Published in final edited form as:

J Phys Chem B. 2017 June 01; 121(21): 5455–5460. doi:10.1021/acs.jpcb.7b04037.

Mean Direct-Transit and Looping Times as Functions of the Potential Shape

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Abstract

Any trajectory of a diffusing particle making a transition between two end points of an interval can be divided into two segments, which we call direct-transit and looping parts. The former is the final segment of the trajectory, when the particle goes from one end point of the interval to the opposite end point, without retouching the starting point. The rest of the trajectory is the looping part. We study mean durations of the two parts in the presence of a symmetric linear cusp potential which, depending on the parameter values, forms either a barrier or a well between the end points. For the cusp barrier, we find that the mean direct-transit time decreases as the barrier height increases at a fixed interval length. This happens because the increase in the barrier height results in the increase of the magnitude of the force acting on the particle on both sides of the barrier. Interestingly, though the mean looping and direct-transit times are different in the case of the barrier and well potentials with equal height and depth, respectively, the mean first-passage times for the two cases are identical.

Graphical Abstract

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The authors declare no competing financial interest.

1. INTRODUCTION

Chemical reactions are transitions between long-living metastable states of the system separated by a sparsely populated region of the phase space. Passage through this region controls the transitions between the metastable states and hence the reaction rates. As a model of chemical reactions consider transitions of a Brownian particle between two deep wells of a one-dimensional double-well potential, separated by a high barrier. The whole range of the one-dimensional reaction coordinate in such a system can be divided into three regions: reactants, products, and the barrier region in between. To make a transition from the reactants into products, the particle first enters the barrier region. Then, depending on the realization of the random force, the particle either returns to the reactants or passes through the barrier region and enters the product region. In recent years, direct transitions of the particle from the reactants to the products, when the particle passes through the barrier region without returning to the reactant region, have attracted attention of many researchers, both experimentalists and theoreticians.^{1–37} In particular, attention was called^{12,27,29,32} to the fact that the higher the barrier the particle must overcome when traversing the barrier region, the faster it passes through this region. This may sound surprising, at least at first glance, because one might expect the opposite, namely, the higher the barrier, the longer it takes for the particle to traverse the barrier region.

In the main part of the present paper, we address this issue by studying transitions of a diffusing particle from $x = -L$ to $x = L$ in the double-well linear cusp potential shown in Figure 1. Any particle trajectory, starting from $x = -L$ and terminated as soon as it reaches $x = L$ for the first time, can be divided into two segments which we call direct-transit and looping parts. The former is the final segment of the trajectory, when the particle makes a direct transition from $x = -L$ to $x = L$, without retouching the starting point. The rest of the trajectory, when the particle returns to the starting point again and again, is the looping part.

We derive analytical expressions for the mean durations of the two parts of the trajectory, which we call mean direct-transit and looping times. These expressions show how these mean times depend on the barrier height U (Figure 1). We will see that the mean direct-transit time monotonically decreases with the barrier height, approaching zero as $1/(\beta U)$, when $\beta U \rightarrow \infty$, where $\beta = 1/(k_B T)$ with k_B and T denoting the Boltzmann constant and absolute temperature. In contrast, the mean looping time monotonically increases with U , approaching its limiting U -dependence $e^{\beta U}/(\beta U)^2$, when $\beta U \rightarrow \infty$.

2. THEORY

We find the mean direct-transit time using a general formula for the mean time required for a diffusing particle, entering an interval, $a < x < b$, terminated by partially absorbing end points, to traverse this interval and be trapped on its opposite end, derived in ref.³⁸ and used to analyze membrane transport through singly occupied channels in refs 39–42. This mean time is independent of the direction in which the particle crosses the interval and given by³⁸

$$\begin{aligned} \bar{t}(a \rightarrow b) &= \bar{t}(b \rightarrow a) \\ &= \left[\int_a^b \left(1 + \kappa_a e^{-\beta U(a)} \int_a^x e^{\beta U(y)} \frac{dy}{D(y)} \right) \left(1 + \kappa_b e^{-\beta U(b)} \int_x^b e^{\beta U(y)} \frac{dy}{D(y)} \right) e^{-\beta U(x)} dx \right] \left[\kappa_a e^{-\beta U(a)} + \kappa_b e^{-\beta U(b)} + \kappa_a \kappa_b e^{-\beta(U(a)+U(b))} \right] \end{aligned} \quad (1)$$

Here κ_a and κ_b are the trapping rates by the interval end points, $U(x)$ and $D(x)$ are the particle potential energy and position-dependent diffusivity, and the bar above t denotes averaging over realizations of the stochastic particle trajectory, responsible for the transition.

The formula in eq 1 gives the direct-transit (dtr) time in the limiting case of $\kappa_a, \kappa_b \rightarrow \infty$, where it reduces to

$$\begin{aligned} \bar{t}_{dtr}(a \rightarrow b) &= \bar{t}_{dtr}(b \rightarrow a) \\ &= \frac{\int_a^b \left(\int_a^x e^{\beta U(y)} \frac{dy}{D(y)} \right) \left(\int_x^b e^{\beta U(y)} \frac{dy}{D(y)} \right) e^{-\beta U(x)} dx}{\int_a^b e^{\beta U(y)} \frac{dy}{D(y)}} \end{aligned} \quad (2)$$

This can be written in an elegant form, proposed by Szabo, in term of the splitting probabilities $\Phi(x \rightarrow a)$ and $\Phi(x \rightarrow b)$, which are the probabilities for a particle injected at point x , $a < x < b$, to be trapped by one and the other perfectly absorbing end points of the interval. These splitting probabilities are

$$\Phi(x \rightarrow a) = \int_x^b e^{\beta U(y)} \frac{dy}{D(y)} / \int_a^b e^{\beta U(y)} \frac{dy}{D(y)} \quad (3)$$

$$\Phi(x \rightarrow a) = \int_x^b e^{\beta U(y)} \frac{dy}{D(y)} / \int_a^b e^{\beta U(y)} \frac{dy}{D(y)} \quad (4)$$

Using these, one can write eq 2 as follows:¹

$$\bar{t}_{dtr}(a \rightarrow b) = \bar{t}_{dtr}(b \rightarrow a) = \left(\int_a^b e^{\beta U(y)} \frac{dy}{D(y)} \right) \left(\int_a^b \Phi(x \rightarrow a) \Phi(x \rightarrow b) e^{-\beta U(x)} dx \right) \quad (5)$$

A detailed derivation of this formula can be found in ref 23.

In our case (see Figure 1), $a = -L$, $b = L$, $D(x) = D = \text{const}$, and $U(x)$ is a double-well (dw) linear cusp potential of the form

$$U_{dw}(x) = \begin{cases} -F|x|, & |x| < L \\ \infty, & |x| > L \end{cases}, \quad F \geq 0 \quad (6)$$

Performing the integrations in eq 2, we obtain

$$\bar{t}_{dtr}^{dw}(-L \rightarrow L) = \frac{2L^2}{D} \frac{2\beta\Delta U - 3 + 4e^{-\beta\Delta U} - e^{-2\beta\Delta U}}{2(\beta\Delta U)^2(1 - e^{-\beta\Delta U})} \quad (7)$$

where $U = FL$ is the barrier height. This expression gives the mean direct-transit time as a product of two factors. The first, $2L^2/D$, providing a time scale for $\bar{t}_{dtr}^{dw}(-L \rightarrow L)$, is the mean first-passage time between the two end points of the interval in the absence of the potential.⁴³ The second, dimensionless factor describes the dependence of $\bar{t}_{dtr}^{dw}(-L \rightarrow L)$ on the barrier height. In the limiting cases of no barrier ($U = 0$) and high barrier ($\beta U \rightarrow \infty$) the mean direct-transit time in eq 7 reduces to

$$\bar{t}_{dtr}^{dw}(-L \rightarrow L) = \frac{2L^2}{D} \times \begin{cases} 1/3, & \Delta U = 0 \\ 1/(\beta\Delta U), & \beta\Delta U \rightarrow \infty \end{cases} \quad (8)$$

The asymptotic behavior at $\beta U \rightarrow \infty$, written in terms of the force parameter, F , takes the form $\bar{t}_{dtr}^{dw}(-L \rightarrow L) = 2L/(\beta DF)$, which gives the mean direct-transit time as the ratio of the interval length, $2L$, to the absolute value of the particle drift velocity, βDF .

It is interesting to compare $\bar{t}_{dtr}^{dw}(-L \rightarrow L)$ in eq 7 with the mean first-passage (FP) time, $\bar{t}_{FP}^{dw}(-L \rightarrow L)$, between the two ends of the interval. One can check that in our case, this time is given by⁴³

$$\bar{t}_{FP}^{dw}(-L \rightarrow L) = \frac{2L^2}{D} \left[\frac{2}{\beta \Delta U} \sinh\left(\frac{\beta \Delta U}{2}\right) \right]^2 \quad (9)$$

In the absence of the barrier, this leads to

$$\bar{t}_{FP}^{dw}(-L \rightarrow L) = \frac{2L^2}{D}, \quad \Delta U = 0. \quad (10)$$

In the opposite limiting case of high barrier, eq 9 reduces to the expression which follows from the Kramers theory

$$\bar{t}_{FP}^{dw}(-L \rightarrow L) = \frac{2L^2}{D(\beta \Delta U)^2} e^{\beta \Delta U} = \frac{2}{D(\beta F)^2} e^{\beta \Delta U}, \quad \beta \Delta U \rightarrow \infty \quad (11)$$

One can see that the mean direct-transit and first-passage times are comparable in the absence of the barrier,

$$\bar{t}_{dtr}^{dw}(-L \rightarrow L) = (1/3) \bar{t}_{FP}^{dw}(-L \rightarrow L), \quad \Delta U = 0 \quad (12)$$

whereas when the barrier is high, $\beta U \rightarrow \infty$, the mean direct-transit time, $\bar{t}_{dtr}^{dw}(-L \rightarrow L)$, is negligibly small compared to the mean first-passage time, $\bar{t}_{FP}^{dw}(-L \rightarrow L)$.

The difference between these two mean times is the mean looping (l) time, denoted by $\bar{t}_l^{dw}$

$$\bar{t}_l^{dw} = \bar{t}_{FP}^{dw}(-L \rightarrow L) - \bar{t}_{dtr}^{dw}(-L \rightarrow L) \quad (13)$$

Using eqs 7 and 9, we obtain

$$\bar{t}_l^{dw} = \frac{2L^2}{D} \frac{2e^{\beta\Delta U} - 3 - 2\beta\Delta U + 2e^{-\beta\Delta U} - e^{-2\beta\Delta U}}{2(\beta\Delta U)^2(1 - e^{-\beta\Delta U})} \quad (14)$$

In the limiting cases of no barrier and high barrier the mean looping time takes the form

$$\bar{t}_l^{dw} = \frac{2L^2}{D} \times \begin{cases} 2/3, & \Delta U = 0 \\ e^{\beta\Delta U} / (\beta\Delta U)^2, & \beta\Delta U \rightarrow \infty \end{cases} \quad (15)$$

Thus, in the absence of the barrier $\bar{t}_l^{dw}$ is two-thirds of the mean first-passage time and twice as large as the mean direct-transit time

$$\bar{t}_l^{dw} = 2\bar{t}_{dtr}^{dw}(-L \rightarrow L) = (2/3)\bar{t}_{FP}^{dw}(-L \rightarrow L)\Delta, \quad U=0 \quad (16)$$

while when the barrier is high, the mean looping time approaches the mean first-passage time $\bar{t}_{FP}^{dw}(-L \rightarrow L)$. It happens because in this limiting case escape from the well is a rare event, and the particle spends a lot of time looping in the well before it escapes.

If, in eq 6, the minus sign is replaced by the plus sign, the double-well potential becomes a single-well (*sw*) one of the form

$$U_{sw}(x) = \begin{cases} F|x|, & |x| < L \\ \infty, & |x| > L \end{cases}, \quad F \geq 0. \quad (17)$$

This potential is shown in Figure 2. One can check that the mean first passage time between the two ends of the interval in this potential, $\bar{t}_{FP}^{sw}(-L \rightarrow L)$, is identical to its counterpart in the double-well potential, given in eq 9,

$$\bar{t}_{FP}^{sw}(-L \rightarrow L) = \bar{t}_{FP}^{dw}(-L \rightarrow L) = \bar{t}_{FP}(-L \rightarrow L) \quad (18)$$

This is not the case with the mean direct-transit and looping times which differ from their counterparts in the double-well case. Performing the integrations in eq 2 with $a = -L$, $b = L$, $D(x) = D = \text{const}$, and $U(x) = U_{sw}(x)$, one can check that the mean direct-transit time, $\bar{t}_{dtr}^{sw}(-L \rightarrow L)$, is still given by eq 7 with U replaced by $-U$,

$$\bar{t}_{dtr}^{sw}(-L \rightarrow L) = \frac{2L^2}{D} \frac{e^{2\beta\Delta U} - 4e^{\beta\Delta U} + 3 + 2\beta\Delta U}{2(\beta\Delta U)^2(e^{\beta\Delta U} - 1)} \quad (19)$$

The same is true for the mean looping time, $\bar{t}_l^{sw}$, which in the case of the single-well potential takes the form (cf. $\bar{t}_l^{dw}$ in eq 14)

$$\bar{t}_l^{sw} = \frac{2L^2}{D} \frac{e^{2\beta\Delta U} - 2e^{\beta\Delta U} - 2\beta\Delta U + 3 - 2e^{-\beta\Delta U}}{2(\beta\Delta U)^2(e^{\beta\Delta U} - 1)} \quad (20)$$

Dependences of $\bar{t}_{dtr}^{sw}(-L \rightarrow L)$ and $\bar{t}_l^{sw}$ on the parameter $\beta U = \beta FL$ differ from the corresponding dependences of their counterparts in the double-well case, $\bar{t}_{dtr}^{dw}(-L \rightarrow L)$ and $\bar{t}_l^{dw}$. These dependences are illustrated in Figure 3. As $\beta U \rightarrow \infty$, $\bar{t}_{dtr}^{sw}(-L \rightarrow L)$ and $\bar{t}_l^{sw}$ approach each other and become equal to one-half of the mean first-passage time,

$$\bar{t}_{dtr}^{dw}(-L \rightarrow L) = \bar{t}_l^{dw} = (1/2)\bar{t}_{FP}(-L \rightarrow L), \beta\Delta U \rightarrow \infty \quad (21)$$

This is quite in contrast with the βU -dependences of $\bar{t}_{dtr}^{dw}(-L \rightarrow L)$ and $\bar{t}_l^{dw}$. The former tends to zero, as $\beta U \rightarrow \infty$, while the latter approaches $t_{FP}(-L \rightarrow L)$ in this limiting case. The reason why $\bar{t}_{dtr}^{sw}(-L \rightarrow L)$ and $\bar{t}_l^{sw}$ become equal in the limiting case of $\beta U \rightarrow \infty$ is that particle spends all the time near the well bottom in the center of the interval. It escapes from the well and touches the reflecting and absorbing end points of the interval with equal probability, 1/2.

3. DISCUSSION

As shown in Figure 3, at a fixed length of the barrier region, the mean direct-transit time $\bar{t}_{dtr}^{dw}(-L \rightarrow L)$, eq 7, is a monotonically decreasing function of the barrier height. This result has been obtained for a linear cusp barrier. Qualitatively similar dependence of the mean direct-transit time on the barrier height was derived by Attila Szabo for a parabolic barrier (pb) potential,

$$U_{pb}(x) = -m\omega_b^2 x^2/2 \quad (22)$$

where m is the mass of the Brownian particle, and ω_b is the barrier frequency. In the high barrier limit, the leading term of the Szabo's formula for the direct transit time between points $x = \pm L$, $\bar{t}_{dtr}^{pb}(-L \rightarrow L)$, is given by (see the derivation in ref.²³)

$$\bar{t}_{dtr}^{pb}(-L \rightarrow L) = \frac{1}{D\beta m\omega_b^2} \ln(\beta\Delta U) \quad (23)$$

where $U = m\omega_b^2 L^2/2$ is the barrier height. Using the relation $m\omega_b^2 = 2U/L^2$, eq 23 can be written as

$$\bar{t}_{dtr}^{pb}(-L \rightarrow L) = \frac{L^2}{2D} \frac{1}{\beta\Delta U} \ln(\beta\Delta U), \quad \beta\Delta U \rightarrow \infty \quad (24)$$

This shows that when the barrier is high, the mean direct-transit time, at $L = \text{const}$, monotonically decreases with the barrier height. This mean direct-transit time is also called the mean transition path time.

Up to now we discussed the decrease of the mean direct-transit time with the barrier height for a diffusing particle, i.e., in the high-friction (diffusion) regime of the Langevin dynamics. Qualitatively similar dependence of the direct-transit time on the barrier height has also been obtained^{12,29} for the parabolic barrier in the moderate friction regime, where the particle is not affected by the friction and random forces in the barrier region. The total energy of the particle in this region is conserved. Therefore, if the particle has velocity v_0 , $v_0 > 0$, when passing the barrier top located at $x = 0$, its velocity, $v(x|v_0)$, at point x is

$$v(x|v_0) = \sqrt{v_0^2 - 2U_{pb}(x)/m} = \sqrt{v_0^2 - \omega_b^2 x^2} \quad (25)$$

The direct-transit time from $x = -L$ to $x = L$ for this particle, denoted as $t_{dtr}^{pb}(-L \rightarrow L|v_0)$, is a deterministic quantity given by

$$t_{dtr}^{pb}(-L \rightarrow L|v_0) = \int_{-L}^L \frac{dx}{v(x|v_0)} = \int_{-L}^L \frac{dx}{\sqrt{v_0^2 - \omega_b^2 x^2}} \quad (26)$$

Performing the integration, one arrives at

$$t_{dtr}^{pb}(-L \rightarrow L|v_0) = \frac{2}{\omega_b} \ln \left[\sqrt{1 + \left(\frac{\omega_b L}{v_0}\right)^2} + \frac{\omega_b L}{v_0} \right] \quad (27)$$

The mean direct-transit time in the moderate-friction (*mf*) regime, denoted by $\langle t_{dtr}^{pb}(-L \rightarrow L|\nu_0) \rangle_{mf}$, is obtained by averaging $t_{dtr}^{pb}(-L \rightarrow L|\nu_0)$ over ν_0 with the probability density $p(\nu_0) = \beta m \nu_0 e^{-\beta m \nu_0^2/2}$,

$$\begin{aligned} p(\nu_0) &= \beta m \nu_0 e^{-\beta m \nu_0^2/2}, \\ \langle t_{dtr}^{pb}(-L \rightarrow L|\nu_0) \rangle_{mf} &= \int_0^\infty t_{dtr}^{pb}(-L \rightarrow L|\nu_0) p(\nu_0) d\nu_0 \\ &= \frac{2}{\omega_b} \int_0^\infty \ln(\sqrt{1+\beta\Delta U/z} + \sqrt{\beta\Delta U/z}) e^{-z} dz \end{aligned} \quad (28)$$

where, as before, $U = m\omega_b^2 L^2/2$ is the barrier height. Using the relation $\omega_b = \sqrt{2\Delta U/m}/L$, eq 28 can be written as

$$\langle t_{dtr}^{pb}(-L \rightarrow L|\nu_0) \rangle_{mf} = \frac{\sqrt{2\pi}L}{\sqrt{\langle v^2 \rangle_{eq}}} \frac{1}{\sqrt{\pi\beta\Delta U}} \int_0^\infty \ln(\sqrt{1+\beta\Delta U/z} + \sqrt{\beta\Delta U/z}) e^{-z} dz \quad (29)$$

where $\langle v^2 \rangle_{eq} = 1/(\beta m)$ is the equilibrium (*eq*) mean square particle velocity. Here, the first factor, $\sqrt{2\pi}L/\sqrt{\langle v^2 \rangle_{eq}}$, is the mean time required for the particle to pass through the interval of length $2L$ in the absence of the potential, whereas the second, dimensionless factor describes the barrier height dependence of $\langle t_{dtr}^{pb}(-L \rightarrow L|\nu_0) \rangle_{mf}$. In the limiting case of high barrier eq 29 reduces to^{12,29}

$$\begin{aligned} \langle t_{dtr}^{pb}(-L \rightarrow L|\nu_0) \rangle_{mf} &= \frac{1}{\omega_b} \ln(\beta\Delta U) \\ &= \frac{\sqrt{2\pi}L}{\sqrt{\langle v^2 \rangle_{eq}}} \frac{1}{2\sqrt{\pi\beta\Delta U}} \ln(\beta\Delta U), \quad \beta\Delta U \rightarrow \infty \end{aligned} \quad (30)$$

This shows that, at $L = \text{const}$, the mean direct-transit time decreases, as the barrier height increases, in the moderate-friction regime also.

The mean direct-transit time in the cusp potential has similar dependence on the barrier height in the moderate-friction regime. In this case the x -dependent velocity of the particle is

$$v(x|\nu_0) = \sqrt{v_0^2 - 2U_{dw}(x)/m} = \sqrt{v_0^2 + 2F|x|/m} \quad (31)$$

This leads to

$$\begin{aligned}
 t_{dtr}^{dw}(-L \rightarrow L|v_0) &= \int_{-L}^L \frac{dx}{v(x|v_0)} \\
 &= \frac{2m}{F} \left(\sqrt{v_0^2 + \frac{2FL}{m}} - v_0 \right)
 \end{aligned} \quad (32)$$

Averaging this direct-transit time over v_0 , we arrive at

$$\begin{aligned}
 \langle t_{dtr}^{dw}(-L \rightarrow L|v_0) \rangle_{mf} &= \int_0^\infty t_{dtr}^{dw}(-L \rightarrow L|v_0) p(v_0) dv_0 \\
 &= \frac{\sqrt{2\pi L}}{\sqrt{\langle v^2 \rangle_{eq}}} \frac{2}{\sqrt{\pi} \beta \Delta U} \int_0^\infty (\sqrt{z + \beta \Delta U} - \sqrt{z}) e^{-z} dz
 \end{aligned} \quad (33)$$

where, as before, $U = FL$ is the barrier height. As $\beta U \rightarrow \infty$, the mean direct-transit time in eq 33 takes the form

$$\langle t_{dtr}^{dw}(-L \rightarrow L|v_0) \rangle_{mf} = \frac{L}{\sqrt{2\langle v^2 \rangle_{eq}}} \frac{4}{\sqrt{\beta \Delta U}}, \quad \beta \Delta U \rightarrow \infty \quad (34)$$

which shows that, at $L = \text{const}$, $\langle t_{dtr}^{dw}(-L \rightarrow L|v_0) \rangle_{mf}$ also decreases, as the barrier height increases, in the moderate-friction regime.

The barrier height dependences of the mean direct-transit time in the moderate friction regime for the parabolic and cusp barriers, given in eqs 29 and 33, are illustrated in Figure 4. The mean direct-transit time in the cusp potential decreases with the barrier height more rapidly than its counterpart in the case of the parabolic barrier. This happens because the local velocity, $v(x|v_0)$, considered as a function of the distance from the barrier top, in the former potential increases faster than in the latter one.

The barrier height dependence is discussed above for a fixed distance, $2L$, between the starting and end points. Under such conditions, the increase of the barrier height results in the increase in the sharpness of the barrier. One can also pose the question of the barrier height dependence at a given barrier sharpness. Here, the increase in the barrier height requires the increase of the distance between the starting and end points. It turns out that the acceleration of the direct transitions with barrier height at fixed L “converts” into a very slow increase of the mean direct-transit time at a fixed sharpness of the barrier.

4. CONCLUDING REMARKS

The main focus of this paper is on the mean direct-transit and looping times in the symmetric cusp barrier and well potentials, shown in Figures 1 and 2. Similar analysis can

be performed for arbitrary potential $U(x)$ using $\bar{t}_{dt}(a \rightarrow b)$ in eq 2 and determining $\bar{t}_l$ from the relation between $\bar{t}_{dt}(a \rightarrow b)$, $\bar{t}_l$, and the mean first-passage time, $\bar{t}_{FP}(a \rightarrow b)$

$$\bar{t}_{FP}(a \rightarrow b) = \bar{t}_{dt}(a \rightarrow b) + \bar{t}_l \quad (35)$$

which has been used to find $\bar{t}_l$ in eq 13. The mean first-passage time entering into eq 35 is given by

$$\bar{t}_{FP}(a \rightarrow b) = \int_a^b e^{-\beta U(x)} dx \int_x^b e^{\beta U(y)} \frac{dy}{D(y)} \quad (36)$$

The advantage of the cusp potential is that when $D(x) = D = \text{const}$, one can perform the integrations analytically. This leads to relatively simple formulas for the three mean times given in eqs 7, 9, 14, 19, and 20. In the general case, similar integrations can also be performed but numerically. Note that the mean first-passage times for the symmetric cusp barrier and cusp well with equal height and depth, U , are identical, though the mean looping and direct-transit times are distinctly different, as shown in Figure 3.

We hope that the general results for the mean direct-transit, looping, and first-passage times will be helpful in the analysis of long equilibrium single-molecule trajectories measured experimentally or obtained from simulations. The point is that such a trajectory can be transformed into the one that describes transitions between the two ends of an arbitrarily chosen interval. This may be achieved by cutting out the pieces of the initial trajectory outside the interval of interest and connecting the points separated by the cut pieces. The trajectory that results from this transformation is composed of looping and direct-transit segments. It can be analyzed as explained in the previous paragraph. It is worth noting that the transformation discussed above is applicable only for diffusion trajectories, i.e., when the inertia effects are negligibly small.

The transformed trajectory contains information about the direct-transit, looping, and first-passage times. Since all three times are controlled by the same dynamics, their mean values predicted by the theory should agree with the values obtained from the trajectory. Thus, analysis of the looping and first-passage times provides a means for independent testing of the assumptions about the system dynamics used for the interpretation of the single molecule trajectories. Importantly, this analysis may be applied to any interval of the one-dimensional coordinate, not just near the barrier top of the potential of mean force along this coordinate.

Acknowledgments

We are grateful to Irina Gopich, Dima Makarov, Eli Pollak, and Attila Szabo for helpful comments on the manuscript. This study was supported by the Intramural Research Program of the NIH, Center for Information Technology, and the Eunice Kennedy Shriver National Institute of Child Health and Human Development.

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Figure 1.
Double-well linear cusp potential $U_{dw}(x)$, defined in eq 6.

Figure 2.
Single-well linear cusp potential $U_{sw}(x)$, defined in eq 17.

Figure 3.

Dependences of the mean direct-transit (*dtr*), looping (*l*), and first-passage (*FP*) times, given in eqs 7, 9, 14, 19, and 20, on the parameter $\beta U = \beta FL$ for the double-well (*dw*) and single-well (*sw*) potentials, defined in eqs 6 and 17, respectively. The mean first-passage times for the two potentials are identical. All mean times are normalized to the mean first passage time at $U = 0$.

Figure 4.

Mean direct-transit times in the moderate friction regime for the parabolic and cusp potential barriers, eqs 29 and 33, normalized to their values at $U = 0$.