

## Torsional effect on the wrapping transition of a semiflexible polymer around a core as a model of nucleosome

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We investigated the effect of the torsional rigidity of a semiflexible chain on the wrapping transition around a spherical core, as a model of a nucleosome, the fundamental unit of chromatin. Through molecular dynamics simulation, we show that the torsional effect has a crucial effect on the chain wrapping around the core under the topological constraints. In particular, the torsional stress (i) induces the wrapping/unwrapping transition, and (ii) leads to a unique complex structure with an antagonistic wrapping direction which never appears without the topological constraints. We further examine the effect of the stretching stress for the nucleosome model in relation to the unique characteristic effect of the torsional stress on the manner of wrapping.

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### I. INTRODUCTION

The structure of DNA wrapping around a cationic protein is called nucleosome, which is a basic unit of chromatin in living cells [1]. In physics, a spherical or cylindrical core and a semiflexible chain are adopted as a model of the nucleosome structure [2–9]. In contrast to a flexible chain, a semiflexible chain wraps the core in an ordered manner [10]. Under usual aqueous conditions, the persistence length  $l_p \approx 50$  nm of DNA is large compared to its molecular thickness  $d \approx 2$  nm. Therefore, DNA with contour length  $L \gg 1$   $\mu\text{m}$  is characterized as a typical semiflexible chain: for example, the contour length of eukaryote DNA is longer than 500  $\mu\text{m}$ . DNA wraps a histone core, which has a diameter of 11 nm, in an ordered manner 1.75 times. To reveal the structures and mechanisms of a nucleosome, some groups have conducted studies that involve the pulling of nucleosomes [10–15]. These studies have shown that unwrapping is generated in a stepwise manner, i.e., the chain unwraps the core from twice to once, then from once to zero as the chain is pulled. These wrapping transitions are controlled by several factors, which are an interaction between the chain and the core, the chain stiffness, and the sphere size. Recently, it is revealed that other factors are also important in determining nucleosome structures and mechanisms. Yanao *et al.* [5] showed that DNA wraps around a protein core in a left-handed manner based on the coupling between bending and twisting rigidities due to the chirality of the right-handed double helix structure of DNA. In the system of a chain wrapping around a core, topology is an important factor that determines the mechanism and the structure of a nucleosome.

In a prokaryote cell, DNA is a circular chain that is topologically constrained. In this case, the topological number  $Lk = Wr + Tw$  is conserved [16].  $Wr$  is calculated through the chain conformation.  $Tw$  is the total twisting of the chain. The effects of topological constraints and torsional rigidity on the conformation have been studied in a circular polymer [17–20]. In a eukaryote cell, DNA is stored compactly by forming a hierarchical structure. At the lowest level, nucleosomes are packed into a 30 nm chromatin fiber. In an interphase cell, this fiber is further organized into Lampbrush chromosomes, which consist of highly condensed chromatin parts and extended chromatin loop parts emanating from the condensed parts. Most parts of DNA are generally not expressed and these are highly condensed. On the other hand, the chromatin loops are expressed actively [21]. The chromatin loop is fixed at both ends and topologically constrained. In a eukaryote, the structure of DNA is also influenced by the torsional rigidity. Some previous studies have examined how topological constraints influence the conformation of nucleosomes or chromatin fiber [22–24]. Torsional stress on a nucleosome and a single chromatin are also studied by using a magnetic bead [25,26]. However, it is still unclear how torsional stress under topological constraints affects the wrapping manner of a nucleosome. In this study, we examine the relation between torsional effects and the stability of the wrapping manner of a nucleosome. We use a coarse-grained torsional model [17] to reveal the simple relation. We use a semiflexible chain and a spherical core model inspired by a nucleosome.

We report the nontrivial relation between a torsional effect and the wrapping transition of a semiflexible polymer based on a systematic molecular dynamics simulation. This paper is organized as follows: In Sec. II, we introduce the model of a core and a semiflexible chain that is used in the simulation.

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In Sec. III, we present the results of simulation. In Sec. IV, we discuss the wrapping transition in terms of free energy. Further results are interpreted in terms of free energy. Finally, we conclude in Sec. V.

## II. METHODS

To investigate the wrapping and unwrapping transition of semiflexible polymers, we carried out off-lattice molecular dynamics simulations in three-dimensional space. The model of one polymer and one core is essentially the same as that studied previously in Refs. [4,10]. Torsional potential is introduced according to methods proposed in Ref. [17]. The polymer is described as a beads-spring with positions  $\mathbf{r}_i$ ; bond vectors  $\mathbf{u}_i=(\mathbf{r}_{i+1}-\mathbf{r}_i)/|\mathbf{r}_{i+1}-\mathbf{r}_i|$ . The position of the spherical core is denoted by  $\mathbf{r}_c$ . To account for the material twisting, two normal vectors  $\mathbf{f}_i$  and  $\mathbf{v}_i$  are set at the center of gravity of monomers  $\mathbf{r}_i$  and obey  $\mathbf{v}_i=\mathbf{u}_i\times\mathbf{f}_i$  and  $\mathbf{f}_i\cdot\mathbf{u}_i=0$ . The potential energy of the system is represented by the following five terms:

$$\frac{U_{bond}}{k_B T} = \sum_{i=1}^N \frac{k_{bond}}{2} (|\mathbf{r}_{i+1} - \mathbf{r}_i| - \sigma)^2, \quad (1)$$

$$\frac{U_{bend}}{k_B T} = \sum_{i=1}^N \frac{k_\theta}{2} (1 - \cos \theta_i)^2, \quad (2)$$

$$\frac{U_{LJ}}{k_B T} = \epsilon \sum_{|i-j|>1} \left[ \left( \frac{\sigma}{|\mathbf{r}_i - \mathbf{r}_j|} \right)^{12} - 2 \left( \frac{\sigma}{|\mathbf{r}_i - \mathbf{r}_j|} \right)^6 \right], \quad (3)$$

$$\frac{U_{tor}}{k_B T} = \sum_{i=1}^N \frac{k_{tor}}{2} (\alpha_i + \gamma_i)^2, \quad (4)$$

$$\frac{U_{ad}}{k_B T} = \epsilon_{ad} \sum \left[ \left( \frac{\sigma'}{|\mathbf{r}_i - \mathbf{r}_c|} \right)^{12} - 2 \left( \frac{\sigma'}{|\mathbf{r}_i - \mathbf{r}_c|} \right)^6 \right], \quad (5)$$

where  $\theta_i$  is the angle between adjacent bond vectors, and  $\alpha_i + \gamma_i$  is the twist angle, which satisfies  $\sin(\alpha_i + \gamma_i) = (\mathbf{v}_i \cdot \mathbf{f}_{i+1} - \mathbf{f}_i \cdot \mathbf{v}_{i+1}) / (1 + \mathbf{u}_i \cdot \mathbf{u}_{i+1})$  and  $\cos(\alpha_i + \gamma_i) = (\mathbf{f}_i \cdot \mathbf{f}_{i+1} + \mathbf{v}_i \cdot \mathbf{v}_{i+1}) / (1 + \mathbf{u}_i \cdot \mathbf{u}_{i+1})$ . The monomer size  $\sigma$  and  $k_B T$  are chosen as the unit length and energy, respectively. We set the spring constant  $k_{bond}=500$ , the bending elasticity  $k_\theta=60$ , which corresponds to a persistence length  $l_p \approx 10\sigma$ , and torsional energy  $k_{tor}=60$ . The excluded-volume effect is included in the Lennard-Jones potential  $U_{LJ}$ , and we set  $\epsilon=0.20$ . For the attractive energy and excluded-volume effect between a polymer and a core, we set  $\epsilon_{ad}=5.0$ . The size of the core  $\sigma_c=2.0\sigma$  and  $\sigma'=(\sigma_c+\sigma)/2$ . We set  $N=60$  polymer beads and one core. In this paper, we use a simplified model of a nucleosome, which consists of a semiflexible chain and a spherical core:  $\sigma$ ,  $l_p$ , and  $\sigma_c$  roughly correspond to 5, 50, and 10 nm.

Even though a tightly wrapped complex is formed, the core slides along the chain and prefers positioning at the chain end [4]. To eliminate possible end effects of the chain and to achieve clear-cut configuration, we fix the center of the core as in Ref. [10].

The force  $\mathbf{f}$  and the torque  $\psi$  are calculated from Eqs. (1)–(5) and Eq. (4), respectively. The monomers obey the stochastic dynamics described by the Langevin equation without a momentum term

$$\eta \frac{d\mathbf{r}_i}{dt} = \mathbf{f}_i^U + \xi_i, \quad (6)$$

$$\eta_R \frac{d\Psi_i}{dt} = \psi_i^U + \xi_i^\psi, \quad (7)$$

where  $\Psi_i$  is the Euler angle of pure rotation,  $\eta$  is the drag coefficient for drift, and  $\eta_R$  is the drag coefficient for rotation. The constant  $\tau = \eta\sigma^2/k_B T$  is chosen to be the unit for the time scale. We set the time step as  $dt=2.5 \times 10^{-5}\tau$ . The Brownian force  $\xi_i$  and torque  $\xi_i^\psi$  satisfy the fluctuation dissipation theorem,

$$\langle \xi_i(t) \xi_j(t') \rangle = 6k_B T \eta \delta_{ij} \delta(t-t'), \quad (8)$$

$$\langle \xi_i^\psi(t) \xi_j^\psi(t') \rangle = 2k_B T \eta_R \delta_{ij} \delta(t-t'). \quad (9)$$

We set  $\eta=1.0$  and  $\eta_R=0.213$  [27].

Let us introduce the following order parameter:

$$P = \sum_{i=1}^N \rho(i), \quad (10)$$

where  $\rho(i)$  is an indicator of the pair contact:  $\rho(i)=1$  if the number of monomers which satisfy  $|\mathbf{r}_i - \mathbf{r}_c| < r_l$ , and otherwise  $\rho_{i,j}=0$ . In the following discussion we set  $r_l=2.5\sigma$ . This quantity represents the degree of contact between the polymer and the core. As we shall see later,  $P$  is directly related to the wrapping number  $N_w$  which measures how many times the chain wraps the core.

In this study, we examine the chain conformation under three different types of constraints; (i) one end is twisted (the other end is fixed), (ii) both ends are fixed, and (iii) one end is pulled (the other end is fixed). In each case, positions of five monomers at the end ( $\mathbf{r}_{N-4}$  to  $\mathbf{r}_N$ ) are fixed and their  $\Psi$  values are also fixed. The positions of the monomers at the other end ( $\mathbf{r}_1$  to  $\mathbf{r}_5$ ) are fixed in cases of (i) and (ii). In case (iii), the positions of the monomers are fixed in the  $y$  and  $z$  directions and pulled in the  $x$  direction.  $\Psi_1$  to  $\Psi_5$  are twisted in (i) and fixed in (ii) and (iii). We set  $\mathbf{r}_N=(60,0,0)$ ,  $\mathbf{r}_{N-1}=(59,0,0)$ ,  $\mathbf{r}_{N-2}=(58,0,0)$ ,  $\mathbf{r}_{N-3}=(57,0,0)$ , and  $\mathbf{r}_{N-4}=(56,0,0)$ . The monomers of  $\mathbf{r}_1$  to  $\mathbf{r}_5$  are set at  $(y,z)=(0,0)$ . The core is set at  $\mathbf{r}_c=(45,2,0)$ . We manipulate five monomers at both ends to prevent the chain crossing over the chain end and for convenience to twist and fix.

We introduce the topological number Lk, Wr, and Tw [16]. Lk is topologically invariant in the case of the circle chain or the case that the both ends of linear polymer are fixed and any part of the chain is forbidden to pass through at the end of the chain. In this paper, Lk is conserved in cases of (ii) and (iii). In the case of (i), we decrease or increase Lk linearly. Lk is defined as follows:

$$\text{Lk} = \text{Wr} + \text{Tw}, \quad (11)$$

Wr is defined as follows:

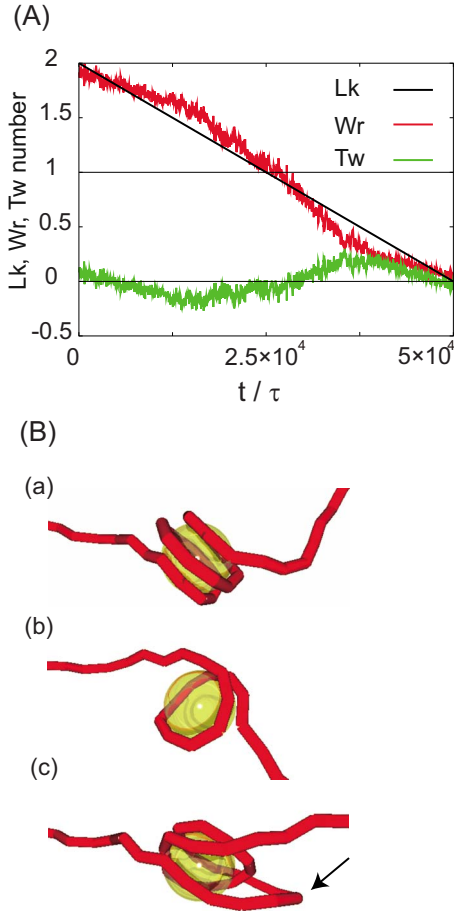


FIG. 1. (Color online) Quasistatic time evolution of the topological numbers and the chain conformation. (A) Changes in  $Wr$  (red) and  $Tw$  (green) numbers accompanied by a linear decrease in  $Lk=2$  to 0 versus time steps. The data represent averages of 10 processes. (B) Typical snapshots of the chain (red) and the core (yellow). The wrapping number  $N_W$  changes  $N_W \approx 2$  (a) to  $N_W \approx 1$  (b), and then changes to  $N_W \approx 2$  (c): (a)  $Lk=2$ ,  $Wr \approx 2$ ,  $Tw \approx 0$  at  $t=0$ , (b)  $Lk=1$ ,  $Wr \approx 1$ ,  $Tw \approx 0$  at  $t=2.5 \times 10^4 \tau$ , (c)  $Lk=0$ ,  $Wr \approx 0$ ,  $Tw \approx 0$  at  $t=5 \times 10^4 \tau$ .

$$4\pi Wr = \int_C \int_C (d\mathbf{r}_1 \times d\mathbf{r}_2) \cdot \mathbf{r}_{1,2} / |\mathbf{r}_{1,2}|^3 \quad (12)$$

where  $\mathbf{r}_1$  and  $\mathbf{r}_2$  are points that pass along the closed curve  $C$ ,  $\mathbf{r}_{12} = \mathbf{r}_2 - \mathbf{r}_1$ . In the calculation, we use the method of Ref. [16]. To make closed curve, we add flat semicircle (virtual loop) to the two ends of the chain. In this paper, the virtual loop is fixed and the radius is  $30\sigma$ .  $Wr$  completely depends on the conformation of the linear part because  $Wr$  is scale invariant and dimensionless.  $Lk$  is invariant if the chain does not cross the loop. This method is similar to the method in Ref. [28]. There is no twist in this virtual loop:  $Tw$  exists only in the linear part.  $Tw$  is defined as follows:

$$2\pi Tw = \sum_{i=1}^N (\alpha_i + \gamma_i). \quad (13)$$

We checked  $Lk$  every 100 steps to look out the unphysical topological breaking.

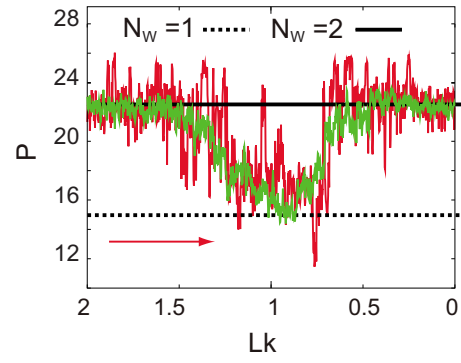


FIG. 2. (Color online) The wrapping number  $N_W$  versus  $Lk$ ;  $N_W=2$  ( $P=22.5$ ) and  $N_W=1$  ( $P=15$ ) are shown by solid and dotted lines, respectively. The chain is twisted from  $Lk=2$  to 0 linearly with time. The red (dark gray) line and green line (light gray) are the result of 1 process and the average of 10 processes, respectively.

### III. RESULTS

We first examine how the chain wraps the core with twisting;  $Lk$  (control parameter) is decreased linearly from  $Lk=2$  to  $Lk=0$  in  $t=5 \times 10^4 \tau$  ( $2 \times 10^9$  steps) without topological breaking. The end-to-end distance is  $33.5\sigma$ . Figure 1 shows (A) the evolution of topological numbers  $Lk$ ,  $Wr$ , and  $Tw$  versus time and (B) snapshots of typical complex structures at  $t=0$ ,  $2.5 \times 10^4$ , and  $5 \times 10^4 \tau$ , respectively. The initial linking number  $Lk=2$  indicates that the chain accommodates itself to the state with no twisting penalty by wrapping around the core twice in a right-handed fashion ( $Wr \approx 2$ ) [Fig. 1(B), (a)]. When the linking number is decreased, the complex first responds by the negative twisting while the writhing number remains almost fixed. This linear response regime is terminated at  $Lk \approx 1.5$ , at about which the complex exhibits a global structural change, i.e., unwrapping transition from  $Wr \approx 2$  to  $Wr \approx 1$ , and releases the torsional stress. Due to the small size of the system, the transition is not very sharp, but there is a finite range for the control parameter ( $Lk$ ), where the bimodal distribution is realized. The state with  $Wr \approx 1$  and  $Tw \approx 0$  is stable around  $Lk=1$  [Fig. 1(B), (b)]. With a further decrease in  $Lk$ , the complex exhibits a second global structural transition at  $Lk \approx 0.5$  to the state with  $Wr \approx 0$ . However, this does not correspond to the unwrapping, but rather to the wrapping transition. Figure 2 plots the order parameter  $P$  as a function of  $Lk$ , which clearly demonstrates that the second structural transition is wrapping. Examination of the snapshot indicates that each of the two turns is characterized by the opposite handedness, and this antagonistic wrapping results in  $Wr \approx 0$ . To realize such an antagonistic wrapping, there must be a “loop” in which the chain segment is not attached to the core [designated by an arrow in Fig. 1(B), (c)]. We have confirmed that its energetic stability is almost the same as that of the natural wrapped state; the total energy and the elastic bending energy of the chain in the case of  $Lk=0$  are almost the same as (a little less than) the energy in the case of  $Lk=2$ . The mean total internal energy  $u = U/(N-10)$  [ $U$  is the summation of Eqs. (1)–(5)], the mean elastic bending energy  $u_{bend} = U_{bend}/(N-10)$ , and the mean adsorption energy  $u_{ad}$

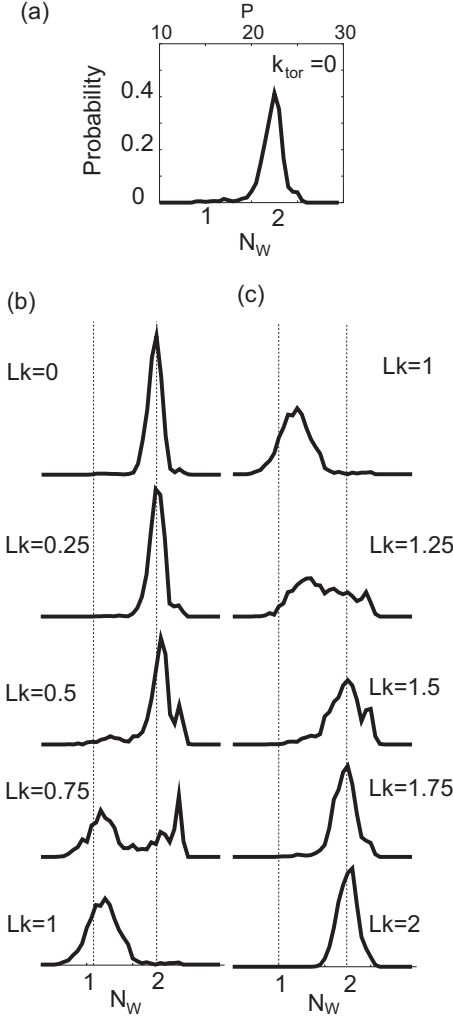


FIG. 3. Distribution of the wrapping number with Lk: (a) Without torsional stress. (b) At Lk=0, 0.25, 0.5, 0.75, and 1. (c) At Lk=1, 1.25, 1.5, 1.75, and 2.

$=U_{ad}/(N-10)$  are given as  $u=1.264$ ,  $u_{bend}=1.066$ ,  $u_{ad}=-0.981$  in the case of Lk=0 and  $u=1.269$ ,  $u_{bend}=1.086$ ,  $u_{ad}=-1.024$  in the case of Lk=2. Interestingly, although the presence of such a loop is an unnatural form, i.e., never observed in the system without topological constraint, the fluctuation of  $P$  is suppressed more in the antagonistic wrapping state ( $N_W \approx 2$  and  $Wr \approx 0$ ) than in the regular wrapping state ( $N_W \approx 2$  and  $Wr \approx 2$ ). This structural stability of the complex is probably due to steric hindrance of the chain segments which cannot cross one another (topological effect of the chain).

We examine how the chain wraps the core with Lk. Both ends of the chain are fixed. The end-to-end distance is  $33.5\sigma$ . Figure 3 shows the distribution of wrapping number versus Lk. For  $k_{tor}=0$  (no torsional effect), the peak is at  $N_W=2$ , which indicates that the chain wraps the core twice. For Lk=0, Lk=0.25, and Lk=0.5, the peak is at  $N_W=2$ . These results are almost the same as the result in Fig. 2. For Lk=0.75, there are two peaks at  $N_W=1$  and  $N_W>2$ , which indicates that the chain wraps the core once and more than twice. For Lk $\approx$ 0.75, the chain wraps and unwraps the core (see Fig. 2). For Lk=1, the peak is at  $N_W=1$ . The chain

wrapping the core once is more favorable than wrapping the core twice although the chain loses adsorption energy. For Lk=1.25, there are no large peaks; the probability is wide from  $N_W=1$  to  $N_W=2$ . For Lk=1.5, Lk=1.75, and Lk=2, the peak is at  $N_W=2$ . These results are also the same as those in Fig. 2.

These results indicate that Lk determines the stable wrapping number, i.e., how many times the chain wraps the core. For Lk=0 to Lk=1, the peak shifts from wrapping the core twice to wrapping the core once. Then, for Lk=1 to Lk=2, the peak shifts from wrapping the core once to wrapping the core twice.

## IV. DISCUSSION

### A. Internal energy

A stiff circular DNA molecule exhibits a buckling transition to a supercoiled state with an increase in Lk [29]. This instability is caused by the balance between the twisting and bending energies. In our case with the twisting of a wrapped complex, similar competition would be conceivable, but with the important difference that the effective bending modulus can be regarded “negative,” i.e., the chain favors wrapping aided by the adsorption energy, in the wrapping state (see discussion below). With this point in mind, we now present a phenomenological theory to describe the properties of the core-chain complex with a torsional effect. We refer to the internal energy in Refs. [10,14]. The internal energy in this case can be written as a sum of the adsorption, bending, and torsional energy terms.

$$E(l) = E_{ad} + E_{bend} + E_{tor}, \quad (14)$$

where  $l$  is the chain length around the core. The energetic gain due to the chain adsorption  $E_{ad}$  is written as  $E_{ad} = \epsilon l$ , where  $\epsilon$  is the adsorption energy density ( $\epsilon < 0$ ). The bending energy  $E_{bend}$  is written as

$$E_{bend} = \kappa l / 2R^2 + 8\sqrt{\kappa f} \left( 1 - \frac{1}{\sqrt{2}} \right) |\sin A|, \quad (15)$$

where  $\kappa$  is chain rigidity,  $R$  is the radius of the core (radius curvature),  $f$  is a extensional force at the end of the chain, and  $A$  is described by  $A = 2\pi l / 4\pi R$ . The second term in Eq. (15), which appears only in the case that both ends of the chain are fixed by pulling, represents the penalty in the bending energy near the core (see Ref. [14]). It has peaks at  $l = \pi R, 3\pi R$ , which makes the half-hearted wrapped state with noninteger  $N_W$  unfavorable. The torsional energy  $E_{tor}$  is written as

$$E_{tor} \approx \int_0^{L_C} \frac{k_{tor}}{2} (2\pi)^2 \left( \frac{Tw}{L_C} \right)^2 = \frac{k_{tor}}{2} (2\pi)^2 \frac{Tw^2}{L_C}, \quad (16)$$

where  $L_C$  is the contour length of the chain associated with the wrapping.  $Wr$  is related to the wrapping number  $N_W$ . We can write  $Tw = Lk - Wr \approx Lk - N_W$  in the regular wrapping state.  $N_W$  is roughly estimated as  $N_W = l / 2\pi R$ . In the antagonistic wrapping state,  $1 < N_W < 2$  and  $|Lk| \leq 1$ , we use simulation results that the chain wraps the core twice but  $Wr=0$ ;  $Wr = |l - 4\pi R| / 2\pi R$ . Finally, we get

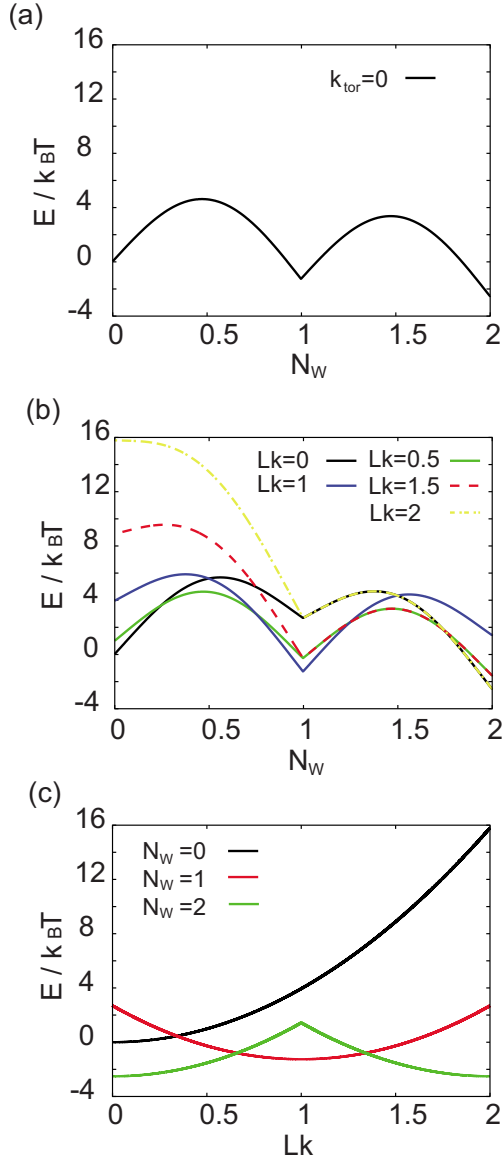


FIG. 4. (Color online) Dependence of internal energy  $E$  [Eq. (14)] on the wrapping number  $N_W$  and  $Lk$  based on the theoretical results. (a) in the case of  $k_{tor}=0$  (without a torsional effect). (b)  $Lk=0$ ,  $Lk=0.5$ ,  $Lk=1$ ,  $Lk=1.5$ , and  $Lk=2$  are shown in black, green, blue, dashed red, and dashed yellow, respectively. (c) The value of internal energy at  $N_W=0$  (black),  $N_W=1$  (red), and  $N_W=2$  (green) versus  $Lk$ .

$$E_{tor} = \begin{cases} \frac{2\pi^2 k_{tor}}{L_C} \left( Lk - \frac{l}{2\pi R} \right)^2 \\ \frac{2\pi^2 k_{tor}}{L_C} \left( Lk - \frac{|l - 4\pi R|}{2\pi R} \right)^2 \end{cases} \quad (1 < N_W < 2, |Lk| \leq 1). \quad (17)$$

We set  $\epsilon = -5.2$ ,  $R = 1.0$ ,  $\kappa = 10$ ,  $k_{tor} = 10$ ,  $f = 0.5$ , and  $L_C = 50$ . Figure 4 shows the internal energy; (a) without a torsional

effect, (b) with a torsional effect as a function of  $N_W$ , and (c) the value of the internal energy at  $N_W=0, 1$ , and  $2$  versus  $Lk$ . In this discussion, we define that the wrapping number  $N_W$  increases from 0 to 2 linearly with a increase of  $l$  from 0 to  $4\pi R$ . Without a torsional effect (see Fig. 4(a)), the most stable state is  $N_W=2$  and the stable state is  $N_W=1$ ;  $E(l)_{N_W=2} < E(l)_{N_W=1} < E(l)_{N_W=0}$ . For  $Lk=0$  to  $Lk=1$ , the internal energy at  $N_W=2$  increases [see Figs. 4(b) and 4(c)]. For  $Lk=1$  to  $Lk=2$ , the free energy at  $N_W=2$  decreases. The internal energy at  $N_W=1$  decreases for  $Lk=0$  to  $Lk=1$  and increases for  $Lk=1$  to  $Lk=2$ . These results indicate that the chain wrapping the core twice  $N_W=2$  is the most stable state for  $Lk \approx 0$  and 2 but not for  $Lk \approx 1$ . On the other hand, the chain wrapping the core once  $N_W=1$  is the most stable state for  $Lk \approx 1$ . Both terms  $E_{ad}$  and  $E_{bend}$  in Eq. (14) have a linear dependence on  $\kappa l / (2R^2) + \epsilon l = \epsilon^* l$ , so the wrapping transition takes place when  $\epsilon^* < 0 \Leftrightarrow \kappa / (2R^2) < |\epsilon|$  in the absence of a torsional effect. Therefore, the torsional effect, if included, is a dominant factor in the total free energy of the system. The stable states are determined by decreasing torsional energy. We present an example here. For  $Lk \approx 0$ , while wrapping the core twice is the most stable state, wrapping the core once is less stable. When the chain wraps the core twice, the gain in adsorption energy is high and the torsional energy is low because  $|Tw| \approx 0$  ( $Lk=0$ ,  $Tw \approx 0$ , and  $Wr \approx 0$ ). When the chain wraps the core once, the gain in adsorption energy is low and the torsional energy is high because  $|Tw| \approx 1$  ( $Lk=0$ ,  $Tw \approx \pm 1$ , and  $Wr \approx \mp 1$ ). For  $Lk=0$  to  $Lk=1$ , the stable state shifts from wrapping the core twice to wrapping the core once. For  $Lk=1$  to  $Lk=2$ , the stable state shifts from wrapping the core once to wrapping the core twice. These discussions are consistent with the results in Fig. 3.

We discuss the internal energy because the entropy in this case should be almost zero: the free energy of this system is estimated as the internal energy. In contrast, fluctuations and entropy are important factors in the case of polynucleosome.

## B. Force responses

We examine the stability of the wrapping around the core versus the stretching. Figure 5(a) shows the tensional forces of the pulled end (at  $\mathbf{r}_5$ ) versus  $L = |\mathbf{r}_5 - \mathbf{r}_{N-4}|$  (like the end-to-end distance). Figure 5(b) shows the number of monomers around the core  $P$  versus  $L$  with and without a torsional effect. For  $k_{tor}=0$  (without a torsional effect), there are two peaks at  $L \approx 30, 40$ ; this is the same result as in Ref. [10]. At  $L \approx 30$ , the chain unwraps the core from twice to once;  $N_W = 2$  changes to 1. At  $L \approx 40$ , the chain unwraps the core from once to zero;  $N_W$  changes to 0. For  $Lk=0$ , there is a large extensional force at  $l \approx 30$  because the chain wrapping the core twice is stable;  $E(l)_{N_W=2} < E(l)_{N_W=1}$ . On the other hand, there is a small peak at  $l \approx 37$  because the potential barrier between  $E(l)_{N_W=1}$  and  $E(l)_{N_W=0}$  is small. The chain unwraps the core easily. For  $Lk=0.5$ , there are two peaks at  $L \approx 30, 40$ .  $N_W$  shows almost the same behavior as in the case of

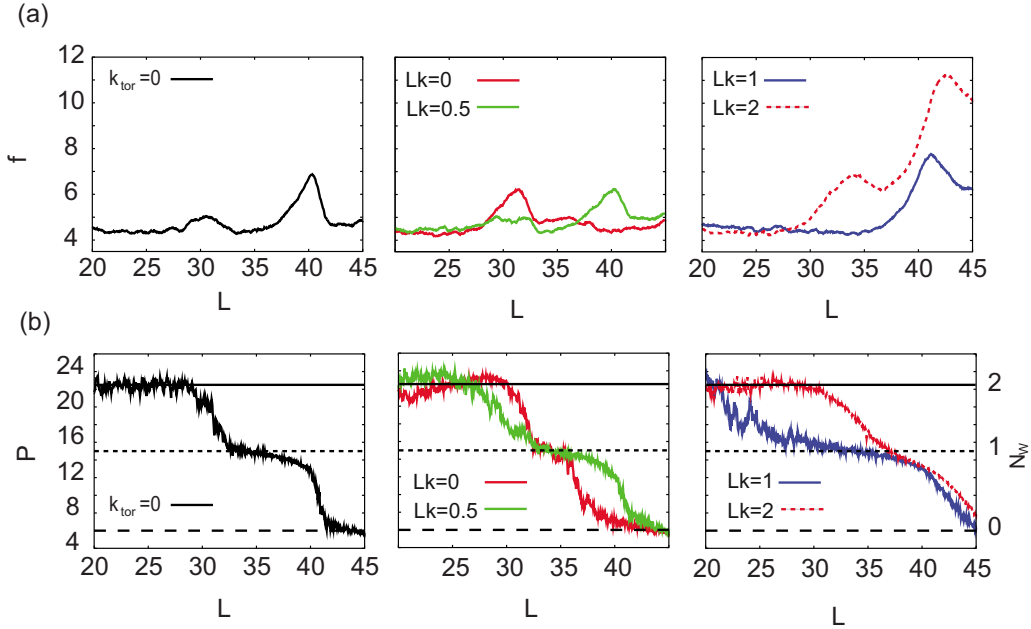


FIG. 5. (Color online) Unwrapping process by stretching. The data are averages of 10 processes:  $k_{tor}=0$  (without a torsional effect),  $Lk=0$ ,  $Lk=0.5$ ,  $Lk=1$ , and  $Lk=2$  are shown in black (left), red (center), green (center), blue (right), and dashed red (right), respectively. (a) Extensional force versus the distance of  $L$  (end-to-end distance). (b)  $N_w$  versus  $L$ . The wrapping numbers  $N_w=2$  (solid line), 1 (dotted line), 0 (dashed line) are defined by  $P=22.5$ , 15, 6, respectively.

$k_{tor}=0$ ; free energy is  $E(l)_{N_w=2} < E(l)_{N_w=1} < E(l)_{N_w=0}$ . For  $Lk=1$ , there is a large extensional force at  $L \approx 37$  because the chain wrapping the core once is stable. There is no peak upon unwrapping the core from twice to once because the chain unwraps the core easily: the potential barrier between  $E(l)_{N_w=2}$  and  $E(l)_{N_w=1}$  is small and the chain wrapping the core twice is metastable [ $E(l)_{N_w=2} > E(l)_{N_w=1} < E(l)_{N_w=0}$ ]. For  $Lk=2$ , there is a large extensional force at  $L \approx 34$  because the chain wrapping the core twice is stable. There is a very large extensional force at  $L \approx 42$  because the chain not wrapping the core is much more unstable than the chain wrapping the core once;  $E(l)_{N_w=2} < E(l)_{N_w=1} < E(l)_{N_w=0}$ . In the case of  $|Lk| > 0$ ,  $E(l)_{N_w=0}$  is large, since  $N_w=0$  implies  $Wr \approx 0$  in the present condition, thus the free energy increases quadratically with  $Lk$ ;  $E(l) \approx E_{tor} \approx (Tw)^2 \approx (Lk)^2$  [see Fig. 4(c)]. Although the actual shape of the real histone core is close to a cylinder, our spherical core model should capture the essential features in the wrapping-unwrapping transition.

In this manipulation, we fixed five monomers at both ends to prevent topological breaking. This corresponds to the case of adsorbing an end of DNA onto a tip of AFM, a microbead, and the surface of a glass. In contrast to the manipulate of a single monomer (DNA fixed at one point), a stronger force is needed to pull monomers (DNA fixed at several points). There is a kink between a free monomer and a fixed monomer, and this causes extra bending energy, which is estimated to be about  $4k_B T$  in this calculation.

## V. CONCLUSIONS

In this study, we used a model inspired by a nucleosome; a single semiflexible chain wraps around a spherical core.

The stable wrapping number, how many times the chain wraps the core, was studied under topological constraints. With twisting once (quasistatic process), an increase in  $Lk$  (topological number) from 0 to 1, the stable states are shifted from the wrapping around the core twice to once. With an additional twist, an increase in  $Lk$  from 1 to 2, the stable states are shifted from the wrapping around the core once to twice. The internal energy of the system including the torsional rigidity were the same as the results of the simulation. The torsional energy is dominant when the bending energy and the adsorption energy cancel each other; they linearly depend on the length around the core. This restrains the wrapping conformation of the chain. The wrapping number, which is related to  $Wr$ , and the torsional stress, which is related to  $Tw$ , are coupled as  $Lk = Wr + Tw$ . To decrease torsional stress, the wrapping number needs to change. The stability of the wrapping number is dependent on  $Lk$  through torsional stress.

Finally, we mention the process of unwrapping by stretching. In the case of increased torsional stress after unwrapping, there is a large extensional force because the chain changes to less stable states. On the other hand, there is a small peak with a decrease in torsional stress after unwrapping because the chain easily unwraps from the core; the chain is in a metastable state and the potential barrier is small. These results are easily verified by experiments. Suitable experimental techniques have recently been developed and it is possible to control torsion. For example, there is a study on the twisting and pulling of DNA [25,26,30]. We expect that it may be possible to apply this experiment to pulling nucleosomes with torsional constraints. We hope that our study will stimulate further experimental and theoretical developments regarding the mechanical stability of chroma-

tin and its association with biological functions.

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