Polymer in a double well: dynamics of translocation of short chains over a barrier

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Abstract
We consider the dynamics of a short chain polymer crossing over a free energy barrier in space. Adopting the continuum version of the Rouse model, we find exact expressions for the activation energy and the rate of crossing. For this model, the analysis of barrier crossing is analogous to semiclassical treatment of quantum tunnelling. Finding the saddle point for the process requires solving a Newton-like equation of motion for a fictitious particle. The analysis shows that short chains would cross the barrier as a globule. The activation free energy for this would increase linearly with the number of units N in the polymer. The saddle point for longer chains is an extended conformation, in which the chain is stretched out. The stretching out lowers the energy and hence the activation free energy is no longer linear in N. The rates in both the cases are calculated using a multidimensional approach and analytical expressions are derived, using a new formula for evaluating the infinite products. However, due to the harmonic approximation made in the derivation, the rates are found to diverge at the point where the saddle point changes over from the globule to the stretched out conformation. The reason for this is identified to be the bifurcation of the saddle to give two new saddles, and a correction formula is derived for the rate in the vicinity of this point. Numerical results using the formulae are presented. As a function of N, it is possible for the rate to have a minimum. This is due to confinement effects in the initial state.

1. Introduction

The dynamics of a long chain molecule crossing over a barrier is an interesting basic problem in physics. It is of great interest in connection with its application to transport of long chain biomolecules through pores in membranes and gel electrophoresis [1]. There have been a number of experiments in which the passage of single macromolecules through pores of nanometre dimensions have been studied. Kasianowicz *et al* [2] forced a single stranded DNA through a haemolysin pore of 2.6 nm diameter and measured the time that it took for

the molecule to pass through the pore (see also [3–5]). In another interesting study, Han *et al* [6] studied the motion of very long double-stranded DNA through nanometre sized channels. The channels had different depths in different regions. In the deep region (depth, 1 μm), the double-stranded DNA could sit comfortably, while in the shallow region (depth 90 nm), it had to stretched out, thus costing entropy. Because of this, the shallower regions would act as entropic barriers for the transport of the macromolecule. Since these studies, a number of papers have appeared on the passage of long chain molecules through nano-sized pores [7–9]— these references may be looked into for more details.

On the theoretical side too, there have been a large number of studies. Park and Sung [10–12] were among the earliest to model the problem theoretically. They studied the free energy profile and the dynamics of the passage of a long chain molecule from the *cis* side to the *trans* side of a membrane through a pore in it. The barrier was taken to be purely entropic. It is rather broad and the motion of the molecule over the barrier was assumed to be diffusive. They assumed the motion to be subject to a friction that is proportional to the number of units N in the long chain. Consequently, the rate of diffusion over the barrier would be inversely proportional to N. They argued that the time that the molecule takes to go through the pore is proportional to N^3 if there is no free energy bias between the two sides, while it is proportional to N^2 if there is a constant free energy bias. Experiments [2] however showed that the residence time is proportional to N. These experiments led Lubensky and Nelson [13] to propose a model in which only the dynamics of the portion of the molecule that is inside the pore is relevant, as a result of which only the friction acting on this part is important. This friction does not depend on the total length of the molecule and hence they found that if there is a bias between the two sides of the pore, the residence time is proportional to N. There have been quite a number of theoretical studies based on these initial studies. Many of these studies make the ad hoc assumption that the diffusion of only the portion that is inside the pore is important. A more microscopic approach to the problem was adopted by Sebastian and Paul [14, 15] and Park and Sung [12]. They start with the Rouse model for a long chain molecule and introduce an additional force due to the externally applied potential into it. Sebastian and Paul consider the very long chain limit ($L = Nl \gg w$, where l is the length of one unit, L the total length of the chain and w is the width of the barrier) and use the continuum version of the Rouse model. They obtain analytical expressions for all the quantities of interest. They argue that in the limit of long chains there are two steps to the process. The first one is the crossing of the barrier by perhaps one end of the molecule. This will have a free energy of activation. Once one end has crossed the barrier, the remaining part of the molecule too has to go over the barrier, for which they suggest a kink mechanism. The kink moves with a steady velocity, as a result of which the time of residence of the molecule over the barrier is proportional to N. On the other hand, Park and Sung [12] consider shorter chains such that $L \lesssim w$. They use the discrete version of the Rouse model. They find that the chain can undergo a coil to stretch transformation above a critical length. Below this length the molecule crosses over in the form of a globule, while above this length the molecule crosses the barrier in a stretched conformation. The stretching of the molecule at the top of the barrier causes a lowering of activation energy and helps the crossing process. They argue that the simple Rouse model breaks down because of the infinite extensibility of a Rouse chain. Using a transfer matrix approach, they estimate the free energy of the polymer at the transition state and evaluate the rate of crossing. They find that rate is non-monotonic—there is a minimum in the rate—and find that longer chains can go over the barrier faster. In a later paper, Lee and Sung [16] have studied barrier crossing by a semi-flexible ring polymer. There have been simulations and analytical approaches to the problem [17–21]. See the interesting review by Slater for a general introduction to rate processes involving long chain molecules [22].

In this paper, we study the barrier crossing by short to intermediate length molecules, as a detailed analysis of the long chain limit has already been published [15]. We make use of the continuum version of the Rouse model. In their calculations, Park and Sung [12] did not take the nonlinearity of the potential into account—for them the barrier was a simple inverted parabola. In comparison, we fully account for non-linearity of the potential, and the problem of 'infinite extensibility' that Park and Sung encountered disappears when the non-linearity of the potential is included in the calculation. The model can be solved analytically and rates obtained. To calculate the rate, we use multidimensional rate theory due to Langer [23]. The Rouse model seems to be one of the very few multidimensional models for which an analytical expression for barrier crossing can be obtained.

We find that for this model the problem of finding the saddle point is similar to the semiclassical treatment of tunnelling [24] and the large amount of literature on dissipative quantum tunnelling, as reviewed by Weiss [25], is relevant to its mathematical analysis. To find the saddle, one needs to analyse a Newton-like equation of motion for a fictitious particle, moving in the inverted potential. As found by Park and Sung, the chain crosses over as a globule if the number of units is less than a critical number N_c. Above this, the transition state is a stretched conformation. The stretching lowers the free energy of activation. The stretched conformation can be easily found by solving the Newton-like equation and activation energy can be calculated. Using Langer's [23] approach to multidimensional nucleation problems, it is possible to express the rate as the product of a pre-factor and an exponential term. The pre-factor involves infinite products of frequencies of the normal modes of the initial and the transition state. We show that the infinite product can be rewritten as a single term (see equation (33)). This result has not been given in the literature. Using this equation, it is easy to calculate the rate. However, this equation has the shortcoming that it gives a rate that diverges at N_c. We point out that the divergence is a result of bifurcation of the saddle point. As N is increased through N_c, the saddle point develops one more unstable direction and consequently becomes a hill top. There are now two new saddles on either side of the old saddle, and realizing this it is easy to derive a new formula, valid in the vicinity of N_c. We present numerical results based upon these formulae.

We now give a brief outline of the paper. In section 2, we present the model that we use for the analysis. Section 3 analyses the crossing by a short chain and shows the existence of globular and stretched transition states. Section 4 gives the results of the calculation of the rates in the two cases as well as results of using the formula valid in the vicinity of N_c. Finally, we present numerical calculations in section 5 and conclusions in section 6.

2. The Rouse model

We consider the simplest possible model for polymer dynamics—the Rouse model [26, 27] in one dimension. The model considers a chain of 'phantom beads', and does not take excluded volume interactions into account, as a result of which the beads can pass through one another. The beads are imagined to be joined together through harmonic springs. We consider the continuum version as it is easier to tackle analytically. In this, the beads are imagined to be smeared out into a continuum. Thus the polymer is just a flexible string of length $L = Nl$, where N is the number of beads in the chain and l is the effective statistical length of a segment [27]. Despite its simplicity, the model captures the essential physics of barrier crossing by a long chain molecule. Further, the model has the advantage of being analytically tractable. The equation describing the dynamics of a chain in one dimension, subject to a free energy barrier $V(R)$, is

$$\zeta \frac{\partial R(n, t)}{\partial t} = m \frac{\partial^2 R(n, t)}{\partial n^2} - V'(R(n, t)) + f(n, t). \tag{1}$$
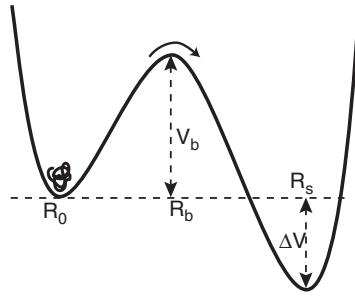
Figure 1. The double-well potential plotted against position R. The minima are at $R = R_0$ and R_s. The minimum at R_s is assumed to be lower. The polymer is initially trapped in the minimum at $R = R_0$. The maximum is at $R = R_b$. It is convenient to take $V(R_0) = 0$.

$R(n, t)$ is the position of the nth bead at the time t. $m = 3k_BT/l^2$ and ζ is the coefficient of friction for a bead. $f(n, t)$ is white noise obeying $\langle f(n, t) f(n_1, t_1) \rangle = 2\pi \zeta k_B T \delta(t - t_1)\delta(n - n_1)$. The two chain ends have to obey the boundary conditions

$$(\partial R/\partial n)_{n=0} = (\partial R/\partial n)_{n=N} = 0 \tag{2}$$

(see the book by Doi and Edwards [27] for futher details). Equation (1) is of the form

$$\zeta \frac{\partial R(n, t)}{\partial t} = -\frac{\delta E[R(n, t)]}{\delta R(n, t)} + f(n, t) \tag{3}$$

where $E[R(n, t)]$ is the free energy functional, depending on the configuration of the chain $R(n, t)$, and is given by

$$E[R(n, t)] = \int_0^N \mathrm{d}n \left[\frac{m}{2} \left(\frac{\partial R(n, t)}{\partial n} \right)^2 + V(R(n, t)) \right]. \tag{4}$$

Energy functionals of this type have been used in describing interesting rate processes involving long chain molecules [28].

We note that the condition for the applicability of the continuum model would be that the relative stretching of the bonds is small, i.e., $\left| \frac{1}{l} \frac{\mathrm{d}R(n)}{\mathrm{d}n} \right| \ll 1$.

3. Barrier crossing by a short chain

We now assume that the potential $V(R)$ has the form of a double well, as shown in figure 1. We take the positions of the two minima to be at $R = R_0$ and at $R = R_s$ and the maximum to be at $R = R_b$. The minimum at R_s is taken to be deeper. It is convenient to take $V(R_0) = 0$. The height of the barrier is then $V(R_b)$, which we shall denote as V_b. The chain starts in the less stable well, located at R_0, and has to climb over the barrier to cross over to the other side. While $V(R)$ is the potential felt by one unit of the chain, $E[R(n)]$ determines the energy of the whole chain. To escape from the well, the chain has to go over a saddle on the free energy hypersurface. The extrema on the free energy hypersurface may be found as solutions of the equation

$$\frac{\delta E[R(n)]}{\delta R(n)} = -m \frac{\partial^2 R(n)}{\partial n^2} + V'(R(n)) = 0. \tag{5}$$

Equation (5) may be thought of as Newton's equation for a fictitious particle of mass m if one takes n to be (analogous to) time. The particle moves in the potential $-V(R)$. That is, the original potential in which the polymer is moving has to be turned upside down to get a
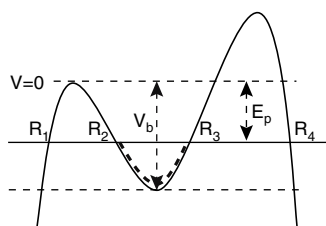
Figure 2. The upside down potential $-V(R)$. The horizontal line represents E_p, and its intersections with the curve the points R_1, R_2, R_3, R_4.

double-humped potential (figure 2). One has to analyse the motion of a classical particle in this potential and the boundary conditions of equation (2) imply that initial velocity and the final velocity after a 'time' N are both equal to zero. The simplest three solutions are the 'n' independent solutions (1) $R(n) = R_0$, (2) $R(n) = R_s$ and (3) $R(n) = R_b$. These correspond to the particle just sitting on top of the two hills or in the valley. In addition, there can be a solution that corresponds to the oscillation of the particle in the potential well in figure 2. If the potential around the minimum in this figure is approximated as harmonic, with an angular frequency ω_b, then the complete oscillation would take a time $2\pi/\omega_b$. In our case, it is not a complete oscillation that we are interested in, but half an oscillation, in which the particle starts from rest on one side of the minimum at the time $n = 0$ and comes to rest in exactly a time N on the other side (remember that we are actually looking for the configuration of a long chain molecule crossing the barrier). In a harmonic potential, this can happen only if $N = N_c$ where $N_c = \pi/\omega_b$, but as our potential is not harmonic, and is approximately harmonic for small amplitude vibrations near the minimum, such solutions will exist if $N \geqslant \pi/\omega_b$. Thus we have the following two situations.

3.1. Case I: $N < \pi/\omega_b$

In this case, the initial state corresponds to the particle sitting on top of the first hill (at R_0) in the inverted double well. The saddle point is the particle sitting at the bottom of this well. This saddle corresponds to the polymer going over the barrier as a globule [12]. The energies of these two solutions may be found by putting the solutions $R(n) = R_0$ and $R(n) = R_b$ into the energy functional which gives the energy of the initial state $E_i = 0$ and the energy at the saddle $E^\ddagger = NV_b$. (In the following, the symbol $\ddagger$ will be used to indicate quantities that are associated with a saddle.) The activation energy for the crossing is thus

$$E^\ddagger = NV_b. \tag{6}$$

3.2. Case II: $N > \pi/\omega_b$

In this case, the oscillating solution mentioned above exists. We shall denote the solution by $R^\ddagger(n)$. As the fictitious particle obeys a Newton like equation, we can define an energy for it which is conserved. If E_p is the value of this energy, then energy conservation gives

$$\frac{m}{2}\left(\frac{dR^\ddagger}{dn}\right)^2 - V(R^\ddagger) = E_p. \tag{7}$$

Looking at figure 2, it is clear that in order to have the oscillating solution E_p must satisfy $0 > E_p > -V_b$. The points at which the particle starts (R_2) and ends (R_3) may be easily found from the energy E_p, because they obey the equation $-V(R^\ddagger) = E_p$. If $0 > E_p > -V_b$, there
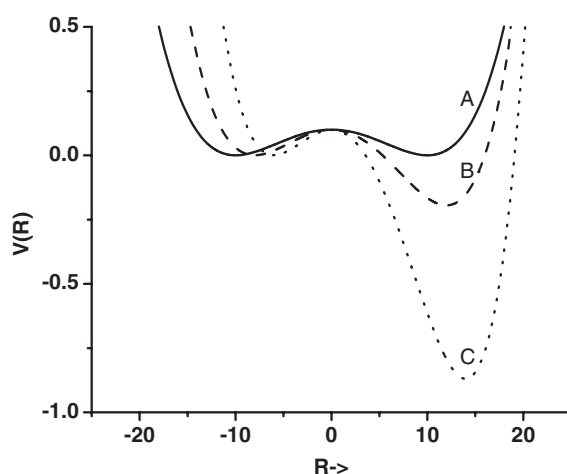
Figure 3. Plot of $V(R)$ against R. Calculations are done for three different choices of parameters. The parameters are chosen such that the barrier height is equal to $1/10$. Also, the width of the potential $(= a_0 + a_1)$ is kept equal to 20. A: $a_0 = 10$ and $a_1 = 10$—the potential is a symmetric double well. B: $a_0 = 8$ and $a_1 = 12$ and C: $a_0 = 6$ and $a_1 = 14$. Dimensionless variables are used for all the plots.

would be four solutions to this equation, because if one draws a horizontal line at the energy E_p as in figure 2 then the line will intersect the upside down potential four times, and the inner two intersections will give the values of R_2 and R_3. The energy of the chain corresponding to this solution is

$$E^\ddagger = E[R^\ddagger(n)] = \int_0^N dn \left[\frac{m}{2} \left(\frac{dR^\ddagger(n)}{dn} \right)^2 + V(R^\ddagger) \right]. \tag{8}$$

On using equation (7) this becomes

$$E^\ddagger = \int_0^N dn \left\{ m \left(\frac{dR^\ddagger(n)}{dn} \right)^2 - E_p \right\} \tag{9}$$

$$= \int_{R_2}^{R_3} dR \sqrt{2m \left(E_p + V(R^\ddagger(n)) \right)} - E_p N. \tag{10}$$

We can also find a relation between the length of the chain and the turning points R_2 and R_3 as

$$N = \int_0^N dn = \int_{R_2}^{R_3} \frac{dR^\ddagger}{(dR^\ddagger/dn)} = \sqrt{\frac{m}{2}} \int_{R_2}^{R_3} \frac{dR^\ddagger}{\sqrt{(E_p + V(R^\ddagger))}}. \tag{11}$$

For any given potential, what one needs is to calculate R_2, R_3, E_p and $E^\ddagger$ for each value of N. In practice, it is easier to fix E_p and then calculate N, R_2, R_3 and $E^\ddagger$ from it. Plots of $E^\ddagger$ versus N are given in figure 4 for three different sets of values of the parameters given in figure 3. Note that in this case the long chain does not go over the barrier as a globule, but is stretched out. This has been pointed out by Park and Sung [12], who call it the 'coil to stretch transition'.

Now we can restate the condition $\left| \frac{1}{l} \frac{dR(n)}{dn} \right| \ll 1$ as the global condition $\left(\frac{2V_b}{ml^2} \right)^{1/2} \ll 1$. If this is satisfied, the model is applicable for all values of N (even for very large). For small values of N this condition can be relaxed.
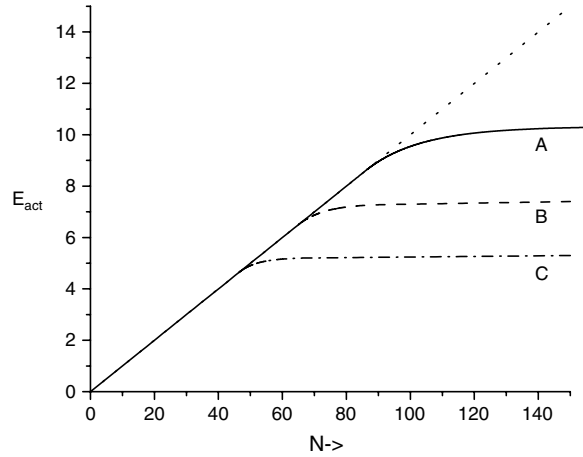
Figure 4. Plot of $E_{act} = E^{\ddagger}$ versus. N for the three cases given in figure 3. At first $E^{\ddagger}$ increases linearly. The straight line passing through origin represents this linear increase. For all the potentials, this happens until $N = \pi/\omega_b$, after which the increase is slower. In the limit of large chains ($N \to \infty$), E_{act} becomes a constant.

4. The rate

Having found the saddle point, we need to calculate the rate. We make use of an approach that is well described in the literature. However, we will have to modify some portions of it to suit the special nature of our problem, particularly in section 4.3, and therefore we give a very brief outline of the method. For a detailed description of the theory of rate processes, we refer the reader to the excellent review by Hanggi et al [29]. The approach that we use is originally due to Langer [23]. The Rouse model in equation (1) leads to the functional Fokker–Planck equation

$$\frac{\partial P}{\partial t} = \frac{1}{\zeta} \int_0^N dn \frac{\delta}{\delta R(n)} \left[k_B T \frac{\delta P}{\delta R(n)} + \frac{\delta E[R(n)]}{\delta R(n)} P \right] \tag{12}$$

for the probability distribution functional P. This equation means that associated with the coordinate $R(n)$ there is a flux $j[R(n)]$ given by

$$j[R(n)] = -\frac{1}{\zeta} \left[k_B T \frac{\delta P}{\delta R(n)} + \frac{\delta E[R(n)]}{\delta R(n)} P \right]. \tag{13}$$

Let us now consider the initial state, which is metastable. We assume the barrier height for the crossing process ($E^{\ddagger}$) to be large. As a result, the rate of crossing is small and one can assume that the probability distribution in the well is given by the equilibrium one. Hence it is

$$P = \frac{1}{Z_0} \exp\left(-E[R(n)]/k_B T\right). \tag{14}$$

Z_0 is defined by

$$Z_0 = \int D[R(n)] \exp\left(-E[R(n)]/k_B T\right). \tag{15}$$

For small amplitude motion around the minimum, one would have $R(n) = R_0 + \delta R(n)$. Using this, the energy functional correct up to second order in $\delta R(n)$ is

$$E[R(n)] = \frac{m}{2} \int_0^N dn \, \delta R(n) \left[-\frac{\partial^2}{\partial n^2} + \omega_0^2 \right] \delta R(n), \tag{16}$$

where we have defined ω_0 by putting $V''(R_0) = m\omega_0^2$ and used the fact that $V(R_0) = 0$. Now we introduce the ψ_k and ε_k which are eigenfunctions and eigenvalues of the operator $H_{ms} = -\frac{\partial^2}{\partial n^2} + \omega_0^2$ in the above equation. We take them to obey the boundary conditions $\partial \psi(n)/\partial n = 0$ at both $n = 0$ and N. These are the normal (Rouse) modes of the system. Now we expand $\delta R(n)$ in terms of ψ_k as $\delta R(n) = \sum_k c_k \psi_k(n)$, c_k being the coefficients of the expansion, and get

$$E[R(n)] = \frac{m}{2} \sum_k \varepsilon_k c_k^2. \tag{17}$$

This expression for the energy may be used in equation (15) and the functional integration performed by integrating over all the c_k. The result is

$$Z_0 = \prod_k (2\pi/m\beta\varepsilon_k)^{1/2}. \tag{18}$$

Now we calculate the flux over the saddle point. As before, we expand $R(n)$ around the saddle as $R(n) = R^{\ddagger}(n) + \delta R(n)$ and get

$$E[R(n)] = E^{\ddagger} + \frac{m}{2} \int_0^N dn\, \delta R(n) \left[-\frac{\partial^2}{\partial n^2} + V''(R^{\ddagger}(n))/m \right] \delta R(n). \tag{19}$$

$E^{\ddagger} = E[R^{\ddagger}(n)]$ is the activation energy. The operator that one has to analyse now is $H^{\ddagger} = -\frac{\partial^2}{\partial n^2} + V''(R^{\ddagger}(n))/m$ and the eigenfunctions are subject to the same conditions as previously. In general, $R^{\ddagger}(n)$ is not a constant, but is a function of n. Therefore, to find the normal modes, we have the Schrödinger-like eigenvalue equation

$$\left[-\frac{\partial^2}{\partial n^2} + V''(R^{\ddagger}(n))/m \right] \psi_k^{\ddagger}(n) = \varepsilon_k^{\ddagger} \psi_k^{\ddagger}(n), \tag{20}$$

$\varepsilon_k^{\ddagger}$ being the eigenvalue of $H^{\ddagger}$. As we are doing a normal mode analysis around a saddle point, there will be only one unstable direction, and this implies that only one of the $\varepsilon_k^{\ddagger}$ will be negative and all others are guaranteed to be positive. We shall take the unstable mode to be the one with $k = 0$. This is the reaction coordinate for the problem. Expanding $\delta R(n) = \sum_k c_k^{\ddagger} \psi_k^{\ddagger}(n)$, we get

$$E[R(n)] = E^{\ddagger} + \frac{m}{2} \sum_k \left(c_k^{\ddagger} \right)^2 \varepsilon_k^{\ddagger}. \tag{21}$$

We write the probability distribution near the saddle as

$$P = \frac{\theta(c_0^{\ddagger}, c_1^{\ddagger}, c_2^{\ddagger}, \ldots)}{Z_0} \exp\left(-\frac{E[R(n)]}{k_B T} \right), \tag{22}$$

where $\theta(c_0^{\ddagger}, c_1^{\ddagger}, c_2^{\ddagger}, \ldots)$ is a function that should approach unity in the vicinity of the initial state, as there one expects to have equilibrium distribution. Taking the functions $\psi_k^{\ddagger}(n)$ to be normalized over the interval $(0, N)$, we can write the analogue of equation (12) in terms of $c_k^{\ddagger}$. The result is

$$\frac{\partial P}{\partial t} = \frac{1}{\zeta} \sum_k \frac{\partial}{\partial c_k^{\ddagger}} \left[k_B T \frac{\partial P}{\partial c_k^{\ddagger}} + \frac{\partial E}{\partial c_k^{\ddagger}} P \right] \tag{23}$$

so that the flux in the direction of $c_k^{\ddagger}$ is

$$j_k^{\ddagger} = -\frac{1}{\zeta} \left[k_B T \frac{\partial P}{\partial c_k^{\ddagger}} + \frac{\partial E}{\partial c_k^{\ddagger}} P \right]. \tag{24}$$

Using equations (21) and (22) in equation (24), we get

$$j_k^{\ddagger} = -\frac{k_B T}{\zeta Z_0} \frac{\partial \theta(c_0^{\ddagger}, c_1^{\ddagger}, c_2^{\ddagger}, \ldots)}{\partial c_k^{\ddagger}} \exp\left(-\beta E^{\ddagger} - \frac{m\beta}{2} \sum_k \left(c_k^{\ddagger}\right)^2 \varepsilon_k^{\ddagger}\right). \tag{25}$$

When a steady state is established, there is flux only in the direction of the unstable mode and this flux has to be constant. This means that only $j_0^{\ddagger}$ is non-zero, implying that θ depends only on $c_0^{\ddagger}$. Thus near the saddle the flux in the unstable direction would be of the form

$$j_0^{\ddagger} = A \frac{k_B T}{\zeta Z_0} \exp\left(-\beta E^{\ddagger} - \frac{m\beta}{2} \sum_{k \neq 0} \left(c_k^{\ddagger}\right)^2 \varepsilon_k^{\ddagger}\right), \tag{26}$$

where A is a constant that is to be determined. Using equation (26) in (25) we get

$$\frac{\partial \theta(c_0^{\ddagger})}{\partial c_0^{\ddagger}} = -A \exp\left(\frac{m\beta}{2} \left(c_0^{\ddagger}\right)^2 \varepsilon_0^{\ddagger}\right) \tag{27}$$

(remember that $\varepsilon_0^{\ddagger}$ is negative). Integrating and using the condition that as $c_0^{\ddagger} \to -\infty$, $\theta(c_0^{\ddagger})$ should approach unity leads to $A = \left(\frac{-m\beta\varepsilon_0^{\ddagger}}{2\pi}\right)^{1/2}$ and hence

$$\theta(c_0^{\ddagger}) = \left(\frac{-m\beta\varepsilon_0^{\ddagger}}{2\pi}\right)^{1/2} \int_{c_0^{\ddagger}}^{\infty} dz \exp\left(\frac{m}{2}\beta\varepsilon_0^{\ddagger}z^2\right). \tag{28}$$

Now that $\theta(c_0^{\ddagger})$ is known, the flux is easily calculated and is found to be

$$\Gamma = \frac{k_B T}{\zeta Z_0} \left(\frac{m\beta\left(-\varepsilon_0^{\ddagger}\right)}{2\pi}\right)^{1/2} \prod_k' (2\pi/m\beta\varepsilon_k^{\ddagger})^{1/2} \exp\left(-\beta E^{\ddagger}\right). \tag{29}$$

The prime in the product $\prod_k'$ indicates that the unstable mode has to be left out. On using equation (18), we get

$$\Gamma = \frac{m}{2\pi\zeta} \left(-\varepsilon_0^{\ddagger}\right)^{1/2} \left(\frac{\prod_k \varepsilon_k}{\prod_k' \varepsilon_k^{\ddagger}}\right)^{1/2} \exp\left(-\beta E^{\ddagger}\right) \tag{30}$$

$$= \frac{m}{2\pi\zeta} \left(-\varepsilon_0^{\ddagger}\right) \left(\frac{\prod_k \varepsilon_k}{(-1)\prod_k \varepsilon_k^{\ddagger}}\right)^{1/2} \exp\left(-\beta E^{\ddagger}\right). \tag{31}$$

This equation can be written in the more interesting form

$$\Gamma = \frac{m}{2\pi\zeta} \left(-\varepsilon_0^{\ddagger}\right) \left(\frac{\left|-\frac{\partial^2}{\partial n^2} + \omega_0^2\right|}{(-1)\left|-\frac{\partial^2}{\partial n^2} + V''(R^{\ddagger}(n))/m\right|}\right)^{1/2} \exp\left(-\beta E^{\ddagger}\right) \tag{32}$$

$\left|-\frac{\partial^2}{\partial n^2} + \omega_0^2\right|$ stands for the determinant of the operator $-\frac{\partial^2}{\partial n^2} + \omega_0^2$. This expression is quite useful because determinants of this type always occur in the semiclassical evaluation of path integrals in quantum mechanics (see for example [30]). However, the boundary conditions for the eigenfunctions in our problem are different from those of quantum mechanics—here the derivatives of the eigenfunction vanish at the boundaries, and not the functions themselves. The formula given by Coleman in the appendix of his article [30] is easily modified to suit this case too and the result is

$$\Gamma = \frac{m}{2\pi\zeta} \left(-\varepsilon_0^{\ddagger}\right) \left(\frac{\phi_0'(N)}{(-1)\phi^{\ddagger'}(N)}\right)^{1/2} \exp\left(-\beta E^{\ddagger}\right), \tag{33}$$

where the prime is used to denote the derivative. $\phi_0(n)$ and $\phi^{\ddagger}(n)$ obey the following equations:

$$\left(-\frac{\partial^2}{\partial n^2} + \omega_0^2\right)\phi_0(n) = 0 \qquad \text{and} \qquad \phi_0(0) = 1; \phi_0'(0) = 0 \qquad (34)$$

and

$$\left(-\frac{\partial^2}{\partial n^2} + V''(R^{\ddagger}(n))/m\right)\phi^{\ddagger}(n) = 0 \qquad \text{and} \qquad \phi^{\ddagger}(0) = 1; \phi^{\ddagger\prime}(0) = 0. \qquad (35)$$

The proof of this would follow closely that given by Coleman [30] and therefore we do not give it here. Equation (34) is easily solved to get $\phi_0(N) = \cosh(\omega_0 N)$, so that

$$\Gamma = \frac{m}{2\pi\zeta}\left(-\varepsilon_0^{\ddagger}\right)\left(\frac{\omega_0 \sinh(\omega_0 N)}{(-1)\phi^{\ddagger\prime}(N)}\right)^{1/2} \exp\left(-\beta E^{\ddagger}\right). \qquad (36)$$

This is the expression for the rate that we shall use in our calculations in the following.

4.1. Case I: $N < N_c = \pi/\omega_b$

In this case, the saddle is just $R^{\ddagger}(n) = R_b$. This means that the whole of the polymer goes over the barrier as a globule. The Rouse modes of the system are eigenfunctions of the operator $H^{\ddagger} = -\frac{\partial^2}{\partial n^2} + V''(R_b)/m$. They are $\psi_k(n) = N_k \cos(n\pi k/N)$, $k = 0, 1, 2, \ldots$. N_k is the normalization factor defined by $N_0 = 1/\sqrt{N}$ and $N_k = \sqrt{2/N}$. These are just the usual Rouse modes, and the corresponding eigenvalues are $\pi^2 k^2/N^2 - \omega_b^2$. The reaction coordinate is the $k = 0$ mode and the associated eigenvalue is $\varepsilon_0^{\ddagger} = -\omega_b^2$. We can solve equation (35) for $\phi^{\ddagger}(n)$ and get $\phi^{\ddagger}(n) = \cos(\omega_b n)$. Thus, the rate is

$$\Gamma_< = \frac{m\omega_b^2}{2\pi\zeta}\left(\frac{\omega_0 \sinh(\omega_0 N)}{\omega_b \sin(\omega_b N)}\right)^{1/2} \exp\left(-E^{\ddagger}/k_B T\right). \qquad (37)$$

As found earlier, $E^{\ddagger} = NV_b$. This expression breaks down as $N \to N_c$ and is not valid if $N > N_c$. It is interesting to note that in the limit of small N such that $\omega_0 N \ll 1$ and $\omega_b N \ll 1$ the prefactor reduces to $\frac{\omega_b \omega_0}{2\pi(\zeta/m)}$, which has exactly the same form as the well known expression in the one-dimensional case [29].

4.2. Case II: $N > N_c = \pi/\omega_b$

In this case, one has the oscillating solution, shown in figure 2 as the saddle point. As one increases the value of N, until it reaches the value N_c, the saddle point is given by $R(n) = R_b$. As N is increased further, $\varepsilon_1^{\ddagger} = (\pi/N)^2 - \omega_b^2$ becomes negative so that there are now two unstable modes ($k = 0$ and 1). So $R(n) = R_b$ is no longer a saddle, but a hilltop. What is happening is that the saddle point bifurcates, resulting in two new saddle points on two sides of the old one on the free energy hypersurface. Each of the new saddle points is given by the oscillating solution, analysed in section 3.2, and corresponds to a transition state in which the chain is stretched out. The reason why there are two saddles is that in the stretched out state it is possible for the molecule to go over the barrier with either of its two ends going over first. These two saddles can be accounted for by multiplying the rate in equation (36) by a factor of two to get

$$\Gamma_> = \frac{m}{\pi\zeta}\left(-\varepsilon_0^{\ddagger}\right)\left(\frac{\omega_0 \sinh(\omega_0 N)}{(-1)\phi^{\ddagger\prime}(N)}\right)^{1/2} \exp\left(-\beta E^{\ddagger}\right). \qquad (38)$$
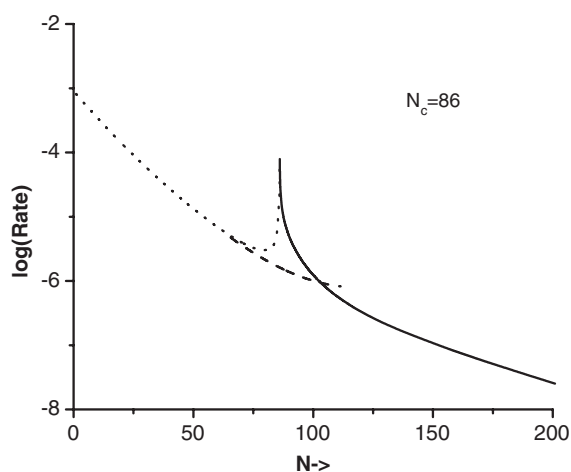
Figure 5. Plot of $\log_{10}$(rate) against N for the symmetric potential, with $a_0 = 10, a_1 = 10$ and $V_b = 1/10$. The dotted line is the rate using equation (37). The full line represents the rate calculated using the extended transition state equation (38), while the dashed line is the result of using equation (40).
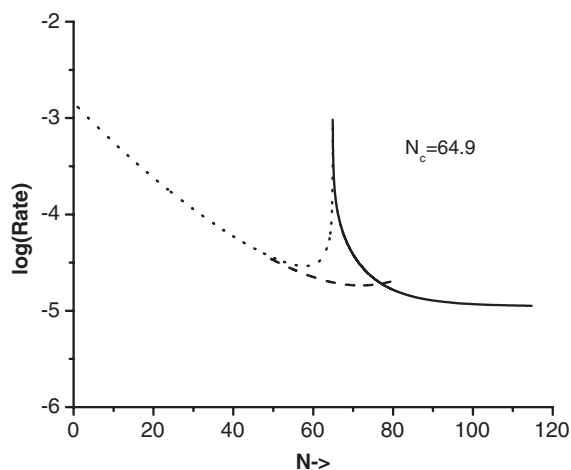

Figure 6. Plot of $\log_{10}$(rate) against N for the symmetric potential, with $a_0 = 8, a_1 = 12$ and $V_b = 1/10$. The dotted line is the rate using equation (37). The full line represents the rate calculated using the extended transition state equation (38) while the dashed line is the result of using equation (40).

4.3. Singular behaviour of the rate and its removal

Even though we have been able to evaluate the rate in the two cases, equation (37) has the problem that the rate would diverge at $N = \pi/\omega_b$. The same problem occurs with equation (38) too (see figures 5–7). This has already been pointed out by Park and Sung [12], and Lee and Sung in a later paper on barrier crossing by semiflexible polymers [16] suggested the solution too, though without pointing out that there is a bifurcation of the saddle point. The solution to the problem is to go to higher order in the expansion of energy for the mode whose eigenvalue $\varepsilon_1^{\ddagger}$ becomes zero. That is, the expression for energy in equation (21) may be modified to include
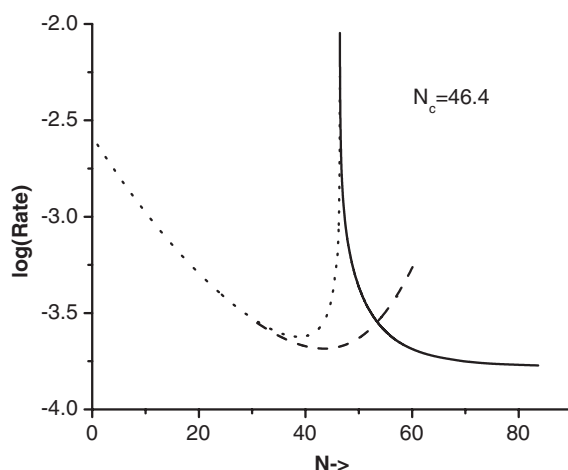
Figure 7. Plot of $\log_{10}$(rate) against N for the symmetric potential, with $a_0 = 6$, $a_1 = 14$ and $V_b = 1/10$. The dotted line is the rate using equation (37). The full line represents the rate calculated using the extended transition state equation (38) while the dashed line is the result of using equation (40).

terms up to fourth order in $c_1^\ddagger$, so that it becomes

$$E[R(n)] = E^\ddagger + \frac{m}{2} \sum_{k \neq 1} \left(c_k^\ddagger\right)^2 \varepsilon_k^\ddagger + \left(c_1^\ddagger\right)^2 \frac{m}{2} \left(\frac{\pi^2}{N^2} - \omega_b^2\right) + \left(c_1^\ddagger\right)^4 \frac{V^{(4)}(R_b)}{16N} \tag{39}$$

where $V^{(4)}(R_b)$ is the fourth derivative of the potential $V(R)$ evaluated at R_b. Using this in the expression for the flux in equation (26) and proceeding as earlier, we get the corrected rate Γ_c to be

$$\Gamma_c = \sigma \left|\Gamma_<\right|. \tag{40}$$

σ is the correction factor given by

$$\sigma = e^{\frac{a^2}{8b}} \sqrt{\frac{\pi}{8b}} \left(|a| I_{-\frac{1}{4}}\left(\frac{a^2}{8b}\right) - a I_{\frac{1}{4}}\left(\frac{a^2}{8b}\right)\right), \tag{41}$$

and $a = \frac{m\beta}{2}\left(\frac{\pi^2}{N^2} - \omega_b^2\right)$ and $b = \frac{\beta V^{(4)}(R_b)}{16N}$. I_n is the modified Bessel function of the first kind. This expression is valid for N above or below N_c, but has to be close to it. Note that for $N > N_c$, $\Gamma_<$ is imaginary, but equation (40) still holds.

5. Numerical calculations

Using the above expressions, it is very easy to calculate the rate using Mathematica. For the calculations, it is convenient to use dimensionless variables defined by $\tilde{V} = V/k_B T$, $\tilde{R} = R/l$ and $\tilde{t} = k_B T t/(\zeta l^2)$. We shall do this, and for the sake of convenience drop the tildes above these variables. Thus in this section all the variables are dimensionless. In these units, the value of $m = 3$. We chose the potential such that it has minima at $R = -a_0$ and a_1 (a_0 and a_1 being positive numbers) and a barrier at $R = 0$. Further, we take $V(-a_0) = 0$. The potential that we use is

$$V(R) = \frac{k}{6}(R + a_0)^2 \left(3R^2 - 2Ra_0 - 4Ra_1 + a_0^2 + 2a_0 a_1\right). \tag{42}$$

The barrier height for this potential is $V_b = \frac{k}{6}a_0^3(a_0 + 2a_1)$ and the free energy difference between the two minima is $\Delta V = V(a_1) - V(-a_0) = \frac{k}{6}(a_0 - a_1)(a_0 + a_1)^3$. By choosing $a_1 > a_0$ the value of ΔV is assured to be negative.

In the limit of large N, the expression for the rate given in equation (38) becomes

$$\Gamma_> = \frac{m}{\pi\zeta}\left(-\varepsilon_0^{\ddagger}\right)\left(\frac{\omega_0}{(-2)\phi^{\ddagger\prime}(N)}\right)^{1/2}\exp\left(-\beta E^{\ddagger} + \frac{\omega_0 N}{2}\right). \tag{43}$$

For large N, we have already seen that $E^{\ddagger}$ becomes a constant. Therefore, the equation predicts that for large enough N there will be an enhancement in the rate of crossing. This is purely an effect of confinement of the long chain in its initial state [12]. The confinement increases its free energy and thus lowers the free energy of activation, causing the increase in the rate.

Calculations were done for three sets of values of the parameters. As there are several parameters that could be varied, we chose them such that V_b was always equal to $1/10$. We also kept the width of the potential, as given by $a_0 + a_1$, equal to a constant ($=20$).

A: $a_0 = 10$, $a_1 = 10$, $V_b = 1/10$. The potential is a symmetric double well.

B: $a_0 = 8$, $a_1 = 12$, $V_b = 1/10$ and

C: $a_0 = 6$, $a_1 = 14$, $V_b = 1/10$.

The shapes of the potential for three set values for the parameters are given in figure 3. As one increases the ratio a_1/a_0, the potential becomes more and more asymmetric. Plots of $E^{\ddagger}$ for these three sets are given in figure 4. As expected, for very short chains, the activation energy increases linearly with N until N_c. From N_c onwards the transition state is the stretched one and the activation energy increases more slowly, and in the limit $N \to \infty$ it reaches a constant value.

In figures 5–7 we give plots of the rate against N for the three cases. The full line in these figures represent the rate calculated using equation (37). This equation holds only for $N < N_c$, and gives a rate that diverges at $N = N_c$. The dashed line in these figures shows the rate calculated using equation (38), which is valid for $N > N_c$. This also diverges as one approaches N_c. The rate near N_c is calculated using equation (40), which takes higher order terms in $c_1^{\ddagger}$ into account. The result is shown by the dotted lines in the figures. It is seen that the result is able to bridge across the singularity at N_c.

6. Conclusions

We have considered the dynamics of barrier crossing by polymer chains. The case of long chains has already been considered in [15], where it was shown that the activation energy is independent of N, and that once the barrier is overcome the chain will continue to cross by a kink mechanism. Here, the analysis is carried out for shorter chains. For very short chains, we find that the molecule will go over the barrier as a globule and the activation energy is proportional to the length of the molecule. Therefore, the rate of crossing will steadily decrease with length. But when the length of the molecule exceeds a critical value ($=N_c = \pi/\omega_b$), which depends on the curvature at the top of the barrier, the globular transition state becomes unstable. It bifurcates into two new saddles, both having the same energy. The two saddles correspond to the fact that the molecule has two ends, either of which may cross over first. For these two saddles, the configuration of the chain is extended (stretched). The stretching of the chain causes a lowering of the activation energy and the rate decreases more slowly. For larger N, the increase in free energy of the chain in the initial well becomes important

and therefore the rate can increase as one increases the length of the chain. Using the harmonic approximation in the vicinity of the initial point and the saddle, we have evaluated the rate using the multidimensional approach of Langer [23]. Analytical expressions have been derived for the rate and used for calculations. These expressions, because of the harmonic approximations made in deriving them, diverge near N_c. In the region near N_c, the corrected rate expression can be derived, and this is found to bridge the rates for globular and extended saddle points.

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