

Supporting Information (SI) for
Translocation Dynamics Of An Asymmetrically Charged Polymer Through A
Pore Under The Influence Of Different pH Conditions

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Description of estimation of error in the calculation of the mean translocation time:

The mean values of translocation times in Table 1 and 2 in the manuscript are obtained from the independent successful translocation runs. The statistical errors in the means (SEMs) are now included in the tables and obtained from the protocol described below.

Following the standard protocol, we have first calculated the standard deviation, SD of the variable X given by $SD = \sqrt{\frac{\sum (x - \bar{x})^2}{n-1}}$ where \bar{x} = mean, and n = size of the sample. Next, the standard error of the mean (SEM) is calculated as: $SEM = \sqrt{\frac{SD}{n}}$

The SEM value quantifies the uncertainty in the estimate of the mean as given in the 3rd and 5th column of Table 1 and 2 in the manuscript.

This can be further used to construct the confidence intervals (CI) to the desired degree (usually 95% CIs) as $CI = \bar{x} \pm Z \sqrt{\frac{SD}{n}}$ where CI = confidence interval, Z = 1.96 (a standardized score for 95% of confidence). This is additionally mentioned in column 4 and 6 in table S1 and S2. CI value indicates the range within which the mean lies with a given confidence.

Table S-1

E	systems	τ_1	95% CI	τ_{21}	95% CI
4.0	S- I	14.78±0.16	[15.09, 14.47]	15.84±0.98	[17.76, 13.91]
	S- II	14.08±0.10	[14.28, 13.89]	3.66±0.04	[3.74, 3.58]
	S- III	15.34±0.13	[15.59, 15.08]	3.18±0.03	[3.24, 3.12]

Table S-2

E	Systems	τ_{22}	95% CI	τ_3	95% CI
0.08	S- I	19.54±0.67	[20.85, 18.23]	192.52±1.94	[196.32, 188.72]
	S- II	35.77±1.63	[38.96, 32.58]	215.43±3.23	[221.76, 209.10]
	S- III	39.91±1.87	[43.58, 36.24]	209.81±3.18	[216.04, 203.58]
0.1	S- I	20.30±0.88	[22.02, 18.57]	203.37±2.39	[208.05, 198.69]
	S- II	31.11±1.70	[34.44, 27.78]	241.39±4.12	[249.47, 233.31]
	S- III	32.42±1.89	[36.12, 28.72]	224.21±4.29	[232.62, 215.80]

The parenthesis [,] indicates the upper and lower range of the CI value. The mean values in both the tables lie within the confidence interval.

Free energy calculation for translocation:

We have a polymer chain with N monomer beads translocating through a nanopore of length $L=26$. We define a translocation coordinate $Q = N_{\text{cis}} - N_{\text{trans}}$ where N_{cis} and N_{trans} are the number of monomer beads on the cis and trans side of the pore respectively. During the onset of the translocation process, the first monomer bead is at the entrance of the pore ($N_{\text{cis}} = 0$, $N_{\text{trans}} = 35$, $Q = -35$) The translocation continues with an increase in the number of monomer beads filling up the pore (at the end of pore filling stage at $N_{\text{cis}} = 0$, $N_{\text{trans}} = 26$, $Q = -26$) followed by the transfer of the polymer across the pore. As the transfer stage continues, the number of beads on the cis side of the pore increases and on the trans side decreases leading to the increase in the value of Q . At the end of the entry stage, an equal number of charged residues is present within the pore as well as an equal number of beads is present on either side of the pore as shown

in Figure 1. ($N_{cis}= 5$, $N_{trans}= 5$, $Q= 0$). Once the transfer stage ends, there are no monomer beads on the trans side of the pore ($N_{trans}= 0$, $N_{cis}= 10$, $Q=10$) and after this, the value of Q is only determined by the value of N_{cis} . During the pore emptying stage, N_{cis} increases and reaches its maximum value ($Q= 36$) when all the monomers are on the cis side of the pore. Between the limits of $Q=-36$ to 0 and $Q= 0$ to 36, one can construct the free energy landscape for the entry stage and exit stage respectively for the different systems under consideration. The free energy of this system has three major components in it: the electrostatic interaction between the polymer and the pore-polymer (F_{elec}), the contribution due to an externally applied electric field (F_{ext}), and the entropy of the chain (F_{ent})

To calculate the electric field contribution we used the protocol employed in Ref 1 and 2.³⁻⁴ It is given by the work done by the external electric field E acting within the pore

$$F_{ext} = aE(N_+q_1 + N_-q_2) \quad (S.1)$$

The electric field E is assumed to be zero outside the pore and is acting parallel to the pore axis directed from trans to cis side of the pore. N_+ and N_- correspond to the number of positively and negatively charged residues inside the pore with charges q_1 and q_2 respectively. Here q_1 is always 1e and q_2 is negative whose magnitude changes with changes for different systems. As mentioned in Ref. 3 and 4, a is a “function that connects the variation in the progress variable Q to the average movement of the mass center of the peptide”. As N_+ and N_- changes, the electric field effect changes and also “ a ” as a function of Q changes. As mentioned in the above references, “ a ” attains a fixed value over two different ranges of Q . In our case $a= 1$ when the pore is fully occupied by the polymer with $N_{cis} \neq 0$ and $N_{trans} \neq 0$ which corresponds to a Q value within the range -8 to 8 for our system of study. For all other values of Q , $a=$

0.5.

In addition to the contribution from the external electric field, we also consider a contribution of the electrostatic interaction between the polymer and pore⁵⁻⁶ adapted from Ref. 5 and also implemented in Ref. 6. The free energy contribution due to the pore-polymer electrostatic interaction is given by a screened Coulombic interaction

$$F_{elec} = \frac{N_r q_{ring}}{4\pi \epsilon_0} \left(\sum_i \frac{q_1}{x(i,1)} e^{-\kappa x(i,1)} + \sum_j \frac{q_2}{x(j,1)} e^{-\kappa x(j,1)} \right) \quad (S.2)$$

where $x(i, 1)$ is the distance between the i^{th} bead of the A end with charge q_1 and $x(j, 1)$ is the distance between the j^{th} bead of the B end with charge q_2 from the pore ring with charge q_{ring} . The cylindrical pore is made up of 26 consecutive rings such that $L=26$. The symbol “1” in the parenthesis denotes the position of the first ring along the pore axis. As seen in Figure 1, q_{ring} is situated at the mouth/ entrance of the pore on the trans side. Note that the sums over index i and j is performed on the position of each of the N_+^{th} and N_-^{th} bead respectively along the pore axis with respect to the ring at the entrance of the pore. The position of a given N_+^{th} or N_-^{th} bead ($x(i,1)$ or $x(j,1)$) changes as translocation progresses and is determined by Q . There can be an attractive or a repulsive interaction between the trans side of the pore and the pore confined polymer depending upon the magnitude of charges on the pore ring and the charges on both tails of the polymer. Also, the number of the attractive or repulsive terms that contribute to the electrostatic energy within the summation depends on the number of N_+ and N_- beads which changes with Q . In Eq. S.1 and S.2, N_+ or N_- or both and their positions within the pore are determined by the value of Q . Thus F_{ext} and F_{elec} are implicit functions of the variable Q . There is also an entropic contribution given by

$$F_{ent} = k_B T \ln \Omega(n) \quad (S.3)$$

where n is the number of monomers at the cis or trans side of the pore which is a

measure of the value of Q . $\Omega(n) = n^{\gamma-1}$, where $\gamma = 0.69$ for a 3D polymer chain.⁷ A free energy landscape is constructed including all the above components with appropriate limits as a function of the translocation coordinate Q .

During the beginning of the exit stage, for example, when $Q=2$, there are 8 monomers on the cis side and 6 on the trans side with $N_{\text{cis}}=6$ and $N_{\text{trans}}=4$, $N_+=6$ and $N_-=8$, the free energy is given by

$$F(Q = 2) = \frac{q_{\text{ring}}}{4\pi\epsilon_0} \left(\sum_{j=0}^7 \frac{q_2}{x(j,1)} + \sum_{i=20}^{25} \frac{q_1}{x(i,1)} \right) + Ea(6q_1 + 8q_2) + k_B T (1 - \gamma) (\ln(4) + \ln(6)) \quad (\text{S.4})$$

Since q_1 corresponds to the charge on the A end, it is always positive. q_2 is negative on the B patch and its magnitude will depend on the pH of the system. Also the sign and magnitude of q_{ring} changes from S-I to S-II. Based on this, one can construct the free energy landscape during different stages of the translocation process. Figure S1 shows the free energy during the entry stage and Figure 4 in the manuscript shows the free energy diagram during the exit stage of the translocation.

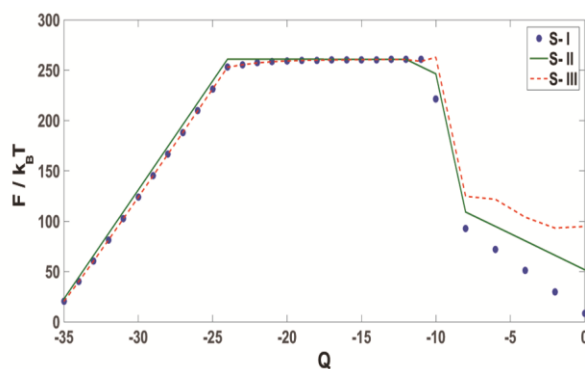


Figure S1: Free energy landscape for the translocation of a polymer chain of length $N = 36$ during the entry stage ($\tau_1 + \tau_{21}$) translocating through a pore of length $L = 26$ for S-I, S-II and S-III at $E = 4$

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