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Monte Carlo Study on Spontaneous Recoil of Confined DNA Chain

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A part of a long DNA chain was driven into a confined environment by an electric field, while the rest remains in the higher-entropy region. Upon removal of the field, the chain recoils to the higher-entropy region spontaneously. This dynamical process was investigated by Monte Carlo simulations. The simulation reproduces the experimentally-observed phenomenon that the recoil of the DNA chain is initially slow and gradually increases in speed due to the presence of the confinement-entropic force. The results show that with increasing the dimension or decreasing the spacing of the nanopillars the recoil velocity of the DNA chain will increase. Further analysis suggests that the characteristic entropy per monomer in the confinement is proportional to the area fraction of the free part in the confinement.

Key words: DNA chain, Spontaneous recoil, Monte Carlo simulation, Effective entropy

I. INTRODUCTION

The dynamical response of biopolymers to external force and confinements is a ubiquitous problem occurring in biological situations. It encompasses various situations such as polymers transport across membranes [1,2], injection of DNA and RNA from a virus to bacteria after their synthesis [3], gene swapping between the guest and the host bacteria through pili, etc. The motion of polymers in a confined medium is also technologically important in biotechnologies and industrial processes, such as DNA sequencing [4,5], oil recovery and separation, and gene therapy [6,7], etc. Accordingly, the dynamical behavior of the polymer in a confined medium has attracted considerable interest in recent years (experimental [8-11], theoretical [12-15], and numerical studies [16,17]).

During moving into a confined environment, the polymer chain faces a large entropic barrier due to the decrease in the number of available configurations [13,18,19]. In order to overcome this barrier and to speed up the motion of the polymer, an external field or interaction is needed [9,20-23]. However, if a DNA chain has been driven by an electric field to enter a region constrained by densely spaced nanopillars and captured with one part of it remaining in the free region, this part will create an impetus for the chain to evacuate the low-entropy region and return to the high-entropy region spontaneously. Turner *et al.* observed, for the first time, this process of long chain motion was caused by a confinement-mediated entropic force [24]. Individual DNA molecules stained with fluorescent dye were observed in a nanofabricated structure while recoiling from a quasi-two-dimensional region constrained by 35 nm pillars densely. Meanwhile, they constructed a simple kinetic model which is consistent with the experimental observations. However, a detailed examination of the recoil process is lacking due to the constraint of the experimental conditions. A careful study of the recoil velocity as a function of the dimension and spacing of the nanopillar is needed, which is helpful for a better understanding of how entropy decreases with confinement.

Inspired largely by this spirit, in the present work we focus on the spontaneous recoil process of single DNA chain in the nanofluidic structure fabricated by Turner *et al.* [24]. Our results agree with experimental observation and the simple model proposed by Turner. Furthermore, a presentation of the results showing how the recoil velocity of the DNA chain depends on the dimension, and spacing of the regular nanopillars is given. The dependence of the confinement entropy on the nanopillar dimension is discussed.

II. MODEL

In the present study, the two-dimensional bond fluctuation model (BFM) combined with single-segment Monte Carlo moves was adopted. This model has been described in detail [25,26] and has been used extensively in polymer simulations, so we only recall its main characteristics. The simulation space is divided into unit cells so as to form an orthogonal lattice, and the macromolecule is represented by a chain of N effective monomers each occupying 2^d lattice sites (where d is the dimensionality of space) to cover one unit cell. A given lattice site can only belong to one monomer at

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a time in order to account for excluded volume interactions, and the bond vector connecting two successive monomers is constrained to a predefined set, chosen so as to avoid bond crossing; there are 36 and 108 allowed bond vectors in 2D and 3D respectively.

The motion of the chain is generated from local elementary moves: for each trial move, we randomly select a monomer and attempt to move it randomly by one lattice unit along one of the axis directions. Provided the volume exclusion and bond constraints are respected, the move is accepted according to the Metropolis criterion [27]. The elementary time unit of the simulation is given by one Monte Carlo step (MCS), defined as N trial moves.

The nanofluidic structures depicted in Fig.1 is incorporated in the simulation by means of occupied lattice sites forming the regular nanopillars that match the device geometry. A periodic boundary condition is employed along the y direction. The dimension and the spacing between the nearest neighboring nanopillars are $D_{\rm pillar}$ and $S_{\rm pillar}$, respectively. A DNA chain of length N=200 is initially placed in the pillar-free region. A pulse electric field is applied to drive it partially into the dense-pillar region. The Metropolis weight associated with the movement of a monomer bearing a unit charge q=1 is then simply given by $\exp(-q\delta V/k_{\rm B}T)$, where δV is the potential difference between the two adjacent lattice sites involved, $k_{\rm B}$ is Boltzmann's constant, and T is the absolute temperature.

When the DNA chain has been driven into the dense-pillar region with some portion still in the pillar-free region, the electric field is removed. The part of the chain in the dense-pillar region recoils into the pillar-free region spontaneously. During this process, the distal-end position of the chain from the interface of two regions, L_1, as well as the number of the monomers in the dense-pillar region, n_1, are recorded as a function of recoil time. It is important to keep in mind that, apart from strict volume exclusion, we neglect interactions between the DNA chain and the nanopillars as well as the electrostatic repulsion between the charged monomers, in accordance with the analysis of Ref.[24]. Statistics were compiled based on at least 100 independent simulations for each set of parameters. It should be pointed out that the time, when all the monomers recoil out of dense-pillar region, is set to be zero and all the data are averaged.

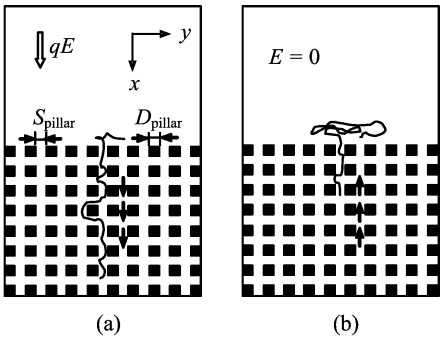

FIG. 1 A schematic representation of the studied system. (a) The DNA chain was driven partway into the low-entropy region by a pulse electric field. (b) The chain recoils to the high-entropy region spontaneously when the field has been removed. The dimension and spacing of the nanopillars are $D_{\rm pillar}$ and $S_{\rm pillar}$ respectively. The arrows point the direction of the chain movement.

III. RESULTS AND DISCUSSION

To explain the observed recoil motion of the DNA chain in their nanofluidic structure, Turner *et al.* have constructed a simple kinetic model, in which the average distal-end position of the chain from the interface of two regions, L_1, exhibits square-root time dependence,

$$L_1 = \sqrt{-\frac{2f(t-t_0)}{\rho}} \tag{1}$$

where t_0 is the time at which the chain completes its recoil, f the impetus, and ρ the specific drag [24]. Following their approximation and replacing the length occupying ith region, L_i, by the monomer number in either region, n_i, the total entropy of the DNA chain can be expressed as

$$\begin{aligned} S &= n_1 s_1 + n_2 s_2 \\ &= n_1(s_1 - s_2) + N s_2 \end{aligned} \tag{2}$$

where n_1 and n_2 are the monomer numbers in either region with n_2=$N-n_1$, and s_1 and s_2 are the characteristic effective entropies per monomer in the two regions. The free energy F=$U-TS$ and the force f is $\mathrm{d}F/\mathrm{d}A_1$, where A_1 is the contour length of the chain occupying the dense-pillar region, A_1=$l_p n_1$, and l_p is the persistence length of the model. So that

$$\begin{aligned} f &= \frac{\mathrm{d}(U-TS)}{\mathrm{d}A_1} = -\frac{T}{l_p}\frac{\mathrm{d}S}{\mathrm{d}n_1} \\ &= -\frac{T}{l_p}(s_1 - s_2) \propto (s_1 - s_2) \end{aligned} \tag{3}$$

From Eq.(3) it is clear that the impetus, f, is proportional to the entropy difference per monomer between the two regions. On the other hand, the model that relates the recoil velocity to the impetus and viscous drag coefficient is f=gv. When, as in our simulations, the chain is long compared with the hydrodynamic screening length the drag coefficient should be approximately proportional to the contour length of the chain [8]. So, we can write the drag coefficient in terms of the specific drag, ρ, as g=ρA_1. Combining these equations we have

$$\frac{\mathrm{d}A_1}{\mathrm{d}t} = -\frac{f}{\rho A_1} \tag{4}$$

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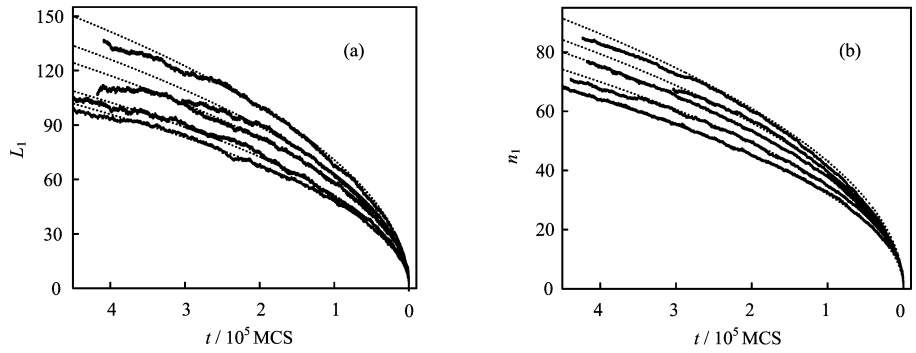

FIG. 2 (a) The average end-monomer position of the chain from the interface of two regions, L_1, as a function of the recoil time t; (b) Average monomer number in the confinement, n_1, as a function of the recoil time t. $S_{\rm pillar}$=3 keeps constant. From upper to lower curves, $D_{\rm pillar}$=8, 5, 4, 3, 2, respectively. The dot lines are the fit lines to the data respectively.

Substituting A_1=$l_p n_1$ into Eq.(4), we get

$$\frac{{\rm d}n_1}{{\rm d}t} = -\frac{f}{\rho {l_p}^2}\frac{1}{n_1} \tag{5}$$

This can be integrated to give

$$n_1 = \sqrt{-\frac{2f(t-t_0)}{\rho {l_p}^2}} \tag{6}$$

where t_0 is the time at which the chain completes its recoil. Before that $(t-t_0)$ is negative. The monomer number of the chain in the confinement, n_1, exhibits square-root time dependence also, but with a different parameter, the ratio $2f/\rho {l_p}^2$.

Figure 2(a) shows the average end-monomer positions of the chain in the confinement from the interface of two regions, L_1, as a function of the recoil time t, as well as the fit lines to them using Eq.(1). In agreement with the experimental observation, the recoil is initially slow and gradually increases in speed. It is quite different from an elastic recoil which is initially rapid followed by a gradual slowing [28-30]. This suggests the presence of a confinement-entropic force, distinct from entropic elasticity. Note that the simulation curves are always below the fit lines at the initial stage of the recoil process, which is consistent with the experimental observation, though the discussion was omitted. At the initial stage of the recoil process, the part of the chain in the dense pillar region is in the relaxation state, and the distal end of the chain is insensitive to the impetus arising from the segments near the interface until the part in the confinement is stretched. In contrast, the monomer number of the chain in the confinement, n_1, displays more sensitive characteristics to the impetus as soon as the field was removed, and the simulation curves of n_1 accord with the fit lines better than L_1 in the total recoil process (Fig.2(b)). On the other hand, the expression of the total entropy of the chain, Eq.(2), is more suitable than that presented by Turner *et al.* [24]. So the measurements of the monomer number in the confinement, n_1, are more suitable to describe the recoil behavior of the DNA chain than the less sensitive, though experimentally simpler, measurements of L_1.

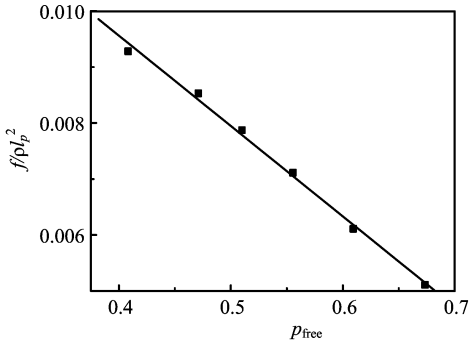

FIG. 3 $f/\rho {l_p}^2$ as a function of the area fraction of free part in the dense-pillar region, $p_{\rm free}$.

When the dimension or spacing of the nanopillars changes, the number of available conformations of the DNA chain in the confined region also varies, and thus the alteration of entropy difference as well as the free energy difference between two regions, influences the recoil velocity of the chain. In order to determine the influence of the nanopillar dimension on the recoil velocity of the chain, we carried out a series of simulations for a fixed spacing between the nearest neighboring nanopillars ($S_{\rm pillar}$=3), and for a range of values of the nanopillar dimension, $2 \le D_{\rm pillar} \le 8$. Figure 2 shows L_1 as well as n_1, as a function of recoil time t. Obviously, the recoil velocity of the DNA chain increases as the dimension of the nanopillar increases. It is quite different from the recoil produced by entropic elasticity, for which the velocity should keep constant when the spacing of the nanopillars is the same. When the dimension of the nanopillars increases, the difference between the numbers of available conformations in two regions becomes larger, bringing a consequent increase of entropy as well as free energy difference between two regions, and thus strengthens the impetus for the recoil of the chain and accelerates its velocity. According to

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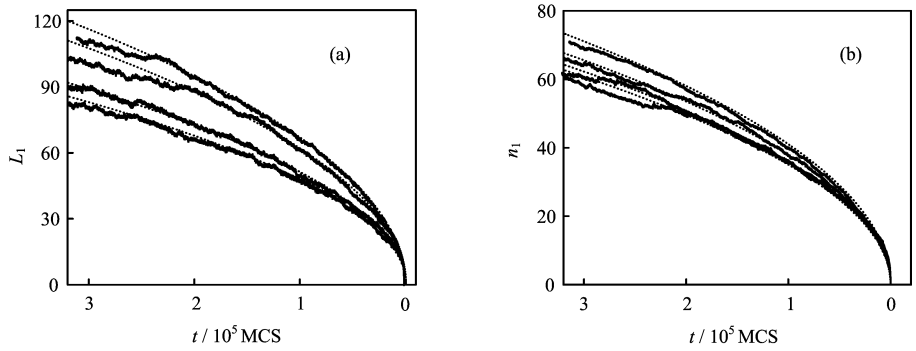

FIG. 4 (a) The average end-monomer position of the chain from the interface of two regions, L_1, as a function of the recoil time t. (b) Average monomer number in the confinement, n_1, as a function of the recoil time t. $D_{\rm pillar}$=6 keeps constant. From upper to lower curves, $S_{\rm pillar}$=3, 4, 5, 6, respectively. The dot lines are the fit lines to the data respectively.

Eq.(6), the ratio, $f/\rho {l_p}^2$, for different $D_{\rm pillar}$, could be obtained from the fit lines. In Fig.3 we present $f/\rho {l_p}^2$ as a function of area fraction of free part in the dense-pillar region, $p_{\rm free}=1-{D_{\rm pillar}}^2/(D_{\rm pillar}+S_{\rm pillar})^2$. It can be seen that there is a clear linear relationship between $f/\rho {l_p}^2$ and $p_{\rm free}$,

$$\frac{f}{\rho {l_p}^2} \propto -p_{\rm free} \tag{7}$$

Since in this situation, the spacing of the nearest nanopillars is fixed, so the specific drag, ρ, which depends only on the distance of adjacent nanopillars, keeps constant [8]. So, we have

$$f \propto -p_{\rm free} \tag{8}$$

Combining Eq.(3) with Eq.(8) yields

$$s_1 - s_2 \propto p_{\rm free} \tag{9}$$

The characteristic entropy per monomer in the pillar-free region, s_2, keeps constant when the spacing of the nearest nanopillars varies. Substituting this result in Eq.(9), we get

$$s_1 \propto p_{\rm free} \tag{10}$$

Therefore, remarkably, the entropy per monomer in the confinement is proportional to the area fraction of free part in the confinement.

Having established the effect of nanopillar dimension on the recoil process, we proceed to determine the influence of the spacing of nanopillars on recoil velocity. Figure 4 presents the average end-monomer position of the chain from the interface, L_1, as well as the monomer number of the chain in the confinement, n_1, as a function of recoil time for different spacing of nanopillars, $S_{\rm pillar}$, by fixing nanopillar dimension $D_{\rm pillar}$=6. It can be seen that as the spacing of nanopillars $S_{\rm pillar}$ increases, the recoil velocity of the chain decreases. Experimental and simulation results [8,30] have indicated the elastic recoil increases in speed when $S_{\rm pillar}$ becomes

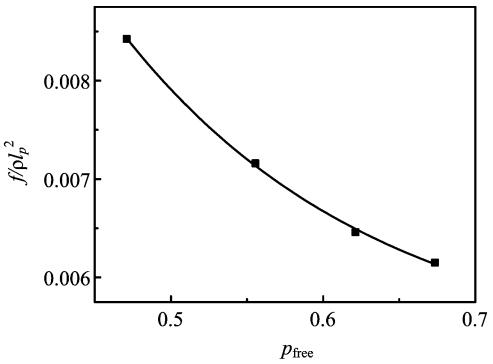

FIG. 5 $f/\rho {l_p}^2$ as a function of the area fraction of free part in the dense-pillar region, $p_{\rm free}$.

larger. This confirms the conclusion that the recoil of the chain in this simulation is due to confinement rather than stretching again. When $S_{\rm pillar}$ increases, the number of available conformations in the dense-pillar region increases while that in the pillar-free region remains unaltered, and the consequent increase of the entropy difference as well as free energy difference between two regions, reduces the impetus for the chain to recoil. However, unlike the previous case (Fig.3), the area fraction of the free part in the dense-pillar region $p_{\rm free}$, in this situation, dependence of the ratio $f/\rho {l_p}^2$, exhibits a nonlinear behavior, as shown in Fig.5. A reasonable explanation of this disagreement relies on the fact that when $S_{\rm pillar}$ varies, the consequent alteration of the lateral fluctuation size of the DNA chain changes the value of the specific drag, ρ. The effect of the lateral fluctuation size of the chain upon ρ has been described in detail by Bakajin *et al.* [8].

IV. CONCLUSION

Using a two-dimensional coarse-grained lattice model, we studied the recoil process of a DNA chain that has been driven partway into a high-entropy re-

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gion populated with densely spaced regular nanopillars. We reproduce the experimentally-observed phenomenon that the recoil of the DNA chain is initially slow and gradually increases in speed. This result suggests the presence of a confinement-entropic force, distinct from the entropic elasticity. Further simulation results show that increasing the dimension of the nanopillars or decreasing the spacing of the nanopillars will accelerate the recoil velocity, and the characteristic entropy per monomer in the confinement is proportional to the area fraction of free part in the confinement. It should be noted that in three dimensions, the scaling relationships expressed by Eq.(1) and Eq.(6) are still valid because the kinetic model is independent of dimensionality of space and our simulation results have confirmed it (data not shown). We hope our results are helpful to understand the behavior of the DNA chain in a confinement.

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