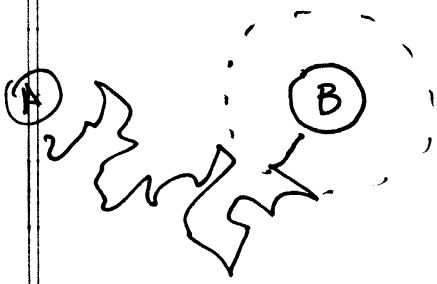
# I. Diffusion Controlled Reactions

$$A + B \rightleftarrows AB$$

Molecules A and B react every time they collide.




How fast are these reactions?

$J_A = -D_A \nabla C_A$ flux of A to B

$J_A = -D_A \partial C_A / \partial r$ radial dep.

$J_A$ = number of molecules flowing across $1\,cm^2/s$

r is the separation distance betw. molecular centers

flux across spherical surface of radius r and surface area $4\pi r^2$:

$$J_A = -4\pi r^2 J_A = -4\pi r^2 D_A \partial C_A / \partial r$$

steady state flow $J_A$ is constant for all values of r.

$J_A$ = number of A molecules that flow into surface of B per unit time.

Cast into a better form:

i $r_0$ = distance of closest approach

Boundary Conditions @ $r = r_0$ and $r = \infty$

ii $r_0$ (cm)

iii $C_A = 0$ at $r = r_0$ (all molecules react upon collision)

iv $C_A = \tilde{C}_A$ (bulk) at $r_\infty$ $r = \infty$

Integrate betw. boundary conditions

$$J_A \int_{r_0}^{\infty} r^{-2} dr = 4\pi D_A \int_0^{\tilde{C}_A} d C_A$$

$$J_A / r_0 = 4\pi D_A \tilde{C}_A$$

$$J_A = 4\pi r_0 D_A \tilde{C}_A$$

number of molecules of A that collide with B per second

* Molecules of B actually move with by diffusion $D_B$ - diffusion coefficient of B.
* Rate ~~is~~ scales with bulk concentration of B.

$$\text{Rate} = 4\pi (D_A + D_B) r_0 C_A C_B = k C_A C_B$$

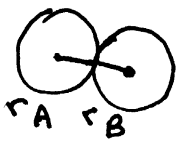
$k'$ $cm^3$ molecule$^{-1}$ sec$^{-1}$

$M^{-1}$ multiple by $10^{-3}$ $N_0$

$$k = 10^{-3} N_0 k'$$

$k' = 4\pi(D_A + D_B)r_o$ $r_o$ = distance of close approach

We'll take this to be the diameter of the molecule colliding (2 × radius)




$r_A + r_B = r_o \simeq 30\,\text{Å}$

Suppose, as an example, we calculate the collision rate, of a 15 kDa protein (globular).

A 15 kDa globular protein ($\bar{v} = 0.73\ cm^3/g$), which is spherical, has a radius of 15 Å and a diffusion coefficient of $1.4 \cdot 10^{-6}\ cm^2/s$

Then $k' = 4 \cdot \pi\ (2 \cdot 1.4 \cdot 10^{-6}\ cm^2/s)\ 30\text{Å} \cdot 10^{-8}\ cm/\text{Å}$

$k' = 1.05 \cdot 10^{-11}\ cm^3/s/\text{molecule}$

$k = k' \cdot 10^{-3}\ dm^3/cm^3 \times 6 \cdot 10^{23}\ \text{molecules/mole}$

$k = 1.05 \cdot 10^{-11}\ cm^3/s/\text{molecule} \cdot 10^{-3}\ dm^3/cm^3 \cdot 6 \cdot 10^{23}\ \frac{\text{mole}}{\text{molecule}}$

$k = 6.3 \cdot 10^9\ M^{-1}s^{-1}$

Reaction rate constant for for diffusion-controlled reaction of a 15 kDa protein

# Features of Diffusion Controlled Reaction Rate Constant

- No activation energy
- 100% react every collision
  (no orientation effect)
- collision rate determine by diffusion
  (no attractive or repulsive interactions)
  - van der Waals
  - charge-charge
  - H-bond
  - etc.

On the other hand most rate constants are much smaller that the 'upper limit' defined by the analysis for Diffusion Controlled Reactions. Why?

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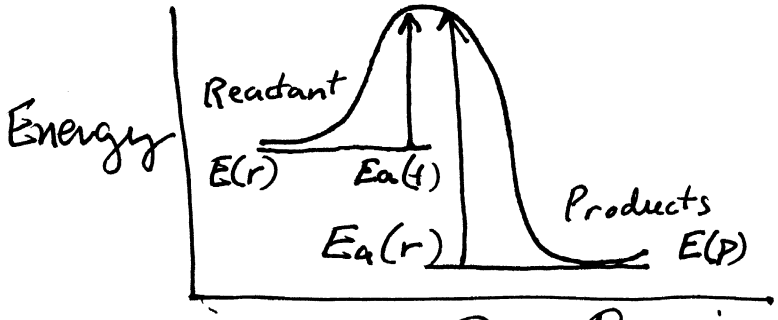
II **Activation Energy**. In transforming from reactants to products, there are often high energy intermediates, referred to as transition states.



- Reactants and Products have energies associated with ~~ten~~ them.
- The transform from Reactant to Product proceeds along a reaction coordinate. The diagram implies this as an independent variable of which the system energy is a function
- The difference in energy between Reactants and products determines the Reaction equilibrium, $\Delta E = E(P) - E(R)$

- The pathway from Reactant to Product (or Product to Reactant) involves passage through a high energy state. The difference in Energy of the transition state and either the reactant or product state defines the Activation energies $E_{act}(f)$, $E_{act}(R)$ (f for ward; r, reverse)

$$E_{act}(f) = E(TS) - E(R)$$

$$E_{act}(r) = E(TS) - E(P)$$

- By definition, there is one transition state in an elementary reaction step. For multi-step reaction schemes, the largest activation energy defines the rate-limiting step.

The Arrhenius Equation, even in its simplest form, gives the activation energy.

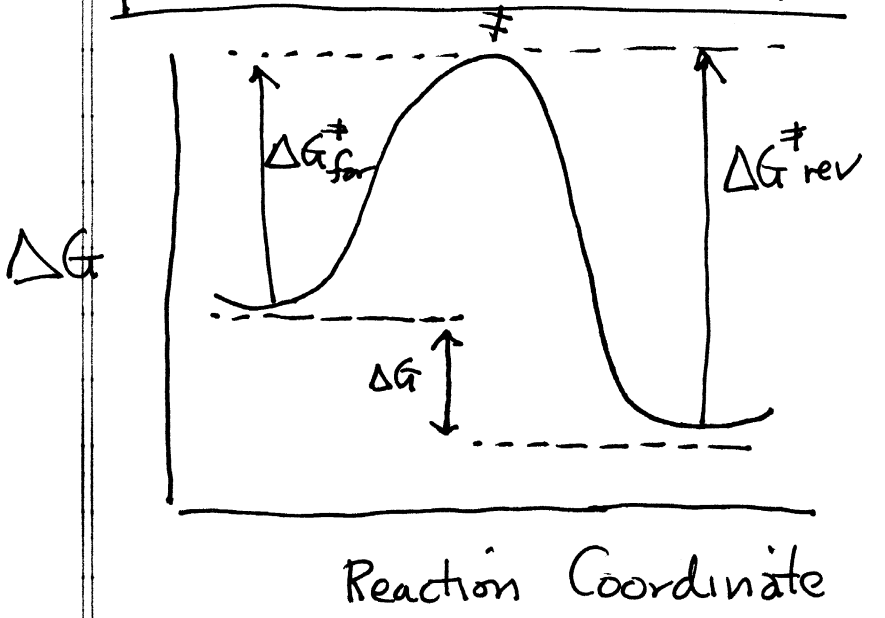
$$k = A \exp\left(-\frac{E_a}{RT}\right)$$

here $E_a$ is a molar energy since $R$ (instead of $k_B$) is used.

Again, an energy (here $E_a$) relative to thermal energy, $RT$, ($k_B T$) gives an exponential dependence to $k$.

- The pre-exponential factor, $A$, is sometimes regarded as a frequency factor, since it can represent the number of collisions per unit time (as in a diffusion controlled reaction) and the term $\exp(-E_a/RT)$ reduces the number of collisions to the number of collisions that result in a reaction. The larger $E_a$ is, relative to $RT$, the smaller this fraction is.

# III Transition State Theory




$$\Delta G(for) = \Delta G^{\ddagger}_{rev} - \Delta G^{\ddagger}_{for}$$

Transition state theory assigns thermodynamic significance to the ‡ transition state, a Gibbs energy, and an analysis of the pre-exponential factor to a universal rate constant.

To illustrate with specific reaction:

$$2A \rightleftharpoons AA^{\ddagger} \xrightarrow{k^{\ddagger}} A_2$$

$$K^{\ddagger}$$

consider protein (A) dimerization ($A_2$)

The rate constant, $k$, is given by

$$k = k^{\ddagger} K^{\ddagger} \qquad (7)$$

in transition theory.

$K^{\ddagger}$ is the equilibrium between the reactant state and transition state

$k^{\ddagger}$ is the rate constant for the decomposition of the transition state to product

$$K^{\ddagger} = \frac{[AA^{\ddagger}]}{[A]^2} \qquad k^{\ddagger} = \frac{k_B T}{h}$$

With the definition of $K^{\ddagger}$, the usual relation to $\Delta G^{\ddagger}$ can be applied

$$k = \frac{k_B T}{h} K^{\ddagger} = \frac{k_B T}{h} \exp\left[-\frac{\Delta G^{\ddagger}}{RT}\right]$$

$$k = \frac{k_B T}{h} \exp\left[\frac{\Delta S^{\ddagger}}{R}\right] \exp\left[-\frac{\Delta H^{\ddagger}}{RT}\right]$$

~~In principle, this value~~

$\Delta H^{\ddagger}$ is analogous to Eact of the Arrhenius equation.

$\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ provide thermodynamic information about the weighting factor ($\exp(-\Delta G^{\ddagger}/RT)$), the extent to which bonding may change ($\Delta H^{\ddagger}$) and configurational effects ($\Delta S^{\ddagger}$) are involved in the formation of the transition state.

IS this of any use to biochemical reactions?

Problem Set 7 investigates how it might be.