Adsorption-assisted translocation of a chain molecule through a pore

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We analyze the free energy for translocation of a polymer from the outside of a spherical vesicle to the inside. The process is assumed to be driven by the adsorption of the polymer on the inner surface of the vesicle. We argue that in the case where the polymer is adsorbed on the outer surface too, the entropic barrier for translocation is absent. We analyze the adsorption process and find the free energy profile for the translocation. We argue that the motion corresponds to a polymer crossing a region with a change in free energy per segment. Based upon our earlier analysis of the behavior of kinks in such a problem, we conclude that the translocation can occur with a crossing time $t_{\mathrm{trans}} \sim N$.

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Park and Sung [1] have studied the translocation time t_{trans} of a polymer through a small pore in a spherical vesicle (see Ref. [1]). They assume both the inner and the outer surfaces of the vesicle to be hard walls, which repel the units of the polymer. They argue (a) that the membrane curvature drives the polymer out of a spherical vesicle (b) capture of a polymer of N segments into a small bud takes a very long time (exponentially dependent on N), which can be reduced to N^3 or even to N^2 by free energy differences between the inside and the outside. In this paper, we consider the case where there may be adsorption on both the surfaces. We construct a free energy profile for the translocation process. We show that in this case, the entropic barrier for penetration in to the pore is absent. Following Refs. [2–4] , we suggest that translocation, when driven by the free energy difference due to the different adsorption strengths can occur with a translocation time $t_{\mathrm{trans}} \sim N$.

We make use of the approach of de Gennes [5] to treat the adsorption of the chain molecule on the surface [6,7]. We go beyond the results of Park and Sung [1] and find the exact partition function for a chain restricted to the outside of a sphere and having an attractive interaction with the surface of the sphere. For a chain molecule confined to the inner region of the sphere and interacting with the surface, we give the exact result for the Laplace transform of the partition function. We analyze the condition for the existence of an adsorbed state and find that they are different for the two cases. Partition function is found in the limit of a long chain and this is used to calculate the free energy of the adsorbed polymer. From this, we construct the free energy profile for the translocation process.

The partition function for a chain of n segments confined to the outer or inner region of a sphere can be calculated from the Green's function $G(\mathbf{r},\mathbf{r}_0;n)$, obeying the equation $[\partial/\partial n-(b^2/6)\nabla^2+V(r)]G(\mathbf{r},\mathbf{r}_0;n)=\delta(n)\delta(\mathbf{r}-\mathbf{r}_0)$ (see Refs. [1,6]). $V(r)$ is the potential of interaction arising from the sphere. The partition function may be calculated from the angle averaged function $Z(r,r_0;n)=\int_0^{\pi}d\theta\int_0^{2\pi}d\phi\,\sin(\theta)G(\mathbf{r},\mathbf{r}_0;n)$. This averaged Green's function obeys [1] $[\partial/\partial n-(a^2/r^2)(\partial/\partial r)r^2\,\partial/\partial r+V(r)]Z(r,r_0;n)=(1/r^2)\delta(n)\delta(r-r')$, where $a=b/\sqrt{6}$. It has to satisfy the conditions $Z(r,r_0;n)\rightarrow 0$ as $r,r_0\rightarrow\infty$. If $V(r)=0$, $Z_0(r,r';n)=(1/rr_0a\sqrt{\pi n})\exp\{-(r^2+r_0^2)/4a^2n\}\sinh(rr_0/2a^2n)$. The presence of a spherical surface at $r=R$ with a short range attractive (or repulsive) potential can be accounted for by imposing a boundary condition [5] (see below). It is easier to work with the Laplace transform of the Green's function $\overline{Z}(r,r_0;s)=\int_0^{\infty}dn Z(r,r_0;n)e^{-sn}$, which obeys

$$\left(s-\frac{a^2}{r^2}\frac{\partial}{\partial r}r^2\frac{\partial}{\partial r}\right)\overline{Z}(r,r_0;s)=\frac{1}{r^2}\delta(r-r_0). \tag{1}$$

We now solve Eq. (1) for the region outside the sphere $(r>R)$. The boundary condition that is to be imposed may be found [7] by imagining that the region $r<R$ is a hard wall, where $V(r)=\infty$, and within a spherical shell with $R<r<R+b$ (b assumed to be small), there exists an attractive potential equal to $V(r)=-w$ and $V(r)=0$ for $r>R$. Then one finds $(d\ln\overline{Z}_{>}(r,r_0;s)/dr)_{r=R}=-1/R+(\pi/2)(\pi/2b-\sqrt{w})$ (see Appendix A of Ref. [7]). We can write the above as

$$\left(\frac{d}{dr}\ln[r\overline{Z}_{>}(r,r_0;s)]\right)_{r=R}=c, \tag{2}$$

where c is determined solely by the nature of the interaction of a monomer with the surface [our definition of c is different from that of Ref. [7]—$c(\text{ours})=c(\text{of Ref. [7]})+1/R$]. With this definition, if $c<0$, there is a bound state on the surface. $c\rightarrow\infty$ corresponds to a hard wall. However, in contrast to the situation on a plane wall, $c=0$ does not represent neutral surface. Rather, $c=1/R$ represents a neutral surface (see below). Solving the Eq. (1) subject to Eq. (2), we get $\overline{Z}_{>}(r,r_0;s)=(1/2arr_0\sqrt{s})(e^{-|r-r_0|\sqrt{s}/a}+e^{-|r+r_0-2R|\sqrt{s}/a})-[c/rr_0(ac+\sqrt{s})\sqrt{s}]e^{-|r+r_0-2R|\sqrt{s}/a}$. On inverting this, we get for a chain of n segments

$$Z_{>}(r,r_0;n)=\frac{1}{2a\sqrt{\pi n}rr_0}\left(\exp\left[-\frac{(r-r_0)^2}{4a^2n}\right]+\exp\left[-\frac{(r+r_0-2R)^2}{4a^2n}\right]\right)-\frac{c}{rr_0}e^{a^2c^2n+c(r-2R+r_0)}\times\operatorname{Erf}c\left(ac\sqrt{n}+\frac{r-2R+r_0}{2a\sqrt{n}}\right), \tag{3}$$

similar to the expression for the case of adsorption on a planar surface [1]. As the surface of the sphere becomes repulsive ($c\rightarrow\infty$), the above reduces to

$$Z_{>}(r,r_0;n)=(1/2arr_0\sqrt{\pi n})\{\exp[-(r-r_0)^2/4a^2N]-\exp[-(r+r_0-2R)^2/4a^2n]\}.$$

The partition function for the polymer with one end fixed at r_0 is

$$\begin{aligned}Q_{>}(r_0,n)&=\textstyle\int_R^\infty drZ_{>}(r,r_0;n)r^2\\&=(1/cr_0)\{1-cR+cr_0\\&\quad+(1-cR)\operatorname{Erf}[(R-r_0)/2a\sqrt{n}]\\&\quad+e^{c(a^2cn-R+r_0)}(-1+cR)\\&\quad\times\operatorname{Erf}c[(2a^2cn-R+r_0)/2a\sqrt{n}]\}.\end{aligned}$$

As $r_0\rightarrow\infty$, $Q_{>}(r_0,n)\rightarrow 1$, which is the value for a free polymer. Also, if $c=1/R$, then $Q_{>}(r_0,n)=1$, thus showing that $c=1/R$ corresponds to a neutral surface. In particular, if one end is on the surface ($r_0=R$), then

$$Q_{>}(R,n)=\frac{1}{cR}[1+e^{a^2c^2n}(-1+cR)\operatorname{Erfc}(ac\sqrt{n})]. \tag{4}$$

$Q_{>}(R,n)$ is always positive, as it should be. We now consider the limit where $n\rightarrow\infty$. If $c<0$, then we can approximate the above as $Q_{>}(R,n)\sim(2/Rc)(Rc-1)e^{a^2nc^2}$. In this limit, the free energy of the polymer, with one end at R is $F(n)=-k_BT\ln Q_{>}(R,n)\simeq-k_BTa^2nc^2$. The free energy per unit is $-k_BTa^2c^2$ for the chain on the outer surface of the sphere. This free energy comes from the adsorbed state on the surface of the sphere, which would be there as long as $c<0$.

For the case where the polymer is inside the vesicle, the boundary condition we impose is $\{d\ln[r\overline{Z}(r,r_0;s)]/dr\}_{r=R}=-d$. Note that we have put a negative sign in front of d [compare Eq. (2)] as increasing the value of r means one is moving towards the surface. On solving Eq. (1) we find

$$\overline{Z}_{<}(r,r_0;s)=\left\{\sinh\left(\frac{r_<\sqrt{s}}{a}\right)\left(\cosh\left(\frac{\sqrt{s}(R-r_>)}{a}\right)+\frac{ad\sinh\left(\frac{\sqrt{s}(R-r_>)}{a}\right)}{\sqrt{s}}\right)\right\}\Bigg/\left\{ar_>r_<\times\left[\sqrt{s}\cosh\left(\frac{R\sqrt{s}}{a}\right)+ad\sinh\left(\frac{R\sqrt{s}}{a}\right)\right]\right\},$$

where $r_<=\min(r_0,r)$ and $r_>=\max(r_0,r)$.

We now find the partition function for the polymer with one end fixed at the inner surface of the sphere and the other end free by putting $r_0=R$ and integrating over all the values of r inside the sphere. We get

$$\overline{Q}_{<}(R,s)=\int_0^R r^2dr\overline{Z}_{<}(r,R;s)=\frac{\sqrt{s}-\tanh(R\sqrt{s}/a)a/R}{s[\sqrt{s}+ad\tanh(R\sqrt{s}/a)]}. \tag{5}$$

The partition function is then $Q_{<}(R,n)=\int_{\gamma-i\infty}^{\gamma+i\infty}dse^{sn}\overline{Q}_{<}(R,s)/(2\pi i)$, where γ is taken such that the line of integration is to the right of all the poles of $\overline{Q}_{<}(R,s)$. To find the poles of $\overline{Q}_{<}(R,s)$, we have to solve the transcendental equation $\sqrt{s}+ad\tanh(R\sqrt{s}/a)=0$. We consider two different possibilities.

(1) d is sufficiently negative so that $Rd<-1$. Then one solution, s_0 exists for real, positive value of s. If $R|d|\gg 1$, then $s_0\approx(ad)^2$ is the solution. For large values of n, the major contribution to $Q_{<}(R,n)$ comes from this pole and hence $Q_{<}(R,n)\sim e^{s_0n}$ and the free energy of the adsorbed chain is $-k_BTs_0n$. The free energy per unit length of the adsorbed chain is $-k_BTs_0$. In contrast to the outer surface, there is a critical value for the logarithmic derivative, for an adsorbed state to exist. The reason for this critical value is quite simple. In the absence of an attractive interaction, the free energy of the polymer inside the sphere is not zero, due to entropic reasons. An attractive interaction with the surface would lead to a negative free energy only if this entropic effect is overcome by the attractive interaction and hence a critical value for d exists.

(2) d is positive. In this case, all the poles have $s<0$ and there is no adsorbed state. There are several states inside the spherical vessel, and the Bromwich integration leads to an infinite sum for the partition function. This type of problem has already been considered in Ref. [1] and we shall not discuss this case further.

Now we consider the free energy profile for translocation. If it is confined to a spherical vesicle, with the outer and inner walls of the vesicle having no affinity to its units, then its free energy inside would be greater than on the outside. Consequently, if there is a pore on the wall of the vesicle, the molecule would move from the inside to the outside. But there are examples where the molecule does the reverse [8–10]. This would require either a motor driving the chain in, or a situation where the chain has a lower free energy inside the vesicle. We consider the latter situation, and we assume that the polymer can adsorb on inner walls of the

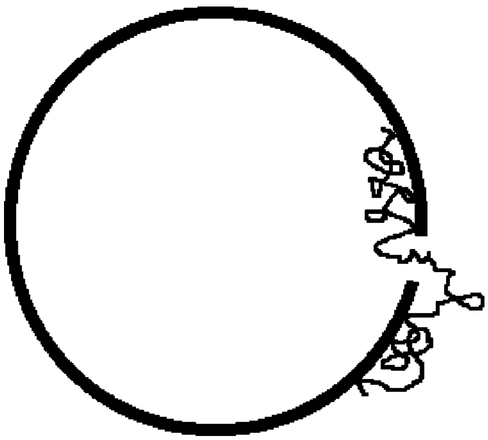

FIG. 1. Translocation in the case where there is adsorption on the inside as well as outside

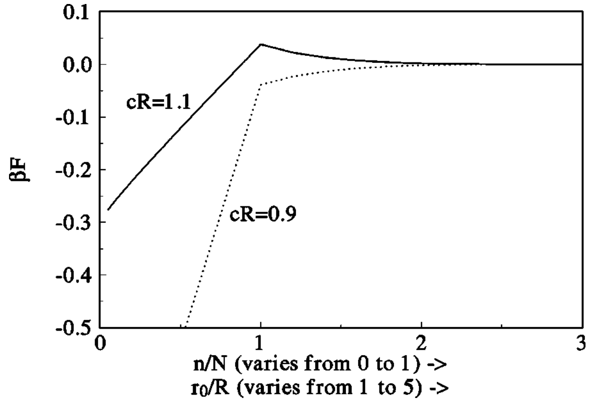

FIG. 2. Plot of $F/(k_BT)$ as functions of r_0/R (varies between 1 and 5) and n/N (varies between 0 and 1) for $cR>1$ and $cR<1$.

vesicle. (It is not necessary that the adsorption should be on the walls, it can be anywhere inside the vesicle.)

The process that we consider is given in the Fig. 1. The translocation from the outside to the inside may be thought of as occurring in two steps. The first consists of the approach of one end of the molecule to the outer surface of the sphere and the second is the passage of the segments of the polymer through the pore. We now consider a chain of total N segments and denote the number of segments left outside by n. Assuming the segments to be adsorbed strongly enough on the inner surface so that one need to take only the bound state contribution to the free energy for the portion inside the sphere, the total free energy for any value of N is the sum of the contributions from the segments n outside and the remaining $(N-n)$ inside. It is $F/(k_BT)=-\ln Q_>(r_0,n)-a^2d^2(N-n)$. We now use the radius of gyration R_g of a polymer having N segments, given by $R_g=a\sqrt{N}$. Using the dimensionless quantities $\underline{r}_0=r_0/R$, $\underline{R}_g=R_g/R$, $\underline{c}=cR$, $\underline{d}=Rd$, $\underline{n}=n/N$, and $\underline{F}=F/(k_BT)$, we rewrite the above as

$$\underline{F}=-\ln\left\{\frac{1}{\underline{c}\,\underline{r}_0}\left((-1+\underline{c})\left[-1+\mathrm{Erf}\left(\frac{1+\underline{r}_0}{2\sqrt{\underline{n}}\,\underline{R}_g}\right)+e^{\underline{c}(-1+\underline{r}_0+\underline{c}\,\underline{n}\,\underline{R}_g^2)}\,\mathrm{Erfc}\left(\frac{-1+\underline{r}_0+2\underline{c}\,\underline{n}\,\underline{R}_g^2}{2\sqrt{\underline{n}}\,\underline{R}_g}\right)\right]+\underline{c}\,\underline{r}_0\right)\right\}-\underline{R}_g^2\,\underline{d}^2(1-\underline{n}).$$

Figure 2 shows the plot of free energy for two values of $\underline{c}$ (1.1 and 0.9). The first corresponds to a repulsive outer surface while the second is an attractive one. In both the cases, the inner surface is taken to be attractive, with $\underline{d}=-2$ and the radius of gyration of the polymer taken to be half the size of the sphere $(\underline{R}_g=1/2)$. If the chain is completely outside the sphere, $\underline{r}_0$ is greater than unity and $\underline{n}=1$. In the figure, the portion with abscissa varying from 3 to 1 represents the change in $\underline{r}_0$ as the end of the chain approaches the surface. Once $\underline{r}_0$ attains the value unity, the chain can go through the pore and this would cause $\underline{n}$ to decrease from unity. So, in the same plot, we show how the free energy changes, as $\underline{n}$ varies from 1 to 0. The plots show that if $\underline{c}>1$, there is an increase in the free energy as the end of the polymer is brought near the surface reaching a maximum when the end touches the surface. This increase is due to the lowering of the entropy as the chain end is brought near the surface. Thus there is an entropic barrier for the approach of the end of the molecule to the surface. As portions of the chain go through the pore, the free energy of the chain decreases. On the other hand, if $\underline{c}<1$, there is no such barrier. Thus an attraction to the outer surface would actually facilitate the translocation process, by completely removing the entropic barrier for the approach of the end of the chain to the surface. If there is no adsorption on the outer surface, translocation is improbable as the end of the chain would have to overcome the entropic barrier and find the pore through which it has to translocate. So, in the following we assume that the chain is weakly adsorbed on the outer surface. However, if it is strongly adsorbed with a barrier for motion parallel to the surface having height ΔV_p, then translocation would become difficult. Thus we have the conditions $c<1/R$ and $\Delta V_p \ll k_BT$, under which translocation is facilitated.

Even though our analysis above has been done for a spherical vesicle, one can take the limit $R\to\infty$, and obtain the results for the planar case too. Now we consider the actual translocation through the pore. The translocating chain may be thought of as divided into three portions—first is the portion adsorbed on the outside, second, the portion on the inside, and the third is the portion inside the pore. We imagine that the polymer is adsorbed on both the surfaces, and the adsorption (physisorption) is such that it is easy for the segments to move in the direction parallel to the surfaces, but movement in the perpendicular direction, away from the surface would cost energy. Hence the net effect is to reduce dimensionality of the motion in directions parallel to the surface. We already have expressions for the free energy per segment of the chain molecule when it is inside or outside and in our considerations above, we did not include the contribution to the free energy from the portion that is inside the pore. The portion that is inside the pore, is not adsorbed anywhere and consequently, the free energy per segment is higher. Often, the pores have a repulsive interaction with the chain segments, and hence the most reasonable form for the free energy per segment for a translocating chain would have the appearance shown by the full line of Fig. 3. An alternate scenario would be to have a pore which has affinity towards the molecule, as a result of which the free energy per segment follows the dotted line in the Fig. 3, for segments inside the chain.

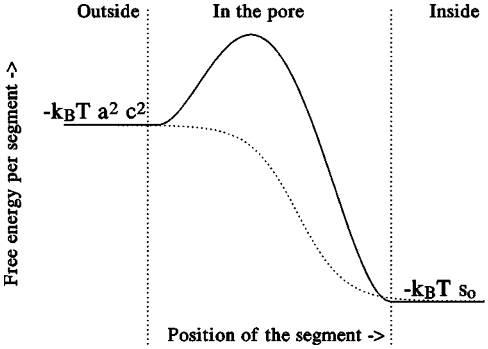

FIG. 3. The Free energy per segment as a function of segment position.

Irrespective of which is the profile, if one uses a one dimensional Rouse model to describe the process, then one has the following picture: the variation of the potential inside the pore would distort the portion of the chain inside it, which we refer to as the kink. As the pore is fixed in space, the kink too is fixed in space and movement of the chain in one direction through the pore is equivalent to the movement of the kink in the reverse direction on the chain. If there is a free energy gain for the segments of the polymer, then the translocation is driven and hence the motion of the kink too is driven. This problem is discussed in detail in Ref. [2], where it is shown that the one-dimensional nonlinear Rouse model that described the motion of a polymer in this type of potential has a special solution, which represent a kink that can move on the polymer chain. The motion of the kink decouples (approximately) from the other modes of the chain. It is to be noted that the kink is a local dynamical mode whose motion on the chain results in the translocation of the polymer through the pore. Further, the motion of the kink is equivalent to that of a particle executing Brownian motion under the influence of a constant external force with a friction that has no dependence on N. Therefore, on an average, the kink will move with a certain velocity determined by the free energy profile for a segment crossing the pore (for an expression for this velocity, see Ref. [2]). Consequently, the polymer will move in to the inner side, at a constant rate. This means that the crossing time $t_{\rm trans}\sim N$. This is to be compared with the mechanism of Ref. [1], where translocation is taken to be equivalent to the motion of the center of mass of the polymer. As the center of mass diffuses with a coefficient proportional to $1/N$, $t_{\rm trans}\sim N^2$ [1]. The difference in $t_{\rm trans}$ in the two mechanisms thus arises from the difference in the N dependence of friction. It is of interest to note that there have been recent experiments in which flexible single stranded DNA molecules have been drawn through a pore by the application of an electric field [3]. In these experiments, the translocation time has been found to be proportional to N, in agreement with the kink mechanism. An alternative mechanism for the translocation, in which the diffusive movement of only the monomers which are inside the pore has been suggested by Lubensky and Nelson (LN) [4]. This too leads to $t_{\rm trans}\sim N$. This LN mechanism is similar to the kink mechanism, but is different in that it does not consider the distortion of the chain by the pore as important. However, both kink and LN mechanisms lead to $t_{\rm trans}\sim N$.

One can also consider the case of translocation from a vesicle of radius $R_1$to another of radius R_2. Analyzing this case, Park and Sung [1] conclude that spontaneous capture in to a small bud can occur only rarely as the chain is losing entropy in going into a small bud. However, adsorption on the surface of the bud, can drive the process. Park and Sung suggest that this will require at least a time $t_{\rm capture}\sim N^2$. Operation of a kink mechanism can lead to capture times proportional to N.

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