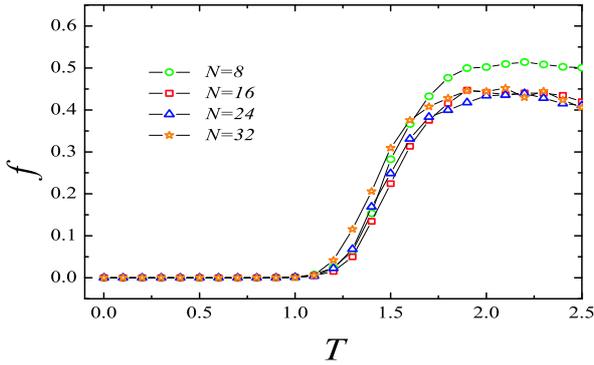
Fig. 1. (Color online) Opening fraction f, defined as the ratio between the number of opened base pairs and the total number of base pairs, versus the temperature T. As T is increased, the DNA denaturation transition is shown to occur around $T_m \approx 1.2$.
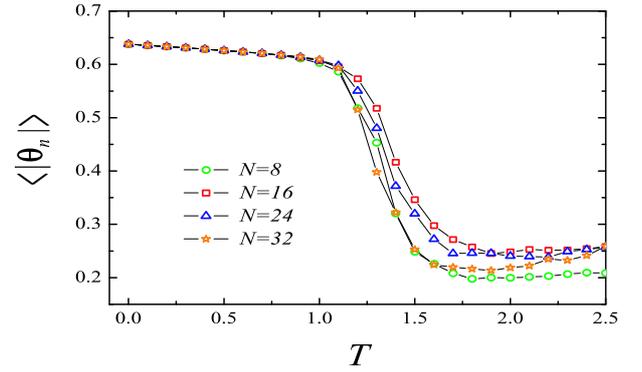

Fig. 2. (Color online) Absolute value of the twist angle $\langle|\theta_n|\rangle$ versus T. As T is increased from zero temperature, the twist angle decreases and takes the value $\langle|\theta_n|\rangle \approx 0.61$ at $T = 1$ (room temperature).

edness, such a harmonic potential can be less effective for examining the possible formation of a B-Z junction. On the other hand, the strength of the potential V_b was arbitrarily taken to be huge as $\kappa_b = 2 \times 10^3 k_B T_R$ [11]. Also, in our consideration, the interaction parameter κ remains arbitrary, depending on the twist modulus ℓ, which is closely related to the bending modulus. Simply by using the persistence length for bending the duplex $\ell_D \approx 50$nm [12], that is, $\ell = \ell_D$, we have $\kappa \approx 10^2 k_B T_R$. Since there exists partial contributions to ℓ_D from the potentials for base stacking and vertical deformation already included, we take a moderate value, $\kappa = 10 k_B T_R$.

The Monte Carlo (MC) simulations are performed with the potential energy given in Eq. (4) with all energy scales in units of $k_B T_R$ and length scales in units of $r = 10$ Å. At each MC step, we use r_n and ϕ_n as dynamic variables, adopting the standard Metropolis algorithm with the open boundary condition. We start from a sufficiently high temperature $T = 4$ (henceforth, temperatures are in unit of T_R) and decrease T slowly in step size $\Delta T = 0.1$ by using the annealing technique for better equilibration. At each T, we disregard 10^6 initial MC steps and compute quantities for $10^7 - 10^8$ steps. All the above procedures are then repeated for 100 times for DNA sizes $N = 6, 8, 10, 12, 16, 20, 24$ and 32. We restrict our simulations to such relatively small sizes to avoid insufficient equilibration during the MC procedure.

III. RESULTS

We first study the structural phase transition related with the opening of the DNA double helix (DNA denaturation), measured by the ensemble averaged fraction f of opened base pairs satisfying $r_n > 2$, i.e., bigger than twice the equilibrium radius. Figure 1 shows that as T is increased beyond the melting temperature $T_m = 1.2(1)$

(i.e., around 350 K), the number of opened base pairs begins to increase, in accord with previous findings [5]. The melting temperature of oligonucleotides (chains of nucleotides with the number of base pairs less than about 50) has been known to depend on various conditions, such as the salt concentration, the heterogeneity of the DNA sequence (most importantly, the GC contents), and the size of the DNA chains [13]. We in this work heavily simplify the real experimental situation, and the heterogeneity in base sequences is neglected. Furthermore, neither the chemical reactions with the surrounding environment nor the interactions with other oligonucleotides are taken into account. We believe that the insignificant size dependence of the melting behavior in this work may originate from the above differences.

In Figure 2, the temperature dependence of $\langle|\theta_n|\rangle$ is displayed, where $\langle\cdots\rangle$ denotes the ensemble average. Although this quantity cannot be used to detect the Z_2 symmetry of the system because it disregards the handedness of twist, it is to be noted that $\langle|\theta_n|\rangle \approx 0.61$ is measured at room temperature $T = 1$, which is in a good agreement with the experimental observation [1] that a DNA double helix makes a full turn at every 10.4 base pairs at room temperature, i.e., $(2\pi/10.4 \approx 0.604)$.

In order to detect the Z_2 symmetry related with the handedness of the twist of a DNA double helix, which is a key issue in the present paper, we define

$$m = \frac{1}{N} \sum_n \text{sgn}(\theta_n), \tag{6}$$

where $\text{sgn}(x) = 1(-1)$ for $x > 0$ $(x < 0)$. For a fully ordered state with all bases right-handed (left-handed), one gets $m = 1$ $(m = -1)$. Accordingly, m in Eq. (6) can detect symmetry breaking related with the handedness. As we anneal the system from the high-temperature region, the mixture of B-DNA and Z-DNA base pairs is clearly seen to undergo a structural change towards only a single type of twist (either B or Z) through the whole DNA. Even though the above order parameter appears
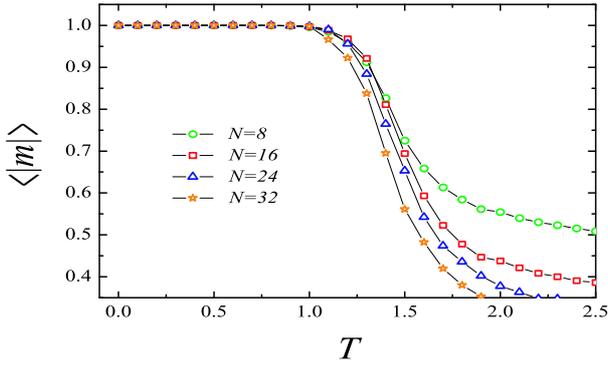
Fig. 3. (Color online) Order parameter m to detect the Z_2 symmetry related with the handedness of the twist in DNA versus T.

Fig. 4. (Color online) A snapshot of the twist angle configuration at $T = 1.3$ for DNA of size $N = 32$. $\theta_n = \phi_n - \phi_{n-1}$ is the twist angle for the nth base pair. The Z-type changes to B-type abruptly, implying the existence of a point-like defect between the two domains with opposite twist handedness.

to exhibit a sudden change around $T \approx 1.5$, it should not be interpreted as a genuine Z_2 symmetry breaking phase transition. The well-known argument of the absence of a finite-temperature phase transition in the locally-coupled Ising system in one dimension still applies to our model of DNA. The quasi-ordered state in the low-temperature region in Figure 3 is only a crossover behavior related with the huge strength (order of magnitude bigger than the room temperature) of the tangential interaction in Eq. (5). We have numerically confirmed (not shown here) that if the tangential interaction strength is reduced much, the quasi-ordered state at low temperatures found for large κ changes to a disordered state.

We finally investigate the spatial structure of the boundary between B-DNA and Z-DNA. A recent experiment [4] revealed, through the use of a crystallographic technique, that the boundary is like a point defect. In itself, this is a rather striking observation because B-DNA is expected to change to Z-DNA along the DNA helix in a spatially continuous way: The positive twist angle of B-DNA approaches zero smoothly and then continuously changes the twist direction, with a bubble like structure between the B- and Z-DNA. In contrast, the experimental observation suggests that this is not the case, and that the DNA changes its handedness very sharply. We repeat our MC simulations many times and take snapshots of configurations. In some cases, the B-Z junction is found to be formed as shown in Figure 4 and does not disappear later on. Around the melting transition, we observe that the twist angle changes abruptly as in Figure 4, in accord with the experimental finding. However, it should be noted that in our simulation, different from the experiment [4], the sudden change of the handedness at the B-Z junction is not accompanied by a sudden breaking of the base pair. Since a number of degrees of freedom are correlated in a complex manner in the present formulation of different potential functions, we are allowed only to surmise that the small junction size observed in Figure 4 is due to the strength of the twist potential taken as ten times the thermal energy: For a strong twist potential, it is advantageous for a system
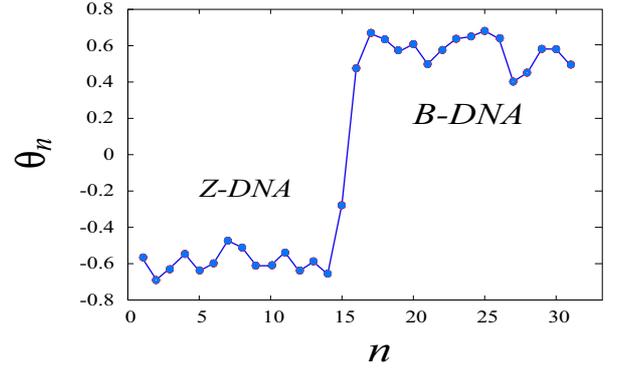
to localize defects, rather than spread them over a large distance.

IV. SUMMARY

In summary, we have investigated the denaturation transition of the DNA melting, with focus on the Z_2 symmetry related with the two opposite handednesses of the DNA double helix. In nature, right-handed B-type DNA is much more abundant than the left-handed Z-type. We have extended the previous model to include the tangential interaction potential to implement the preference for a single-handed DNA. As the temperature is increased from low temperatures, the interstrand distance is found to increase beyond the melting transition temperature $T_m = 1.2(1)$, and the twist angle has a magnitude of about 0.61, in good agreement with previous studies. Furthermore, we have also revealed, through the use of a properly defined order parameter to detect Z_2 symmetry, that the B- and the Z-type DNA coexist at high temperatures while at sufficiently low temperatures, the whole DNA helix prefers a single form of either B-type or Z-type. However, the Z_2 symmetry breaking cannot be interpreted as a true phase transition. We also confirmed the recent experimental observation that the boundary between the B-type and the Z-type domains is like a point defect; accordingly, a DNA helix changes its handedness abruptly along the direction of the DNA. In the present theory, we do not consider sequence heterogeneity. The simplest way to do so would be to introduce a nonuniform strength of the Morse potential that depends on the base-pair species: an AT pair with two hydrogen bonds and a GC pair with three hydrogen bonds. Also, if the crucial role of the stacking potential in determining the nature of the melting transition is noted [8], a better description can be made by taking account of the stacking parameter's variation. Al-

though finding an appropriate parameter set of (at least) 16 variables might be demanding, unveiling the frequent formation of Z-DNA at specific sequences with alternating GC base pairs is, nevertheless, essential. Knowing that the B-Z transition can be driven by high-salt concentration, it is also desired to incorporate the screening effects served by counterions on the molecular structural dynamics [14], which is left for further study. We believe that an understanding of the structural and the mechanical properties [15], which has been the main motivation of the present study, can be of great benefit in the study of transport phenomena [16] in DNA molecules.

ACKNOWLEDGMENTS

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