Pore-blockade Times for Field-Driven Polymer Translocation

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Abstract. We study pore blockade times for a translocating polymer of length N, driven by a field E across the pore in three dimensions. The polymer performs Rouse dynamics, i.e., we consider polymer dynamics in the absence of hydrodynamical interactions. We find that the typical time the pore remains blocked during a translocation event scales as $\sim N^{(1+2\nu)/(1+\nu)}/E$, where $\nu \simeq 0.588$ is the Flory exponent for the polymer. In line with our previous work, we show that this scaling behavior stems from the polymer dynamics at the immediate vicinity of the pore — in particular, the memory effects in the polymer chain tension imbalance across the pore. This result, along with the numerical results by several other groups, violates the lower bound $\sim N^{1+\nu}/E$ suggested earlier in the literature. We discuss why this lower bound is incorrect and show, based on conservation of energy, that the correct lower bound for the pore-blockade time for field-driven translocation is given by $\eta N^{2\nu}/E$, where η is the viscosity of the medium surrounding the polymer.

1. Introduction

Molecular transport through cell membranes is an essential mechanism in living organisms. Often, the molecules are too long, and the pores in the membranes too narrow, to allow the molecules to pass through as a single unit. In such circumstances, the molecules have to deform themselves in order to squeeze — i.e., translocate — themselves through the pores. DNA, RNA and proteins are such naturally occurring long molecules [1–5] in a variety of biological processes. Translocation is also used in gene therapy [6, 7], and in delivery of drug molecules to their activation sites [8]. Consequently, the study of translocation is an active field of research: as a cornerstone of many biological processes, and also due to its relevance for practical applications.

More recently, translocation has found itself at the forefront of single-molecule-detection experiments [9–11], as new developments in the design and fabrication of nanometer-sized pores and etching methods may lead to cheaper and faster technology for the analysis and detection of single macromolecules. In these experiments, charged polymeric molecules, suspended in an electrolyte solution, are initially located on one side of a membrane. The membrane is impenetrable to the molecule except for a nanometer-sized pore. Between the two different sides of the membrane, a DC voltage difference is then applied, which drives the molecule through the pore. When the molecule enters the pore, it affects the electrical resistivity of the circuit, leading to a dip in the electric current supplied by the voltage source. The magnitude and the duration of these dips have proved to be very effective in determining the size and the length of the molecule. The usage of protein pores (modified α-haemolysin, mitochondrial ion channel, nucleic acid binding/channel protein etc.) and the etching of specific DNA sequences inside the pores [6, 12] have opened up promising new avenues of fast, simple and cheap technology for single macromolecule detection, analysis and characterization, perhaps even allowing DNA sequencing at the nucleotide level.
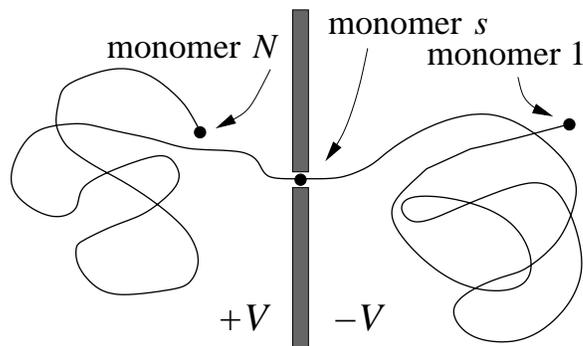
Figure 1. Snapshot of a translocating polymer in a two-dimensional projection of our three-dimensional system. Across the pore of size unity a voltage difference $2V$ is applied. The monomer located within the pore is labeled s.

The subject of this paper is (charged) polymer translocation in three dimensions through a narrow pore in an otherwise impenetrable membrane placed at $z = 0$, as

the polymer is driven by a DC voltage across the pore. Our interest is in the scaling behavior for the typical pore-blockade time during a translocation event with polymer length N. In practice, the electric field due to the applied voltage decays rapidly with increasing distance from the pore, and for simplicity it is often assumed that only those polymer segments residing within the pore feel the driving force due to the field. For our theory and simulations too, we consider a polymer which only experiences a force acting on its monomers that reside in the pore, as illustrated in Fig. 1.

To substantiate our theoretical analysis we use extensive Monte Carlo simulations with a three-dimensional self-avoiding lattice polymer model. For the voltage difference across the pore we choose

$$V(z) = \begin{cases} +V & (z \leq -1) \\ 0 & (z = 0) \\ -V & (z \geq 1) \end{cases}.$$ (1)

Thus, during translocation through the pore, the energy gained by each monomer carrying a charge q, in dimensionless units, is given by $\Delta U = 2qV/k_BT$. From now on, favoring notational simplicity, we choose both q and k_BT to be unity. Since we also choose the lattice spacing to be unity in our simulations, the strength of the electric field acting on each monomer within the pore is given by $E = V$.

Details of the lattice polymer model used in this paper can be found in Ref. [13,14]: the polymer moves through a sequence of random single-monomer hops to neighboring lattice sites. These hops can either be "reptation"-moves, along the contour of the polymer, or Rouse moves, in which the monomer jumps "sideways" and changes the contour. The definition of time used throughout this paper is such that every monomer attempts a "reptation"-move as well as a "sideways"-move with rate unity. There is no explicit solvent in our analysis, i.e., the polymer performs Rouse dynamics.

Our conventions to study this problem, all throughout this paper, are the following. We place the membrane at $z = 0$. We fix the middle monomer (monomer number $N/2$) of a polymer of total length N at the pore, apply the voltage as in Eq. (1) and thermalize the polymer. At $t = 0$ we release the polymer and let translocation commence. We define the typical time when the polymer leaves the pore as the dwell time τ_d: it scales with N in the same way as the pore-blockade time in a full (field-driven) translocation event.

This problem has recently been studied in Ref. [15], in which a lower bound $\propto N^{1+\nu}/E$ has been argued for τ_d. This lower bound was derived in the limit of unimpeded polymer movement, i.e., for an infinite pore, or equivalently, in the absence of the membrane. In Ref. [15] the authors also suggested that the dynamics of translocation is anomalous (see also Ref. [16] in this context).

In the recent past, some of us have been investigating the microscopic origin of the anomalous dynamics of translocation. We have set up a theoretical formalism, *based on the microscopic dynamics of the polymer*, and showed that the anomalous dynamics of translocation stem from the polymer's memory effects, in the following

manner. Translocation proceeds via the exchange of monomers through the pore: imagine a situation when a monomer from the left of the membrane translocates to the right. This process increases the monomer density in the right neighborhood of the pore, and simultaneously reduces the monomer density in the left neighborhood of the pore. The local enhancement in the monomer density on the right of the pore *takes a finite time to dissipate away from the membrane along the backbone of the polymer* (similarly for replenishing monomer density on the left neighborhood of the pore). The imbalance in the monomer densities between the two local neighborhoods of the pore during this time causes an enhanced chance of the translocated monomer to return to the left of the membrane, thereby giving rise to *memory effects*. The ensuing analysis enabled us to provide a proper microscopic theoretical basis for the anomalous dynamics. Further theoretical analysis then led us to the conclusion that in the case of unbiased translocation, i.e., when the polymer is not subjected to an external force, the dwell time scales with length as $\tau_d \sim N^{2+\nu}$ [13, 17, 18], both in two and three dimensions. Our approach based on the polymer's memory effects also works beautifully for pulled translocation, during which a force F is applied at the head of the polymer: we have shown that if FN^ν is sufficiently large, then the dwell time scales as $\tau_d/N^{2+\nu} \sim (FN^\nu)^{-1}$ [19]. In this work, we push ahead with the same formalism to demonstrate that it reveals the physics of field-driven translocation too, thus providing a *unified underlying theoretical basis* for translocation, based on the theory of polymer dynamics.

authors	two dimensions	three dimensions
Kantor *et al.* [15]	1.53 ± 0.01	–
Luo *et al.* [20]	1.72 ± 0.06	–
Cacciuto *et al.* [21]	1.55 ± 0.04	–
Wei *et al.* [22]	–	1.27
Milchev *et al.* [23]	–	1.65 ± 0.08
Dubbeldam *et al.* [24]	–	1.5

Table 1. Existing numerical results on the exponent for the scaling of τ_d with N for field-driven translocation. Note that the proposed lower bound $1 + \nu$ of Ref. [15] is 1.75 and 1.59 in two and three dimensions respectively.

Returning to the lower bound for the scaling of the dwell time with polymer length N for field-driven translocation as proposed in Ref [15], we note that subsequent numerical studies did not immediately settle the scaling for τ_d with N, including the one by the authors of Ref. [15] themselves. In Table 1 we present a summary of the existing numerical results on the exponent for the scaling of τ_d with N for field-driven translocation. All results quoted are for self-avoiding polymers in the absence of hydrodynamical interactions in the scaling limit.

More recently, this lack of consensus prompted three of us to investigate the issue of field-driven translocation in two dimensions, via a proxy problem, viz., polymer

translocation in three dimensions out of strong planar confinements [18]. We showed that the actual lower bound for τ_d for field-driven translocation is given by $\eta N^{2\nu}/E$, where η is the viscosity of the surrounding medium. This inequality is derived from the principle of conservation of energy: it was shown in Ref. [18] that although the presence of the memory effects suggests that the scaling of τ_d could behave as $N^{(1+2\nu)/(1+\nu)}$, since $(1+2\nu)/(1+\nu) < 2\nu$ in two dimensions, conservation of energy overrides the memory effects in the polymer — high precision simulation data suggested, in accordance with those of Refs. [15, 21] that the actual scaling of τ_d for field-driven translocation in two dimensions is given by $\tau_d \sim N^{2\nu}$. In three dimensions $2\nu < (1+2\nu)/(1+\nu)$, implying that in three dimensions $\tau_d \sim N^{(1+2\nu)/(1+\nu)}$, which is the central result of this paper.

This paper is organized in the following manner. In Sec. 2 we derive the lower bound $N^{2\nu}$ for τ_d for field-driven translocation. In Sec. 3.1 we discuss a method to measure the polymer's chain tension at the pore. In Sec. 3.2 we analyze the memory effects in the imbalance of the polymer's chain tension at the pore. In Sec. 4 we discuss the consequence of these memory effects on the translocation velocity $v(t)$, and obtain the scaling relation of τ_d with the polymer length N. We end this paper with a discussion in Sec. 5.

2. Lower bound for τ_d for field-driven translocation

As noted in Sec. 1, a lower bound for the dwell time $\tau_d \sim N^{1+\nu}/E$ has been proposed in Ref. [15]. The underlying assumption behind this result is that, with or without an applied field, the mobility of a polymer translocating through a narrow pore in a membrane will not exceed that of a polymer in bulk (i.e., in the absence of the membrane). This mobility is then obtained under two more assumptions for the behavior of a polymer under a driving field:

(i) To mimic the field acting on a translocating polymer, the field on the polymer in bulk has to act on a monomer whose position along the backbone of the polymer changes continuously in time. As a result, there is no incentive for the polymer to change its shape from its bulk equilibrium shape, i.e., the polymer can still be described by a blob with radius of gyration $\sim N^\nu$ in the appropriate dimension.

(ii) The polymer's velocity is proportional to DE, where E is the applied field, and D is the diffusion coefficient scaling as $D \sim 1/N$ for a Rouse polymer.

Of these two assumptions, note that (ii) is obtained as the steady state solution of the equation of motion of a Rouse polymer, in bulk, with uniform velocity and vanishing internal forces, see for instance Ref. [25], Eq. VI.10. We have already witnessed in many occasions [13, 15–17, 19, 24, 26, 27] that the dynamics of translocation through a narrow pore is anomalous (subdiffusive), as a consequence of the strong memory effects discussed in the previous section, and also that these memory effects are so strong that the velocity of translocation is not constant in time [18, 19]. The anomalous dynamics and the memory effects are crucial ingredients that question the validity of the lower

bound $N^{1+\nu}$ for τ_d for field-driven translocation.

It is however possible to derive a lower bound for τ_d for field-driven translocation, based on the principle of conservation of energy. Consider a translocating polymer under an applied field E which acts only at the pore. By definition, the N monomers of the polymer translocate through the pore in a time τ_d. The total work done by the field in this time τ_d is then given by EN. During translocation, each monomer travels over a distance of order $\sim R_g$, leading to an *average* monomer velocity $v_m \sim R_g/\tau_d$. The rate of loss of energy due to the viscosity η of the surrounding medium per monomer is given by ηv_m^2. For a Rouse polymer, the frictional force on the entire polymer is a sum of frictional forces on individual monomers, leading to the total energy loss due to the viscosity of the surrounding medium during the entire translocation event scaling as $\sim N\tau_d \eta v_m^2 = N\eta R_g^2/\tau_d$. This loss of energy must be less than or equal to the total work EN done by the field, which yields us the inequality $\tau_d \geq \eta R_g^2/E = \eta N^{2\nu}/E$ [28].

3. Memory effects in the chain tension perpendicular to the membrane

A translocating polymer can be thought of as two segments of polymers tethered at the pore, while the segments are able to exchange monomers between them through the pore. In Ref. [17] we developed a theoretical method to relate the dynamics of translocation to the imbalance of chain tension between these two segments across the pore. The key idea behind this method is that the exchange of monomers across the pore responds to $\phi(t)$, this imbalance of chain tension; in its turn, $\phi(t)$ adjusts to $v(t)$, the transport velocity of monomers across the pore. Here, $v(t) = \dot{s}(t)$ is the rate of exchange of monomers from one side to the other.

The memory effects discussed in Sec. 1 in terms of relaxation of excess monomers (or the lack of monomers) in the immediate vicinity of the pore translates immediately to that of the imbalance of the chain tension across the pore — local accumulation of excess monomers reduce the chain tension, while local lack of monomers enhance it. Quantitatively speaking, in the presence of memory effects, the chain tension imbalance across the pore $\phi(t)$ and the velocity of translocation $v(t)$ are related by

$$\phi(t) = \phi_{t=0} + \int_0^t dt' \mu(t - t')v(t') \tag{2}$$

via the (field-dependent) memory kernel $\mu(t)$, which could be thought of as time-dependent 'impedance' of the system. Using the Laplace transform, this relation could be inverted to obtain $v(t) = \int_0^t dt' a(t - t')[\phi_{t=0} - \phi(t')]$, where $a(t)$ can be thought of as the 'admittance' of the system. In the Laplace transform language, these are related to each other as $\mu(k) = a^{-1}(k)$, where k is the Laplace variable representing inverse time [13, 17–19].

3.1. Chain tension perpendicular to the membrane

Measuring chain tension directly is difficult. We therefore use a method developed earlier [18, 19] to monitor the chain tension near the pore.

By definition, the chain tension imbalance $\phi(t)$ is the difference of the chain tensions on the right and the left side of the pore: $\phi(t) = \Phi_R(E, t) - \Phi_L(E, t)$. Both $\Phi_R(E, t)$ and $\Phi_L(E, t)$ are functions of the applied electric field E across the pore. Note, from the applied potential (1), that the field E acts on the monomers at site $z = -1$ towards the pore, while it acts on those at site $z = 1$ away from the pore. Using the convention that $E < 0$ (resp. $E > 0$) implies a field acting towards (resp. away from) the membrane, we have

$$\Phi(E, t = 0) = \begin{cases} \Phi_L(t = 0) & (E < 0) \\ \Phi_R(t = 0) & (E > 0) \end{cases}. \tag{3}$$

Now consider a different problem, where one end of a polymer is tethered to a fixed membrane, yet the number of monomers are allowed to spontaneously enter or leave the tethered end, under the effect of an electric field E. Then, following the methodology described in Refs. [18, 19], we have

$$\Phi(E, t = 0) = k_B T \ln \frac{P_+}{P_-}, \tag{4}$$

where P_- (resp. P_+) is the probability that the left (or the right) polymer segment has one monomer less (resp. one extra monomer).
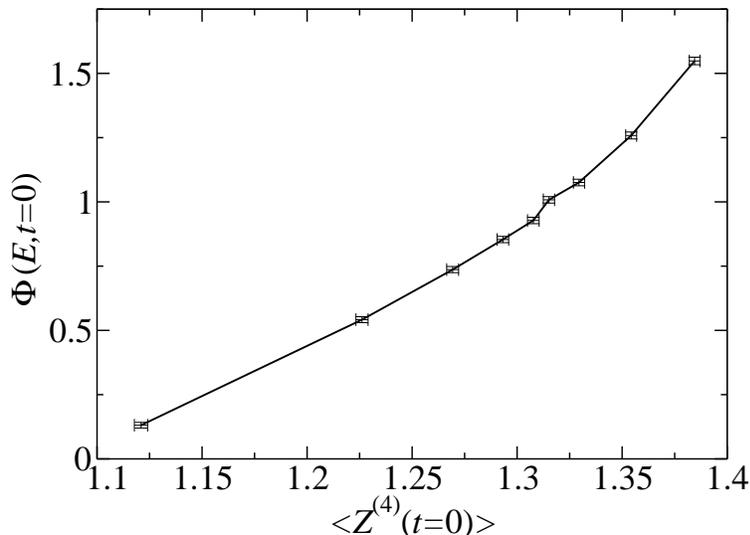
Figure 2. $\langle Z^{(4)}(t = 0) \rangle$ vs. $\Phi(E, t = 0)$, for $N/2 = 200$ and electric field values $E = -0.5. - 0.25, -0.1, -0.05, 0, 0.05, 0.1, 0.25$ and 0.5 respectively. The angular brackets for $\langle Z^{(4)}(t = 0) \rangle$ indicate an average over 32000 polymer realizations, which are also used to obtain $\Phi(E, t = 0)$.

Note that even for $E = 0$, as already stressed in Ref. [19], there is nonzero chain tension Φ_0 at the pore, due to the presence of the membrane. A polymer's free energy close to a membrane is higher than its free energy in bulk. In other words, the membrane repels the polymer, and as a result, for a polymer with one end tethered to a membrane, the monomers close to the membrane are more stretched than they would be in the bulk.

For a translocating polymer Eq. (4) cannot be used, so to compute $\Phi_R(t)$ and $\Phi_L(t)$ one needs a suitable proxy. In the cases of unbiased translocation [13, 17], translocation with a pulling force [19] and translocation out of planar confinements [18], we have seen that the center-of-mass distance of the first few, say 4 to 5 monomers from the membrane provides an excellent proxy for Φ. In this paper we follow the same line. The average distance $\langle Z^{(4)}(t = 0) \rangle$ is plotted as a function of the chain tension $\Phi(E, t = 0)$ for various values of E in Fig. 2. This figure shows that under an applied field, $\Phi(E, t = 0)$ is a reasonably linear function well-proxied by $Z^{(4)}$. The positive curvature seen in Fig. 2, i.e., the deviation from linearity, is seen only for $E > 0$. We believe that this is partly due to the saturation of $Z^{(4)}$. [By definition, in our lattice model the distance of the center-of-mass of the first 4 monomers from the membrane cannot exceed $(1+2+3+4)/4 = 2.5$.]

3.2. Memory effects in the chain tension

From Eq. (2), the behavior of the memory kernel $\mu_R(t)$ for the polymer segment on the right side of the membrane can be obtained with a sudden introduction of p extra monomers at the pore, corresponding to an impulse current $v(t) = p\delta(t)$. Physically, $v(t) = p\delta(t)$ with $p > 0$ (resp. $p < 0$) means that we tether a polymer of length N halfway through the pore at the pore at $t \to -\infty$, let it thermalize till $t = 0$, and then introduce p extra monomers at the tethered end of the right (resp. left) segment at $t = 0$. We then ask for the time-evolution of the mean response $\langle \delta\Phi_R(t) \rangle$, where $\delta\Phi_R(t)$ is the shift in chemical potential for the right segment of the polymer at the pore. This means that for the translocation problem (with both right and left segments), we would have $\phi(t) = \delta\Phi_R(t) - \delta\Phi_L(t)$, where $\delta\Phi_L(t)$ is the shift in chemical potential for the left segment at the pore due to an opposite input current to it.

In earlier works [13, 17], using $v(t) = p\delta(t)$ for a polymer of length N tethered halfway at the pore as described in the above paragraph, three of us showed that for unbiased polymer translocation, i.e., for $E = 0$, this mean response, and hence $\mu(t)$ takes the form $\mu(t) \sim t^{-\alpha} \exp[-t/\tau_{\text{Rouse}}(N/2)]$ [note that for $E = 0$ there is a trivial symmetry between the right and the left segment of the polymer, hence $\mu_R(t) = \mu_L(t) \equiv \mu(t)$].

When the electric field is applied at the pore, and the same monomer injection method is used to probe the memory kernels $\mu_R(t)$ and $\mu_L(t)$, we expect the above arguments to hold again: since the field is applied very locally at the base of the tethered polymer segments, it does not destroy the broader structure of the polymer. However, we do expect to see deviations from the $t^{-\alpha} \exp[-t/\tau_{\text{Rouse}}(N/2)]$ at short times. Indeed, we have confirmed this picture — for various field strengths we tracked $\langle \delta\Phi_R(t) \rangle$ and $\langle \delta\Phi_L(t) \rangle$ by measuring the distance of the average centre-of-mass of the first 4 monomers

from the membrane, $\langle Z^{(4)}(t)\rangle$, in response to the injection of extra monomers near the pore at $t = 0$. Specifically we consider the equilibrated right and left segments of the polymer, each of length $N/2 = 200$ (with the middle monomer threaded at the pore), adding 5 extra monomers at the tethered end of the right and the left segment each at $t = 0$, corresponding to $|p| = 5$, bringing the length of each segment up to $N/2 + |p|$. Using the proxy $\langle Z^{(4)}(t)\rangle$ for both segments we then track $\langle \delta\Phi_R(t)\rangle$ and $\langle \delta\Phi_L(t)\rangle$, denoting them by values $E > 0$ and $E < 0$ respectively in Fig. 3. The deviations from the expected power-law $t^{-(1+\nu)/(1+2\nu)}$ at short times and the $\exp[-t/\tau_{\mathrm{Rouse}}(N/2)]$ at long times makes the precise identification of the power-law $t^{-(1+\nu)/(1+2\nu)}$ difficult. Nevertheless, there is an extended regime where this power law can be identified reasonably clearly, yielding us $\mu_R(t) = \mu_L(t) \equiv \mu(t) = t^{-(1+\nu)/(1+2\nu)} \exp[-t/\tau_{\mathrm{Rouse}}(N/2)]$.
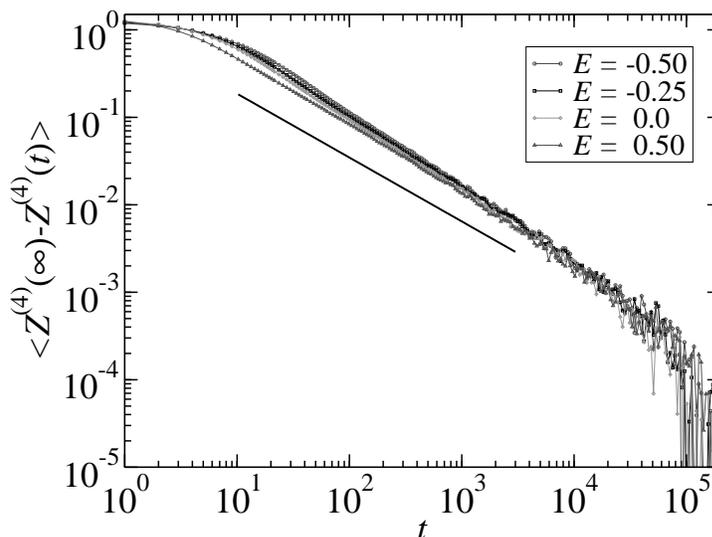
Figure 3. Probing the memory kernels by $\langle Z^{(4)}(\infty) - Z^{(4)}(t)\rangle$ following monomer injection at the pore corresponding to $v(t) = p\delta(t)$, with $|p| = 5$. Physically, $v(t) = p\delta(t)$ with $p > 0$ (resp. $p < 0$) means that we tether a polymer of length N halfway at the pore at $t \to -\infty$, let it thermalize till $t = 0$, and then introduce $|p|$ extra monomers to the right (resp. left) segment at the tether point at $t = 0$. Following our notation in Eq. (3), the $E < 0$ data (resp. $E > 0$ data) correspond to $\mu_L(t)$ [resp. $\mu_R(t)$]. The data presented correspond to an average over $500,000$ polymer realizations, with $N/2 = 200$. The steeper drop at longer times correspond to the exponential decay $\exp[-t/\tau_{\mathrm{Rouse}}(N/2)]$. The solid line corresponds to the power law $t^{-\frac{1+\nu}{1+2\nu}} \approx t^{-0.73}$.

4. Scaling behavior of τ_d with N

The memory kernel we obtained in Sec. 3 can be termed as the "static memory kernel", as it is obtained under the condition that before the injection of the extra monomers both segments were thermalized. When the applied field is not too strong, we can expect

the static memory kernel to yield the scaling of translocation velocity with time, in the following manner.

An inverse Laplace transform of Eq. (2) yields us

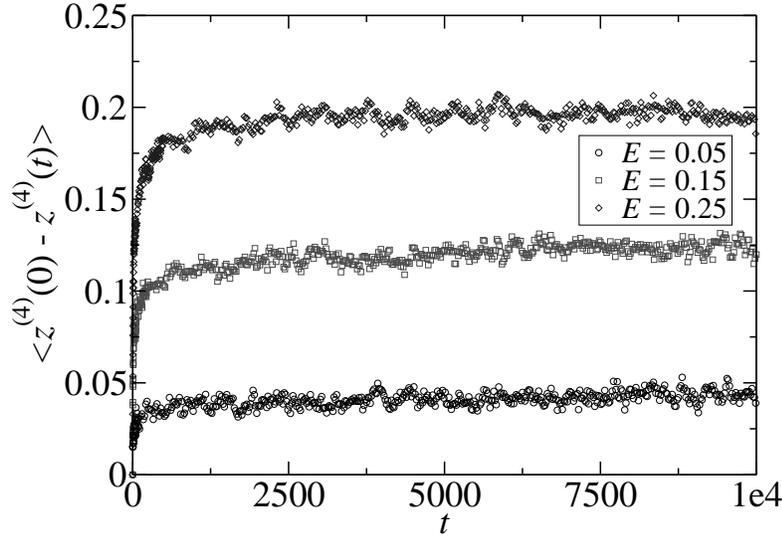$$v(k) = \frac{\phi_{t=0}}{k\mu(k)} - \frac{\phi(k)}{\mu(k)}, \tag{5}$$

where k is the Laplace variable representing inverse time. Thereafter, using the power-law part of $\mu(t) \sim t^{-(1+\nu)/(1+2\nu)}$, i.e., $\mu(k) \sim k^{(1+\nu)/(1+2\nu)-1}$, and Laplace-inverting Eq. (5), we get

$$v(t) = \int_0^t \mathrm{d}t' \, (t - t')^{-\frac{1+3\nu}{1+2\nu}} \left[\phi_{t=0} - \phi(t') \right]. \tag{6}$$

If $\phi(t)$ goes to a constant $\neq \phi_{t=0}$, then Eq. (6) reduces to

$$v(t) \sim t^{-\frac{\nu}{1+2\nu}}, \ \text{ i.e., } s(t) = N/2 + \int_0^t \mathrm{d}t' \, v(t') \sim t^{\frac{1+\nu}{1+2\nu}}, \tag{7}$$

where $[s(t) - N/2]$ is the distance unthreaded after time t [29]; the $N/2$ appears in Eq. (7) as $s(0) = N/2$.

Figure 4. Behaviour of $[\phi_{t=0} - \phi(t)]$ for $N = 200$ as a function of t, shown by means of the proxy variable $< z^{(4)}(0) - z^{(4)}(t) >$. demonstrating that $[\phi_{t=0} - \phi(t)]$ reduces to a constant very quickly: $E = 0.05$ (circles), 0.15 (squares), and 0.25 (triangles). To generate these averages $16,000$ individual polymers were unthreaded for each value of E.

In Fig. 4 we show the behavior of $[\phi_{t=0} - \phi(t)]$ by means of the proxy variable $\langle z^{(4)}(0) - z^{(4)}(t) \rangle$ for $E = V = 0.05$, 0.15, and 0.25 respectively, where $z^{(4)}$ is the difference between the $Z^{(4)}$ values of the right and left segment of the polymer, i.e., $z^{(4)}(t) = Z_R^{(4)}(t) - Z_L^{(4)}(t)$. Indeed the quantity $[\phi_{t=0} - \phi(t)]$ approaches a constant

rather quickly. We also note that the relation between this constant and the applied field E is almost linear.
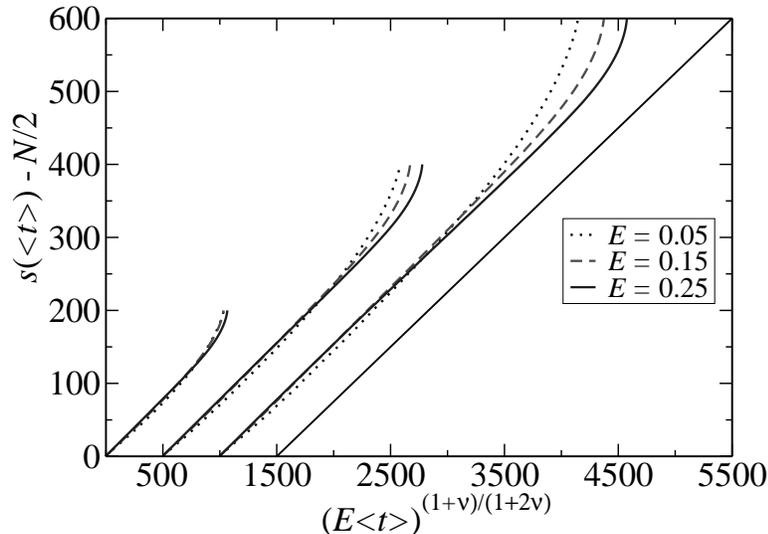
Figure 5. The average time $\langle t \rangle$ to unthread distance s for three different field strengths, for $N = 400$ (average over $16,000$ polymer realizations for each field), $N = 800$ (average over $16,000$ polymer realizations for each field), and $N = 1,200$ ($5,000$ polymer realizations for $E = 0.05$, and $7,500$ polymer realizations each for $E = 0.15$ and $E = 0.25$). The data for $N = 800$ correspond to real time value, while the data for $N = 400$ and $N = 1,200$ have been shifted by ∓ 500 units along the x-axis for clarity. The solid line has been added for a guide to the eye.

For strong fields, there is no *a priori* reason that the dynamics can still be described by the static memory kernel instead of a suitably replacing "dynamic memory kernel", but we find that the scaling $s(t) \sim t^{(1+2\nu)/(1+\nu)}$ is obeyed for fairly strong fields as well: in Fig. 5 we plot the average time $\langle t \rangle$ to unthread a distance s to show this scaling. Note the strong finite-size effects for the scaling behavior as shown by the deviation from the $t^{(1+2\nu)/(1+\nu)}$ for larger values of s. The presence of such strong finite-size effects indicates that without the aid of $s(t)$ vs. t curves, determining the scaling of τ_d with N will almost certainly lead to erroneous identification of the scaling laws — we believe that these finite-size effects are responsible for the wide range of existing numerical scaling results, as summarized in Table 1. Nevertheless, Fig. 5 shows that these finite-size effects do not increase linearly with N, leading us to the scaling for τ_d as

$$\tau_d \sim N^{(1+2\nu)/(1+\nu)}/E\,, \tag{8}$$

which is obtained from the condition that $s(\tau_d) = N$. For the above analysis to hold, the dwell time must be less than τ_{Rouse}, which Eq. (8) confirms. Note that the E-dependence of Eq. 8 is only numerically obtained from Fig. 5. Note also that the curves in Fig. 5 for $E = 0.05$ tend to 'sag' a bit. We attribute this to our numerically inspired definition

of $s(\langle t \rangle)$, as the mean time to unthread a distance s, as opposed to, e.g., the numerically less favorable measure of distance $\langle s(t) \rangle$, i.e.,the monomer which is most likely to reside in the pore at time t. At small fields, the polymer has ample time for fluctuations, pushing the time of first arrival up. Numerically, for $E = 0.15$ and 0.25, the exponent $\partial[\log s(t)]/\partial(\log t)$ is found to be 0.73 ± 0.02, in agreement with the theoretical value $(1+\nu)/(1+2\nu)$. The sagging and finite-size effects discussed above cause the apparent exponent to be slightly larger, ranging from 0.74 to 0.79, for $E = 0.05$.

With decreasing field strength, especially in the range where the thermal fluctuations are comparable to the work done by the field to translocate the entire polymer, given by $EN \simeq k_B T = 1$, one should obtain a crossover from the above scaling (8) to $\tau_d \sim N^{2+\nu}$ for unbiased translocation [13, 17]. This suggests that if $\tau_d/N^{2+\nu}$ is plotted as a function of EN, then one should obtain a scaling collapse; i.e., there exists a scaling function f such that $\tau_d = N^{2+\nu} f(EN)$. However, EN as a scaling variable is simply numerically inconsistent with Fig. 5 and Eq. (8). Instead $\tau_d = N^{2+\nu} f(E, N)$ is the proper description of the situation, with $f(E, N)$ approaching a constant for $E \to 0, N \to \infty$ and $f(E, N)$ behaving as $E^{-1} N^{-\nu-1/(1+\nu)}$ for $E \sim O(1)$ and $N \to \infty$. Note that E in this paragraph should be interpreted as the dimensionless quantity $qV/(k_B T)$.
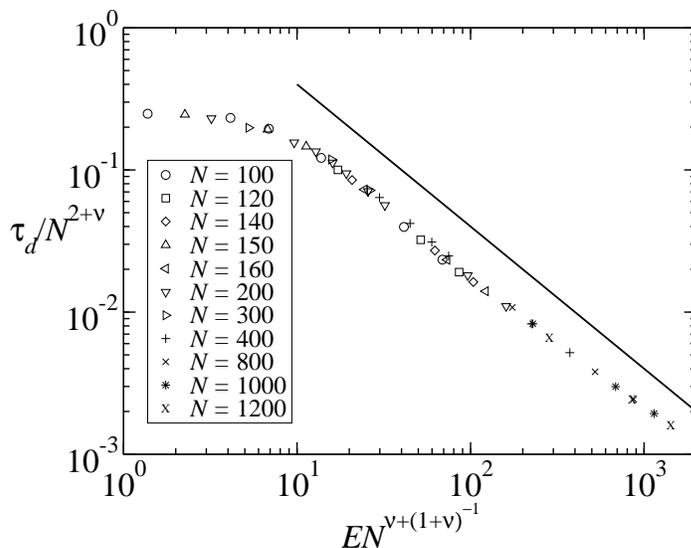
Figure 6. Data collapse in terms of $x = EN^{\nu+1/(1+\nu)}$ and $y = \tau_d/N^{2+\nu}$ for various fields. The mean unthreading times τ_d have been obtained with at least $1,000$ polymers (up to $32,000$ for smaller N values) for each N and field strength E: the statistical error bars are smaller than the size of the symbols. The solid line $y \sim 1/x$ for moderate field strengths in support of Eq. (8) has been added for a guide to the eye.

To demonstrate the scaling behavior of Eq. (8) for $E \simeq O(1)$, we plot $\tau_d/N^{2+\nu}$ as a function of $EN^{\nu+1/(1+\nu)}$ in Fig. 6. Keeping in mind that this way of plotting the data does not necessarily yield a data collapse at small but nonzero E, as discussed above,

we also plot several data points for small E, in order to demonstrate that for $E \to 0$ our results in this paper are consistent with that of unbiased translocation [13, 17, 18].

5. Discussion

In this paper, we studied polymer translocation in three dimensions through a narrow pore in an otherwise impenetrable membrane, as the polymer is driven by a field E across the pore. The polymer performs Rouse dynamics, i.e., we considered polymer dynamics in the absence of hydrodynamical interactions. We found that the typical time the pore remains blocked during a translocation event, for moderate field strengths scales as $\sim N^{(1+2\nu)/(1+\nu)}/E$, where $\nu \simeq 0.588$ is the Flory exponent for the polymer. In line with our previous works, we showed that this scaling behavior stems from the polymer dynamics at the immediate vicinity of the pore — in particular, the memory effects in the polymer chain tension imbalance across the pore [13, 17–19]. We also showed that our results in this paper are consistent with that of unbiased translocation [13, 17, 18] in the limit $E \to 0$.

The above results for finite E, along with the numerical results by several other groups, violate the lower bound $\sim N^{1+\nu}/E$ suggested earlier in the literature [15]. We also discussed why this lower bound is incorrect and showed, based on conservation of energy, that the correct lower bound for the pore-blockade time for field-driven translocation is given by $\eta N^{2\nu}/E$, where η is the viscosity of the medium surrounding the polymer. Our theoretical analysis has been supported by high precision computer simulation data, generated with a three-dimensional self-avoiding lattice polymer model.

Having worked out the physics of field-driven polymer translocation in the absence of hydrodynamical interactions, it is worthwhile to reflect on the scaling of pore-blockade times as a function of the polymer length N in the presence of hydrodynamical interactions. Hydrodynamical interactions will modify the memory kernel $\mu(t)$ — changing it from $t^{-(1+\nu)/(1+2\nu)} \exp(-t/\tau_{\text{Rouse}})$ to $t^{-(1+\nu)/(3\nu)} \exp(-t/\tau_{\text{Zimm}})$ [13, 17], where τ_{Zimm} is the Zimm relaxation time, scaling as $N^{3\nu}$ in good solvent for a polymer of length N. This implies that the pore-blockade time will behave as $N^{3\nu/(1+\nu)}$ under the influence of hydrodynamical interactions. In this context we note that the scaling of the pore-blockade time has been experimentally measured to scale as $N^{1.26\pm0.07}$ [11]. In the scaling limit $3\nu/(1 + \nu) \simeq 1.11$. The value for ν suggested in Ref. [11] is 0.611 ± 0.016, for which $3\nu/(1+\nu) \simeq 1.14\pm0.02$, a bit closer to 1.26 ± 0.07. For a physical explanation of the scaling of the pore-blockade times with polymer length, the authors of Ref. [11] arrived at an answer 2ν using a macroscopic view of the translocating polymer, assuming that the translational velocity of the centre-of-mass of the untranslocated part is constant in time, and (implicitly) that the memory kernel is a δ-function. Our analysis in this paper, as well as in Refs. [13, 17–19] based on memory effects, therefore, casts serious doubts on the physical interpretation of Ref. [11]: as we have repeatedly shown that the velocity of translocation is not uniform in time, and the same part of the polymer visits the pore a multitude number of times. Although so far our work has

not incorporated hydrodynamical interactions explicitly, it is difficult to imagine that introducing hydrodynamical interactions will mysteriously wipe out the entire memory effects in the polymer.

Acknowledgements

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[28] For unbiased translocation, EN in this argument is to be replaced by the difference in free energy (or entropy) of a threaded polymer, corresponding to $s = N/2$, and the translocated polymer, corresponding to $s = N$. This leads to the inequality $\tau_d \geq \eta N^{1+2\nu}$.

[29] Note that with $\phi(t)$ a constant, strictly speaking, the integral (6) does not converge. The divergence stems from the assumption that $\mu(t) \sim t^{-(1+\nu)/(1+2\nu)}$ holds all the way to $t \to 0$. This is clearly not true as can be seen from Fig. 3, which provides the required cutoff for the convergence of the integral (6).