Pulling a polymer out of a potential well and the mechanical unzipping of DNA

K. L. Sebastian
Department of Inorganic and Physical Chemistry, Indian Institute of Science, Bangalore 560012, India

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Motivated by experiments on DNA under torsion, we consider the problem of pulling a polymer out of a potential well by a force applied to one of its ends. If the force is less than a critical value, then the process is activated, and has an activation energy proportional to the length of the chain. Above this critical value, the process is barrierless and will occur spontaneously. We use the Rouse model for a description of the dynamics of the peeling out, and study the average behavior of the chain by replacing the random noise by its mean. The resultant mean-field equation is a nonlinear diffusion equation, and hence rather difficult to analyze. We use physical arguments to convert this to a moving boundary value problem, which can then be solved exactly. The result is that the time t_{po} required to pull out a polymer of N segments scales like N^2. For models other than the Rouse model, we argue that $t_{po} \sim N^{1+\nu}$.

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I. INTRODUCTION

Considerable attention has been paid to the replication of the DNA molecule [1]. The first step in the replication is the unzipping of the two strands. Usually, this is caused by enzymes, and mechanical force at the molecular level is involved in the action of these enzymes. Recently, micromanipulation techniques have been developed to study single molecules of DNA under stress [2]. Most such single molecule experiments have concerned the stretching properties of DNA, but very recently, the response of the DNA to external torques was also studied [3,4]. Mechanical unzipping of the two strands of the DNA, in the absence of enzymes, has been carried out [6]. There have been interesting investigations of the theory of stretching DNA [5], and its denaturation under a torque (see Fig. 1) [7,8]. In an interesting recent e-print, Bhattacharjee [7] suggested a minimal model to study the unzipping. He treated the DNA as consisting of two flexible interacting elastic strings which are bound together by an attractive interaction. The two are tied together at one end, and at the other end there are forces acting on the two strands, trying to separate them. Winding was ignored in his analysis. He assumed that in relative coordinates, the Hamiltonian for the unzipping problem is equivalent to that for a single chain, subject to an attractive short range potential well with a force acting at one of its ends. It is shown that the polymer can be pulled out only if the force exceeds a critical value. The model is of interest in other contexts as well. For example, one can imagine constructing microfabricated channels having different depths in different regions to trap the polymer by entropic barriers (see the recent experiments by Han *et al.* [9]), and then pulling it out from the traps by the application of a force at one end. Another possible application is the desorption of a long chain molecule adsorbed on a surface by pulling at one end. Our aim in this paper is to investigate the dynamics of the escape of a chain from a potential well as a result of applying a force at one of its ends. We consider only the one-dimensional problem, and our approach is much less sophisticated than that of Ref. [7], as we do not take into account the excluded volume interaction. We bring out the physical reason for the existence of the critical force. For describing the dynamics, we use the simple Rouse model. We find that t_{po}, the time required to pull out a chain molecule of N segments, scales as N^2.

In Sec. II we give an outline of the statistical mechanics of a polymer, trapped by an attractive potential, with a force acting at one end. Section III outlines the Rouse model that is applicable for a polymer subject to a force, and analyzes why the force has to exceed a critical force for pulling it out. In Sec. IV, we argue that the problem can be approximated by a moving boundary value problem and then solve the problem. Finally, Sec. V summarizes our conclusions.

II. STATISTICAL MECHANICS OF A TRAPPED POLYMER WITH A FORCE AT ONE OF ITS ENDS

In this section we consider the statistical mechanics of a polymer in one dimension, trapped in an attractive potential $V(R)$, that is located near $R=0$ (see Fig. 2 for the nature

FIG. 1. The forced unzipping of DNA.

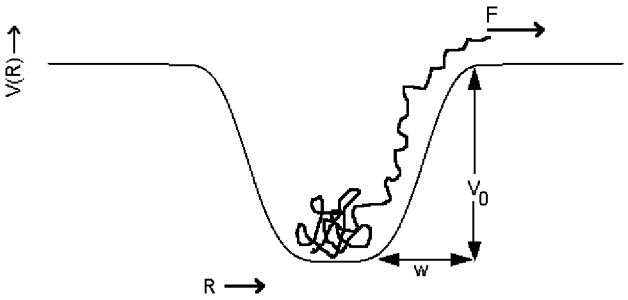

FIG. 2. The polymer trapped in a potential well, subject to a force F.

of the potential) and subject to a force F at one of its ends. We take the number of segments in the polymer to be N. The partition function for a free polymer, that is not subject to any force but has one end at $R=0$, may be calculated as $Z=\int dRG(R,0,N)$, where $G(R,0,N)$ is the propagator for the unforced molecule, which obeys the differential equation

$$\left(\frac{\partial}{\partial N}-\frac{l^2}{6}\frac{\partial^2}{\partial N^2}+\frac{1}{k_BT}V(R)\right)G(R,R_0,N)=\delta(N)\delta(R-R_0)$$

(see Ref. [10]). l is the Kuhn length for the chain, and R and R_0 denote the positions of the two ends of the chain.

In the presence of a force F acting at the end at R, the partition function becomes

$$Z=\int_{-\infty}^{\infty}dRG(R,0,N)e^{RF/k_BT}. \qquad (1)$$

Using the ground state dominance approximation for the propagator, valid for long polymers [10], we can write the above as

$$Z=\int_{-\infty}^{\infty}dR\psi_0^*(R)\psi_0(0)e^{(RF-E_0N)/k_BT}, \qquad (2)$$

where $\psi_0(R)$ is the lowest eigenfunction of the operator $H=-(l^2/6)(\partial^2/\partial R^2)+(1/k_BT)V(R)$, having the eigenvalue $E_0/(k_BT)$. Now, for large values of R, the eigenfunction $\psi_0(R)\sim\exp(-\sqrt{(-6E_0/l^2k_BT)}R)$ $\sim\exp(-\sqrt{(6V_0/l^2k_BT)}R)$, where in the last step we have neglected the "zero point energy" contribution to the lowest eigenvalue and approximated it by $-V_0$, where V_0 is the depth of the potential well. On using this in Eq. (2), we realize that for $F>F_c=\sqrt{6k_BTV_0/l^2}$, the contribution from large values of R make the integral diverge, indicating that for $F>F_c$, the polymer is pulled out of the hole. For $F<F_c$, the partition function is finite, indicating that the molecule remains trapped. In this analysis, we have neglected the zero-point energy, which, in the polymer problem, is equivalent to neglecting the effect of thermal fluctuations. Thermal fluctuations make F_c slightly lower [7].

III. ROUSE MODEL AND THE FREE ENERGY PROFILE FOR THE PULLED POLYMER

The process that we study is shown in Fig. 2. For its description, we use the continuum limit of the Rouse model, discussed in detail by Doi and Edwards [10], which was recently used to study the related problem of escape of a polymer over a barrier [11]. The chain is approximated as a string, with segments (beads) labeled by their position n along the chain. n is taken to be a continuous variable, having values ranging from $-N$ to 0 (this is convenient for the present problem). The position of the nth segment in space (one dimension) is denoted by $R(n,t)$, where t is time. In the Rouse model, this position undergoes overdamped Brownian motion, and its time development is described by the equation

$$\zeta\frac{\partial R(n,t)}{\partial t}=m\frac{\partial^2R(n,t)}{\partial n^2}-V'(R(n,t))+f(n,t). \qquad (3)$$

In the above, ζ is a friction coefficient for the nth segment. The term $m[\partial^2R(n,t)/\partial n^2]$ comes from the fact that stretching the chain can lower its entropy and hence increase its free energy. Consequently, the parameter $m=3k_BT/l^2$ [see Doi and Edwards [10], Eq. (4.5). They used the symbol k for the quantity that we call m]. $V(R)$ is the free energy of a segment of chain, located at the position R and $V'(R)=\partial V(R)/\partial R$. $f(n,t)$ are random forces acting on the nth segment, and have the correlation function $\langle f(n,t)f(n_1,t_1)\rangle=2\zeta k_BT\delta(n-n_1)\delta(t-t_1)$ [see Ref. [10], Eq. (4.12)]. The deterministic part of Eq. (3), which will play a key role in our analysis, is obtained by replacing the random noise term in Eq. (3), by its mean. As we are applying a force at one end of the polymer (at $n=0$), and as the other end is free, the boundary conditions to be satisfied are

$$\left\{\frac{\partial R(n,t)}{\partial n}\right\}_{n=0}=\frac{F}{m}, \qquad (4)$$

$$\left\{\frac{\partial R(n,t)}{\partial n}\right\}_{n=-N}=0. \qquad (5)$$

The above equations may equivalently be written as

$$\zeta\frac{\partial R}{\partial t}=-\frac{\delta}{\delta R(n)}E[R)]+f(n,t), \qquad (6)$$

where we have defined the free energy functional

$$E[R]=\int_{-N}^{0}dn\left\{\frac{m}{2}\left(\frac{\partial R}{\partial n}\right)^2+V(R)-FR(n)\delta(n+\varepsilon)\right\}. \qquad (7)$$

$\varepsilon(\to 0)$ is a small positive number. The process of pulling out may be made physically clearer by analyzing this free energy functional. For this, we consider the free energy hypersurface that results from Eqs. (4), (5), and (7). We find the extrema on this surface by putting $(\delta/\delta R)E[R]=0$, which leads to

$$m\frac{\partial^2R}{\partial n^2}=V'(R) \quad \text{for } n<0. \qquad (8)$$

This has to be solved, subject to the conditions of Eqs. (4) and (5). Imagining and speaking of n as time for the rest of this section, we realize that this is just Newton's equation for

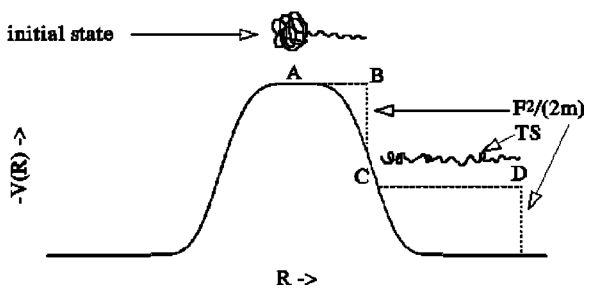

FIG. 3. The upside down potential $-V(R)$. The lines AB and CD represent the solutions of Eq. (8), corresponding to initial and transition states, respectively. The corresponding configurations of the polymer are represented by the coiled curves above them. TS stand for the transition state. The kinetic energy at the $n=0$ end is $F^2/2m$, and this must be less than the height of the potential V_0, if the extrema are to exist.

a particle of mass m, moving in the upside down potential $-V(R)$. In Fig. 3, we show this potential. The boundary condition of Eq. (5) means that the particle has to start at the time $n=-N$, with zero velocity and end at the time $n=0$, with the velocity F/m. This means that at the end of its path, its kinetic energy is $F^2/2m$. At $n=-N$, the particle can at the most start at the top of the potential, where its total energy is V_0. If it obeyed Eq. (8), then, at $n=0$, its kinetic energy has to be less than this amount. Thus we obtain the condition that $V_0>F^2/2m$ (or equivalently, $F_c>F$) for the free energy surface to have a local minimum). If this condition is satisfied, then for any finite value of N, we can find two solutions to Eq. (8) satisfying the boundary conditions (this is true for potentials of the shape shown in the figure). These two solutions are shown in Fig. 3. In the first solution (shown as line AB in the figure), the particle starts near the maximum of $-V(R)$, at the time $n=-N$, and takes a very long time to move away from the maximum; it eventually arrives at point B at the final time $n=0$, with exactly the right kinetic energy of $F^2/2m$. As this corresponds to a configuration for the polymer where almost all its N (assumed to be large) segments are near the minimum of the potential well $V(R)$, we can estimate the free energy for this configuration to be $\sim -NV_0$. The second solution, CD, also shown in Fig. 3, corresponds to the particle starting from rest from an appropriate value of R (point C in Fig. 3) at the time $n=-N$ and arriving at $n=0$ with the kinetic energy $F^2/2m$. The particle spends only relatively small amount of time in the region where the potential energy $-V(R)$ is nonzero. One easily estimates the free energy of the polymer to be $\sim -N(F^2/2m)$. Thus, for a polymer of N segments, there is a barrier of height $N(V_0-(F^2/2m))=N(F_c^2-F^2)/2m$, to be overcome for the pulling the polymer out. As $F\to F_c$ this barrier is reduced, and if $F>F_c$ then the free energy surface has no local minimum—its minimum is at infinity—which means that the pulling out is barrierless and would occur spontaneously. A pictorial representation of this scenario is given in Fig. 4.

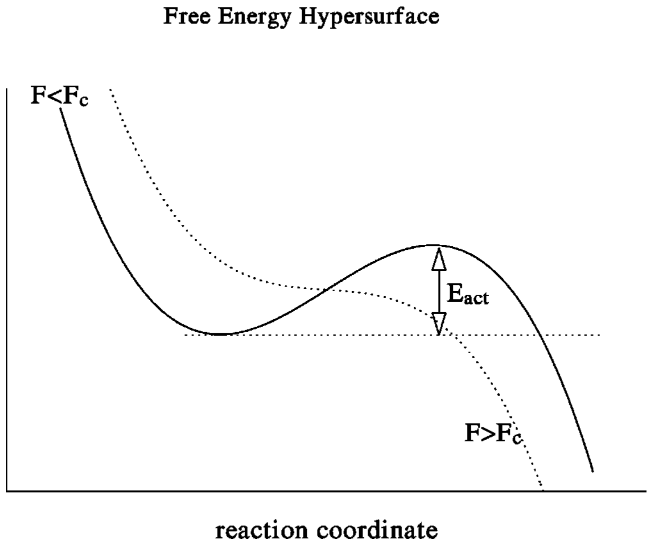

FIG. 4. The free energy hypersurface. For $F<F_c$ it has both a local maximum and a minimum, while for $F>F_c$ no local extrema exist. E_{act} is the activation energy and is equal to $N(F_c^2-F^2)/2m$.

IV. DYNAMICS

We now consider the case with $F>F_c$, so that the pulling out of the chain has no activation barrier. We are interested in only the average behavior of the segments, in the process of pulling out. This may be obtained by analyzing the deterministic equation

$$\zeta\frac{\partial R(n,t)}{\partial t}=m\frac{\partial^2 R(n,t)}{\partial n^2}-V'(R(n,t)), \tag{9}$$

where we have replaced the random term $f(n,t)$ by its average value, viz. 0. We now wish to analyze this equation subject to the two boundary conditions of Eqs. (4) and (5). This equation is just a nonlinear diffusion equation.

Equation (9) is very difficult to solve for any realistic $V(R)$. However, we can use the following physical picture. We take $V(R)$ to be a short ranged well, having a depth of V_0, and to have a rather sharp boundary like the one in Fig. 2. The change over from $-V_0$ to the flat region where $V(R)=0$ occurs over a region of width w, which is assumed to be small. This means that $V'(R(n,t))$ resembles a Dirac δ function, which implies that $\partial R(n,t)/\partial n$ has to change very rapidly across this region, and would resemble a step function. If we consider the process of escape from the well, then, at any time, the units of the polymer with $n<n_i(t)$ would have $R(n,t)=0$, and the segments from $n_i(t)$ to $n_o(t)$ would be spread across the region of width w. We shall refer to $n_o(t)$ as the peeling point. On multiplying Eq. (9) by $\partial R(n,t)/\partial n$, and integrating from $n_i(t)$ to $n_o(t)$, we obtain

$$\frac{m}{2}\left(\frac{\partial R(n,t)}{\partial n}\right)^2_{n_o(t)}-V_0=\zeta\int_{n_i(t)}^{n_o(t)}\frac{\partial R(n,t)}{\partial t}\frac{\partial R(n,t)}{\partial n}dn. \tag{10}$$

In arriving at Eq. (10) we have used the fact that $(\partial R(n,t)/\partial n)_{n_i(t)}=0$ and $V[R(n_i(t))]=-V_0$. If the width w is small, then we are justified in neglecting the right hand side of the Eq. (10), and then we find that $(\partial R(n,t)/\partial n)^2_{n_o(t)}=2V_0/m$, which on taking the square root may be written as

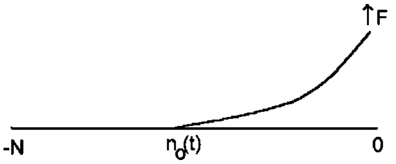

FIG. 5. The moving boundary value problem. The force F is applied at $n=0$. n varies from $-N$ to 0. At a given time t, the portion with $0>n>n_o(t)$ has been pulled out from the well.

$$\left(\frac{\partial R(n,t)}{\partial n}\right)_{n_o(t)}=\frac{F_c}{m}, \tag{11}$$

where $F_c=\sqrt{2mV_0}$. (If we picture the process as in Fig. 5, then we need not worry about the case where $F_c=-\sqrt{2mV_0}$). Now all that we have to do is to solve the diffusion equation (9), outside the well region, subject to the above boundary condition. Outside the well, Eq. (9) becomes the simpler diffusion equation

$$\zeta\frac{\partial R(n,t)}{\partial t}=m\frac{\partial^2 R(n,t)}{\partial n^2}, \tag{12}$$

which is a linear equation. As the range of the potential well is small in comparison with the total length of the polymer, we can take

$$R(n,t)=0 \quad \text{for} \quad n<n_o(t). \tag{13}$$

Thus we now have a moving boundary value problem: we have to solve Eq. (12) for $R(n,t)$, and determine $n_o(t)$, such that conditions (4), (11), and (13) are satisfied (see Fig. 5 for a pictorial representation of the process). In thus simplifying the equation, our assumption of neglecting the right hand side of the Eq. (10) is crucial. Physically, what is being done is that near the point of breaking away from the potential, the segments are assumed to be at equilibrium. This means that the time scale for peeling the polymer away from the well is slow in comparison with the time scale for the establishment of local equilibrium near the peeling point.

Usually, moving boundary value problems are difficult to solve. However, in this case, it is possible to find similarity solutions to these equations. For this, we put $R(n,t)=\sqrt{t}\rho(z)$, where $z=n/(\alpha\sqrt{t})$, with $\alpha=\sqrt{2m/\zeta}$:

$$\frac{d^2\rho(z)}{dz^2}+z\frac{d\rho(z)}{dz}-\rho(z)=0. \tag{14}$$

Note that $z \epsilon (-\infty,0)$. The boundary conditions become

$$\left(\frac{d\rho(z)}{dz}\right)_{z=0}=\frac{\alpha F}{m}, \tag{15}$$

$$\left(\frac{d\rho(z)}{dz}\right)_{z=zo}=\frac{\alpha F_c}{m}, \tag{16}$$

and

$$\rho(z_o)=0, \tag{17}$$

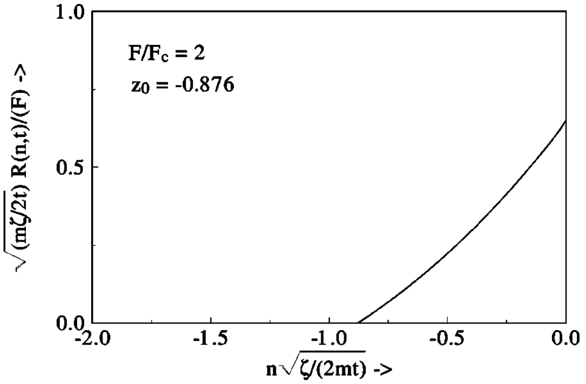

FIG. 6. Plots of $\sqrt{m\zeta/2t}R(n,t)/F$ against $n\sqrt{\zeta/2mt}$.

where z_o is related to $n_o(t)$ by

$$n_o(t)=z_o\alpha\sqrt{t}.$$

These equations can be solved to find $\rho(z)$ and z_o. The result is

$$\rho(z)=\frac{\alpha}{m\,\mathrm{erf}\left(\frac{z_0}{\sqrt{2}}\right)}\left[(F_c-F)\sqrt{\frac{2}{\pi}}e^{-z^2/2}+z\left((F_c-F)\mathrm{erf}\left(\frac{z}{\sqrt{2}}\right)+F\,\mathrm{erf}\left(\frac{z_0}{\sqrt{2}}\right)\right)\right], \tag{18}$$

where $z_o(<0)$ is the solution of the equation

$$\sqrt{\frac{\pi}{2}}\,\mathrm{erf}\left(\frac{z_0}{\sqrt{2}}\right)e^{z_0^2/2}z_0=\frac{(F-F_c)}{F_c}. \tag{19}$$

Note that z_0 is a function of $(F-F_c)/F_c$ only. Using all the above results, we obtain

$$\frac{R(n,t)}{F}\sqrt{\frac{\zeta m}{2t}}=n\sqrt{\frac{\zeta}{2mt}}-\frac{(F-F_c)}{F\,\mathrm{erf}\left(\frac{z_0}{\sqrt{2}}\right)}\left(\sqrt{\frac{2}{\pi}}e^{-n^2\zeta/4mt}+n\sqrt{\frac{\zeta}{2mt}}\,\mathrm{erf}\left(\frac{1}{\sqrt{2}}n\sqrt{\frac{\zeta}{2mt}}\right)\right). \tag{20}$$

To demonstrate the nature of this solution, we note that the right hand side is a function of $n\sqrt{\zeta/2mt}$ alone, and make a plot of the left hand side against this variable in Fig. 6. The important conclusion that we can draw from the above is that the point of detachment of the polymer from the well is given by the equation $n_o(t)=z_0\sqrt{2mt/\zeta}$, where z_0 is the solution of Eq. (19) and is t independent. As the left hand side of Eq. (19) is positive, one has a solution for z_0 only if $(F-F_c)/F_c>0$, and again this just means the existence of the critical force (a similar conclusion was arrived at by Bhattacharjee [7]). His answer was slightly different, as his analysis took the noise term too into account). The pulling out of the polymer is complete when $n_o(t)=-N$. Hence the time required to pull out the chain is given by

$$t_{po}=\left(\frac{N}{z_0\alpha}\right)^2.$$

For forces slightly exceeding the critical force, one can solve Eq. (19) and obtain

$$z_0=-\left(\frac{(F-F_c)}{F_c}\sqrt{\frac{2}{\pi}}\right)^{1/2}.$$

Hence we conclude that $t_{po}\sim N^2$. Further, for small $(F-F_c)$,

$$t_{po}\sim(F-F_c)^{-1}. \tag{21}$$

V. CONCLUSIONS

We now summarize our results and point out the drawbacks of our analysis. Using the Rouse model, we find that for a polymer trapped in a potential well, subject to a force at one of its ends, there exists a critical force F_c. Below this critical force the pulling out is an activated process, with an activation energy proportional to the number of segments in the chain. So the pulling out would not occur. For forces higher than F_c, there is no barrier, and the process would occur spontaneously. The dynamics of the pulling out is described by a nonlinear Rouse equation, which is rather difficult to solve. We find an approximate solution by (a) confining ourselves to the average behavior of the positions of the segments, and (b) introducing a local equilibrium assumption, which enables us to convert the nonlinear equation to a moving boundary value problem. This moving boundary value problem has a similarity solution, and this leads to the conclusion that the time required to pull the chain out scales like N^2.

Obviously, there is scope for improvement of our analysis. One would like to perform a more detailed analysis, including the effects of noise. Also, the effects of hydrodynamic interactions and the excluded volume interactions have to be included. Inclusion of these may be done by modifying Eq. (3) to

$$\zeta\frac{\partial R(n,t)}{\partial t}=m\int dn_1 h(n-n_1)\frac{\partial^2 R(n_1,t)}{\partial n_1^2}-V'(R(n,t))+f(n,t)$$

[see Eq. (4.50) of Ref. [10]]. In general, $h(n)\sim n^{-\nu}$, with $v<1$ (different values can be used for ν to account for Zimm dynamics or excluded volume interactions—see Eqs. (4.49) and (4.69) of Ref. [10]). With the boundary conditions same as in our Eqs. (5), (11), and (13), one finds that $t_{po}\sim N^{1+\nu}$.

Our results above, however, are only the first few steps in the analysis of this very interesting problem. The most important next step, obviously, is to go beyond our mean-field description by including the fluctuations. It seems likely that fluctuations can modify the long time behavior qualitatively.

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