Dynamical Scaling Exponents for Polymer Translocation through a Nanopore

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We determine the scaling exponents of unbiased and driven polymer translocation through a nanopore by carrying out extensive computer simulation studies using Monte Carlo (MC), Molecular Dynamics (MD), and Langevin Dynamics (LD) methods for two dimensional (2D) and three dimensional (3D) systems for a large span of chain lengths from $N = 8 - 800$. We focus on how the average translocation time $\tau$ and the mean-square change of the translocation coordinate $\langle s^2(t) \rangle$ scale as a function of the chain length $N$ characterized by the scaling exponents $\alpha$ ($\tau \sim N^\alpha$) and $\beta$ ($\langle s^2(t) \rangle \sim t^\beta$) respectively. We verify universality of the the relations $\alpha = 1 + 2\nu$ and $\beta = 2/\alpha$ for unbiased translocation in both 2D and 3D, and find the latter relation to be valid even for driven translocation in 2D. For the driven case there is a crossover scaling between the theoretically suggested bounds $\alpha = 2\nu$ for short chains to $\alpha = 1 + \nu$ for long chains in 2D. However, this cross-over is virtually absent in 3D and the exponent $\alpha$ saturates for $N \approx 40$ where we find $\alpha = 1.42 \pm 0.01$ up to $N = 800$. These results invalidate recently suggested alternate scaling theories for polymer translocation.

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The transport of a polymer through a nanopore plays a crucial role in numerous biological processes, such as DNA and RNA translocation across nuclear pores, protein transport through membrane channels, and virus infection. Due to various potential technological applications, such as rapid DNA sequencing, gene therapy and controlled drug delivery, polymer translocation has become a subject of intensive experimental [1, 2] and theoretical studies [3, 4, 5, 6, 7, 8, 9]. However, as Chuang et al. [3] noted, the quadratic scaling behavior for unbiased translocation cannot be correct for a self-avoiding polymer. The reason is that the translocation time is shorter than the Rouse equilibration time of a self-avoiding polymer, $\tau_R \sim N^{1+2\nu}$, where the Flory exponent $\nu = 0.588$ in 3D and $\nu = 0.75$ in 2D [23], thus rendering the concept of equilibrium entropy and the ensuing entropic barrier inappropriate for translocation dynamics. Chuang et al. [3] performed numerical simulations with Rouse dynamics for a 2D lattice model to study the translocation for both phantom and self-avoiding polymers. They decoupled the translocation dynamics from the diffusion dynamics outside the pore by imposing the artificial restriction that the first monomer, which is initially placed in the pore, is never allowed to cross back out of the pore. Their results show that for large $N$, $\tau \sim N^{1+2\nu}$, which scales approximately in the same manner as the equilibration time but with a much larger prefactor. This result was recently corroborated by extensive numerical simulations based on the Fluctuating Bond (FB) [4] and Langevin Dynamics (LD) models with the bead-spring approach [5, 6, 7, 8, 9, 10]. In Refs. [6, 7] the translocation time $\tau$ was found to scale as $N^{2.50\pm0.01}$ in 2D, which is in excellent agreement with $\tau \sim N^{1+2\nu}$.

For driven translocation, Kantor and Kardar [11] have demonstrated that the assumption of equilibrium in polymer dynamics by Sung and Park [3] and Muthukumar [4] breaks down more easily and provided a lower bound $\tau \sim N^{1+\nu}$ for the translocation time by comparison to the unimpeded motion of the polymer. Using FB [12] and LD [13] models, a crossover from $\tau \sim N^{1.46\pm0.01} \approx N^{2\nu}$ for relatively short polymers to $\tau \sim N^{1.70\pm0.03} \approx N^{1+\nu}$ for longer chains was found in 2D.

Recently, however, alternate scaling scenarios have been presented [10, 13, 14, 15, 16, 17, 18, 19, 20], which contradict the above results. To resolve the apparent discrepancy, we have undertaken an extensive effort to determine $\tau$ as function of $N$, $\tau \sim N^\alpha$, and the mean-square change of the translocation coordinate $\langle s^2(t) \rangle \sim t^\beta$ based on high-accuracy numerical simulations. The independent models employed here include the fluctuating bond (FB) model with Monte Carlo (MC) dynamics [6, 12] in 2D, Langevin dynamics (LD) of the bead-spring model of polymers [7, 8, 13, 14, 15] in both 2D and 3D, and...
atomistic Molecular Dynamics (MD) simulations using the GROMACS [26] simulation engine in both 2D and 3D.

In the 2D lattice FB model for MC simulation of a self-avoiding polymer [8,13,14], each segment excludes four nearest and next-nearest-neighbor sites on a square lattice. The bond lengths $b_i$ are allowed to vary in the range $2 \leq b_i \leq \sqrt{13}$ in units of the lattice constant, where the upper limit prevents bonds from crossing each other. Dynamics is introduced in the model by Metropolis moves, with probabilities of acceptance $\min[1/e^{-U/kT},1]$, where $U$ is the energy difference between the new and old states, $k_B$ the Boltzmann constant, and $T$ the absolute temperature. As to an elementary MC move, we randomly select a monomer and attempt to move it onto an adjacent lattice site (in a randomly selected direction). If the new position does not violate the excluded-volume or maximal bond-length restrictions, the move is accepted or rejected according to Metropolis criterion. $N$ elementary moves define one MC time step.

In LD simulations [8,13,14], the polymer chains are modeled as bead-spring chains of Lennard-Jones (LJ) particles with the Finite Extension Nonlinear Elastic (FENE) potential. Excluded volume interaction between monomers is modeled by a short range repulsive LJ potential with a cutoff of $2^{1/6}\sigma$, where $\sigma$ is the diameter of a bead. Between all monomer-wall particle pairs, there exist the same short range repulsive LJ interaction. In the LD simulations, each monomer is subjected to conservative, frictional, and random forces, respectively. GROMACS [26] is currently one of the most commonly used programs in soft matter and biophysical simulations, and has also been used extensively by some of us in various problems (see e.g., Ref. [27] and references therein). As in the MC and LD methods, the hydrodynamic effects are excluded from our GROMACS MD simulations, which have been performed by using both overdamped Brownian and Langevin dynamics thermostats.

Unbiased translocation. For unbiased translocation, the middle monomer is initially placed in the center of the pore. The polymer can escape the pore from either side in time defined as the translocation time $\tau$. We simulated the escape of chains of lengths varying from $N = 15$ up to $N = 255$ for the scaling of $\tau$ and averaged over 200 samples for MC simulations in both 2D and 3D and over 2000 samples for MC and LD simulations in 2D to minimize statistical errors.

Figure 1 shows $\tau \sim N^\alpha$ for different models. For MD simulations we find that $\alpha = 2.44 \pm 0.03$ in 2D and $\alpha = 2.22 \pm 0.06$ in 3D, in complete agreement with $\alpha = 2.50 \pm 0.01$ from MC simulations in 2D [6], and $\alpha = 2.48 \pm 0.07$ from LD simulations in 2D [8]. All these results confirm $\tau \sim N^{1+2\nu}$ [6,8,14] and also agree with the recent results by Wei et al. [14], where $\tau \sim N^{2.51 \pm 0.03}$ in 2D and $\tau \sim N^{2.2}$ in 3D based on LD simulations.

The scaling $\tau \sim N^{1+2\nu}$ implies that $\tau$ scales in the same manner as the chain equilibration time $\tau_R$. Here, $\tau_R$ is the time taken for a polymer to move a distance equal to its radius of gyration $\tau_R \sim R_g^2/D$ with $D = 1/N$ being the diffusion coefficient. Most recently, Slater et al. [22] used MD simulations with explicit solvent to study the impact of hydrodynamic interactions in 3D. The results show that the scaling of the translocation time varies from $\tau \sim N^{1+2\nu}$ to $\tau \sim N^{3\nu}$ with increasing pore size, which indicates that the hydrodynamic interaction is screened for smaller pore sizes. These results also support $\tau \sim R_g^2/D$ by taking into account $D \sim 1/N$ and $D \sim 1/N^\nu$ without and with hydrodynamic interactions, respectively. Using a similar argument, it was also predicted, and numerically confirmed, that $\tau \sim (R_g + L)^2/D \sim N L^2$ for a long pore of length $L \gg R_g$, resulting from the fact that the mass center of the polymer moves a distance of $L + R_g \approx L$ [8]. For a long pore $L \gg N$ we have $\tau \sim N L^2 \gg N^3$, which is longer than the reptation time of the chain $\sim N^3$. In addition, for translocation under a pulling force $F$ acting on one end of the chain, $\tau \sim N^{2\nu+1}$ is recovered for $F \to 0$ [8]. Altogether, these results further confirm the argument that $\tau$ scales in the same manner as $\tau_R$.

For the mean-square change of the translocation coordinate $s(t)$, we use chains of length $N = 201$ for LD simulations in 2D and $N = 100$ for MD simulations in both 2D and 3D, and average over 2000 samples. As shown in Fig. 2, we observe sub-diffusive behavior $\langle s^2(t) \rangle \sim t^{\beta}$, where $\beta = 0.80 \pm 0.01$ in 2D for LD simulations and $\beta = 0.81 \pm 0.01$ in 2D and $\beta = 0.91 \pm 0.01$ in 3D for MD simulations, as predicted by Chuang et al. [8], where $\beta = 2/\alpha = 2/(1 + 2\nu)$ gives 0.80 in 2D and 0.92 in 3D. All the above results demonstrate that $\alpha = 1 + 2\nu$. 

![Figure 1: Scaling of the translocation time for unbiased translocation.](image-url)
and $\beta = 2/(1+2\nu)$ for the range of $N$ studied here. However, in a recent paper, Wolterink et al. [10] present different results for unbiased translocation using a 3D lattice model using Monte Carlo (MC) simulations. According to their scaling argument $\tau \sim N^{1+2\nu}\phi(b/R_{gs})$, where $R_{gs}$ is the radius of gyration, $b$ the pore width, and the scaling function $\phi(x) \sim x^{-0.38\pm 0.08}$ for $x \rightarrow 0$. This leads to $\tau \sim N^{2.40\pm 0.08}$ in 3D. For $\tau/N^{1+2\nu}$ as a function of $N$, as shown in the insert of Fig. 1, we found that the scaling function $\phi(b/R_{gs})$ does not depend on $N$, in contrast with their claims. Furthermore, they have also computed $\langle s^2(t) \rangle \sim t^\beta$, with $\beta = 0.81$ in 3D [17]. In addition, in a more recent paper [18], two of these authors argue that $\beta = (1+\nu)/(1+2\nu) \approx 0.73$ in 3D for $t < \tau_R$ and it crosses over to $\beta = 1$ for $t > \tau_R$. Correspondingly, they have changed their previous results to $\tau \sim N^{2+\nu}$, where the exponent is 2.75 in 2D and 2.588 in 3D. In the data shown in Fig. 2, there is no sign of such a crossover to a behavior $\langle s^2(t) \rangle \sim t$ even at the longest times studied. In fact, $\tau_R$ is the relaxation time for the whole chain without confinement. During the translocation process, the chain is always confined by the pore and thus it is impossible for the whole chain to be relaxed even if $t > \tau_R$. Therefore, the crossover to $\beta = 1$ regime cannot exist. Most recently, based on the fractional Fokker-Planck equation Dubbeldam et al. [20] have argued that $\beta = 2/(2\nu+2-\gamma_1)$ and $\tau \sim N^{2/\beta} = N^{2\nu+2-\gamma_1}$. This gives $\alpha = 2.554$ and $\beta = 0.78$ in 2D, where $\gamma_1 = 0.945$ in 2D, and $\alpha = 2.496$ and $\beta = 0.80$ in 3D. However, our results invalidate these claims as well.

**Driven translocation.** First, we present a scaling argument for $\tau$. Under the driving force $F$ in the pore, the Rouse time $\tau_R \sim N^{1+2\nu}$ is the solitary relevant time scale, and all other relevant parameters appear in the dimensionless combination $FR_{gs}$. Thus, the translocation time $\tau$ scales as $\tau = \tau_R\phi(FR_{gs})$. The scaling function $\phi$ is determined from the requirement that the speed of the process, $N/\tau$, must be linear in the applied force, leading to $\tau \sim N^{1+\nu}/F$. However, at least in 2D, short chains are easier to be deformed and $FN$ appears as a natural scaling variable, resulting in $\tau \sim N^{2\nu}/F$ for short chains. If we assume that $\langle s^2(t) \rangle \sim t^\beta$, and then from the correspondence to the scaling laws of $\tau$ with $N$ for short and long chains, one may estimate $\beta$.

The translocation time as a function of the polymer length is presented in Fig. 3. One of the main features is that a crossover scaling behavior is observed in 2D for using different models. For short chains $N \leq 200$, $\alpha = 1.46 \pm 0.01$ was found for MC simulations [12], and $\alpha = 1.50 \pm 0.01$ for LD simulations [7], and here we find $\alpha = 1.52 \pm 0.02$ for MD simulations, all of which are in good agreement with $\tau \sim N^{2\nu}$. For longer chains, the exponents cross over to $\alpha = 1.70 \pm 0.03$ for MC simulations [12], $\alpha = 1.69 \pm 0.04$ for LD simulations [7] and $\alpha = 1.64 \pm 0.03$ for MD simulations, which are slightly below the bound $\tau \sim N^{1+\nu}$. For simulations in 3D, however, we find no clear evidence of a crossover for the range of $N$ studied here. For $N = 8-32$ the effective $\alpha$ (running slope) is close to $2\nu$; however, it rapidly increases with $N$ saturating to a value of $\alpha = 1.42 \pm 0.01$, which is our best estimate from the new MD data up to $N \leq 800$. We note that this value lies between $2\nu$ and $1+\nu$, as expected. This is fully consistent with LD data in 3D where $\alpha = 1.41 \pm 0.01$. As emphasized in the previous works, driven translocation is a highly non-equilibrium process [12] and thus simple scaling arguments may not be fully accurate. We indeed find that some aspects of the driven translocation dynamics are sensitive to the physical system parameters, such as polymer-pore interactions [14, 15]. Details of these results will be published elsewhere.

In Fig. 4, we show our data for $\langle s^2(t) \rangle \sim t^\beta$, where $\beta = 1.36 \pm 0.01$ in 2D and $\beta = 1.53 \pm 0.01$ in 3D for LD simulations with $N = 128$ and $\beta = 1.38 \pm 0.01$ in 2D and $\beta = 1.50 \pm 0.01$ in 3D for MD simulations with chain length $N = 100$ and $N = 500$, respectively. These numerical results show that relationship $\beta = 2/\alpha$ is also correct for driven translocation in 2D. However, in 3D $\beta = 2/\alpha \approx 1.4$, in contrast to 1.5 from $\langle s^2(t) \rangle$.

In contrast to our results, Dubbeldam et al. [20] have argued that $\langle s^2(t) \rangle \sim t^\beta$, where $\beta = 4/(2\nu+2-\gamma_1)$. This gives $\beta = 1.56$ in 2D and 1.60 in 3D. They further obtain $\alpha = 2/(\beta/2) - 1 = 2\nu + 1 - \gamma_1$, which gives $\alpha = 1.55$ in 2D and $\alpha = 1.50$ in 3D. Most recently, Panja et al. [19] have argued that $\beta = (1+\nu)/(1+2\nu)$, which is 1.40 in 2D and 1.46 in 3D. Numerically, they find that $\tau \sim N^{(1+2\nu)/((1+\nu))}$, which is 1.43 in 2D and 1.37 in 3D. This result also implies $\beta = 2/\alpha$. Using the same argument as Storm et al. [23], Panja et al. [19] further claim that the lower bound for $\alpha$ is $\tau \sim N^{2\nu}$, which gives $\alpha = 1.50$ in 2D. Obviously, this contradicts both the prediction
short chains to $\alpha$ translocation, there is crossover scaling from $\alpha = 1 + 2\nu$ is observed for all the simulations. In 3D, there is no clear evidence of the crossover for the range of $N$ studied here.

![FIG. 3: Scaling of translocation times under the driving force. To be clear, the data are shifted. In 2D, the crossover from $\alpha = 1 + 2\nu$ to $\alpha = 1 + \nu$ is observed for all the simulations. In 3D, the relationship of $\beta = 2/\alpha$ does not change for driven translocation. These results invalidate both the lattice model results of Refs. 16, 17, 18, 19 and those of Dubbeldam et al. 20, 21.]

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