Unwinding dynamics of double-stranded polymers

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We consider the unwinding of two lattice polymer strands of length N that are initially wound around each other in a double-helical conformation and evolve through Rouse dynamics. The problem relates to quickly bringing a double-stranded polymer well above its melting temperature, i.e., the binding interactions between the strands are neglected, and the strands separate from each other as it is entropically favorable for them to do so. The strands unwind by rotating around each other until they separate. We find that the process proceeds from the ends inward; intermediate conformations can be characterized by a tightly wound inner part, from which loose strands are sticking out, with length $l \sim t^{0.39}$. The total time needed for the two strands to unwind scales as a power of N as $\tau_u \sim N^{2.57 \pm 0.03}$. We present a theoretical argument, which suggests that during this unwinding process, these loose strands are far out of equilibrium. © 2010 American Institute of Physics. [doi:10.1063/1.3505551]

I. INTRODUCTION

There are several known examples of polymers in nature that are composed by two or more strands arranged in a helical conformation. One is the double-helical structure of DNA, in which two complementary sequences are held together by hydrogen bonding between A/T or C/G nucleotides. Another example is the triple helical structure of collagen. Under the appropriate thermodynamic conditions, the multistranded structure becomes unstable and the strands dissociate from each other. For a DNA molecule, the dissociation of the two strands is usually referred to as the melting transition or denaturation; this happens when the temperature is increased typically above 80 °C in standard conditions.[1] In view of its importance in many biological and biotechnological processes, various models of DNA melting have been developed to study the thermodynamical behavior as function of the sequence length and composition. Models originally proposed by Poland and Scheraga[2] and by Peyrard and Bishop[3] take into account the different unbinding energies required to dissociate complementary G/C or A/T pairs using various types of approximations, yet they are simple enough to deal with very long DNA sequences. Using an appropriate choice of parameters, they both fit reasonably well experimental data for the melting temperature of DNA sequences.[4]

The melting *dynamics* has also been studied. In 1986, Baumgärtner and Muthukumar[5] performed Monte Carlo simulations of the disentangling of two initially intertwined chains. After an initial softening of the original double helix, they reported that the time required for the actual unraveling of the chains scales with polymer length as a power law with exponent 3.3 ± 0.2. Computer technology at that time allowed for simulations of 2, 4, and 8 turns only, and their fitted exponent might very well change with increasing chain length. The dynamics of the opening of bubbles in an entangled chain has also been studied.[6–9] In addition, different extensions of the Poland–Scheraga (PS) and Peyrard–Bishop (PB) models were considered to include helical degrees of freedom of DNA molecules.[10–13] These extensions allow for rapid computations of equilibrium and dynamical properties of the melting transition, at the cost of introducing approximations that are poorly controlled and sometimes even questionable. The moves introduced to update PS models usually neglect the helicity of double-stranded DNA, which is locally conserved due to impenetrability of the two strands (the unbinding of the two strands forming the double helix requires a release of the twist through a rotation of these strands with respect to each other). With the denaturation times τ_d characterized by the scaling law $\tau_d \sim N^\beta$ for the DNA strand length N (in base pairs), the resulting values of β thus range from $\beta = 0$ (Ref. 8) to $\beta = 4/3$.[7] If local moves preserving the DNA helicity are introduced, a very slow melting is instead observed, with $\beta \approx 3$.[9] A second simplification intrinsic in PS models is that helical fragments and loops are described by equilibrium partition functions. This description can be too simplified in systems where the dynamics of the unwinding process is too fast to allow for the full structural relaxation within these loops. PB models have as a major simplification the possibility for complementary bases to orbit around a virtual central axis of the macromolecule. This yields denaturation times scaling linearly with the chain length.[13] Given such spread of results and uncontrolled simplifications in these models, we must conclude that we are still missing the understanding of how DNA length affects the time for its strands to disentangle.

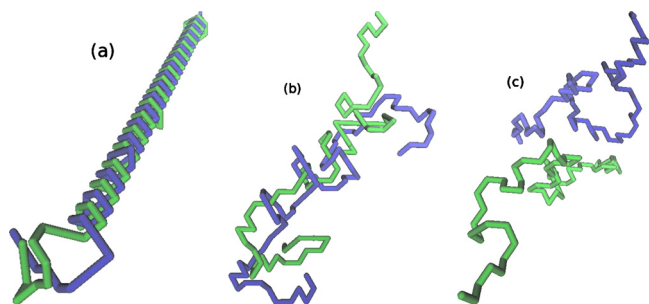a)Electronic mail: enrico.carlon@fys.kuleuven.be.

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FIG. 1. Snapshots of the polymer configurations during unwinding for two strands of length $N=100$ each. The initial conformation is fully double-helical all along its length. (a) Snapshot after short time from the beginning of the simulation; opening begins mainly from the two ends, although small bubbles within the chain are also visible. (b) Snapshot at later times. (c) Separation.

In order to gain more direct insight into the dynamics of the melting process of double-stranded molecules, we investigate the unwinding dynamics of double-stranded three-dimensional long polymers using Monte Carlo simulations in the absence of hydrodynamic interactions. No binding energies between the two strands are taken into account during the unwinding process, corresponding to the case of a double helix brought rapidly to a temperature well above its melting point. For such a setup, the strands unwind from each other as it is entropically favorable for them to do so. We follow a procedure very similar to that of Ref. 5, except that our chains are longer and more tightly wound. Figure 1 shows three configurations: (a) at the early stages of unwinding, (b) during the unwinding process, and (c) at the end of the unwinding, when the two stands are separating from each other. The main scope of this manuscript is twofold: in Sec. II, we study the unwinding time τ_u as a function of N—high precision simulations for polymers of length up to $N=1000$ show that τ_u scales as a power law $\tau_u \sim N^{\beta}$ with $\beta=2.57 \pm 0.03$. In Sec. III, we show that the intermediate conformations can be characterized as a tightly wound inner part, to which unwound single strands are connected. The length of the unwound strands increases with time in a power law fashion as $l(t) \sim t^{0.39}$. With a theoretical argument, we find an upper bound for the radius of gyration of the loose ends, which excludes the equilibrium value. This demonstrates that the unwinding is a far from equilibrium process.

II. UNWINDING TIME

In the simulation, the polymers reside on a face-centered-cubic lattice with a lattice spacing of $\sqrt{2}$ and are initialized in a double-helical state. The polymers evolve in time through a long sequence of single-monomer moves, under the restriction that at all times, the polymer backbones are self- and mutually avoiding. Each allowed move occurs with a statistical rate of unity. To give the polymers some elasticity, the self-avoidance condition is lifted for monomers that are direct neighbors along the same chain. A detailed description of this lattice polymer model, its computationally efficient implementation, and a study of some of its properties and applications can be found in Ref. 14. This model reproduces known features of the Rouse dynamics[15] and of
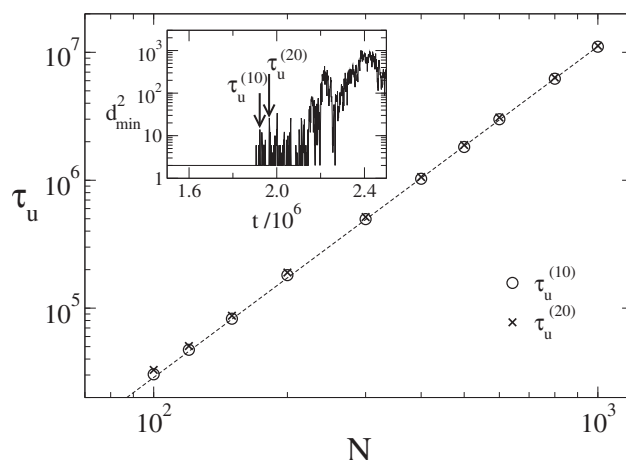

FIG. 2. Double-logarithmic plot of the average unwinding time as a function of strand length. The circles are obtained with an unwinding threshold of $d_0^2=10$, while the crosses correspond to a threshold of $d_0^2=20$. The straight dashed line is a fit to the data corresponding to an unwinding exponent of $\beta=2.57$. Inset: Plot of $d_{\min}^2(t)$ vs time for a run with strands of length $N=500$. The arrows indicate the first time that this distance reaches its threshold value $d_0^2=10$ or 20.

the equilibrium properties[16] of single self-avoiding polymers. As the moves respect the no-crossing condition between strands, we expect that the long time behavior of unwinding discussed in this study is of universal nature and is not affected by microscopic details and lattice effects.

Let $\vec{r}_i^{(1)}(t)$ and $\vec{r}_i^{(2)}(t)$ be the lattice positions of the ith monomers on the two strands at time t ($0 \le i \le N$). We consider the minimal distance between two strands defined as $d_{\min}(t) = \min_{i,j}|\vec{r}_i^{(1)}(t) - \vec{r}_j^{(2)}(t)|$. The inset in Fig. 2 shows a plot of $d_{\min}^2(t)$ as a function of time for a run. The choice of an initial double-helical conformation implies that $d_{\min}=\sqrt{2}$ at $t=0$. Note that $d_{\min}(t)$ remains constant up to a time $t \approx 1.9 \times 10^6$ in the inset in Fig. 2 and then starts fluctuating and increasing in time. We define the unwinding time τ_u as the time at which $d_{\min}(t)$ exceeds some threshold value for the first time. For the threshold value d_0, we took $d_0^2=10$ and $d_0^2=20$. The higher threshold value gives a slightly higher estimate of the unwinding time [$\tau_u^{(10)}$ and $\tau_u^{(20)}$ in Fig. 2]. However, as the polymer length increases, the ratio of $\tau_u^{(10)}/\tau_u^{(20)}$ converges to 1, as shown in Table I; hence, the two quantities have the same scaling behavior in N.

Figure 2 and Table I show the behavior of $\tau_u^{(10)}$ and $\tau_u^{(20)}$ as a function of polymer length. We note that the scaling of unwinding times is a power of the strand length: from a linear regression of the data for $N>30$, we find the values $\beta=2.58 \pm 0.03$ ($d_0=10$) and $\beta=2.56 \pm 0.03$ ($d_0=20$), from which we obtain the result anticipated above, $\beta=2.57 \pm 0.03$.

III. CHARACTERIZATION OF INTERMEDIATE CONFORMATIONS

Given the topological constraint, each strand faces while unwinding, we expect the unwinding dynamics to unroll from the two ends of the initial double-stranded complex, progressing inwards with increasing time (Fig. 3). Note that because of the elasticity of the model used in the simulations,

TABLE I. Average unwinding times $\tau_u^{(10)}$ and $\tau_u^{(20)}$ as a function of polymer length N for threshold values $d_0^2=10$ and $d_0^2=20$, and the ratio of these two times. Times are obtained by averaging over 120 simulations.

N	$\tau_u^{(10)}$	$\tau_u^{(20)}$	$\tau_u^{(20)}/\tau_u^{(10)}$
60	1.23×10^4	1.12×10^4	1.093
80	1.80×10^4	1.97×10^4	1.096
100	3.04×10^4	3.29×10^4	1.082
120	4.73×10^4	5.06×10^4	1.070
150	8.27×10^4	8.75×10^4	1.055
200	1.81×10^5	1.90×10^5	1.048
300	4.97×10^5	5.16×10^5	1.038
400	1.03×10^6	1.06×10^6	1.032
500	1.82×10^6	1.88×10^6	1.036
600	3.00×10^6	3.10×10^6	1.032
800	6.22×10^6	6.35×10^6	1.021
1000	1.11×10^7	1.13×10^7	1.017

a partial opening up of the inner wound part is not ruled out by the model: it is the physics of the problem that seems to suppress this. In order to connect this physical picture with the observed scaling $\tau_u \sim N^{2.57 \pm 0.03}$, we considered the quantity $d_{\min}(i,t) = \min_j |\vec{r}_i^{(1)}(t) - \vec{r}_j^{(2)}(t)|$, which is the minimal distance from the ith monomer of the first strand to any other monomer of the second strand. Its average square $\langle d_{\min}^2(i,t) \rangle$ is plotted in Fig. 4 for a strand length equal to $N=500$. The different data are for increasing time step snapshots taken at time intervals equal to $t/10^5 = 1, 2, \ldots, 10$ (from bottom to top). The quantity $\langle d_{\min}^2(i,t) \rangle$ is minimal in the middle, while it increases in time from the two edges, in agreement with the physical picture proposed in Fig. 3. We consider now the normalized profile $\langle d_{\min}^2(i,t) \rangle / \langle d_{\min}^2(0,t) \rangle$. For this quantity, we expect the following scaling behavior, as a function of the distance from the end monomer ($i=0$)

$$\frac{\langle d_{\min}^2(i,t) \rangle}{\langle d_{\min}^2(0,t) \rangle} = f(i/l(t)), \qquad (1)$$

with $f(\ )$ being a scaling function and $l(t)$ a characteristic length depending on time. The inset in Fig. 4 show that the normalized profiles at different times collapse when a rescaling $i/t^{0.39}$ is used, which implies that $l \sim t^{0.39}$. This is consistent with the exponent determined from the scaling of unwinding time as $l \sim t^{1/\beta} = t^{0.39}$.

In order to gain insight into the unwinding, we set up a simple analytical model of the process, assuming that the unwinding is sufficiently slow so that the conformation of
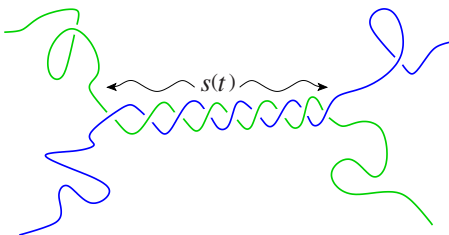
FIG. 3. Sketch of a double-stranded polymer during the unwinding dynamics. At time t, we expect to find a double-stranded region of curvilinear length $s(t)$ terminates with two single strands of lengths $(N-s(t))/2$ at both edges, $s(t)$ being a decreasing function of t.
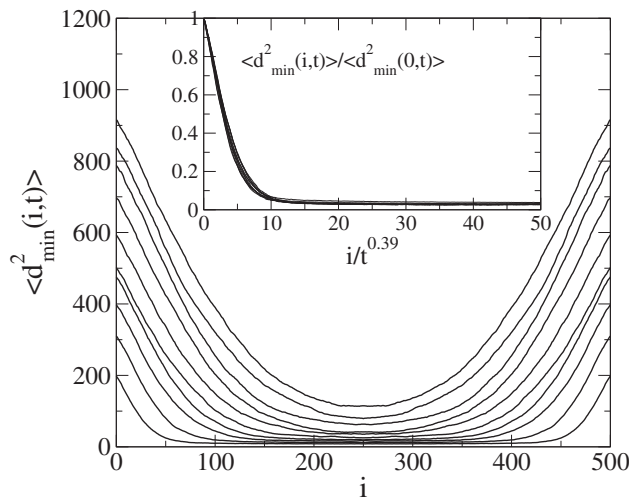
FIG. 4. Average squared minimal distance $\langle d_{\min}^2(i,t) \rangle$ as a function of monomer number i, for polymers with length $N=500$. From bottom to top, the curves are obtained at times $t/10^5 = 1, 2, \ldots, 10$. Inset: collapse of $\langle d_{\min}^2(i,t) \rangle / \langle d_{\min}^2(0,t) \rangle$ for polymers of length $N=1000$ again at times $t/10^5 = 1, 2, \ldots, 10$. The vertical scale is normalized so that all curves start from a common value at $i=0$. The horizontal scale is divided by $t^{0.39}$. This exponent is consistent with that obtained from the scaling of the unwinding time.

the loose strands can be approximated by equilibrium ones at all times. We will show that this approach predicts an unwinding dynamics which is slower than what is observed in simulations. We therefore conclude that the unwinding we observe is a far from equilibrium process.

Consider an intermediate conformation that consists of two single-stranded coils of $N-s(t)$ attached to a double-stranded helical part of length $s(t)$. We estimate the free energy F as a function of $s(t)$ from the partition function for a double-helical segment of length s is $Z_{\text{helix}} \sim \mu_h^s$ and that of a single-stranded coil $Z_{\text{coil}} \sim \mu_c^{N-s}$, where μ are the connectivity constants. In other words,

$$\beta F = -s \log(\mu_h) + 2(N-s)\log(\mu_c). \qquad (2)$$

As an infinitesimal portion ds of the double helix unwinds, the change in free energy is thus given by

$$dF = -\beta^{-1} \log(\mu_c^2/\mu_h)ds \equiv -K_1 ds. \qquad (3)$$

During this infinitesimal unwinding, the single-stranded coils are displaced over a distance dr due to the rotational motion around the axis of the helix: the coils describe a fraction of a circle of radius R_v perpendicular to the axis of the helix, where R_v is the distance from the helix axis to the coil's center of mass. In equilibrium, we expect $R_v \sim (N-s)^\nu$, with ν being the Flory exponent. This implies that

$$dr \propto R_v ds \propto (N-s)^\nu ds. \qquad (4)$$

During this process, the work done against friction equals

$$dW = \gamma \dot{r} dr = \gamma R_v^2 \dot{s} ds, \qquad (5)$$

where for Rouse dynamics, the friction on the single-stranded coils is proportional to their lengths: $\gamma \propto N-s$. Since the work done against friction cannot exceed the available free energy, we obtain the inequality

$$K_2(N-s)^{1+2\nu}\dot{s}\,ds \leq K_1\,ds. \tag{6}$$

If this inequality were saturated, the unwinding process would be described by

$$K_1/K_2 = -[N-s(t)]^{2\nu+1}\frac{ds}{dt}. \tag{7}$$

The integration of Eq. (7) yields a scaling of the unwinding time as $\tau_u \sim N^{2\nu+2} = N^{3.18}$ (since $\nu = 0.59$), which is obtained from Eq. (7) by setting $s(\tau_u) = N$. Indeed, a visual investigation of the unwound parts during simulations reveals that these show a tendency to be spiral-like and contain a significant amount of coiling. A precise quantification of the amount of spiraling is very difficult due to the lack of a clean definition of the central axis of the spiral. This argument predicts a very slow unwinding compared to that which is actually observed in simulations, suggesting that unwinding proceeds through nonequilibrium states. In an early study of unwinding,[5] the scaling $\tau \sim N^{3.3(2)}$ was computed for shorter polymers (up to $N=65$; with 2, 4, or 8 turns in the double helix) and for helices less tightly bound than considered here. The exponent of Ref. 5 most likely describes a preasymptotic scaling regime. The exponent reported in Ref. 5 is however compatible with that predicted from Eq. (7). This suggests that the early stages of unwinding are probably well captured by the mechanisms underlying the derivation of Eq. (7), but that the asymptotic scaling regime is dominated by a mechanism that is faster for longer chains.

IV. SUMMARY AND CONCLUSIONS

Summarizing, we introduced a lattice model for studying the unwinding dynamics of a long three-dimensional double-stranded polymer, with excluded volume effects taken into account. The lattice nature of the model, combined with an efficient encoding of the dynamics, allows one to simulate long polymers (up to $N=10^3$) for very long time ($t=10^7$ Monte Carlo steps). Our numerical results show that the unwinding time scales with the polymer length as a power law with exponent $\beta = 2.57(3)$ with Rouse dynamics. An analysis of a simple analytical model of the process suggests that the unwinding we observe is a far from equilibrium process; therefore, it cannot be understood in terms of a slow dynamics evolving through quasiequilibrium states, e.g., using free energy arguments.

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