

Rapid Communications

Statistics of Polymer Capture by a Nanopore: A Brownian Dynamics Simulation Study*

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Abstract We investigate the statistics of polymer capture by a nanopore using Brownian dynamics simulations. It is found that when the velocity flux is greater than a critical velocity flux, the capture picture is a random selection process, otherwise it tends to a statistical process governed by energetic considerations. In addition, the chain ends capture probability decreases as the chain length increases and satisfies a power-law scaling of $P_0(N) \sim N^{-0.8}$.

Keywords: Polymer capture; Critical velocity flux; Brownian dynamics.

Recently single-molecule experiments probing single-stranded DNA or RNA translocation through a membrane nanopore have fueled considerable interest. In fact, the translocation of biopolymers is a complex phenomenon, thus, coarse-grained computational models capable of describing the conformation and motion of polymer chains in confined geometries would be of considerable significance for the physical nature and application foreground of such a phenomenon^[1,2].

However, most of simulation work focused on head-to-tail translocation type (unfolded type), that is to say, one end of a chain is pinned inside the nanopore before simulations. In contrast, some studies found that the nanopore can capture polymer chain some distance from its ends and pull it through in a folded configuration (folded type)^[3–7]. So there is a unanswered question concerning the fundamental physics behind such a result and the competition between unfolded type and folded type may alter the translocation dynamics. Importantly, the study of capture process can not only provide snapshots of insertion moment, but also offer clues about probing mechanisms and applications of single-molecule experiments. Storm *et al.*^[5] inferred the polymer chain ends are more likely to be captured due to the lower energetic cost, which implies the capture picture is a statistical process governed by energetic considerations. Instead, Stein *et al.*^[6] inferred the bias of unfolded type to be a consequence of random selection by the nanopore. So a simple model that can systematically investigate the capture process and evaluate these competing pictures is still missing.

Here, we employed Brownian dynamics (BD) to simulate the capture process of linear polymer chains in a channel of dimensions (L_x, L_y, L_z). In the middle of this geometry we create a narrow pore of size (L, D, D) as depicted in Fig. 1(a). In the simulations, the polymer chains are modeled as bead-spring chains of Lennard-Jones (LJ) particles with the finite extension nonlinear elastic (FENE) potential. Both excluded volume and van der

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Waals interactions between beads are taken into account by a repulsive LJ potential:

$$U_{\text{LJ}}(r) = \begin{cases} 4\epsilon[(\sigma/r)^{12} - (\sigma/r)^6] + \epsilon, & r \leq 2^{1/6}\sigma \\ 0, & r > 2^{1/6}\sigma \end{cases} \quad (1)$$

where r is the center-of-mass distance between two beads, σ is the diameter of a bead, and ϵ is the depth of the potential. The connectivity between neighboring beads is modeled as a FENE spring with

$$U_{\text{FENE}}(r) = -0.5\kappa R_0^2 \ln[1 - (r/R_0)^2] \quad (2)$$

where κ is the spring constant and R_0 is the maximum allowed separation between connected beads. As shown in Fig. 1(a), the channel and the nanopore are formed by the same stationary particles within distance σ from one another which interact with the beads by the same repulsive LJ interaction as described above.

The background flow field is simulated by using Lattice-Boltzmann method (LBM). In LBM, the single-particle distribution function $f_i(\mathbf{r}, t)$ constitutes the fundamental quantity. According to the Bhatnagar-Gross-Krook approximation, the time evolution of $f_i(\mathbf{r}, t)$ at lattice node $\mathbf{r}$ and time t is

$$f_i(\mathbf{r} + \mathbf{e}_i \Delta t, t + \Delta t) = f_i(\mathbf{r}, t) - 1/\tau_0 [f_i(\mathbf{r}, t) - f_i^{\text{eq}}(\mathbf{r}, t)] + F_i^{\text{ext}}(\mathbf{r}, t) \quad (3)$$

where i labels a lattice vector, $\mathbf{e}_i$ is a unit vector in i direction, Δt is the time step of the algorithm, τ_0 is the relaxation time related to the fluid viscosity, f_i^{eq} is the local equilibrium distribution function defined in D3Q19 model, and F_i^{ext} is the external force density which can model a pressure-driven flow field^[8–10]. The parameters are the same as in ref. [8]. Accordingly, the fluid density $\rho = \sum_i f_i$ and the velocity $u = 1/\rho \sum_i f_i \mathbf{e}_i$, then the velocity flux of the nanopore center is $J = \sum u_x$, where u_x is the velocity in x direction (flow field direction). Here, the well-known bounceback collision rule is introduced to consider solid walls with no-slip boundary conditions in LBM. Just as remarked in ref. [10], a linear relationship between J and F_{ext} is found as Darcy's Law, that is $J = kF_{\text{ext}}$, where k is the proportional coefficient related to nanopore width. Therefore from the linear relationship, the background flow field with different J can be simply obtained by introducing corresponding F_{ext} .

The BD equation of motion for monomer i is^[11]

$$\dot{\mathbf{R}}_i = -1/\xi \nabla(U_{\text{LJ}} + U_{\text{FENE}}) + 1/\xi (\mathbf{f}_i(t) + \mathbf{F}_{\text{LB}}) \quad (4)$$

Here ξ is the friction coefficient, $\mathbf{f}_i(t)$ is a random force related to ξ by the fluctuation dissipation theorem $\langle \mathbf{f}_i(t) \mathbf{f}_j(t') \rangle = 2\xi k_B T \delta_{ij} \delta(t-t') \mathbf{I}$, where $\mathbf{I}$ is the unit tensor. And $\mathbf{F}_{\text{LB}}$ is the drag force from the background flow field, which is defined as $\mathbf{F}_{\text{LB}} = -\xi[\mathbf{v} - \mathbf{u}(\mathbf{R})]$, where $\mathbf{v}$ is the monomer velocity and $\mathbf{u}(\mathbf{R})$ is the flow velocity at monomer's position $\mathbf{R}$. A linear interpolation is implemented to estimate $\mathbf{u}(\mathbf{R})$ ^[12, 13], that is $\mathbf{u}(\mathbf{R}) = \sum_r \sigma_r \mathbf{u}(\mathbf{r})$, where σ_r is the fractional distance from monomer to adjacent grid points $\mathbf{r}$ with the velocity $\mathbf{u}(\mathbf{r})$. Here, we should mention that the effect of hydrodynamic interactions mediated by the fluid is neglected in our simulation, which is screened out in a narrow pore.

In this model, we use the LJ parameters ϵ and σ and the monomer mass m to fix the energy, length and mass scales, respectively. Then the time scale is given by $\tau = (m\sigma^2/\epsilon)^{1/2}$. The equations are integrated with a time step $\Delta t = 10^{-4}\tau$ and the temperature is $k_B T = 1.0$. The lattice spacing in LBM, Δx , is uniform (σ) along the lattice axes. The other dimensionless parameters in our simulations are $\kappa = 7$, $R_0 = 2$ and $\xi = 0.5$. For the channel and nanopore, we set $L_x = 83$, $L_y = L_z = 17$, and $L = 3$.

Initially, a linear polymer chain is put into the left-hand side of nanopore and the beads of polymer chain are under thermal collisions to obtain an equilibrium configuration. The beads are prevented from entering the nanopore during the equilibration by means of a soft virtual wall. The wall is then removed and a background flow field with certain velocity flux is applied. A successful translocation corresponds to the polymer ending up on the right-hand side of nanopore within a time $10^3\tau$. For the present study, we restrict our attention to two capture types as shown in Fig. 1(b) (unfolded type) and Fig. 1(c) (single folded type). Typically, we average our data over 2000 independent runs.

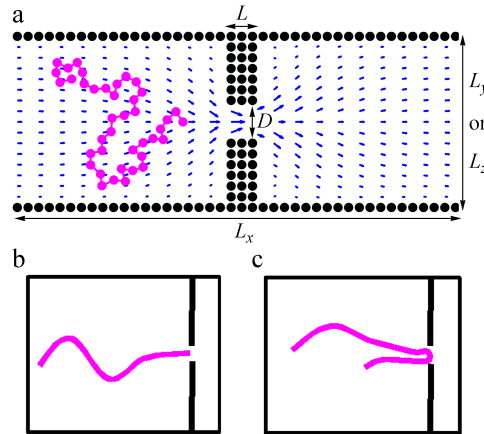


Fig. 1 (a) Geometry used in the simulations of polymer capture by a nanopore (The size of the simulation channel and nanopore is respectively (L_x, L_y, L_z) and (L, D, D) .) (b) unfolded capture type and (c) single folded capture type

For each successful translocation event, following the approach of Storm *et al.*^[5], we define the capture location as $x = N_i/N$, where N_i is the distance from the folding point to the nearest end of the polymer chain and N is the chain length. And the distribution probability $P(x)$ is calculated as the fraction of successful translocation captured at location x . Figure 2 depicts the distribution probability $P(x)$ as a function of capture location x with the velocity flux $J = 10$, the chain length $N = 40$, and the nanopore width $D = 3$. For comparison, some experimental and theoretical results from Stein *et al.*^[6] are also summarized and plotted. The inset of Fig. 2 shows the translocation probability $P'(J)$ as a function of velocity flux J at same conditions, where the translocation probability $P'(J)$ is calculated as the fraction of runs leading to successful translocation at given velocity flux. The simulation results show that the probability of unfolded type is the highest, decreasing rapidly but smoothly with distance away from the ends and becoming a slowly increasing function of x near $x = 0.2$, which is slightly different from experimental and theoretical results. This implies that when the capture location is near the ends, there may be a biased conversion from folded type to unfolded type. Furthermore, from the inset of Fig. 2 we can find when the velocity flux is $J = 10$, the translocation probability is about 100%, which implies that all available configurations of polymer chain can pass through the nanopore. And from the views of statistics this gives the definition of $J = 10$.

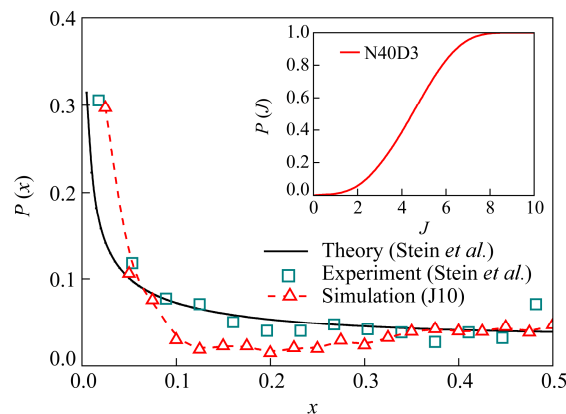


Fig. 2 Distribution probability $P(x)$ as a function of capture location x with the velocity flux $J = 10$, the chain length $N = 40$, and the nanopore width $D = 3$

For comparison, some experimental and theoretical results from Stein *et al.* [6] are also summarized and plotted. Inset: translocation probability $P'(J)$ as a function of velocity flux J at same conditions.

Figure 3 shows the distribution probability $P(x)$ as a function of capture location x for different velocity fluxes $J = 5$, $J = 10$ and $J = 20$ with the chain length $N = 40$ and the nanopore width $D = 3$. There is the same trends of distribution for $J = 10$ and $J = 20$. However, the distribution probability of $J = 5$ is obviously different from that of the other two velocity flux, especially the probability of locations with some distance away from the ends is almost zero, which reveals a strong bias of unfolded type. The inset of Fig. 3 shows the probability of unfolded type $P_0(J)$ as a function of velocity flux J with the nanopore width $D = 4$, where $P_0(J)$ rapidly decreases and then becomes independent of velocity flux. In addition, from the inset of Fig. 2 we can find the translocation probability of $J = 5$ is about 50%, which implies only partial configurations of polymer chain can pass through the nanopore. In a random selection model of Stein *et al.*^[6], the effect of velocity flux can't be taken into account. However, our simulation results prove that unless there is a enough large velocity flux ($P'(J) = 1$), the distribution probability of capture location is independent of velocity flux, and if not, free energy barrier of translocation will affect the capture process. This implies that random selection is decisive only when all available configurations can complete translocation, otherwise energetic considerations gradually governs the capture process, where energy cost is important.

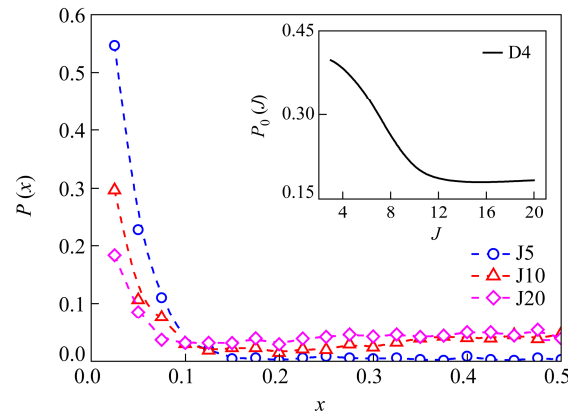


Fig. 3 Distribution probability $P(x)$ as a function of capture location x for different velocity fluxes $J = 5$, $J = 10$ and $J = 20$ with the chain length $N = 40$ and the nanopore width $D = 3$. Inset: probability of unfolded type $P_0(J)$ as a function of velocity flux J with the nanopore width $D = 4$.

Figure 4 depicts the probability of unfolded type $P_0(D)$ as a function of nanopore width D for different velocity fluxes $J = 5$, $J = 10$ and $J = 20$ with the chain length $N = 40$. The probability of unfolded type rapidly decreases as the nanopore width increases for $J = 5$, however, it is almost independent of nanopore width for $J = 20$. Importantly, the probability of unfolded type rapidly decreases and then becomes independent of nanopore width for $J = 10$. These imply that the dependence of probability of unfolded type on nanopore width is associated with the velocity flux. Just as Wu *et al.*^[14] reported that the critical flow rate of polymer translocation decreases with the nanopore width increase. We infer the effect of nanopore width on the distribution probability can come down to the change of critical velocity flux, which is defined as $J_c = J$ when $P'(J) = 1$. Namely, the chain could pass through a nanopore much smaller than its unperturbed radius only when the velocity flux is higher than a certain value. In another word, when the velocity flux is enough to make all available configurations of polymer chain to pass through the nanopore, the probability of unfolded type is independent of nanopore width. The inset of Fig. 4 describes the ratio of cross-sectional area of polymer size in vertical to flow direction and nanopore cross-sectional area as a function of nanopore width with the velocity flux $J = 10$. The ratio is greater than 1 for nanopore width $D = 2$, closes to 1 for nanopore width $D = 3$ and $D = 4$ and is less than 1 for nanopore width $D = 5$ and $D = 6$, which gives the microscopic picture of whether all available configurations of polymer chain can pass through the nanopore at a given velocity flux.

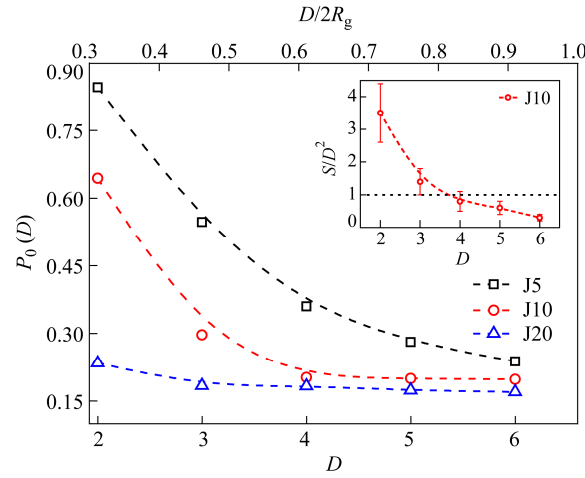


Fig. 4 Probability of unfolded type $P_0(D)$ as a function of nanopore width D for different velocity fluxes $J=5$, $J=10$ and $J=20$ with the chain length $N=40$ and the gyration radius $R_g=3.34$

Inset: the ratio of cross-sectional area of polymer size in vertical to flow direction and nanopore cross-sectional area as a function of nanopore width with the velocity flux $J=10$

Because the critical velocity flux has been proven that it is independent of chain length^[9, 14–17], we can generally divide two physical mechanisms of polymer capture as shown in Fig. 5. For certain nanopore width, when the velocity flux is greater than critical velocity flux, the capture picture is a random selection process, otherwise it tends to a statistical process governed by energetic considerations.

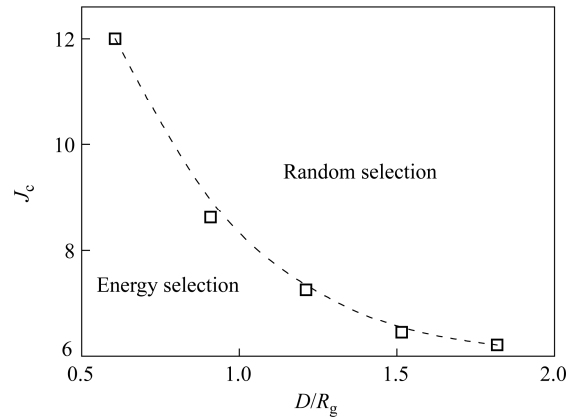


Fig. 5 Capture picture for different nanopore widths and velocity fluxes

In addition, to our knowledge, the effect of chain length on probability of unfolded type is not clear. We find the probability of unfolded type versus chain length satisfies a power-law scaling of $P_0(N) \sim N^{-0.8}$ as shown in Fig. 6, which is in agreement with the result from random selection model. But as the chain length decreases, the polymer chain gradually approaches to non-Gaussian chain and the probability of unfolded type breaks away from the power-law scaling.

This work reports a simple, coarse-grained computational model for polymer capture by a nanopore, which can systematically investigate the capture process and help to deeply understand the fundamental physics behind such a process. The present work clearly indicates that when the velocity flux is greater than the critical velocity flux, the capture picture is a random selection process, otherwise it tends to a statistical process governed by energetic considerations. In addition, the chain ends capture probability decreases as chain length increases and

satisfies a power-law scaling of $P_0(N) \sim N^{-0.8}$. Our results offer a comprehensive understanding of snapshots of insertion moment, especially for microscopic capture mechanisms.

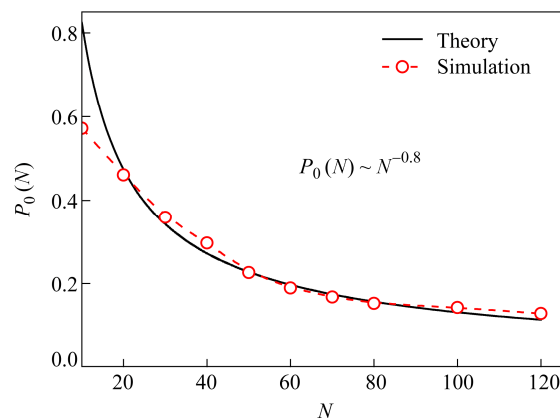


Fig. 6 Probability of unfolded type $P_0(N)$ as a function of chain length N with the velocity flux $J = 10$ and the nanopore width $D = 3$. The probability of unfolded type versus chain length satisfies a power-law scaling of $P_0(N) \sim N^{-0.8}$, which is in agreement with result from random selection model.

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