Thermal activation at moderate-to-high and high damping: Finite barrier effects and force spectroscopy

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We study the thermal escape problem in the moderate-to-high and high damping regime of a system with a parabolic barrier. We present a formula that matches our numerical results accounting for finite barrier effects, and compare it with previous works. We also show results for the full damping range. We quantitatively study some aspects on the relation between mean first passage time and the definition of an escape rate. To finish, we apply our results and considerations in the framework of force spectroscopy problems. We study the differences on the predictions using the different theories and discuss the role of $γ\dot{F}$ as the relevant parameter at high damping. © 2013 American Institute of Physics. [http://dx.doi.org/10.1063/1.4793983]

I. INTRODUCTION

Seventy years ago, Kramers1 proposed an equation for the thermal escape of a Brownian particle out of a metastable well. This problem is considered as an issue of fundamental interest and it has received great attention from an impressive number of scientific areas.2–4 We present here a minor contribution to this vast field: a detailed numerical study, by using Langevin dynamics simulations, of the activation problem in the moderate-to-high and high damping regime of the system.

This work is motivated by a recent numerical study of the Kramers problem at low damping.5 There, important finite barrier effects were described, a very slow convergence to the infinite barrier limit of the system was reported, and the accuracy of the Drozdov-Hayashi (DH) theory6 was proved. As it is shown there, an accurate theory is of fundamental interest to understand experiments in this physical regime.

On the other side of the same coin, the high damping limit of the problem is found. This is the typical case for many of the current friction1–11 and biological-physics works,12–14 where escape rate is the fundamental concept to understand force spectroscopy experiments. In many of these works, the Kramers result for the escape rate at high damping,

$$r_{KHD} = \frac{\omega_a \omega_b}{2\pi \gamma} e^{-\Delta U / k_B T},$$

(1.1)

appears as the theoretical starting point to understand experimental results.

In his famous work,1 Kramers also derived an expression for the escape rate in the moderate-to-high damping limit,

$$r_{KMHD} = k_{KMHD} \times \frac{\omega_a}{2\pi} e^{-\Delta U / k_B T},$$

(1.2)

where the damping dependent prefactor is given by $k_{KMHD}(\gamma / \omega_b) = [1 + (\gamma / 2\omega_b)^2]^{-1/2} - (\gamma / 2\omega_b)$. There, $\omega_a$ and $\omega_b$ are related with the potential curvature at the well and the barrier, respectively, see Fig. I. $\Delta U$ stands for the potential barrier and $\gamma$ for the damping of the system. For high damping, $\gamma / \omega_b \gg 1$, we have $k_{KHD} := \omega_b / \gamma$ for the prefactor and we recover the extensively used result of Eq. (1.1). The given results were obtained for a parabolic barrier15 in the so-called infinite barrier regime of the system, where $\Delta U / k_B T \gg 1$.

Another important concept in thermal activation theory is the mean first passage time (MFPT), This is defined as the mean time (t) for particles injected with zero velocity at point a, to reach a point b, where they are absorbed. In the overdamped limit, given the potential $U(x)$, the MFPT can be exactly computed as

$$\langle t \rangle_{HD} = \frac{m \gamma}{k_B T} \int_a^b dy e^{U(y) / k_B T} \int_{-\infty}^y dz e^{-U(z) / k_B T}.$$

(1.3)

There exists an important literature studying the relation between transition rates and mean first passage times.2–4, 16, 17 It has been usually assumed, and theoretically proved, that there is a close relation between both quantities and in fact

$$r = \frac{1}{\langle t \rangle},$$

(1.4)

whenever the injection and adsorbing points correspond to two potential minima separated by a barrier. Thus, Eqs. (1.3) and (1.4) allow for computing the exact escape rate in the overdamped limit of the system and for comparing to the Kramers infinite barrier and other escape rate results in this physical regime.

We devote Sec. II of the paper to this end where a critical review of existing theories is presented. There, we propose a relatively simple equation, Eq. (2.3), to compute the escape rate for any barrier and damping in the moderate-to-high and high damping domains. Then, in Sec. III we study the time to reach the barrier problem. This time, $\langle t \rangle_M$, differs from the previously calculated $\langle t \rangle$ by a factor that changes from 1 to 1/2 when damping increases, and it is the relevant quantity in some situations.

Armed with our previous results, we attack in Sec. IV the so-called force spectroscopy problems. There, the system is continuously biased by an external field and the escape field probability distribution function is recorded. We compare
results for the mean escape field based in different theories. We stress the differences between results for field to reach
the next metastable state and field to reach the barrier. We also show that damping times field ramp is the relevant pa-
parameter in the overdamped limit, and that there exists a value of this parameter beyond which important nonequilibrium ef-
facts dominate the problem. We finish by showing results in the full damping spectrum.

II. MODEL AND RESULTS

We use Langevin dynamics simulations to compute the mean time for a particle with a given initial condition to reach
a defined point beyond the barrier. To be precise, we will be first interested in computing the mean time for a particle sit-
ed with zero velocity in the minimum of a metastable well A to reach for first time the next available potential minimum C,
see Fig. 1. For us this will be the definition of the relevant MFPT \( t \) of the problem.

To be definite, we study the dynamics of a Brownian particle in a metastable potential,

\[
m \ddot{x} + m \gamma \dot{x} = - \frac{dV}{dx} + \xi(t),
\]

where for the potential, we use

\[
V(x) = V_0 (1 - \cos x) - F x,
\]

and \( \xi(t) \) is the stochastic force describing the thermal fluctuations. Here we consider white thermal noise, \( \langle \xi(t) \rangle = 0 \) and \( \langle \xi(t) \xi(t') \rangle = 2m\gamma k_BT \delta(t-t') \).

The tilted sinusoidal potential describes a particle in a per-
iodic potential subjected to an external field, a situation of in-
terest in many fields. In particular, Eq. (2.1) is experimentally
realized by a biased Josephson junction, and the high damp-
ing regime can be addressed with resistively shunted tunnel
junctions or with superconducting-normal-superconducting
ones.

We compute the escape rate of a particle out of the meta-
stable well (see Fig. 1) as a function of the damping of the system and for different values of the \( \delta := \Delta U/k_BT \) ratio, which is the most relevant parameter of the problem.

A. High damping

First, we compare in Fig. 2 exact results from the MFPT theory [Eqs. (1.3) and (1.4)] to the Kramers infinite barrier
one, Eq. (1.1). We show also the Pollak and Talkner \( \text{PT} \) and Drozdov \( \text{TST} \) results, which include finite barrier correc-
tions to the escape rates. As a reference we also plot the \( r_{\text{exact}} \) result \( \text{TST} \) [Eq. (A5) in the Appendix]. These results were pro-
posed for the high damping limit of the system. The figure gives a quantitative estimation of the accuracy of the Kramers
high damping result for every barrier. As it can be seen, finite barrier effects are not very severe (below 10%) for normal-
ized barriers above 5. However, some cares have to be taken when considering effects involving barriers below this value.

The figure also shows the convergence of the escape rate to the Kramers infinite barrier result.

As we also see in Fig. 2, PT theory gives a simple ex-
pression very close to the exact result except for small barri-
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of the damping. PT approach fails at low barriers and Drozdov
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FIG. 1. Potential profile. Due to thermal fluctuations, a particle sited in state
A is able to overcome a barrier \( \Delta U \) and escape to state C.

FIG. 2. Theoretical estimations of the escape rate in the high damping limit nor-
malized by the Kramers result. Red line shows the exact mean first pas-
sage time result which accounts for the finite barrier effects in the system. We
also show PT, Drozdov, and exact TST results (see text and the Appendix).
to the moderate damping region where (we will show below that this value of damping corresponds to Eq. (1.3). The formula recovers the correct transition between the moderate-to-low and the moderate-to-high damping region.

B. Moderate-to-high damping

We propose below an expression for the escape rate, which gives a good approximation for any barrier height and damping. Equation (1.3) is exact in the overdamped limit of the system. However, there is no result for the MFPT at other values of the damping of the system.

Our proposal is based in observing our numerical results for the escape rate at different values of damping as a function of the normalized barrier \( \Delta U/k_B T \). Figure 3 shows results for \( \gamma r/\gamma \) (inset) and \( r/r_{KHMHD} \) [note that, different from Fig. 2, now we normalize the rate with respect to Eq. (1.2)] as a function of \( \Delta U/k_B T \) for \( T = 0.01 \) and \( \gamma = 0.1, 0.2, 0.3, 1, \) and 10. There, we see first that our numerical results for high damping agree the theoretical prediction from the MFPT expression, Eq. (1.3).

Figure 3 also shows that, except for the \( \gamma = 0.1 \) curve (we will show below that this value of damping corresponds to the moderate damping region where \( r/r_{KHMHD} \) gets a maximum), all data approximately lie in a same curve when compared to the \( r_{KHMHD} \) prediction. Thus, we propose the following simple extension of the MFPT results of Eq. (1.3) to the moderate-to-high damping region:

\[
r_{MHD} = \frac{\gamma}{\omega_b} \times k_{KHMHD} \left( \frac{\gamma}{\omega_b} \right) \times \left( \frac{1}{t} \right)_{HD}.
\]  

The formula recovers the correct \( r_{HD} = 1/(t)_{HD} \) result for \( \gamma/\omega_b \gg 1 \) and incorporates the \( \gamma \) dependence suggested in Fig. 3. As we will see, this expression gives account of our numerical results in the moderate-to-high damping regime of the problem in a simpler and better way than any previous approach.

In order to evaluate the accuracy of Eq. (2.3), we have performed numerical simulations of the escape rate of the system as a function of \( \gamma \) for different values of the barrier. In particular, Fig. 4 shows our numerical results obtained for four different values of the \( \Delta U/k_B T \) ratio (3, 5, 7, and 10). For better understanding, we plot results in three different ways. Figure 4(a) shows the rate versus the damping. As we see, the theoretical expression is valid for values of \( \gamma \) larger than 0.1, approximately. This value is at the lower limit of the moderate-to-high damping region. Smaller values of \( \gamma \) sets in the moderate-to-low damping regime that we studied previously. These kinds of plots have been extensively used in the literature, however, due to the log scale dependence of the rate, it is not convenient to use them to evaluate the precision of the theoretical equations.

Figure 4(b) plots \( r/r_{HD} \) as a function of \( \gamma/\omega_b \) to check the validity of our ansatz in Eq. (2.3). Plotted in this way, all the curves approximately collapse in a single function given by \( (\gamma/\omega_b) \times k_{KHMHD}(\gamma/\omega_b) \). As expected, deviations appear for the lowest values of damping.

To finish, we present in Fig. 4(c) the direct comparison of our numerical results to Eq. (2.3) and PT theory for \( \delta = 3 \) and \( \delta = 10 \). In this figure, we plot the escape rate normalized by our theoretical expression, \( r/r_{MHD} \) versus \( \gamma/\omega_b \). We conclude that Eq. (2.3) reproduces our numerical results in a better way than previous theories for any barrier and in the full moderate-to-high damping regime.

As we have seen, our numerical results are well fitted by Eq. (2.3) for damping values above \( \gamma \sim 0.2 \) in our units. At these intermediate values of the damping parameter, we are into the so-called turnover region, which characterizes the transition between the moderate-to-low and the moderate-to-high damping regimes.
high damping regimes. There, the classical transition state theory establishes $r_{TST} = (\omega_a/2\pi) \exp(-\Delta U/k_B T)$. 

C. Full damping

In order to supplement the information given in previous works, Fig. 5(a) shows the escape rate divided by the $r_{TST}$ result for a wide range of damping values with special emphasis on the turnover region. As expected, when plotted as a function of the normalized damping $\gamma/\omega_b$, all curves collapse on each other only in the high damping limit. As barrier increases, the maximum moves to lower values of $\gamma/\omega_b$. In any case, rate approaches very slowly to the infinite barrier limit. The figure also shows the theoretical results studied in Ref. 5 and here. We see that the combination of the Drozdov-Hayashi result for moderate-to-low damping values and our extension of the mean first passage time result for moderate-to-high ones gives a fairly good approximation to the numerically computed result for all damping of the system.

Figure 5(b) shows the results for $\Delta U/k_B T = 10$ and also plots three other theoretical approaches. On the one hand, we use the Kramers moderate-to-high damping result and the Buttiker-Harris-Landauer (BHL) one. We see that the latter deviates importantly in the moderate damping region of the system. To finish, we also plot the result of the simplest analytical expression which approaches the escape rate for all damping, which is given by the following interpolation formula: 

$$r^{-1}_{simple} = r^{-1}_{KLD} + r^{-1}_{KMHD},$$

where for a linear-cubic barrier we have $r_{KLD} = (7.2\gamma/2\pi)(\Delta U/k_B T)e^{-\Delta U/k_B T}$, and $r_{KMHD}$ is given by Eq. (1.2). This is a simple expression which, as seen in the figure, gives a first glance good idea of the escape rate behavior in the full damping spectrum of the system.

III. TIME TO REACH THE BARRIER

The general expression for the MFPT, Eq. (1.3), depends on the injection, $a$, and absorption, $b$, points. It is interesting to remark that the adequate choice for both numbers in order to keep Eq. (1.4) valid usually relies on relatively vague criteria, since for particles starting in a metastable well $far$ $enough$ the barrier and adsorbed in another well $well$ $beyond$ the barrier, the dependence on $a$ and $b$ is negligible. Thus, $a$ and $b$ should be both far from the barrier. Equation (1.3) allows for a direct study of the $\langle t(a, b) \rangle$ dependence. Figure 6 explores $\langle t(a, b) \rangle$ as a function of $b = x_a$ (the potential minimum position) and different values of the model parameters. As it can be seen, the MFPT changes importantly in the barrier region. As expected, the time to reach the next potential minimum approximately doubles the time to get the maximum. A similar study can be done to know the dependence of the MFPT on the injection position of the system, $a$.

There exist problems where the relevant physical magnitude is the mean time spent by the system to reach the maximum of the potential barrier (the transition state $B$ in Fig. 1). We call here this time $\langle t \rangle^M$ to distinguish it from $\langle t \rangle$, defined above as the time to reach state $C$ beyond the barrier.

Let us introduce the factor $\epsilon := \langle t \rangle^M/\langle t \rangle$ for the ratio between both times. As can be seen in Fig. 6, a rough estimation

![Diagram](image-url)
in the high damping limit is that $\epsilon_{HD} \simeq 0.5$, showing that a particle in the maximum has a probability close to one half to cross the barrier and close to one half to move backwards to the original well. However, this is not exactly the case and as it is well known\textsuperscript{16} the so-called stochastic separatrix is sited beyond the barrier and differs from the deterministic separatrix. There, interesting dynamic effects appear in the Brownian dynamics of the system.\textsuperscript{28, 29}

The value of $\langle t \rangle^M$ can be computed in the overdamped limit from Eq. (1.3) fixing absorption limit $b$ at the potential barrier position. We have numerically explored how $\epsilon$ depends on the normalized barrier height $\Delta U/k_BT$ and damping of the system. We should expect a weak dependence on the damping $\epsilon$ changes smoothly from a value close to 0.5 for high damping to 1 for small damping. At small damping any particle that reaches the maximum has enough energy to overcome the barrier and rapidly slides down to the next potential minimum.

Figure 7(a) plots $\epsilon$ as a function of $\Delta U/k_BT$ at different values of the damping $\gamma$. Figure 7(b) shows $\epsilon$ as a function of the normalized damping $\gamma \omega_b$ at different values of the normalized barrier $\Delta U/k_BT$. We can see that $\epsilon$ depends very weakly on the barrier except for values of $\Delta U \leq 3k_BT$. In these respects to the damping dependence, $\epsilon$ changes from $\epsilon_{HD} \simeq 0.55$ at our parameters for $\gamma > 10$ to $\epsilon \simeq 1$ for $\gamma < 0.1$.

In a similar way that for evaluating escape rates, it would be useful to get an analytical expression to computing the mean time to reach the maximum at different values of the parameters of the system. From Fig. 7(b) we see that for every barrier we can write $\langle t \rangle^M = f(\gamma \omega_b)(t)$. Following the ansatz used to derive Eq. (2.3), we now propose\textsuperscript{30}

$$
\frac{1}{\langle t \rangle^M_{HD}} = \frac{1}{\gamma \omega_b^2} \epsilon_{HD} \times k_{MHD} \left( \frac{1}{\epsilon \omega_b} \epsilon_{HD} \right) \times \frac{1}{\langle t \rangle^M_{HD}}
$$

for the case of a parabolic barrier. There, $\epsilon_{HD} = (\langle t \rangle^M_{HD}/\langle t \rangle_{HD})$ is computed from Eq. (1.3). Figure 7 compares this equation to the numerical results for two possible values of $\epsilon_{HD}$, 0.5 and 0.545. Though agreement is worse than that for the escape rate case, to our knowledge this is the first attempt to propose an expression for the $\langle t \rangle^M(\gamma)$ dependence.

IV. FORCE SPECTROSCOPY

In a typical force spectroscopy experiment the probability distribution function of the escape force $P(F)$ is measured performing many experiments where force is continuously increased at a given rate $\dot{F}$. From these results the mean escape force $(\bar{F})$ and its standard deviation can be trivially computed. Such $P(F)$ can be easily related to the escape rates $r(F)$ as\textsuperscript{31}

$$
P(F) = r(F) \left( \frac{dF}{dt} \right)^{-1} \left( 1 - \int_0^F P(u) du \right).
$$

Alike, escape rates can be computed from measured $P(F)$. In this section we will show results of the mean escape force in our system for different parameter conditions and compare to available theories.

As in the case of the escape rate and its relation with the MFPT, it is possible to introduce different definitions of escape force. In our simulations we start at zero force with particles in a metastable state (state $A$ in Fig. 1) and increase the force at a given ramp. Then we define the escape force as the mean force for which particles first reach the next metastable state (state $C$). However, in some circumstances the relevant escape force can be related with a different state, for instance the potential barrier (state $B$). In the first case we say that a particle has escaped if it has reached a new potential minimum, in the second if it has just passed the potential maximum.

Figure 8 shows the results of the mean escape force computed for both cases. As expected, $\langle F \rangle$ increases with the damping and both curves overlap for moderate damping and differ at larger ones. The figure also shows the theoretical results obtained from Eq. (4.1) with $r(F)$ computed as Eqs. (2.3) and (3.1), in this last case using $\epsilon_{HD} = 0.545$. As expected, such curves give account of the numerical results in all the studied range. We want to remark that the difference between both curves at high damping is due to the factor close to 0.5 between the MFPT for reaching states $B$ or $C$. Thus, a factor of 0.5 in the prefactor of the rates has a measurable effect in the measured critical force value, see Fig. 8.

We also compare our results with predictions from Eqs. (1.1) and (1.2) and analytical results by Garg\textsuperscript{32} see the Appendix. Based on the small error found in the estimation...
of the system escape rates, we can advance that even the simplest theories give fairly good results. Such analysis is made in the top inset of Fig. 8 where the theoretical results obtained from the Kramers high damping and the Kramers moderate-to-high damping results (red lines), and the first order Garg theory (black dashed lines) for high and moderate damping are shown.

It is interesting to remark that in this numerical experiment escape happens at moderate-to-low values of the barrier over temperature ratio (see bottom inset in Fig. 8). Thus, we see that results obtained from the infinite barrier limit give reasonable estimations for physical processes involving such small barrier values.

Next, we are going to discuss an important issue, regarding the validity of the available theories at very high damping values or force rates, where strong nonequilibrium effects play a role. At high damping escape events are very rare and, if the force is varied fast enough, the critical force of the model (for which barrier disappears) is reached before particles have reached the barrier. Then we can say that the escape problem is somehow ill-defined.

These observations are studied in Fig. 9 where the high $\gamma F$ limit is reached. At high damping the probability distribution function $P(F)$ depends on $F$ and $\gamma$ through the $\gamma F$ product. As seen in the figure, the nonequilibrium high $\gamma F$ regime appears in our simulations for $\gamma F > 10^{-4}$ ($\langle F \rangle > 0.13$ and $\Delta U/k_B T < 2$). There, we observe that an increasingly important fraction of the realizations does not escape before getting the critical force value ($V_0 = 0.155$) for which the potential profile does not show a metastable well structure anymore. This situation is shown by the filled-circles curves in Fig. 9, where the mean escape force of the fraction of particles that have escaped from the potential well for $F < V_0 = 0.155$ is plotted. An adequate theoretical calculation based on the MFPT results allows for reproducing the observed results even in this regime. To compare, we have also computed the mean force for the particles to advance from the starting point $a$ to a point $b = a + 2\pi$. Result is shown by open circles in the figure and, as expected, the theoretical results based in MFPT theory are also able to explain our results.

For the sake of completeness we present in Fig. 10, a plot of the normalized mean escape force for a wide range of damping values, $10^{-5} < \gamma < 10^2$, and two different force rates. As shown before, the escape rate has a maximum for $\gamma \sim 0.1$ and thus the escape force presents a minimum for such damping value. For larger values of $\gamma$, our Eq. (2.3) correctly estimates the escape force. For smaller values of $\gamma$, as shown in Ref. 5, the DH equation for low damping escape6 is valid. However, given the relative complexity of both approaches, we want to compare the results to those obtained with a simple interpolation formula, and the Garg analytical predictions.

The simplest analytical expression which approaches the escape rate for all damping is given by the interpolation formula of Eq. (2.4). As seen in Fig. 10, such expression gives a very good approach to the computation of the mean escape force and can be useful to analyze experiments at moderate damping values. In addition, the figure also shows the simple
approximation published by Garg\textsuperscript{32} (see also the Appendix). We plot first order approach for moderate and high damping cases and second order for the low damping one. Such results also give a good approach to our numerical results in a wide damping area. It is important to remark now that as ramp is decreased, the moderate damping area enlarges. Thus, the border between the different damping regions is also given by the force ramp and a good knowledge of both parameters is needed to correctly understand any experimental result.

V. CONCLUSIONS AND DISCUSSION

In this paper we have presented a number of results concerning the escape problem for moderate-to-high and high damping and its consequences in force spectroscopy experiments. Such problems include for instance cell to cell adhesion and molecular bond experiments,\textsuperscript{13,34–36} dissociation of molecular complexes,\textsuperscript{37} mechanical unfolding of proteins,\textsuperscript{12} single-molecule pulling experiments,\textsuperscript{14,38–42} free-energy reconstruction,\textsuperscript{43–47} and study of friction at the nanoscale.\textsuperscript{8–11,48–50,52,53}

Our work gives an accurate expression, Eq. (2.3), for the escape rate in the moderate-to-high and high damping domains and allows for a quantitative evaluation of errors made in the use of different approaches to the problem. This result combined with the DH one for the moderate-to-low and low damping regime allows for a study of the thermal activation problem over a parabolic barrier for any barrier and damping and a comparison with other simpler theoretical approaches. Then we have quantitatively studied some issues concerning the relation between mean first passage time and the very definition of an escape rate. We have also considered the time to reach the barrier problem and computed its ratio with the usual definition of escape rate at different values of the damping. Activation theory at high damping is a central concept in order to understand force spectroscopy results. We have focused in comparing predictions from the different available theories. Infinite barrier results are usually assumed in literature without an estimation of the real barrier values involved in each case. We have explored this issue and showed that finite barrier effects do not importantly affect force spectroscopy results though escape indeed may occur at very low barrier values (Fig. 8). This was also obtained in Ref. 51. We have also discussed the role of $\gamma F$ as the relevant parameter at high damping.

As discussed in Sec. III and Fig. 6, the very concept of escape rate loses its significance if position initial conditions play a role. This happens when the two relevant time scales, equilibrium at the metastable well and escape time, are not separate. Separation of time scales is a central issue in the theory that has been qualitatively discussed in most of the seminal papers. Figure 6 summarizes our quantitative study. Then, it appears that the concept of an escape rate becomes questionable for barrier heights below 3 (in units of $k_B T$). In relation to this, Fig. 3 shows that theory correctly accounts for our numerical expectations at lower barriers, but certainly it has been obtained with well-defined initial conditions. However, Fig. 8 also shows a good agreement, and there, see bottom inset of the figure, escape happens at very low normalized mean barriers. In this case, force has been adiabatically increased and results are not affected by the chosen initial conditions at $F = 0$. To finish, Fig. 9 gives, in terms of the $\gamma F$ product, the limit of validity of theory when applied to force spectroscopy problems. This limit is certainly reached when the separation of time scales concept fails.

Another important issue is the role played by the damping parameter. This is a pretty difficult issue to evaluate in many real systems, although the validity of the high damping approach is usually assumed. We see that, on the one hand, high damping theories work fine for dimensionless damping $\gamma/\omega > 2$. On the other hand, if the $\gamma F$ product goes above $10^{-4}$, important non-equilibrium effects appear and usual escape rate theories are not valid any more. We have pointed out the existence of a high $\gamma F$ limit beyond which the escape problem is not well defined (see Fig. 9).

Frequently, the main source of uncertainty in the problem is the potential profile itself. Then, sometimes it is assumed $r \sim r_0 \exp(-\Delta U/k_B T)$ with $r_0$ some empirical prefactor. In such cases, all interest is focused on the barrier value and the field dependence of this barrier, and the weak $r_0$ dependence with $F$ is neglected. However, in general, $r_0$ contains information about the damping, the bias field, and the barrier shape.

In adhesion and other similar problems, free energy is frequently modeled by a tilted Morse-type potential. Then, the applied field creates a barrier.\textsuperscript{36} However, next potential minimum is sited at $+\infty$ and escape rate is vaguely defined in terms of being far (but not too far) from the potential barrier. In addition, in some force spectroscopy experiments, the measured maximal spring force corresponds to a rupture event.\textsuperscript{14} Then the particle over barrier picture may fail and the problem can be studied as time to reach a given force, position, or a maximum of a potential profile. Mean time to reach the maximum can be a useful concept for some specific problems and sometimes, when a cusplike barrier is assumed, it is the only meaningful one. However, since in many cases the prefactor is not carefully considered, possible errors on choosing the correct picture are unwittingly integrated in uncertainties on the different parameters involved in the escape rate prefactor. This is an interesting problem that we are currently studying in depth.

In force friction experiments, mean friction force is computed from the maximum force in each stick-slip\textsuperscript{8,9,52,53} cycle. A study using expressions for the escape rate beyond the usual Kramers approach to the escape rate is lacking.

Most of the previously discussed issues are also relevant when analyzing single-molecule pulling experiments\textsuperscript{38,41,54} An interesting question here is that of the reconstruction of free-energy landscapes.\textsuperscript{43} Moreover, in such, and other systems, additional issues beyond the scope of this paper as diffusion in a multidimensional landscape\textsuperscript{42,55} have a fundamental importance.

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APPENDIX: SOME AVAILABLE THEORIES

Here we will give some numerical expressions that have been used along the paper.

1. Pollak and Talkner

Pollak and Talkner proposed\textsuperscript{19} the following expression for the escape rate:

\[ r_{PT} = k_{KMHD} \times r_{TST}^{\text{exact}} \times \left(1 + \frac{f(\chi)}{\chi}\right), \]  
\[ (A1) \]
where \( \chi = \frac{\Delta U/k_b T}{\gamma} \) and \( \chi \) the following function of \( \bar{\gamma} = \frac{\gamma}{\omega_b} \),

\[ \chi = \frac{(1 + \bar{\gamma}^2/4)^{1/2}}{\bar{\gamma}/2} \]  
\[ (A2) \]
and

\[ f(\chi) = \frac{1}{36} \left[ 2 - 3\chi - \frac{1}{2}(\chi + 1)^3 + \frac{3}{2} \left(\chi - 1\right)^2(\chi + 1)(3\chi^2 + 12\chi + 1) \right]/9\chi^2 - 1 \]  
\[ (A3) \]

In the high damping limit \( \chi \to 1 \) and \( f(\chi) \to -5/36 \) then

\[ r_{PT, HD} = \frac{0_b}{\gamma} \times r_{TST}^{\text{exact}} \times \left(1 - \frac{5}{36\chi}\right). \]  
\[ (A4) \]

In this theory it is necessary to compute the term

\[ r_{TST}^{\text{exact}} = \left\{\sqrt{2\pi \beta m} e^{\beta V(x_{\text{max}})} \int_{-\infty}^{x_{\text{max}}} dx \ e^{-\beta V(x)}\right\}^{-1}. \]  
\[ (A5) \]

Note that in the high barrier limit \( r_{TST}^{\text{exact}} \sim \frac{0_b}{\gamma} e^{-\Delta U/k_b T} \) := \( r_{TST} \), the usual result given by the transition state theory and used in Eq. (1.2).

2. Drozdov

The problem was also studied by Drozdov in a series of papers,\textsuperscript{6,21,33} where he proposed

\[ r_D = k_D \times r_{TST}^{\text{exact}}. \]  
\[ (A6) \]

Here,

\[ k_D = \left[1 + \frac{\gamma^4}{\omega_e^4} \left(1 + \frac{4\theta}{n\omega_e \gamma^2}\right)\right]^{-1/4}, \]  
\[ (A7) \]

being \( n = 8/7 \) a good choice,

\[ \omega_e = \sqrt{2\pi / \beta} \left[\int_{-\infty}^{+\infty} dx \ e^{\beta V(x)}\right]^{-1} \]  
\[ (A8) \]

and

\[ \theta = \frac{\omega_e^2 \beta^{3/2}}{\sqrt{2\pi}} \int_{-\infty}^{+\infty} dx \ V'(x) e^{\beta V(x)}. \]  
\[ (A9) \]

3. Garg

To finish, we will present a short comparative study of Garg\textsuperscript{32} predictions for the mean escape force and its variance. There, both quantities are given as a series expansion of a certain parameter. Figure 11 shows a numerical study of the results reported by Garg\textsuperscript{32} for two different force ramps. Barrier height is given by

\[ 4\sqrt{2V_0/3(1 - F/V_0)^{3/2}}; \]  
oscillation frequency by

\[ 2^{1/4}(V_0/m)^{1/2}(1 - F/V_0)^{1/4}, \]

\( T = 0.01, \) and

\( \dot{F} = 2.5 \times 10^{-7} \) and \( 2.5 \times 10^{-12}. \) The figure shows that for
the case of $(F)$ first order approximation is very good for the moderate and high damping cases (even better that considering the second order approximation). On the contrary, in the low damping result only the second order approximation correctly estimates the exact escape rate. With respect to the variance, results are not that good. For the case of moderate and low damping first order approximation is not that bad and second order is better. However, for low damping first order result is not very good but second order is much worse.


22 To normalize Eq. (2.1), we divide it by $V_0$ and time by $\omega^{-1} = \sqrt{m/V_0}$. Then, the dimensionless parameters are $\tilde{\tau} = \gamma/\omega$, $\tilde{F} = F/(\omega V_0)$, and $\tilde{t} = \tilde{\tau}/(\omega V_0) = 9.70F$.

23 $r_{\text{TST}}$, Eq. (1.1), results from the infinite barrier approximation to $r_{\text{TST}}$ for parabolic barrier.


29 This is equivalent to say $\langle t^{\text{M}}/t \rangle = k_{\text{KMHD}}(\gamma/\omega)/k_{\text{KMHD}}(\epsilon HY/\omega)$.


