Translocation of a heterogeneous polymer

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We present results on the sequence dependence of translocation kinetics for a partially charged heteropolymer moving through a very thin pore using theoretical tools and Langevin dynamics simulation techniques. The chain is composed of two types of monomers of differing frictional interaction with the pore and charge. We present exact analytical expressions for passage probability, mean first passage time, and mean successful passage times for both reflecting/absorbing and absorbing/absorbing boundary conditions, showing rich and unexpected dependence of translocation behavior on charge fraction, distribution along the chain, and electric field configuration. We find excellent qualitative and good quantitative agreement between theoretical and simulation results. Surprisingly, there emerges a threshold charge fraction of a diblock copolymer beyond which the success rate of translocation is independent of charge fraction. Also, the mean successful translocation time of a diblock copolymer displays non-monotonic behavior with increasing length of the charged block; there is an optimum length of the charged block where the mean translocation rate is the slowest; and there can be a substantial range of higher charge fractions which make the translocation slower than even a minimally charged chain. Additionally, we find for a fixed total charge on the chain, finer distribution along the backbone significantly decreases mean translocation time.
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I. INTRODUCTION

The movement of a linear, flexible polymer through a small channel is a phenomenon of fundamental interest in biology as well as having significant potential for technological applications. Experimental work by Kasianowicz and co-workers¹ and Bezrukov and co-workers² demonstrated the feasibility of monitoring single molecule translocation with ionic currents. Subsequent work has refined this technique in the context of both biological^{3–9} and synthetic nanopores,^{10–16} revealing a rich dependence of translocation behavior on many factors such as the tertiary structures of the polymer,^{7,16–20} salt concentration,^{21,22} field strength,¹⁵ and pH.^{9,23} The experimental literature in this field continues to expand rapidly.²⁴

The complex phenomenology of polymer translocation has attracted significant theoretical work.^{24–41} By assuming that the ends of the chain are in equilibrium throughout the translocation process, the large number of degrees of freedom of the polymer can be captured by a one-dimensional free energy landscape, thereby mapping the process of translocation to a one-dimensional diffusion process along the length of the chain.^{25–27} The local nature of the interaction between the chain and the pore is usually accounted for by a kinetic parameter^{27,28} in order to correctly capture experimentally observed scaling behavior. The basic assumption in this free energy landscape picture is that the translocation time is long enough to allow equilibration of chain conformations at all

stages of the translocation process. If this condition is not satisfied, nonlinear effects on the translocation kinetics set in Refs. 29 and 30.

In efforts to address nonuniversal features of polymer translocation, subsequent computational and theoretical work has sought to capture the effects of details of the pore geometry,^{31,32} interactions between the chain and pore/membrane,^{31,33,34} and heterogeneities along the chain.^{35–37} Such heterogeneous systems have been studied using a variety of computational techniques, notably via 2D Langevin dynamics simulation by Luo and co-workers³⁸ and via Monte Carlo and numerical methods by Gauthier and Slater^{39–41} and Slutsky and co-workers.³³ Interest in heterogeneous chains has been intensified due to interest in methods to obtain additional control over the process of translocation^{42–45} by a variety of means. One possibility of particular interest in this paper is to manipulate the kinetics of translocation of a charged molecule via the addition of an uncharged tag^{42,46} or a tag with differing chemical potential driving force across the pore.^{47,48} The resulting system is then modeled as the translocation of a partially charged diblock copolymer across the entropic barrier of the pore. Here, we use a Langevin dynamics simulation setup up as in Fig. 1(a) and exact analytic methods based on the theory by one of the present authors,^{27,49} pictured in Fig. 1(b), to study the kinetics and success rates of translocation for a heterogeneously charged polymer. We use these simulation and theoretical models to explore the kinetic behavior of the sequences shown in Fig. 1(c).

Previous theoretical calculations^{35,49} of the translocation kinetics for a homopolymer have predicted qualitatively similar behavior whether, once having overcome the

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FIG. 1. (a) Simulation setup with m th monomer in the pore. (b) Theoretical model of translocation through infinitely thin pore. (c) Distributions of charge. All chains have $f = 45$ charged monomers (solid lines) and 15 uncharged monomers (dotted lines).

nucleation barrier, the chain is allowed to retract unsuccessfully back to the *cis* chamber or whether such a motion is forbidden. Theoretical studies of heterogeneous systems by Muthukumar³¹ and Mohan and co-workers³⁶ have made the assumption that the chain is forbidden from retracting back into the *cis* chamber. We find that for non-uniformly charged chains such considerations lead to significantly different qualitative predictions of the translocation behavior as a function of the total charge on the chain. As discussed below, in the theory there are two conditions corresponding to absorbing/absorbing boundary conditions and reflecting/absorbing boundary conditions on the chain. The words “reflecting” and “absorbing” refer to the behavior of the monomers on either end of the chain. If the end monomer is able to pass through the pore it is “absorbed” by the pore; if it cannot pass through the pore but is pushed back into the chamber where it came from, it is “reflected” by the pore. Absorbing/absorbing boundary conditions are physically natural in both experiment and simulation. A reflecting/absorbing boundary condition often allows for computational convenience in theoretical calculation as well as allowing for more efficient simulation. The effects of differing boundary conditions will be studied primarily for a diblock copolymer consisting of one block of charged monomers and a second block of uncharged monomers.

In typical experiments¹ an external voltage is imposed across a cell volume containing a membrane with a pore allowing for translocation in it. The great part of the voltage drop across the volume occurs across the pore itself. How-

ever, there remains a small voltage gradient outside the pore.⁵⁰ When a uniformly charged polymer translocates across the pore, the process will be dominated by the driving force on the monomers inside the pore and any potential gradient outside the pore will have insignificant effects. However, if the chain is not uniformly charged and the monomers inside the pore are uncharged, then the strong field inside the pore is not felt and the translocation will be affected by the small extended field outside the pore. We simulate translocation with an identically zero field outside the pore and with a small outside field to explore such effects.

Finally the role of charge distribution along the chain backbone is studied by fixing the total charge and varying the placement of charged monomers according to Fig. 1(c). The sequences have been ordered according to the total number of blocked monomers along the backbone. Thus, sequence 1 is a diblock with 2 blocks of monomers, one charged block and one uncharged block. Similarly, sequence 11 is a multi-block with seven blocks of monomers, four charged blocks and three uncharged blocks.

We have organized the remainder of the paper as follows: In Sec. II we define our simulational and theoretical models, giving relevant parameter values and assumptions. In Sec. III we give results for these models, with comparison between theory and simulation. In light of the issues outlined above, we organize our results according to two sets of boundary conditions. Thus, we first discuss translocation for systems experiencing with a reflecting/absorbing boundary condition. Within this context we explore the effect of charge distribution along the backbone and the presence of an extended electric field outside the pore. We then impose the more physically natural absorbing/absorbing boundary conditions and focus on a simple diblock copolymer with one leading block of charged monomers and a second block of uncharged monomers. We calculate the probability of successful translocation, the average time for successful translocation, and the average dwell time of such a chain in the pore as functions of field strength and length of the charged block. Unexpectedly, we find that there is an optimum length of the charged block where the mean translocation time will be longest. Finally, we close with brief concluding remarks in Sec. IV.

II. MODEL

A. Simulation setup

We simulate a polymer chain moving through a narrow pore using a Langevin dynamics simulation with implicit solvent, implemented through the LAMMPS package.⁵¹ As shown in Fig. 1(a), the chain is composed of $N = 60$ spherical beads of diameter $l_0 = 3.4$ Å and mass $m = 96$ Da connected by bonds of average length l_0 . The beads in the chain carry either a negative unit charge $-e$ or are neutral, shown in Fig. 1(a) by dark and light beads, respectively. The membrane separating *cis* and *trans* compartments is composed of uncharged beads of diameter 3.0 Å fixed in space, shown by the hatch marked beads in the figure. The cylindrical pore is constructed from uncharged beads of diameter 0.75 Å,

represented by open beads in the figure. The length of the pore is 3.0 Å, the same as the thickness of the membrane and has a diameter of 6 Å, prohibiting hairpins so that the chain must translocate in single file.

The bonds between beads in the chain obey a harmonic potential of the form $U_{bond} = k(l - l_0)^2$, with l the instantaneous length of the bond and $k = 171$ kcal/(mol Å²) a spring constant chosen such that U_{bond} will be large relative to the thermal energy in the system, $k_B T$.⁵⁰ Here, k_B is the Boltzmann constant and T is the absolute temperature. We fix the average temperature in the simulation to be 300 K, such that $k_B T \approx 0.59$ kcal/mol. The strength of the harmonic potential is large enough that the instantaneous bond length l varies from l_0 by less than 5% throughout the simulation.

All pairs of beads in the simulation experience a Lennard-Jones (LJ) potential between them given by

$$U_{LJ}(r_{ij}) = \begin{cases} 4\epsilon_{LJ} \left[\left(\frac{\sigma}{r_{ij}} \right)^{12} - \left(\frac{\sigma}{r_{ij}} \right)^6 \right] + \epsilon_{LJ} & \text{for } r_{ij} \leq 1.12\sigma, \\ 0 & \text{for } r_{ij} > 1.12\sigma, \end{cases} \quad (1)$$

where r_{ij} is the distance between the centers of the i th and j th beads and σ is the diameter of a bead, i.e., the distance at which two beads come in contact. Thus, for beads in the membrane, $\sigma_{mm} = 3$ Å, while for beads in the chain, $\sigma_{pp} = 3.4$ Å. The depth of the potential well is $\epsilon_{LJ} = 0.1$ kcal/mol, which is $0.167 k_B T$ when $T = 300$ K.

Charged beads interact with an additional potential between themselves given by the Debye-Hückel screened Coulombic potential

$$U_{DH}(r_{ij}) = \frac{e^2}{4\pi\epsilon_0\epsilon r_{ij}} e^{-\kappa r_{ij}}. \quad (2)$$

Here, e is the unit charge, ϵ is the dielectric constant of the medium, taken to be 80 in all simulations (corresponding to water), and κ^{-1} is the Debye length, giving the range of electrostatic interactions. In principle, the charge of each bead is only a fraction of e , due to counterion condensation. The Debye length of a solution is given by $\sqrt{\epsilon\epsilon_0 k_B T / e^2 \sum_i n_i q_i}$, where q_i and n_i are the charge and concentration of the i th dissociated ion species. For typical translocation experimental systems at 1 M KCl, $\kappa^{-1} = 0.3$ nm, which is the value we have employed in our simulations.

Finally, we impose an external potential, $V(\mathbf{r})$, which leads to a potential for charged beads of $U_V(\mathbf{r}) = -eV(\mathbf{r})$. The externally imposed potential is spatially dependent, as will be emphasized below.

Using these four potentials, the equation of motion for the i th bead is⁵²

$$m_i \frac{d^2 \mathbf{r}_i}{dt^2} = -\zeta_i \mathbf{v}_i - \nabla_{\mathbf{r}_i} (U_{bond,i} + U_{LJ,i} + U_{DH,i} + U_{V,i}) + \mathbf{F}_i, \quad (3)$$

where t is the time, $\mathbf{r}_i$ is the position vector of the i th monomer, ζ_i is the friction coefficient of the i th monomer moving through the implicit solvent, and $\mathbf{F}_i$ is a random force acting on the i th bead. The random force has a white

noise spectrum, with the fluctuation-dissipation theorem dictating a relationship with the friction coefficient given by $\langle \mathbf{F}_i(t) \cdot \mathbf{F}_i(t') \rangle = 6k_B T \zeta_i \delta(t - t')$.

The equation of motion, Eq. (3), is integrated using a Verlet algorithm⁵³ implemented through LAMMPS. In performing the simulations, all physical parameters are specified in dimensionless LJ units of length, mass, time, energy, charge, and temperature. The LJ unit of length is specified so that the diameter of a membrane bead is $\sigma_{mm} = 1$ LJ unit. In these units the Debye length is 1 LJ unit, the diameter of a bead in the chain and the average length of a bond vector is 1.13 LJ units, the diameter of the beads comprising the cylindrical pore is 0.25 LJ units, and the diameter of the pore itself is 2 LJ units. The LJ unit of mass is set to be the mass of the bead, m . The unit of energy is given by the depth of the Lennard-Jones potential well, so that $\epsilon_{LJ} = 1$ LJ unit. These units of length and mass determine the LJ unit of time to be $\sqrt{\sigma_{mm}^2 m / \epsilon_{LJ}}$, the LJ unit of charge to be $\sqrt{4\pi\epsilon_0\epsilon_{LJ}\sigma_{mm}}$, and the LJ unit of temperature to be ϵ_{LJ}/k_B . In these units the temperature in the simulation is 6 LJ units and the friction coefficient $\zeta_i = 0.1$ LJ units. The ratio of the bead mass to the friction coefficient is the damping constant used in LAMMPS and is 10 LJ time units. One simulation time step is equal to 0.0002 LJ time units. The position of all beads in the system is recorded every 1000 time steps throughout the process of translocation.

The simulation takes place in a box with periodic boundary conditions of size $L_x \times L_y \times L_z$, with $L_x = 120$ LJ units, $L_y = 36$ LJ units, and $L_z = 36$ LJ units. The pore is oriented along the x axis such that the membrane lies in the y - z plane. To initialize the system, an initial monomer (defined as the $m_0 + 1$ monomer here and below, with m_0 monomers in the *trans*) is placed in the center of the pore and the total energy of the system is monitored. When the energy converges to a stable value with minor fluctuations of less than 10%, the system is taken to be equilibrated and the initial monomer is allowed to move freely. It is at the time step when the initial monomer is allowed to move that translocation is said to begin. The translocation is taken to end when the center of mass of either end monomer exits the volume of the pore.

In typical translocation studies involving uniformly charged polymers, the detailed specification of the externally imposed potential outside the pore has not been found to play a major role in the kinetics of translocation (although the polymer capture is dominated by the electrophoretic drift outside the pore). However, we have found that for non-uniformly charged polymers the exact specification of the imposed potential (or, equivalently, electric field) outside the pore can have a significant influence on the translocation kinetics. In order to explore these effects we define two field configurations in our simulations. In the first field configuration, E_1 , the externally imposed field is identically zero everywhere outside the pore (i.e., $U_V(\mathbf{r})$ is constant). This field configuration has been chosen to match with assumptions necessary to do theoretical calculations, described below. When a reflecting boundary is imposed on the first monomer of the chain, we set $E_1 = 5.88$ LJ units, which is a driving potential of approximately $32.7 k_B T / \sigma_{mm}$. Such a high value of the field is chosen in the interest of obtaining

reliable statistics with reasonable computational time. In experiments, however, the external voltage is applied across an experimental cell containing some volume of free solution as well as the membrane and pore. Thus, while the greater part of the voltage drop occurs across the pore, there is always a small, non-zero voltage drop outside the pore.⁵⁴ We model this second field configuration by imposing a small extended field outside the pore, in addition to the potential gradient inside the pore. This configuration will be referred to as E_2 . The magnitude of this external field is 0.005 LJ units, which is a driving potential of approximately $0.027k_B T/\sigma_{mm}$. This choice is based on Poisson-Nernst-Planck calculations.⁵⁴ Although there is generally an azimuthal angle dependence of the electric field, we consider the field only along the pore axis. In the remainder of the paper, when absorbing boundary conditions are used for both chain ends the magnitude of the potential drop will be given explicitly. With these boundary conditions the field outside the pore is always identically zero.

The correspondence between the simulation units and the experimental quantities is as follows. One LJ unit of length is 0.3 nm so that the diameter of the beads of the chain (1.13 LJ units) is 0.34 nm. Taking the LJ unit of mass as 96 Da, the LJ unit of time is $\Delta t = \sqrt{\sigma^2 m / \epsilon_{LJ}} = 4.55$ ps. Since we use $0.0002\Delta t$ as one simulation time step, each time step corresponds to roughly 1 fs. One $k_B T$ corresponds to 25.9 mV at room temperatures. As an example, $32.7k_B T$ corresponds to 847 mV.

In order to explore the effect of boundary conditions on the kinetics of translocation, we have imposed the two boundary conditions as follows. The reflecting boundary condition is enforced in the simulation by fixing a phantom bead in the mouth of the pore. This bead interacts only with the end bead of the chain which is in the *trans* compartment at the start of translocation via a Lennard-Jones potential, identical to that given in Eq. (1). No other beads on the chain interact with the phantom bead, and in this way the end monomer which began in the *trans* compartment is forbidden from retracting into the *cis* chamber. When reflecting/absorbing boundary conditions are discussed below, the initial monomer is always simply the first monomer of the chain. Absorbing/absorbing boundary conditions are physically natural and require no modification to the setup shown in Fig. 1(a). When absorbing/absorbing boundary conditions are discussed m_0 will be explicitly given.

B. Theoretical model

1. Free energy landscape

Theoretically, we consider a long heterogeneous flexible polymer of length N moving through an infinitely thin pore as shown in Fig. 1(b). The polymer is driven through the pore by an electrochemical gradient, which the m th monomer experiences as $\mu_m = \mu'_{m,trans} - \mu'_{m,cis}$. Uncharged monomers will have $\mu_m = 0$. Borrowing standard results from the theory of random walks,⁵⁵ a chain of n segments in a half space will have $Z_n = e^{-\mu n} n^{\gamma-1}$ possible configurations, where γ is a critical exponent describing the quality of the solvent. For theta solvents, $\gamma = 0.5$; for electrolyte solutions $\gamma \approx 0.69$ at high salt and $\gamma \approx 1$ at low salt. We may use this result

to write the free energy of one section of the chain in one compartment as

$$\frac{F_n}{k_B T} = (1 - \gamma) \ln n + \sum_i \mu'_i, \quad (4)$$

where μ'_i is the chemical potential of the monomer in the solution of one compartment. Considering Fig. 1(b), it is clear that when m monomers are in the *trans* chamber the free energy of the entire chain is given by the sum of the two half chains on either side of the pore²⁷

$$F_m = (1 - \gamma_{trans}) \ln m + (1 - \gamma_{cis}) \ln(N - m) + \sum_i \mu_i. \quad (5)$$

Free energy and chemical potential are in units of $k_B T$. Here μ_i has the meaning of a chemical potential *difference* for the i th monomer moving from the *cis* to the *trans* chamber as defined above. The logarithmic terms in Eq. (5) give rise to an entropic barrier for translocation such that a critical number of monomers, m^* , must nucleate into the *trans* chamber before translocation becomes a downhill process. The number of monomers corresponding to the nucleation barrier is given by $\partial_m F_m = 0$. Even for modest driving potentials of $1k_B T$ (~ 25 mV), this gives m^* on the order of a single monomer. Therefore, the kinetics in overcoming this barrier are not significantly affected by the distribution of charges along the chain, provided that the initial monomer into the pore is charged. We refer the reader to previous work⁴⁹ regarding the homopolymer problem for details.

Using the free energy landscape of Eq. (5) we make a familiar mapping of the translocation process onto a one-dimensional random walk problem,²⁷ controlled by the Fokker-Planck equation,

$$\frac{\partial}{\partial t} W_m(t) = \frac{\partial}{\partial m} \left[\frac{k_m}{k_B T} \frac{\partial F_m}{\partial m} W_m(t) + \frac{\partial}{\partial m} k_m W_m(t) \right]. \quad (6)$$

In making this mapping, we assume that the translocation kinetics are slow enough that the chain is in equilibrium throughout the process. Here, $W_m(t)$ is the probability of m monomers being in the *trans* chamber at time t , related to a general transition probability (which satisfies a similar Fokker-Planck equation) by $W_m(t) \equiv P(m, t; m_0, 0)$ through the initial condition $W_m(t_0) = P(m, t_0; m_0, t_0) = \delta(m - m_0)$. This relation shows the dependence of $W_m(t)$ on the initial monomer, m_0 . k_m is a frictional coefficient encapsulating the local interaction of the m th monomer and the pore due to, e.g., hydrodynamics or details of charge interactions. In making comparisons with simulation and experimental results, it is important to recognize that k_m is a parameter which must be fitted to the data within this model.

We wish to draw attention to the fact that the driving electrochemical potential drop μ_i for a given monomer is modeled to occur only across the pore. The free energy landscape is a function only of the number of monomers in the *trans* chamber, and assumes that anchored chain on either side of the membrane freely assumes all available conformations. This picture is closely analogous to the field configuration E_1 discussed above in the simulations. The equilibrium assumption

will be a good one so long as the relaxation time for the chain tails in the *cis* and *trans* chamber are shorter than the typical dwell time for a single monomer in the pore. This assumption is valid for the lengths of the chain in the present simulations.⁹

A primary quantity of interest is the mean dwell time given by

$$\tau(m_0) = \int_0^N dm \int_0^\infty dt t \dot{W}_m(t). \quad (7)$$

It can be shown to obey a differential equation (related to the Backward Fokker-Planck equation⁵⁶)

$$\frac{k_{m_0}}{k_B T} \frac{\partial F_{m_0}}{\partial m_0} \frac{\partial}{\partial m_0} \tau(m_0) + k_{m_0} \frac{\partial^2}{\partial m^2} \tau(m_0) = -1. \quad (8)$$

Imposing appropriate boundary conditions Eqs. (6) and (8) can be solved for various quantities of physical interest. Here, we simply quote results and refer the reader to the Appendix B as well as references by Muthukumar²⁴ and Gardiner⁵⁶ for details of the solutions.

2. Reflecting chain

A polymer which is physically prohibited from exiting the pore into the *cis* chamber is described using a reflecting boundary condition at the first monomer through the pore and an absorbing boundary condition at the N th monomer to solve Eq. (6). This type of process can be created artificially in experiments,^{16,20,57} as under these conditions all translocation attempts are ultimately successful. The primary quantity of interest is the mean first passage time, which is identical to the dwell time of the polymer in the pore. From Eq. (8) it can be shown²⁴ for reflecting-absorbing boundaries that

$$\tau(m_0) = \int_{m_0}^N dy \frac{1}{\psi(y)} \int_0^y dz \frac{\psi(z)}{k_z}, \quad (9)$$

with

$$\psi(y) = \exp \left[-\frac{1}{k_B T} \int_0^y dx \left. \frac{\partial F_m}{\partial m} \right|_x \right]. \quad (10)$$

We assume that the polymer has already overcome the nucleation barrier discussed above and begins with m_0 monomers threaded through the pore. In the case of a reflecting boundary condition all translocation attempts are successful and m_0 may be as small as we wish. A system of particular interest experimentally⁴² is that of a charged block affixed to an uncharged “drag tag” used to manipulate the kinetics of the composite molecule. Taking a diblock polymer with charged block 1 of length f which experiences a chemical potential difference μ_1 across the pore and an uncharged block 2 of length $N - f$ we assign frictional coefficients k_1 and k_2 , respectively, take $m_0 \rightarrow 0$, and obtain

$$\tau = \frac{1}{\mu_1 k_1} \left[f - \frac{1}{\mu_1} (1 - e^{-\mu_1 f}) \right] + \frac{1}{\mu_1 k_1} (N - f) (1 - e^{-\mu_1 f}) + \frac{1}{2k_2} (N - f)^2. \quad (11)$$

This has an intuitive physical interpretation: the first and third terms represent the mean first passage times for the first, charged, block and for the second, uncharged, block to pass

through the pore, respectively. In the limit of a completely charged chain, $f \rightarrow N$, we recover drift dominated behavior such that $\tau \sim N$ while in the limit of no driving force (either $f \rightarrow 0$ or $\mu \rightarrow 0$), we recover a diffusion dominated process, where $\tau \sim N^2$. The total passage time is the first moment of the convolution of the underlying distribution of times to translocate over each block. The second term in Eq. (11) is a cross-term arising from this convolution of underlying distributions. It is insufficient to simply add mean first passage times of different stages of the translocation process in order to arrive at a time for the entire process.

Using Eqs. (9) and (10) exact expressions for the mean first passage time have been computed for arbitrary distributions of charge along the chain. These full expressions are given in Appendix A and are used to compute expected mean first passage times for the sequences shown in Fig. 1(c).

3. Absorbing chain

If the chain is allowed to escape from the pore in either direction then we must impose absorbing-absorbing boundary conditions on Eqs. (6) and (8). The probability that the chain will “successfully” translocate into the *trans* chamber, given that m_0 monomers are initially nucleated through the pore is²⁴

$$\pi_+(m_0) = \frac{\Psi(0, m_0)}{\Psi(0, N)}, \quad (12)$$

with

$$\Psi(x, y) = \int_x^y dz \frac{1}{\psi(z)}, \quad (13)$$

where $\psi(z)$ captures information about the free energy landscape and is given by Eq. (10). For a diblock copolymer with one block of length f charged and the remaining $N - f$ monomers uncharged, we obtain

$$\pi_+(m_0) = \begin{cases} \frac{(1 - e^{-\mu_1 m_0})}{(1 - e^{-\mu_1 f}) + \frac{\mu_1}{\mu_2} e^{-\mu_1 f} (1 - e^{-\mu_2 (N-f)})} & f > m_0, \\ [1.2em] \frac{(1 - e^{-\mu_1 f}) + \frac{\mu_1}{\mu_2} e^{-\mu_1 f} (1 - e^{-\mu_2 (m_0 - f)})}{(1 - e^{-\mu_1 f}) + \frac{\mu_1}{\mu_2} e^{-\mu_1 f} (1 - e^{-\mu_2 (N-f)})} & f < m_0. \end{cases} \quad (14)$$

The mean time taken for the chain to complete a successful translocation, where events in which the chain exits back into the *cis* chamber are not counted, is given by²⁴

$$\tau_+(m_0) = \frac{\Psi(0, m_0) \phi_+(m_0, N) - \phi_+(0, m_0) \Psi(m_0, N)}{\Psi(0, m_0) \Psi(0, N)}, \quad (15)$$

with $\Psi(x, y)$ given in Eq. (13) and $\phi_+(x, y)$ given by

$$\phi_+(x, y) = \int_x^y dp \frac{1}{\psi(p)} \int_0^p dq \frac{\psi(q) \Psi(0, q)}{k_q}. \quad (16)$$

The expressions for $\Psi(x, y)$ and $\phi_+(x, y)$ yield a final expression for $\tau_+(m_0, f)$, which is omitted here as its exact form is unwieldy. The relevant expressions are included in Appendix A for completeness.

Also of interest is the mean first passage time, defined as the mean time for the chain to exit the pore in either direction,

which is given by²⁴

$$\tau(m_0) = \frac{\int_{m_0}^N dy \frac{1}{\psi(y)} \int_0^{m_0} dy' \frac{H(y')}{\psi(y')} - \int_0^{m_0} dy \frac{1}{\psi(y)} \int_{m_0}^N dy' \frac{H(y')}{\psi(y')}}{\int_0^N dy \frac{1}{\psi(y)}}, \quad (17)$$

where $\psi(y)$ is given in Eq. (10) and the function $H(x)$ is given by

$$H(x) = - \int_0^x dy \frac{\psi(y)}{k_y}. \quad (18)$$

We have again computed exact analytical expressions and they are included in Appendix A.

III. RESULTS AND DISCUSSION

A. Reflecting/absorbing boundary conditions

1. Field across the pore

We show in Fig. 2 histograms for a simple diblock copolymer using field configuration E_1 . The chain is composed of one block of f charged monomers which passes through the pore first and a second block of $N - f$ uncharged monomers, with $N = 60$ the total length of the chain. We assume that the friction coefficient is constant within each block

and assign the values k_1 to monomers in the charged block and k_2 to those in the uncharged block. By fitting the first moment of the distribution of passage times for a completely charged chain shown in Fig. 2(a) to the theoretical expression given in Eq. (B14) we obtain in reduced LJ units $k_1 = 0.023$. Similarly we find $k_2 = 0.043$ using the distribution shown in Fig. 2(d) for the completely uncharged chain. We note that translocation of a completely uncharged chain is meaningful only because of the reflecting boundary condition, which forces the chain to translocate through the entire pore. The translocation is simply a diffusive random walk near a wall in this case. Using the values of k_1 and k_2 obtained through this procedure, theoretical expectations for the distribution of translocation times for different lengths of the charged block have been computed and are shown overlaid on the simulation data in Fig. 2.

From distributions like those shown in Fig. 2 we extract the first moment, which is the mean translocation time. These mean times are plotted in Fig. 3 as a function of the length of the charged block and compared to theoretically computed values from Eq. (11). By the definition of k_1 and k_2 discussed above the times for the homopolymer cases at $f = 0$ and $f = 60$ are identically equal between theory and simulations. The theoretical values for intermediate values of f involve no

FIG. 2. Histograms of normalized number of translocation events with passage time τ for diblock copolymers with various lengths of the charged block f , compared against theoretical prediction. Total length of the chain, $N = 60$. (a) Homopolymer, $f = 60$. (b) Diblock copolymer, $f = 40$. (c) Diblock copolymer, $f = 20$. (d) Homopolymer, $f = 0$.

FIG. 3. Mean first passage time of a diblock copolymer for various lengths of the charged block ($N = 60$).

additional fitting. We find good agreement between simulation and theoretical expectations. Our results are in keeping with the physically intuitive expectation that an increase in the amount of charge along the backbone decreases translocation time monotonically.

We find that charge distribution along the chain can have a large effect on the mean translocation time. In order to explore the effect of different distributions of charge along the backbone we fix the total number of charged monomers to be $f = 45$ for a chain of total length $N = 60$. These charges are distributed along the backbone according to the schematic shown in Fig. 1(c). The mean translocation times for these sequences are shown in Fig. 4 in comparison with theoretical predictions from Eq. (A1). The squares represent the average translocation times for the end A going first to the *trans* side; filled circles represent the end B going first. The star symbol repre-

FIG. 4. Mean first passage times for a fixed total charge $f = 45$ distributed according to sequences shown in Fig. 1(c). Open symbols are theoretical predictions, closed symbols are simulation results. Squares represent translocation from end A to end B, circles from end B to end A, stars are the average of the simulated times.

sents the average between these two data. The error bars are within the sizes of the symbols in the plot. The open squares (end A going first) and open circles (end B going first) are theoretical predictions. The sequence labels along the x axis correspond to labels in Fig. 1(c) and are grouped first according to the total number of blocks of similar monomers in the sequence and secondarily arranged according to the number of uncharged blocks in the sequence. Thus, sequence 1 has two total blocks, one charged and one uncharged. Sequences 2, 3, 4, 5, and 6 have three blocks of monomers. Sequences 7 and 8 have four blocks while sequences 9 and 10 have five blocks and sequence 11 has seven blocks. Within these groupings, we have further ordered the individual sequences according to the number of uncharged blocks. As an example, within the grouping of sequences comprised of three total blocks, sequences 2 and 3 have one uncharged block while sequences 4, 5, and 6 have two uncharged blocks.

This ordering makes evident that a finer distribution of charge leads to faster translocation, in good agreement with theory. This effect can be quite significant, as a comparison of the longest average translocation time for sequence 1 to the shortest for sequence 11 shows an almost 80% reduction due to a finer distribution of charge. Some sequences additionally show a significant effect from the direction of translocation, as in the case of sequences 1, 4, and 5. This asymmetry appears to be correlated to the chain having uncharged endcaps. Nonetheless, the effect is muted for sequences 6 and 10. This effect is not predicted by the theory, and its origin is unclear at present. However, we note that the translocation of a chain with an uncharged initial monomer in the pore relies on an artificially imposed reflecting boundary condition, and will be difficult to realize experimentally. We have included these configurations to make the overall trend of faster translocation with finer charge distributions evident. When only experimentally relevant sequences are considered the agreement between theory and simulation is excellent.

This trend can be intuitively understood by considering that a block of monomers with no charge of length n will have a mean translocation time proportional to n^2 , as alluded to briefly in the discussion of Eq. (11). The total number of uncharged monomers for all sequences in Fig. 1(c) is 15. Thus for the diblock, sequence 1, the contribution to the mean translocation time of the uncharged block will be proportional to $15^2 = 225$. In contrast, sequence 11 presents three blocks of five uncharged monomers, which contribute to the mean translocation time proportional to $5^2 + 5^2 + 5^2 = 75$. Clearly, the cross-term of Eq. (11) (or the equivalent terms in Eq. (A1)) complicates this picture. However, this simple intuitive argument captures the general trend.

2. Extended field

As alluded to in the Introduction, in typical experimental setups it is impossible to strictly limit the imposed field to the volume of the pore itself as we have done above. There is inevitably some small field outside the pore in the *cis* and *trans* chambers. As such, we have maintained the strong field

FIG. 5. Comparison of simulated translocation times in field configurations E_1 and E_2 . (a) Mean translocation time as a function of f . Red line is theory from Eq. (A1), black circles are with field configuration E_1 (same as in Fig. 3), and blue triangles with field configuration E_2 . (b) Mean translocation times for a fixed total charge $f = 45$ distributed according to the sequences shown in Fig. 1(c). Black diamonds are with field configuration E_1 , red triangles with field configuration E_2 .

inside the pore and imposed a small extended field of constant strength outside the pore in both the *cis* and *trans* chambers. We refer to this configuration of the fields as E_2 . We show the effect of field configuration E_2 in Fig. 5. Comparison is made with analogous results from Figs. 3 and 4.

From Fig. 5(a) it is evident that the effects of E_2 are most pronounced for chains with lower fractions of charge. At present a good theoretical understanding of this effect is lacking. The theory presented in Sec. II captures only the potential drop across the pore and explicitly excludes any free energy drop due to an uncharged monomer moving across the pore, so that the motion of uncharged monomers is purely diffusive. In simulations with field configuration E_2 , the situation is different. Although there is no explicit driving potential acting on an uncharged monomer passing through the pore, when there is an electric field present outside the pore, all charged monomers in the chain experience a potential gradient, although they may be far from the pore. Thus, although an uncharged monomer experiences no driving force from the field itself, the chain will nonetheless experience a free energy gradient pushing towards the *trans* chamber. Due to the connectivity of the chain, this results in a small effective driving potential across the pore even for uncharged monomers. When the chain is completely uncharged, this effective potential disappears as does the discrepancy between the two field configurations.

In Fig. 5(b), we have plotted average translocation times for the various sequences of Fig. 1(c) in field configurations E_1 and E_2 . We have averaged over translocation events from both chain end A and chain end B. We find that the effect of the extended field is significantly smaller for finer distributions of charge. We note that in contrast to results for homopolymer translocation, details of the field far from the pore appear to have an important effect on the kinetics of translocation.

B. Absorbing/absorbing boundary conditions

In order to make contact with realistic experimental and biological systems we must allow the chain to escape from the pore in either direction, whether back into the *cis* chamber or forward into the *trans* chamber. This physical situation is described theoretically by imposing absorbing/absorbing boundary conditions on Eqs. (6) and (8). Here, it is important to note that the mean first passage time is the mean time taken for the chain to exit the pore *in either direction* and is more accurately thought of as a “dwell” time for the chain in the pore. A calculation of the mean first passage time will therefore include both “successful” and “unsuccessful” events (where unsuccessful means exit into the *cis* chamber and successful means exit into the *trans* chamber). We will therefore refer to this time, τ , as the mean dwell time. Further, because the chain can exit the pore in either direction, we wish to know the probability of “successful” translocation, which we define as the quantity π_+ . Finally, we wish to know the mean first passage time in the event of a successful translocation. We define this quantity to be τ_+ , which is the average dwell time for the chain in the pore given that the chain exits into the *trans* chamber. We will refer to this time as the successful translocation time. In this section we will limit ourselves to the case of a simple diblock copolymer, composed of f charged monomers, which thread through the pore first, followed by $N - f$ uncharged monomers. We assume that the chain has already nucleated m_0 monomers into the *trans* chamber.

1. Probability of successful translocation

Given this initial threading, we have computed the probability of successful translocation, using Eq. (12). In Fig. 6(a), we show the probability of successful translocation for a diblock copolymer against the length of the charged fraction of

FIG. 6. Probability of successful translocation for a diblock with various lengths of the charged fraction. (a) Probability of successful translocation for various initially nucleated lengths. $\mu = 0.5k_B T$. (b) Probability of successful translocation for various driving potentials across the pore. Connected dots are simulation data, solid lines are theoretical curves. $m_0/N = 0.05$.

the chain for various values of the initially nucleated length m_0 . We find that the probability of successful translocation exhibits a distinct shoulder when plotted against the length of the charged block, shown in Fig. 6. As exemplified for a driving force of $\mu = 0.7k_B T$, the probability of successful translocation of a chain which is $\sim 25\%$ charged is nearly equal to that of a fully charged homopolymer. Increasing the length of the charged block beyond $\sim 25\%$ of the chain length does not significantly increase the probability of successful translocation. Further, the value of f at which the probability saturates is shown in Fig. 6(a) to be independent of the details of the initial nucleation into the *trans* chamber as the location of the shoulder in the probability remains unchanged with changing values of m_0/N . As expected, the probability of successful translocation increases along with the initially nucleated length, shown by the upward shift of the curves in Fig. 6(a) with increasing m_0/N . The more monomers that are initially placed in the *trans* chamber the higher is the probability of successful translocation for each value of f/N . The increase of π_+ with m_0 arises from the numerator of Eq. (14). For $f/N > 0.25$, the denominator of Eq. (14) (for $f > m_0$) is essentially unity, resulting in the saturation values shown in Fig. 6.

We have also marked a point on each curve in Fig. 6(a) at a value of f we define to be f^* . As will be discussed below, this corresponds to a maximum in the average successful translocation time. For the present discussion we note that f^* corresponds closely with the value of f at which additional charge along the backbone has a decreasing effect on the probability of successful translocation.

In Fig. 6(b), we have plotted the probability of successful translocation against the charged fraction of the chain for various values of the driving potential. Clearly, the saturation value of f does depend on the strength of the driving potential. At a driving potential of $2k_B T$, the probability saturates at only 10% of the chain being charged. At room temperature this corresponds to a driving voltage of 50 mV, the lower range of experimental voltages reported in the literature. Thus, we ex-

pect this saturation in the probability of successful translocation (and the corresponding maximum in successful translocation time, discussed below) to be evident at low experimental voltages and short lengths of the charged block relative to the overall length of the chain. In the limit of an infinite driving force we recover the reflecting case, where $\pi_+ = 1$ identically for all lengths of the charged block.

2. Average successful translocation time

Given that the chain successfully translocates through the pore, the average translocation time is plotted in Fig. 7(a). Theoretical curves are plotted from explicit analytical formulas given in Appendix A and data from simulations are shown for comparison. We find good agreement in spite of the simplifying assumptions made in the theoretical model. We note that no additional fitting has been done between simulation and theory, with values of k_1 and k_2 in the theoretical formula taken from those computed in homopolymer simulations with reflecting boundary conditions, as described above. The black dashed line is to guide the eye and represents the mean successful translocation time for an uncharged chain. For absorbing/absorbing boundary conditions, this quantity is a purely theoretical construct and is not experimentally accessible. In a more practical sense, it may be thought of as the mean time for a minimally charged chain. As the simulation data show, even a chain with 3% of the backbone length being charged will experience successful translocation events. We have included this black dashed line to show that the mean translocation time for a diblock is larger than that of a minimally charged (or, theoretically, an uncharged) chain up to a significant fraction of the chain being charged. As an example, for a driving potential of $2k_B T$ (≈ 50 mV), the chain on average will be slower than a minimally charged chain for fractions of the charged block up to nearly 50% of the chain.

We find a maximum in the successful translocation time with increasing length of the charged block length, f , as evident from Fig. 7(a). We define the location of this maximum

FIG. 7. Mean successful translocation time $m_0/N = 0.05$. (a) τ_+ vs f for various values of the driving potential. Connected dots are simulation data, solid lines are theoretical curves. (b) f^*/N vs driving potential. (c) τ_+ vs driving potential μ for various lengths of the charged block. $f/N = 0.05$ (blue), 0.1 (green), 0.25 (red), 0.5 (aqua), 1 (purple).

to be f^* . The existence of a maximum implies the counterintuitive fact that at small lengths of the charged fraction of the chain, $f < f^*$, increasing the amount of charge along the backbone (and therefore increasing the fraction of the chain that is subjected to the driving force across the pore) leads to an *increase* in the average time taken for a successful translocation. The location of this maximum is controlled by the strength of the driving potential across the pore, shown in Fig. 7(b). f^* is inversely related to the driving potential. At very large values of the driving potential, f^* approaches 0. In such a case, essentially all translocation events will be successful and we recover a reflecting-like boundary on the charged end of the chain as the energy barrier required to retract even one monomer unsuccessfully into the *cis* chamber becomes very large. In the limit of an infinite μ , the mean successful translocation time becomes identical to the mean dwell time as with a reflecting boundary condition. In this limit the plots shown in Fig. 7(a) become identical to that

shown in Fig. 3, corresponding to $f^* \rightarrow 0$. The presence of the maximum in the mean successful translocation time will be most evident experimentally for low driving voltages or short lengths of the charged block.

The existence of the maximum in Fig. 7(a) implies that at a short, fixed length of the charged fraction an increase in the driving potential leads to an increase in the mean successful translocation time. This behavior is illustrated in Fig. 7(c) where we plot the mean successful translocation time against the driving potential for various lengths of the charged block based on theory. At a high enough driving voltage, all chains approach a saturation value for τ_+ , where further increases in the driving potential no longer appreciably changes the successful translocation time. The time taken to translocate over the length of the uncharged block is unaffected by changes in the driving potential so that its length entirely dominates τ_+ at these high driving potentials, where the contribution from the charged block to successful translocation time is minimized

FIG. 8. Histograms for mean successful translocation times. (a) Expected histograms of successful translocation time for $f/N = 0.01$ (brown), 0.05 (blue), 0.15 (red), 0.25 (green), 0.35 (orange). $\mu = 0.7k_B T$, $m_0/N = 0.05$. Vertical lines mark the first moment of the distribution. (b) Comparison of theoretically predicted normalized histogram with simulation data with $f = 20$, $\mu = 2k_B T$, and $m_0/N = 0.05$.

and $\tau_+ \sim (N - f)^2$ for $f < N$. When $f = N$ (homopolymer) $\tau_+ \sim N/(\mu_1)$. These limits are apparent in Fig. 7(c). For short lengths of the charged block, e.g., $f/N = 0.05$ and $f/N = 0.1$, Fig. 7(c) shows that increasing the driving potential leads to a monotonic increase in the mean translocation time up to a maximum translocation time. For a longer values of the charged block, $f/N = 0.25$ and $f/N = 0.5$, a maximum is evident with increasing driving potential. For driving potentials below the location of this maximum, an increase in potential “captures” translocation events that would have quickly exited the pore unsuccessfully into the *cis* chamber, forcing them instead to translocate over their entire length through the pore, a much longer time process. We also note that as the length of the charged block is increased, the position of this maximum moves to lower driving potentials until it vanishes for the homopolymer, $f/N = 1$. This conversion of short time translocation events into longer time events is discussed below with regard to the maximum in successful translocation time with increasing f/N shown in Fig. 7(a). The discussions are entirely parallel, and we could replace the definition of f^* with a value of the driving potential, μ^* instead. We choose to focus here on alteration of f and simply note the parallel.

In order to understand the origin of this counterintuitive maxima in successful translocation time, we have marked the position of f^* in Fig. 6(a) with a dot on each π_+ curve to show the relationship between f^* and the value of f at which the probability of successful translocation saturates. As discussed above, addition of charge along the backbone when $f < f^*$ leads to an increase in the probability of successful translocation. This increase in the probability of success means that additional charged length captures translocation events that would otherwise retract unsuccessfully into the *cis* chamber for a shorter length of the charged block. This effect is illustrated more clearly in Fig. 8(a) which shows the theoretically computed unnormalized distributions of successful translocation time. The total area under the histogram is the probability of successful translocation plotted in Fig. 6(a). For $f < f^*$, the lengthening of the charged block leads to an in-

crease in the total area under the curve in going from, e.g., $f/N = 0.05$ to $f/N = 0.15$. This increase in the total area under the curve occurs disproportionately in the tail of the distribution, as events which otherwise would have quickly exited the pore in the unsuccessful direction are “captured” by the additional length of the charged block and then diffuse over the entire length of the chain. This capturing of additional long time events leads to the first moment of the distribution being pulled towards longer times.

When $f > f^*$, a competing effect emerges. Above f^* , the probability shown in Fig. 6(a) does not change, implying that the total area under the histogram in Fig. 8(a) is conserved and that addition of charged length does not capture additional events. Instead, the length of the uncharged block is decreased with additional charged length. Thus, monomers which experience no driving force across the pore are exchanged for monomers which experience a potential drop across the pore. Long time events in the tails of the distribution are reduced and take less time because they experience a drift force over more of their length, leading to thinner tails in the distribution and pushing the first moment back towards shorter times. This dynamic is evident in going from, e.g., $f/N = 0.15$ to $f/N = 0.25$. Figure 8(b) compares the theoretically predicted histogram to that computed in a simulation for a half charged chain of length $N = 60$, $f = 20$ ($\mu = 2k_B T$, $m_0/N = 0.05$). We find good agreement, as expected.

3. Mean dwell time

Even for a chain which is initially threaded into the pore, some translocation events will end with the chain retracting unsuccessfully into the *cis* chamber. The average time the chain is in the pore before exiting in either direction, defined to be the mean dwell time τ , is given in Fig. 9(a) as a function of the length of the charged block. Partially charged chains have average dwell times longer than either the minimally charged chain or the fully charged chain.

The mean dwell time also exhibits a maximum value at a certain value of f . Examination of the histograms in

FIG. 9. Mean dwell time and associated histograms. (a) Mean dwell time against length of the charged block for various driving potentials. Connected dots are simulation data, solid lines are theoretically computed. (b) Expected histograms of successful translocation time for $f/N = 0.01$ (brown), 0.05 (blue), 0.15 (red), 0.35 (orange). $\mu = 0.7 k_B T$, $m_0/N = 0.05$. Vertical lines mark the first moment of the distribution. (c) Comparison of theoretically predicted normalized histogram with simulation data with $f/N = 0.5$, $\mu = 0.7 k_B T$, and $m_0/N = 0.05$.

Fig. 9(b) shows that its origin is similar to that discussed above for τ_+ , but is more pronounced. At small values of f , increasing the length of the charged block, e.g., in going from $f/N = 0.01$ to $f/N = 0.05$, captures events that would quickly exit the pore into the *cis* chamber and converts them to successful events. Because a successful event requires the entire chain to pass through the pore, these events are longer time events and increase the weight of the long-time tails of the distribution, pulling the first moment towards longer times. At $f/N = 0.15$, two distinct peaks are evident, one at $\tau \approx 0$ representing unsuccessful events which very quickly withdraw from the pore into the *cis* chamber while the second, broader peak has a very long-time tail representing successful translocation events. Above the value of f where the peak in τ occurs, the shortening length of the uncharged block begins to compensate for this capturing of additional successful events, so that events which are successful experience a drift force over a long enough section of chain that the time taken for translocation does not increase the width of the tails of the distribution. In Fig. 9(c), we show a simulation histogram of dwell times for $f/N = 0.5$, $\mu = 0.7 k_B T$, and $m_0/N = 0.05$ and find good agreement.

IV. CONCLUSION

We have investigated the translocation of a sequenced linear polymer through a narrow pore using theoretical tools and Langevin dynamics simulations by imposing reflecting and absorbing boundary conditions. With the reflecting boundary condition at one end of the chain, such that retraction into the *cis* chamber is forbidden, we have explored the translocation kinetics of a partially charged diblock and have found good agreement between theoretical predictions for event time distributions and mean first passage times. At a constant charged fraction of the chain, a finer distribution of charge leads to lower mean translocation times. This has an intuitive basis in the $\tau \sim N^2$ scaling law for free translocation, as we have discussed in the text. We note that the theory presented here is based on the key assumption that the chain conformations are equilibrated throughout the process of translocation, thus allowing the use of the free energy landscape in the calculation of various features of the kinetics. The agreement we find between theory and simulation results gives confidence that this assumption is well founded for the chain lengths and field strengths we have investigated.

Nevertheless, it is known⁵⁸⁻⁶³ that non-equilibrium effects can be significant in the behavior of the translocation coordinates corresponding to labelled monomers. Extensions of the present simulations to monitor the details of monomer dynamics and the accompanying non-equilibrium effects are in progress and will constitute a future publication.

In the presence of an extended field outside of the pore, good qualitative agreement remains, but simulated kinetics show significantly reduced mean passage times. This sensitivity to the extended field is in contrast to homopolymer translocation, where the kinetics are almost entirely dominated by the potential across the pore. We conjecture that uncharged monomers experience a small effective potential across the pore due to chain connectivity in an extended field. At present a rigorous theory for the strength of this effective potential is lacking and we have described an intuitive picture with the hope of inspiring further theoretical investigation.

Removal of the reflecting boundary condition leads to qualitatively different predictions for a partially charged diblock copolymer, which are born out by simulation. We find that the probability of successful translocation saturates at a threshold length of the charged block independent of nucleation details and well below the length of the entire chain. Below this length of the charged block, additional charge leads to an *increase* in the mean successful translocation time and probability of successful translocation. Above this threshold length of the charged block, additional charge leads to a decrease in the mean time for successful translocation, but does not increase the probability of successful translocation. This maximum in the mean translocation time with increasing length of the charged block can also be understood by considering a diblock with a fixed length of charge and fixed overall length. If the ratio of the length of the charged block is below the saturation value in the probability, an increase in the driving potential will lead to an increase in the mean translocation time. Both of these effects have their origin in the saturation of the probability. Below the saturation value of f , increasing f at fixed μ (or vice versa) “captures” events that would otherwise quickly exit the pore and converts them into long time events which must slowly diffuse over the entire length of the chain, thus pulling the average time upward while also increasing the probability of successful translocation.

We are at present not aware of a systematic experimental study of the effect of the length of the charged fraction on the translocation of a diblock copolymer and hope

that the present work will stimulate further experimental investigation. We note that these effects will be most evident at low driving strengths and short lengths of the charged block.

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APPENDIX A: AVERAGE TRANSLOCATION TIME

1. Reflecting/absorbing boundary condition

For reflecting/absorbing boundary conditions, we consider a chain of length N broken into $i_{\max}$ blocks, the i th block being of length l_i and having monomers which experience a chemical potential difference μ_i across the pore and friction coefficient k_i . Using Eqs. (9) and (10) we obtain for $m_0 < l_1$,

$$\begin{aligned} \tau(m_0) = & \frac{1}{\mu_1 k_1} \left[(f - m_0) - \frac{1}{\mu_1} (e^{-\mu_1 m_0} - e^{\mu_1 l_1}) \right] \\ & + \sum_{i=2}^{i_{\max}} \frac{1}{\mu_i k_i} \left[l_i - \frac{1}{\mu_i} (1 - e^{-\mu_i l_i}) \right] \\ & + \sum_{i=1}^{i_{\max}-1} \sum_{j=i+1}^{i_{\max}} \frac{1}{\mu_i \mu_j k_i} \\ & \times [(1 - e^{-\mu_i l_i}) e^{-\sum_{k=i+1}^{j-1} \mu_k l_k} (1 - e^{-\mu_j l_j})]. \quad (\text{A1}) \end{aligned}$$

For a diblock copolymer with $m_0 \rightarrow 0$, $\mu_1 \rightarrow \mu$, and $\mu_2 \rightarrow 0$, this reduces to Eq. (11).

2. Absorbing/absorbing boundary condition

In order to compute τ_+ and τ from Eqs. (15) and (17) for a diblock copolymer with the first block of length f and the second block of length $N - f$ experiencing driving potentials across the pore of μ_1 and μ_2 and friction coefficients k_1 and k_2 we require the functions $\Psi(x, y)$ and $\phi_+(x, y)$ in three regimes: $x < y < f$, $x < f < y$ and $f < x < y$. For a diblock copolymer $\Psi(x, y)$ is given by evaluating Eq. (13) as

$$\Psi(x, y) = \begin{cases} \frac{1}{\mu_1} (e^{-\mu_1 x} - e^{-\mu_1 y}) & x < y < f, \\ \frac{1}{\mu_1} (e^{-\mu_1 x} - e^{-\mu_1 f}) + \frac{1}{\mu_2} e^{-\mu_1 f} (1 - e^{-\mu_2 (y-f)}) & x < f < y, \\ \frac{1}{\mu_2} e^{(\mu_2 - \mu_1) f} (e^{-\mu_2 x} - e^{-\mu_2 y}) & f < x < y. \end{cases} \quad (\text{A2})$$

The limit $\mu_2 \rightarrow 0$ discussed in the text is straightforward.

Likewise, computing the integrals in Eq. (16) for a diblock copolymer gives for $x < y < f$,

$$\phi_+(x, y) = \frac{1}{\mu_1^2 k_1} \left[(y - x) + \frac{2}{\mu_1} (e^{-\mu_1 y} - e^{-\mu_1 x}) + (y e^{-\mu_1 y} - x e^{-\mu_1 x}) \right]. \quad (\text{A3})$$

For $x < f < y$, we obtain

$$\begin{aligned}\phi_+(x, y) = & \frac{1}{\mu_1^2 k_1} \left[(f - x) - \frac{2}{\mu_1} (e^{-\mu_1 x} - e^{-\mu_1 f}) - (x e^{-\mu_1 x} - f e^{-\mu_1 f}) \right] \\ & + \frac{1}{\mu_1 \mu_2 k_1} e^{-\mu_1 f} (1 - e^{-\mu_2(y-f)}) \left[\frac{1}{\mu_1} (e^{\mu_1 f} - 1) - f \right] \\ & + \frac{1}{\mu_1 \mu_2 k_2} (1 - e^{-\mu_1 f}) \left[(y - f) - \frac{1}{\mu_2} (1 - e^{-\mu_2(y-f)}) \right] \\ & + \frac{1}{\mu_2^2 k_2} e^{-\mu_1 f} \left[(y - f) - \frac{2}{\mu_2} (1 - e^{-\mu_2(y-f)}) + (y - f) e^{-\mu_2(y-f)} \right].\end{aligned}\quad (\text{A4})$$

Finally, for $f < x < y$ we have

$$\begin{aligned}\phi_+(x, y) = & \frac{1}{\mu_1 \mu_2 k_1} e^{-\mu_1 f} e^{\mu_2 f} (e^{-\mu_2 x} - e^{-\mu_2 y}) \left[\frac{1}{\mu_1} (e^{\mu_1 f} - 1) - f \right] \\ & + \frac{1}{\mu_1 \mu_2 k_2} \left[(y - x) - \frac{1}{\mu_2} e^{\mu_2 f} (e^{-\mu_2 x} - e^{-\mu_2 y}) \right] (1 - e^{-\mu_1 f}) + \frac{y - x}{\mu_2^2 k_2} e^{-\mu_1 f} e^{\mu_2 f} \\ & + \frac{1}{\mu_2^2 k_2} e^{-\mu_1 f} e^{\mu_2 f} \left[f (e^{-\mu_2 x} - e^{-\mu_2 y}) - \frac{2}{\mu_2} (e^{-\mu_2 x} - e^{-\mu_2 y}) - (x e^{-\mu_2 x} - y e^{-\mu_2 y}) \right].\end{aligned}\quad (\text{A5})$$

In the limit $\mu_2 \rightarrow 0$, $\phi_+(x, y)$ becomes

$$\phi_+(x, y) \rightarrow \begin{cases} \frac{1}{\mu_1^2 k_1} \left[(y - x) + \frac{2}{\mu_1} (e^{-\mu_1 y} - e^{-\mu_1 x}) + (y e^{-\mu_1 y} - x e^{-\mu_1 x}) \right] & x < y < f, \\ \frac{1}{\mu_1^2 k_1} \left[(f - x) - \frac{2}{\mu_1} (e^{-\mu_1 x} - e^{-\mu_1 f}) - (x e^{-\mu_1 x} - f e^{-\mu_1 f}) \right] \\ \quad - \frac{y - f}{\mu_1 k_1} \left[f e^{-\mu_1 f} - \frac{1}{\mu_1} (1 - e^{-\mu_1 f}) \right] & x < f < y, \\ \quad + \frac{(y - f)^2}{2 \mu_1 k_2} (1 - e^{-\mu_1 f}) + \frac{(y - f)^3}{6 k_2} e^{-\mu_1 f} \\ \frac{(y - x)}{\mu_1 k_1} e^{-\mu_1 f} \left[\frac{1}{\mu_1} (e^{\mu_1 f} - 1) - f \right] \\ \quad + \frac{(y^2 - x^2)}{2 \mu_1 k_2} (1 - e^{-\mu_1 f}) - \frac{y - x}{\mu_1 k_1} f (1 - e^{-\mu_1 f}) & f < x < y. \\ \quad + \frac{(y^3 - x^3)}{6 k_2} e^{-\mu_1 f} - \frac{y^2 - x^2}{2 k_2} f e^{-\mu_1 f} + \frac{y - x}{2 k_2} f^2 e^{-\mu_1 f} \end{cases} \quad (\text{A6})$$

In order to compute the mean dwell times five separate integrals are required in Eq. (17). They are

$$I_1 \equiv \int_{m_0}^N dy \frac{1}{\psi(y)} = \frac{1}{\mu_2} e^{-\mu_1 f} (e^{-\mu_2(m_0-f)} - e^{-\mu_2(N-f)}), \quad (\text{A7a})$$

$$\begin{aligned}I_2 \equiv \int_0^{m_0} dy \frac{H(y)}{\psi(y)} = & \frac{1}{\mu_1 k_1} \left[\frac{1}{\mu_1} (1 - e^{-\mu_1 f}) - f \right] \\ & - \frac{1}{\mu_1 \mu_2 k_1} (1 - e^{-\mu_1 f}) (1 - e^{-\mu_2(m_0-f)}) \\ & - \frac{1}{\mu_2 k_2} \left[(m_0 - f) - \frac{1}{\mu_2} (1 - e^{-\mu_2(m_0-f)}) \right],\end{aligned}\quad (\text{A7b})$$

$$I_3 \equiv \int_0^{m_0} dy \frac{1}{\psi(y)} = \frac{1}{\mu_1} (1 - e^{-\mu_1 f}) + \frac{1}{\mu_2} e^{-\mu_1 f} (1 - e^{\mu_2(m_0-f)}), \quad (\text{A7c})$$

$$I_4 \equiv \int_{m_0}^N dy \frac{H(y)}{\psi(y)} = \frac{1}{\mu_1 \mu_2 k_1} (1 - e^{-\mu_1 f}) (e^{-\mu_2(N-f)} - e^{-\mu_2(m_0-f)}) - \frac{1}{\mu_2 k_2} \left[(N - m_0) - \frac{1}{\mu_2} (e^{-\mu_2(m_0-f)} - e^{-\mu_2(N-f)}) \right], \quad (\text{A7d})$$

$$I_5 \equiv \int_0^N dy \frac{1}{\psi(y)} = \frac{1}{\mu_1} (1 - e^{-\mu_1 f}) + \frac{1}{\mu_2} e^{-\mu_1 f} (1 - e^{-\mu_2(N-f)}). \quad (\text{A7e})$$

From Eq. (17) the mean first passage time for absorbing/absorbing boundary conditions is given by

$$\tau = \frac{I_1 I_2 - I_3 I_4}{I_5}, \quad (\text{A8})$$

for $m_0 > f$.

APPENDIX B: DISTRIBUTION OF TRANSLOCATION TIME

The full probability distribution for the position of the diblock chain in the pore at any time t given that at time $t = 0$ the chain is at the m_0 th monomer is obtained by solving the Fokker-Planck equation, Eq. (6), subject to the boundary conditions of interest. The solution can be written as a sum of eigenfunctions

$$P(m, t; m_0, t_0) = \sum_{\lambda} A_{\lambda}(m_0) P_{\lambda}(m) \exp[-\lambda(t - t_0)], \quad (\text{B1})$$

with $P_{\lambda}(x)$ satisfying the equation,

$$\partial_m [Q(m) P_{\lambda}(m)] + \partial_m^2 [k_m P_{\lambda}(m)] = -\lambda P_{\lambda}(m), \quad (\text{B2})$$

where for a diblock with a charged block of length f , $Q(m)$ is given by

$$Q(m) = \begin{cases} -k\mu & m < f \\ 0 & m > f. \end{cases} \quad (\text{B3})$$

1. Absorbing/absorbing boundary conditions

For absorbing boundary conditions at both ends of the chain $P_{\lambda}(m)$ is given by

$$P_{\lambda}(m) = \begin{cases} e^{\frac{\mu}{2}m} \sin[\beta_{\lambda}m] & m < f, \\ e^{\frac{\mu}{2}f} \frac{\sin[\beta_{\lambda}f]}{\sin[\gamma_{\lambda}(f-N)]} \sin[\gamma_{\lambda}(m-N)] & m > f, \end{cases} \quad (\text{B4})$$

where $\gamma_{\lambda}^2 \equiv \lambda/k$ and $\beta_{\lambda}^2 \equiv \gamma_{\lambda}^2 - (\frac{\mu}{2})^2$ for convenience. The allowed modes are determined by the condition at f on the discontinuity in the derivative

$$\Delta \partial_m P_{\lambda}|_f = -\mu P_{\lambda}|_f. \quad (\text{B5})$$

This gives

$$\left[\gamma_{\lambda} + \frac{\mu}{2} \tan[\gamma_{\lambda}(f-N)] \right] \tan(\beta_{\lambda}f) = \beta_{\lambda} \tan[\gamma_{\lambda}(f-N)]. \quad (\text{B6})$$

It can be shown generally⁵⁶ that enforcing the initial condition $P(m, t; m_0, t_0) = \delta(m - m_0)$ gives $A_{\lambda}(m_0) = [p_s(m_0)]^{-1} P_{\lambda}(m_0)$,

where p_s is the steady state solution to the equation with reflecting boundary conditions. It is given by

$$p_s(m_0) = \begin{cases} e^{\mu m_0} & m_0 < f \\ e^{\mu f} & m_0 > f. \end{cases} \quad (\text{B7})$$

This gives

$$A_{\lambda}(m_0) = \begin{cases} e^{-\frac{\mu}{2}m_0} \sin[\gamma_{\lambda}m_0] & m_0 < f, \\ e^{-\frac{\mu}{2}f} \frac{\sin[\sqrt{\gamma_{\lambda}^2 - (\frac{\mu}{2})^2}f]}{\sin[\gamma_{\lambda}(f-N)]} \sin[\gamma_{\lambda}(m_0 - N)] & m_0 > f. \end{cases} \quad (\text{B8})$$

Combining Eqs. (B4) and (B8) into Eq. (B1) and summing over solutions to Eq. (B6) gives the solution to Eq. (6).

The distribution of exit times from either end of the pore is given by the flux at that boundary, where $J(m, t; m_0, t_0) = Q(m)P(m, t; m_0, t_0) + \partial_m[k_m P(m, t; m_0, t_0)]$. Evaluating this at the boundary $m = N$ gives the expected distribution of successful passage times as

$$g_+(m_0, t) = \sum_{\lambda} k \gamma_{\lambda} A_{\lambda}(m_0) e^{\frac{\mu}{2}f} \frac{\sin[\beta_{\lambda}f]}{\sin[\gamma_{\lambda}(f-N)]} e^{-\lambda(t-t_0)}, \quad (\text{B9})$$

with $A_{\lambda}(m_0)$ given by Eq. (B8). This distribution is plotted in Fig. 8. A similar calculation accounting for exit at both ends of the chain gives the distribution of dwell times plotted in Fig. 9,

$$g(m_0, t) = \sum_{\lambda} A_{\lambda}(m_0) \lambda \left\{ \frac{4\beta_{\lambda}}{\gamma_{\lambda}^2} [1 - e^{\frac{\mu}{2}f} \cos(\beta_{\lambda}f)] + e^{\frac{\mu}{2}f} \frac{\sin[\beta_{\lambda}f]}{\tan[\gamma_{\lambda}(f-N)]} \right\} e^{-\lambda t}. \quad (\text{B10})$$

As alluded to in the text discussion of absorbing/absorbing boundary conditions, for small values of f increasing the length of the charged block leads to an increase in the number of diffusion dominated long time events in the far right tails of the distributions, counterintuitively moving the experimentally measured first moment of the distribution towards longer times. As the length of the charged block is increased further (and the length of the uncharged block decreased), the overall translocation process become progressively more drift dominated and the tails of the distribution shrink once again, with a coincident decrease in the translocation time.

2. Reflecting/absorbing boundaries

Following the same procedure as above, we impose a reflecting boundary condition at $m = 0$ in equation by requiring the flux evaluated there to be zero: $J|_{m=0} = -k\mu P_\lambda + k\partial_m P_\lambda = 0$. We obtain

$$P_\lambda(m) = \begin{cases} \sin[\alpha_\lambda m] + \frac{\alpha_\lambda}{\mu - \gamma_\lambda^2} \cos[\alpha_\lambda m] & m < f, \\ (\sin[\gamma_\lambda m] - \tan[\gamma_\lambda N] \cos[\gamma_\lambda m]) \frac{\sin[\alpha_\lambda f] + \frac{\alpha_\lambda}{\mu - \gamma_\lambda^2} \cos[\alpha_\lambda f]}{\sin[\gamma_\lambda f] - \tan[\gamma_\lambda N] \cos[\gamma_\lambda f]} & m > f, \end{cases} \quad (\text{B11})$$

where we have defined $\gamma_\lambda^2 \equiv \frac{\lambda}{k}$ for convenience as above. Using the same relation for A_λ as for absorbing/absorbing boundaries we obtain

$$A_\lambda(m_0) = \begin{cases} e^{-\mu m_0} (\sin[\alpha_\lambda m_0] + \frac{\alpha_\lambda}{\mu - \gamma_\lambda^2} \cos[\alpha_\lambda m_0]) & m_0 < f, \\ e^{-\mu f} (\sin[\gamma_\lambda m_0] - \tan[\gamma_\lambda N] \cos[\gamma_\lambda m_0]) \frac{\sin[\alpha_\lambda f] + \frac{\alpha_\lambda}{\mu - \gamma_\lambda^2} \cos[\alpha_\lambda f]}{\sin[\gamma_\lambda f] - \tan[\gamma_\lambda N] \cos[\gamma_\lambda f]} & m_0 > f. \end{cases} \quad (\text{B12})$$

α_λ is given by solutions to the equation,

$$\begin{aligned} & \gamma_\lambda [(1 + \tan[\gamma_\lambda N] \tan[\gamma_\lambda f]) + \mu (\tan[\gamma_\lambda f] - \tan[\gamma_\lambda N])] \left[\tan[\alpha_\lambda f] + \frac{\alpha_\lambda}{\mu - \gamma_\lambda^2} \right] \\ & = \alpha_\lambda \left(1 - \frac{\alpha_\lambda}{\mu - \gamma_\lambda^2} \tan[\alpha_\lambda f] \right) (\tan[\gamma_\lambda f] - \tan[\gamma_\lambda N]). \end{aligned} \quad (\text{B13})$$

Solving Eq. (B13) gives α_λ for each $\lambda = 0, 1, 2, \dots$ and combining Eqs. (B11) and (B12) in Eq. (B1) then summing over $\lambda = 0, 1, 2, \dots$ gives the full probability distribution. The un-normalized distribution of exit times is given by the flux at the absorbing boundary, $m = N$,

$$\begin{aligned} g(m_0, t) &= \sum_\lambda k \gamma_\lambda A_\lambda(m_0) (\cos[\gamma_\lambda N] + \tan[\gamma_\lambda N] \sin[\gamma_\lambda N]) \\ &\times \frac{\sin[\alpha_\lambda f] + \frac{\alpha_\lambda}{\mu - \gamma_\lambda^2} \cos[\alpha_\lambda f]}{\sin[\gamma_\lambda f] - \tan[\gamma_\lambda N] \cos[\gamma_\lambda f]} e^{-\lambda t}. \end{aligned} \quad (\text{B14})$$

This equation is plotted in Fig. 9.

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