Statistical mechanics of a polymer chain attached to the interface of a cone-shaped channel

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Abstract – A polymer chain confined in nano-scale geometry has been used to investigate the underlying mechanism of Nuclear Pore Complex (NPC), where transport of cargoes is directional. It was shown here that depending on the solvent quality (good or poor) across the channel, a polymer chain can be either inside or outside the channel or both. Exact results based on the short chain revealed that a slight variation in the solvent quality can drag the polymer chain inside and vice versa similarly to one seen in NPC. Furthermore, we also report the absence of crystalline (highly dense) state when the pore size is less than a certain value, which may have potential application in packaging of DNA inside the preformed viral proheads.

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Understanding of equilibrium properties of biopolymers confined in a nano-scale geometry may delineate the possible mechanism involved in many biological processes, e.g., translocation, transport of proteins from the nucleus, ejection of viral DNA from the capsid, etc. [1–11]. Such processes have potential applications in designing nanotechnology devices including polymer separation, DNA sequencing, protein sensing, etc. [12–18]. While most experiments and theories focus on driven systems [19–27], there is also considerable interest related to the unforced translocation [28–33]. An interesting example is when a pore connects two volumes of the solvent of different quality in case of nascent polypeptides, which translocates from the cytoplasm of eukaryotic cells to the lumen of the endoplasmic reticulum [34]. There are few studies related to this phenomenon where scaling in translocation time has been reported [31–33]. However, besides the scaling in translocation time, understanding of the equilibrium properties of a polymer chain attached to the edge of a pore-interface of two liquids still remains elusive.

It is pertinent to mention here that in some cases the shape of the pore-interface (e.g., Mycobacterium smegmatidis porin A (MspA), HIV-1 capsid), looks similar to the cone-shaped channel (fig. 1) [35,36]. Though, the polymer translocation through the cone-shaped channel has been studied experimentally [37–39], the interest here is for the theoretical understanding in the framework of statistical mechanics [40–43]. Moreover, for the translocation of the polymer from the pore to the outside, it was shown that the pore size ($r_p$) and the size of polymer play an important role [44–47]. The radius of gyration, which gives the information about the size of the polymer chain, scales as $N^{\nu}$, where $N$ is the number of monomers, and $\nu$ is the gyration exponent. In the globule state (low temperature), $\nu = 1/d$, while at high temperature the polymer is in the swollen state, and its value is given by the Flory approximation $\nu = \frac{3}{d+2} [1–3]$. Here, $d$ is the dimension. For a chain of finite length, high-precision numerical simulations also show the existence of a crystalline-like...
(highly dense) state \([48–51]\) of the polymer in addition to a globule phase at low temperature. This is in accordance with findings of Doniach et al. \([52]\). However, they termed it as “molten globule” state. Interestingly, many viruses use molecular motors that generate large forces to package DNA to near-crystalline (high) densities inside preformed viral proheads \([9]\). Therefore, it is a prerequisite to explore the existence of such states in the confined geometry and its relationship with the pore size.

A cone-shaped channel of varying pore size on the square lattice has been constructed to model the nanopore. Two walls of the channel separate two liquids in such a way that \(\approx \frac{1}{4}\) volume is available to one type of liquid inside the pore (from the interface and above), while the remaining \(\approx \frac{3}{4}\) volume is available to the liquid outside the pore (fig. 1). One end of the polymer chain is fixed at the interface of the cone-shaped channel, whereas the other end is free to be anywhere (fig. 2). The polymer chain is not allowed to cross the wall of the channel, except through the pore at the interface. The aim of the present study is twofold: first to understand the effect of asymmetry arising due to the cone-shaped channel, and secondly to investigate the role of the solvent quality on the equilibrium properties of a polymer confined in a pore. For this, we consider a self-attracting self-avoiding walk model of semi-flexible polymer, and use the exact enumeration technique \([1–3,51]\) to obtain the equilibrium properties. Since we have the exact information about the density of states, it is possible to explore the low-temperature behavior of the system and its dependence on the pore size. Previous studies for other systems have shown that the chain length considered here is sufficient to predict the correct qualitative behavior, and increasing the chain length only yields a better estimate of the phase boundary \([53–56]\). The partition function of such a composite system may be written as

\[
Z(T) = \sum_{(N_{pc}, N_{po}, N_b)} C_N(N_{pc}, N_{po}, N_b) u^{N_{pc}} \omega^{N_{po}} b^{N_b}. \tag{1}
\]

Here, \(C_N(N_{pc}, N_{po}, N_b)\) is the total number of different conformations of walk of length \(N = 28\) steps.

Fig. 2: Schematic representations of a polymer chain on the square lattice having the cone-shaped channel of the pore size one. \(\epsilon_c\) and \(\epsilon_o\), shown by the dotted lines, correspond to the attractive interaction between non-bonded monomers inside and outside the cone-shaped channel, respectively. \(\epsilon_o\) represents the bending energy. Depending on the solvent quality, the polymer chain can stay on both sides (a), or only inside (b), or outside the cone-shaped channel (c).

...(Remaining text continues as in the original document)
change and almost all monomers prefer to stay outside (in a good solvent) rather inside the pore which has a relatively poor solvent (fig. 3(b)). With the increase in temperature, one can see a tendency to decrease in relative poor solvent (fig. 3(b)). With the increase in temperature, one can see a tendency to decrease in relative poor solvent (fig. 3(b)).

Panels (c), (d) and (e), (f) show the variation of fluctuation and specific heat with temperature, respectively. The arrow on the x-axis (panel (e)) corresponds to the coil-globule transition in free space (in the absence of a cone-shaped channel).

In figs. 5(a), (b), we plot the variation of \( \langle N_{pc} \rangle \) and \( \langle N_{po} \rangle \) with temperature for different sets of interactions at fixed \( \epsilon_b \). If the nature of the solvent on both sides is the same (\( \epsilon_c = \epsilon_o = -1 \)), \( \langle N_{po} \rangle \) decreases with temperature, whereas \( \langle N_{pc} \rangle \) remains almost negligible. The system undergoes a globule-coil transition outside the pore, which can be seen from the fluctuation curve (fig. 5(c)) or the specific-heat plot (fig. 5(e)). It may be noted that the transition temperature of the polymer chain in the free space is \( \sim 0.93 \) [51] shown by an arrow on the x-axis in fig. 5(e). This shift is because of the reduction of the entropy induced by the cone-shaped channel. For a relatively poor solvent inside the pore (\( \epsilon_c = -1 \) and \( \epsilon_o = -0.8 \), and \( \epsilon_b = 0.2 \)), we find that \( \langle N_{pc} \rangle \) decreases with temperature much faster (fig. 5(b)). Instead of going to the coil state in the pore, the increase in \( \langle N_{po} \rangle \) indicates that the polymer prefers to be in the globule state outside the pore. With a
increase the monomer-monomer attraction of that side. shows that to drag polymer on the preferred side, one has to side of the solvent, whereas

\[ \langle M \rangle \]

the outside solvent is relatively poor than that of the in-

conformations outside the pore (figs. 5(d) and (f)). When

Fig. 6: Same as fig. 3, but for the flat interface of the pore size one. Here, \( m_c \) corresponds to the number of monomers on one side of the solvent, whereas \( m_o \) for the other side. Panel (d) shows that to drag polymer on the preferred side, one has to increase the monomer-monomer attraction of that side.

further increase in temperature, the polymer acquires coil conformations outside the pore (figs. 5(d) and (f)). When the outside solvent is relatively poor than that of the inside, \( \langle N_{po} \rangle \) decreases with temperature, and globule-coil transition occurs outside the pore.

In order to rule out that this is not an artifact of the lattice model or a finite-size effect, we revisited the model with a flat interface of a pore size one. One end of the poly-

mer chain is attached to the edge of the pore. In this case, the polymer will not experience any confinement, but the interface will separate two volumes of the liquid. We show the variation in the average number of monomers on both sides of the solvent with temperature for four different sets of interactions (fig. 6). In the absence of confinement, a major fraction of polymer chain prefers to stay on the poor solvent side at low temperature. At high temperature or when both sides of the solvent are the same, there is no preferential choice, and monomers are uniformly distributed, i.e., half of the monomers stays on one side and the remaining half on the other side. These results provide unequivocal support to the fact that confinement arising due to the cone-shaped channel gives rise to such an effect, and we anticipate that experiments will be able to verify these findings.

For \( N = 28 \), the average size of the polymer is \( \approx 5 \) and \( \approx 12 \) at low and high temperature, respectively. If \( r_p \) is less than 5, migration of polymer from inside to outside at low temperature should be difficult. For this, a polymer has to first unfold and then cross the interface, therefore, dynamics appears to be slow, whereas for a bigger pore size (5 and above), dynamics would be fast. In view of the above, we enumerate all possible walks of step as 28 for different \( r_p \) (fig. 1), and calculate the partition function for
each case. Here, we focus now only on the solvent quality inside the pore, which is poorer than that of the outside, i.e., \( \epsilon_c = -1 \) and \( \epsilon_o = -0.8 \) (fig. 3(a)).

In fig. 7(a), we depicted the variation of specific heat \( c \) inside the pore with temperature for different pore sizes \( (r_p = 1–11) \). One can see from the plot that when \( r_p \) is less than 4, the system has one peak corresponding to the globule-coil transition and the transition temperature shifts to the right as the pore size increases. Above the pore size 4, the system exhibits two peaks. This is in accordance with earlier studies which exhibited a frozen structure (beta sheet) for the semiflexible chain at low temperature [48–52]. In fig. 8, we plot the density of states \( D(N_p) \) as a function of nearest-neighbor contacts \( (N_p) \) at different temperature (around the peak positions). It is evident from the plot that at high temperature, the polymer is in the coil-state, where contributions are from \( N_p = 1–19 \). Near the globule-coil transition, contributions are from \( N_p = 11–19 \). This implies that the globule has some voids, and, therefore, the entropy of the globule state is relatively high. At low temperature, the dominant contribution is from \( N_p = 19 \) only, which corresponds to the highly dense state, where all lattice sites are occupied. Thus, the emergence of the new peak is the signature of the highly dense state (frozen) to globule transition [48,50], whereas the second peak corresponds to globule-coil transition. For the pore size 6 and higher, all plots fall on each other indicating that the pore size has no effect for a given length. Similar behavior has been seen for the polymer chain outside the pore (fig. 7(b)).

To the best of our knowledge, this is the first study on correlating the effect of temperature, solvent quality, and pore size on a polymer chain attached to the edge of a cone-shaped channel. When the outside solvent is poorer than the inside one, the polymer always stays outside the pore. This is because the free energy of the system is less compared to the inside. Even if the solvent quality inside and outside the channel is the same, the polymer prefers to stay outside. This is due to the reduction of the entropy inside the pore with respect to the outside, which pushes
the polymer from the pore. The most surprising finding is the ejection of the polymer from the pore and vice versa with a slight change in solvent quality. This happens in the case when the solvent quality inside is relatively poor with respect to the outside. The competition between gain in energy and loss of entropy inside the pore, together with a gain of entropy outside the pore leads to this interesting behavior. Such process can be found in the case of a nuclear pore complex (NPC), where transport through the NPC is directional so that many cargoes are only imported into or exported from the nucleus, although other cargoes do shuttle in and out continuously [59]. The estimation of barrier height across the interface (fig. 4) suggests that the polymer of different length may collapse on a single curve. In fact for a small chain we do find such collapse [57], however, to be sure one has to go for higher chain length preferably using high-precision Monte Carlo simulation.

The absence of crystalline (highly dense) state, when the pore size is less than four, may be understood recalling that the average size of the polymer is ≈5 for a given length. On a square lattice, one expects a square-like frozen structure. Since the polymer is attached to the edge of the pore, such structure cannot exist in the cone-shaped channel. When the size of the pore approaches 5, one can see the signature of the first peak corresponding to the highly dense state. Once the pore size exceeds 5, a polymer of the present length will not experience confinement and such structure can exist. One may recall that for the semi-flexible polymer chain (e.g., proteins), the crystalline state is more prominent in the form of β-sheet at low temperature [55]. Hence, at this stage our studies warrant further investigation on the relation between the pore size and the length of the polymer preferably using numerical simulations of a longer chain. It will be also interest to investigate the adsorption of biopolymers (e.g., nucleic acids) onto the inner surface of the cone [60–62] and its consequence on transport.

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