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Confinement-Driven Translocation of a Flexible Polymer

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We consider the escape of a flexible, self-avoiding polymer chain out of a confined geometry. By means of simulations, we demonstrate that the translocation time can be described by a simple scaling law that exhibits a nonlinear dependence on the degree of polymerization and that is sensitive to the nature of the confining geometry. These results contradict earlier predictions but are in agreement with recently confirmed geometry-dependent expressions for the free energy of confinement.

Translocation through a nanopore is one of the fundamental biological mechanisms through which long molecules can be exchanged between different regions compartmentalized by biological membranes [1]. Examples of this phenomenon include the injection into host cells of DNA packed inside virus capsids [1] and the transport of proteins through biological membranes. Furthermore, pioneering experiments have demonstrated that DNA can be translocated through a nanopore by means of an external electric field, and that this event can be probed by measuring the variation in ionic current through the pore [2–4]. This has opened the prospect of creating efficient and economical DNA sequencing devices and has resulted in a widespread theoretical and experimental interest in polymer translocation [5–15].

The passage of a flexible chain through a narrow opening involves a large entropic barrier, so that most polymer translocation phenomena require a driving force. A typical experimental setup [2] consists of two chambers separated by an interface. A DNA molecule is placed in one of the chambers and passes through the interface via a small orifice, either a protein complex embedded in a membrane or a solid state nanopore. In this case, the required driving force is provided by an external electric field. However, one can also envisage the use of other forces, e.g., generated by optical tweezers or by an osmotic pressure resulting from the geometrical confinement of the polymer in one of the chambers.

In the study of polymer translocation, the duration of the sequential passage of a chain through a membrane—measured from the entrance of the first monomer into the pore—occupies a central place, because it is one of the few dynamical parameters that is accessible to current experiments [2,15–17]. In particular, there have been various efforts to determine and to understand the dependence of translocation time τ on the degree of polymerization and the magnitude of the driving force. Sung and Park [5] proposed treating polymer translocation as a diffusion process across a free energy barrier. Muthukumar [8] reproduced this approach using nucleation theory, employing

a corrected diffusivity. This analysis reveals the existence of two distinct regimes. If the chemical potential gradient per monomer $\Delta\mu$ is sufficiently small, the entropic barrier dominates the diffusion process,

$$\tau \sim N^2 \quad \text{for } N|\Delta\mu| \ll 1, \tag{1}$$

whereas stronger driving forces lead to a drift-dominated regime,

$$\tau \sim \frac{N}{\Delta\mu} \quad \text{for } N|\Delta\mu| > 1. \tag{2}$$

Chuang *et al.* [10] observed an inconsistency in the reasoning leading to Eq. (2), since it assumes that the polymer chain is equilibrated at all times during the translocation, whereas the Rouse equilibration time scales as $N^{2\nu+1}$ and hence for sufficiently long chains exceeds the predicted translocation time. Furthermore, it was argued [13] that the unhindered motion of a chain provides a lower bound for the translocation time, such that Eq. (2) should be replaced by

$$\tau \sim \frac{N^{1+\nu}}{\Delta\mu}. \tag{3}$$

The difference in chemical potential of the monomers on either side of the interface clearly is a crucial ingredient in all estimates of the translocation time. Unlike other simulation studies [11,12], here we concentrate on the situation where this difference originates from polymer confinement, i.e., where the chain is ejected out of a restricted geometry. This situation has been analyzed in Refs. [6,9], where numerical results were presented that agree with Eq. (2), rather than with the corrected prediction Eq. (3). To confuse matters further, it was recently established that the driving force exhibits a nontrivial dependence on geometry [18,19] that was not taken into account properly in Refs. [6,9]. In this Letter we resolve this contradictory situation by means of an accurate numerical study of the escape of a polymer chain out of *different* confining geometries, in which we *independently* vary the degree of

polymerization and the strength of the osmotic driving
force.

The free energy cost of confining a linear, flexible
polymer within a planar or cylindrical geometry (uniaxial
or biaxial confinement, respectively) is given by a well-
known blob scaling result [20],

$$\beta \Delta F \sim \left(\frac{R_G}{R}\right)^{1/\nu} \sim N\left(\frac{\sigma}{R}\right)^{1/\nu}, \quad (4)$$

where R is the separation between the plates or the radius
of the cylinder and $R_G \sim \sigma N^\nu$ is the radius of gyration of
the polymer in its *unconfined* state. σ is the size of a
monomer, $\nu \simeq 0.588$ is the Flory exponent and $\beta = 1/(k_B T)$, with k_B the Boltzmann constant and T the abso-
lute temperature. As has been argued on theoretical
grounds [18] and confirmed numerically [19], this predic-
tion is *invalid* for a spherical geometry (triaxial confine-
ment) and must be replaced by a scaling law that has a
much stronger dependence on the sphere radius R,

$$\beta \Delta F \sim \left(\frac{R_G}{R}\right)^{3/(3\nu-1)} \sim N\phi^{1/(3\nu-1)}, \quad (5)$$

where $\phi = N(\sigma/(2R))^3$ is the monomer volume fraction.
This result can be understood within blob scaling theory by
realizing that, unlike the planar or cylindrical case, the
monomer concentration within a spherical cavity increases
with increasing polymer size N. The extensivity of the free
energy of confinement is then recovered only when a
change in polymer size is accompanied by a corresponding
change in volume of the cavity such that the monomer
concentration remains invariant [18,21].

Since the free energy of confinement per monomer,
$\Delta F/N$, represents the chemical potential gradient that
drives the translocation, a combination of Eqs. (4) and
(5) with Eq. (3) leads to predictions for the translocation
out of a planar or a spherical geometry,

$$\tau \sim \begin{cases} N^{1+\nu}\left(\frac{R}{\sigma}\right)^{1+\nu} & \text{planar confinement} \\ N^{1+\nu}\phi^{1/(1-3\nu)} & \text{spherical confinement} \end{cases} \quad (6)$$

where the exponent $1 + \nu$ in the prefactor represents the
lower bound proposed in Ref. [13]. To validate this pre-
diction, we study the translocation of a flexible polymer
chain which is modeled as a linear series of N spherical
beads of diameter σ, connected by bonds that are freely
extensible up to a fixed value ℓ_M. All monomers interact
via a hard-core repulsion,

$$u_m(r_{ij}) = \begin{cases} 0 & r_{ij} > \sigma \\ \infty & r_{ij} \le \sigma \end{cases}, \quad (7)$$

where r_{ij} is the center-to-center distance between beads i
and j. The nearest-neighbor bonds are represented by

$$u_b(r_{i,i-1}) = \begin{cases} 0 & r_{i,i-1} \le \ell_M \\ \infty & r_{i,i-1} > \ell_M \end{cases}. \quad (8)$$

We mimic the dynamical properties of this model by means
of Monte Carlo simulations in which only local, short-
ranged displacements are employed. The monomer dis-
placement per Monte Carlo step equals $(\Delta x, \Delta y, \Delta z)$, in
which each Cartesian component is chosen uniformly in
the range $[-0.15\sigma, 0.15\sigma]$ [22]. To avoid dynamical in-
consistencies that could result from crossing polymer
bonds, we choose $\ell_M = \sqrt{2}\sigma$. Confinement is imposed
by means of a spherical or planar boundary of thickness
σ, which exerts a hard-core repulsion on the monomers.
For the planar case, the system is periodically replicated in
the directions parallel to the plates, with a period $2N\sigma$. The
setup is depicted schematically in Fig. 1.

The polymer chain is first equilibrated within the con-
fining geometry. Subsequently, we create a smooth pore
(shaped as the hole in a torus) of radius 1.3σ to allow
ejection of the polymer (see Fig. 1). This radius is suffi-
ciently small to practically exclude the translocation of
folded chains. A translocation event is considered success-
ful when the entire polymer escapes from the confining
geometry. We define the translocation time τ as the differ-
ence between the time t_N when the last monomer has left
the cavity and the time t_1 when, within a successful event,
the first monomer has entered the pore. We systematically
vary the degree of confinement R and determine the aver-
age escape time for chains with lengths ranging from $N = 40$ to $N = 512$ monomers. For each choice of R and N, we
generate between 400 and 1400 independent translocation
events. All simulations are performed in the drift-
dominated regime, i.e., $N\Delta\mu > 1$, which requires $R < R_G$.

To focus on the role of the degree of confinement, we
calculate τ for a fixed, long chain length ($N = 256$ for
planar and $N = 512$ for spherical confinement). Figure 2
displays τ as a function of R. The escape times from both
geometries are accurately described by a power-law de-
pendence, but with strikingly different exponents. For
confinement within a planar geometry, the driving force
is relatively weak and we use smaller separations than for
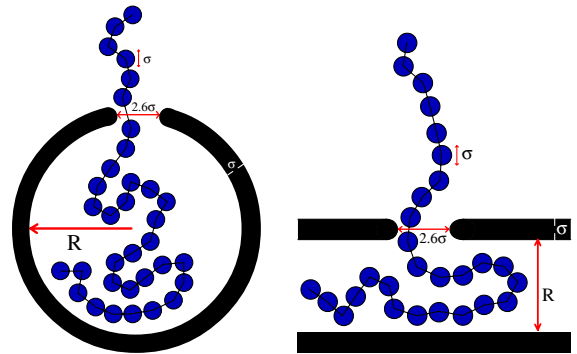

FIG. 1 (color online).   Schematic setup of the Monte Carlo
simulations. In the left-hand panel, a polymer chain is released
from a spherical geometry of radius R. In the right-hand panel,
the chain is confined between two parallel plates at separation R
and escapes via a circular opening in one of the plates. The
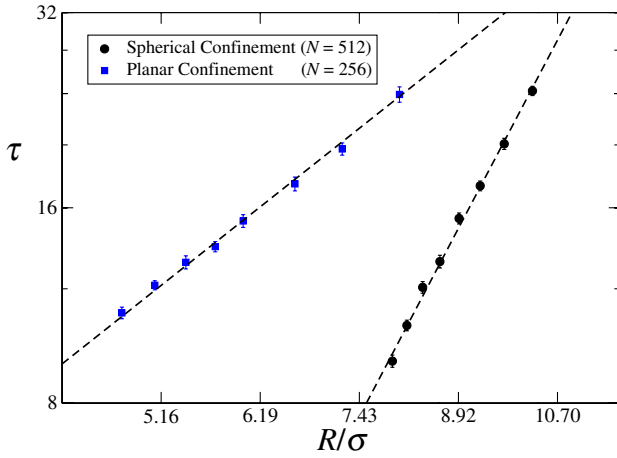actual simulations are performed in three dimensions.

FIG. 2 (color online). Double logarithmic plot of the average translocation time τ for a linear, flexible polymer escaping from a spherical and a planar geometry, as a function of the degree of confinement R. The translocation times are expressed in units of 10^6 Monte Carlo sweeps. These data confirm the striking dependence on confinement geometry, Eq. (6).

the spherical geometry (as small as $R = 4.8\sigma$). A least-squares fit of both data sets to the expression $\tau(R) = \tau_0 + aR^\gamma$ yields $\gamma = 1.54 \pm 0.10$ for planar confinement and $\gamma = 3.65 \pm 0.08$ for spherical confinement, with chi square per degree of freedom ($\bar{\chi}^2$) equal to 1.06 and 0.86, respectively. These results are in good agreement with the exponents in $1/\nu$ [Eq. (4)] and $3/(3\nu - 1)$ [Eq. (5)] and thus confirm the linear dependence of τ on $1/\Delta\mu$ predicted by Eq. (6). The agreement is even closer if one notes that for the chain lengths employed here the effective Flory exponent is slightly larger than $\nu = 0.588$.

Additional information about the translocation process can be obtained from the probability distribution function of translocation times $P(\tau)$. Theoretical [7] and experimental results [2,16,17] indicate that this distribution deviates from a Gaussian distribution and may be considerably skewed. Consequently, the *average* translocation time is not fully representative of the experimental data. We sample $P(\tau)$ for a chain of $N = 128$ monomers, comparable to the chain length employed in the experimental determination of $P(\tau)$ for single-stranded DNA [2]. For escape from a spherical cavity, the driving force depends on the monomer volume fraction. As shown in Fig. 3, for strong confinement ($\phi = 0.15$), the distribution is narrow and nearly Gaussian. However, at weaker confinement ($\phi = 0.08$), $P(\tau)$ broadens and the skewness becomes clearly visible. Lubensky and Nelson [7] derived an expression that provides a reasonable description of the data in Fig. 3; however, this expression is not valid for large τ. Following the experimental analysis [16] we therefore fit the data to an empirical expression of the form $\tau^{a_1} \exp(-a_2\tau)$. Just as in the experiments, the exponential term provides a good description of the long-time tail. It is argued in Ref. [7] that the distribution of passage times can be characterized
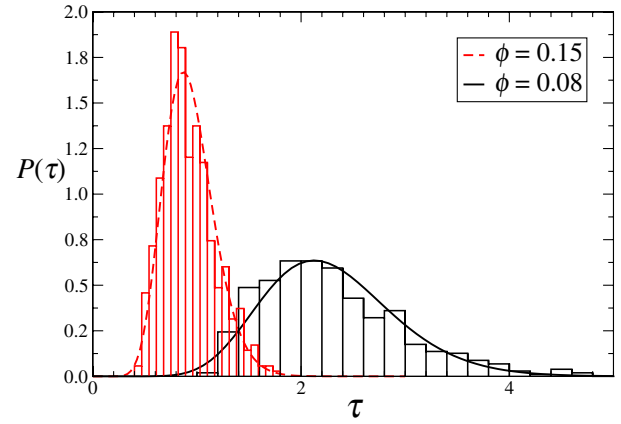

FIG. 3 (color online). Probability distribution $P(\tau)$ of translocation times τ, for a polymer of $N = 128$ monomers confined in a spherical cavity. The translocation times are expressed in units of 10^6 Monte Carlo sweeps. The narrow distribution corresponds to a strongly confined chain (monomer volume fraction $\phi = 0.15$) and the wider distribution is obtained for a smaller driving force ($\phi = 0.08$). As discussed in the text, the curves represent empirical expressions of the form $\tau^{a_1} \exp(-a_2\tau)$, with a characteristic ratio Δ of the width and the peak position that is close to typical experimental results.

in a useful way via the ratio $\Delta \equiv \delta\tau/\tau_{\max}$ between the width $\delta\tau$ of the distribution (as defined in Ref. [7]) and its peak position $\tau_{\max}$. For the distributions shown in Fig. 3 we find values in the range 0.53–0.56, indeed in agreement with experimental values $\Delta \approx 0.5$ [2,7] and $\Delta \approx 0.55$ [16].

We now proceed to determine the dependence of translocation time on the degree of polymerization N. For the spherical case, we perform a series of simulations at constant initial volume fraction $\phi = 0.1$, and for the planar geometry we perform a series of simulations at fixed separation $R = 4.8\sigma$. For both geometries τ is accurately described by a power-law dependence $\tau \sim N^\delta$ that is independent of geometry, in accordance with the observation [18,19] that the free energy of confinement is extensive [cf. Equations (4) and (5)]. For planar confinement, a least-squares fit yields $\delta = 1.55 \pm 0.04$ ($\bar{\chi}^2 = 1.16$) and for spherical confinement we find $\delta = 1.59 \pm 0.03$ ($\bar{\chi}^2 = 0.87$). Both results agree with $1 + \nu \approx 1.59$, confirming the lower bound established by Eq. (3). Accordingly, all results for a given geometry can be combined in a single data collapse. Figure 4(a) (plates) shows the translocation time τ normalized by $N^{1+\nu}$ as a function of the inverse driving force $(\Delta\mu)^{-1} \sim (R/\sigma)^{1/\nu}$, for five different chain lengths ($N = 32, 64, 96, 128,$ and 256). Likewise, Fig. 4(b) (sphere) displays $\tau/N^{1+\nu}$ as a function of $(\Delta\mu)^{-1} \sim \phi^{1/(1-3\nu)}$ for $N = 64, 128, 192, 256,$ and $N = 512$. In both cases, all data are described by a single master curve with $\bar{\chi}^2 = 1.40$ and 1.45, respectively.

In view of the striking difference between planar and spherical geometry that we observe for the R dependence of the translocation time (Fig. 2), it is remarkable that
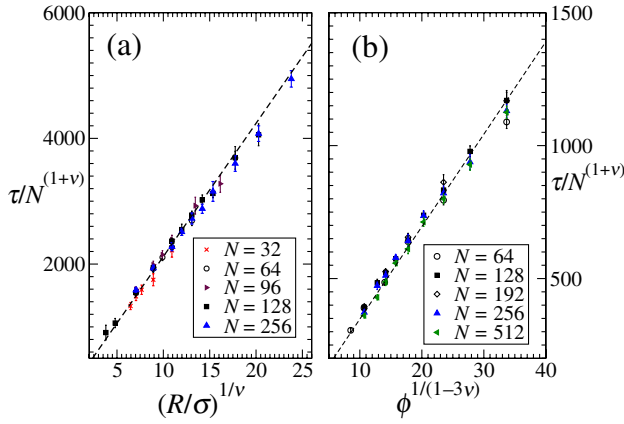
FIG. 4 (color online).   Average translocation time τ (in units of Monte Carlo sweeps) normalized by $N^{1+\nu}$ for chains escaping from (a) planar confinement, as a function of the inverse driving force per monomer $(\Delta\mu)^{-1} \sim (R/\sigma)^{1/\nu}$, and (b) spherical confinement, as a function of $(\Delta\mu)^{-1} \sim \phi^{1/(1-3\nu)}$. The collapse of the data points for different chain lengths confirms the validity of Eq. (6).

earlier work [9] found good agreement between numerical results for *spherical* confinement and a theoretical prediction based upon Eqs. (2) and (4) i.e., a driving force obtained from the free energy of *uniaxial* (i.e., planar) confinement. We ascribe this finding to the fortuitous cancellation of two errors. Indeed, in Ref. [9] the translocation time is predicted to scale as

$$\tau \sim N\left(\frac{\sigma}{R}\right)^{1/\nu} \sim N\left(\frac{N}{\phi}\right)^{1/(3\nu)}. \tag{9}$$

Combination of the linear N dependence of Eq. (2) and the inappropriate expression for the free energy of confinement yields an overall chain-length dependence $N^{1+1/(3\nu)}$, so that, at fixed concentration, τ is predicted to scale as $N^{1.567}$, which coincidentally is in approximate numerical agreement with the lower bound $\tau \sim N^{1+\nu}$ [Eq. (3)]. In fact, since the data in Ref. [9] exhibit a collapse when scaled by the N dependence of Eq. (9) we conclude that those data corroborate our findings. It is more difficult to reconcile our findings in Fig. 2 with the apparent confirmation of the concentration dependence of Eq. (9). However, we note that the evidence in Ref. [9] consists of a scaling collapse rather than an explicit numerical analysis of the power law. When performed over a narrow range of densities, such a collapse can be relatively insensitive to the precise power of ϕ.

In summary, we have investigated the translocation of a flexible polymer chain through a hole, when the driving force is generated by confinement of the polymer. To clarify the role of the confinement geometry, we have considered the escape of a polymer from a planar as well as a spherical geometry. For both cases, we demonstrate that the translocation time has a chain-length dependence that follows the nonlinear lower bound established by Kantor and Kardar [13]. The driving force affects the translocation time via a *linear* dependence on the inverse chemical potential gradient, as predicted on analytical grounds [5,8]. Thus, the average translocation time can be described by a simple scaling relation, $\tau \sim N^{1+\nu}/\Delta\mu$, which results in a *geometry-dependent* power law when expressed in terms of the length scale of confinement—the distance between parallel plates for a planar geometry and cavity radius for a spherical geometry.

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