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doi: 10.1063/1.1758939
Phase transitions of a polymer threading a membrane coupled to coil-globule transitions

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(Received 23 February 2004; accepted 13 April 2004)

We theoretically study phase transitions of a polymer threading through a pore imbedded in a membrane. We focus on the coupling between a partition of the polymer segments through the membrane and a coil-globule transition of the single polymer chain. Based on the Flory model for collapse transitions of a polymer chain, we calculate the fraction of polymer segments and the expansion factor of a polymer coil on each side of the membrane. We predict a first-order phase transition of a polymer threading a membrane; polymer segments in one side are discontinuously translocated into the other side, depending on solvent conditions and molecular weight of the polymer. We also discuss the equilibrium conformation of the polymer chain on each side of the membrane. © 2004 American Institute of Physics. [DOI: 10.1063/1.1758939]

I. INTRODUCTION

Translocation processes of polymer molecules [deoxyribose nucleic acid (DNA), ribonucleic acid (RNA), proteins, and biopolymers] threading through a pore imbedded in a membrane play an important role for many biological processes and for biological applications. Examples include the translocation of RNA through nuclear pores and the incorporation of proteins into membranes in nearly all cells. In vitro experiments show that single-strand DNA polymers can be driven through a single α-hemolysin pore (inside diameter ~2 nm) by an external field.

The problems of a polymer threading a membrane have both kinetics and equilibrium aspects. Recent theoretical studies have described the polymer translocations as a diffusion processes through a pore imbedded in a flat membrane. DiMarzio et al. have considered the equilibrium properties of a polymer molecule whose two ends reside on opposite sides of a membrane or partition separating two solutions in the limit of no self-excluded volume. They have pointed out that the polymer threading a membrane transition is coupled to the other phase transitions of a single polymer chain, such as a helix-random coil transition, collapse transitions, and adsorption onto a surface, and showed many possible translocation pair couplings.

The insertion of a single polymer chain into a pore occurs in most biological cells which can transport polymers across membrane to function. The number of conformations of a polymer can produce an entropy force tending to pull the chain out of the pore. It is well known that, in polymer physics, the conformation of a polymer chain depends on solvent conditions, temperature, and ionic strength. In a good solvent condition, a polymer is in a coiled state, while in a poor solvent region a polymer has a globular conformation. The change in temperature and solvent conditions can undergo a coil-globule transition of a single polymer chain in a solution. Then it is important to study the coupling between a polymer threading a membrane and a coil-globule transition.

In this paper we study the equilibrium properties of a polymer threading a membrane, taking into account interactions between polymer and solvent molecules, based on the Flory model for coil-globule transitions of a single polymer chain. The polymer segments on one side (region 1) of the membrane can translocate to the other side (region 2) by going through a pore in the flat membrane, depending on the interaction between polymer and solvent molecules. The interaction between polymer and solvent molecules in region 1 (2) can be described in terms of the Flory–Huggins interaction parameter \( \chi_1 (\chi_2) \). In a thermal equilibrium state, the polymer segments are partitioned into the two regions, where the conformation of the polymer are determined by the balance between the elastic free energy and the interaction energy. We calculate the fraction of polymer segments and the expansion factors of a polymer coil on each side of the membrane and predict a first-order phase transition of a polymer threading a membrane, depending on the solvent conditions and the molecular weight of the polymer.

II. FREE ENERGY OF A POLYMER THREADING A MEMBRANE

Consider a polymer threading through a pore imbedded in a membrane. The segments of the polymer on one side (side 1) of the membrane can translocate to the other side (side 2) only by going through this pore whose diameter is comparable to the size of the chemical repeat units on the polymer. In a thermal equilibrium state, the monomer segments are divided among side 1 and side 2 as shown in Fig. 1. To derive the equilibrium conformation of the polymer and the fraction of polymer segments on each side of the membrane, we consider the thermodynamics of the system based on the Flory–Huggins theory for polymer solutions.
Let $n$ be the number of segments (each of size $a$) on a polymer and $n_1$ and $n_2$ are the numbers of segments on sides 1 and 2, respectively. The polymer chain can translocate through a membrane with finite thickness corresponding to $an_0$. Then we have $n = n_0 + n_1 + n_2$. The free energy of the polymer chain is given by

$$ F = F_1 + F_2 + F_0, $$

where $F_1$ ($F_2$) shows the free energy of the polymer on side 1 (side 2) and $F_0$ is the free energy of the segments in the pore.

Let $R_1$ ($R_2$) be the mean radius of the occupied region of the monomer segments on side 1 (2). Then the volume fraction of the segments in the sphere $R_i$ is given by

$$ \phi_i = \frac{4}{3} \pi a^3 n_i / (\frac{4}{3} \pi R_i^3) = a^3 n_i / R_i^3, $$

where $(4/3)\pi a^3$ corresponds to the volume of an unit segment on the polymer. Hereafter the suffix $i$ shows side 1 or 2 ($i = 1, 2$). We here define the expansion factor $\alpha_i$ of the polymer chain in region $i$ as

$$ \alpha_i = R_i / R_{0,i}, $$

where $R_{0,i} = a \sqrt{n_i}$ is the radius of gyration of the ideal chain with $n_i$ segments. The volume fraction, Eq. (2), of the monomer segments in the sphere $i$ is then given by

$$ \phi_i = \frac{1}{\alpha_i^3 \sqrt{n_i}}. $$

The presence of the surface (membrane) may change the polymer conformation. The chain is stretched by a factor $v_2$ in the perpendicular direction. In our model, we neglect the stretching of the chain near the wall.

The free energy $F_i$ on side $i (i = 1, 2)$ is given by

$$ F_i = F_i,\text{el} + F_i,\text{mix}, $$

where $F_i,\text{el}$ shows the elastic free energy due to the deformation of the segment distribution from the ideal state. This free energy is given by Flory

$$ \beta F_i,\text{el} = \frac{3}{\alpha_i^3} (\alpha_i^3 - 1 - \ln \alpha_i), $$

where $\beta = 1/k_B T$, $T$ is the absolute temperature, and $k_B$ is the Boltzmann constant. The second term in Eq. (5) shows the free energy for a mixing of a polymer chain with solvent molecules on side $i$ and is given by the Flory–Huggins theory

$$ \beta F_i,\text{mix} = \frac{R_i^3}{a_0} \left[ (1 - \phi_i) \ln (1 - \phi_i) + \chi_i \phi_i (1 - \phi_i) \right], $$

where $\chi_i$ shows the Flory–Huggins interaction parameter between a polymer segment and a solvent molecule on side ($i$).

The translational entropy term $(\phi_i/n) \ln \phi_i$ of the polymer chain can be neglected since the center of gravity of the polymer chain is fixed near a membrane in a thermal equilibrium state. The prefactor $R_i^3/a_0^3$ is the total number of unit cells in the sphere of the radius $R_i$.

The free energy $F_0$ of the segments in the pore is simply given by

$$ \beta F_0 = \beta \epsilon_0 n_0, $$

where $\epsilon_0$ is the interaction energy between a polymer segment and a pore. We assume here that the diameter of the pore is of the order of the segment of the polymer. Then we can choose the value of $n_0$ as one numerical parameter characterizing the thickness of the membrane. In this assumption, the free energy Eq. (8) becomes a constant, but it is an important factor for the dynamics.

When the interaction energy between a polymer segment and a pore is weak, the polymer can escape completely from the vicinity of the membrane (or either side) because of the conformational entropy of the chain. In our model, however, the chain is tethered to the membrane. This would occur for a polymer chain which has a large end group on the both ends.

In a thermal equilibrium state, the expansion factors $\alpha_i$ of the polymer in side $i(=1, 2)$ are determined by minimizing the free energy (1) with respect to $\alpha_i$:

$$ (\partial F / \partial \alpha_i)_{\alpha_{j\neq i}, n_j} = 0, $$

$$ (\partial F / \partial n_i)_{\alpha_i, n_{j\neq i}} = 0. $$

These lead to

$$ \alpha_i^2 - 1 + n_1 \left[ \frac{1}{\phi_i} \ln (1 - \phi_i) + 1 + \chi_1 \phi_i \right] = 0, $$

$$ \alpha_i^2 - 1 + n_2 \left[ \frac{1}{\phi_i} \ln (1 - \phi_i) + 1 + \chi_2 \phi_i \right] = 0. $$

The number $n_1$ of the segments in side 1 is determined by

$$ (\partial F / \partial n_1)_{\alpha_1, \alpha_2} = 0, $$

FIG. 1. A polymer molecule consisting of $n$ monomers is threaded through a pore in a flat membrane. The hole is sufficiently small that double threading does not occur.
where we have used $n_2 = n - n_0 - n_1$ before the differentiation. We then obtain

$$\alpha_1^3 \sqrt{n_1} \left[ (\frac{1}{2} - \phi_1) \ln(1 - \phi_1) + \frac{1}{2} \phi_1 + \chi_1 \phi_1 (1 - \phi_1) \right]$$

$$= \alpha_2^3 \sqrt{n_2} \left[ (\frac{1}{2} - \phi_2) \ln(1 - \phi_2) + \frac{1}{2} \phi_2 + \chi_2 \phi_2 (1 - \phi_2) \right].$$

(14)

where the volume fractions are given by

$$\phi_1 = \frac{1}{\alpha_1^3 \sqrt{n_1}},$$

(15)

$$\phi_2 = \frac{1}{\alpha_2^3 \sqrt{n - n_0 - n_1}}.$$  

(16)

The equilibrium values of $\alpha_1$, $\alpha_2$, and $n_1$ are determined from the three coupled Eqs. (11), (12), and (13).

III. RESULTS AND DISCUSSION

In this section we show some results of our theory. Here we put $n_0 = 1$ and assume that the value of the parameter $\chi_2$ in region 1 remains constant when the parameter $\chi_1$ in region 1 is changed. The Flory–Huggins parameter $\chi$ can be changed by $p$H, ionic strength, solvent conditions, and temperature.\(^1\)

Figure 2 shows the fraction of polymer segments on each side of the membrane plotted against the Flory–Huggins parameter $\chi_1$ with $\chi_2 = 0.1$. The number $n$ of the segments on the polymer is varied. The solid curve shows the fraction $n_1/n$ and the dotted curve corresponds to $n_2/n$.

at $\chi_1 = \chi_2$. On increasing the molecular weight of the polymer, the width of the jump becomes larger. Figure 3 shows the expansion factor of the polymer chain on each side of the membrane plotted against $\chi_1$ with $\chi_2 = 0.1$ for various values of $n$. The solid curve shows the expansion factor $\alpha_1$ and the dotted curve corresponds to $\alpha_2$. When $\chi_1 = 0$, the value of the expansion factor $\alpha_1$ in region 1 is large and the polymer is in a coiled state. On increasing $\chi_1$, the value of the expansion factor $\alpha_1$ is decreased and jumps at $\chi_1 = \chi_2 = 0.1$. For $\chi_1 > \chi_2 = 0.1$, the polymer in region 2 is in a coiled state with an expanded conformation because $\chi_2 = 0.1$.

Figure 4(a) shows the fraction of polymer segments on each side of the membrane plotted against $\chi_1$ with $\chi_2 = 0.5$. The number $n$ of the segments on the polymer is changed. The solid curve shows the fraction $n_1/n$ and the dotted curve corresponds to $n_2/n$. For $n = 10$, the fraction of polymer segments in region 1 is continuously decreased with increasing $\chi_1$ and the polymer segments in region 1 are translocated into region 2 through a hole in the membrane. For larger values of $n$, we find the first-order phase transition of the polymer threading a membrane. When the solvent condition becomes poorer, the polymer segments of a short polymer chain are continuously translocated into region 2. Figure 4(b) shows the expansion factors of the polymer chain on each side of the membrane plotted against $\chi_1$ with $\chi_2 = 0.5$ for $n = 10, 100$. The solid curve shows the expansion factor $\alpha_1$ and the dotted curve corresponds to $\alpha_2$. On increasing $\chi_1$, the value of the expansion factor $\alpha_1$ is decreased and slightly jumps at $\chi_1 = \chi_2 = 0.5$. As shown in Fig. 4(a), the value of the fraction $n_1$ is almost constant when $\chi_1 < 0.5$ and drastically changed near $\chi_1 = \chi_2 = 0.5$. The polymer chain in region 1 is condensed with increasing $\chi_1$ and most polymer segments remain in region 1 for $\chi_1 < \chi_2$. At $\chi_1 = \chi_2 = 0.5$, the polymer segments in region 1 are translocated into region 2.

Figure 5(a) shows the fraction of polymer segments on each side of the membrane plotted against $\chi_1$ with $\chi_2 = 0.7$ for various values of $n$. The solid curve show the fraction $n_1/n$ and the dotted curve corresponds to $n_2/n$. When $n$
The fraction \( n_1 / n \) of the polymer segments in region 1 is continuously decreased with increasing \( x_1 \). For larger values of \( n_1 \), we find the first-order phase transition of the polymer threading a membrane at \( x_1 = x_2 = 0.7 \). As increasing the number of segments on a polymer, the width of the jump becomes larger. Figure 5 gives the corresponding expansion factors plotted against \( x_1 \) with \( x_2 = 0.7 \) for various values of \( n_1 \). The solid curve shows the expansion factor \( \alpha_1 \) and the dotted curve corresponds to \( \alpha_2 \).}

From Eq. (3), the gyration radius \( R_i \) of the polymer chain in region \( i = 1, 2 \) is given by

\[
R_i / a = \alpha_i \bar{u}_i. \tag{17}
\]

Figure 6 shows the radius \( R_i \) plotted against \( x_1 \) with \( n_1 = 100 \) for \( x_2 = 0.1, 0.5, \) and 0.7. The solid curve shows the radius \( R_1 / a \) and the dotted curve corresponds to \( R_2 / a \). When \( x_1 < x_2 \), the radius of the polymer coil in region 1 is larger than that in region 2. At \( x_1 = x_2 \), it is switched the radius of the polymer coil in region 1 and that in region 2. The radius of the polymer coil in region 1 becomes smaller than that in region 2 for \( x_1 > x_2 \). We find that the radius of the polymer chain on each side of the membrane is discontinuously changed when the first-order phase transition of a polymer threading a membrane takes place.
In Fig. 7, we schematically show the conformation of the polymer chain \( n = 100 \) occupied in regions 1 and 2 in a thermal equilibrium state. The equilibrium value of the radius for each sphere is given in Fig. 6. Circles show the occupied region of polymer segments and the vertical line shows the flat membrane. When \( \chi_1 < \chi_2 \), the radius of the polymer in region 1 is larger than that in region 1. On increasing \( \chi_1 (\leq \chi_2) \), the polymer chain is condensed. Note that most polymer segments remain in region 1 for \( \chi_1 < \chi_2 \). At \( \chi_1 = \chi_2 \), the conformation of the polymer chain on each side of the membrane is drastically changed.

IV. CONCLUSION

We have theoretically studied phase transitions of a polymer threading through a pore imbedded in a membrane. The theory takes into account the coupling between a partition of the polymer segments through the membrane and a coil-globule transition of a single polymer chain. Based on the Flory model for the collapse transition of a polymer chain, we have calculated the fraction of polymer segments and the expansion factor of a polymer chain on each side of the membrane.

It was found that the change in a solvent condition and molecular weight of a polymer is an important role for phase transitions of a polymer threading a membrane. When \( \chi_1 < \chi_2 \), most polymer segments is in region 1. At \( \chi_1 = \chi_2 \) we find that the segments on the polymer in one side can be translocated into the other side by changing the solvent condition. A first-order phase transition of the polymer threading a membrane occurs at \( \chi_1 = \chi_2 \). We also have found that the radius of the polymer coil on each side of the membrane is discontinuously changed when the first-order phase transition of a polymer threading a membrane takes place. When the solution of region 2 is in a poor solvent condition \( (\chi_2 > 0.5) \), a continuous phase transition of a polymer threading a membrane can occur for short polymer chains. In this paper we have focused on the dependence of the phase transition on molecular weight and solvent conditions. On increasing the value of \( n_0 \) (thicker membranes) the first-order phase transition becomes the continuous one.

Our results may offer insights into an invasion of RNA viruses into cells, incorporation of membrane proteins into a lipid bilayer, and drug delivery systems.

ACKNOWLEDGMENT

This work was supported by a Grant-in-Aid from the Ministry of Education, Culture, Sports and Technology, Japan.