Phase transitions of a polymer escaping from a pore

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Abstract
We theoretically study 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. We take into account the radius of the pore and the polymer–
pore interaction and predict a first-order escape transition coupled to the
conformational change of the polymer chain. We also study the kinetics of
the polymer under an external electric field based on Langevin equations. The
translocation time t_t is predicted to be $\propto n^{1+\nu}$ for a large number n of polymer
segments, where ν is the radius of gyration exponent. The exponent of the
translocation time decreases with increasing the electric field.

1. Introduction

Translocation of a polymer escaping from a pore plays an important role for many biological
processes and for technological applications. For example, protein transport through channels
in a biological membrane, the motion of DNA across a pore into the cell nucleus, and size
exclusion chromatography are a few examples where a polymer escapes from a pore.

The problems of a polymer escaping through a pore have recently received great attention
in experimental [1–5] and theoretical [6–19] studies. *In vitro* experiments show that DNA
polymers can be driven through nanopores by an external electric field [1–3]. Many theoretical
studies focus on solving Fokker–Plank equations which give some physical pictures about the
translocation time through a pore [7–9]. The deformation of a polymer that is compressed
between two planar plates has also been discussed as escape transitions of an end-tethered ideal
chain [20–22]. When the size of the pore is large, the polymer remains a state of confinement
within the pore. On decreasing the width of a pore, the number of the conformations of the
polymer can produce an entropy force tending to pull the chain out of the pore. Therefore it is
important to understand the escape processes in terms of some variables such as a pore size,
length of a polymer, and external fields.

In this paper we study escape processes of a polymer chain coupled to the conformational
change of the polymer and address how the size of a pore, the length of a polymer, the interaction
between the pore and polymer, and the electric fields affect the escape processes. Based on
the Flory model for coil–globule transitions of a single polymer chain, we predict a first-order
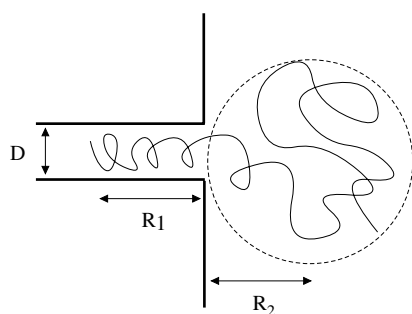
Figure 1. A polymer molecule consisting of n monomers is escaping from a long pore. As the diameter D of the pore is decreased, the chain inside the pore is compressed.

phase transition between an imprisoned state, where the polymer segments are completely included into the pore, and an escaped state, where the polymer segments are divided both into the pore and solution. We also study the kinetics of a polymer escaping from a pore under an external field based on Langevin equations and find some scaling behaviours. The problems addressed here provide valuable insight into the physics of DNA confinement in structures with biological relevant length scale [1–3].

2. Free energy of a polymer escaping from a pore

Consider a polymer escaping from a long square pore, as pictured in figure 1. To derive the equilibrium state of the polymer we first consider the thermodynamics of our system, based on the Flory–Huggins theory for polymer solutions [24].

Let n be the number of polymer segments, and n_1 and n_2 the number of segments inside (side 1) and outside (side 2) the pore, respectively. We then have $n = n_1 + n_2$. As the diameter D of the pore is decreased, the chain is compressed and the chain inside the pore has a dimension of R_1 along the pore (z direction). Its dimensions in the x and y directions are bound to D. Let R_2 be the mean radius of the occupied region of the polymer segments outside the pore. Then the volume fraction of the polymer segments inside the pore is given by

$$\phi_1 = \frac{(4\pi/3)a^3 n_1}{D^2 R_1},\tag{1}$$

and the volume fraction of the segments in the sphere of radius R_2 is given by

$$\phi_2 = \tfrac{4}{3}\pi a^3 n_2/(\tfrac{4}{3}\pi R_2^3) = a^3 n_2/R_2^3,\tag{2}$$

where $(4/3)\pi a^3$ corresponds to the volume of a unit segment on the polymer. We here define the expansion factors of the chain inside the pore as $\alpha_x = \alpha_y = D/R_{0,1}$ and $\alpha_z = R_1/R_{0,1}$, where $R_{0,1} = a\sqrt{n_1}$ is the radius of gyration of the ideal chain with n_1 segments. The expansion factor of the polymer outside the pore is given by $\alpha_2 = R_2/R_{0,2}$, where $R_{0,2} = a\sqrt{n_2}$ is the radius of gyration of the ideal chain with n_2 segments. Using these expansion factors, the volume fractions are then given by $\phi_1 = (4\pi/3)/(\alpha_x^2 \alpha_z \sqrt{n_1})$ and $\phi_2 = 1/(\alpha_2^3 \sqrt{n_2})$. The expansion factor α_x is also given as a function of n_1: $\alpha_x = (D/R_0)\sqrt{n}/\sqrt{n_1}$, where $R_0 = a\sqrt{n}$ is the radius of gyration of the ideal chain with n segments. The fraction D/R_0 is an important parameter which characterizes the pore size.

The free energy of the polymer chain is given by

$$F = F_1 + F_2,\tag{3}$$

where F_1 (F_2) represents the free energy of the polymer on side 1 (side 2). The free energy of the polymer inside the pore is given by

$$F_1 = F_{1,el} + F_{1,mix} + F_{int}, \tag{4}$$

where $F_{1,el}$ represents the elastic free energy due to the deformation of the segment distribution from the ideal state. This free energy is given by Flory [24]:

$$\beta F_{1,el} = \tfrac{1}{2}(\alpha_x^2 + \alpha_y^2 + \alpha_z^2 - 3) - \ln \alpha_x \alpha_y \alpha_z, \tag{5}$$

where $\beta \equiv 1/k_B T$, T is the absolute temperature, and k_B is the Boltzmann constant. The second term in equation (4) represents the free energy for a mixing of a polymer chain with solvent molecules inside the pore, and is given by [24]

$$\beta F_{1,mix} = \frac{n_1}{\phi_1}[(1 - \phi_1) \ln(1 - \phi_1) + \chi \phi_1 (1 - \phi_1)], \tag{6}$$

where χ represents the Flory–Huggins interaction parameter between a polymer segment and a solvent molecule. The translational entropy term $(\phi_1/n) \ln \phi_1$ of the polymer chain can be neglected since the centre of gravity of the polymer is fixed near a pore in a thermal equilibrium state. The pre-factor n_1/ϕ_1 is the total number of unit cells of the pore. The free energy F_{int} in equation (4) is given by $\beta F_{int} = \beta \epsilon_0 n_1 = \beta \epsilon_0 (n - n_2)$, where ϵ_0 represents the polymer–pore interaction energy.

The free energy F_2 of the polymer outside the pore is given by $F_2 = F_{2,el} + F_{2,mix}$, where $F_{2,el}$ represents the elastic free energy due to the deformation of the segment distribution from the ideal state, and is given by [24]

$$\beta F_{2,el} = 3[\tfrac{1}{2}(\alpha_2^2 - 1) - \ln \alpha_2], \tag{7}$$

and the free energy for a mixing of a polymer with solvent molecules on side 2 is given by

$$\beta F_{2,mix} = \frac{n_2}{\phi_2}[(1 - \phi_2) \ln(1 - \phi_2) + \chi \phi_2 (1 - \phi_2)], \tag{8}$$

where the pre-factor n_2/ϕ_2 is the total number of unit cells in the sphere of the radius R_2.

In a thermal equilibrium state, the expansion factors α_i ($i = z, 2$) and the fraction n_2 are determined by minimizing the free energy (3) with respect to α_i and n_2: $(\partial F/\partial \alpha_2)_{\alpha_z,n_2} = 0$, $(\partial F/\partial \alpha_z)_{\alpha_2,n_2} = 0$, and $(\partial F/\partial n_2)_{\alpha_z,\alpha_2,} = 0$,

Figure 2 shows the numerical results of the number n_2 of polymer segments outside the pore (a), the expansion factor α_2 (b), and α_z (c) as a function of the confinement width D/R_0 for $n = 100$ and $\chi = 0$ (good solvent conditions). The interaction parameter $\epsilon \equiv \beta \epsilon_0$ between the polymer segment and pore is changed. The dashed curves show the unstable regions. For larger values of D/R_0, most polymer segments are inside the pore. On decreasing the width D of the pore, the polymer segments suddenly escape from the pore to the solution. We predict a first-order phase transition between an imprisoned state, where the polymer segments are completely included into the pore, and a partially escaped state, where the polymer segments are divided into the pore and solution. On increasing ϵ, the phase transition point shifts to smaller values of D, since the attractive interaction between the pore and polymer segments becomes strong. The width of the jump in n_2 becomes larger with increasing ϵ.

3. Kinetics of a polymer escaping from a pore

We next consider the kinetics of a polymer escaping from a pore by using our free energy function (3). We also take into account the effects of an external electric field acting on a polymer chain which has an electric charge q. The dynamics of the escape processes of polymer segments can be describe by Kramer's model [23] for a chemical reaction consisting
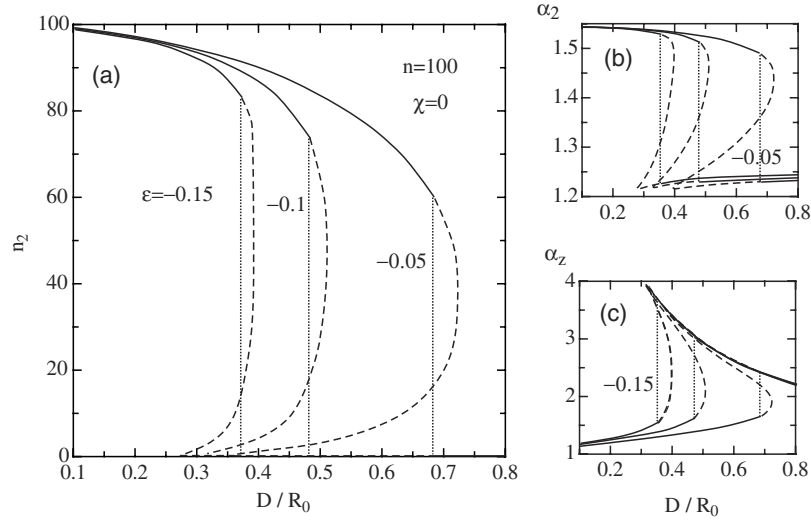
Figure 2. Numerical results of the number n_2 of polymer segments outside the pore (a), the expansion factor α_2 (b), and α_z (c) as a function of the confinement width D/R_0 for $n = 100$ and $\chi = 0$. The interaction parameter $\epsilon \equiv \beta\epsilon_0$ between a polymer segment and a pore is changed.

of a classical particle moving in a one-dimensional asymmetric double-well potential. The particle coordinate x corresponds to the number n_2 of polymer segments that have escaped from a pore. At a temperature T, the dynamics of a polymer escaping from a pore is described by a fluctuating force $\xi(t)$ and by a linear damping force $-\gamma\dot{n}_2$, where γ is a friction constant. These forces enter Newton's equation of motion in the form of a Langevin equation

$$\frac{\partial^2 n_2}{\partial t^2} = -\frac{\partial F}{\partial n_2} - \gamma\frac{\partial n_2}{\partial t} + \xi(t) + qE, \tag{9}$$

where the fluctuating force $\xi(t)$ denotes Gaussian white noise with zero mean, which obeys the fluctuation–dissipation theorem $\langle\xi(t)\rangle = 0$, and $\langle\xi(0)\xi(t)\rangle = 2\gamma k_B T\delta(t)$. The friction constant γ is given by $\gamma = 6\pi\eta R_2$, where η represents the viscosity of a solvent [25]. The gyration radius R_2 of the polymer chain on side 2 is given by $R_2/a = \alpha_2\sqrt{n_2}$ as a function of n_2 and α_2. The friction constant γ is then changed with time in our model. The last term represents the Coulomb force acting to the polymer chain of an electric charge q under an external electric field E.

We also need the kinetic equations for the expansion factors α_2 and α_z. The relaxation process can be described by the following Lagevin equations:

$$\gamma_1\frac{\partial\alpha_z}{\partial t} = -\frac{\partial F}{\partial\alpha_z} + \xi_1(t), \tag{10}$$

$$\gamma_2\frac{\partial\alpha_2}{\partial t} = -\frac{\partial F}{\partial\alpha_2} + \xi_2(t), \tag{11}$$

where we assume that the friction constants γ_1 and γ_2 are constant ($6\pi\eta a$).

In our numerical calculations, we focus on the case of $n = 100$, $\chi = 0$, and $\epsilon = -0.05$ for a typical example. The equilibrium properties are shown in figure 2. As most polymer segments exist inside the pore at the initial stage, we put $n_2 = 1$, $n_1 = n - n_2$, $\alpha_2 = 1.1$, and $\alpha_z = 1.1$. To derive time evolutions of a polymer escaping from a pore at a given confinement width D/R_0, we numerically solve the three coupled Langevin equations (9), (10), and (11).
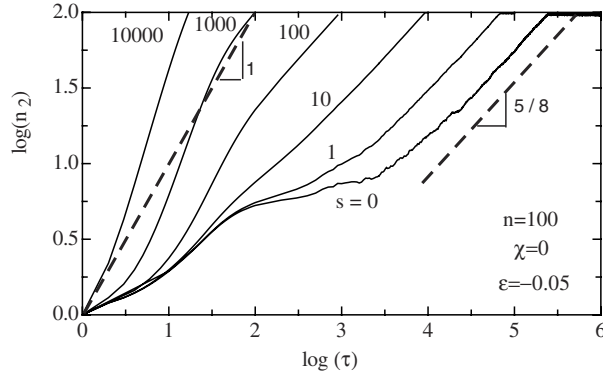
Figure 3. Time evolution of n_2 plotted against the reduced time $\tau = (k_B T/6\pi\eta a)t$ for various value of an external field $s \equiv qE$ with $D/R_0 = 0.2$, $n = 100$, $\chi = 0$, and $\epsilon = -0.05$.

Figure 3 shows the time evolution of n_2 for various values of the external electric field $s \equiv qE$ with $D/R_0 = 0.2$, $n = 100$, $\chi = 0$, and $\epsilon = -0.05$. With time, the number n_2 is increased and has a power law $n_2 \propto t^{5/8}$ at late stages for $s = 0$. In the case of weak external field, the growth of the exponent becomes small in the intermediate time region, which corresponds to a saddle point of the free energy. At a late stage, the friction of the chain dominates the dynamics and so equation (9) is given by $n_2^\nu(\partial n_2/\partial t) \propto$ constant, where we have used that the friction constant is proportional to $R_2 = an_2^\nu$ as in the Zimm model [25]. Then we obtain the time evolution of n_2 as $n_2 \propto t^{1/(1+\nu)}$ for a late stage. When $\nu = 3/5$, the exponent is 5/8. We here define the translocation time t_t as the time which satisfies $n_2 \sim n$. We then obtain $t_t \propto n^{1+\nu}$ [19]. When $\nu = 3/5$, we get $t_t \propto n^{8/5}$ for long flexible polymer chains. When the hydrodynamic interaction between polymer segments is neglected, as in the Rouse model ($\nu = 1$), we have $t_t \propto n^2$, which has been obtained by Sung–Park [8] and Muthukumar [9]. When $\nu = 0$, or the friction is independent of the polymer length, we have $t_t \propto n$.

On increasing the strength of the electric field, the translocation time becomes shorter and the exponent δ of the power law $n_2 \propto t^\delta$ at late stages is increased from 5/8 to 2. The effect of thermal fluctuations in the time evolution of n_2 is less with increasing s. For larger external fields, we have $\ddot{n}_2 \sim$ constant: $n_2 \propto t^2$ ($t_t \propto n^{1/2}$). Recent experiments show that polynucleotides thread through the alpha-hemolysin (αHL) channel as extended chains under electric fields: the translocation time is proportional to the polymer's contour length [1–3]. Our numerical results suggest that the DNA translocation can be controlled by the competition between the external electric fields and the entropic elasticity due to the deformation of the polymer in the pore.

4. Conclusion

We have studied the kinetics and phase transitions of a polymer escaping from a pore. Depending on the pore size and the polymer–pore interaction, we predict a first-order escape transition coupled to the conformational change of the polymer chain. The time evolution of the polymer segments escaping from a pore is scaled as $n_2 \propto t^{1/(1+\nu)}$ at late stages. The exponent increases with increasing the external electric field. We hope that our approach will provide useful insights into translocations of DNA under external fields, a invasion of RNA viruses into a cell, incorporation of membrane proteins into a lipid bilayer, and drug delivery systems.

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