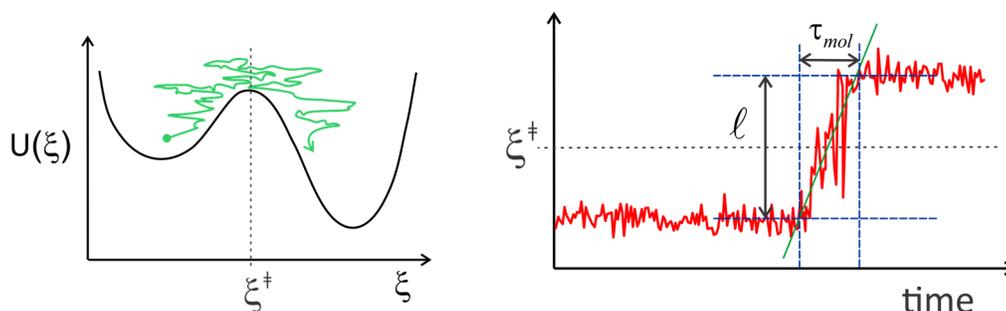


## 19. Barrier Crossing and Activated Processes<sup>1</sup>

“Rare but important events”

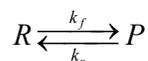


The rates of chemical reaction are obtained by calculating the forward flux of reactant molecules passing over the transition state, i.e. the time rate of change of concentration, population, or probability for reactants passing over the transition state.

$$\langle J_f^\ddagger \rangle = dP_R^\ddagger / dt \quad (1)$$

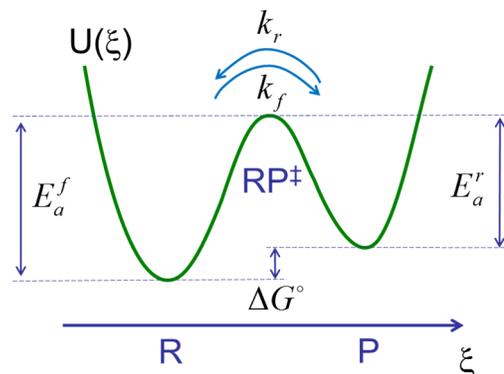
### Transition-State Theory<sup>2</sup>

Transition state theory is an equilibrium formulation of chemical reaction rates that originally comes from classical gas-phase reaction kinetics. We'll consider a two-state system of reactant  $R$  and product  $P$  separated by a barrier  $\gg k_B T$ :



which we obtain by projecting the free energy of the system onto a reaction coordinate  $\xi$  (a slow coordinate)

by integrating over all the other degrees of freedom. There is a time-scale separation between the fluctuations in a state and the rare exchange events. All memory of a trajectory is lost on entering a state following a transition.



1. D. Chandler, "Barrier Crossings: Classical Theory of Rare but Important Events" in *Classical and Quantum Dynamics in Condensed Phased Simulations*, edited by B. J. Berne, G. Ciccotti and D. F. Coker (World Scientific, Singapore, 1998), pp. 3-23.
2. J. I. Steinfeld, *Chemical Kinetics and Dynamics*, 2nd ed. (Prentice Hall, Upper Saddle River, N.J., 1998).

Our goal is to describe the rates of crossing the transition state for the forward and reverse reactions. At thermal equilibrium, the rate constants for the forward and reverse reaction,  $k_f$  and  $k_r$ , are related to the equilibrium constant and the activation barriers as

$$K_{eq} = \frac{[P]}{[R]} = \frac{P_{P,eq}}{P_{R,eq}} = \frac{k_f}{k_r} = \exp\left(-\frac{(E_a^f - E_a^r)}{k_B T}\right)$$

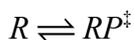
$E_a^f, E_a^r$  are the activation free energies for the forward and reverse reactions, which are related to the reaction free energy through  $E_a^f - E_a^r = \Delta G_{rxn}^0$ .  $P_i$  refers to the population or probability of occupying the reactant or product state.

The primary assumptions of TST is that the transition state is well represented by an activated complex  $RP^\ddagger$  that acts as an intermediate for the reaction from  $R$  to  $P$ , that all species are in thermal equilibrium, and that the flux across the barrier is proportional to the population of the activated complex.



Then, the steady state population of the activated complex can be determined by an equilibrium constant that we can express in terms of the molecular partition functions.

Let's focus on the rate of the forward reaction considering only the equilibrium



We relate the population of reactants within the reactant well to the population of the activated complex through an equilibrium constant

$$K_{eq}^\ddagger = \frac{[RP^\ddagger]}{[R]}$$

which we will evaluate using partition functions for the reactant and activated complex

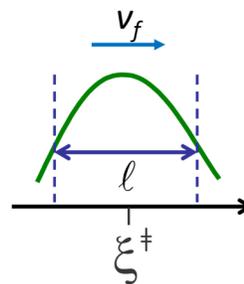
$$K_{eq}^\ddagger = \frac{q^\ddagger/V}{q_R/V} e^{-E_a^f/k_B T}$$

Then we write the forward flux in eq. (1) proportional to the population of activated complex

$$\begin{aligned} \langle J_f^\ddagger \rangle &= v[RP^\ddagger] \\ &= vK_{eq}^\ddagger[R] \end{aligned}$$

Here  $v$  is the reaction frequency, which is the inverse of the transition state lifetime  $\tau_{mol}$ .  $v^{-1}$  or  $\tau_{mol}$  reflects the time it takes to cross the transition state region.

To evaluate  $v$ , we will treat motion along the reaction coordinate  $\xi$  at the barrier as a translational degree of freedom. When the reactants gain enough energy ( $E_a^f$ ), they will move with a constant forward velocity  $v_f$  through a transition state region that has a width  $\ell$ . (The exact definition of  $\ell$  will not matter too much).



$$\tau_{\text{mol}} = \frac{\ell}{v_f}$$

Then we can write the average flux of population across the transition state in the forward direction

$$\begin{aligned} \langle J_f^\ddagger \rangle &= K_{eq}^\ddagger [R] \frac{v_f}{\ell} \\ &= \frac{q^\ddagger}{q_R} e^{-E_a^f/k_B T} [R] \frac{1}{\ell} \sqrt{\frac{k_B T}{2\pi m}} \end{aligned} \quad (2)$$

where  $v_f$  is obtained from a one-dimensional Maxwell–Boltzmann distribution.

For a multidimensional problem, we want to factor out the slow coordinate, i.e., reaction coordinate ( $\xi$ ) from partition function.

$$q^\ddagger = q_\xi q'^\ddagger$$

$q'^\ddagger$  contains all degrees of freedom except the reaction coordinate. Next, we calculate  $q_\xi$  by treating it as translational motion:

$$q_\xi \text{ (trans)} = \int_0^\ell d\xi e^{-E_{\text{trans}}/k_B T} = \sqrt{\frac{2\pi m k_B T}{h^2}} \ell \quad (3)$$

Substituting (3) into (2):

$$\langle J_f^\ddagger \rangle = \frac{k_B T}{h} \frac{q'^\ddagger}{q_R} e^{-E_a^f/k_B T} [R]$$

We recognize that the factor  $v = k_B T/h$  is a frequency whose inverse gives an absolute lower bound on the crossing time of  $\sim 10^{-13}$  seconds. If we use the speed of sound in condensed matter this time is what is needed to propagate 1–5 Å. Then we can write

$$\langle J_f^\ddagger \rangle = k_f [R]$$

where the forward rate constant is

$$k_f = A e^{-E_a^f/k_B T} \quad (4)$$

and the pre-exponential factor is

$$A = v \frac{q^{\ddagger}}{q_R}$$

$A$  determines the time that it takes to cross the transition state in the absence of barriers ( $E_a \rightarrow 0$ ).  $k_f$  is also referred to as  $k_{TST}$ .

To make a thermodynamic connection, we can express eq. (4) in the Eyring form

$$k_f = v e^{\Delta S^{\ddagger}/k_B} e^{-\Delta E_f^{\ddagger}/k_B T}$$

where the transition state entropy is

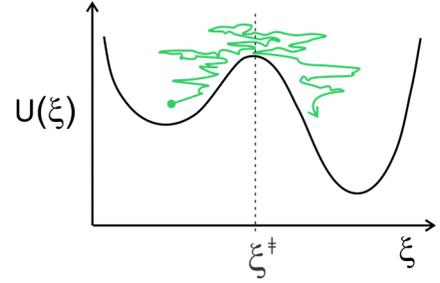
$$\Delta S^{\ddagger} = k_B \ln \frac{q^{\ddagger}}{q_R}$$

$\Delta S^{\ddagger}$  represents a count (actually ratio) of the reduction of accessible microstates in making the transition from the reactant well to the transition state. For biophysical phenomena, the entropic factors are important, if not dominant!

Also note implicit in TST is a dynamical picture in which every trajectory that arrives with forward velocity at the TST results in a crossing. It therefore gives an upper bound on the true rate, which may include failed attempts to cross. This is often accounted for by adding a transmission coefficient  $\kappa < 1$  to  $k_{TST}$ :  $k_f = \kappa k_{TST}$ . Kramers' theory provides a physical basis for understanding  $\kappa$ .

## Kramers' Theory

In our treatment the motion of the reactant over the transition state was treated as a free transitional degree of freedom. This ballistic or inertial motion is not representative of dynamics in soft matter at room temperature. Kramers' theory is the leading approach to describe diffusive barrier crossing. It accounts for friction and thermal agitation that reduce the fraction of successful barrier crossings. Again, the rates are obtained from the flux over barrier along reaction coordinate, eq. (1).



One approach is to treat diffusive crossing over the barrier in a potential using the Smoluchowski equation. The diffusive flux under influence of potential has two contributions:

- 1) Concentration gradient  $dC / d\xi$ . Proportional to diffusion coefficient,  $D$ .
- 2) Force from gradient of potential.

$$J(\xi) = -D \frac{dC(\xi)}{d\xi} - \frac{C(\xi)}{\zeta} \frac{dU(\xi)}{d\xi}$$

As discussed earlier  $\zeta$  is the friction coefficient and in one dimension:

$$\zeta = \frac{k_B T}{D}$$

Written in terms of a probability density  $P$

$$J = D \left( -\frac{P}{k_B T} \frac{dU}{d\xi} - \frac{dP}{d\xi} \right)$$

$$J = -D e^{-U/k_B T} \frac{d}{d\xi} (P e^{U/k_B T})$$

or

$$J e^{U/k_B T} = -D \frac{d}{d\xi} P e^{U/k_B T} \quad (5)$$

Here we have assumed that  $D$  and  $\zeta$  are not functions of  $\xi$ .

The next important assumption of Kramers' theory is that we can solve for the diffusive flux using the steady-state approximation. This allows us to set:  $J = \text{constant}$ .

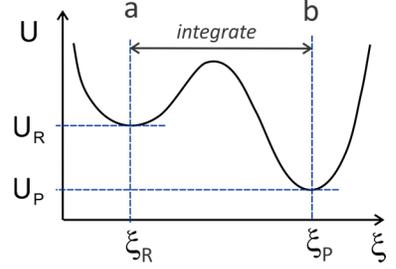
Integrate along  $\xi$  over barrier.

$$J \int_a^b e^{U/k_B T} d\xi = -D \int_a^b dP e^{U/k_B T}$$

$$J \int_a^b e^{U(\xi)/k_B T} d\xi = D \{ P_R e^{U_R/k_B T} - P_P e^{U_P/k_B T} \}$$

$P_i$  are the probabilities of occupying the  $R$  or  $P$  state, and  $U_i$  are the energies of the  $R$  and  $P$  states. The right hand side of this equation describes *net flux* across barrier.

Let's consider only flux from  $R \rightarrow P$ :  $J_{R \rightarrow P}$ , which we do by setting  $P_P \rightarrow 0$ . This is just a barrier escape problem. Also as a reference point, we set  $U_R(\xi_R) = 0$ .



$$J_{R \rightarrow P} = \frac{D P_R}{\int_a^b e^{U(\xi)/k_B T} d\xi} \quad (6)$$

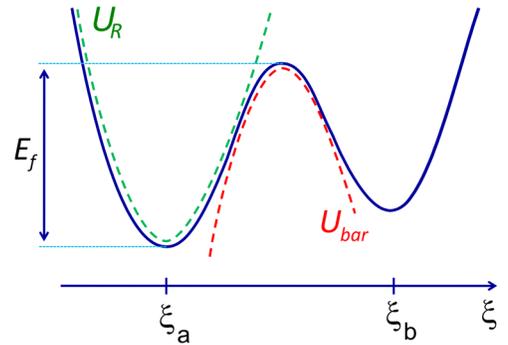
The flux is linearly proportional to the diffusion coefficient and the probability of being in the reactant state. The flux is reduced by a factor that describes the energetic barrier to be overcome.

Now let's evaluate with a specific form of the potential. The simplest form is to model  $U(\xi)$  with parabolas. The reactant well is given by

$$U_R = \frac{1}{2} m \omega_R^2 (\xi - \xi_R)^2 \quad (7)$$

and we set  $\xi_R \rightarrow 0$ . The barrier is modeled by an inverted parabola centered at the transition state with a barrier height for the forward reaction  $E_f$  and a width given by the barrier frequency  $\omega_{bar}$ :

$$U_{bar} = E_f - \frac{1}{2} m \omega_{bar}^2 (\xi - \xi^\ddagger)^2$$



In essence this is treating the evolution of the probability distribution as the motion of a fictitious particle with mass  $m$ .

First we evaluate the denominator in eq. (6).  $e^{U_{bar}/k_B T}$  is a probability density that is peaked at  $\xi^\ddagger$ , so changing the limits on the integral does not affect things much.

$$\int_a^b e^{U_{bar}/k_B T} d\xi \approx \int_{-\infty}^{+\infty} d\xi \exp \left[ -\frac{m \omega_B^2 (\xi - \xi^\ddagger)^2}{2 k_B T} \right] = \sqrt{\frac{2 \pi k_B T}{m \omega_B^2}}$$

Then eq. (6) becomes

$$J_{R \rightarrow P} = \omega_{\text{bar}} D \sqrt{\frac{m}{2\pi k_B T}} e^{-E_f/k_B T} P_R \quad (8)$$

Next, let's evaluate  $P_R$ . For a the Gaussian well in eq. (7), the probability density along  $\xi$  is  $P_R = e^{-U_R/k_B T}$ :

$$P_R(\xi) = \exp\left[-\frac{1}{2} m \omega_R^2 (\xi - \xi_R)^2 / k_B T\right]$$

$$P_R \approx \int_{-\infty}^{+\infty} P_R(\xi) d\xi = \omega_R \sqrt{\frac{m}{2\pi k_B T}}$$

Substituting this into eq. (8) we have

$$J_{R \rightarrow P} = \omega_R \omega_{\text{bar}} D \left( \frac{m}{2\pi k_B T} \right) e^{-E_f/k_B T}$$

Using the Einstein relation  $D = k_B T / \zeta$ , we find that the forward flux scales inversely with friction (or viscosity).

$$J_{R \rightarrow P} = \frac{\omega_R \omega_{\text{bar}}}{2\pi \zeta} e^{-E_f/k_B T} \quad (9)$$

Also, the factor of  $m$  disappears when the problem is expressed in mass-weighted coordinates  $\omega_{\text{bar}} = \sqrt{m} \omega_{\text{bar}}$ . Note the similarity of eq. (9) to transition state theory. If we associate the period of the particle in the reactant well with the barrier crossing frequency,

$$\frac{\omega_R}{2\pi} \Rightarrow \nu = \frac{k_B T}{h}$$

then we can also find that we an expression for the transmission coefficient in this model:

$$k_{\text{diff}} = \kappa_{\text{diff}} k_{\text{TST}}$$

$$\kappa_{\text{diff}} = \frac{\omega_{\text{bar}}}{\zeta} \ll 1$$

This is the reaction rate in the strong damping, or diffusive, limit.

Hendrik Kramers actually solved a more general problem based on the Fokker–Planck Equation that described intermediate to strong damping. The reaction rate was described as

$$k_{Kr} = \kappa_{Kr} k_{\text{TST}}$$

$$\kappa_{Kr} = \frac{1}{\omega_{\text{bar}}} \left( -\frac{\zeta}{2} + \sqrt{\frac{\zeta^2}{4} + \omega_{\text{bar}}^2} \right)$$

$$\zeta = \frac{1}{m k_B T} \int_0^\infty dt \langle \xi(0) \xi(t) \rangle$$

This shows a crossover in behavior between the strong damping (or diffusive) behavior described above and an intermediate damping regime:

$$\text{Strong damping/friction: } \zeta \rightarrow \infty \quad \kappa_{K_r} \rightarrow \frac{\omega_{bar}}{\zeta}$$

$$\text{Intermediate damping: } \zeta \ll 2\omega_B \quad \kappa_{K_r} \rightarrow 1 \text{ and } k_{K_r} \rightarrow k_{TST}$$

In the weak friction limit, Kramers argued that the reaction rate scaled as

$$k_{weak} \sim \zeta k_{TST}$$

That is, if you had no friction at all, the particle would just move back and forth between the reactant and product state without committing to a particular well. You need some dissipation to relax irreversibly into the product well. On the basis of this we expect an optimal friction that maximizes  $\kappa$ , which balances the need for some dissipation but without so much that barrier crossing is exceedingly rare. This “Kramers turnover” is captured by the interpolation formula

$$\kappa^{-1} = \kappa_{K_r}^{-1} + \kappa_{weak}^{-1}$$

