Translocation of Polymers through Nanopores at Weak External Field, Direct Approach with Monte Carlo Simulations

Stanislav Kotsev

Max-Planck-Institut für Polymerforschung,
Ackermannweg 10, D-55128 Mainz, Germany

I did off-lattice 3D Monte Carlo simulations for polymer translocation through a narrow pore at low external field, trying to be as close to a direct approach as possible. The process was found non equilibrium globally, but dynamics of the monomers close to the pore (the *fold*) was found close to quasi equilibrium. I observed a tension (or pressure) buildup near the pore, and subdiffusion for the displacement of the middle monomer in the pore, as reported in the literature. I did not find the distribution of the reaction coordinate after some time of free diffusion predicted by the fractional diffusion equation.
I. INTRODUCTION

Translocation of polymer molecules through nanopores is an important process in biology. Examples are the transport of DNA and RNA molecules across pores of the nuclear membranes, injection of the virus genetic information, gene swapping etc. Translocation of single-stranded DNA/RNA through a pore forced by external voltage was demonstrated in vitro as a single molecule signal by Kasianowicz et al. In such experiment voltage is applied across a membrane with a single pore in it. Due to its negative charge, the DNA or RNA molecule is forced to drift across (see the topical review by Meller). While inside the pore the polymer blocks the ion current, thus increasing the resistance, which effect can be detected with a single event resolution. Such experiments showed sensitivity to the nucleotide composition, etc. It is now believed that by using the blockage current only, no sequencing can be achieved. Yet electrophoretic translocation through a hole combined with another method is still one of the prime candidates for fast DNA sequencing in the future (see the review by Zwolak). Maybe most experiments use a pore made by self assembly of α-hemolysin in lipid bilayer. Such pores are so narrow (1.4 nm diameter in the most narrow place), that only a single stranded DNA or RNA can pass. Typically the RNA/DNA is of the order of hundreds base units, the applied voltage is few hundreds mV (or less), and the blockage times are hundreds of microseconds. More recently experiments with silicone membranes have been reported. A big development in silicone nanopore production has been made in the last years. A pore of 1 nm diameter is reported, which similarly to the α-hemolysin can translocate only single stranded DNA. Obviously wider pores can be created and used, but this is outside the emphasis of this paper.

The translocation of a polymer through a narrow pore driven by electric field is also extensively simulated. Some authors use MD simulations with simplified (e.g. cylinder like) pore, some consider more detailed pore structure (α-hemolysin). Another approach is dynamic Monte Carlo simulations (only with simplified cylinder/square like pore). The last approach allows the case without external field to be simulated. No friction forces can be considered in a natural way in Monte Carlo simulations, hence the hydrodynamic interactions are neglected. Using some tricks that shorten the computer time, MD simulations on the low external field problem have been recently reported.
The low external field behavior observed in simulations invoked some controversy. Considering equilibrium entropic barrier one gets for the translocation time, reflecting boundary conditions at the beginning $\tau = CN^2$, where $N$ is the number of bases of the polymer (or other parameter proportional to the length of the chain). For ideal chain $C = \frac{\pi^2}{16D}$ where $D$ is 1D diffusion constant. In the above mentioned result no friction is considered. How noticed, the non forced translocation time has a simple lower limit - the time the polymer diffuses its radius of gyration (or translocation with no barrier). That gives $\tau \geq N^{2\nu}$, where $D$ is the diffusion constant of the whole molecule. In Rouse model $D \sim \frac{1}{N^\nu}$ giving $\tau \geq N^{2\nu+1}$. $\nu$ is the Flory exponent, which in 3D is $\nu = 0.5$ for ideal chain, and $\nu = 0.588$ for self avoiding random walk, corresponding to polymer in a good solvent. The self avoiding case contradicts $\tau \sim N^2$.

Also, for long enough chains, the polymer shouldn’t have time to equilibrate at each step of it translocation. Equilibration time goes as $n^{1+2\nu}$ with the number of monomers outside on one of the sides of the membrane $n$. For ideal chain this gives $N^2$, making equilibrium at each step possible if not probable, and $N^{2.18}$ in the self avoiding case, resulting in equilibration slower than translocation.

Extrapolating the result of 2D Monte Carlo simulations, a $\tau \sim N^{1+2\nu}$ big $N$ behavior, good solvent was proposed (reflecting beginning, self avoiding chain, no external field). Later this result was supported in 3D by MD. Based on 3D lattice or off lattice Monte Carlo much higher scaling exponents have been proposed for the above system, reaching up to $\tau \sim N^{2+\nu} = N^{2.588}$. Diffusion time scaling longer than squared length means subdiffusive behavior.

I performed off-lattice Monte Carlo simulations equivalent to direct trial by transparent assumptions. The whole dynamics of the process was obtained this way as transition rates, and then $\tau$ was calculated. I obtained for the above described system a smaller scaling exponent limited only by $\tau \geq N^{2\nu+1}$ in Rouse model.

II. THE MODEL

I regard the mean translocation (or first passage) time $\tau$ of polymer through a hole in a flat membrane. I start with the first monomer passed, it cannot exit back (reflecting boundary conditions), and finish when one monomer is left not translocated. The membrane is thin
only $\sim 1$ monomer is in the pore, the others are outside. The hole is cylindrical and narrow, so the chain cannot enter folded, and in the theoretical fit, the monomer inside is assumed without degrees of freedom.

The polymer consists of $N$ beads. I use dynamic off-lattice Monte Carlo model close to the bead-spring model, which gives Rouse dynamics. Instead using springs, I just give some allowance for the distance between the nearest neighboring monomers. For the self avoidance I assume the bead is a hard sphere with radius that prevents self crossing. I pick a monomer at random and attempt to move it $\pm 0.5$ at each $x$, $y$, and $z$ direction simultaneously with uniform distribution of the probability. The move is rejected if it places the beads to close to (far from) one another or to the membrane, or accepted otherwise. This is equivalent to 0 or $\infty$ potential, or there are no attractive or repulsive interactions. $N$ such attempts are the unit of time (one MC step). No external field is applied - all the motion is completely stochastic by nature.

I regard self avoiding and phantom chains. For the self avoiding case the distance between two nearest neighbors is between $r_{min} = 0.5$, and $r_{max} = 0.7$. With respect to not nearest neighbors, and the membrane the bead is a hard sphere with radius 0.3, which makes the self crossing of the chain practically impossible. The membrane is 0.11 in thickness, so no additional care is needed for the polymer not to drift with no bead in the pore. A thicker membrane slows down the translocation. The pore is cylindrical with radius 0.4 -just a little bit bigger than the bead.

For the phantom polymers only nearest neighbors distance is controlled, self crossing is allowed. The distance between two nearest neighbors is again between $r_{min} = 0.5$, and $r_{max} = 0.7$. The membrane is 0.71 in thickness for the same reasons as above. The pore is cylindrical with radius 0.1.

I checked the two models by using a polymer of $n$ monomers with the first one fixed on the membrane surface. $\vec{r}$ connects the first and the last bead. First I compared the mean of the component of $\vec{r}$ in direction perpendicular to the membrane. Similarly to the bulk case this should give scaling as $n^\nu$. I also checked the equilibration time of such chain defined as the correlation coefficient between $\vec{r}$ and its initial position as a function of the time. As mentioned one expects scaling as $n^{1+2\nu}$. I did this for chains of $n = 294$ and $n = 6$ monomers for each model. For the phantom case I got $\nu \sim 0.5$ within our accuracy from the both tests, as expected. For the self avoiding case I got $\nu \sim 0.6$ from the distance test, and
$n^{2.3}$ as an approximation of $n^{1+2\nu}$ from the correlation test. Thus I overestimated a little bit the theoretical expectation of $\nu = 0.588$. Note that for similar polymer lengths similar scaling is reported for dynamical exponent\textsuperscript{22} as a reasonably close to the theoretical one (which should be observed when $n \to \infty$). The obtained exponents proof that the polymer is effectively in a good solvent.

The number of translocated monomers is the reaction coordinate $k$. I actually simulate the effective rates for the polymer to jump step monomer forwards or backwards. Then one can calculate the translocation time $\tau$ from (1) and (2). I use step = 6 monomers (unless otherwise specified). This is much (about a order of magnitude for the regarded systems) faster than to wait for a direct escape starting from the beginning. I start from $k = \tilde{k}$ and simulate till the chain reaches both $k = \tilde{n} + \text{step}$ and $k = \tilde{k} - \text{step}$ at least once. Than I start from $k = \tilde{n} + \text{step}$. The program keeps the configuration of the polymer when first reached translocation to $k = \tilde{k} + \text{step}$ and use it as the initial state when starting from the new $k = k + \text{step}$ state. I use (3) to calculate the effective rates $u_{m}^{\text{effective}}$ and $w_{m}^{\text{effective}}$.

I did 500 or more trials for every simulated point shown, unless otherwise mentioned.

I define $k = \tilde{k} \pm \text{step}$ or $\tilde{k}$ when the corresponding monomer is at the middle along it translocation in the pore. In the off-lattice MC monomers jump randomly, which introduce some error in defining the position. Reducing the relative error, a bigger step makes the result more accurate, but demands longer computer time.

Please note, that in this work I regard the mean translocation time. This is the case for most theoretical works and simulations. In experimental works the most probable passage time is measured. For theoretical works dealing with the shape of the translocation time distribution (not zero external field) see\textsuperscript{11,12,13}.

### III. THEORETICAL APPROACH

I use the formula for the mean time $\tau$ to first reach $b$ or $e$. Let’s $b$ is before $e$, and we start from $s$ between $b$ and $e$. For discrete 1D walk\textsuperscript{14,15},

$$
\tau(b-1,s,e+1) = \pi(b-1,s,e+1) \left( \sum_{k=b}^{e} \frac{1}{u_{k}} + \sum_{k=b}^{e-1} \frac{1}{u_{k}} \sum_{i=k+1}^{e} \prod_{j=k+1}^{i} \frac{w_{j}}{u_{j}} \right) - \left( \sum_{k=b}^{s} \frac{1}{u_{k}} + \sum_{k=b}^{s-2} \frac{1}{u_{k}} \sum_{i=k+1}^{s-1} \prod_{j=k+1}^{i} \frac{w_{j}}{u_{j}} \right)
$$

(1)
where
\[ \pi(b - 1, s, e + 1) = \frac{1 + \sum_{k=b}^{s} \prod_{j=b}^{k} w_j}{1 + \sum_{k=b}^{e} \prod_{j=b}^{k} w_j} \] (2)

is the probability starting at \( s \) to reach \( e + 1 \) before ever reaching \( b - 1 \). Above \( u_k \) is the rate per unit time to jump forwards from \( k \) to \( k + 1 \). \( w_k \) is the same but backwards from \( k \) to \( k - 1 \).

We also need the ansatz (see Fig. 1)

\[
\begin{align*}
\left. u \right|_{m} \text{effective} &= \frac{\pi(b_m, s_m, e_m)}{\tau(b_m, s_m, e_m)} \\
\left. w \right|_{m} \text{effective} &= \frac{1 - \pi(b_m, s_m, e_m)}{\tau(b_m, s_m, e_m)} \\
\small e_m &= s_{m+1}; \quad b_m = s_{m-1} \tag{3}
\end{align*}
\]

the last is consistent with the formula for mean first passage time, or if one uses \( u \left|_{m} \right. \text{effective} \), and \( w \left|_{m} \right. \text{effective} \) instead of \( u_k \), and \( w_k \) in Eqs.\( (1) \), one gets the same time. Note that the set of \( u \left|_{m} \right. \text{effective} \), and \( w \left|_{m} \right. \text{effective} \) should be less in number than the one of \( u_k \), and \( w_k \) in order \( (3) \) to be needed.

To estimate the rates theoretically I use:

\[
\begin{align*}
\left. u \right|_{k} &= \frac{\tilde{D}}{\Delta^2} \exp \left( \frac{F(k) - F(k + 1)}{2k_B T} \right) = \frac{\tilde{D}}{\Delta^2} \sqrt{\frac{Z_{k+1}}{Z_k}} \\
\left. w \right|_{k} &= \frac{\tilde{D}}{\Delta^2} \exp \left( \frac{F(k) - F(k - 1)}{2k_B T} \right) = \frac{\tilde{D}}{\Delta^2} \sqrt{\frac{Z_{k-1}}{Z_k}} \tag{4}
\end{align*}
\]

where \( \tilde{D} \) is the 1D diffusion constant if the distance traveled for a jump between 2 neighboring states is \( \Delta \). \( F(k) \) is the free energy at state \( k \). The factor of 2 in denominator insures the detailed balance between the neighboring states.

One may assume a smooth continuous along \( k \) potential and put additional states between the original ones, shortening \( \Delta \). One sees from \( (3) \) that \( \tilde{D} \) should be kept constant to reproduce \( u \left|_{m} \right. \text{effective} \) and \( w \left|_{m} \right. \text{effective} \) between the original states the same as the original rates if \( F \) is constant, and \( \Delta \to 0 \). This way one obtains from \( (4) \) and \( (1) \) the continuous limit for the case we start from state \( 0 \), with reflecting boundary conditions there (\( w_0 = 0 \)):

\[
\tau(0, 0, N)_{w_0=0} = \int_0^N dk \exp \left( \frac{F(k)}{k_B T} \right) \sum_{i=0}^k \frac{1}{D(i)} \exp \left( -\frac{F(i)}{k_B T} \right) \tag{5}
\]
For polymer of \( n \) segments attached at one of its end to a flat surface the partition function is:\(^{29}\)

\[
Z_n \sim n^{\gamma'-1}
\]  

(6)

Hence the entropic potential of our system has the form

\[
\frac{F(k)}{k_B T} = (1 - \gamma') \ln(k) + (1 - \gamma') \ln(N - M - k) + \text{const}
\]  

(7)

In the last equation \( M \) is the number of the monomers inside the pore, which is assumed without degrees of freedom. \( k \) is the number of translocated monomers or our reaction coordinate, and:

\[
\gamma' = \begin{cases} 
\frac{1}{2}; & \text{phantom chain} \\
0.69; & \text{self avoiding chain} \\
1; & \text{rigid rod}
\end{cases}
\]  

(8)

According to (1) and (7) our system have the symmetry:

\[
u_k = w_{N-M-k}
\]

\[
w_k = u_{N-M-k}
\]  

(9)

How we know\(^{6,7,8,10}\) (7) with (3) gives \( \tau(0,0,N-M)_{w_0=0} = C(N-M)^2 \) with \( C = \frac{\pi^2}{16D} \) for ideal chain.

IV. HOW EQUILIBRIUM IS THE TRANSLOCATION PROCESS?

I first use the data for phantom chain. How noted, the translocation process for them is expected to be closer to quasi equilibrium one. All the simulated data shown are fitted to the theory by one constant. I calculate and simulate the first exit time for the polymer starting with one base passed, which cannot reenter back - \( w_1 = 0 \) (reflecting boundary conditions), and finish at one monomer left - \( \tau(0,1,N-1-M)_{w_1=0} \). In all the data \( M = 1 \). Note that in this case the forward reaching probability \( \pi = 1 \) in (1).

In Fig. 2 is shown a fit of the effective forward rate \( u_m^{\text{effective}} \) for ideal polymer to jump \( \text{step} = 6 \) monomers forwards, \( N = 303 \). The theoretical values are calculated using (1), (7) and then (3) to get the effective value for \( \text{step} = 6 \) monomers. One sees almost perfect
agreement with quasi equilibrium theory. The simulated data for \( \tau(0, 1, N - 1 - M)_{w_1=0} \) as function of the number of the monomers in the chain - \( N \) are shown in the Fig. 3 for the case of ideal chain. Since the rates agree very well with theory, I simulate only half of them, than use their symmetry \( 9 \) to find the rest (and \( \tau(0, 1, N - 1 - M)_{w_1=0} \)). The slope goes down with \( N \), reaching \( N^{2.2} \). In this graph one sees again a very good agreement with the quasi equilibrium discrete process theory, given by \( 4 \), \( 7 \), and \( 1 \). I believe for bigger \( N \) the exponent will drop to 2.

The next question is if these data correspond to quasi equilibrium process. To estimate a lower limit of the equilibration time of a chain of \( n \) monomers anchored to the pore at one end, I use the correlation coefficient \( c(n, t) \):

\[
c(n, t) = \left( \frac{(\vec{r}(t) - \langle \vec{r} \rangle)(\vec{r}(0) - \langle \vec{r} \rangle)}{\sqrt{(\vec{r}(t) - \langle \vec{r} \rangle)^2(\vec{r}(0) - \langle \vec{r} \rangle)^2}} \right)
\]  

(10)

In the above definition \( \vec{r} \) is the vector from the end of the polymer fixed in the membrane (the pore) to it free end, and \( \langle \, \, \rangle \) means averaging over ensemble or over time which I assume equivalent. \( c(n, t) \) is correlation coefficient of the direction of \( \vec{r} \), hence it should vanish the same as or faster than the real memory of the whole chain. I did simulations for anchored chains of \( n = 294 \) and \( n = 6 \) monomers for both self avoiding and phantom models. The observed behavior is \( c(n, t) = \exp(-u_{\text{phantom}} t) \) where for \( n \to \infty \) one should have \( \omega = 1 + 2\nu \), and \( u \) is specific for each model. As noted for the phantom case I really have the big \( n \) value \( \omega = 2 \), while for the self avoiding model \( \omega = 2.3 \). Similar approach and results with slightly different correlation coefficient, and using lattice dynamics are reported\(^{30}\) for the same system. For the phantom case I show the times \( t_e(n) \) and \( t_{10}(n) \), (where \( c(n, t_e) = \frac{1}{e} \), and \( c(n, t_{10}) = \frac{1}{10} \)) in Fig. 4. Together are the mean time for the polymer to move step = 6, monomers forwards or backwards which are directly simulated, as well the mean lifetime the polymer to move one monomer left or right (which come as \( \frac{1}{w+u} \) from the theoretical values from \( 4 \), \( 7 \), also used to get the theoretical fit in Fig. 2). One sees that (with probable exception of near the center), there was not been a real equilibrium.

To see why in such case the data look like equilibrium again the phantom chain is used. In Fig.5 effective forward rate \( u^{\text{effective}}_m \) is given for the polymer to jump step = 6 monomers forwards, \( N = 303 \), and \( N = 807 \). This is the very beginning of the process (\( k \) close to 0). I also give the theoretical prediction for the rate with the same translocated number of polymers, but replacing the rest (non translocated end) of the chain with much shorter or
longer one (total number becomes \( N = 40 \), or \( N = 4000 \)). One sees, that this doesn’t change much the translocation rate. Or, if the monomers on one of the sides of the membrane have a counter part on the other of few tens of monomers or of few hundreds, this doesn’t change much the dynamics around the pore. It worths to mention, that (4) with (7) saturates to limiting values for the beginning of the process (or by (9) the end of the process) as \( N \) grows:

\[
\begin{align*}
    u_k &= \frac{\hat{D}}{\Delta^2} \left( \frac{k}{k+1} \right)^{\frac{1-x}{2}} \\
    w_k &= \frac{\tilde{D}}{\Delta^2} \left( \frac{k}{k-1} \right)^{\frac{1-x}{2}} \\
    k &- \text{ small}, \quad N \to \infty
\end{align*}
\]

So, I believe that the process is equilibrium for chains of few tens of monomers. In case of bigger chains, the ones close to the pore do not feel the rest of the chain more than few tens of monomers apart. In other words the rates are close to ones if everything greater than few tens monomers each side of the pore is cut. How suggested\cite{31,33} there is a partial equilibrium for the few tens of monomers close to the pore.

In Fig. 5 one also sees that \( u_{i, \text{effective}}^{\text{effective}} \) is consistently lower than the theoretical prediction. I interpret this fact as that there was a local equilibrium, and the rest of the monomers (not being equilibrated), just pull slightly backwards.

**V. DOES THE SELF AVOIDANCE KEEPS THE THEORY?**

Next I present data for self avoiding chain. Again they all are fitted with one constant. Due to the different lengths of the pores (thicknesses of the membranes), this constant is incompatible to the one for phantom chain.

In Fig. 6 are given the the effective forward rate \( u_{m, \text{effective}}^{\text{effective}} \) for the polymer to jump \( \text{step} = 6 \) monomers forwards for \( N = 75 \), and the same for \( \text{step} = 30 \) monomers forwards for \( N = 123 \). One may see that for the larger chain, there is some deviation from the theory. That is why I do not use (9), but rather simulate all the rates needed to calculate the translocation time. For the same reason, I also give in Fig. 7 times obtained by direct trials. One may observe the nearly perfect match between the theory, and the two ways of simulation. The translocation time \( \tau(0,1,N-1-M)_{w_1=0}, M = 1 \) ends up scaling as \( N^2 \). I conclude, that the hypothesis for local equilibrium next to the pore is still valid.
What violates slightly the theory is that the number of translocated monomers is not a perfect reaction coordinate. It doesn’t give all the information for the state of system, namely that the polymer is stretched when it just advances (see the next section).

VI. SHORT TIME DYNAMICS OF SELF AVOIDING POLYMER

The procedure described above (but with step = 2 which shortens the computation time) is used to thread a self avoiding polymer exactly to the position where the middle monomer is in the pore. Then I set the time to zero, and observe the further dynamics. The entropic potential is then zero, and doesn’t affect the process.

It is believed that for small enough times the dynamics is subdiffusive. The data for $SD^2$ of the displacement of the middle monomer along the pore really scale as $t^{0.7}$ for the range shown in Fig. 8, $N = 127$. Interestingly the $SD^2$ for the reaction coordinate $k$ scales linearly for this range. The displacement of the middle monomer along the pore also scales differently than the change of $k$. The author explains this with the stretching of the chain. Unfortunately very short time intervals are hardly accessible. In the off lattice Monte Carlo monomers jump to random positions, and for small times the error in defining $k$ will become compatible to it value.

Within the accuracy, there is no deviation from Gaussian distribution of the reaction coordinate $k$ at some fixed time after starting from the middle (for the range shown in Fig. 8). The last is in agreement with the lattice simulations described$^{30}$ where they have observed minute deviation far from the mean value for small times. This is also in agreement with the simulations$^{40}$, for phantom polymer in 1D. Deviation from Gaussian distribution in the middle - a non smooth cusp is predicted by the fractional diffusion equation, describing subdiffusion with diverging mean waiting times between the consecutive moves. So, my results are in parallel with the statement$^{40}$ that for the polymer translocation we may have a different type of subdiffusion.

The average shift of the reaction coordinate $k$ is shown in Fig. 8. One sees that the average position consistently goes back. That is why we didn’t get perfect agreement with the theory for $N = 123$. The reason is the accumulated tension in the chain. My results for the mean displacement of $k$ due to the relaxation of the over stretching confirm the tension relaxation exponent $\alpha = \frac{1+\nu}{1+2\nu}$ introduced in$^{32}$. The evolution of the $SD(k)$ is completely
diffusive for the times shown in Fig. 8 within our accuracy. In parallel with what I said the
dynamics is again local, $SD$ of $k$ is practically independent on $N$ - see Table 1. The data
for the average shift $k$ shown in Fig. 8 are less independent on $N$.

The author speculates that such dependence of the dynamics from the history is the
explanation of the subdiffusive behavior expected for longer chains.

VII. WHAT IS THE LONG CHAIN TRANSLOCATION TIME SCALING?

The last point is to check why the exponent is lower than the theoretical limit $\tau \geq N^{2\nu+1}$
for the Rouse dynamics. I performed a direct simulations (200 trials) for the self avoiding
polymer using pore much bigger than the polymer length (or practically absent). I did trials
for $N = 125$ and $N = 175$. In agreement with our equilibration times (using the correlation
coefficient (10)) the time scales as $N^{2.3}$. Comparing them with the self avoiding data for
normal pore shown on Fig. 7 they are $\sim 50$ times smaller. I estimated, that following such
behavior this time will surpass the one for the regular data for $N \sim 10^{12}$. In other words the
data are too far from the point where the the scaling $N^{1+2\nu}$ will become important. Let’s
note that it is hard to extrapolate the same physics for such big $N$. On the other hand, all
the simulation data (including the ones presented here ) start with larger exponent, which
goes down with increasing the $N$. Here an exponent lower than the limit for the Rouse
model is reached, which suggests that $\tau \sim \frac{N^{2\nu}}{D}$ is the real exponent. Also, Rouse model (and
hence MC) overestimates the hydraulic friction in $D$. For the real systems, $D \sim \frac{1}{N^{\nu}}$ (Zimm
exponent) which doesn’t contradict $\tau \sim N^{2}$. For arguments that the Zimm exponent may
not be valid for our problem, see$^{8,35}$.

VIII. ACKNOWLEDGMENTS

The author is grateful to Anatoly B. Kolomeisky for the support and for the useful
discussions.

* Electronic address: kotsev@mpip-mainz.mpg.de

1 C. Dekker, Nature Nanotechnology, 2, 209 (2007).
J. Heng, C. Ho, T. Kim, R. Timp, et al. Biophys. J., 87, 2905 (2004).
J.J. Kasianowicz, E. Brandin, D. Branton, and D.W. Deamer, Proc. Natl. Acad. Sci. USA 93, 13770 (1996).
A. Meller, J. Phys.: Cond. Matter 15, R581 (2003).
H. Lodish et al., Molecular Cell Biology, 4-th ed. (W.H. Freeman and Company, New York, 2000).
W. Sung and P. Park, Phys. Rev. Lett. 77, 783 (1996).
M. Muthukumar, J. Chem. Phys. 111, 10371 (1999).
J. Chuang, Y. Kantor, M. Kardar, Phys. Rev. E 65, 011802 (2001).
K. Luo, T. Ala-Nissila, S. Ying, J. Chem. Phys. 124, 034714 (2006).
E. Slonkina, A.B. Kolomeisky, J. Chem. Phys. 118, 7112 (2003).
R. Metzler and J. Klafter, Biophys. J. 85, 2776 (2003).
D. Lubensky and D. Nelson, Biophys. J. 77, 1824 (1999).
O. Flomenbom and J. Klafter, Phys. Rev. E 68, 041910 (2003).
N. G. van Kampen, Stochastic Processes in Physics and Chemistry, (Elsevier, Amsterdam, 1992).
P. Pury and M. Cáceres, J. Phys. A: Math. Gen. 36, 2695 (2003).
J. Mathè, A. Aksimentiev, D.R. Nelson, K. Schulten, and A. Meller, Proc. Natl Acad. Sci. USA 102, 12377 (2005).
Y. Lansac, P. Maiti, M, Glaser, Polymer 45, 3099 (2004).
S. Matysiak, A. Montesi, M. Pasquali, A.B. Kolomeisky, and C. Clementi, Phys. Rev. Lett. 96, 118103 (2006).
M. Muthukumar and C.Y. Kong, Proc. Natl Acad. Sci. USA 103, 5273 (2006).
S.-S. Chern, A.E. Càrdenas, and R.D. Coalson, J. Chem. Phys. 115, 7772 (2001).
A. Milchev, K. Binder, and A. Bhattacharya, J. Chem. Phys. 121, 6042 (2004).
I. Gerroff, A. Milchev, K. Binder, W. Paul, J. Chem. Phys. 98, 6526, (1993)
C. Kong, M. Muthukumar, Electrophoresis, 23, 2697, (2002).
P. Tian, G. Smith, J. Chem. Phys. 119, 11475, (2003).
R. Randel, H. Loebl, C. Matthai, Macromol. Theor. Simul., 13, 387, (2004).
H. Loebl, R. Randel, S. Goodwin, C. Matthai, Phys. Rev. E , 67, 041913, (2003).
J. Wolterink, G. Barkema, D. Panja, Phys. Rev. Lett., 96, 208301, (2006).
28 Y. Rabin, M. Tanaka, Phys. Rev. Lett. 94, 148103 (2005).

29 E. Eisenriegler, K. Kremer, K. Binder, J. Chem. Phys. 77, 6296, (1982).

30 D. Panja, G. Barkema, R. Ball, arXiv:cond-mat/0610671v2 [cond-mat.soft]

31 J. Dubbeldam, A. Milchev, V. Rostiashvili, T. Vilgis, Phys. Rev. E 76, 010801(R), (2007).

32 D. Panja, G. Barkema, R. Ball, J. Phys.: Cond. Matter, 19, 432202, (2007).

33 J. Dubbeldam, A. Milchev, V. Rostiashvili, T. Vilgis, EPL, 79, 18002, (2007).

34 M. Zwolak, M. Di Ventra, Rev. Modern Phys. 80, 141, (2008).

35 S. Guillouzic, G. Slater, Phys. Lett. A 359, 261, (2006).

36 M. Fytas, S. Melchionna, E. Kaxiras, S. Succi, Multiscale Model. Simul. 5, 1156 (2006)

37 D. Wells, V. Abramkina, A. Aksimentiev, J. Chem. Phys. 127, 125101, (2007)

38 K. Luo, T. Ala-Nissila, S. Ying, P. Pomorski, M. Karttunen, arXiv:0709.4615v3 [cond-mat.soft]

39 D. Wei, W. Yang, X. Jin, Q. Liao, J. Chem. Phys. 126, 204901, (2007)

40 Y. Kantor, M. Kardar, Phys. Rev. E 76, 061121 (2007).
| time | $N = 127$ | $N = 179$ | $N = 299$ |
|------|-----------|-----------|-----------|
| $10^4$ | 0.80 | 0.79 | 0.76 |
| $10^5$ | 2.6 | 2.6 | 2.7 |
| $10^6$ | 8.3 | 8.2 | 7.8 |

Table 1. The $SD(k)$ of a self avoiding polymer with time, due only to diffusion. $SD(k) = 0$ at $t = 0$. 
**Figure Captions:**

Fig 1. Using the effective rates $u_{\text{effective}}$ and $w_{\text{effective}}$ turns the system into equivalent one, consisting of smaller number coarse grained states.

Fig 2. Simulated and theoretical rates $u_{\text{effective}}$, $\text{step} = 6$ as function of the number of the monomers passed. The theoretical fit is done using quasi equilibrium approach.

Fig 3. Translocation time $\tau$ as a function of the length of the chain $N$. One monomer stays in the pore, process starts with one base passed, which cannot reenter back - $w_1 = 0$ (reflecting boundary conditions), and finish at one monomer left. The theoretical fit is done using quasi equilibrium theory for discrete states.

Fig 4. Equilibration time at one of the sides of the pore (thin lines) and the time to pass $\text{step}$ monomers during spontaneous translocation (thick lines). Upper thin lines is the time the correlation coefficient (10) to vanish down to $c(n, t) = \frac{1}{10}$, the lower thin line - the same for $c(n, t) = \frac{1}{e}$. Upper thick line is the average time the polymer of $N = 303$ needs to move $\text{step} = \pm 6$ monomers which is simulated to get $u_{\text{effective}}$ and $w_{\text{effective}}$, lower thick line - the same for $\text{step} = 1$. The diamonds are for $N = 807$ and $\text{step} = \pm 6$.

Fig 5. First few rates $u_{\text{effective}}$, $\text{step} = 6$ for big phantom chains. The lines are calculated, as the original polymer is replaced with one having much shorter non translocated tail (total length $N = 40$, upper curve), or much longer non translocated tail (total length $N = 4000$, lower curve). Quasi equilibrium discrete theory is used.

Fig 6. Simulated and theoretical rates $u_{\text{effective}}$ as function of the number of the monomers passed. The theoretical fit is done using quasi equilibrium approach. In the case of $N = 75$, $\text{step} = 6$ and the fit is good. In the case $N = 123$ $\text{step} = 30$, and we have performed only 200 trials. In the last data one sees a consistent deviation from the theory, due to the accumulation of tension in the chain. That is the reason that $\text{step} = 6$ cannot be used.

Fig 7. Translocation time $\tau$ as a function of the length of the chain $N$. One monomer stays in the pore, process starts with one base passed, which cannot reenter back - $w_1 = 0$ (reflecting boundary conditions), and finish at one monomer is left. The theoretical fit is
done using quasi equilibrium theory for discrete states. 3 of the times are simulated using average of 200 direct trials.

Fig 8. The polymer was threaded in using the procedure described in the text, $step = 2$, equivalent to spontaneous translocation. When the middle is reached, the further dynamics is observed, which is due entirely to the accumulated tension. The line corresponds to $t^\alpha$ with tension relaxation exponent $\alpha = \frac{1+\nu}{1+2\nu}$ as predicted by$^{32}$. 
Figure 1. Kotsev
Figure 2. Kotsev
Figure 3. Kotsev
Figure 4. Kotsev
Figure 5. Kotsev
Figure 6. Kotsev
Figure 7. Kotsev
Figure 8. Kotsev