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Velocity of polymer translocation through a pore

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Abstract

We theoretically study the translocation time and the mean velocity of a long polymer threading a long nanopore on an external electric field. Theoretical method, which explicitly takes into account the nucleation theory, is presented based on the built polymer expanded model. We overcame the previous theory's defect which did not consider the real length of the pore. The present model implies that the length scale of a pore plays a very important role in the process of polymer translocation. Our calculation results are in agreement with those of previous experiments.

Keywords: Polymer; Translocation time; Mean velocity; Polymer expanded model; Partition function

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Translocation of polymers across a narrow pore is ubiquitous in biology. Examples include the motion of DNA and RNA molecules across nuclear pores, the injection of viral DNA into a host cell, gene swapping through bacterial pili, DNA packaging into viral capsids, translocation of protein from cis to trans side of a membrane through channels, and involvement of the motion of biopolymers across membranes [1–3]. Alpha-hemolysin, which effectively creates an aqueous nanopore across a lipid membrane, can serve as a model system to study the dynamics of polymer translocation. Some mechanisms of polymer translocation have recently been getting great attention in numerous experimental studies [4–11]. All of these are helpful to understand the basic biological process and even develop a cheaper method of DNA sequencing.

The problem of chain molecule threading through a membrane is a complicated phenomenon. At present, most theoretical models suppose that the polymer chain is made of N monomers in order to explain these experimental findings, which provide useful insights for understanding the basic features of a polymer threading membrane. W. Sung and P.J. Park utilized the Fokker–Plank equation to study the Gaussian chain translocation dynamics through a pore embedded in a flat membrane where the monomer friction across the pore is proportional to the length scaling of the polymer [12–16]. M. Muthukumar dealt this process with nucleation theory [17–19]. G.F. Oster group used modified one-dimensional drift diffusion equation to build a Brownian ratchet mechanism for protein translocation [20,21]. Lubensky and Nelson also studied one-dimensional drift diffusion equations incorporating a simple model of monomer-pore interaction [22]. E.A. Di Marzio studied thermodynamic phase transitions for an isolated polymer molecule in the limitation of infinite molecular weight [23–25]. Pu. Tian carried out Brownian dynamics simulation study of the translocation of single polymer chain across a nanopore [26]. C.-M. Chen used off-lattice Monte-Carlo simulations to study the driven translocation dynamics of a polynucleotide chain through a nanopore [27]. A. Matsuyama theoretically studied the phase transitions of a polymer escaping from a pore based on the Flory theory of the coil-globule transitions of a single polymer chain [28–30]. Ambjörnsson et al. [31] took into account the nanopore length and studied both the polymer entrance into the pore and the translocation process. K.L. Sebastian viewed the polymer translocation as the motion of a kink, which travelled in the direction opposite to polymer

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transport [32]. And S. Chern's three-dimensional model illustrated that it is indeed impossible to capture many essential features of the translocation process by using an appropriate one-dimensional model [33]. And Y.J. Xie [34] used metropolis molecular dynamics simulation [35,36] combined with the bond-fluctuation method to study the dynamics process of single DNA chain through an entropic trapping channel driven by an electric force.

In this paper, we overcame the previous models' defect which employed the classic theory without considering the realistic length of the pore [3,17,18,30] in order to study the threading of polymer through a pore imbedded in a membrane on external electric field. Based on our polymer expanded model [37], we numerically calculated the overall time of polymer translocation and the velocity of chain through a pore, which is agreement with the previous result [5].

Materials and methods

Suppose a single long polymer with N monomers (each of size a) moves from region I to region III through a membrane pore of length $l_0(=n_0 a)$ and diameter D, as shown in Fig. 1. a is the length of each monomer. In realistic experiments [5], a, n_0 are equal to 4 and 12 Å, respectively. The monomer segments can be divided into region I, II, and III. The free energy of polymer can be derived from the classic nucleation theory [18]. Under the experimental condition, we suppose that the monomer cannot return when it enters into the pore in the external electric field. We simply assume that the interaction between the polymer and the pore can [illegible] ignored and chemical potential inside the pore is uniform. Let the chemical potential of the monomer in region I, II, and III be [illegible] and ε_3, respectively (see Fig. 1). In this paper, the process of translocation is assumed to start as soon as the leading monomer enters the pore and to end when the end of monomer leaves the pore. The whole process [illegible] be divided into process I, process II, and process III (see Fig. 1). We also assume the length of polymer to be much larger than the pore's, that is, $N > n_0$.

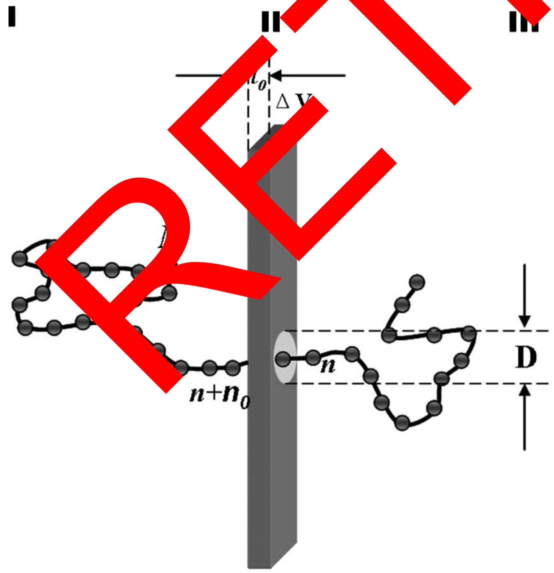

Fig. 1. Schematic representation of an N-monomer polymer in the process of translocation through a cylindrical nanopore of length l_0 and diameter D. n is the number of monomers on one side; n_0 is the number of monomers on the nanopore. ΔV is the potential energy (about 50–200 mV) in realistic experimental condition.

Consider the free energy associated with a translocation of a polymer of N monomer from region I to III. The free energy of the polymer chain can be expressed by

$$F = F_{\mathrm{I}} + F_{\mathrm{II}} + F_{\mathrm{III}}, \tag{1}$$

where F_{I}, F_{II}, and F_{III} are free energies of the polymer on region I, II, and III, respectively. Based on the partition function [3] and our analysis, the overall free energy of polymer is given by

$$F = \begin{cases} (1-\gamma_1')\beta^{-1}\ln(N-n) + n\Delta\varepsilon_{21} & 0 \leqslant n \leqslant n_0 \\ (1-\gamma_1')\beta^{-1}\ln(N-n) + (1-\gamma_2')\beta^{-1}\ln(n-n_0) & \\ +(n-n_0)\Delta\varepsilon_{31} & n_0 < n \leqslant N-1 \\ (1-\gamma_2')\beta^{-1}\ln(n-n_0) + (n-n_0)\Delta\varepsilon_{32} & N \leqslant n \leqslant N+n_0 \end{cases} \tag{2}$$

The first term is the entropic contribution due to the $(N-n)$ free monomers in region I. The second represents the energy gained by moving n monomers into the pore, including the effect of the external field and chemical changes. $\beta^{-1} = k_{\mathrm{B}}T$, where k_{B} is the Boltzmann constant and T is absolute temperature. $\gamma_1'\gamma_2'$, the parameter describing the properties of end-anchored polymer chains in region I, II, is equal to 0.5, 0.69, and 1 for Gaussian, self-avoiding, and rod-like chains, respectively [3]. $\Delta\varepsilon_{21} = \varepsilon_2 - \varepsilon_1$, $\Delta\varepsilon_{31} = \varepsilon_3 - \varepsilon_1$, and $\Delta\varepsilon_{32} = \varepsilon_3 - \varepsilon_2$ are the chemical potential difference per monomer that will depend on the type of monomer. Seen from (2), F exhibits a free energy barrier of the polymer, which depends on the conformational statistics of polymer chain and the values of the chemical potential ε_1, ε_2, and ε_3.

The overall free energy is not a continuous function for the parameter n, the result is shown in Fig. 2 with our assumption: $N = 100$, $n_0 = 12$ for free energy. When $\Delta\varepsilon_{21} = \Delta\varepsilon_{21} = \Delta\varepsilon_{21} = 0$, $\gamma_1' = \gamma_2' = 0.5$, the free energy is symmetric in the whole polymer translocation process, see Fig. 2. But, the barrier becomes asymmetric if $\Delta\varepsilon \neq 0$. The chemical potential difference is crucial for determining the tendencies of polymer free energy. This is illustrated in Fig. 2. When the leading monomer reaches the region III and the end of monomer escapes from the region I, the free energy of polymer has a transition, which illustrates that the structure of polymer has undergone a large transformation.

It is necessary for us to evaluate the mean translocation time from the previous experiments [4–11]. Following the nucleation theory [38], the transport of the polymer across the nanopore can be described by a Master equation [17]

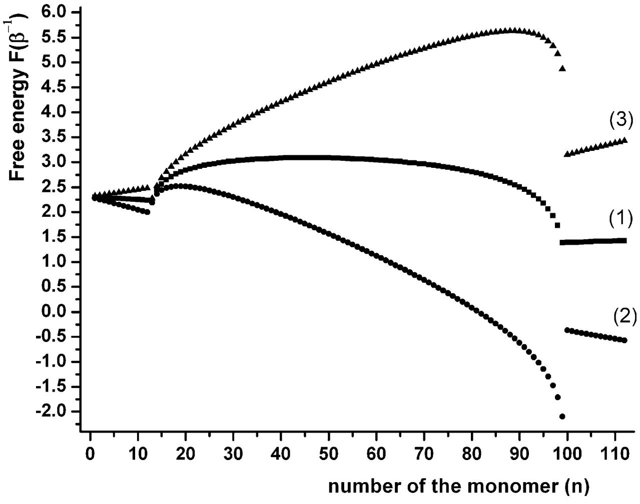

Fig. 2. Plot of F in unit of β^{-1} against n. (1) $N = 100$, $n_0 = 12$, $\gamma_1' = \gamma_2' = 0.5$, $\Delta\varepsilon_{21} = \Delta\varepsilon_{21} = \Delta\varepsilon_{21} = 0$, (2) $N = 100$, $n_0 = 12$, $\gamma_1' = \gamma_2' = 0.5$, $N\beta\Delta\varepsilon_{21} = N\beta\Delta\varepsilon_{32} = -2$, $N\beta\Delta\varepsilon_{31} = -4$, and (3) $N = 100$, $n_0 = 12$, $\gamma_1' = \gamma_2' = 0.5$, $N\beta\Delta\varepsilon_{21} = N\beta\Delta\varepsilon_{32} = 2$, $N\beta\Delta\varepsilon_{31} = 4$.

$$\frac{\partial}{\partial t}P_n(i,t) = k_{n-1}P_{n-1}(i,t) - k'_nP_n(i,t) - k_nP_n(i,t) + k'_{n+1}P_{n+1}(i,t), \tag{3}$$

where $P_n(i, t)$ is the probability of emerging a "core" of n segments in region i = I, II or III at time t. k_n is the rate constant associated with the local friction in transferring one monomer through the hole so that a nucleus of n monomers grows into $n + 1$ monomers, and k'_n is the rate constant of removing one monomer from the n monomers. Here, we assume that the rate constant k_n is independent of n and can be indicated by the ratchet potential arising from the details of the pore. Following the Fokker–Planck Equation [H. Riskin, The Fokker–Planck Equation (Springer-Verlag, Berlin, 1984)] and Smoluchovskii equation [39], therefore, we obtain,

$$\frac{\partial}{\partial t}P_n(i,t) = \frac{\partial}{\partial n}\left[k_n\beta\frac{\partial F_{n,i}}{\partial n}P_n(i,t) + k_n\frac{\partial}{\partial n}P_n(i,t)\right], \tag{4}$$

where the first term is polymer drift contribution. When the first term in this (11) dominates the problem, the mean translocation time τ can be driven as a sum of mean first-passage times in each region, that is, $\tau = \tau_{\mathrm{I}} + \tau_{\mathrm{II}} + \tau_{\mathrm{III}}$. τ_{I}, τ_{II}, and τ_{III} are mean first-passage times in region I, II, and III, respectively. The translocation time can be expressed by

$$\begin{aligned}\tau =& K_0\int_0^{n_0}\mathrm{d}m\exp(\beta F_{m,\mathrm{I}})\int_0^m\mathrm{d}n\exp(-\beta F_{n,\mathrm{I}}) + K_0\int_{n_0}^{N}\mathrm{d}m\exp(\beta F_{m,\mathrm{II}})\\ &\times\int_0^m\mathrm{d}n\exp(-\beta F_{n,\mathrm{II}}) + K_0\int_N^{N+n_0}\mathrm{d}m\exp(\beta F_{m,\mathrm{III}})\int_0^m\mathrm{d}n\exp(-\beta F_{n,\mathrm{III}}).\end{aligned} \tag{5}$$

Here, we assume that $k_i = K_0^{-1}$ (i = I, II, III) is taken to be a nonuniversal constant independent N. As clearly seen from the Ref. [17,18], the potential chemical difference controls the polymer translocation time τ.

For simplicity, if the chemical potential gradient is absent, that is, $\Delta\varepsilon_{21} = \Delta\varepsilon_{31} = \Delta\varepsilon_{32} = 0$, the exact expression of the translocation time $\tau(=\tau_{\mathrm{I}} + \tau_{\mathrm{II}} + \tau_{\mathrm{III}})$ can be obtained from:

$$\begin{aligned}\tau =& \frac{K_0(N+n_0)^2}{\gamma'_1}\left[\frac{\left(\frac{N}{N+n_0}\right)^{\gamma'_1} - \left(\frac{N}{N+n_0}\right)^2}{(2-\gamma'_1)\left(\frac{N}{N+n_0}\right)^{\gamma'_1}} - \frac{1-\left(\frac{N}{N+n_0}\right)^2}{2}\right] + \text{[illegible]}\\ &+ \frac{K_0(N+n_0)^2}{2-\gamma'_2}\left[\frac{1-\left(\frac{N}{N+n_0}\right)^{\gamma'_2}}{\gamma'_2} - \frac{1-\left(\frac{N}{N+n_0}\right)^2}{2}\right].\end{aligned} \tag{6}$$

Here, a is a constant depending on [illegible] and [illegible] which is equal [illegible] 0.5 for the special case of $\gamma'_1 = \gamma'_2 = 0.5$. From this equation, we know that the polymer entering the long pore is more difficult than that entering the short pore and the longer the polymer is, the shorter the translocation time of process III is, which are [illegible] agreement with the previous result [40]. Supposing the length of the translocated pore is variable for a given polymer. Fig. 3 illustrates the translocation time against the pore length n under this condition. We can draw a conclusion that the length of the pore determines the polymer translocation process to some degree.

Under the experimental condition, we assume that the polymer is to start as soon as the [illegible] monomer of the polymer enters the pore and to end when the end monomer escapes the pore. If we consider that the translocation time was measured only when a current passing through the pore dropped [illegible] a level below 65% of an open channel current in the experiments of Meller et al. [5] So, based on considering the translocation process starting when 35% of the polymer entered into the pore and ending when only 35% of the polymer was left in the pore, the whole translocation time can be expressed by being based on the polymer expansion model [37]

$$\tau = \beta^{-1}\left(\frac{0.30n_0}{k_{\mathrm{I}}|\Delta\varepsilon_{21}|} + \frac{N}{k_{\mathrm{II}}|\Delta\varepsilon_{31}|} + \frac{0.30n_0}{k_{\mathrm{III}}|\Delta\varepsilon_{32}|}\right), \quad (N > n_0). \tag{7}$$

Here, we use 0.30 n_0, $N + 0.3$ n_0 instead n_0 and $N + n$, respectively. So the polymer translocation velocity is given by

$$\bar{v} = (N + 0.30n_0)a\beta\left(\frac{0.30n_0}{k_{\mathrm{I}}|\Delta\varepsilon_{21}|} + \frac{N}{k_{\mathrm{II}}|\Delta\varepsilon_{31}|} + \frac{0.30n_0}{k_{\mathrm{III}}|\Delta\varepsilon_{32}|}\right)^{-1}. \tag{8}$$

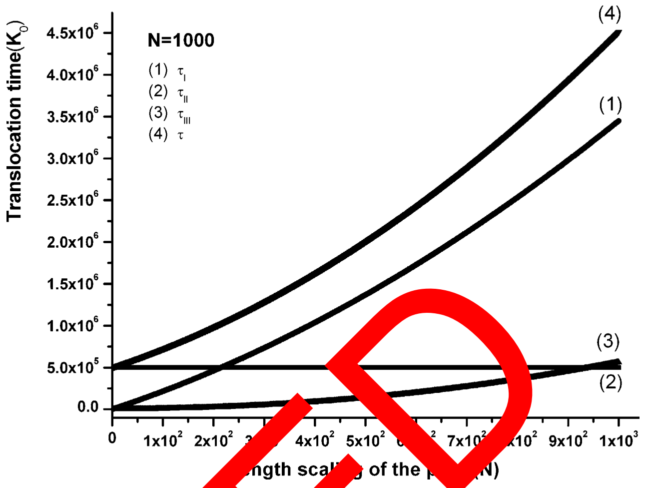

Fig. 3. Translocation time in unit of K_0 against the pore length n. $N = 1000$, $\gamma'_1 = \gamma'_2 = 0.5$.

In order to compare our theoretical predictions with the experimental data [5], we use this equation to fit the experiment data, see the curve (3) in Fig. 4. Curve (2) in Fig. 4 is the modified equation picture and curve (1) is the original equation picture, that is, the expanded length of the polymer is $N + n_0$. We assume that the total length of polymer and pore is 100a and 12a, respectively. And the monomer size is given by $a = 4$ Å. The fitted curve indicates that $\Delta\varepsilon_{21} = \Delta\varepsilon_{32} = 2.9\ \beta^{-1}$, $\Delta\varepsilon_{31} = 5.8\ \beta^{-1}$, $k_{\mathrm{I}} = k_{\mathrm{III}} = 2.2 \times 10^7$ [illegible], $k_{\mathrm{II}} = 1.58 \times 10^4$ μs. This predicts that for long polymers the translocation velocity approaches a constant value and the velocity increases remarkably with decreasing polymer length, which is in excellent qualitative and quantitative agreement with experiments whenever [illegible] modified model and original model.

Discussion

In this paper, a simple model of polymer threading through a long pore was presented on the external electric fields. We have derived explicit expression for the translocation time and the mean velocity of polymer translocation across a pore without considering the interaction between the polymer and the pore and the fluctuation of the

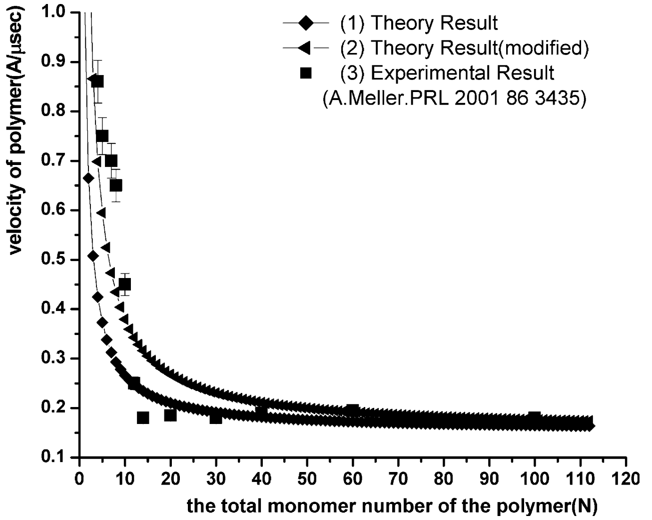

Fig. 4. Translocation velocities as a function of polymer size, the filled squares being experimental data from Ref. [5] at an external field of 120 mV.

chemical potential inside the pore. Both the length scaling of polymer and pore are crucial factors for dynamics of polymer translocation. The original theoretical model and modified theoretical model predict the mean velocity of polymer translocation for experimental condition. It is found that short polymers move faster than long polymers whose velocity is nearly constant, which is in excellent agreement with previous experiments results qualitatively and quantitatively.

We have provided a reasonable model for polymer translocation, but there are many factors that have not been considered in this paper, such as interaction between the polymer and the pore, temperature of the solvent, electrostatic interaction, and realistic geometry of pore. We hope that our results encourage further experimental and analytical studies of forced translocation including these factors. In particular, how to control the polymer velocity is helpful to develop new DNA sequencing methods.

Acknowledgments

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References

[1] H. Lodish et al., Molecular Cell Biology, thi[illegible] ed., [illegible]ientific American Books, New York, 1995.

[2] B. Alberts, Molecular Biology of the Cell, Ga[illegible]d Publi[illegible] York, 1994.

[3] R. Eisenriegler, Polymers Near Surfaces, W[illegible]d Scientific, [illegible]gapore, 1993.

[4] A. Aksimentiev, J.B. Heng, G. T[illegible] K. Schulten, [illegible]icroscopic kinetics of DNA translocation thr[illegible]gh sy[illegible]etic nanopores, [illegible]iophys. J. 87 (2004) 2086–2097.

[5] A. Meller, L. Nivon, D. Bra[illegible]on, Voltage-drive[illegible]NA translocations through a nanopore, Ph[illegible] Rev. Lett. 86 (2001) 3[illegible]5–3438.

[6] L. Movileanu, H. Bay[illegible], Partitio[illegible]g of a polymer into a nanoscopic protein pore obeys a si[illegible]le scal[illegible]g law, Proc. Natl. Acad. Sci. USA 98 (2001) 10137–10141.

[7] S. Howorka[illegible]ileanu, [illegible] Braha[illegible]. Bayley, Kinetics of duplex formation[illegible]or indi[illegible]dual D[illegible]ands within a single protein nanop[illegible], Proc. Na[illegible]. Acad. Sci. [illegible]SA 98 (2001) 12996–13001.

[8] A. Mel[illegible]L. Ni[illegible]lin, J. Golovchenko, D. Branton, Rapid nanopore [illegible]ination between single polynucleotide molecules, Proc. Natl. A[illegible]d. Sci. USA 97 (2000) 1079–1084.

[9] S.E. Henrickso[illegible]M. Misakian, B. Robertson, J.J. Kasianowich, Driven DNA tran[illegible]ort into an asymmetric nanometer-scale pore, Phys. Rev. Lett. 85 (2000) 3057–3060.

[10] J.J. Kasianowich, E. Brandin, D. Branton, D.W. Deamer, Characterization of individual polynucleotide molecules using a membrane channel, Proc. Natl. Acad. Sci. USA 93 (1996) 13770–13773.

[11] M. Akeson, D. Branton, J.J. Kasianowich, E. Brandin, D.W. Deamer, Microsecond time-scale discrimination among polycytidylic acid, Biophys. J. 77 (1999) 3227–3233.

[12] W. Sung, P.J. Park, Polymer translocation through a pore in a membrane, Phys. Rev. Lett. 77 (1996) 783–786.

[13] P.J. Park, W. Sung, Dynamics of a polymer surmounting a potential barrier: the Kramers problem for polymers, J. Chem. Phys. 111 (1999) 5259–5266.

[14] P.J. Park, W. Sung, A stochastic model of polymer translocation dynamics through biomembranes, Int. J. Bifurcat. Chaos. 8 (1998) 927–931.

[15] P.J. Park, W. Sung, Polymer release out of a spherical vesicle through a pore, Phys. Rev. E 57 (1998) 730–734.

[16] P.J. Park, W. Sung, Polymer translocation induced by adsorption, J. Chem. Phys. 108 (1998) 3013–3018.

[17] M. Muthukumar, Polymer translocation through a hole, J. Chem. Phys. 111 (1999) 10371–10374.

[18] M. Muthukumar, Translocation of a confined polymer through a hole, Phys. Rev. Lett. 86 (2001) 3188–3191.

[19] M. Muthukumar, Polymer escape throu[illegible]opore, J. Chem. Phys. 118 (2003) 5174–5184.

[20] S.M. Simon, C.S. Peskin, G.F. Oste[illegible]What drives th[illegible]ranslocation of proteins? Proc. Natl. Acad. Sci. U[illegible]89 (1992) 377[illegible]774.

[21] C.S. Peskin, G.M. Odell, G.F[illegible]ster, C[illegible]lar motion[illegible]nd thermal fluctuations: the Brownian[illegible]chet, Biophys[illegible]65 (1[illegible]) 316–324.

[22] D.K. Lubensky, D.R. N[illegible]on, Drive[illegible]polymer[illegible]ocation through a narrow pore, Biophy[illegible]. 77 (19[illegible]) 1824–1838.

[23] E.A. Di Marzio, A[illegible] Ma[illegible]ell[illegible]hase transi[illegible]n behavior of a linear macromolecule[illegible]reading a[illegible]mbrane, [illegible]Chem. Phys. 107 (1997) 5510–5514.

[24] E.A. Di M[illegible]zio, [illegible]e ten classes o[illegible]lymeric phase transitions: their use as models for se[illegible]ssembly, Prog. Polym. Sci. 24 (1999) 329–377.

[25] E.A[illegible]Di Marzio, J.J.[illegible]asianowicz, Phase transitions within the i[illegible]ated polymer molecu[illegible]coupling of the polymer threading a [illegible]embrane transition to the helix-random coil, the collapse, the [illegible]dsorption, an[illegible]e equilibrium polymerization transitions, J. Chem. [illegible]hys. 119 (2003[illegible]378–6387.

[26] [illegible]Tian, G.D.[illegible]mith, Translocation of a polymer chain across a na[illegible]ownian dynamics simulation study, J. Chem. Phys. 119 (2003) [illegible]–11483.

[2[illegible]M. Chen, Driven translocation dynamics of polynucleotides thro[illegible]h a nanopore: off-lattice Monte-Carlo simulations, Physica A 350 (2005) 95–107.

[28] A. Matsuyama, Phase transitions of a polymer escaping from a pore, J. Phys.: Condens. Matter 17 (2005) S2847.

[29] A. Matsuyama, Phase transitions of a polymer threading a membrane coupled to coil-globule transitions, J. Chem. Phys. 121 (2004) 604–608.

[30] A. Matsuyama, Kinetics of polymer translocation through a pore, J. Chem. Phys. 121 (2004) 8098–8103.

[31] T. Ambjörnsson, S.P. Apell, Z. Konkoli, E.A. Di Marzio, J.J. Kasianowicz, Charged polymer membrane translocation, J. Chem. Phys. 117 (2002) 4063–4073.

[32] K.L. Sebastian, A.K.R. Paul, Kramers problem for a polymer in a double well, Phys. Rev. E 62 (2000) 927–939.

[33] S. Chern, E. Cárdenas, D. Coalson, Three-dimensional dynamic Monte Carlo simulations of driven polymer transport through a hole in a wall, J. Chem. Phys. 115 (2001) 7772–7782.

[34] Y.J. Xie, Q.W. Shi, X.P. Wang, P.P. Zhu, H.Y. Yang, X.Y. Zhang, Simulation of translocation of long DNA chain through an entropic trapping channel, Acta Phys. Sin. 53 (2004) 2796–2800.

[35] Y.L. Li, C.L. Luo, Tight-binding molecular dynamics simulation: the structure and stability if Si60 cluster, Acta Phys. Sin. 51 (2002) 2589–2593.

[36] X.R. Zhang, Z.G. Shen, J.F. Chen, W.C. Wang, Adsorption of linear ethane molecules in MCM-41 by molecular simulation, Acta Phys. Sin. 52 (2003) 163–167.

[37] K.J. Ding, D.Q. Cai, F.R. Zhan, L.J. Wu, Y.J. Wu, Z.L. Yu, Long polymer translocation through a long pore, Chin. Phys. (final review).

[38] E.M. Lifshitz, L.P. Pitaevskii, Physical Kinetics, Pergamon, New York, 1989.

[39] N. Ithaca, M. Doi, S.F. Edwards, The Theory of Polymer Dynamics, Clarendon, Oxford, UK, 1986.

[40] J. Han, S.W. Turner, H.G. Craighead, Entropic trapping and escape of long DNA molecules at submicron size constriction, Phys. Rev. Lett. 83 (1999) 1688.