Polymer in a pore: Effect of confinement on the free energy barrier

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We investigate the transfer of a polymer chain from *cis*-side to *trans*-side through two types of pores: cone-shaped channel and flat-channel. Using the exact enumeration technique, we obtain the free energy landscapes of a polymer chain for such systems. We have also calculated the free-energy barrier of a polymer chain attached to the edge of the pore. The model system allows us to calculate the force required to pull polymer from the pore and stall-force to confine polymer within the pore.

1. Introduction

Homeostasis is the property of living systems (humans and other mammals) in which the temperature is actively regulated to remain almost constant [1]. Biological processes in such living systems, therefore, take place at roughly constant temperature. Translocation, transport of proteins from the nucleus, ejection of viral DNA from capsid *etc.* [2–15] are few examples, where the processes are not driven by temperature but some other thermodynamic parameters *e.g.* chemical potential, entropy, nature of the solvent *etc.* The combined effect of all these parameters exerts some sort of force on the molecule of interest. An interesting example is nuclear pore complexes (NPCs) [16]. NPCs perforate the nuclear envelope and allow the exchange of macromolecules between the nucleus and the cytoplasm. Transport through the NPC is directional in nature such that specific cargoes are only imported into or exported from the nucleus, although other cargoes do shuttle across the interface continuously [17].

In vitro, the transfer of polymer from one region of the solvent to other through the pore may be achieved either by the relative change in the solvent quality or by shifting the conformational entropy (inside and outside the pore) of the system. It should be noted that the NPCs are supramolecular assemblies, 60125MDa in molecular weight, constitute the sole gateway through the nuclear envelope (NE), which is computationally difficult to model. Interestingly, in some cases, the shape of the pore-interface (*e.g.* Mycobacterium smegmatis porin A (MspA), HIV-1 capsid), looks similar to a cone-shaped channel (Fig. 1) [18,19]. Therefore, the polymer translocation through the cone-shaped channel has been studied experimentally [20–22] and theoretically [23–26] in recent years. However, the emphasis so far is limited to obtain scaling associated with translocation [27–30]. On the other hand equilibrium properties of the self-avoiding walks inside the cone has been studied using the conformal invariance technique by Cardy and Redner [31]. These results are in good agreement with the exact enumeration technique followed by the series analysis by Guttmann and Torrie [32]. Batchelor et al. [33] studied the polymer networks and linear polymer inside the cone, and calculated various exponents, which are in good agreement with earlier reported values [31,32]. However, these studies were limited to a polymer chain in a good solvent.

Equilibrium properties of a polymer in confined geometry are important because of the shift in the balance between conformational entropy and internal energy, which leads polymers to modify their shape under external parameter, such as

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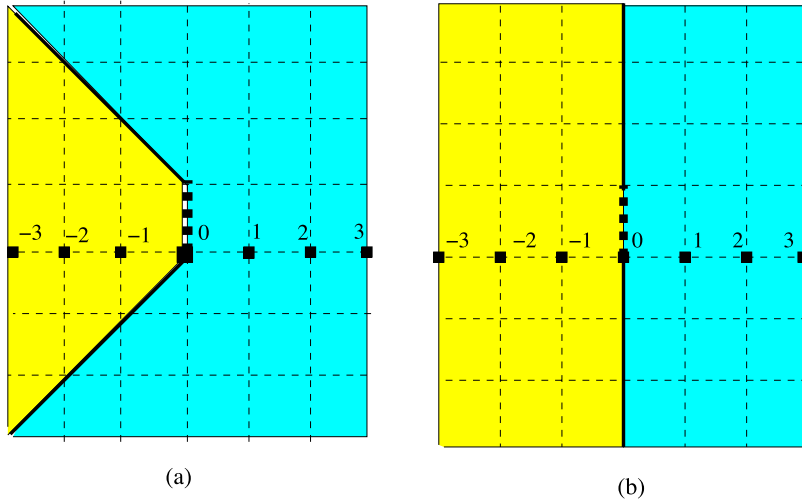
Fig. 1. Figures show the schematic representations of (a) a cone-shaped channel and (b) flat-channel of unit pore-size. The thick lines represent the impenetrable walls of the channel, which separate two regions of the liquid. The dashed line shows the penetrable interface of two liquids, which can be crossed by the polymer. Edge of the pore is chosen as the reference point and marked it as 0.

changes in temperature or pH of the solvent or external force. Prominent among such transformations are the coil-globule transition, protein unfolding etc., where a polymer can switch from an entropy-dominated coil conformation to a globular one, governed by energy [2]. In this context, a polymer chain in presence of a pore on a flat interface has been studied quite extensively [7]. It was shown that the total free energy ($F(m)$) of chain, where m monomers of the chain are translocated to other region, can be expressed as:

$$\frac{F(m)}{k_B T} = (1 - \gamma_2') \ln m + (1 - \gamma_1') \ln(N - m) - m \frac{\Delta \mu}{K_B T}. \tag{1}$$

Here, γ_1' and γ_2' are the critical exponents associated with two sides (say, *cis* and *trans*) across the pore and its values are different than the bulk values [7]. Its values depend on the ionic strength, the solvent quality, and geometry of two sides. $\Delta \mu$ is the chemical potential difference between the two sides. It should be pointed here that the contribution to $\Delta \mu$ may be from different sources *e.g.* polymer concentration asymmetry, gradients in salt concentration and pH, differential adsorption of the polymer on the membrane surfaces, complexities with other macromolecules, *etc.* Eq. (1) is general enough to describe the behaviour of polymer in different kind of solvents (*e.g.* poor or good). For this, one has to take appropriate values of γ_1', γ_2', and $\Delta \mu$ corresponding to that solvent.

To initiate the translocation of a polymer through the pore, it must be guided towards the pore and then threaded inside. This is called the capture process. The probability for a capture event on a cubic lattice is estimated to be $\approx cN^{-1.48}$, where c is the monomer concentration [9]. For a long polymer chain in a dilute solution, the probability of the polymer being captured in the pore is quite small. Therefore, the determination of equilibrium properties either experimentally or numerically is quite difficult. *In vitro*, such processes have been achieved by the application of external fields [34]. Recently, single molecule force techniques were used to pull a polymer chain from a pore and measure the drag force [35–38]. Efforts have also been made to measure the stall-force to confine polymer in a pore. DNA packaging in bacteriophages is one of the interesting examples [39,40], where process is driven by powerful molecular motors *in vivo*, which work against the large forces resisting the confinement induced by the entropy.

In a recent publication [41], we reported on the development of a coarse-grained description of the pore modelled by a cone-shaped channel of varying pore-size on a square lattice. Exact results based on a short chain revealed that when the solvent quality remains same across the interface, the polymer prefers to stay outside the channel. Surprisingly, when the quality of solvent inside the channel is relatively poor than the outside, even then, the polymer prefers to stay outside at lower temperatures. Our results demonstrate that a slight variation in the solvent quality can drag a polymer chain inside the pore and *vice versa*. However, dependence of free energy barrier on the external parameters (e.g. solvent quality across the interface) remains elusive. The aim of the present study is twofold: first to calculate the free-energy barrier arising due to the cone-shaped channel and its dependence on the solvent quality across the interface. The second aim is to estimate the force required to pull a polymer chain from inside the pore, and the stall-force to confine polymer in a pore at constant temperature.

The paper is organized as follows: in Section 2, we briefly describe the model and the method used to obtain the equilibrium properties of a polymer chain attached to the interface of a pore. In Section 3, we obtain the free energy profile of a polymer as a function of distance from the pore for different solvent conditions and estimate the free energy barrier.