Probability distributions for polymer translocation

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We study the passage (translocation) of a self-avoiding polymer through a membrane pore in two dimensions. In particular, we numerically measure the probability distribution $Q(T)$ of the translocation time T, and the distribution $P(s,t)$ of the translocation coordinate s at various times t. When scaled with the mean translocation time $\langle T \rangle$, $Q(T)$ becomes independent of polymer length, and decays exponentially for large T. The probability $P(s,t)$ is well described by a Gaussian at short times, with a variance of s that grows subdiffusively as t^α with $\alpha \approx 0.8$. For times exceeding $\langle T \rangle$, $P(s,t)$ of the polymers that have not yet finished their translocation has a nontrivial stable shape.

I. INTRODUCTION

Translocation of a long polymer through a narrow pore in a membrane has been extensively studied experimentally during the last decade [1–3]. It is important in many biological and chemical processes such as viral injection of DNA into a host and RNA transport through a nanopore of the nuclear membrane [4]. It may also have practical applications such as the possibility to "read" a DNA or RNA sequence by passing it through a nanopore such as microfabricated channels or the α-hemolysin channel [5]. Understanding the dynamics of translocation is also of inherent fundamental interest. Theoretically, the short time behavior has been investigated [6] by considering ever more detailed models of the interaction between the polymer and the pore in the membrane. The microscopic details should not be necessary to understand the scaling of the passage time for very long polymers, where it should suffice to resort to rather simple models of the polymer and the membrane.

It is convenient to track the process with a single variable s, called the *translocation coordinate*, that is the monomer number at the pore [7–10], and also indicates how much of the polymer has passed to the other side. In terms of this variable, the translocation process begins when the first monomer enters the pore ($s=1$) and ends when the last monomer exits to the other side at $s=N$, at the translocation time T. If the translocation process is sufficiently slow (to allow for the equilibration of the polymer), the mean force acting on the monomer at the hole can be obtained from a simple calculation of free energies. This is a reasonable approximation for the experimental results of relatively short polymers [5]. The reduction of entropy creates a weak potential barrier, and the translocation problem becomes equivalent to the escape of a "particle" (the translocation coordinate) over this barrier. As is the case for diffusion over an interval of length N, the mean translocation time is found to scale as $\langle T \rangle \sim N^2$. (The logarithmic potential due to entropy is too weak to modify this scaling.)

In the absence of hydrodynamic interactions, the relaxation time τ of a polymer scales with the number of monomers as $N^{1+2\nu}$ [11,12], where the exponent ν characterizes

scaling of the radius of gyration R_g of the polymer by $R_g \sim N^\nu$. In good solvent $\nu=3/4$ in two dimensions (2D), and $\nu \approx 0.59$ in three dimensions (3D). Note that τ is of the order of the time the polymer needs to diffuse its own R_g. Since τ grows faster than N^2, the quasiequilibrium approach to translocation, described in the previous paragraph, must fail for sufficiently large N. The relaxation process slows down the passage of the polymer, and the stochastic forces acting on the translocation coordinate must be anticorrelated. Initial numerical simulations suggest [13] that the resulting mean translocation time $\langle T \rangle$ scales like the relaxation time τ, i.e., $\langle T \rangle \sim N^{1+2\nu}$. This suggests that, to the extent that the resulting process can be regarded as stationary, the translocation coordinate s executes anomalous (subdiffusive) motion. Simple scaling considerations lead to the conclusion [13], that the variance of the translocation coordinate δs^2 increases with time t as t^α with $\alpha=2/(1+2\nu)$. This power is obtained by the requirement that for $t=\langle T \rangle$, $\delta s^2 \sim N^2$, i.e., the translocation is complete.

Anomalous diffusion in translocation is closely related to the behavior of a tagged monomer in a long polymer [14]: At short time scales, before a monomer feels the effects of its neighbors, it undergoes rapid normal diffusion with diffusion constant D_o. At very long times, exceeding the relaxation time τ, the entire polymer (and hence each monomer) diffuses along with the center of mass of the polymer, with a slow diffusion constant of D_o/N. At intermediate times, the fluctuations of the monomer are independent of the total length, and to match the final N-dependent diffusion constant must be characterized by anomalous diffusion [14]. Both the tagged monomer and the translocation coordinate are slowed down by the couplings to the rest of the polymer, and undergo *subdiffusion* since the variances of the relevant variables increase sublinearly ($\alpha<1$). There are of course important differences: the diffusion of a tagged monomer is executed in d-dimensional real space, while the translocation coordinate moves along the one-dimensional axis of monomer numbers. The scaling exponents are also different, although their values are derived from closely related considerations. Recently we studied the constrained motion of a tagged monomer as an indirect means of gaining insight into the distribution of translocation times [15].

There has been much recent progress in the theoretical modeling of translocation: hydrodynamic interactions were taken into account [16,17], and an intuitive scaling picture of polymer translocation under the influence of a force [18,19] was developed. A variety of scaling regimes with force applied to the end point or at the pore have been investigated numerically in some detail [20]. Some recent studies [21,22] suggest that the translocation process in 3D may be even slower than dictated by the relaxation time. If so, this would weaken the analogy between translocation and the motion of a tagged monomer. (The accuracy of these claims is questioned in further work [23].)

Since the translocation process is terminated when s reaches one end of the polymer, one may draw an analogy to the anomalous diffuser in the presence of absorbing boundaries. One approach frequently used to describe subdiffusion is the fractional diffusion equation (FDE) [24]. Solutions of FDE in the presence of absorbing boundaries predict that for large t the absorption probability $Q(t)$ decays as $1/t^{\alpha+1}$ [25]. In the case of subdiffusion ($\alpha < 1$) this decay is so slow that the mean absorption time diverges. By applying this analogy to translocation it has been suggested [26] that the mean translocation time is infinite, and there is a numerical study [22] that lends support for a power-law tail in the distribution of translocation times. If so, this would imply that the experimentally and numerically measured translocation times are artifacts of the finite duration of the experiment. However, this proposition is not supported by experiments or other numerical simulations.

To address this controversy, we recently considered [15] the motion of a tagged monomer belonging to a very long phantom (Gaussian) polymer, moving in one dimension between two absorbing boundaries. We demonstrated that at least in this case, $Q(t)$ decays exponentially even though the monomer undergoes subdiffusion. While this casts strong doubts to the generality and relevance of the conclusions based on FDE, it does not directly address the dynamics of translocation, and thus does not necessarily contradict the conclusions of Ref. [22]. Thus, in this work, we perform a direct and detailed study of the translocation process for a self-avoiding polymer in 2D. We concentrate on the behavior of the distribution of the translocation times, and also on the stationary distribution of the translocation coordinate at very long times. In Sec. II we describe our numerical model and the Monte Carlo (MC) procedure. The results presented in Sec. III demonstrate that for large t the distribution of the translocation times decays exponentially, while the long-time distribution of the translocation coordinate takes a nontrivial form.

II. MODEL AND SIMULATIONS

Simulations of the self-avoiding polymer translocating through a membrane were performed with a fluctuating bond polymer model [27] in 2D. In this model, the N monomers are restricted to the sites of a square lattice. Excluded volume interactions are implemented by forbidding two monomers to be closer than two lattice constants, while the polymeric character is enforced by requiring the separation between

monomers adjacent along the chain to be less than $\sqrt{10}$ lattice constants. This choice of minimal and maximal distances ensures that the polymer never intersects itself. The model contains no energy scale, leading to an extremely simple Monte Carlo procedure: An elementary move consists of an attempt to move a randomly selected monomer by one lattice spacing in an arbitrarily chosen direction. If the new configuration is permitted, the step is executed; otherwise, the configuration remains unchanged. One MC time unit is composed of N elementary moves. This model closely resembles tethered spheres used in continuum [28] simulations. We previously used this model to demonstrate the anomalous dynamics of polymer translocation [13]. The intervening membrane in simulations has a thickness of two lattice constants, with a hole that is three lattice spacings wide. The tight size ensures that only one monomer can pass through the hole, and enables a unique designation of the monomer s which separates the polymer segments on the two sides of the membrane.

The translocation process in actuality involves several complicating factors: The polymer located on one side of the membrane must first reach the pore such that one end enters the pore. In the absence of a strong driving force, it is then quite likely that the polymer retracts and does not pass through to the other side until a number of such attempts. Both of these processes have been discussed in the literature. Since we are only interested in the anomalous dynamics during the translocation process, we implement a computation procedure that is different from the usual experimental conditions. In our simulations, the initial configuration is constructed by fixing the monomer $s = N/2$ in the hole, and equilibrating the remaining monomers for more than the relaxation time (which is proportional to $N^{2.5}$) [11]. After this equilibration is finished, at time $t = 0$, the fixed monomer is allowed to move freely. The simulation ends at time $t = T$ when the entire polymer is on *either side* of the membrane. We denote T the *translocation time*. The procedure is repeated a large number of times for each polymer size N, to construct the probability $Q_N(T)$. For each simulation run, we also record the trajectory $s(t)$ of the translocation coordinate. Consequently, we are able to monitor the evolution of the distribution $P(s,t)$. At the starting moment $P(s,0) = \delta_{s,N/2}$, and it subsequently broadens as the time increases. It should be noted that as t reaches typical translocation times, the fraction of polymers that has completed the process starts to grow, and consequently the probability distribution $P(s,t)$, which is normalized for each t, is obtained from a decreasing sample of runs. Another drawback is that the simulation times increase as $N^{3.5}$, making it difficult to obtain good statistics in the interesting limit of large N. We performed simulations for $N = 8, 16, \ldots, 128$, and 256. Most of the results presented in the paper correspond to $N = 128$, for which we are able to obtain sufficiently many samples.

III. RESULTS

Each of our simulations begins at $s = N/2$, and as the time t increases the distribution $P(s,t)$ becomes broader. As long as t is significantly shorter than the mean translocation time
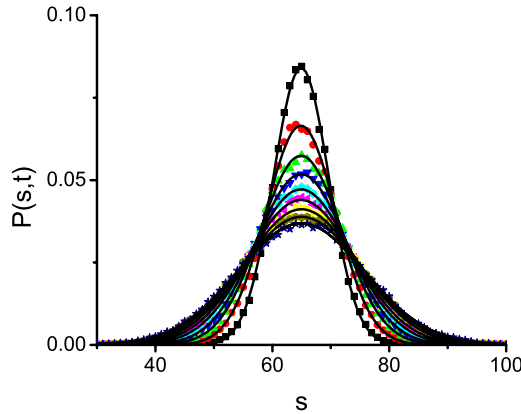
FIG. 1. (Color online) Probability distribution of the translocation coordinate s, of a polymer with $N=128$ monomers for MC times $t=10^4$, $2\times10^4,\ldots,$ and 9×10^4 (from narrowest to the widest distribution), which are significantly shorter than the mean translocation time. The results are obtained from 10 000 independent runs. Continuous lines represent Gaussian fits to these distributions.
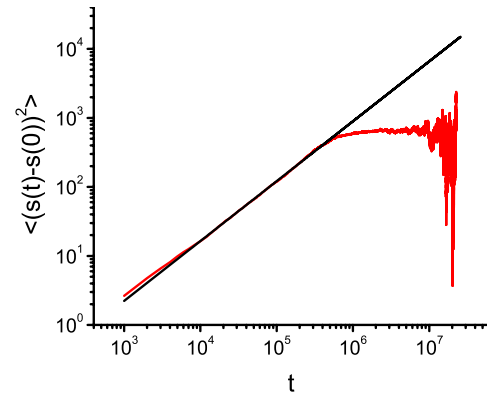

FIG. 2. (Color online) The mean squared displacement of the translocation coordinate s as a function of MC time t, obtained from 10^4 runs of a 128-monomer polymer. The straight line represents the power-law fit t^α in the interval $10^4 < t < 1.2\times10^5$ with exponent $\alpha=0.86$.

$\langle T \rangle$, the distribution of s resembles a Gaussian, as can be seen in Fig. 1, and is very different from the shapes obtained from the solutions of FDE. The plots depict the behavior of s for $N=128$, where $\langle T\rangle \approx 2.9\times10^6$ MC time units. Similar shapes were observed in the simulations of a tagged monomer in a phantom polymer (see Fig. 1 in Ref. [15]), where one can *prove* that the distributions are indeed Gaussian. In our case, there is no analytical proof, and we instead numerically examined the fourth cumulant κ_4 of the distribution, which vanishes for a Gaussian probability density function (PDF). Since the variable s is discrete, κ_4 does not vanish, but should become significantly smaller than the squared second cumulant (which is the variance of the distribution δs^2), as the width of the distribution increases. We find that once this width exceeds 2, the cumulant κ_4 becomes only a few percent of $(\delta s^2)^2$, and the deviation from zero is probably caused by the statistical errors. Thus within our statistical accuracy, the PDF at short times is indistinguishable from a Gaussian. The observed Gaussian behavior does not strongly constrain the choice of the effective theories describing the diffusion of s, since such distribution can be produced by a variety of equations.

As time goes on, the variance δs^2 is expected to increase as t^α, with $\alpha=2/(1+2\nu)=0.8$, and eventually saturate at values of order N^2. Figure 2 depicts such dependence on a logarithmic scale. For a range of times longer than 10^4 this line has a straight segment with slope 0.86, which is slightly larger than the above value, and is consistent with the other numbers quoted in the literature [13,20]. The statistical accuracy of the calculated exponent is better than the last significant digit of the number. However, we believe that systematic errors related to crossovers and specific choice of the fitting range introduce significantly larger (few percent) errors. Curves for various values of N saturate approximately at $\delta s^2 \approx (N/5)^2$, and corresponding saturation time T_1 is obtained by extrapolating the (low-t) power-law behavior to this value. For the various lengths N used in our simulations the ratio $\langle T\rangle/T_1$ is approximately constant (≈ 4).

As the simulation time t exceeds $\langle T\rangle$, a significant fraction of polymers complete their translocation process. For the subsets of runs that survive into such long times, the distribution of $P(s,t)$ reaches a stable shape. In the case of normal diffusion between two absorbing boundaries, the limiting shape is a sine function that vanishes linearly near the boundaries. This shape reflects the lowest eigenfunction of the diffusion operator (Laplacian), corresponding to the longest decay time (eigenvalue). Since we do not know of a corresponding differential equation for the translocation coordinate, we do not know the corresponding limiting shape. Some insight into possible solutions can be gleaned by considering a fractional diffusion operator, as in the case of the Laplacian raised to the power $1/\alpha$, with absorbing boundary conditions (see, e.g., Zoia *et al.* [29]). In the absence of absorbing boundaries the squared width of the distribution produced by such a fractional Laplacian increases as t^α. In the presence of the boundaries, the eigenstates are not known for general α. However, it is known that near the absorbing boundaries the eigenfunction goes to zero nonlinearly, with an exponent of $k=1/\alpha$. For normal diffusion, this naturally reduces to the expected linear form. For subdiffusion, the eigenvalues of this operator vanish faster than linearly; in the case $\alpha=0.8$ with exponent $k=1.25$. Figure 3 depicts $P(s,t)$ for $N=128$ and for times exceeding $\langle T\rangle$. The statistical accuracy of these results is not very good, since a significant fraction of the polymers have already translocated. The accuracy is particularly poor near the end points of the graph where the probability approaches zero. Nevertheless, we observe that the function seems to decay faster than linearly and slower than quadratically. The overall shape of the distribution can be approximated by the function $A\sin^k[s\pi/(N+1)]$. We find a good fit with $k=1.44$. Qualitatively, Fig. 3 resembles the results obtained for tagged monomer diffusion (see Fig. 8 in Ref. [15]), but with a different exponent k.

We also studied the probability distribution $Q(T)$ of the translocation time. In the range from $N=8$ to $N=256$ we find that the mean translocation time $\langle T\rangle$ increases as $N^{2.51}$ consistent with $1+2\nu=2.5$, and in accord with previous work [13,20]. As in the case of the numerical estimate of α, the statistical errors are smaller than the last significant digit, but we should beware of systematic errors. For example, the ex-
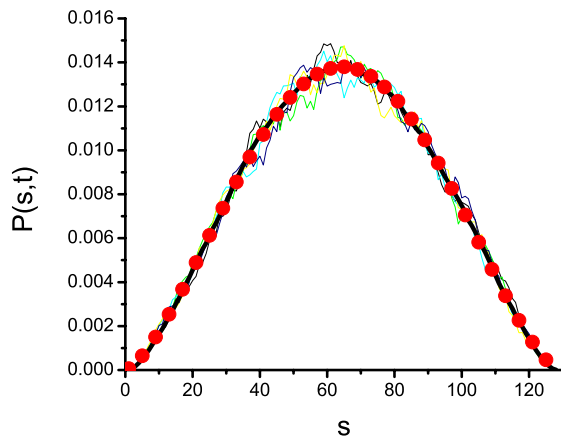
FIG. 3. (Color online) Probability distribution of the transloca-tion variable s of the subset of polymers with $N=128$ monomers that did not complete translocation at MC times $t=40\times10^5$, 42×10^5,..., and 48×10^5 (thin lines), which exceed the mean trans-location time. These graphs were obtained by performing 10^4 inde-pendent runs out of which only 15–20 % survive to the times when the data is collected. The thick solid line is the average of ten graphs in the range $4\times10^6\leqslant t\leqslant4.9\times10^6$. The dotted line depicts the fit function $A\sin^k[s\pi/(N+1)]$ with $k=1.44$.

ponent 2.51 should correspond to $\alpha\approx0.80$, which is smaller than the directly measured value of 0.86, and indicates the importance of systematic errors. Figure 4 depicts $Q(T)$ for three values of N on a semilogarithmic scale. We clearly see an exponential decay $Q(T)\sim\exp(-T/T_0)$ for large T in each of the graphs. The decay constant T_0 increases with increas-ing N. The ratio $\langle T\rangle/T_0$ is approximately a constant (≈1.8). Moreover, in terms of rescaled times $T'=T/\langle T\rangle$ the distribu-tion becomes independent of N, as can be seen in the inset in Fig. 4. The exponential decay is evident over two decades on the vertical axis. (Note that analogous tail of the distribution in Fig. 2(b) of Ref. [22] ranges over 2/3 of a decade and has a large scatter.)

IV. DISCUSSION AND CONCLUSION

In this work we performed a detailed study of distribution functions associated with the translocation of a 2D model of a self-avoiding polymer. Our results clearly indicated an ex-
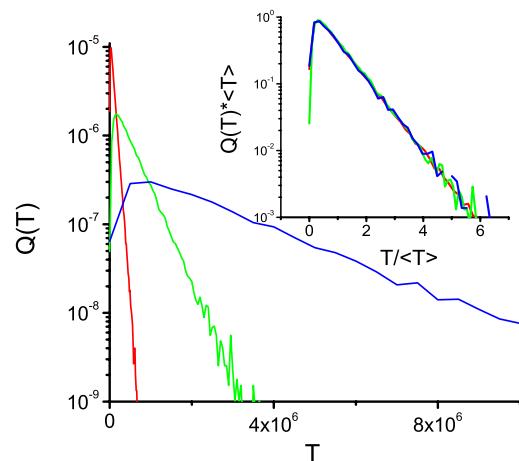

FIG. 4. (Color online) Probability distribution of translocation time T for $N=32$, 64, and 128 (left to right), obtained from 100 000, 78 600, and 8600 runs, respectively. The inset demonstrates the collapse of the probabilities when T is scaled with its average value $\langle T\rangle$.

ponential decay of the PDF $Q(T)$ for large translocation times T, and thus exclude power-law [22] or stretched expo-nential [30] behavior. The distribution of the translocation variable s both at short and long times exhibits the behavior resembling that of a tagged monomer [15]. There is some similarity in the behavior of the long-time stationary distri-butions from our simulations, and solutions of a fractional Laplacian with absorbing boundaries [29]. However, the ac-curacy of our results precludes definitive statements regard-ing these long-time distributions.

Strong crossover effects are present in translocation for surprisingly high values of N. In fact, the values of various exponents reported in the literature differ beyond their nomi-nal error bars. One may hope that for N as large as 1000 this difficulty can be overcome. Unfortunately, accumulating very large statistics for such large N is currently beyond our ability.

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