Polymer translocation through nanopore into active bath

Mingfeng Pu, Huijun Jiang, and Zhonghuai Hou

Department of Chemical Physics and Hefei National Laboratory for Physical Sciences at Microscales, iChEM, University of Science and Technology of China, Hefei, Anhui 230026, China

(Received 22 July 2016; accepted 12 October 2016; published online 1 November 2016)

Polymer translocation through nanopores into a crowded environment is of ubiquitous importance in many biological processes. Here we investigate polymer translocation through a nanopore into an active bath of self-propelled particles in two-dimensional space using Langevin dynamics simulations. Interestingly, we find that the mean translocation time $\langle \tau \rangle$ can show a bell-shape dependence on the particle activity $F_a$ at a fixed volume fraction $\phi$, indicating that the translocation process may become slower for small activity compared to the case of the passive media, and only when the particle activity becomes large enough can the translocation process be accelerated. In addition, we also find that $\langle \tau \rangle$ can show a minimum as a function of $\phi$ if the particle activity is large enough, implying that an intermediate volume fraction of active particles is most favorable for the polymer translocation. Detailed analysis reveals that such nontrivial behaviors result from the two-fold effect of active bath: one that active particles tend to accumulate near the pore, providing an extra pressure hindering the translocation, and the other that they also aggregate along the polymer chain, generating an effective pulling force accelerating the translocation. Such results demonstrate that active bath plays rather subtle roles on the polymer translocation process. Published by AIP Publishing. [http://dx.doi.org/10.1063/1.4966591]

I. INTRODUCTION

The phenomenon of polymer translocation through nanopores and channels has gained extensive research attention in the latest decade. On the one hand, polymer translocation is closely relevant with many crucial biological processes, such as DNA and mRNA translocation through nuclear pores, protein transport across membrane channels, virus injection into cell,1 and so on. On the other hand, it also has far-reaching technological potentials, including gene therapy, rapid DNA sequencing, and controlled drug delivery.2–7 A considerable number of works in the literature, both experimentally,2,6–15 and theoretically,16–28 have been devoted to study the polymer translocation process, which may be influenced by many factors, such as the pore structure,2–9,29 the polymer-pore interaction,9,22,24,29,30 the solvent property,31 the polymer concentrations,32,33 and so on.

In real systems, polymer translocation process usually involves crowded environments. For instance, the volume fraction of large macromolecules and other inclusions in cell interior can be as large as 50%.34 Experiments have shown that crowded environment can affect the dynamic properties of polymer such as reaction rates, protein folding rates, and equilibria in vivo compared with those in dilute solutions remarkably.35–37 It was also revealed that crowded environment strongly influences the polymer translocation through nanopore. For instance, Gopinathan et al. have considered a simple model wherein crowding was modeled by randomly distributed spherical static obstacles, and novel scaling behaviors of the translocation time have been discovered by treating the entropic penalty due to crowding.38 Cao et al. have used Monte Carlo simulation to investigate the influence of crowding on three-dimensional polymer translocation, they have found that normal diffusion can only be observed in dilute solution without obstacles, or in a crowded environment with weak polymer-obstacle attraction, otherwise, a sub-diffusion behavior of polymer is observed.39 Chen and Luo have used both theoretical analysis and Langevin dynamics simulation to study the size effect of the mobile crowding agents. It is found that the translocation undergoes a maximum value by changing the diameters of agents at trans side with the fixed diameters at cis side while the crowding agents have equal area fraction at both cis and trans sides.40

The above studies for polymer translocation all take into account the crowded media as passive particles, i.e., the particles will finally relax to an equilibrium state determined by the interaction potential and temperature. Nevertheless, the crowded media may also be active particles that are subjected to some external driving force which renders the system to be out of equilibrium. Actually, dynamics of active matter has gained extensive research attention in recent years, including those in living systems such as bacteria,41 spermatozoa, and mammals.42–44 A wealth of new non-equilibrium phenomena have been reported, such as active swarming, large scale vortex formation,45,46 and phase separation,47–51 both experimentally and theoretically. In particular, dynamics of polymer in active media also shows many nontrivial phenomena. For instance, Kaiser and Löwen have considered a fully flexible polymer chain in a bacterial bath(or an active solvent), finding that active bacteria can stiffen and expand the chain in a...
non-universal way. J. Harder et al. found that rigidity of polymer can lead to interesting behaviors in active bath, e.g., a rigid filament can breath between a tight hairpin and an ensemble of extended conformation for intermediate activities. Recent works on filaments formed by active Brownian particles showed very interesting dynamic behaviors, including periodic beating and rotational motions, and so on. To the best of our knowledge, however, how the active media would influence the dynamics of polymer translocation process has not been studied yet.

Motivated by this, in the present paper, we have studied the translocation process of a polymer through a small pore into an active bath. For simplicity, we have considered a two-dimensional system with only active particles at the trans side (see Figure 1). We mainly focus on how the mean translocation time $\tau$ would depend on the particle activity $F_a$ as well as the volume fraction $\phi$ of the particles. Very interestingly, we find that $\langle \tau \rangle$ shows a bell-shape dependence on the particle activity at a fixed volume fraction, indicating that the translocation process becomes slower for small activity compared to the case of passive media. Only for large activity, can the polymer translocation be accelerated. On the other hand, we find that $\langle \tau \rangle$ also shows a non-monotonic dependence on the volume fraction $\phi$ at a fixed particle activity, but now with a minimum, implying that the translocation process is mostly accelerated at an intermediate volume fraction. Such findings clearly demonstrate the nontrivial role that the active media plays in the polymer translocation process.

The remainder of this paper is organized as follows. In Sec. II, we describe our model and simulation method. In Sec. III, we present our results and discussion followed by conclusion in Sec. IV.

II. MODEL

The polymer is modeled by a fully flexible self-avoiding bead-spring chain consisting of $N$ beads with diameter $\sigma$. Neighboring beads are linearly connected via a harmonic potential $U_h(r_{ij}) = \epsilon_h(r_{ij} - r_0)^2$, where $r_{ij}$ is the center-to-center distance between each pair of adjacent beads, $\epsilon_h$ is the spring constant, and $r_0$ denotes the equilibrium distance. The excluded volume effect is realized by a short range repulsive Lennard-Jones(LJ) potential,

\[
U_{LJ}(r_{ij}) = \begin{cases} 
4\epsilon \left( \frac{\sigma}{r_{ij}} \right)^{12} - \left( \frac{\sigma}{r_{ij}} \right)^6 + 4 \epsilon, & r_{ij} \leq 2^{1/6} \sigma \\
0, & r_{ij} > 2^{1/6} \sigma 
\end{cases},
\]

where $r_{ij}$ is the distance between beads $i$ and $j$, and $\epsilon$ denotes the potential strength.

We consider a two-dimensional rectangular box of size $2L \times L$ as depicted in Fig. 1, wherein the polymer passes across the wall in the middle through a pore of width $\omega$. The trans side is an active bath of self-propelling particles (SPPs), which repel each other via the LJ potential same as Eq. (1). The purely repulsive wall consists of one monolayer of immobile repulsive LJ particles. The dynamics of the SPPs is governed by the following Langevin equations:

\[
m\ddot{r}_i = -\gamma \dot{r}_i + F_a \eta_i(\dot{\theta}_i) - \frac{\partial V_i}{\partial r_i} + \sqrt{2\gamma k_BT\xi_i(t)},
\]

\[
\dot{\theta}_i = \sqrt{2D_r\xi_{i,r}(t)},
\]

where $m$ is the particle mass, $\gamma$ is the friction coefficient, $k_B$ is the Boltzmann constant, $T$ is the temperature, $D$ and $D_r$ are, respectively, the translational and rotational diffusion coefficients with $D = 3D_r/\sigma^2$, $V_i = \sum_{j \neq i} U_{LJ}(r_{ij})$, where the summation $j$ runs over all the other particles except $i$ at the trans side, including the SPPs, polymer beads, and wall-particles. $F_a$ denotes the magnitude of the self-propelling force exerted on the particle along the direction given by $\mathbf{n}_i(\dot{\theta}_i) = (\cos \theta_i, \sin \theta_i)$. $\xi_i(t)$ and $\xi_{i,r}(t)$ are the Gaussian white noises for translational and rotational motion, respectively, which satisfy $\langle \xi_i(t) \rangle = 0$, $\langle \xi_i(t)\xi_j(t') \rangle = \delta_{ij}\delta(t-t')$, and $\langle \xi_{i,r}(t) \rangle = 0$, $\langle \xi_{i,r}(t)\xi_{j,r}(t') \rangle = \delta(t-t')$. Similarly, the dynamics of a polymer bead $i$ is described by

\[
m\ddot{r}_i = -\gamma \dot{r}_i + F_{ext} - \frac{\partial V'_i}{\partial r_i} + \sqrt{2\gamma k_BT\xi_i(t)},
\]

where $V'_i = \sum_{j \neq i} U_{LJ}(r_{ij}) + U_h(r_{i,i+1}) + U_h(r_{i,i-1})$ includes the interactions of bead $i$ with its two nearest neighbor beads (note that each of the two end-beads has only one nearest neighbor) and all other particles. For simplicity, the bead mass $m$, friction coefficient $\gamma$, the temperature $T$, and the diffusion constant $D$ are chosen to be the same as those of the SPPs in Eq. (2). In particular, $F_{ext} = F_{ext} \hat{X}$ denotes a constant external force inside the pore toward the trans side.

We use $m$, $\sigma$, and $k_BT$ as the fundamental units for mass, length, and energy, respectively. The dimensionless time unit is then $\tau_0 = \sqrt{\frac{k_BT}{m\sigma^2}}$. The parameters for our simulation are fixed to be $\epsilon_h = 800k_BT/\sigma^2$, $r_0 = 2^{1/6}\sigma$, $\epsilon = 10k_BT$, $\gamma = 10.0\tau_0^{-1}$, $L = 50$, and $\omega = 1.3\sigma$. The external force in the pore is $F_{ext} = 100.0$, the length of polymer is $N = 100$, and the volume fraction of active particles is $\phi = 0.1$, if not otherwise stated. In case of varying $\phi$ at the trans side, the value is in the range from 0.01 to 0.3, which is below the threshold value for the spontaneous phase separation induced by activity. At the beginning of translocation, the first monomer is fixed at the center of the pore and released after necessary relaxations. All of the obtained results presented in this paper are averaged over at least 1000 independent runs.
III. RESULTS AND DISCUSSION

In the present work, we are mainly interested in how the activity bath at the trans side would influence the polymer translocation. To this end, we have investigated how the average translocation time $\langle \tau \rangle$ would depend on the particle activity $F_a$. To highlight the effect of activity, we have calculated the relative translocation time $\langle \tau \rangle_{net} = \langle \tau \rangle - \langle \tau \rangle_0$, where $\langle \tau \rangle_0$ is the translocation time without particles at the trans side. In Fig. 2, $\langle \tau \rangle_{net}$ as a function of $F_a$ at a fixed volume fraction $\phi = 0.1$ is presented. Very interestingly, $\langle \tau \rangle_{net}$ shows a non-monotonic dependence on the active force $F_a$, i.e., $\langle \tau \rangle_{net}$ first increases gradually for small values of $F_a$, reaches a maximum at a certain intermediate value of $F_a$, and then decreases for large $F_a$. Moreover, $\langle \tau \rangle_{net}$ is larger than 0 for small $F_a$, indicating that the particle activity at the trans side hinders the polymer translocation in this case. When the particle activity becomes large enough, however, the active bath can obviously accelerate the translocation process. Note that the occurrence of this nontrivial phenomenon can be observed for varying $F_{ext}$ as also shown in Fig. 2.

With decreasing external force, the non-monotonic behavior becomes more pronounced with the peak position shifted towards small values of $F_a$.

One should note that the nontrivial dependence of $\langle \tau \rangle$ on $F_a$ as demonstrated above is quite counter-intuitive at the first glance. Since an active particle tends to keep its direction during the persistence time period until it takes random rotation, the effect of active bath should be different from that of a passive bath. Generally, one expects that the active particles should considerably influence the polymer translocation, since they may exert some kind of force on the polymer segments that have already passed across the pore. This force could accelerate or suppress the translocation, depending on how active particles interact with the polymer beads, as one may think. Nevertheless, that the effect can change from a negative one, i.e., $\langle \tau \rangle_{net} > 0$, to a positive one with $\langle \tau \rangle_{net} < 0$ as shown in Fig. 2, is quite not easy to be understood straightforwardly.

In order to understand in more detail about such nontrivial dependence of $\langle \tau \rangle$ on $F_a$, we have analyzed the translocation process by studying the waiting time $W(s)$ which is the average time between monomer $s$ and monomer $s+1$ to first pass through the pore. $W(s)$ then measures how long it takes on average for the monomer $s$ to pass through the pore. We can also investigate the accumulative waiting time $\tau(s)$ defined as $\tau(s) = \sum_{i=1}^{s} W(s)$, which describes how long it takes from the beginning to the moment as the monomer $s+1$ passes through the pore. In Fig. 3, the dependences of $W(s)$ and $\tau(s)$ as functions of $s$ for $F_{ext} = 100.0$ are depicted for a relatively small active force $F_a = 15.0$ and a larger one $F_a = 50.0$, respectively, compared to the case $F_a = 0$ for a passive system. For small activity $F_a = 15.0$ as shown in Fig. 3(a), the curve for $W(s)$ is slightly above that for passive system with $F_a = 0$, for all the monomers. Accordingly, $\tau(s) (F_a = 15.0)$ is always larger than $\tau(s) (F_a = 0.0)$ for any $s$ as shown in Fig. 3(b) and its inset. Therefore, for $F_a = 15.0$, the polymer translocation is always suppressed during the translocation process, as compared to the passive case with $F_a = 0$. For relatively large activity $F_a = 50.0$ as shown in Figs. 3(c) and 3(d), the situation is quite different. Overall, we see that the curve for $W(s) (F_a = 50)$ is apparently below that for $F_a = 0$, indicating that particle activity at the trans side now apparently accelerates the translocation process in accordance with Fig. 2. Interestingly, for small $s (\leq 12)$, one can see that $W(s) (F_a = 50)$ is still larger than $W(s) (F_a = 0)$, indicating that the translocation is hindered by the active particles in the early stage. After that, $W(s) (F_a = 50)$ becomes considerably smaller than $W(s) (F_a = 0)$ indicating apparent acceleration by particle activity. This is also demonstrated in Fig. 3(b), where the difference $\tau(s) (F_a = 50) - \tau(s) (F_a = 0)$ first increases a little and then decreases substantially with the increment of monomer index $s$.

The above analysis suggests that the active particles tend to suppress the translocation process at the early stage, whether the active force is large or not. While at the latter stage, large active force may help the translocation process. To get more insight into these effects, we have depicted some typical snapshots of the polymer and active particles at the trans side in Fig. 4 at early and late translocation stages for $F_a = 15$ and $F_a = 50$, respectively. In the early stages, for both small and large particle activities, one can see that the particles aggregate near the pore and thus produce an extra effective pressure to the cis side which is unfavorable to the translocation. Actually, this is in accordance with the phenomenon reported in the literature that active particles tend to accumulate near walls or angles when they move in a confined space.\cite{58,59} Such an activity-induced aggregation is more pronounced for larger driving forces; hence, the deceleration effect is larger for $F_a = 50$ than that for $F_a = 15$ at the early stage as discussed in the last paragraph. However, at the late stage when many monomers have passed across the pore, the active particles can also aggregate along the long exposed part of the polymer chain at the trans side as shown in Figs. 4(b) and 4(d). Active particles aggregating around the polymer tend to maintain their movement directions and thus also exert a force on the chain to bring the polymer moving together. For large active force $F_a = 50$ as demonstrated
FIG. 3. Waiting time $W(s)$ ((a) and (b)) and cumulative waiting time $\tau(s)$ ((c) and (d)) for the translocation of flexible polymer into different active environments with $F_a = 15.0$ ((a) and (c)) and $F_a = 50.0$ ((b) and (d)). Ones for $F_a = 0.0$ are also plotted for comparison. The values of $\tau(s)$ for $F_a = 15.0$ and $F_a = 50.0$ relative to the one for $F_a = 0.0$ are presented in insets of (c) and (d), respectively.

FIG. 4. Typical snapshots of polymer configuration at the very beginning of translocation process for (a) $F_a = 15.0$ and (c) $F_a = 50.0$, and at the latter stage for (b) $F_a = 15.0$ and (d) $F_a = 50.0$. Here, active particles away from the polymer are rendered with a semitransparent filter to give a clear picture.

in Fig. 4(d), this extra force leads to an extension of the polymer chain and thus accelerates the polymer translocation process. Therefore, we think that it is the two-fold effect of the active particles: one that they tend to accumulate near the pore and the other that they also aggregate along the polymer chain, the relative strength of which depends on the active force, that results in the non-monotonic dependence of the translocation time $\tau$ on the active force as shown in Fig. 2.

The above results are obtained at a fixed volume fraction of the active particle $\phi = 0.1$. One may then wonder how the translocation process depends on the volume fraction $\phi$. In Fig. 5, the dependences of the mean translocation time $\langle \tau \rangle$ on $\phi$ for three different values of active force $F_a$ are presented. Interestingly, we find that $\langle \tau \rangle$ undergoes a clear-cut minimum with the increment of $\phi$, indicating that there exists an optimal volume fraction of active particles in the trans bath that is most favorable to the polymer translocation. This optimal behavior is more pronounced for a larger active force, and for $F_a = 30$ as shown in the figure, the curve already becomes nearly monotonic-increasing with $\phi$. Therefore, this non-monotonic dependence on $\phi$ would not be observed for a passive bath where $F_a = 0$. We have also analyzed the behaviors of $W(s)$ and $\tau(s)$ at different volume fractions with given $F_a = 50$, as demonstrated in Fig. 6. Compared to the case $\phi = 0.1$, where the translocation time $\langle \tau \rangle$ is the smallest, $W(s)$ for $\phi = 0.3$ is larger for all $s$, indicating that the translocation is
slower during the whole process. For $\phi = 0.01$, overall the translocation is also slower than that for $\phi = 0.1$, while it is a little bit faster in the early stage ($s \leq 18$) as shown in Figs. 6(a) and 6(c).

The reason why there exists an optimal value of $\phi$ which is the most helpful for translocation is not easy to be understood. Here we just try to give a qualitative illustration. For $F_a = 50$, the activity is already large enough such that the positive “pulling” effect of the active particles dominates the negative “pressure” effect, as discussed in the last paragraph. Nevertheless, to make this positive “pulling” effect work, enough number of active particles should be necessary to aggregate along the polymer chain. In Figs. 3 and 4, the volume fraction is $\phi = 0.1$ which is demonstrated to be enough. If we reduce the volume fraction of active particles (equally decrease the number of active particles), say 0.01, the number of particles aggregating along the polymer chain decreases, such that the translocation becomes slower in Fig. 7(a). However, if the volume fraction is too large, say 0.3 here, the trans side gets crowded and the particles may form clusters as shown in Fig. 7(c), thus also leading to a slowing down of the translocation.

The above findings strongly suggest us to perform extensive simulations to study the dependence of the translocation time $\langle \tau \rangle$ in the $F_a - \phi$ parameter plane. Fig. 8 presents the contour plot of $\langle \tau \rangle_{net}$. Clearly, two types of non-monotonic behaviors can be observed. On the one hand, at a fixed volume fraction $\phi$, $\langle \tau \rangle_{net}$ undergoes a maximum with increasing $F_a$, indicating that an intermediate level of particle activity suppresses the translocation process most strongly. Moreover, the position of maximum shifts to larger $F_a$ with increasing volume fraction $\phi$. On the other hand,
FIG. 7. Typical snapshots of polymer configuration at the later stage of translocation process for (a) $\phi = 0.01$, (b) $\phi = 0.10$, and (c) $\phi = 0.30$. The active force is $F_a = 50.0$. For the sake of clarity, the active particles away from the polymer are rendered with a semitransparent filter.

$\langle \tau \rangle_{\text{net}}$ shows a clear-cut minimum with the variation of $\phi$ if the active force $F_a$ is fixed and large enough. This means that the translocation process is mostly accelerated in an active bath with an intermediate volume fraction. The optimal value of $\phi$ becomes larger with increasing active force $F_a$. Therefore, the active bath facilitates us to control the polymer translocation via tuning the particle activity or volume fraction. To suppress the translocation most efficiently, an intermediate value of $F_a$ and a high volume fraction are preferred. On the other hand, to accelerate the translocation, the volume fraction should be at an optimal value and the particle activity should be large.

Finally, we have also investigated the dependence of the translocation time $\langle \tau \rangle$ on the chain length $N$. Both experiments and numerical simulations have suggested a power law dependence between $\langle \tau \rangle$ and $N$, i.e., $\tau \sim N^\alpha$. The exponent $\alpha$ may depend on the friction force the polymer is experienced, or the range of the polymer length. It was found that for transmembrane process at moderate values of the friction, the scaling exponents are close to $2\nu$ and $1 + \nu$ for relatively short and long polymers, respectively, where $\nu$ is the Flory exponent. At high friction, only $\alpha = 1 + \nu$ is observed even for short chains. For our system considered here, due to that trans side contains a great amount of active particles, the space confinement only allows us to consider relatively short polymers. Fig. 9(a) shows the log-log plots of $\langle \tau \rangle$ as a function of $N$ for different $F_a$ under a fixed volume fraction $\phi = 0.10$. The scaling exponent presented here should be considered as an effective value due to the fact that the simulated polymer is relatively short. It is shown that the effective scaling exponent $\alpha$ is not a constant but varies with $F_a$ in the range of chain length under consideration. For comparison, the scaling law for $\phi = 0.0$ is also shown (dashed line) where the exponent is $\alpha = 1.66$ which is slightly larger than $2\nu$ and close to $1 + \nu$, where $\nu = 0.75$ is the Flory exponent in two dimension. As demonstrated in Fig. 9(a), the exponent $\alpha$ decreases with the increment of $F_a$, which is in accordance with the fact that a higher friction usually leads to a larger effective value of $\alpha$. We have also studied how the exponent $\alpha$ depends on the volume fraction $\phi$, as shown in Fig. 9(b). Generally, $\alpha$ decreases monotonically with $\phi$, and the decreasing tendency becomes stronger with increasing particle activity. Overall, larger $F_a$ and $\phi$ result in smaller $\alpha$ since active force balances the friction force or increases the driving force.

FIG. 8. Contour plot of the relative translocation time $\langle \tau \rangle_{\text{net}} = \langle \tau \rangle - \langle \tau \rangle_0$ in the $F_a-\phi$ plane.

FIG. 9. (a) Translocation time $\langle \tau \rangle$ as a function of the chain length $N$ and (b) the scaling exponent $\alpha$ as a function of the volume fraction $\phi$ for a different active force $F_a$. The black dashed line in (a) indicates the one without particles at the trans side.
IV. CONCLUSIONS

In conclusion, the dynamics of polymer translocation into an active environment has been investigated in a two-dimensional space. It has been found that active bath can result in two-fold effects on polymer translocation: one of which is that accumulation of active particles near the pore provides an extra “pushing” force and the other is that aggregation of active particles near the polymer generates an effective “pulling” force. Such effects lead to a non-monotonic mean translocation time (τ) varying with active force $F_a$ at a fixed volume fraction $\phi$, or with varying $\phi$ at a fixed particle activity. Consequently, the polymer translocation process may become slower in an active bath than that in a passive one, if the particle activity is small. The translocation process can be accelerated by the active bath only when the particle is large enough. Interestingly, an intermediate number of particles in the active bath may be the most favorable for the translocation due to the competition between activity-induced pulling and the crowding effect. Such a global picture is clearly demonstrated in the contour plot of $\langle \tau \rangle$ in the $F_a$-$\phi$ plane, which guides how one can control the translocation process via tuning the particle activity or volume fraction. We have also investigated how $\langle \tau \rangle$ depends on the chain length $N$, finding that good power-law scaling relations hold while the exponent decreases monotonically with $N$. Our results highlight the nontrivial role of active bath on polymer translocation which may shed some new lights on understanding such an important process in real biological systems.

ACKNOWLEDGMENTS

This work is supported by the National Basic Research Program of China (Grant No. 2013CB834606), by the National Science Foundation of China (Grant Nos. 21521001, 21473165, and 21403204), by the Ministry of Science and Technology of China (Grant No. 2016YFA0400904), and by the Fundamental Research Funds for the Central Universities (Grant Nos. WK206003018, 2030020028, and 2340000074).
