

Translocation of polymers out of confined geometries

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Available online 23 February 2007

Abstract

We consider the free energy of confinement for a flexible self-avoiding polymer inside a spherical cavity. Accurate numerical calculations allow us to arbitrate between competing scaling predictions. We find that, for moderate confinement, the free energy exhibits a power-law dependence on cavity size that is different from what is observed for planar and cylindrical confinement. At high monomer concentrations, crossover to another scaling regime occurs. One of the consequences of these findings is a new prediction for the escape time of a polymer from a spherical confinement. By means of additional simulations, we confirm that the translocation time can be described by a scaling law that exhibits a nonlinear dependence on the degree of polymerization that is sensitive to the nature of the confining geometry. The geometry dependence contradicts earlier predictions but is in quantitative agreement with findings for the free energy of confinement.

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Keywords: Polymers; Translocation; Confinement

1. Introduction

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]. 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 [3–8].

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. In a typical experimental setup [2] the driving force is provided by an external electric field; however, one can also imagine the use of other forces, e.g., an osmotic pressure resulting from the geometrical

confinement of the polymer in one of the chambers. This last case is the focus of this article.

Confinement of a polymer drastically reduces its number of accessible conformations and thus results in an excess free energy ΔF . The dependence of the excess free energy on geometry, degree of confinement and chain length determines the partitioning of polymers and the entropic force on the polymer.

As the translocation time τ is expected to be inversely proportional to the driving force acting on each monomer [6–8], $\tau \sim (\Delta F/N)^{-1}$, it is crucial to understand how ΔF scales with the degree of confinement.

The calculation of the entropy loss due to the confinement of an ideal chain is an old problem [9–11]. For a polymer confined between two parallel plates at separation R the free energy $\beta\Delta F$ increases as $(R_G/R)^2$, where R_G is the radius of gyration of the unperturbed chain and $\beta = 1/(k_B T)$, with k_B Boltzmann's constant and T the absolute temperature. This result, that Casassa [9] has proven to also hold for a long capillary and a spherical geometry, can be obtained by means of a “blob” description of the polymer [11]. For planar and cylindrical geometries, the generalization to self-avoiding (non-ideal) polymers is straightforward [11],

$$\beta\Delta F \sim \left(\frac{R_G}{R}\right)^{1/\nu} \sim N\left(\frac{\sigma}{R}\right)^{1/\nu} \approx N\left(\frac{\sigma}{R}\right)^{1.70}, \quad (1)$$

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where $\nu \approx 0.588$ is the Flory exponent and σ denotes the monomer size. However, it is less widely appreciated that the applicability of Eq. (1) to *spherical* cavities is controversial. While some studies explicitly state [12] and employ [6] this relation for such a geometry, two alternative theories have been put forward. First, self-consistent field theory (SCFT) predicts [13]

$$\beta \Delta F \sim N^2 \left(\frac{\sigma}{2R} \right)^3 = N\phi, \quad (2)$$

where $\phi = N(\sigma/(2R))^3$ is the monomer volume fraction. This mean-field estimate is just the leading correction to the free energy of an ideal polymer due to excluded-volume interactions [14]. Secondly, a blob scaling description has been proposed [13,15] which explicitly recognizes that—unlike in a planar or cylindrical geometry—the monomer concentration in a spherical geometry increases upon confinement,

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

The differences between these predictions are by no means minor: Eq. (3) predicts $\Delta F \propto R^{-3.93}$, compared to $\Delta F \propto R^{-3}$ in Eq. (2) and $\Delta F \propto R^{-1.70}$ in Eq. (1). Here, we resolve this controversy by means of numerical simulations and measure how the translocation time of confined flexible polymers is affected by the specific geometrical constraint. A more detailed account is given in Refs. [16,17].

2. Methods

The polymer is described via a bead–spring model, i.e. a linear series of N spherical beads of diameter σ connected by bonds of maximal extension $\ell_{\max} = 1.9\sigma$. All monomers interact via a hard-core repulsion and the nearest-neighbor bonds are described as entropic springs

$$u_b(r_{i,i-1}) = \begin{cases} 0 & \text{if } r_{i,i-1} \leq \ell_{\max}, \\ \infty & \text{if } r_{i,i-1} > \ell_{\max}. \end{cases} \quad (4)$$

We explore the statistical properties of the model by means of Monte Carlo simulations involving local monomer moves. Confinement is enforced using an external spherically symmetric potential centered around the origin,

$$u_\alpha(\lambda) = \sum_{i=1}^N \frac{1}{(\lambda - r_i)^\alpha} \quad (\alpha > 0), \quad (5)$$

so that r_i is the distance of monomer i from the center of the sphere and λ represents the radius of the cavity. The computation is performed in two stages. In the first stage the polymer chain is equilibrated within the confining geometry and the free energy of confinement is computed via thermodynamic integration [18] in the NVT and the NPT ensemble. Next, a smooth pore of radius 1.3σ is created to allow ejection of the polymer and the translocation time of the polymer is recorded.

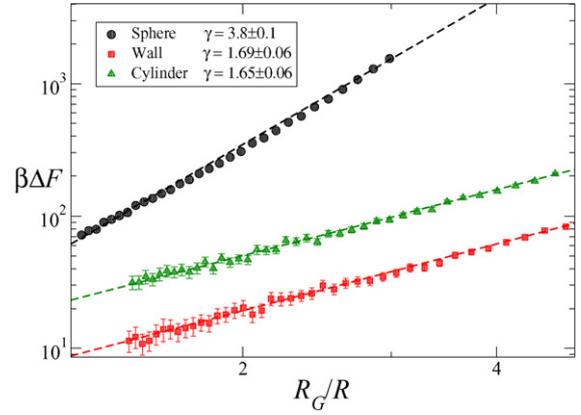


Fig. 1. Free-energy cost of planar, cylindrical and spherical confinement of a self-avoiding flexible polymer chain of $N = 256$ monomers as a function of the compression parameter R_G/R .

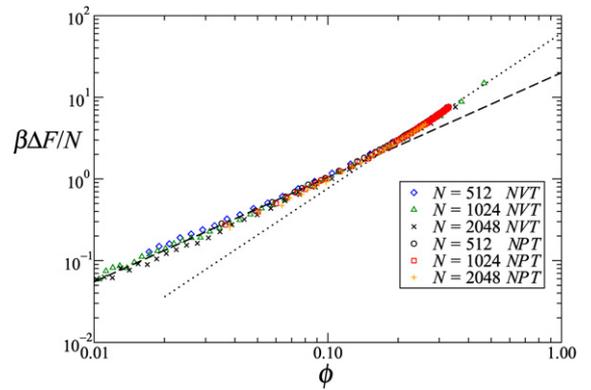


Fig. 2. Concentration dependence of the free energy of confinement per monomer, obtained at constant volume (NVT) and constant pressure (NPT). The coinciding curves for different chain lengths confirm the extensive character of the free energy. For $\phi < 0.15$ the data exhibit a power-law behavior $\Delta F \propto \phi^{1.28}$ (dashed line), in agreement with Eq. (3). The dotted line is a guide to the eye, indicating the systematic deviations at high concentrations (see text).

3. Results

Fig. 1 summarizes the free energy calculations for $N = 256$ and permits two crucial observations [19]. First, it confirms that ΔF exhibits the *same* power-law dependence $R^{-\gamma}$ for planar and cylindrical confinement and shows that our approach yields a quite accurate estimate of this power law: $(R_G/R)^{1.69 \pm 0.06}$ for parallel plates and $(R_G/R)^{1.65 \pm 0.06}$ for a cylinder, both in good accordance with $(R_G/R)^{1/\nu}$. Secondly, spherical confinement clearly shows a *much stronger* increase of the free energy with decreasing R .

To accurately determine the corresponding power law and to minimize possible artifacts due to the use of short chains, we compute (see Fig. 2) the free energy of confinement as a function of monomer volume fraction ϕ for three different chain lengths ($N = 512, 1024, 2048$), as measured in the NPT and in the NVT ensemble. It is rewarding that the results for both ensembles are in good agreement, ruling out ensemble-dependent artifacts. Furthermore, upon normalization per monomer, all curves collapse [20], confirming the extensive character of the

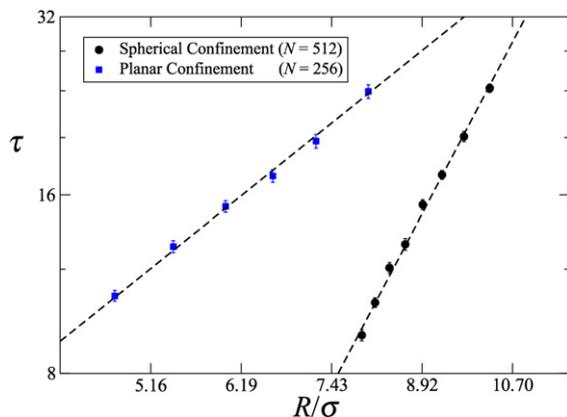


Fig. 3. Double logarithmic plot of the average translocation time τ for a linear, flexible polymer escaping from a spherical and a planar geometry, as a function of the degree of confinement R . The translocation times are expressed in units of 10^6 Monte Carlo steps. These data confirm the striking dependence on confinement geometry.

free energy at fixed ϕ . For moderate values of ϕ , all data coincide on a line with slope $\gamma = 1.28 \pm 0.06$, in agreement with the prediction of Eq. (3), $\gamma = 1/(3\nu - 1) = 1.31$, and in contrast with the linear concentration dependence predicted by SCFT (Eq. (2)).

It is of interest to also discuss the limitations of the scaling prediction. For concentrations exceeding approximately 0.2, the data cross over to an effective power-law behavior with an exponent $\gamma \approx 2$. The break-down of the blob scaling description at these concentrations should not come as a surprise as the number of monomers per blob at large volume fractions becomes rather small; already for $\phi \simeq 0.2$ there are only about five monomers per blob. On the other hand, in the dilute regime we anticipate considerable finite-size effects, since there the total number of blobs becomes very small. For example, at $\phi = 0.01$ there are approximately 200 monomers per blob, so that even our longest chain (with $N = 2048$) consists of only 10 blobs.

Now that we understand how the free energy of a polymer increases upon spherical, cylindrical and planar confinement, we turn to the problem of translocation. As already stated, the free energy of confinement per monomer, $\Delta F/N$, is responsible for driving the polymer out of the restricted geometry. In light of our results we can expect that for a planar, cylindrical or spherical geometry the following scaling laws apply, respectively,

$$\tau \sim \begin{cases} N^{1+\nu} (R/\sigma)^{1/\nu} & \text{plane/cylinder,} \\ N^{1+\nu} \phi^{1/(1-3\nu)} & \text{sphere,} \end{cases} \quad (6)$$

where the exponent $1 + \nu$ in the prefactor represents the lower bound proposed in Ref. [8].

First, we consider 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). Fig. 3 displays τ as a function of R . The escape times from both geometries are accurately described by a power-law dependence, but with strikingly different exponents. For confinement within a planar geometry, the driving force is relatively weak and we use

smaller separations than for 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. These results are in good agreement with the exponents in $1/\nu$ and $3/(3\nu - 1)$, respectively, and thus confirm the linear dependence of τ on $(\Delta F/N)^{-1}$.

The dependence of the translocation time on the degree of polymerization N is determined via a similar analysis, at constant $\Delta F/N$. We find that for both geometries τ is accurately described by a power-law dependence $\tau \sim N^\delta$ with $\delta = 1.55 \pm 0.04$ for planar confinement and $\delta = 1.59 \pm 0.03$ for spherical confinement. Both results agree with $1 + \nu \approx 1.59$ [8].

4. Summary

We have demonstrated, for the first time, that the free energy of a flexible self-avoiding polymer confined to a spherical cavity exhibits a different dependence on pore size than the free energy of a polymer confined between parallel plates or within a cylindrical geometry. We have also shown that the average confinement-driven translocation time can be described by a simple scaling relation, $\tau \sim N^{1+\nu}/(\Delta F/N)$, which results in a *geometry-dependent* power law when expressed in terms of the length scale of confinement—distance between parallel plates for a planar geometry and cavity radius for a spherical geometry.

Acknowledgements

This material is based upon work supported by the U.S. Department of Energy, Division of Materials Sciences under Award No. DEFG02-91ER45439, through the Frederick Seitz Materials Research Laboratory at the University of Illinois at Urbana-Champaign.

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- [19] The free energy depicted in the figures does not include energetic contributions resulting from the monomer–wall interactions (Eq. (5)) and is thus of purely entropic origin.
- [20] The results for $N = 256$ (not shown in this figure) exhibit minor deviations in the amplitude, owing to the short chain length.