Polymer translocation in a double-force arrangement

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Abstract. Using Langevin dynamics simulations, we investigate the translocation dynamics of an externally driven polymer chain through a nanopore, where a pulling force \( F \) is exerted on the first monomer whilst there is an opposing force \( F_E < F \) within the pore. Such a double-force arrangement has been proposed recently to allow better dynamical control of the translocation process in order to sequence biopolymers. We find that in the double-force arrangement translocation becomes slower as compared to the case under a single monomer pulling force of magnitude \( F - F_E \), but scaling of the translocation time as a function of the chain length \( \tau \sim N^2 \) does not change. The waiting time \( \tau(m) \) for monomer \( m \) to exit the pore is found to be a monotonically increasing function of the bead number almost until \( m \approx N \), which indicates relatively well-defined slowing down and control of the chain velocity during translocation. We also study the waiting time distributions for the beads in the chain, and characterize in detail fluctuations in the bead positions and their transverse position coordinates during translocation. These data should be useful in estimating position-dependent sequencing errors in double-force experiments.

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1 Introduction

Transport of nucleic acids and other biological molecules through membrane channels of nanometer scale is ubiquitous in nature, such as the movement of RNA molecules and transcription factors across nuclear pores, viral DNA injected through a bacterium membrane in phage infection, and the uptake of specific oligonucleotides by membrane proteins. Understanding how biomolecules thread through nanopores is a major task of modern molecular biology and biophysics. Recent intensive experimental [1–19] and theoretical [19–54] studies on the passage of polymers through nanopores have been motivated by the exciting possibility of developing a practical technique for rapid DNA sequencing. In a seminal experimental paper, Kasianowicz et al. [1] have demonstrated that an electric field can drive single-stranded DNA and RNA molecules through the water-filled \( \alpha \)-hemolysin channel and that the passage of each molecule is signaled by a blockade in the channel current, whose magnitude and duration depend on the structure of the DNA or RNA molecule. Currently, based on the modulation of the ionic current through the \( \alpha \)-hemolysin pore, the length of the DNA or RNA molecule can be characterized [1,5,2,19]. Moreover, it has been demonstrated in experiments [4,6,3] that translocation through a nanopore can be used to discriminate between polydeoxycytidylic acid (poly(dC)) and polydeoxyadenylic acid (poly(dA)) molecules of the same chain length based on the blockage level and the translocation time histogram. Similar experiments have been done recently using solid-state nanopores which can be tuned in pore size and are more stable over changes in external conditions, such as voltage, temperature, salinity and the solution pH. On the theoretical side, it has recently been confirmed by computer simulations that different translocation behavior between poly(dA) and poly(dC) comes from the different base-pore interactions [39]. Moreover, by adjusting the base-pore interactions, the arrangement of the nucleotides could be determined from the waiting time distribution of the biopolymer [40]. However, since sequencing through translocation requires precise control over the dynamics of the process, several serious technical problems remain to be solved for single base resolution in such nanopore-based DNA sequencing approaches [13,17]. The most important one is that the measured DNA translocation speed under an electric field requires an electronic sensing system at extremely high bandwidth, and the concomitant electronic noise poses serious limitations in electrically discriminating between bases. Thus, a key to DNA sequencing is to develop the capability to control the motion or translocation of DNA molecules through the pore. It has been demonstrated that DNA translocation speeds can be reduced by an order of...
magnitude over previous results by controlling the electrolyte temperature, salt concentration, viscosity, and the electrical bias voltage across the nanopore [13]. However, this comes at the cost of decreased ionic current, reducing the signal-to-noise ratio. From the experimental side, it is highly desirable to measure the DNA translocation process at either a lower constant velocity or constant force. To do this, the widespread use of optical tweezers in single-molecule biophysics suggests their utility to control sample presentation to a pore or channel, to reduce polymer propagation speeds without impairing ionic currents, and to repeatedly characterize one DNA molecule [14–16]. Ideally, one would like to measure the ionic current while the DNA molecule is fully stretched inside the pore where fluctuations in the ionic current due to DNA thermal motion can be reduced or avoided. To this end, in recent experiments [14] the 3′ end of a single-stranded DNA is attached to a streptavidin-coated magnetic bead through a single biotin molecule. Initially, the 5′ end of a DNA is drawn through the solid-state nanopore to the trans side by means of electrophoresis while the 3′ end stays in the cis side with the magnetic bead. Under a large enough magnetic-field gradient generated by a set of permanent magnets or electric coils, the DNA can be pulled out of the nanopore by the bead. The net force on the magnetic bead determines this reverse translocation speed. By carefully tuning the magnetic-field gradient and the voltage bias on the nanopore, one can make the reverse translocation much slower than the conventional forward translocation, in which case the DNA is driven only by the electric force. The goal of the above-mentioned double-force experiments is to sequence single-stranded DNA by reading the nucleotides off the taut translocated part of the polymer. Thus, it is important to characterize in detail the dynamics of the chain during the translocation process in this case. It is also of theoretical interest to compare this case to the case where the chain is simply pulled through the nanopore from one end only [37, 55]. To this end, in the present paper we investigate in detail various features of the dynamics of polymer translocation as described in the above-mentioned double-force experiments. For computational efficiency we employ here the bead-spring model of a flexible polymer chain within the Langevin dynamics (LD) simulation scheme. Such a model allows us to characterize all the stages of the translocation process and can be directly compared to our previous study of the pulled polymer translocation case [37].

2 Model and methods

In accordance with our previous works [34–39], the polymer is modeled as a fully flexible bead-spring chain. The van der Waals interaction and the excluded-volume effect are modeled using a repulsive Lennard-Jones (LJ) potential that reads

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

where \(\sigma\) is the diameter of a bead, and \(\epsilon\) is the depth of the potential. Adjacent beads in the polymer chain are connected via the finitely extensible nonlinear elastic (FENE) potential

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

where \(r\) is the separation between the beads, \(k\) the spring constant and \(R_0\) the maximum elongation of the nearest-neighbor bond. The setup of the system is shown schematically in Figure 1. In this study, translocation takes place in a two-dimensional geometry where the wall in the \(y\)-direction is described as \(w\) columns of stationary particles within distance \(\sigma\) from one another and they interact with the beads via the repulsive part of the LJ potential. Wall particles are fixed in place throughout the simulation. The pore is formed in the wall by removing \(w_p\) rows of beads from it. In the Langevin dynamics (LD) simulation method, the equation of motion for each bead reads

\[
\ddot{\mathbf{r}}_i = \frac{1}{m_i} \left[ \nabla U_i + F_i^\text{C} + F_i^\text{F} + F_i^\text{R} \right],
\]

where \(M\) is the monomer mass and the force superscripts denote conservative, frictional and random components, respectively. The conservative force \(F_i^\text{C}\) is a combination of the potentials given above and two external forces, \(F^\text{pore}\) and \(F^\text{pore}\) in the present case. The pulling force is expressed as

\[
F^\text{pulling} = F \hat{x},
\]

where \(F\) is the pulling force strength exerted on the first bead in the chain and \(\hat{x}\) is a unit vector in the direction perpendicular to the wall. We note that the \(y\) coordinate of the first bead is not confined to be \(y_1 = 0\). For the force opposing the polymer motion, according to the experiments [14], we set

\[
F^\text{pore} = -F_E \hat{x},
\]

when the bead is in the pore. Here, \(F_E\) is the strength of the force exerted by an applied electric field, \(w\) is the wall width and \(w_p\) is the pore width. The conservative force is thus

\[
F_i^\text{C} = -\nabla U_i + \nabla U_{\text{FENE}} + F^\text{pulling} + F^\text{pore}.
\]

The frictional force acting on an individual monomer is

\[
F_i^\text{F} = -\zeta v_i,
\]

where \(\zeta\) is the friction coefficient and \(v_i\)
is the velocity of the monomer. The Brownian motion of a monomer resulting from the random collisions with solvent molecules is included in \( F_i^R \) and it satisfies the fluctuation-dissipation theorem [56].

### 3 Scaling for chains under tension

The way a polymer stretches under external tension can be understood in terms of scaling theory [57,58]. We denote the average end-to-end distance of the polymer as \( L(F) \) when two opposite (and equal) forces of strength \( F \) are pulling at its ends. Ultimately, the chain becomes straight as the force \( F \) exceeds \( k_B T/\sigma \), where \( k_B \) is the Boltzmann constant and \( T \) the temperature, and the average end-to-end separation is comparable to a fully extended chain, that is

\[
L(F) \sim N\sigma. \tag{4}
\]

In a recent study [37], the scaling theory above and the results of reference [59] were applied to the polymer translocation problem with an external pulling force. In reference [37], it was shown that forces above \( k_B T/\sigma \) straighten the whole chain and the translocation time becomes

\[
\tau \sim \frac{N\sigma}{F_0} \sim N^2 F^{-1}. \tag{5}
\]

These results were numerically verified in reference [37] using the same bead-spring model with LD as in the present work.

### 4 Results

As mentioned above, the model and the parameters used in the present case are analogous to references [36,37], where the cases with an electric-field–induced force in the pore and an external pulling force were studied separately. The main difference in the double-force setup is, of course, that now these forces act in opposite directions, with the force across the pore opposing translocation. In the present study, the LJ parameters \( \epsilon \) and \( \sigma \) set the energy and the length scales, respectively. The simulations were run with \( \sigma = 1, k_B T = 1.2 \epsilon \), and the time scale determined by \( t_{LJ} = \sqrt{M \sigma^2 / \epsilon} \), which is in the picosecond range. The friction parameter is set to \( \zeta = 0.7 M / t_{LJ} \). As in reference [37], the values \( R_0 = 2\sigma \) and \( k = 7\epsilon / \sigma^2 \) were used for the FENE potential. These parameters are put in context by noting that \( k_B T/\sigma = 4 \) pN for a chain of Kuhn length \( \sigma = 1 \) nm at room temperature of 295 K, the time scale is about 11.3 ps for a monomer of mass \( M = 312 \) amu. The pulling force \( F \) has the scale \( \epsilon/\sigma \), which is close to 3.3 pN. The pore size was fixed at \( w = \sigma \) and \( w_p = 2\sigma \). The Langevin equations were integrated in time by a method set forth by Ermak and Buckholz [60]. The initial configuration was created by placing the first monomer of the chain in the pore entrance. The polymer is then let to relax to an equilibrium configuration. After this the polymer was released and translocation took place as determined by the difference \( F - F_E \). All the simulations were performed with uncorrelated initial configurations. The translocation time is defined as the time interval between the entrance of the first segment into the pore and the exit of the last segment from the pore. The translocation time was estimated as the average over the durations of successful translocations. In this investigation we define that a monomer \( m \) resides inside the pore when its \( x \) coordinate \( x_m \) is for the first time within the interval \([0, 0.5\sigma, 0.5\sigma]\) as defined by the width of the wall. A monomer is said to leave the pore when its \( x \) coordinate exceeds 0.5\( \sigma \).

#### 4.1 Translocation times

The distribution \( p(\tau) \) of translocation times for a polymer of length \( N = 100 \) pulled with a force \( F = 10 \) and an opposing force \( F_E = 5 \) is depicted in Figure 2. For this particular value of the force difference, virtually all translocation events are successful [37], and thus the distribution is relatively sharp and well defined. The average translocation time \( \tau \) is much larger and there is a longer tail in \( p(\tau) \) than in the pure pulling case with \( (F, F_E) = (5, 0) \), where \( p(\tau) \) is close to a Gaussian. This is because the dynamics of the chain is controlled by the effective friction in the pore which is larger when there is an opposing force inside the pore. For the double-force arrangement the \( \text{cis} \) side of the polymer chain fluctuates less than for the pure pulling case resulting in a weaker entropic driving force for translocation.

Here, we define \( \tau \) as

\[
\tau \equiv \int_0^\infty d\tau' p(\tau')\tau'. \tag{6}
\]

In Figure 3 we show the scaling of \( \tau \) as a function of the chain length \( N \) in the strong force regime with \((F, F_E) = (10, 5)\). For a pore of width \( 2\sigma \), the result \( \tau \sim N^{1.90 \pm 0.06} \) is
in excellent agreement with the pure pulling case [37,31] and with the theoretical prediction in the absence of the wall \( \tau \sim N^2 \), which is attained when \( N \) becomes very large (cf. Eqs. (5)).

### 4.2 Waiting time distributions

It is of interest to examine how each bead passes from one side of the wall to the other. By letting \( t_m \) be the time when the monomer \( m \) exits the pore, the passing of beads can be quantified by calculating the waiting time of bead \( m \) defined as the average over \( t_{m+1} - t_m \) [38,36,37]. The index \( m \) ranges from 1 to \( N - 1 \), thus making \( m = 1 \) the first bead to pass through the pore. A driving force due to an external field across the pore was used in references [36,38] and it was discovered that the waiting time depends strongly on the position of the monomer on the chain (see the curve plotted with diamonds in Fig. 4). It was also concluded that the high density of segments of a long polymer near the pore slows down the translocation. These numerical results suggest that controlling the chain velocity during DNA sequencing is nontrivial. In reference [37], the translocation was expedited by pulling the polymer from one end, which made the peaks of the waiting time curves shift towards the back end of the chain for all chain lengths and pulling forces studied, see reference [37] and the data points plotted as circles in Figure 4.

In the present double-force arrangement, the aforementioned monotonicity is even more pronounced and the influence of the chain length becomes less important. Figure 4 reflects the extended regime of monotonicity, which originates in an increase in the chain free energy as its configurational entropy decreases while being held taut. Short chains slow down until the chain entropies in the trans and cis parts are equal on the average. As the figure reveals, the waiting times may be shortened by increasing the difference \( F - F_E \) from, e.g., five to ten, which also makes the bead-by-bead progress steadier and more controllable.

The translocated part of long enough a chain will eventually have sufficient leeway so that its entropy exceeds that of the tail. This results in the maximum waiting time appearing at the very end of the translocation process. Thus, the chain velocity slows down in a relatively well-defined manner until \( m \approx N \), when the very last beads of the chain escape the pore rapidly. Time sequences of typical chain conformations in the driven, pulled and double-force case are illustrated in Figure 5.

In Figure 6 we show the actual waiting time distributions for the 6th, 50th and 90th bead along the chain for the case \( N = 100 \). This distribution is relatively sharp for \( m \ll N \), but develops a long tail with increasing \( m \).

### 4.3 Fluctuations in positions of translocated beads

The goal of the double-force setup is to sequence single-stranded DNA by reading the nucleotides off the taut translocated part of the polymer and thus it is important to know how much the chain can deviate along the direction of pulling. To this end, we have calculated and show in Figure 7 how much, on the average, selected beads deviate from their ideal positions \( i \cdot x_{0,FENE} \), defined as the
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Fig. 5. A driving force in the pore results in a tangle on the right side of the wall as the chain does not have time to equilibrate. Pulling the polymer at one end slows down the translocation. The index $m$ denotes here the bead currently in the pore. The chain consists of $N = 100$ beads.

Fig. 6. Waiting time distributions of the 6th, 50th and 90th bead. The chain has $N = 100$ monomers and the external forces are $(F, F_E) = (10, 5)$. The vertical lines show the corresponding averages.

distance given by $\nabla (U_{LJ}(r) + U_{FENE}(r))|_{r=x_0 \cdot FENE} = 0$. The fluctuation is then measured as

$$\Delta x_i \equiv x_i - i \cdot x_0 \cdot FENE$$

along the axis as defined by the pulling force vector. $x_i$ is the displacement of the $i$-th translocated bead with respect to the bead $i = 0$ currently in the pore. When $s$ beads have translocated, $\Delta x_i$ can be measured for all beads for which $i \leq s$. At different times different monomers occupy the pore, but $\Delta x_i$ is always measured for some fixed set $I_N \ni i$, which means that the distribution of the $\Delta x_i$ is averaged over the whole process. The data for the sets $I_{100} = \{3, 9, 15, 30, 75\}$ and $I_{300} = \{9, 30, 100, 200, 250\}$ in Figure 7 suggest the additive nature of the deviation: if each bond is stretched by $\delta x$, the $i$-th bead will approximately be displaced by $i \delta x$ in the direction of the pulling from the ideal position. The insets in Figure 7 show the kurtosis $\gamma_2 = \mu_4/\mu_2^2 - 3$ and skewness $\gamma_1 = \mu_3/\mu_2^{3/2}$ that characterize the peakedness and the asymmetry of the distributions, $\mu_j$ is the $j$-th central moment [61]. Both $\gamma_1$ and $\gamma_2$ exhibit the approach to a Gaussian distribution as a function of $i$.

In the transverse direction, spatial fluctuations have a mean value of zero by symmetry. There are no fluctuations in the pore as it fixes the $y$ coordinate of the chain, and the pulling force prevents large departures from the $y = 0$ axis. The behavior of the $i$-th bead is illustrated in Figure 8 for different pairs of forces. The data assume parabolic shapes for $(F, F_E) = (10, 5)$, since for each value of $i$, there is an effective spring constant $k_i$ that determines the amplitude $A$ of the fluctuation: $A \sim \sqrt{k_i T / k_0}$. The amplitude becomes small as $i$ approaches the endpoint indices. We remark again that data are collected at each instance for certain fixed values $I_N = \{i\}$ in the range $\{0, 1, \ldots, s\}$, where $s$ is the number of translocated beads. Toward the end of the translocation process $s$ approaches the number of the beads $N$, i.e., for $(i, N) = (99, 100)$ we

![Fig. 5. A driving force in the pore results in a tangle on the right side of the wall as the chain does not have time to equilibrate.](image1)

![Fig. 6. Waiting time distributions of the 6th, 50th and 90th bead.](image2)

![Fig. 7. (a) The fluctuations of the 3rd (○), 9th (□), 15th (♦), 30th (△) and the 75th (♥) beads about their ideal position for a chain of length $N = 100$. Inset shows the kurtosis and the skewness of the distributions as a function of the bead index $i$ for $(F, F_E) = (10, 5)$ (●) and $(F, F_E) = (15, 5)$ (■). (b) The fluctuations of the 9th (○), 30th (□), 100th (♦), 200th (△) and the 250th (♥) bead for $N = 300$. Inset as in (a). The errors in all plots are of the size of the symbols or less.](image3)
get only one sample per translocation for the deviation $y(i = 99)$. The parabolic shape is maintained for pairs of forces $(F, F_{E}) = (6, 1)$ and $(F, F_{E}) = (13, 5)$, but the amplitudes change. This suggests that transverse fluctuations are suppressed both as a function of the absolute value of the pulling force $|F|$ and of the relative value $|F - F_{E}|$.

4.4 Fluctuations in bead positions about the pore and the translocating bead

From the point of view of sequencing, it is also important to know how much statistical error there is in the position of each bead as measured either form the pore or from the position of the bead currently within the pore. To this end, we use again the monomer index $m$ as defined in Section 4.2. Once a monomer enters the pore, it may be pulled back out by the opposing force $F_{E}$ and random fluctuations. Thus, with bead $m$ inside the pore, the $(m + 1)$-th monomer along the chain is expected to lag $\approx \sigma$ behind it and the $(m - 1)$-th monomer’s position is bounded above by $x = 0.5\sigma + R_{0}$ due to the FENE potential. Figure 9(a) depicts the position distribution for beads $m = 31$ and $m = 91$ in two cases. We show both the distribution of $x_{m+1} - x_{m}$ and the distribution of the positional coordinate $x_{m+1}$ when the $m$-th bead is inside the pore as defined above. As seen in the figure, in contrast to the case where fluctuations are measured from the ideal bead positions, all these distributions have a non-Gaussian tail in the direction of the pore regardless of the phase of the translocation process. This means that standard error analysis of bead positions based on Gaussian statistics is not correct.

Also, the 31st bead follows the 30th bead with a mean distance of less than $\sigma$ implying a compressed bond. The distance is larger for the pair $(m, m + 1) = (90, 91)$ as the push experienced by the monomer next to the pore becomes smaller as more of the chain recedes on average after the $m$-th bead has reached the pore for the first time. In Figure 9(b), we draw attention to the position of the most recently translocated bead $(m - 1)$: $(30 - 1) = 29$ (●) and $(90 - 1) = 89$ (△ and ○). The pulling force $F$ makes the peaks well defined compared to those of the untranslocated beads.

Fig. 8. Variance of the transverse position coordinate $y$ of translocated beads for chains of length $N = 100$ and $N = 300$. The continuous line is a parabolic fit to the data points. For $N = 100$, the data points are $i = 3, 6, 9, 12, 15, 30, 50, 75$ and 90. For $N = 300$, they are 3, 6, 9, 15, 30, 60, 100, 150, 200 and 250. The symbols ▲, ■ and ○ of the small parabolas correspond to force pairs $(F, F_{E}) = (13, 5), (10, 5)$ and $(6, 1)$, respectively. The forces $(F, F_{E}) = (10, 5)$ were also exerted on the $N = 300$ chain (●).

Fig. 9. (a) Fluctuations in the positions of the $(30 + 1) = 31$st (● and □) and the $(90 + 1) = 91$st (△ and ○) bead with respect to the bead in the pore and the wall coordinate (♦) bead with respect to the bead in the pore and the wall coordinate (♦) bead. The calculations were carried out with the 30th and the 90th bead in pore, respectively. The distributions have an increasingly longer right tail as a function of the bead index $m$. (b) As above, but the distributions are now for the most recently translocated bead $(m - 1)$: $(30 - 1) = 29$ (● and □) and $(90 - 1) = 89$ (△ and ○). The pulling force $F$ makes the peaks well defined compared to those of the untranslocated beads.
4.5 Fluctuations in bead positions inside a long pore

Two experimentally relevant quantities are the absolute and the relative positions of the beads currently in the pore. To quantify these, we set up a pore consisting of six LJ particles centered at coordinates $(-3 + i, 1)\sigma$ and $(-3 + i, -2)\sigma$, $i = 0, \ldots, 5$. We denote the $x$ coordinate of the bead most recently to enter the pore by $x_L$. We then measured the distributions of $\Delta x_{mL} := x_m - x_L$ for the beads $M = \{m = L - 1, \ldots, L - 5\}$ and of $x_m$ for $M \cup \{L\}$ while they are inside the pore. The endpoints of the pore are determined by the LJ potential of equation (1). In practice, there are usually five beads situated in the potential minima created by the wall particles, and a sixth bead seldomly enters the pore. Our result for the relative probability for there to be six beads in the pore is $P_r(\text{six}) = N(\text{six})/(N(\text{six}) + N(\text{five})) \approx 0.08$. Figure 10(a) and (b) depict the probability distributions of the relative position $\Delta x_{mL}$ in the order of entry to the pore for the beads $M$ in the case of a 100-monomer chain averaged over 100 independent runs. The forces used were $(F, F_E) = (10, 5)$. Figure 10(a) shows the case with five beads in the pore and it is an average over the whole translocation process. The distributions show a slight tail to the left, but the beads are mostly confined to reside in the potential minima of the pore. Ergo, consecutive peaks have a separation close to the bond length. The tail is explained by thermal fluctuations and $F_E$ pulling a given bead backward. The distributions of Figure 10(b) in the six-bead case are noisier than in (a) as the configuration is rarer. There are more beads in the pore than available minima, which makes the distributions clearly non-Gaussian. Compression is visible in the means being slightly closer than in (a). The absolute positions $x_m$ of the beads $m \in M \cup \{L\}$ are plotted in Figure 10(c). Again, the data is an average over the whole process in which the entry of chain to the pore contributes to the left tails. The leftmost distribution for the sixth bead shows the extent of the compression that may occur. The possibility of compression in the chain suggests that in experiments the reading errors should be better controlled and suppressed by extending the chain to disallow six-bead configurations in the pore.

5 Summary and conclusions

As compared to the traditional techniques for DNA sequencing, polymer translocation through nanopores would offer an inexpensive and rapid technique for reading of nucleotide sequences. However, as discussed in the Introduction, there are several technical difficulties in the actual application of this technique for sequencing. One of the problems concerns controlling the dynamics of the translocation when facilitated by external forces. To this end, the double-force arrangement proposed by Ling et al. [14] offers one promising way of better controlling the dynamics. In the present work, we have carried out a comprehensive study of the dynamics of a flexible polymer chain under the double-force translocation arrangement. We have employed the simple bead-spring model within the Langevin dynamics approach in 2D to be able to fully characterize the dynamics of the translocation process. In order to model the double-force setup, in our simulations a pulling force $F$ is exerted on the first monomer of the chain whilst there is an opposing force $F_E < F$ in the pore. We find that overall the translocation process is slower than the case under a pure pulling force of magnitude $F - F_E$, but the scaling of the translocation time as a function of the chain length $\tau \sim N^2$ remains unchanged. We have
studied in detail the waiting time of the monomers and found $\tau(m)$ to be a monotonically increasing function of the bead number $m$ almost until the end of the process. This indicates that the slowing down of the chain during the translocation is better controlled than in the pore-driven or end-pulled cases. We have also studied the waiting time distributions for the beads in the chain, and characterized in detail fluctuations in the bead positions and their transverse position coordinates during translocation. In particular, we have demonstrated here that these quantities may display significant deviations from Gaussian statistics, which should be taken into account in experimental measurements of the nucleotide positions. These data should be useful in estimating position-dependent sequencing errors in double-force experiments.

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