Translocation of a semi-flexible polymer through a nano-pore in presence of attractive binding particles

Ramesh Adhikari and Aniket Bhattacharya*
Department of Physics, University of Central Florida, Orlando, Florida 32816-2385, USA
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We study the translocation dynamics of a semi-flexible polymer through a nanopore from the cis into the trans compartment containing attractive binding particles (BPs) using the Langevin dynamics simulation in two dimensions (2D). The binding particles accelerate the threading process in two ways: (i) reducing the back-sliding of the translocated monomer and (ii) providing the pulling force towards the translocation direction. We observe that for certain binding strength (εc) and concentration (ρ) of the BPs, the translocation is faster than the ideal ratcheting condition as elucidated by Simon, Peskin, and Oster [M. Simon, C. S. Peskin, and G. F. Oster, Proc. Natl. Acad. Sci. U.S.A. 89, 3770 (1992)]. The asymmetry produced by the BPs at the trans-side leads to similarities of this process to that of a driven translocation with an applied force inside the pore manifested in various physical quantities. Furthermore, we provide analytic expression for the force experienced by the translocating chain as well as for the scaled Mean first passage time (MFPT) for which we observe that for various combinations of N, ε and ρ the scaled MFPT ⟨τ⟩/N^{1.5}ρ^{0.8} collapses on to the same master plot. Based on the analysis of our simulation data we provide plausible arguments how scaling theory of driven translocation can be generalized for such directed diffusion process by replacing the externally applied force with an effective force.

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I. INTRODUCTION

Transfer of bio-molecules through a nanopore is a crucial process in living organisms [1] and is equally important in the application of biotechnology [2]. Translocation of biomolecules from the cis to the trans compartment often requires a driving force. This driven translocation of bio-molecules under the influence of external forces has been studied extensively experimentally and using various theoretical and computational methods [2]. However, it is well known in molecular biology that certain transportation of biomolecules occurs without involvement of molecular motors [3, 4]. Examples include translocation of polymers in presence of binding particles (BPs) (e.g., Chaperones) [4–17] and the translocation of chains due to asymmetric solvent condition some of which has been studied recently using coarse-grained (CG) models [18–20].

Simon, Peskin, and Oster (SPO) [6] while searching for a generic but a faster mechanism than diffusion used Brownian ratchet (BR) mechanism [21] to interpret the translocation of proteins, where the BPs present in the trans-compartment rectify the pure diffusive motion along the translocation direction. The difference between simple diffusion and directed diffusion can be understood quite easily in the context of a one dimensional (1D) diffusion along a line. In a medium characterized by the monomer friction Γ, the diffusion time of the chain of the order of its own contour length \(L = (N - 1)\sigma \simeq N\sigma\) (\(N\) and \(σ\) are the number and size of the monomeric building blocks of the chain, respectively) is given by \(τ_{\text{chain}} = L^2/2D_{\text{chain}}\), where \(D_{\text{chain}} = k_BT/(NT)\) is the diffusion coefficient of the chain, and \(k_B\) and \(T\) are the Boltzmann constant and temperature, respectively. In the simplified 1D model SPO introduced equally spaced \(M\) binding sites along the chain (so that the separation between successive binding sites is \(δ = Lσ/M\)) with the stipulation that the binding particles attach irreversibly once and for all at these sites as soon as these binding sites are available at the trans side immediately after translocation [6]. SPO further assumed that once the particles are bound to the specific sites of the chain, the trans segment of the chain cannot go back to the cis side. For this directed translocation it is then easy to see that the efficiency for this directed diffusion rectified by ratchet increases \(M\) fold and

\[
τ_{\text{ratchet}} = Mδ^2/2D_{\text{chain}} = τ_{\text{chain}}/M \tag{1}
\]

However, there are several assumptions in this derivation by SPO, namely the 1D motion of a rod, ideal ratchet condition, etc. which in reality are not met. For example, biopolymers are semiflexible and not strictly rods, translocation of a rod through a nanopore in most cases is not a 1D diffusion, the binding and unbinding of particles depend on the interaction strength between the particles and the binding sites, which in turn can depend on the surrounding solvent conditions, and the ready availability of the binding particles, which may be kinetically hindered. However, the simplicity of this idea has resulted in exploring how these factors affect a realistic translocation process [8–18] through a nanopore. Zandi et al. [8], using Brownian dynamics (BD) simulations for short 1D rigid rods, found the role of BPs is not only lim-
ited to the ratchet mechanism but also provides a pulling force in the direction of translocation which makes the actual translocation process faster than the ideal BR process. Yu et al. [9] have repeated the same argument for longer 1D compressible rods. The effects of size mismatch between BPs and binding sites [10–15], sequence dependent binding affinity [13–15], and some aspects of chain flexibility have also been studied [17].

The asymmetry introduced by the presence of BPs at the trans compartment introduces several new features of single file translocation across the pore. In this study we consider translocation of a semi-flexible chain facilitated by attractive BPs present at the trans compartment. We demonstrate the similarity as well as the differences of this process with that of the well studied problem of driven translocation through a nanopore where the force is present only inside the pore [2]. However, unlike the case of driven translocation of a semiflexible chain [23, 24], in addition to the chain flexibility, there are other factors, e.g., concentration and strength of the attractive binding particles affect the translocation process in a non-trivial way, and much more, the interdependency of the various factors is subtle. Despite these additional complications we have been able to make a thorough analysis of our simulation results and came up with algebraic equations which we believe will promote further theoretical work. Before we go to the subsequent sections we first show some snapshots produced from the coordinates of the translocating chain and the BPs so as to provide a picture (Fig. 1) of how the ratcheting mechanism is affected by chain flexibility and the concentration of BPs which are explained in detail in section-III. These snapshots also help to appreciate the model introduced in the next section. The organization of the rest of the paper is as follows. In Sec. II we briefly discuss the model and the simulation techniques. The results and their interpretation are presented in Sec. III. In Sec. IV we provide a broader perspective of the problem and suggest generalization of our recently proposed scaling ansatz [25] to include other factors that affect the translocation as studied in this paper.

FIG. 1: (Color online) Snapshots of translocation from BD simulations for a fully flexible (left column) and very stiff chain (right column) for three different values of binding particle (BP) densities: (a), (c), and (e) correspond to flexible chains (κ = 0) and for ρ = 1%, 5% and 10% respectively, and (b), (d), and (f) correspond to a stiff chain (κ = 256) for the same densities. In each case the length of the translocated segments are the same. The cyan circles represent BPs and the red circles depict the chain monomers.

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FIG. 2: (Color online) Bead-spring model of a polymer chain with bending angle θi subtended by the vectors \( \vec{b}_{i-1} = \vec{r}_i - \vec{r}_{i-1} \) and \( \vec{b}_i = \vec{r}_{i+1} - \vec{r}_i \).

II. MODEL

We have used the bead spring model [26] of a polymer chain with excluded volume, spring, and bending potentials as follows. The excluded volume interaction between any two monomers is given by a short range Lennard-Jones (LJ) potential.

\[
U_{LJ}(r) = 4\epsilon \left( \frac{\sigma}{r} \right)^{12} - \left( \frac{\sigma}{r} \right)^{6} + \epsilon, \text{ for } r \leq 2^{1/6}\sigma;
\]

\[
= 0, \text{ for } r > 2^{1/6}\sigma
\]

Here, \( \sigma \) is the effective diameter of a monomer, and \( \epsilon \) is the strength of the potential. The connectivity between neighboring monomers is modeled as a Finite Extension Nonlinear Elastic (FENE) spring with

\[
U_{\text{FENE}}(r) = -\frac{1}{2}kR_0^2 \ln \left( 1 - r^2/R_0^2 \right)
\]

where \( r \) is the distance between the consecutive monomers, \( k \) is the spring constant and \( R_0 \) is the maximum allowed separation between connected monomers. The chain stiffness is introduced by adding an angle dependent three body interaction term between successive bonds as (Fig. 2)

\[
U_{\text{bend}}(\theta_i) = \kappa_b \left( 1 - \cos \theta_i \right)
\]
Here \( \theta_i \) is the angle between the bond vectors \( \vec{b}_{i-1} = \vec{r}_i - \vec{r}_{i-1} \) and \( \vec{b}_i = \vec{r}_{i+1} - \vec{r}_i \), respectively, as shown in Fig. 2. The strength of the interaction is characterized by the bending rigidity \( \kappa_b \) associated with the \( i \)th angle \( \theta_i \).

The BPs are chosen to be of the same size and mass as that of the polymer beads and they interact with each other with the same repulsive LJ interaction as given by Eq. (2). The attractive interaction of the BPs with those of the chain monomers is denoted as \( U_{\text{binding}} \) and is modeled by an attractive LJ interaction with a cut-off distance of \( 2.5\sigma \) and a strength \( \epsilon_c \), which is kept as a variable parameter in our studies and is given by

\[
U_{\text{binding}}(r) = 4\epsilon_c \left[ \left( \frac{\sigma}{r} \right)^{12} - \left( \frac{\sigma}{r} \right)^6 \right] + \epsilon, \quad \text{for} \quad r \leq 2.5\sigma; \\
0, \quad \text{for} \quad r > 2.5\sigma
\] (5)

The strength of the interaction parameter \( \epsilon_c \) controls the rate of reversible binding and unbinding of the BPs to and from the chain during the translocation process.

The purely repulsive wall consists of one mono-layer (line) of immobile LJ particles of diameter \( \sigma \) at \( x = 0 \). The LJ interaction between the mobile particles (monomers or the BPs) and immobile wall particles is given by

\[
U_W(r) = 4\epsilon_c \left[ \left( \frac{\sigma}{r} \right)^{12} - \left( \frac{\sigma}{r} \right)^6 \right] + \epsilon, \quad \text{for} \quad r \leq 2^{1/6}\sigma; \\
0, \quad \text{for} \quad r > 2^{1/6}\sigma
\] (6)

The pore is created by removing two particles at the center of the wall. The wall divides a square box into two rectangular compartments on each side (cis and trans) as shown in Fig. 1. We use the Langevin dynamics with the following equations of motion for the \( i \)th monomer

\[
m\ddot{r}_i = -\nabla(U_{\text{LJ}} + U_{\text{FENE}} + U_{\text{bend}}) + U_W + U_{\text{binding}} - \Gamma \vec{v}_i + \vec{\eta}_i
\] (7)

and for the \( i \)th binding particle as:

\[
m\ddot{\eta}_i = -\nabla(U_{\text{LJ}} + U_W + U_{\text{binding}}) - \Gamma \vec{v}_i + \vec{\eta}_i
\] (8)

Here \( \vec{\eta}_i(t) \) is a Gaussian white noise with zero mean at temperature \( T \), and satisfies the fluctuation-dissipation relation:

\[
< \vec{\eta}_i(t) \cdot \vec{\eta}_j(t') > = 4k_BT \delta_{ij} \delta(t-t')
\] (9)

We express length and energy in units of \( \sigma \) and \( \epsilon \), respectively. The parameters for the FENE potential in Eq. (3), \( k \) and \( R_0 \), are set to \( k = 500\epsilon/\sigma^2 \) and \( R_0 = 1.5\sigma \), respectively. The friction coefficient and the temperature are set to \( \Gamma = 0.7\sqrt{m\epsilon/\sigma^2} \), \( k_BT/\epsilon = 1.2 \), respectively. The equation of motion is integrated with the reduced unit time step \( \Delta t = 0.005 \) following the algorithm proposed by van Gunsteren and Berendsen [27].

### III. RESULTS

We carried out simulations for chain lengths \( N \) from 16 - 256 for different chain rigidity \( \kappa_b \) (in 2D the chain persistence length \( \ell_p = 2\kappa_b/k_BT \)) and for several choices of concentration \( \rho \) and the strength of the attractive interaction \( \epsilon_c \) for the BPs. Due to a large number of runs for a variety of combinations of parameters most of our runs are carried out for chain lengths \( N = 64 \) and 128 respectively, although in certain cases we have extended our calculations for chain length \( N = 256 \).

The polymer chain is equilibrated for times proportional to \( N^{1+2\gamma_{2D}} \) (Rouse relaxation time) [29] fixing the first monomer at the pore with the rest of the chain at the cis-compartment. Here, \( \nu_{2D} = 0.75 \) is the Flory exponent in 2D [29, 30]. The chain is then allowed to thread through the pore. When the last monomer exits the pore towards the trans-compartment we stop the simulation and note the translocation time. To get good statistics for all the quantities presented here, we have taken average over at least 1000 independent runs. We do not apply any external force at the pore to drive the polymer but the BPs present in the trans-compartment provide an effective force to make the translocation possible.

In a previous theoretical treatment based on simplified models, polymer translocation has been analyzed in terms of relative time scales of the BPs and the translocating chain [10], i.e., the diffusion time of the BPs (\( \tau_{BP} \)), the diffusion time for the chain (\( \tau_{chain} \)), and the MFPT \( \langle \tau \rangle \) of the chain respectively. We define \( \tau_{chain} \sim \sigma^2/4D_{chain} \) as the diffusion time for the chain to travel a distance of the size of the monomer \( \sigma \). Likewise, \( \tau_{BP} \sim \sigma^2/(4D_{BP}) \), where \( D_{BP} \) is the diffusion coefficient of the BPs. We have also looked at two other quantities \( \tau_{unocc} \) and \( \tau_{occ} \) defined as the the average time the binding sites (chain monomers) remain unoccupied and the average time that a BP needs to bind to the chain [10], respectively. For the simpler case of one dimensional diffusion of a rod one can show [10] that \( \tau_{unocc} \sim \sigma^2/(4\pi\rho D_{BP}) \) and \( \tau_{occ} \sim \rho \exp(\beta\sigma) \tau_{unocc} = \exp(\beta\sigma) \sigma^2/D_{BP} \). We have used these estimates to quantify the regimes of our simulation studies in two dimensions.

We have calculated these quantities from the coordinates of the chain and the BPs. In all cases studied here we find \( \tau_{BP} \ll \langle \tau \rangle \) so that the BPs attach almost instantaneously to the segment of the chain on the trans side. Thus the diffusive regime characterized by \( \tau_{unocc}, \tau_{occ} \gg \tau_{chain} \) is absent in our studies. Furthermore we find that for interaction strength \( \epsilon_c/k_BT = 5.0 \), \( \tau_{occ} \gg \tau_{unocc}, \tau_{chain} \), so that for all practical purposes the BPs bind irreversibly during the translocation process and relatively insensitive to the density of the BPs. However, reversible binding and unbinding take place for \( \epsilon_c/k_BT = 2.0 \) and in this case we find \( \tau_{chain} \gg \tau_{occ}, \tau_{unocc} \).

We further find that in this case \( \tau_{unocc} \gg \tau_{occ} \) for low density of the BPs and gets reversed for larger density of the BP. This subtle interplay of BP density and interaction strength, as well as the chain flexibility is a cou-
A. Perfect Ratchet and translocation

We begin presenting our results by making a comparison of the MFPT $\langle \tau(s) \rangle$ as a function of the s-coordinate of the polymer chain in 2D for different concentrations of the BPs ($\rho \approx 1\% - 10\%$) and chain rigidity $\kappa_b$ ranging from 0 to 256. In each figure the black dashed line represents the perfect ratcheting [9]. Here $d$ is the physical dimension. It is noteworthy in this point that for (1DBR). (ii) For a given density, the translocation becomes slower for a stiffer chain and (iii) in the limit of a very stiff chain the translocation time is longer than the 1DBR time except for a high density of BPs. We believe the results are quite general and will be valid for a more realistic situation in three dimensions (3D) [31]. Therefore, efficient design of translocation based devices may benefit from these conclusions. From our previous studies of driven polymer translocation of semi-flexible chains, we know that a stiffer chain translocates slower which can be explained using the tension propagation (TP) theory of Sakaue [22]. It is tempting to think that the binding particles produces a pulling force and therefore the BP assisted translocation would share similarities with driven translocation [8]. We will come back to this issue. This result shows that the 1DBR (where the chain cannot slide back) time is not the lower limit for translocation of semi-flexible chain driven by BPs through a nano-pore. For a 1D rod Zandi et al. [8] and Yu et al. [9] have seen this trend. Our studies establishes a far more general result in this context.

B. How efficient is the actual ratcheting mechanism?

The ratcheting of the chain through the pore due to the presence of BPs depends on the density $\rho$ and interaction strength $\varepsilon_c$ of the binding particles. The chain flexibility parameter $\kappa_b$ also plays a crucial role in attractive sites to be available to the binding particles (see Fig. 1). Unlike 1DBR (where once a monomer translocates to the trans
side it cannot go back to the cis side) we expect that there will be some backward translocation for the monomers. Thus in order to study the efficiency of the ratcheting process we calculate the average of the quantity \( n_b(m) \) which represents the number of times the \( m \)-th monomer goes back and forth from the cis to the trans side and vice versa, before finally exiting to the trans side. This captures the back and forth motion of the monomers across the pore. Fig. 4(a) shows \( \langle n_b(m) \rangle \) as a function of the monomer index \( m \) for various combinations of \( \rho \), \( \epsilon_c \), and \( \kappa_b \). A common feature of these plots is that for a low density and a low binding energy the translocation of the chain is most affected by its flexibility. It is worth noting that when the frequency \( f_b \) of binding and unbinding is small, \( \nu_x \) the time period \( T_b = 1/f_b \simeq \langle \tau \rangle \), for all practical purposes we can think that the particles are bound reversibly and make further analysis based on this assumption. However, one can expect qualitative changes in the limit of \( T_b = 1/f_b \approx \langle \tau \rangle \). If the particles bind and unbind several times during the time the chain translates, this will be reflected in an oscillatory behavior in \( \langle n_b \rangle \). Fig. 4(a)-(b) shows \( \langle n_b \rangle \) for a fully flexible and very stiff chain for several binding energies. For a fully flexible chain and for weak binding strength \( \epsilon_c = 2 \epsilon \), \( \langle n_b(m) \rangle \) shows a nearly symmetric behavior as a function of the index \( m \), while for very stiff chain one can clearly see an oscillatory pattern for back-sliding. Fig. 1 can help us in getting a better physical understanding. For a fully flexible chain the trans-segment forms a near spherical “blob” and beyond a critical size this blob hinders the back translocation of the incoming monomers; as a result for a fully flexible chain this back and forth motion saturates and then eventually decreases. On the contrary, for a stiff chain when \( \kappa_b \gg \epsilon_c \), the trans-segment of the chain is relatively straight and binding and unbinding is relatively insensitive to the monomer index \( m \). However, binding/unbinding of BPs makes the chain more/less sluggish reducing/increasing the back-sliding, which is reflected in the slightly oscillatory behavior. We think for \( \epsilon_c > k_B T \) this will be a generic feature but will be hard to see in a simulation as lowering the strength of the attractive interaction drastically reduces the probability of successful translocation. For \( \epsilon_c > k_B T \) increasing the chain stiffness will enhance the probability of particles getting adsorbed on the chain more permanently in the time scale of the translocation process and hence will decrease the back-sliding as is clearly seen in Fig. 4(c)-(d). Therefore, the back-sliding of the chain is controlled by the total number of bound BPs and the total force exerted by that bound particles. The number of bound BPs and force exerted on the chain by the bound BPs will be discussed in Sec. III D.

C. Waiting time distribution and back-sliding

The waiting time distribution \( W(s) \) is defined as the amount of time a monomer \( s \) spends inside the pore such that

\[
\sum_{s=1}^{N} W(s) = \langle \tau \rangle
\]  

Evidently a plot of \( W(s) \sim s \) reveals detailed information about the translocation process of the individual monomers. This quantity has been studied in detail in the past for fully flexible chains and more recently for driven translocation of semi-flexible chains [23, 24], and for translocation driven by binding particles [17]. For the case of driven translocation the shapes of the plots have been rationalized using TP theory [22]. Here we briefly mention the salient features of \( W(s) \) in presence of binding particles and compare the graphs of Fig. 5 with those of Fig. 4.

At low concentration of the BPs the qualitative features of \( W(s) \sim s \) (Fig. 5(a)-(b)) and \( n_b(s) \sim s \) (Fig. 4(a)-(b)) are very similar. However a point worth noting is that although the back-sliding is reduced drastically for a stiffer chain (Fig. 4(c)-(d)), the chain takes longer time to translocate as also seen in the \( W(s) \) of the individual monomer. This is partly due to the fact that a stiffer chain takes longer time to translocate as shown by us previously in the context of driven translocation [23, 24], and partly due to the fact that a stiffer translocating segment adsorbs more bound particles (see Fig. 1). For smaller \( \epsilon_c \) we also notice a slight oscillatory behavior for the middle monomers. Contrary to Figs. 5(a)-(b) which look similar to Figs. 4(a)-(b), for larger binding strength the behavior of \( n_b \) and \( W \) are opposite. At a larger binding energy \( n_b \) decreases with the chain stiffness but \( W \) increases in general. For low concentrations (Fig. 5(c)) \( W(s) \) is distinct for each stiffness. Both Fig. 5(c) and (d) share the features of a driven translocation in that the position of the maximum for a stiffer chain shifts toward a smaller value of the monomer index. Also, a noticeable feature is that it is the extreme stiff chain which exhibits very different behavior than the

\[\text{FIG. 5: (Color online) The corresponding waiting time distribution of Fig. 4.}\]
semi-flexible chains whose contour length \( L \leq \ell_p \). Increasing the concentration of the BPs markedly reduces the values of \( W(s) \) and hence the MFPT \( \langle \tau \rangle \). The similarity of the variation of the waiting time distribution as a function of chain stiffness for larger strength of the attractive interaction leads us to think that the TP theory can also be extended to the case, where no external bias is present, however, the chemical potential difference may produce an effective force on the chain monomer leading to a propagating tension front.

### D. Number of bound BPs and driving force

An important aspect of the polymer translocation facilitated by attractive binding particles is how these particles impart an effective force on the translocating segment and how the force depends on various factors. Since this force is a function of the number of bound particles \( n_{\text{bound}}(s) \), we first look at this quantity as a function of the translocated segment \( s \) as shown in Fig. 6. We also find the quantity \( \bar{n}_{\text{bound}}(s) = n_{\text{bound}}(s)/s \), is useful in depicting the evolution of the bound pairs shown in the insets of Figs. 6(a) and (b). Several noticeable features of Fig. 6 are the following. We consider two concentrations of the binding particles, namely 1% (Fig. 6(a)) and 10% (Fig. 6(b)) of strength \( \epsilon = 5\epsilon \). This value of \( \epsilon \) is close to the bending stiffness of the moderately flexible chain \( (k_b = 8\epsilon) \). We observe that the dependence of \( n_{\text{bound}}(s) \) on the chain stiffness is markedly different for a stiff chain \( (\ell_p \gg L \text{ or equivalently } k_b \gg \epsilon_c) \) than that of a fully flexible chain, or a moderately flexible chain. While for a stiff chain \( n_{\text{bound}} \propto s \) (or \( \bar{n}_{\text{bound}} \approx 0.8 \text{ or } 1.4 \) for 1% and 10% density of the BPs respectively), \( n_{\text{bound}}(s) \) either saturates at \( \rho = 1\% \), or decreases as a function of \( s \). These qualitative behaviors of \( n_{\text{bound}}(s) \) as a function of chain stiffness are rightly captured in various snapshots of Fig. 1. As long as \( k_b < \epsilon_c \), the binding particles are capable of bending the chain and more than one monomer attach to the same binding particle. For a larger value of \( \rho = 10\% \) preexisting binding particles accommodate the incoming translocated monomers and hence \( \bar{n}_{\text{bound}} \) decreases. For stiff chains, at least for the concentration considered here, the number of bound particles continues to increase linearly with the translocated segment.

The attractive interaction between the BPs and translocated monomers of the chain causes a net force on the translocated segment of the chain. We calculate the \( x \)-component (the component in the direction of translocation) of this force as:

\[
F_x(s) = -\sum_{i=1}^{s} \sum_{j=1}^{N_{BP}} \frac{\partial U_{\text{binding}}(r_{ij})}{\partial x} \tag{12}
\]

Here, \( N_{BP} \) is the total number of the BPs. Fig. 7 shows the force \( F_x \) due to the BPs along the direction of translocation as a function of \( n_{\text{bound}}(s) \). For stiff chain it is clear that \( F_x(s) \propto n_{\text{bound}}(s) \) and hence \( F_x(s)/n(s) \) remains roughly constant for a stiff chain. For a fully flexible or moderately flexible chain the force reaches a maximum value which is expected from Fig. 6. For extreme stiff chains our results qualitatively are the same as the previous work of Zandi et al. [8] who found similar behavior for the translocation of a rod, although they considered the motion of the rod to be restricted along the translocation axis only. In the extreme stiff limit it is expected that the qualitative feature will be the same. We have also calculated the concentration dependence of the \( F_x \) from the asymptotic values of \( F_x(s)/n(s) \) in the limit of extreme stiff chains shown in the inset (i) of Fig. 7(b). We find \( F_x \propto \ln \rho \) as expected as the free energy is proportional to \( \ln \rho \).

### E. Universal aspects and scaling of MFPT

We now discuss the MFPT for translocation facilitated by binding particles. The dependence of MFPT on chain length \( N \) has been a matter of considerable interest for the last two decades [2] and theoretical studies have achieved a rather mature state in delineating the factors affecting the translocation exponent \( \alpha \) \( (\langle \tau \rangle \sim N^\alpha) \). For the case of driven translocation a scaling ansatz has been established [25]

\[
\langle \tau \rangle = A(f, \eta_{\text{olv}}) N^{1+\nu} + B(f, \eta_{\text{olv}})/(\eta_{\text{pore}}/\eta_{\text{olv}}) N \tag{13}
\]

Here, \( f, \eta_{\text{olv}}, \eta_{\text{pore}} \) are the external force, the solvent friction, and the pore friction, respectively, and \( A \) and \( B \) are
nonuniversal quantities whose numerical values are close to unity. Eq. (13) explains the non-universal finite $N$ effect arising out of the second term due to relative influence of pore friction over solvent friction. Detailed numerical calculations [32] show that Chuang-Kantor-Kardar limit [(\tau) \sim N^{1+\nu}] is achieved only in the limit of very large $N \rightarrow 10^6$. For moderate chain length of 100-1000 most of the reported translocation by various groups exponent is within $2\nu \leq \alpha \leq 1 + \nu$ [39–41]. In the case of translocation assisted by the BPs we also find that the translocation exponent $\alpha \approx 1.5$ which is another reason to believe that TP theory can be generalized for chemical potential induced tension propagation. In the following subsections we discuss how the MFPT depends on the density and strength of the binding particles as well as on the persistence length of the chain.

1. Density dependence of MFPT

Consistent with Eq. (13), we also find that the translocation exponent $\alpha$ is within the above mentioned bound. This is first verified in Fig. 8 where we observe that the nonuniversal quantities whose numerical values are close to unity. Eq. (13) explains the non-universal finite $N$ effect arising out of the second term due to relative influence of pore friction over solvent friction. Detailed numerical calculations [32] show that Chuang-Kantor-Kardar limit [(\tau) \sim N^{1+\nu}] is achieved only in the limit of very large $N \rightarrow 10^6$. For moderate chain length of 100-1000 most of the reported translocation by various groups exponent is within $2\nu \leq \alpha \leq 1 + \nu$ [39–41]. In the case of translocation assisted by the BPs we also find that the translocation exponent $\alpha \approx 1.5$ which is another reason to believe that TP theory can be generalized for chemical potential induced tension propagation. In the following subsections we discuss how the MFPT depends on the density and strength of the binding particles as well as on the persistence length of the chain.

1. Density dependence of MFPT

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translocation process [35]. However, this argument will not hold for a stiff chain. As a matter of fact from the figure, we observe that for the stiffer chains the effect of increasing the density of the BPs in reducing the MFPT is more pronounced as compared to a fully flexible chain. Thus an “effective pulling” force is responsible for the reduction of the MFPT.

2. Binding strength dependence of MFPT

Now we discuss the effect of the binding strength of the BPs on the MFPT. For a driven translocation process we know that \( (\tau) \propto f^{-1} \) [2]. Here as we just discussed the dependence of MFPT on the “effective force” \( f \) produced by the BPs is expected to be more complex as \( f = \tilde{f}(s, \rho, \epsilon_c, \kappa_b) \), in addition to the pore and the solvent friction. We show the dependence of MFPT on \( \epsilon_c \) in Fig. 9 for a low density of the BPs. We observe that for large binding energies asymptotes of the rescaled MFPT

\[
\frac{\langle \tau \rangle}{N^{1.5}} \text{ for different stiffness roughly saturate at a common value. From further analysis of these graphs we note that for all chain stiffness each curve could be fitted to a polynomial as follows:}
\]

\[
\frac{\langle \tau \rangle}{N^{1.5}} = a_0 - a_1\epsilon_c + a_2\epsilon_c^2 - a_3\epsilon_c^3 + a_4\epsilon_c^4 \quad (15)
\]

We further notice that to a first approximation \( a_1 \approx 0.5a_0, a_2 \approx 0.14a_0, a_3 \approx 0.01a_0, \) and so on. We provide a physical picture as follows which we have verified for at least two different chain lengths and for several low concentrations of the BPs. The first term \( a_0 \) represents the density and stiffness dependence of translocation in the limit \( \epsilon_c \to 0 \) and approximately we find \( a_0 \approx \rho^{-\beta} \). We have seen it before [24] that the MFPT increases with the chain stiffness. Once the attractive BPs are introduced the translocation acquires signature of a driven translocation and MFPT decreases which is reflected in the negative contribution of the linear term \( a_1\epsilon_c \). The quadratic term \( a_2\epsilon_c^2 \) and the higher order terms represent many-body effect where two or more binding particles would be attached to the same monomer and introduce “crowding” and increase the MFPT. It is worth noticing each graph in principle can exhibit minima for certain combination of the coefficients are reported previously [17, 34] but have not been analyzed adequately. We re-confirm our analysis in Fig. 9 by showing data collapse of \( \langle \tau \rangle / \rho^{0.8} \) for two different concentrations for a stiff chain.

3. Chain stiffness and MFPT

Finally in Fig. 10 we analyze the translocation data as a function of the chain stiffness for a moderate strength of the attractive interaction \( (\epsilon_c/k_B T \approx 4\epsilon) \) for several densities. For \( \ell_p \leq L \) the MFPT varies approximately linearly as a function of the chain stiffness. However, beyond \( \ell_p \geq L \) the strict linearity will no longer be valid as the effect of the chain stiffness will saturate. The inset of Fig. 10 shows the saturation effect.

![Figure 9](image-url) (a) Scaled MFPT \( \langle \tau \rangle / N^{1.5} \) as a function of binding strength \( \epsilon_c \) of BPs for different chain stiffness \( \kappa = 0, 8, 32, 256 \epsilon \) and for \( N = 64 \) (open symbols) and \( N = 32 \) (closed symbols) respectively. Black-solid, red-dashed and green-dotted lines are 4-th degree polynomial fits to the data for \( \kappa = 256 \epsilon, 32 \epsilon \) and \( 8 \epsilon \), respectively. The fitted line for the data corresponding to \( \kappa = 8 \epsilon \) is almost the same as for \( \kappa = 0 \). (b) Scaled MFPT \( \langle \tau \rangle / \rho^{0.8} \) as a function of binding strength \( \epsilon_c \) of BPs for stiff chain \( (\kappa = 256 \epsilon) \) of length \( N = 64 \). Open symbols correspond to \( \rho = 1\% \) and closed symbols correspond to \( \rho = 5\% \). The solid line represent the 4-th degree polynomial fit to the data.

![Figure 10](image-url) (Color online) The MFPT varies linearly with the chain rigidity \( \kappa_b \) for the smaller values of \( \kappa_b \). After certain value of rigidity the MFPT saturates. Red-squares, green-diamonds and blue-triangles represent the density \( \rho = 2.5\%, 5\% \) and \( 10\% \), respectively. The inset is the same plotted in log-log scale.
IV. SUMMARY & DISCUSSION

To summarize, we have studied translocation of a homopolymer through a nanopore in presence of attractive BPs at the trans side responsible for the directed motion of the chain. The motivation of the problem stems from a seminal paper by Simon, Peskin and Oster [6] which raised an important issue of non-specific transport in the biological world which is as generic as diffusion, albeit a faster process, and suggested directed diffusion rectified by binding particles as a possible solution. As an example, this process occurs in the biological world when a DNA enters a nucleopore the chaperonin proteins provides the necessary driving force for the translocation. Thus a study of a coarse-grained model is of practical value. Theoretical studies based on idealized and simpler models, based on several assumptions predict how the attractive BPs enhances the directed diffusion and exert a force on the translocating chain. However, the assumptions are often not satisfied which resulted some numerical works in the past. One of the important results is that the ratcheting mechanism introduced through the reversible binding of the BPs under certain conditions can outperform the ideal ratchet. This was demonstrated earlier by Zandi et al. [8] for the 1D translocation of a rod. Here we have demonstrated its generic validity.

There is no net external force in this system, however, we have demonstrated that there is an effective pulling force exerted by the attractive BPs on the translocating chain. Indeed we observe that we can find consistent explanations to some of our simulation data using the original TP theory [22] and the results from our previous simulation studies of driven translocation of a semi-flexible chain through a nanopore [24], where we demonstrated how the chain stiffness affects the tension propagation and hence the translocation process. A plausible physical reason for this connection is that unlike the case of driven translocation, here the asymmetry in chemical potential creates and drives a tension in the cis side. Therefore, for the stronger interaction strength of the BPs, the waiting time distribution is asymmetric and qualitatively is similar to that of driven translocation. Based on these evidences from simulation results, we have suggested that by generalizing the external force to an effective force so as to include other factors responsible for a pulling force, it is likely that the TP theory can be extended to such directed diffusion process. In most cases we have provided scaling relations for the dependence of MFPT on various variables and provided phenomenological equations and data collapse in the limit of extreme stiff chains which will be useful for further theoretical studies.

We now like to comment on the relevance of our work and the choice of the parameters in regard to actual biological processes. The experimental values of diffusion coefficient for short chains translocating through a nanopore is $D_{\text{chain}} \sim 10^{-8} \text{ cm}^2/\text{s}$ [36, 37]. The diffusion constant for the short macromolecules in cellular solution is $D_{\text{BP}} \sim 10^{-6} \text{ cm}^2/\text{s}$ [38], so that the ratio $D_{\text{BP}}/D_{\text{chain}} \sim 100$. For the parameters used in our simulation we find that this ratio $D_{\text{BP}}/D_{\text{chain}} \sim 20 – 50$, which implies that the choice of the parameters can be associated with actual biological processes. We have also checked that the diffusion time of the chain $\tau_{\text{chain}} \ll \langle \tau \rangle$. Thus we expect that our numerical studies augmented by good theoretical estimates will promote further theoretical and experimental work in this field.

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For stiff chains the total force on the chain increases linearly with the number of bound particles \( n_b \) which is proportional to the physical dimension \( d \) (Fig. 7). We also know that \( \langle \tau \rangle \propto 1/F \) [2] which implies that \( \langle \tau \rangle \propto 1/d \). Thus from Eqn. 10, to a first approximation \( \tau_{\text{ratchet}}/\langle \tau \rangle \) will be independent of the physical dimension \( d \). However how the “perfect ratchet” condition will be over or under satisfied will depend on the parameters of the model.