Luo, K.; Huopaniemi, I.; Ala-Nissila, T.; Ying, S.C.

Polymer translocation through a nanopore under an applied external field

Published in:
Journal of Chemical Physics

DOI:
10.1063/1.2179792

Published: 01/01/2006

Please cite the original version:
Luo, K., Huopaniemi, I., Ala-Nissila, T., & Ying, S. C. (2006). Polymer translocation through a nanopore under an applied external field. Journal of Chemical Physics, 124(11), 1-7. [114704]. https://doi.org/10.1063/1.2179792
Polymer translocation through a nanopore under an applied external field

Kaifu Luo and Ilkka Huopaniemi Tapio Ala-Nissila See-Chen Ying

Citation: The Journal of Chemical Physics 124, 114704 (2006); doi: 10.1063/1.2179792
View online: http://dx.doi.org/10.1063/1.2179792
View Table of Contents: http://aip.scitation.org/toc/jcp/124/11
Published by the American Institute of Physics

Articles you may be interested in

Langevin dynamics simulations of polymer translocation through nanopores
The Journal of Chemical Physics 125, 124901 (2006); 10.1063/1.2357118
Polymer translocation through a nanopore under an applied external field

Kaifu Luo a) and Ilkka Huopaniemi
Laboratory of Physics, Helsinki University of Technology, P.O. Box 1100, FIN-02015 HUT, Espoo, Finland
Tapio Ala-Nissila b)
Laboratory of Physics, Helsinki University of Technology, P.O. Box 1100, FIN-02015 HUT, Espoo, Finland and Department of Physics, Brown University, Providence, Box 1843, Rhode Island 02912-1843
See-Chen Ying c)
Department of Physics, Brown University, Providence, Box 1843, Rhode Island 02912-1843

(Received 15 November 2005; accepted 31 January 2006; published online 15 March 2006)

We investigate the dynamics of polymer translocation through a nanopore under an externally applied field using the two-dimensional fluctuating bond model with single-segment Monte Carlo moves. We concentrate on the influence of the field strength $E$, length of the chain $N$, and length of the pore $L$ on forced translocation. As our main result, we find a crossover scaling for the translocation time $\tau$ with the chain length from $\tau \sim N^{2+\nu}$ for relatively short polymers to $\tau \sim N^{1+\nu}$ for longer chains, where $\nu$ is the Flory exponent. We demonstrate that this crossover is due to the change in the dependence of the translocation velocity $v$ on the chain length. For relatively short chains $v \sim N^{-\nu}$, which crosses over to $v \sim N^{-1}$ for long polymers. The reason for this is that with increasing $N$ there is a high density of segments near the exit of the pore, which slows down the translocation process due to slow relaxation of the chain. For the case of a long nanopore for which $R_g$, the radius of gyration $R_g$ along the pore, is smaller than the pore length, we find no clear scaling of the translocation time with the chain length. For large $N$, however, the asymptotic scaling $\tau \sim N^{1+\nu}$ is recovered. In this regime, $\tau$ is almost independent of $L$. We have previously found that for a polymer, which is initially placed in the middle of the pore, there is a minimum in the escape time for $R_g = L$. We show here that this minimum persists for weak fields $E$ such that $EL$ is less than some critical value, but vanishes for large values of $EL$. © 2006 American Institute of Physics. [DOI: 10.1063/1.2179792]

I. INTRODUCTION

Many crucially important processes in biology involve the translocation of a biopolymer through nanometer-scale pores, such as DNA and RNA translocations across nuclear pores, protein transport through membrane channels, and virus infection.1-5 Due to various potential technological applications, such as rapid DNA sequencing,4,5 gene therapy, and controlled drug delivery,6 polymer translocation has been the subject of a number of experimental,7-17 theoretical,17-35 and numerical studies.32-43 In order to overcome a large entropic penalty of binding particles,28,29,43 several theoretical studies on chain translocation in the presence of binding particles.28,29,43

The nanopore detection and analysis of single molecules is based on the working principle of a Coulter counter.44 When a particle passes through a nanopore, the electrolyte in the solution is displaced, resulting in blockades in the ionic current. The magnitude of these blockades is roughly proportional to the volume of the particle. Kasianowicz et al.7 demonstrated that an electric field can drive single-stranded DNA (ssDNA) and RNA molecules through the water-filled α-hemolysin channel and that the passage of each molecule is signaled by a blockade in the channel current. The translocation process includes two essential steps. First, one end of the polymer enters the pore directed by diffusion and by the action of an electric field near the pore. Second, the polymer is translocated from one side of the membrane to the other, driven by the electric field. For the first step, the experimental results show that the ability of the polymer to enter the nanopore depends linearly on polymer concentration.7,10 For the second step, the translocation time is highly sensitive to the polynucleotide sequence of ssDNA and RNA and secondary structure of RNA.8 As to the dependence of the polymer translocation on the chain length, two regimes are found, depending on the polymer length.11 For long polymers, the mean translocation time appears to be linear with the chain length,7,11 while it decreases rapidly with decreasing chain length in a nonlinear way.11 In addition, an inverse linear dependence and an inverse quadratic dependence of the translocation time on applied voltage are observed for different experiments.7,11

Only a limited voltage range can be applied across a biological pore. Furthermore, there are difficulties in analyzing the current variations because the shot noise is compa-
rable to the expected signal. Recently, solid-state nanopores have been used for similar experiments.\textsuperscript{14–17} Storm et al.\textsuperscript{17} carried out a set of experiments on double-stranded DNA (dsDNA) molecules with various lengths that translocate through a solid-state nanopore. Surprisingly, a power-law scaling of the most probable translocation time with the polymer length was observed with an exponent of 1.27, in contrast to the linear behavior observed for the experiments on α-hemolysin channel.\textsuperscript{\textsuperscript{11}}

Thus existing theories\textsuperscript{17,19,22,23} provide different predictions for the scaling behavior of the translocation time as a function of polymer length, ranging from $\tau \sim N$ to $\tau \sim N^{1+\nu}$, where $\nu$ is the Flory exponent.\textsuperscript{45,46} Moreover, they do not agree with the recent experimental finding\textsuperscript{17} that $\tau \sim N^{1.27}$. To clarify these issues, here we perform numerical simulation studies based on a two-dimensional (2D) fluctuating bond lattice model for polymers to investigate the translocation dynamics under an external driving field within the pore. As our main result, we find that for short nanopores, the translocation time crosses over from $N^{2\nu}$ to $N^{1+\nu}$ with increasing chain length. In three dimensions (3D), the exponent\textsuperscript{45,46} $2\nu=1.18$, which is in reasonably good agreement with the experimental result of 1.27. We demonstrate that the crossover is due to a change in the translocation velocity of the polymer as a function of the chain length. Finally, we also discuss the influence of the pore length on forced translocation.

II. THE FLUCTUATING BOND MODEL

The fluctuating bond (FB) model\textsuperscript{47} with single-segment Monte Carlo (MC) moves is an efficient model to study various static and dynamic properties of polymers. Here, we consider the 2D lattice FB polymer model for MC simulations of a self-avoiding polymer, where each segment excludes four nearest and next nearest neighbor sites on a square lattice. The bond lengths $b_i$ are allowed to vary in the range $2 \leq b_i \leq \sqrt{13}$ in units of the lattice constant, where the upper limit prevents bonds from crossing each other. With these restrictions each segment can occupy 36 different lattice sites and there are 28 different bond angles $\phi \in [0, \pi)$, thus yielding a reasonable approximation for continuum behavior.

The external driving force in the present work was modeled as a potential difference applied linearly across the length of the pore with the profile in the manner described by Chern et al.\textsuperscript{46}

$$\frac{U_e}{k_B T} = \begin{cases} -\frac{E}{k_B T}x, & x > L/2 \\ -\frac{E}{k_B T}L, & L/2 \geq x \geq -L/2 \text{ and } y^2 \leq (W/2)^2 \\ \frac{E}{k_B T}L, & x < -L/2 \\ \infty, & \text{otherwise,} \end{cases}$$

where $L$ and $W$ are the length and width of the pore, respectively, and $E$ is the strength of the external field.

Dynamics is introduced by Metropolis moves of a single segment, with a probability of acceptance $\min\{e^{-\Delta U_e/k_B T}, 1\}$, where $\Delta U_e$ is the energy difference between the new and old states. As to an elementary MC move, we randomly select a monomer and attempt to move it onto an adjacent lattice site (in a randomly selected direction). If the new position does not violate the excluded-volume or maximal bond-length restrictions, the move is accepted or rejected according to Metropolis criterion. $N$ elementary moves constitute one MC time step. In the FB model, each effective monomer corresponds to several real chemical monomers along the backbone of the chain. Each segment separating two adjacent effective monomers has a physical meaning corresponding approximately to the Kuhn length $a$ which measures the length scale at which the polymer is stiff and not flexible.

III. RESULTS AND DISCUSSION

To begin the simulation of translocation of the polymer through the pore, a chain is placed on one side of the pore with one end of it in the pore entrance. Then the chain is allowed to reach an equilibrium state using MC moves, but with the constraint that the first monomer is fixed. Once the polymer is in its equilibrium state, the first monomer at the entrance of the pore is released, and that moment is designated as $\tau=0$. The translocation time $\tau$ is defined as the duration of time it takes for the chain to move through the pore in the direction of the driving force. In our simulations, the pore width is fixed as two lattice units unless otherwise stated.

A. Polymer translocation through a short nanopore

1. Influence of the electric field strength on translocation time

To determine how translocation time depends on the electric field strength $E/k_B T$, we considered a polymer chain of length $N=75$. The length and the width of the pore were chosen as 3 and 2 lattice units, respectively. It is important to note that not all the simulation runs result in a successful translocation and even when they do, the translocation times vary over a wide range of values. We define the translocation time $\tau$ as the average time over all successful runs. For the present case where the driving force is relatively strong, the distribution of translocation times is narrow without a long tail and symmetric with respect to the most probable translocation time, as noted by Kantor and Kardar.\textsuperscript{33} Therefore, the average is well defined. With increasing electric field the translocation time decreases rapidly for weak fields and saturates to a constant value for strong fields, as shown in Fig. 1. This is because the electric field interacts with the polymer only inside the pore and therefore within our model, the translocation rate has a finite maximum. For weak fields, we find that $\tau \sim E^{-0.83 \pm 0.01}$, which is in agreement with the experiments of Kasianowicz et al.\textsuperscript{7} who found that the channel blockade lifetime was inversely proportional to the applied voltage. By contrast, Meller et al.\textsuperscript{11} found an inverse quadratic dependence of apparent translocation velocities on the applied field.
2. Numerical results for a crossover scaling behavior of \( \tau \) with \( N \)

Next, we consider the influence of the chain length on translocation for the short pore case \( (L=3) \). Figure 2 shows the dependence of \( \tau \) on \( N \) for two different fields. One of the main features is that there is a crossover for both cases. For a smaller chain of length \( N<200 \), \( \tau \sim N^{1.46 \pm 0.01} \) is observed. This exponent is close to \( 2\nu \), where \( \nu=0.75 \) is the Flory exponent for a self-avoiding walk in 2D. For longer chains of length \( N>300 \), the slopes become 1.70 and 1.72, which are in good agreement with \( \nu+1=1.75 \). With increasing the width of the pore from 2 to 5 lattice units, we observed the same exponents and crossover behavior. Thus, we conclude that for smaller chain length, translocation time versus polymer chain length satisfies \( \tau \sim N^{2\nu} \) and it crosses over to \( \tau \sim N^{1+\nu} \) for larger \( N \) independent of the strength of the field. A crossover of \( \tau \) as a function of \( N \) has also been reported in very recent Langevin dynamics simulations.\(^{48}\)

Our results are in contrast with the experimental data that \( \tau \) depends linearly on \( N \) in the case of \( \alpha \)-hemolysin,\(^{7,11}\) but the predicted short chain exponent \( 2\nu=1.18 \) in 3D agrees reasonably well with the solid-state nanopore experiments of Storm et al.,\(^{17}\) who found an exponent of 1.27. The ssDNA is a flexible polymer and the Kuhn length \( a \sim 1-5 \text{ nm} \sim 2-10 \text{ bps} \) (base pairs),\(^{39,50}\) while the dsDNA is a semiflexible polymer and typically \( a \sim 100 \text{ nm} \sim 340 \text{ bps} \).\(^{51,52}\) The beginning of the crossover region occurs at \( N=200 \), which corresponds to real lengths of the ssDNA and the dsDNA about 400–2 kbps (kilo-base-pairs) and 68 kbps, respectively. These lengths are beyond or near the longest ssDNA and dsDNA used in the experiments so far.\(^{7,11,17}\) Thus, it is not surprising that crossover in scaling behavior has not been experimentally observed yet.

3. Comparison with theoretical scaling predictions

A number of recent theories\(^{17–35}\) have been developed for the dynamics of polymer translocation. Sung and Park\(^{19}\) considered equilibrium entropy of the polymer as a function of the position of the polymer through the nanopore. Under the instantaneous equilibrium approximation during the translocation process, the translocation problem is reduced to the escape of a “particle” over an entropic barrier. The limiting case of an extremely long chain, an infinitely thin membrane, and narrow pore was considered. For a Gaussian chain under an external force, it is shown that \( \tau \sim N/D \), where \( D \) is the relevant diffusion coefficient. Muthukumar\(^{22}\) suggested that \( D \) is not that of the whole chain, but rather the diffusion coefficient of the monomer that just passes the pore, and hence it is a constant independent of \( N \). As a result, a linear dependence \( \tau \sim N \) is obtained under a strong field. This is in agreement with some experimental results\(^{7,11}\) for polymer translocation through \( \alpha \)-hemolysin channel. In addition, there is support for the linear scaling behavior from the 3D Gaussian chain MC simulations of Chern et al.\(^{36}\) and Langevin dynamics simulations for relatively short polymers.\(^{37,42}\) However, the above theories cannot explain the recent experimental result, namely, that \( \tau \sim N^{1.27} \) for polymer translocation through a solid-state nanopore.\(^{17}\) Incidentally, according to our present results in the short chain limit, \( \tau \) scales as \( N^{2\nu} \) which would also yield a linear scaling result for the Gaussian chain since \( 2\nu=1 \) in this case.

Chuang et al.\(^{32}\) and Kantor and Kardar\(^{31}\) have argued that the assumption of equilibrium in Brownian polymer dynamics by Sung and Park,\(^{19}\) and Muthukumar\(^{22}\) breaks down when the translocation time is shorter than the equilibration time for the polymer, which occurs for a self-avoiding polymer in the long chain limit. For a Gaussian polymer, the equilibrium assumption is marginal even in the absence of a driving field. Instead, a lower bound for translocation time was obtained by considering the unimpeded motion of a polymer that best mimics the situation with a chemical potential difference applied across the pore.\(^{33}\) Absent the restriction imposed by the membrane, there is a force that is applied to a single monomer, at the spatial position where the membrane would reside. Because the monomer to which the force is applied changes constantly, it was assumed that there is no incentive for a drastic change in the shape of the polymer and the scaling of the size remains the same, independent of \( \Delta \mu \). At each moment a force is applied to the polymer. The drift velocity \( u \) of the polymer due to the applied force \( F \) can be written in the scaling form as\(^{32}\) \( u(F) \sim (R_g/\tau_c)\phi(FR_g/k_BT) \sim N^{-1+\nu} \phi(FN^n) \), where \( R_g \) is the radius of gyration which scales as \( R_g \sim N^{1/2} \), and \( \tau_c \) is the relaxation time of the polymer that scales as \( \tau_c \sim N^{1+2\nu} \) for Rouse dynamics. If \( u \) is proportional to the force, the scaling func-
tion $\phi$ is linear and thus the mobility $u/F$ scales as $1/N$. They thus conclude that the time for such unhindered motion scales as
\[ \tau(\Delta \mu) \sim \frac{R_g}{u} \sim \frac{N^{1+\nu}}{\Delta \mu}. \] (2)

This provides a lower bound for the scaling of the translocation time which agrees with our numerical results for large $N$. The fact that the numerical study of Kantor and Kardar did not yield the scaling form $N^{1+\nu}$ was attributed to the fact that the large $N$ limit has not been reached yet.\(^{33}\)

For the shorter polymers, the situation under an electric field driving force is different. In this case, the equilibrium radius of gyration $R_g$ is not an appropriate variable for the scaling form, since the shape of the polymer can be greatly distorted by the applied field. Instead, if we denote by $N_{\text{trans}}(t)$ the number of segments that have passed through the pore, we can write a scaling form for $dN_{\text{trans}}(t)/dt$ as suggested in Refs.\(^{32,34}\):
\[ \frac{dN_{\text{trans}}(t)}{dt} \sim \frac{N}{\tau_r} \frac{\Delta \mu N}{k_BT} \sim N^{1-2\nu} \Delta \mu, \] (3)

where $\Delta \mu$ is the chemical potential difference between two sides of the membrane. Integrating both sides from the beginning to the end of the translocation process yields the result for the scaling of the translocation time as
\[ \tau \sim N^{2\nu}, \] (4)
in agreement with our result for short chains. We note that the same scaling law in Eq. (4) was recently derived by Storm et al.\(^{33}\) based on the force balance between the driving force and the hydrodynamic friction experienced by the polymer. They thus attributed their experimentally observed nonlinear scaling to hydrodynamic interaction. However, further theoretical and numerical support for their argument is currently missing. The effect of hydrodynamic interaction on polymer translocation is nontrivial and will be investigated in future work.

4. Crossover behavior of translocation time

Although the above scaling arguments support our numerical results for small and large $N$, the crossover scaling behavior cannot be understood based on these arguments. Theoretically, we need to answer two questions: Does $R_g$ remain constant during the translocation under an external field, and is the translocation velocity really inversely proportional to $N$ for a wide range of $N$?

To study these assumptions, we have numerically calculated $R_g$ during the translocation process for $L=3$ and $W=2$, as shown in Fig. 3. For both $N=100$ and $N=500$, during translocation $R_g$ first increases and reaches a maximum, and then decreases with time. The same behavior was verified even for a relatively wide pore with $W=200$. In addition, there is a slight asymmetry of $R_g$ with time in that it is somewhat larger before the translocation than immediately after it. This indicates that the chain remains in a nonequilibrium state, and the assumption that there is no drastic change in the shape of the polymer during the translocation is invalid.

To study this issue in detail, we calculated the average initial horizontal distance between the last monomer of the polymer and the wall $R_0$, as shown in Fig. 4. According to the definition of the translocation time, at the completion of the translocation process, the chain has moved a distance of $R_0$ along the direction parallel to the axis of the pore. Here we should point out that $R_0$ is the component of an end-tethered chain along the pore and we thus have $R_0 = (R_0)/\tau$. We now define the translocation velocity as $\nu = (R_0)/\tau$. For a change in the shape of the polymer during the translocation is invalid.
crossover scaling behavior of $\tau$ with $N$, the scaling of $v$ with $N$ must have a crossover, too. According to our numerical results, we must have that

$$v \sim \frac{N^{\nu}}{\tau} \sim \begin{cases} \frac{N^\nu}{N^{2\nu}} \sim N^{-\nu} & \text{for small } N \\ \frac{N^\nu}{N^{1+\nu}} \sim N^{-1} & \text{for large } N. \end{cases} \quad (5)$$

Figure 5 shows the influence of the chain length on the translocation velocity. As expected, there is a crossover. For $N > 200$, we find $v \sim N^{-0.97}$, where the exponent is indeed close to $-1$. For $N < 200$, we find $v \sim N^{-0.63}$. This is in reasonably good agreement with $-\nu = -0.75$.

The reason why the translocation velocity slows down for large $N$ can be seen in Fig. 6, which shows the chain configurations for $N=100$ and $600$ just at the moment after translocation. The density of segments near the pore is much higher for a long chain than for a short chain. At the late stages of translocation, the high density of segments near the pore slows down the translocation velocity. The translocation time is much shorter than the Rouse relaxation time for a self-avoiding chain, and thus Fig. 6 demonstrates the fact that the polymer remains in a nonequilibrium state, as the translocated segments do not have enough time to diffuse away from the vicinity of the pore.

5. Waiting times for monomers

An important issue from the experimental point of view concerns the dynamics of single monomers passing through the nanopore during translocation. The nonequilibrium nature of the driven translocation problem should have a significant effect on this. To this end, we numerically calculated the average waiting time for each monomer to pass through the pore. This is defined as the time duration between the events when monomers $s$ and $s+1$ exit the pore. In Fig. 7 we show the results for two chain lengths. There is strong dependence of the waiting time on the position of the monomer in the chain. For $N=100$, the longest waiting time approximately corresponds to the middle monomer of the chain. However, for $N=400$, approximately the 300th monomer needs the longest time to thread the pore, which indicates that during the late stages of translocation the high density of segments of a long polymer near the pore slows down the translocation. For sequencing DNA, one expects to distinguish monomers one by one according to the blockade of current and the waiting time. From our numerical results, even for identical monomers, the waiting times are different and are determined by the monomer positions in the chain. For heteropolymers, it thus becomes very difficult to distinguish based on the waiting time how many monomers of the same kind are connected together in the chain, which is very important for successful sequencing DNA.

B. Polymer translocation through a long nanopore

In this section, we discuss the influence of the pore length on translocation dynamics. Here we fixed the field strength to be $E/k_BT=5$, which means that the voltage drop increases with increasing the pore length. Figure 8(a) shows the translocation time as a function of the chain length for different pore lengths $L$. For $R_i/L \gg 1$, where $R_i$ is the radius of gyration along the pore, the asymptotic scaling $\tau \sim N^{1+\nu}$ is recovered for all $L$. However, for a smaller ratio of $R_i/L$ the situation is more complicated. For $L=6$, scaling follows the previous short pore result $\tau \sim N^{2\nu}$ as expected, while for longer pores there is no obvious power-law scaling. Our data also indicate that translocation times decrease rapidly with decreasing chain length in a nonlinear way for short polymers, which is in good agreement with the experimental results. The dependence of $\tau$ on $L$ is shown in Fig. 8(b).
For relatively short polymers, $\tau$ increases with increasing $L$, while it is independent of $L$ for long polymers. On one hand, with increasing $L$ the voltage drop increases, which leads to a faster translocation. On the other hand, with increasing $L$ the polymer needs to move a longer distance, which results in a longer translocation time. For long enough polymers, the cancellation of these two factors leads to the lack of dependence of $\tau$ on $L$.

Next, we fixed $EL/2k_BT=2$, which means that the voltage drop across the pore does not change with the length of the pore. Figure 9 shows $\tau$ as a function of the pore length $L$ for different chain lengths. It can be seen that $\tau$ increases with increasing $L$. This is because the field decreases and the distance that the polymer has to move increases with increasing $L$.

In our previous work, in the absence of an external driving force we considered a polymer which is initially placed in the middle of the pore and studied the escape time $\tau_e$ required for the polymer to completely exit the pore on either end. We showed that $\tau_e$ has a minimum as a function of $L$ when the radius of gyration along the pore $R_g=L$. To study whether this still holds for the forced case, we investigated the influence of driving on $\tau_e$ as a function of $L$ with constant voltage drop, as shown in Fig. 10. The width of the pore is $W=7$ here. For a weak field of $EL/2k_BT=0.05$, we still observe the “optimal” pore length for minimum passage time, in agreement with our previous results for $EL/2k_BT=0$. However, the minimum in the escape time rapidly vanishes with increasing field such that for $EL/2k_BT=0.1$, $\tau_e$ already changes into a monotonously increasing function of $L$.

### IV. CONCLUSION

In this work, we have investigated the problem of polymer translocation through a nanopore under an electric field based on the 2D fluctuating bond model with single-segment Monte Carlo moves. We examined the influence of the field strength, chain length, and pore length on translocation dynamics. As our main result, we have found a crossover...
scaling for the translocation with chain length from $\tau \sim N^{2+}$ for relatively short polymers to $\tau \sim N^{1+r}$ for longer polymers. With increasing $N$, there is a high density of segments near the exit of the pore due to slow relaxation of the chain, which slows down the translocation process. We demonstrated that the change in the dependence of the translocation velocity $v$ on the chain length determines this crossover behavior. For relatively short polymers $v \sim N^{-2}$, which crosses over to $v \sim N^{-1}$ for long chains. In addition, we also examined the translocation through a long pore for constant field strength. For short polymers, i.e., where $R_p$ along the pore direction is less than the pore length, translocation times decrease rapidly with decreasing chain length in a nontrivial way. In the long polymer limit, the scaling relation $\tau \sim N^{1+r}$ is recovered. Finally, we have also shown that for a polymer which is initially placed in the middle of the pore, there exists a minimum in the escape time, which occurs at $R_p = L$, provided that the applied field is sufficiently weak such that $EL$ is less than some critical value. For larger $EL$, the escape time becomes a monotonously increasing function of the pore length.

ACKNOWLEDGMENTS

This work has been supported in part by a Center of Excellence grant from the Academy of Finland. We also wish to thank the Center for Scientific Computing Ltd. for allocation of computer time.

---

1. B. Alberts and D. Bray, Molecular Biology of the Cell (Garland, New York, 1994).
2. J. Darnell, H. Lodish, and D. Baltimore, Molecular Cell Biology (Scientific American Books, New York, 1995).
3. R. V. Miller, Sci. Am. 278(1), 66 (1998).
4. J. Han, S. W. Turner, and H. G. Craighead, Phys. Rev. Lett. 83, 1688 (1999).
5. S. W. P. Turner, M. Calodi, and H. G. Craighead, Phys. Rev. Lett. 88, 128103 (2002).
6. D.-C. Chang, Guide to Electroporation and Electrofusion (Academic, New York, 1992).
7. J. J. Kasianowicz, E. Brandin, D. Branton, and D. W. Deamer, Prog. Natl. Acad. Sci. U.S.A. 93, 13770 (1996).
8. M. Akton, D. Branton, J. J. Kasianowicz, E. Brandin, and D. W. Deamer, Biophys. J. 77, 3227 (1999).
9. A. Meller, L. Nivon, E. Brandin, J. A. Golovchenko, and D. Branton, Proc. Natl. Acad. Sci. U.S.A. 97, 1079 (2000).
10. S. E. Henrichson, M. Misikian, B. Robertson, and J. J. Kasianowicz, Phys. Rev. Lett. 85, 3057 (2000).
11. A. Meller, L. Nivon, and D. Branton, Phys. Rev. Lett. 86, 3435 (2001).
12. A. F. Sauer-Budge, J. A. Nymwanda, D. K. Lubensky, and D. Branton, Phys. Rev. Lett. 90, 238101 (2003).
13. A. Meller, J. Phys.: Condens. Matter 15, R581 (2003).
14. J. L. Li, D. Stein, C. McMullan, D. Branton, M. J. Aziz, and J. A. Golovchenko, Nature (London) 412, 166 (2001).
15. J. L. Li, M. Gershov, D. Stein, E. Brandin, and J. A. Golovchenko, Nat. Mater. 2, 611 (2003).
16. A. J. Storm, J. H. Chen, X. S. Ling, H. W. Zandbergen, and C. Dekker, Nat. Mater. 2, 537 (2003).
17. A. J. Storm, C. Storm, J. Chen, H. Zandbergen, J.-F. Joanny, and C. Dekker, Nano Lett. 5, 1193 (2005).
18. S. M. Simon, C. A. Reskin, and G. F. Oster, Proc. Natl. Acad. Sci. U.S.A. 89, 3770 (1992).
19. W. Sung and P. J. Park, Phys. Rev. Lett. 77, 783 (1996).
20. P. J. Park and W. Sung, J. Chem. Phys. 108, 3013 (1998).
21. E. A. dIoriozio and A. L. Mandell, J. Chem. Phys. 107, 5510 (1997).
22. M. Muthukumar, J. Chem. Phys. 111, 10371 (1999).
23. M. Muthukumar, J. Chem. Phys. 118, 5174 (2003).
24. D. K. Lubensky and D. R. Nelson, Biophys. J. 77, 1824 (1999).
25. E. Slonkina and A. B. Kolomeisky, J. Chem. Phys. 117, 4063 (2002).
26. T. Ambjörnsson, S. P. Apell, Z. Konkoli, E. A. DiMarzio, and J. J. Kasianowicz, J. Chem. Phys. 117, 4063 (2002).
27. R. Metzler and J. Klafter, Biophys. J. 85, 2776 (2003).
28. T. Ambjörnsson and R. Metzler, Phys. Biol. 1, 77 (2004).
29. T. Ambjörnsson, M. A. Lomholt, and R. Metzler, J. Phys.: Condens. Matter 17, S3945 (2005).
30. U. Gerland, R. Bundschuh, and T. Hwa, Phys. Biol. 1, 19 (2004).
31. A. Baumgärtner and J. Skolnick, Phys. Rev. Lett. 74, 2142 (1995).
32. J. Chuang, Y. Kantor, and M. Kardar, Phys. Rev. E 65, 021802 (2001).
33. Y. Kantor and M. Kardar, Phys. Rev. E 69, 021806 (2004).
34. A. Milchev, K. Binder, and A. Bhattacharya, J. Chem. Phys. 121, 6042 (2004).
35. K. F. Luo, T. Ala-Nissila, and S. C. Ying, J. Chem. Phys. 124, 034714 (2006).
36. S.-S. Chern, A. E. Cardenas, and R. D. Co asphalt, J. Chem. Phys. 115, 7772 (2001).
37. H. C. Loebl, R. Randel, S. P. Goodwin, and C. C. Matthai, Phys. Rev. E 67, 041913 (2003).
38. R. Randel, H. C. Loebl, and C. C. Matthai, Macromol. Theory Simul. 13, 387 (2004).
39. Y. Lansac, P. K. Maiti, and M. A. Glaser, Polymer 45, 3099 (2004).
40. C. Y. Kong and M. Muthukumar, Electrophoresis 23, 2697 (2002).
41. Z. Farkas, I. Derenyi, and T. Vicsek, J. Phys.: Condens. Matter 15, S1767 (2003).
42. P. Tian and D. G. Smith, J. Chem. Phys. 119, 11475 (2003).
43. R. Zandi, D. Reguera, J. Rudnick, and W. M. Gelbart, Proc. Natl. Acad. Sci. U.S.A. 100, 8649 (2003).
44. R. W. DeBlois and C. P. Bean, Rev. Sci. Instrum. 41, 909 (1970).
45. M. Doi and S. F. Edwards, The Theory of Polymer Dynamics (Clarendon, Oxford, 1986).
46. P. G. de Gennes, Scaling Concepts in Polymer Physics (Cornell University Press, Ithaca, NY, 1979).
47. L. Guo and E. Luijten, in Computer Simulation Studies in Condensed-Matter XVIII edited by D. P. Landau, S. P. Lewis, and H.-B. Schüttler (Springer, Heidelberg, 2006).
48. S. B. Smith, Y. Cui, and C. Bustamante, Science 271, 795 (1996).
49. C. Danilowicz, Y. Kafri, R. S. Conroy, W. V. Coljee, J. Weis, and M. Prentiss, Phys. Rev. Lett. 93, 078101 (2004).
50. P. Cluzel, A. Lebrun, I. L. Lavery, J. L. Voiv, D. Chatenay, and F. Caron, Science 271, 792 (1996).
51. C. G. Baumann, S. B. Smith, V. A. Bloomfield, and C. Bustamante, Proc. Natl. Acad. Sci. U.S.A. 94, 6185 (1997).
52. We also used the definition $v=(R_p/\tau)$ for the translocation velocity and observed a crossover for the scaling of $v$ with $N$. Here $R_p$ and $\tau$ denote the values of $R_p$ and $\tau$ for each successful run. In addition, our result also applies to velocity defined through the center of mass velocity.