Anomalous dynamics of translocation

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We study the dynamics of the passage of a polymer through a membrane pore (translocation), focusing on the scaling properties with the number of monomers N. The natural coordinate for translocation is the number of monomers on one side of the hole at a given time. Commonly used models that assume Brownian dynamics for this variable predict a mean (unforced) passage time τ that scales as N^2, even in the presence of an entropic barrier. In particular, however, the time it takes for a free polymer to diffuse a distance of the order of its radius by Rouse dynamics scales with an exponent larger than two, and this should provide a lower bound to the translocation time. To resolve this discrepancy, we perform numerical simulations with Rouse dynamics for both phantom (in space dimensions $d=1$ and 2), and self-avoiding (in $d=2$) chains. The results indicate that for large N, translocation times scale in the same manner as diffusion times, but with a larger prefactor that depends on the size of the hole. Such scaling implies anomalous dynamics for the translocation process. In particular, the fluctuations in the monomer number at the hole are predicted to be nondiffusive at short times, while the average pulling velocity of the polymer in the presence of a chemical-potential difference is predicted to depend on N.

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I. INTRODUCTION

The process of translocation, in which a polymer worms its way through a narrow pore, is an event important to many biological systems. Examples include the viral injection of DNA into a host, DNA packing into a shell during viral replication, gene swapping through bacterial pili, and the genetic technique of cell transformation by DNA electroporation [1]. There are also a number of recent *in vitro* experiments on translocation, the electric-field-induced migration of DNA through microfabricated channels [2], or through an α-hemolysin protein channel in a membrane [3,4]. The driving force is an essential ingredient in the above process, as are the entropic and cooperative factors that arise from the connectivity of the polymer. An interesting statistical consequence of the latter is that the polymer faces an entropic barrier, as the number of available configurations is least when the chain is halfway through the hole. In this regard it shares similarities with other entropically controlled polymer systems, e.g., polymer trapping in random environments [5–7], DNA gel electrophoresis [8], or reptation [9]. In these cases, the geometry of the obstacles around which the polymer must diffuse constrains the kinetics of the process.

A number of recent theoretical works have shed light on the translocation process [3,10–14], mostly in the presence of a driving force. A common approach is to focus on the dynamics of a single variable representing the monomer number at the pore [10,13,15]. Due to its resemblance to the ''reaction coordinate'' for chemical processes, we shall refer to this parameter as the translocation coordinate. Assuming that the segments on the two sides of the hole are in equilibrium leads to a force acting on the trapped monomer that may be derived from the entropic barrier mentioned before, as well as any chemical-potential differences that may provide a driving force. The translocation problem is thereby reduced to the escape of a ''particle'' (the translocation coordinate) over a potential barrier.

Assuming *Brownian dynamics* for the translocation coordinate, and in the absence of a driving force, the characteristic first passage time scales as N^2, where N is the number of monomers. This result cannot be reconciled with the equilibration time of a polymer that scales as N^α, with a dynamic scaling exponent α that is larger than two for Rouse dynamics of self-avoiding chains. Clearly, we expect the constraint of passage through a hole to slow down rather than speed up the dynamics of the polymer, conceivably leading to an exponent even larger than α. Previous work recognizes this difficulty; for example, Ref. [13], while using the Brownian particle analogy, clearly explains why it is applicable to the preasymptotic region of interest in this paper. In this paper, we consider the true asymptotic scaling of the translocation time for large N, and find that its scaling is similar to the corresponding equilibration time, albeit with a larger prefactor. Since we cannot rely on the Brownian particle picture in this regime, we reach this conclusion by numerical simulations.

The problem is to calculate the time required for a polymer to move from one side of a rigid wall to the other through a narrow hole. This is schematically depicted in Fig. 1, with the space on both sides of the wall being infinite. Although frequently a driving force, such as an external field or chemical potential difference is present in the problem, we shall restrict ourselves to a model without external forces. For translocation to occur, there must be two events. The first is the collective diffusion of the polymer to the vicinity of the pore; the second is its threading through the pore. For a finite system, or in the presence of a finite concentration, the first event takes a time determined by the concentration of polymers in solution, their diffusion constant, and the effective cross section of the hole. This time is decoupled from the time for the second event, which is constrained by the

passage of all monomers through the hole. Since we are interested only in the latter event, we shall assume that in the initial state, the first monomer of the polymer chain is already threaded through the hole. To avoid the situation in which the polymer withdraws from the hole and drifts away to infinity, we add the restriction that the first monomer is never allowed to cross back out of the hole. These constraints effectively isolate the translocation time from the time for the polymer to find the hole [11].

Despite the conceptual simplicity of the translocation problem, it has been difficult to solve analytically. Even the simplified case of a Gaussian polymer in a one-dimensional space moving past a potential barrier is nontrivial [16]. Consequently, theoretical treatments resort to approximations such as reducing the problem to Brownian dynamics of the translocation coordinate. As reviewed in Sec. II, the focus of this approach is the probability density function $p(s,t)$ that a particular monomer (labeled by its sequential number s along the chain) is located at the hole at time t. For such a constrained configuration, one may derive the entropy of the polymer if the segments on the two sides are in equilibrium. This entropy is then assumed to generate a force acting on the monomer, favoring its motion to one side or the other. Naturally, stochastic forces are also present (and, in fact, necessary to push the chain over the entropic barrier). Assuming that the translocation coordinate obeys Brownian dynamics, this leads to a Fokker-Planck equation for the evolution of $p(s,t)$. The standard Kramers' approach to escape over a potential barrier yields a mean translocation time that scales with the number of monomers as N^2, i.e., the entropic barrier does not modify the diffusive scaling. We supplement this result with a numerical integration of the Fokker-Planck equation that yields the complete distribution function for transit times. The Rouse model for the dynamics of a *phantom chain* also predicts a time of order of N^2 for the equilibration of the polymer. Since such equilibration is essential to the use of the entropy function as the driving force, the internal consistency of the approach is in doubt. This is even more so when considering self-avoiding polymers, where the relaxation times are much larger than N^2. Noting this contradiction, we proceed to numerical simulations in the rest of the paper.

In Sec. III, we report on simulations of a phantom chain in one dimension. In this case, the relaxation time of the chain scales as N^2, and is thus not inconsistent with the predictions of the Brownian particle analogy. We do indeed find that the probability density function for translocation times (once appropriately scaled) is quite similar to that obtained from solving the Fokker-Planck equation. However, the mean translocation time, while appearing to scale as N^2, has a much larger prefactor, which depends on the size of the hole. Unfortunately, in one dimension, self-avoiding chains are fully stretched, and do not provide a fair model for translocation of a coiled polymer.

Two-dimensional polymers as described in Sec. IV, are ideal for studying the scaling of translocation times in a more complex situation. On the one hand simulations are faster and easier than in three dimensions, while on the other hand, the effects of self avoidance are more pronounced. Our simulations for phantom chains reproduce the trends observed in one dimension, i.e., a mean translocation time scaling as N^2 with a larger prefactor. However, once self avoidance is included, the translocation times increase dramatically, the mean translocation time appearing to scale as N^α, with $\alpha \approx 2.5$, which is the exponent for Rouse relaxation of self-avoiding chains in two dimensions. We find that (for the parameters of our model) translocation times are roughly ten times longer than typical equilibration times. Thus, translocation is indeed much slower than diffusion of the polymer, but appears to scale with the same exponent.

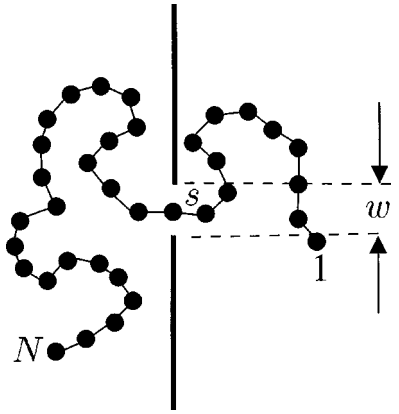

FIG. 1. Schematic representation of a N-monomer polymer in the process of translocation through a hole of size w. The ''translocation coordinate'' s is the number of monomers on one side.

Consequences of this observation are discussed in Sec. V. The observed nontrivial scaling of translocation times is a clear indication of the failure of the Brownian picture for the dynamics of the translocation coordinate. Instead, we suggest that the anomalous dynamics of a specified monomer in a chain provides a better analogy. Following scaling arguments used for the latter, we predict anomalous behaviors for the translocation coordinate $s(t)$. In particular, fluctuations in s are predicted to scale as t^ζ, while in the presence of a chemical-potential $\Delta\mu$, the pulling velocity is predicted to behave as $u \propto \Delta\mu N^\eta$, with $\zeta \approx 0.46$, and $\eta \approx -0.18$ for Rouse dynamics in three dimensions.

II. BROWNIAN TRANSLOCATION

The reduction of the translocation problem to the Brownian dynamics of a single coordinate was introduced in Ref. [17], and further explored in Ref. [10]. Here, we review the main features of this approximation and its consequences. Consider a polymer moving through a pore in a membrane, where the hole is so narrow that only a single strand of polymer may pass through. (Thus, the parameter describing the width of the hole in Fig. 1 is $w=1$.) The progress of the polymer may be tracked by following the number s of the monomer, which is located in the hole at a particular time, as depicted in Fig. 1. Let us denote the probability of monomer s being in the hole at time t by $p(s,t)$. As the monomer s moves forward or backward through the hole a distance a (of order of the typical separation between monomers) the relevant monomer number increases or decreases by unity.

Treating s as a continuous variable, we may write a continuity equation for the probability as

$$\frac{\partial p}{\partial t}+\frac{\partial j}{\partial s}=0, \tag{1}$$

where $j(s,t)$ is the probability current.

The central difficulty is to find an appropriate expression for j that correctly reflects the correlated motion of the whole polymer. If the progress of the polymer is sufficiently slow for the segments on the two sides to come to equilibrium, the monomer at the hole experiences a mean force that can be obtained from the variations of a constrained free-energy $F(s)$. How such a force may be used to deduce the dynamics of the monomer label is not clear. The analogy to Brownian motion suggests that the rate of change of s is related to the force by a mobility μ. Since the polymer fluctuates back and forth between the two sides, there must also be a stochastic element that may be represented by a random force. If there are no correlations in this force at different times (as in the standard Langevin formulation for a Brownian particle), there is a current that depends on the local probability density as

$$j=-D\left(\frac{\partial p}{\partial s}+\frac{p}{k_BT}\frac{\partial F}{\partial s}\right), \tag{2}$$

where the diffusion parameter D is proportional to the variance of the stochastic force [18]. As in standard Brownian processes, the above equation assumes that the mobility is related to the temperature T by $\mu=D/k_BT$, where k_B is the Boltzmann constant. No similar restriction is made in Ref. [13], which obtains the diffusion term from considerations of symmetry and locality. However, as elaborated in Sec. V, the assumption of locality need not be valid in this case, since the true dynamics of s must reflect the collective behavior of the whole polymer.

Calculating the restricted free-energy $F(s)$ is reasonably straightforward, and equivalent to finding the number of possible configurations of a polymer attached at one point to an impenetrable barrier. The exact solution is known for the case of one-dimensional discrete random walks with fixed step length (see, e.g., Ref. [19]): It can be shown that (in the large N limit) the number of N-step walks that start at a boundary and never return to it is $\sqrt{2/\pi N}\times 2^N$. Thus, the number of configurations with s monomers on the right and $N-s$ monomers on the left has the s-dependence $A/[(N-s)s]^\gamma$, where A is independent of s and $\gamma=1/2$, giving the s-dependent part of the free energy as

$$F=\gamma k_BT\ln[(N-s)s]. \tag{3}$$

To this result we add the conditions that the first monomer can never be withdrawn from the hole, and that after the Nth monomer crosses the wall, the polymer will no longer return to it. Figure 2 depicts the resulting free energy for the case of $N=1000$. The two conditions are shown by two vertical lines on the sides of the graph: the line on the left (infinite barrier) signifies our assumption that the first monomer may never cross back through the hole, while the vertical line on the right ($-\infty$) represents the escape of a polymer that has crossed the barrier. The numbers of configurations of polymers in higher-space dimensions d, whether phantom or self avoiding (SA), cannot be calculated exactly. However, it is known that they have the same dependence on the polymer length [20], with γ in Eq. (3) replaced by a number that depends on d ($\gamma=1/2$ for phantom chains). Thus, the s-dependent part of the free energy will have a different prefactor, but the logarithmic dependence remains unchanged.

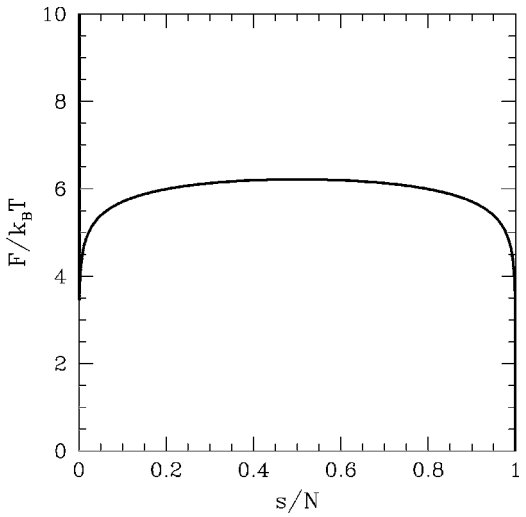

FIG. 2. The entropic potential barrier found in the single variable equivalent to the polymer translocation problem.

By inserting Eq. (3) into Eqs. (1) and (2), we reduce polymer translocation to a standard single-particle problem of escape over a potential barrier. It is interesting to note that if we rescale the variables according to $s\to sN$, $t\to tD/N^2$, all N and D dependence is eliminated from the equation, resulting in

$$\frac{\partial p}{\partial t}=\frac{\partial^2 p}{\partial s^2}+\gamma\frac{\partial}{\partial s}\left(\frac{1-2s}{(1-s)s}p\right). \tag{4}$$

The solution to this dimensionless equation may be converted back to real time by multiplying the t axis by N^2/D. Thus, under the assumptions listed above, the escape time of a particle, and thus the translocation time of a polymer are proportional to N^2/D. Note that this conclusion is *independent* of the value of the parameter γ, and remains valid even for a SA chain in which γ has a different value.

The problem of escape from a *deep* well in one dimension was considered by Kramers [21]. Assuming that the escape rate is slow, i.e., if at every moment in time the probability distribution of a particle in the well can be represented by an equilibrium (Boltzmann) weight, Kramers' method enables an analytic calculation of the mean escape time. Applying Kramers' formula to the logarithmic potential of the problem, one finds [17,10] (for $\gamma=1/2$) that the mean escape time τ is $(\pi^2/16)N^2/D$. The distribution of escape times in Kramers' formula is by construction a simple exponential. Equation (4) may also be solved numerically, by placing a delta function at the left edge of the potential depicted in Fig. 2 at $t=0$ and integrating in time. There are some differences between the numerical solution to Eq. (4), and the Kramers

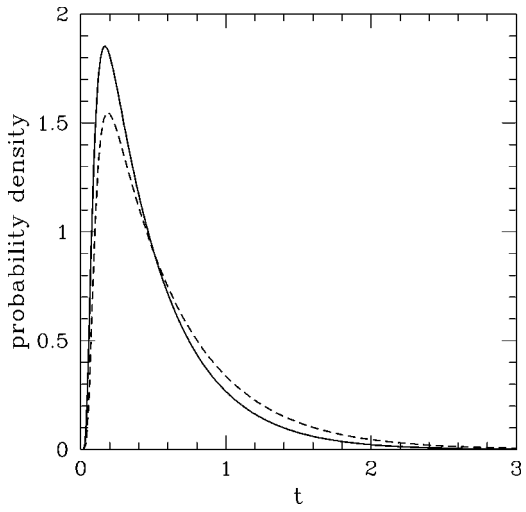

FIG. 3. Probability distribution of escape times measured in reduced, dimensionless, units. The dashed curve corresponds to the logarithmic potential depicted in Fig. 2, while the solid line is in the absence of the entropic barrier. The curves were obtained by numerical integration of the Fokker-Planck equation.

solution, e.g., the former decays to zero for $t \to 0$ due to the time it takes for the delta function to diffuse out of the well. However, the mean escape time for the numerical solution is $\tau \approx 0.6N^2/D$, which almost coincides with the approximate Kramers result. The distribution of escape times calculated from integrating the Fokker-Planck equation is shown by the dashed line in Fig. 3.

If the potential barrier is absent altogether, then the distribution of escape times may again be calculated (e.g., by numerical integration), and is depicted by the solid line in Fig. 3. The mean escape time in this case is $\tau \approx 0.5$ (in reduced units of N^2/D). There is only a 20% difference between the mean escape times of the problems with and without the logarithmic potential barrier. More strikingly, there is little difference in the distribution of times with or without a barrier. (This barrierless version of the problem can be thought of as describing the adsorption of a particle starting at a unit distance from a sink. From a polymer perspective, it corresponds to the passage of a polymer through a *ring*—although the polymer must pass through a constricted space, its free ends may have any possible configuration.) In view of the minute effect of the entropic potential, the notion of ''escape over a barrier'' does not provide a particularly useful analogy.

A central assumption in the reduction of the polymer problem to a single coordinate is that translocation is slow. Specifically, it should be slow enough that the polymer segments on the two sides of the membrane are in equilibrium at every value of s. We may check for the self consistency of this assumption: The equilibration time of a free polymer may be estimated [9] as the time required for it to diffuse its own radius of gyration R_g. Under Rouse dynamics (which ignores hydrodynamic effects), the diffusivity of the center of mass of an N-monomer polymer is reduced to D/N, where D is the diffusion constant of a single monomer, resulting in an equilibration time of order of $R_g^2 N/D$. For phantom polymers $R_g^2 \sim N$, and, consequently the equilibration time is of the same order (N^2/D) as the mean passage time obtained with Brownian translocation dynamics. Thus, the equilibrium assumption is marginally (in)valid in this case. On the other hand, for self-avoiding polymers $R_g \sim N^\nu$, where $\nu = 0.75$ and 0.59 for dimensions $d=2$ and 3, respectively. The resulting relaxation times $(\sim N^{1+2\nu}/D)$ are now longer than the translocation times predicted $(\sim N^2/D)$ by Brownian dynamics, and consequently, the approximations involved are not self consistent. In the following sections, we try to gain further insights into the problem by numerical simulations of the translocation of a polymer in one and two dimensions.

III. SIMULATIONS IN ONE DIMENSION

We begin by examining the translocation of a *one-dimensional phantom* polymer via a Monte Carlo simulation with Rouse-like dynamics as follows. Our model consists of a chain of N ''atoms'' placed on the sites of a one-dimensional lattice. No excluded volume interactions are present, and the spatial distance between two neighboring atoms (along the sequence of the chain) can be 0, 1, or 2 lattice spacings, i.e., the ''bond'' between adjacent atoms has a maximal length of 2. This represents a trivial implementation of the fluctuating-bond method [22]. Initially, the first atom of the chain is placed on, say, the right of the membrane, while all other atoms are on the left. (We assume that the membrane is located between the coordinates $x=0$ and $x=1$ and, consequently, the first atom is initially placed at $x=1$, while the rest of the atoms are at $x \leqslant 0$.) During the simulation, the first atom of the chain is never allowed to move to the left of the membrane. The ''width'' w of the hole is adjusted by changing the maximal number of bonds allowed to be simultaneously present at the hole. An elementary move consists of randomly picking an atom and attempting to move it one lattice step in a randomly selected direction. If the configuration does not violate any of the restrictions of the model it is accepted. N elementary atom move attempts are defined as one Monte Carlo time unit.

Each simulation is terminated when all monomers are on one side. Figure 4 depicts the distribution of translocation times of such phantom chains measured for several chain lengths, and for unit width of the hole. If we normalize the time for each N by the mean translocation time τ for that length, we observe that the resulting curves are quite similar and closely resemble the theoretical curve obtained assuming a Brownian translocation coordinate. While the similarity may appear to support this picture, we should note that since the distribution is constrained to vanish at both short and long times, qualitative similarities are dubious. Moreover, the absolute values of the mean translocation time τ, as depicted in Fig. 5, are significantly larger than the estimates from Brownian dynamics. This log-log plot indicates that the apparent exponent is somewhat larger than two for small N, and only gradually approaches the scaling form $\tau \sim N^2$. However, the prefactor of the power law for $N=256$ is roughly two orders of magnitude larger than expected for a Brownian translocation coordinate. Such discrepancy should not be surprising—the translocation time predicted by this

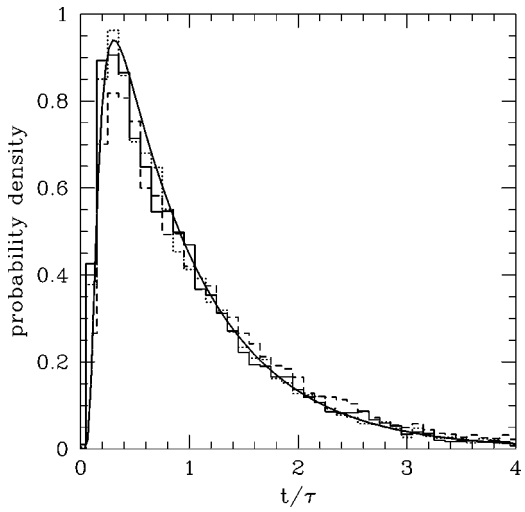

FIG. 4. Probability density of translocation times for one-dimensional phantom polymers. Solid, dotted, and dashed lines correspond to polymer lengths $N=32$, 64, and 128, respectively, and were extracted from 10 000 simulations, each. The times have been normalized by their respective mean translocation time $\tau(N)$ in each case. The continuous curve corresponds to the solution of the Fokker-Planck equation in the single-particle approximation.

model is similar to the time required for a polymer to diffuse its own radius of gyration. It is reasonable to expect that passage through a narrow hole should be slower than diffusion without a wall.

Not surprisingly, translocation times are strongly effected by the width w of the hole, as indicated in Fig. 6. When w reaches the size R_g of the chain ($\sim\sqrt{N}$) the translocation time should become independent of w. This is supported by the saturation of the rescaled times τ/N^2 at roughly the same value of $w/R_g \sim w/\sqrt{N}$ in this figure. For small holes, the translocation times are strongly dependent on the hole size,

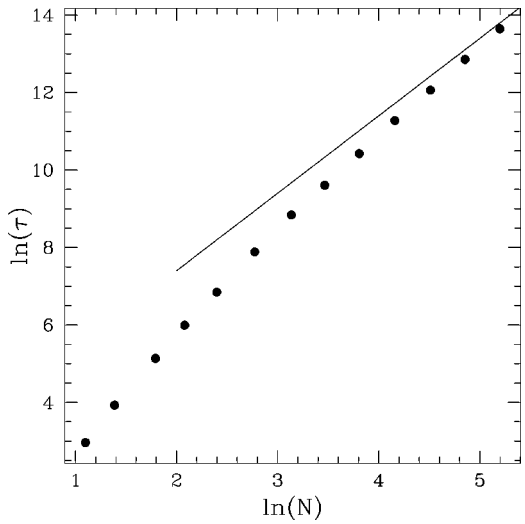

FIG. 5. Logarithmic plot of the mean translocation time τ as a function of chain length N for a one-dimensional phantom polymer. Each data point represents an average over 10 000 realizations. The solid line has slope 2.

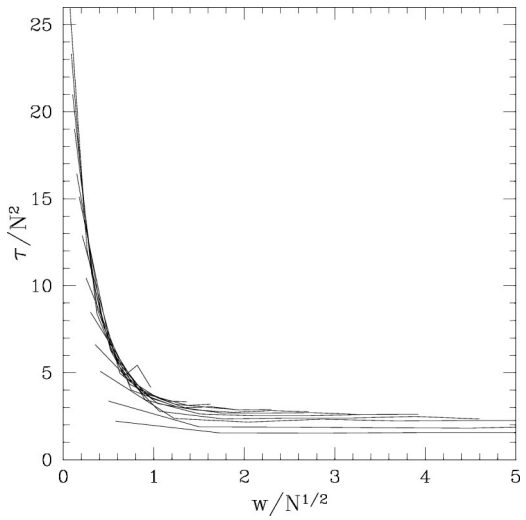

FIG. 6. Dependence of the mean translocation time τ on the width of the hole w, for $N=3$, 4, 6, 8, . . . 91, 128, and 181. The times have been normalized by N^2 to focus on the behavior of the prefactor. Each curve corresponds to fixed N, and is obtained by averaging over 1,000 cases.

and show some indications of collapse onto a universal curve, but the N^2 dependence is not as clear as for the wider holes.

IV. SIMULATIONS IN TWO DIMENSIONS

Excluded volume effects drastically modify the shape and properties of the one-dimensional phantom polymer considered in the previous section. The chain becomes stretched, and its dynamics are then limited by reptation [9]. To study the effects of self avoidance on translocation in the coiled state, higher-dimensional simulations are necessary. Two-dimensional polymers are ideally suited to this purpose for the dual reasons that excluded volume effects are more apparent, while computation times are shorter than in the three-dimensional case.

As in the one-dimensional (1D) system, we employ a fluctuating-bond model for simulations [22], implementing Rouse-like dynamics for linear polymers of several different lengths N. Simulations were performed both with and without excluded volume constraints. In this model, the monomers of the polymer lie on a $2D$ square lattice. Random motion is simulated through a series of elementary moves of single monomers. In each move, a monomer is selected randomly and then moved a single lattice unit in one of the $+x, -x, +y$, or $-y$ directions. If the move violates any of several constraints, it is rejected. For phantom chains, bonds have a maximal allowed length of $\sqrt{10}$ lattice units. For excluded volume chains, in addition, the distance between any two monomers is constrained to be at least two lattice units. For excluded volume chains, these constraints also prevent the chain from crossing itself [22]. The wall has a thickness of three units and the hole has a width of two lattice units. At these sizes, only one monomer may be in the hole at a time, but the hole is large enough that translocation may occur with the given move set. Each N elementary atom move attempts are defined as one Monte Carlo time unit.

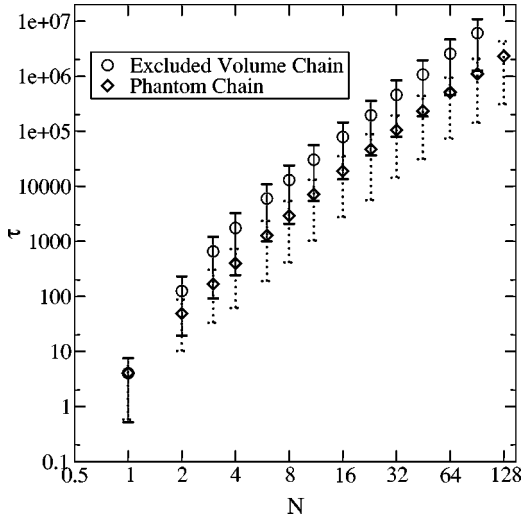

FIG. 7. Logarithmic plot of the mean translocation time τ as a function of chain length N, for two-dimensional phantom and excluded volume polymers. Errorbars indicate the standard deviation over runs.

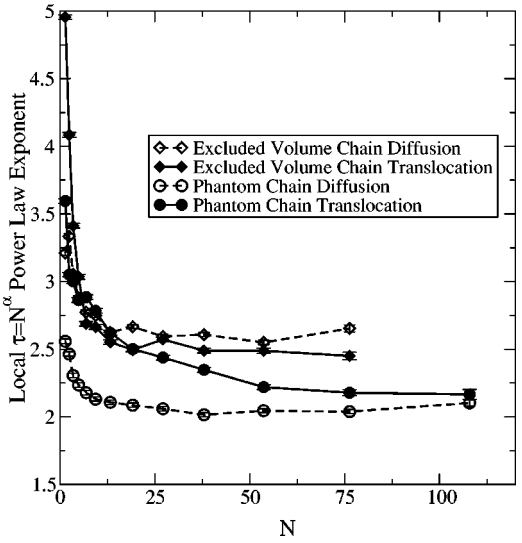

FIG. 8. The effective power-law exponents for translocation and diffusion times as a function of length N for $2D$ polymers. For both translocation and free diffusion, self-avoiding chains exhibit a dynamic exponent that approaches 2.5, equal to $1+2\nu$ given the $d=2$ swelling exponent of $\nu=3/4$. For phantom chains, the exponent is noticeably smaller, and approaches two. In both the self-avoiding and phantom cases, the asymptotic exponent for translocation time nearly equal to that for Rouse relaxation.

The simulation begins by placing the first monomer at the hole, while the remaining $N-1$ monomers are in a random conformation on the left side of the wall. (To generate the initial random configuration, the chain is first allowed to fluctuate subject to the constraints of impermeability of the wall and fixed location of the first monomer. The fluctuation time is $20N^2$, which should be sufficient to randomize the initial condition for the purposes of our simulations, at the length scales employed. In any case, the time it takes for translocation is many times longer than the Rouse relaxation time, and any initial condition effects will be transients.) Once the initial configuration has been established, the polymer is allowed to move in accordance with the restrictions of the model. We measure the time between the beginning of the translocation, and the moment when the last monomer enters the hole. Because only one monomer may lie in the aperture at a time, this condition is equivalent to the complete translocation of the polymer through the hole. As in the one-dimensional case, the first monomer is not allowed to move to the left of the hole.

Translocation times were calculated for a number of different chain lengths N, with several thousand runs at each length. (The number of runs decreases with increasing N, due to CPU limitations.) Theses results are shown for both phantom and self-avoiding chains in Fig. 7. Errorbars indicate the standard deviation of translocation times over runs.

We then attempted to fit the results to a dynamic scaling form, with the effective exponent depicted in Fig. 8. The points are a plot of the local exponent α, assuming a power-law $\tau \sim N^{\alpha}$, as determined from two neighboring polymer lengths N_1 and N_2 via the formula $\alpha(\sqrt{N_1 N_2}) = \log[\tau(N_2)/\tau(N_1)]/\log(N_2/N_1)$. The exponent α for the excluded volume translocation approaches an asymptotic limit that is definitely larger than two. This clearly indicates that excluded volume effects are inconsistent with Brownian dynamics for the translocation coordinate. The data for the translocation times of a phantom polymer (in which the self-avoiding constraint of the bond-fluctuation model is removed) are also included in this figure. The power-law exponent in this case asymptotically approaches a value close to 2, in agreement with the one-dimensional results, and consistent with Brownian dynamics. At each N, the uncertainty in the average translocation time (equal to the standard deviation of $\tau(N)$ over runs divided by the square root of the number of runs) has been translated into an uncertainty in the local power law. This uncertainty, as depicted by the error bars, is quite small, indicating that our conclusion is not due to statistical fluctuations.

The observed scaling laws for self-avoiding and phantom polymers in fact agree with the exponents expected theoretically for Rouse relaxation in the absence of a wall. As stated previously, translocation across the barrier requires that, minimally, the chain diffuses a distance equal to its radius of gyration. The time for such diffusion is $\tau_R \sim R_g^2 N/D \sim N^{1+2\nu}$. For a self-avoiding walk in two dimensions, $\nu = 3/4$ and $\tau_R \sim N^{2.5}$, while for a phantom chain, ν is replaced by 1/2, leading to the relationship $\tau_R \sim N^2$. For comparison, Fig. 8 also shows the derived power-law exponents from simulations of simple diffusion in the absence of a wall. For an excluded volume chain, we approach the scaling $\tau \sim N^{2.5}$, while for the phantom chain $\tau \sim N^2$. The latter results were generated as follows: We started with the same type of random initial configurations (generated by annealing near an impermeable wall) as for the translocation case, and again imposed the constraint that the first monomer cannot pass to the left side of an imaginary wall. The other monomers, however, are allowed to diffuse without feeling this wall. The simulation was stopped when all monomers moved to the right of the imaginary wall.

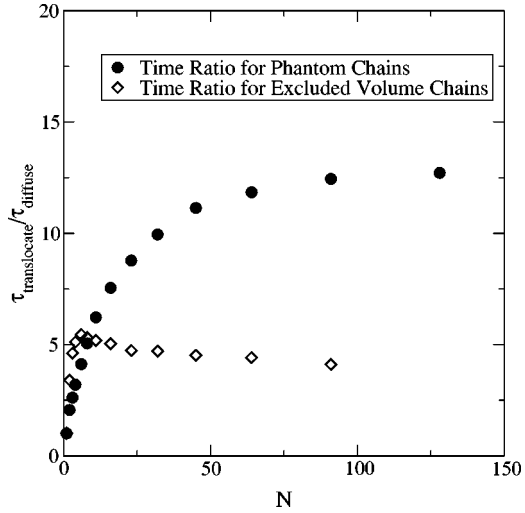

FIG. 9. Comparison of simulation results for diffusion through a hole that may fit one monomer versus free diffusion. Translocation times through the hole are larger than the free diffusion for both phantom and self-avoiding chains. In both cases, the ratio of these times levels off to a constant.

At least in these examples, we find that the scaling of translocation times is the same as that for equilibration of the polymer in the absence of a wall. However, the constraint of passing through the hole must clearly slow down the dynamics of the polymer compared to the case of free diffusion over a similar distance. This slowdown must then be reflected in an overall prefactor that determines how much slower translocation is relative to pure diffusion. The data that address this issue are displayed in Fig. 9. The ratio of crossing times for translocation compared to pure diffusion (as described in the previous paragraph) are plotted for both self-avoiding and phantom chains. For self-avoiding polymers, the hole slows down the chain by a factor of about 5; while for phantom chains the ratio is about 13. These numbers are roughly N independent for $N>10$ (for excluded volume chains) and $N>50$ (for phantom chains). It is interesting to note that translocation slows down the phantom chain more than it does the excluded volume chain. However, these ratios should not be taken too seriously, since for more realistic systems such as the translocation of DNA molecules through a cell membrane, the details of the shape and interaction forces at the pore play a significant role [3,13,4].

V. DISCUSSION

The central result of this paper is the nontrivial scaling of the mean translocation time τ for unforced passage of a polymer through a hole with its length N. For the diffusive dynamics of a self-avoiding chain in $d=2$, numerical simulations indicate $\tau\sim N^{2.5}$. By extension, we expect $\tau\sim N^{\alpha}$ with $\alpha=1+2\nu$ for diffusive dynamics. Possibly even more generally for other types of dynamics $\alpha=\nu z$, where the swelling exponent ν relates the radius of gyration of the polymer to its length by $R_g\sim N^{\nu}$, while its relaxation time scales as $\tau_r \sim R_g^z$ with the dynamic exponent z.

The natural parameter for following the progress of the translocation process is the label $s(t)$ for the monomer in the hole at time t (see Fig. 1). A commonly used analogy is that this ''reaction coordinate'' undergoes stochastic motion, as in a Brownian particle in a force field [10,15,13]. For unforced translocation (with or without the inclusion of an entropic barrier), such approaches lead to $\tau\sim N^2$, which is inconsistent with our numerical results, except for the case of diffusing phantom polymers. Such scaling is also at odds with the expectation that constraining the polymer to pass through a hole should slow down its dynamics compared to free motion over a similar distance. The numerically observed scaling is thus indicative of *anomalous dynamics* of the translocation coordinate $s(t)$—we propose instead an alternative analogy that incorporates this observation.

The dynamics of the polymer is the result of cooperative motions of its many monomers. When described by just a single variable, say the translocation coordinate, the effect of the other degrees of freedom is to exert correlated forces leading to anomalous dynamics. This is best illustrated by the well-studied case of the dynamics of a single monomer in a polymer: Consider the position $\vec{r}(t)$ of a particular atom in the background of all the other monomers. The dynamics of $\vec{r}(t)$ has indeed been studied by numerical, analytical, and experimental methods [23]; its anomalous features are easily captured by the following scaling argument: For short times, we expect that the squared change in the position has a scaling form $\langle\Delta r^2(t)\rangle\sim t^{2\tilde{\zeta}}$, with no dependence on N since the monomer does not yet feel any effects from the finite size of the polymer. At a time of the order of the relaxation time τ_r for the whole chain, the monomer should have moved by a distance of the order of its radius of gyration, giving $R_g^2 \sim \tau_r^{2\tilde{\zeta}}$. Since $\tau_r\sim R_g^z$, we immediately obtain the exponent $\tilde{\zeta}=1/z$ describing the anomalous fluctuations of the specified monomer at short times.

We now adapt a similar scaling argument to describe the squared change in the translocation coordinate, assuming $\langle\Delta s^2(t)\rangle\sim t^{2\zeta}$ at short times. This behavior should saturate when s becomes of the order of the chain length in a time $\tau\sim R_g^z\sim N^{\nu z}$ (assuming that translocation times always scale in the same way as equilibration times). Substituting this in the former equation allows us to identify the exponent $\zeta=1/(z\nu)$ for anomalous dynamics of the translocation coordinate. For the case of diffusive polymer dynamics, we thus obtain $\zeta=1/(1+2\nu)$ resulting in $\zeta=2/5$ and $\zeta\approx 0.46$ for self-avoiding chains in two and three dimensions, respectively; i.e., in this case, the fluctuations are *subdiffusive*. If we naively use the Zimm exponent $z=d$ describing the relaxation of polymers in hydrodynamic flows in d dimensions, we obtain $\zeta(d=2)=2/3$, while $\zeta(d=3)\approx 0.56$, i.e., the fluctuations are predicted to be *superdiffusive* in this case. The usual origin of the speed up of polymer dynamics in a fluid is attributable to the velocity flow field set up by the other monomers. It is doubtful that using the bulk Zimm exponent remains valid for flows that must vanish in the vicinity of the wall. Thus, the above prediction of superdiffusive behavior should not be taken seriously prior to a proper analysis of the hydrodynamic correlations in the vicinity of the wall.

It is experimentally hard to directly probe the motion of the translocation coordinate. The quantity that is easily measured in experiments [4] is the distribution of the translocation times *in the presence of a force* introduced via a chemical-potential difference $\Delta\mu$ for monomers on the two sides of the wall. While our results so far were in the absence of such a driving force, anomalous dynamics has consequences for the length dependence of the forced velocity. Let us first recall the arguments for the drift velocity v of a polymer in a force $\vec{F}$: Scaling considerations suggest $v(F) \sim (R_g/\tau_r)\phi(FR_g/k_BT) \sim N^{\nu(1-z)}\phi(FN^{\nu})$, where ϕ is a scaling function depending on the ratio of two quantities having dimensions of energy. The proportionality of the velocity to the force requires a linear scaling function, leading to a mobility $v/F \sim N^{-\nu(z-2)}$. For Rouse and Zimm dynamics, this leads to the well-known scalings of mobility as $1/N$ and $1/R_g^{d-2}$, respectively. Similarly, for the pulling velocity $u \equiv \dot{s}$ of the translocation coordinate, scaling suggests $u \sim N/\tau\phi(\Delta\mu N/k_BT) \sim N^{2-z\nu}\Delta\mu$. Only for the case of diffusive dynamics of a phantom chain is this velocity independent of N. The anomalous slowdown due to Rouse dynamics leads to a mobility that scales as $N^{-1/2}$ in $d=2$, and $N^{-0.18}$ in $d=3$. By contrast, hydrodynamic speeding up with Zimm dynamic exponents leads to a mobility that grows as $N^{1/2}$ and $N^{0.23}$ in two and three dimensions, respectively. Once more, the latter results are not to be taken seriously without full hydrodynamic calculations in the presence of a wall. Experiments so far [4] do not indicate anomalous scaling, but the size range may not be sufficient to detect the rather small exponent.

In the experiments of Ref. [4], the pulling velocity of single-stranded DNA through a nanopore was observed to be independent of N in the range of 10 to 100 base pairs, although it exhibited a nonlinear dependence on the applied voltage. While the latter is attributed to the strong interactions of DNA with the pore, it is intriguing to inquire if nonlinearities could be intrinsic to translocation dynamics. In particular, in the previous paragraph we assumed that the function $\phi(\Delta\mu N/k_BT)$ is linear in its argument. While this is likely true for small applied force, it may well cross over to a nonlinear form at larger values of its argument. If the pulling velocity is then independent of N, it acquires the nonlinear form $u \sim (\Delta\mu)^{z\nu-1}$. This possibility provides impetus for further numerical studies of forced translocation.

We conclude by listing two other avenues of potential exploration. The first is to note that the distribution of translocation times should also be modified by the anomalous dynamics, potentially to include power-law tails that are distinct from the exponential tails in Fig. 3 [24]. Secondly, it may be possible to construct an experimental system close to our two-dimensional simulations, using vibrated granular chains in a variation on the setup used in Ref. [25], with a chain that is threaded through a hole in a wall.

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