

1.2 Chemical Kinetics

Biophysics

Outline

- Importance of kinetics
 - Kinetics vs. Thermodynamics
- Concepts and nomenclature
- Reaction rates
 - Methods to obtain reaction rates
- Effect of temperature
 - Arrhenius plot
- Transition state theory
- Catalysis, enzyme kinetics

Kinetics vs thermodynamics

- Thermodynamics allows to know whether a process is “in equilibrium” ($\Delta G = 0$) or “spontaneous” ($\Delta G < 0$), but **does not predict** whether the process takes place in a reasonable **time** frame.
- Chemical kinetics aims to understand the actual **rate** of the process.

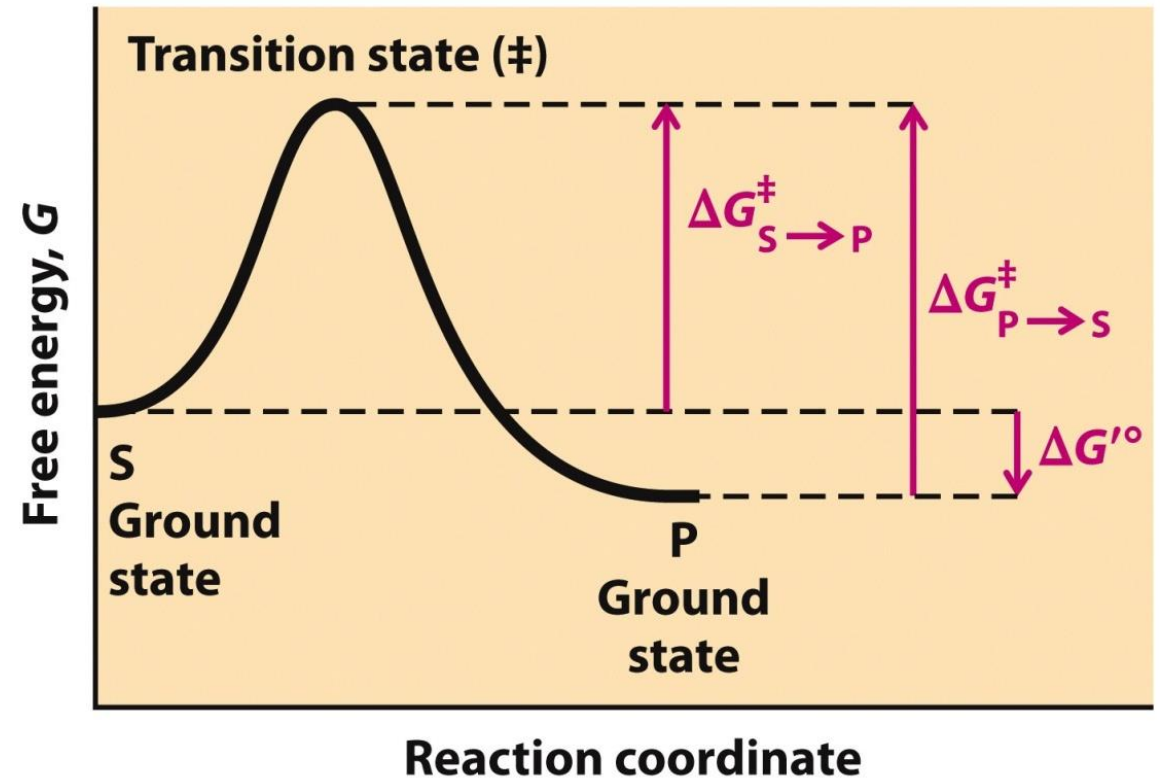


Figure 6-2
Lehninger Principles of Biochemistry, Fifth Edition
© 2008 W. H. Freeman and Company

Kinetics vs thermodynamics

- Reaction progress requires (in most cases) that system overcomes an **energy barrier**
- Even when the system reaches the necessary energy there is still just a probability of going forward.
- Reaction progress is conditioned by reactant, and product concentrations, T, P, ...

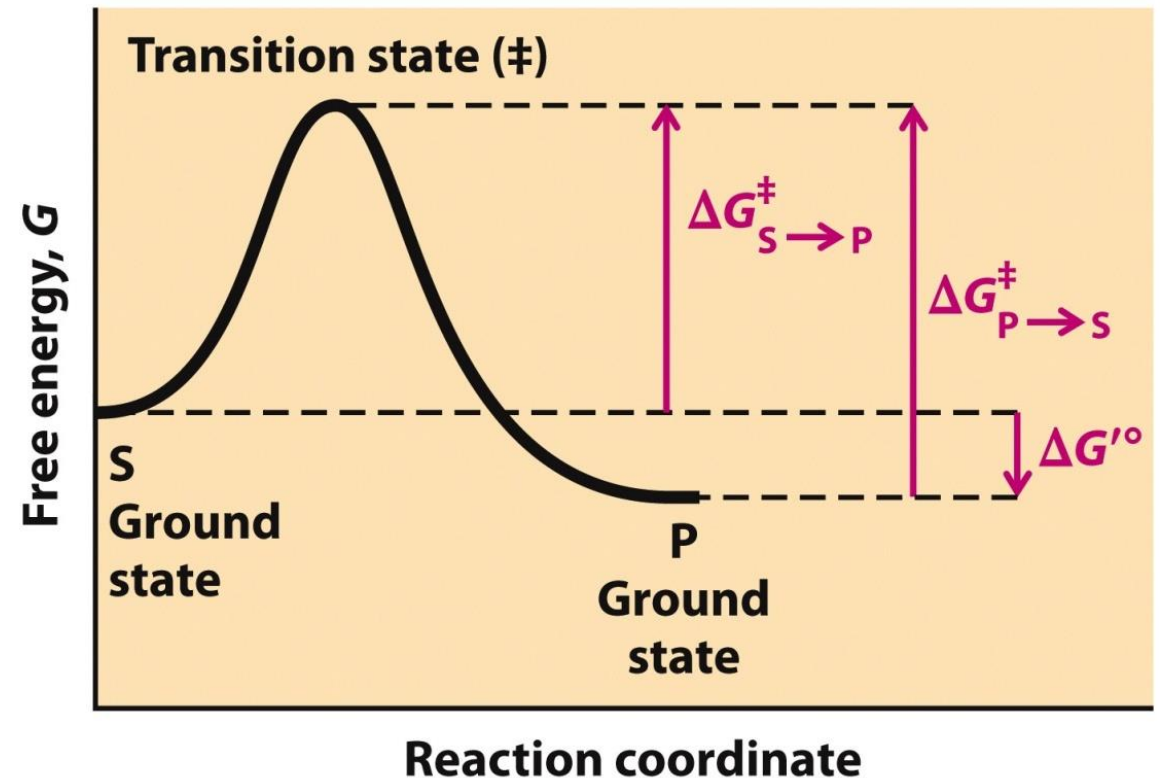
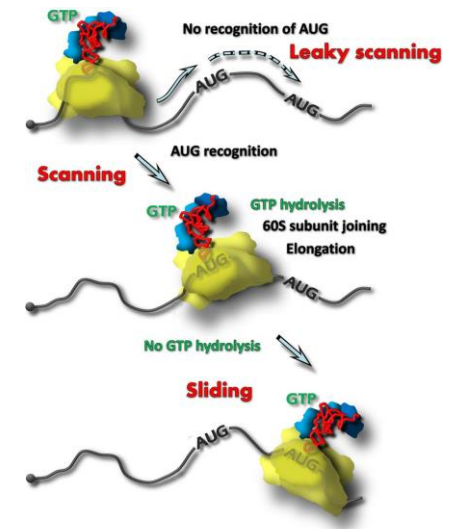
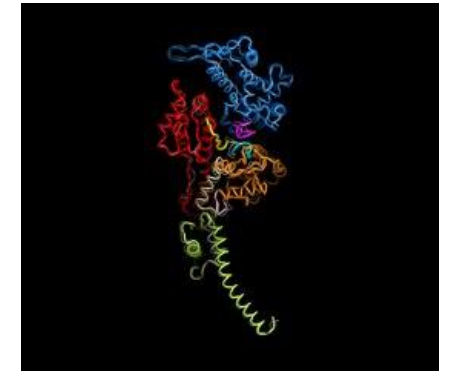
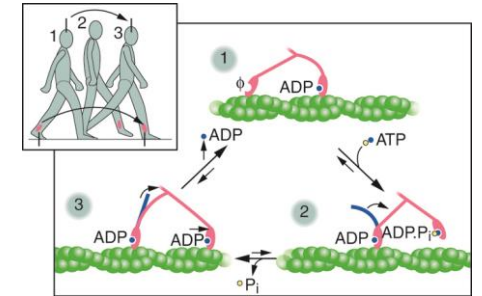
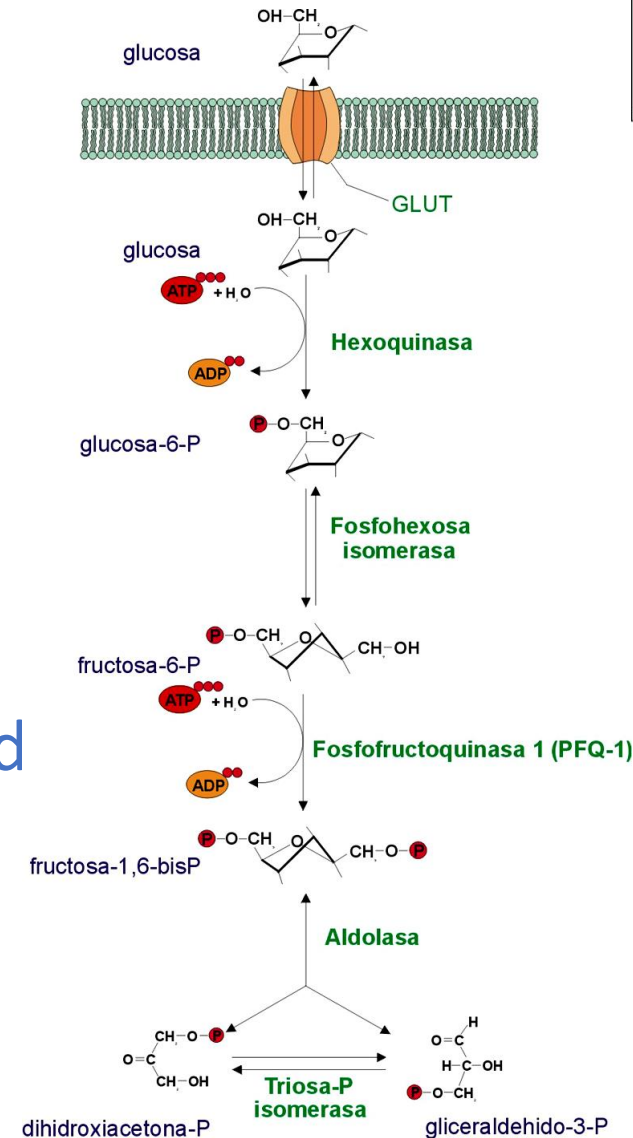


Figure 6-2
Lehninger Principles of Biochemistry, Fifth Edition
© 2008 W. H. Freeman and Company

Kinetics in Biology

- Relevant processes
 - chemical reactions
 - transport across membranes
 - physical movement
- All biological processes are controlled through kinetics regulation!!



Concepts and nomenclature

Reaction rate

- The amount of product that is formed per time. Also the amount of reactant that disappears per time

Order of reaction

- The number of different concentrations required to evaluate reaction rate

Half live

- Time to reduce the concentration of reactants to 50%

Chemical Mechanism

- The process of chemical transformation that occurs

Kinetic Mechanism

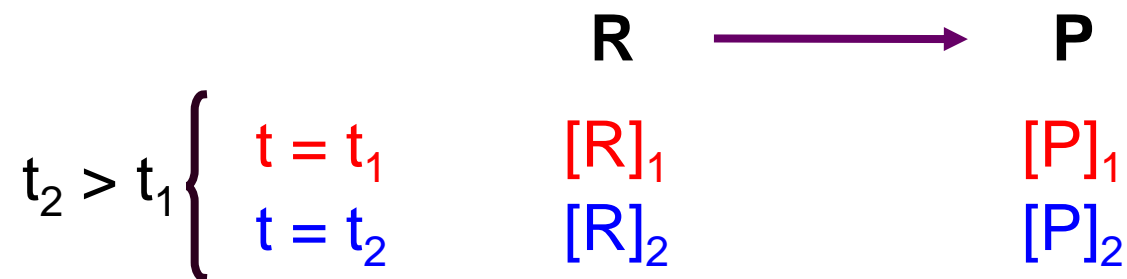
- The expression of how and when the different components interact

Rate law or rate equation

- The mathematic expression that relates component's concentrations and global rate

Reaction rates

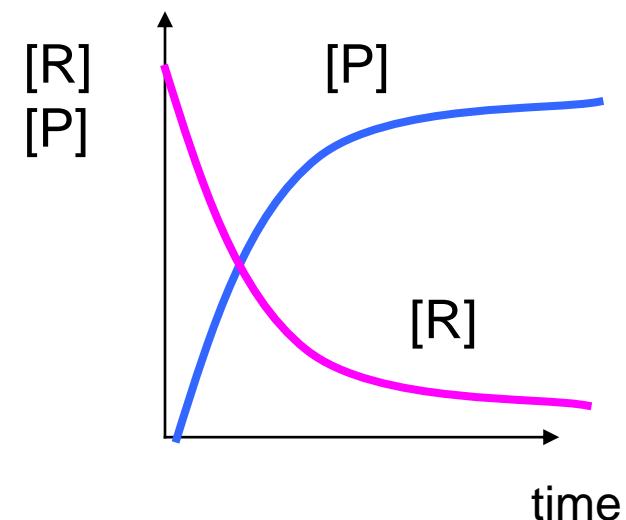
- Velocity of a reaction (rate): the **variation of concentration** of a reactant or product per time unit



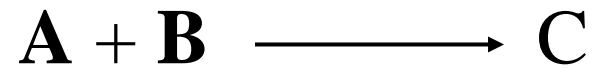
$$\frac{\Delta[R]}{\Delta t} = \frac{[R]_2 - [R]_1}{t_2 - t_1} \quad \frac{\Delta[P]}{\Delta t} = \frac{[P]_2 - [P]_1}{t_2 - t_1} \quad \longrightarrow \quad v = \frac{\Delta[P]}{\Delta t} = -\frac{\Delta[R]}{\Delta t}$$

In general $v = \frac{d[P]}{dt} = -\frac{d[R]}{dt}$ Units = Concentration/time (M/s)

The general case for $aA + bB \rightarrow cC$ $v = -\frac{1}{a} \frac{dA}{dt} = -\frac{1}{b} \frac{dB}{dt} = \frac{1}{c} \frac{dC}{dt}$



Expressions for reaction rates. Effect of concentrations (reaction orders)



$$v = k [A]^{\alpha} [B]^{\beta}$$

Rate constant

Reaction orders

Order: Empiric magnitude (experimental) determined through the rate law

Partial order: exponent of each component in the rate law.

Global order: sum of all partial orders of the rate law ($n = \alpha + \beta$).

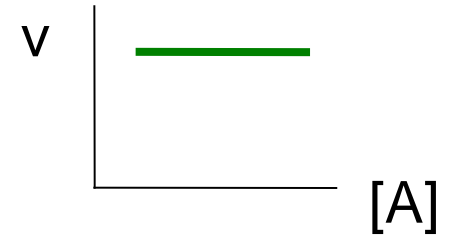
α and β could be integer, fractional numbers or zero.

They have not to coincide with the stoichiometric coefficients, however at the microscopic level they correspond to the number of molecules participating in the reaction.

Rate laws at different reaction orders

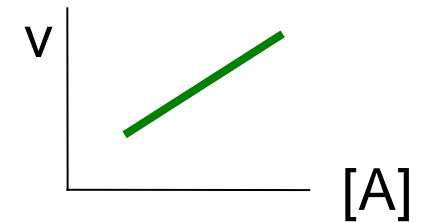
- **Zero order** ($n=0$): The velocity of the reaction is **independent** of the concentration of the reactants

$$v = k$$



- **First order** ($n=1$): The velocity of the reaction is proportional to the concentration of one of the reactants

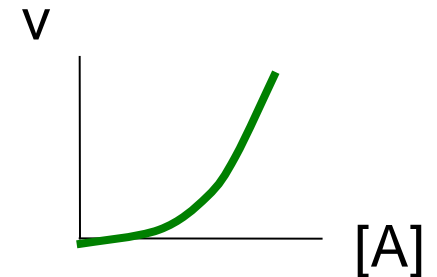
$$v = k[A]$$

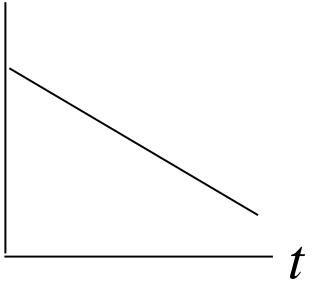
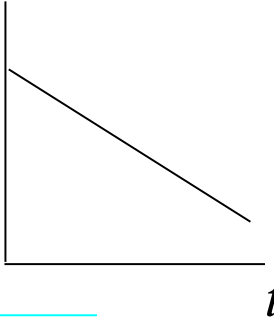
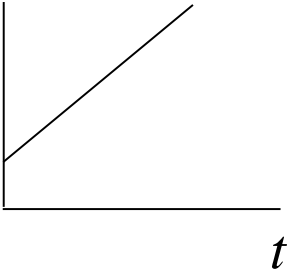
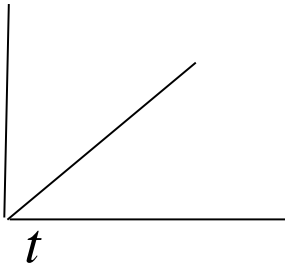


- **Second order** ($n=2$): The velocity of the reaction is proportional to the concentration of two reactants. or proportional to the square of one of them.

$$v = k[A][B]$$

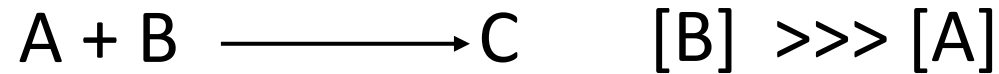
$$v = k[A]^2$$



| Order | Differential form | Integrated form | Half live | Units of k | Graphic representation |
|-----------|------------------------------|--|---------------------|-------------------------------|--|
| 0 | $-\frac{d[A]}{dt} = k$ | $[A] = [A]_o - k_A t$ | $\frac{[A]_0}{2k}$ | M s^{-1} | <div> <div>[A]</div>  <div>t</div> </div> |
| 1 | $-\frac{d[A]}{dt} = k[A]$ | $[A] = [A]_o e^{-k_A t}$ | $\frac{\ln 2}{k}$ | s^{-1} | <div> <div>$\ln[A]$</div>  <div>t</div> </div> |
| 2 | $-\frac{d[A]}{dt} = k[A]^2$ | $\frac{1}{A} = \frac{1}{A_o} + kt$ | $\frac{1}{[A]_0 k}$ | $\text{M}^{-1} \text{s}^{-1}$ | <div> <div>$1/[A]$</div>  <div>t</div> </div> |
| 2' | $-\frac{d[A]}{dt} = k[A][B]$ | $\frac{1}{[A]_0 - [B]_0} \ln \frac{[B]_0[A]}{[A]_0[B]} = kt$ | | $\text{M}^{-1} \text{s}^{-1}$ | <div> <div> $\frac{1}{[A]_0 - [B]_0} \ln \frac{[B]_0[A]}{[A]_0[B]}$ </div>  <div>t</div> </div> |

Reactions of “pseudo”first order

- Bi molecular reactions (usually second order) can be simplified keeping one of the concentrations constant (and much larger)
 - Allow to treat the process as first order



$$v = k [A][B] \rightarrow (k [B]) [A] = k' [A]$$

where k' is the ‘pseudo’ first order constant depending on $[B]$

Methods to determine reaction orders

Integration method

- The experimental values of concentration or pressure (for gases) as a function of time are plotted with the different integrated equations of velocity.
- The order of reaction is found by the representation that yields a constant value during all the profile for the velocity constant.

Half live method:

- The experimental values of concentration or pressure (for gases) are used to calculate the different expressions of half live.
- The expression that gives a constant value for the velocity constant indicates the order of the reaction.

The method of Initial Rates:

- It is based in the measure of different initial rates (v_o) with experiments that change the concentration of one of the reactants.
- A plot of $\log v_o$ as a function of $\log [A]_o$ gives the order of the reactant A.
- The same procedure is followed for all reactants.

S. Arrhenius
Nobel Priz. 1903



Effect of temperature

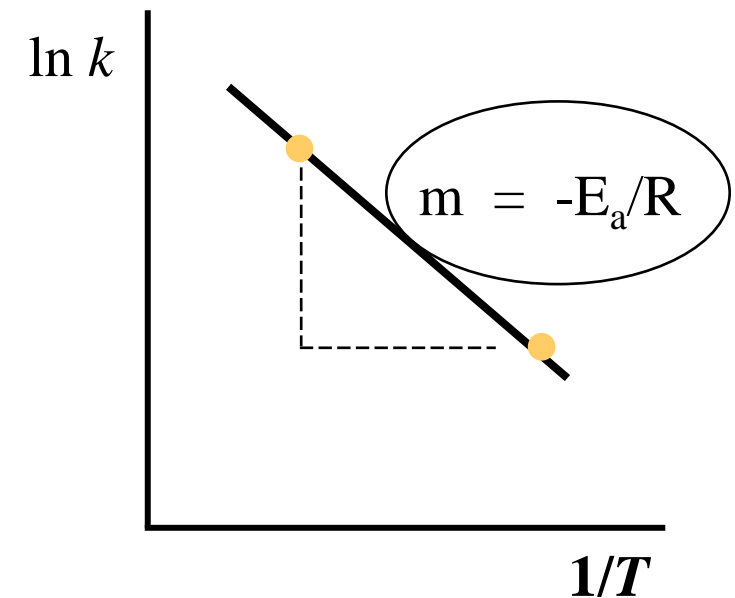
- The progress of the reaction requires the system to surmount an energy barrier
 - Hint: Increase of T increases the probability of exploring high energy states
- Arrhenius obtained an **empirical** relation between T and k (spoiler: Boltzmann strikes again)

$$k = Ae^{-E_a/RT}$$

where E_a is called the **activation energy**, and A is a measure of the probability of collisions between reactants being productive.

$$\ln k = \ln A - \frac{E_a}{RT}$$

$$\ln \frac{k_1}{k_2} = - \frac{E_a}{R} \left(\frac{1}{T_1} - \frac{1}{T_2} \right)$$

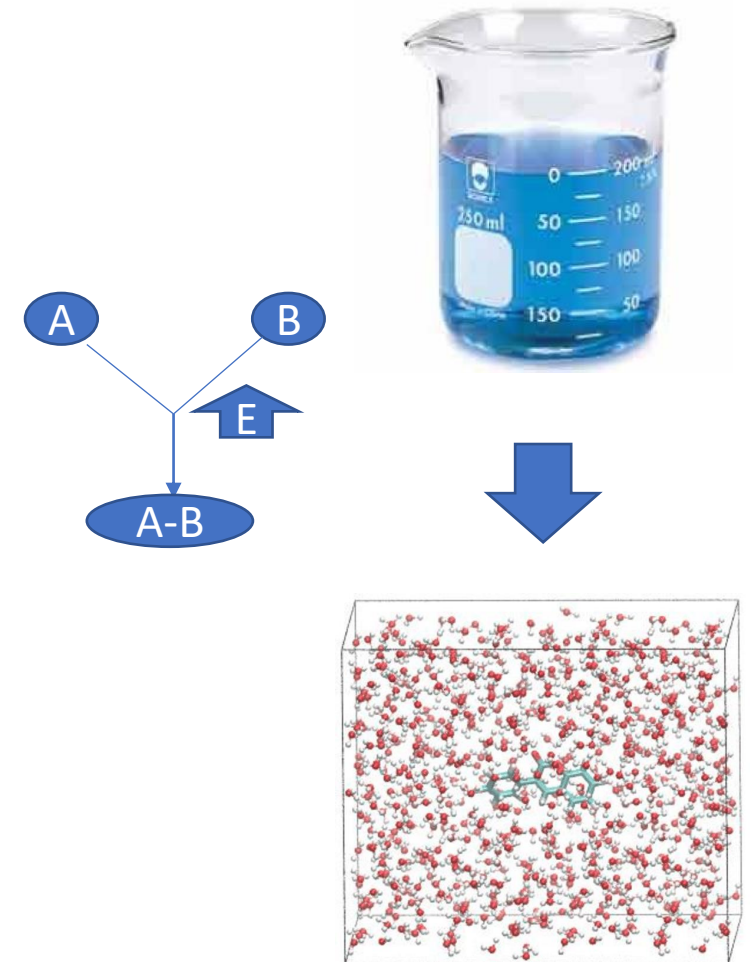


Reaction rates (from the microscopic view)

- There are two main theories to understand (and evaluate) rate constants from the microscopic view
- Collision theory:
 - Reactant molecules must collide (in a specific orientation) before a reaction can occur. Using Maxwell-Boltzmann distribution and defining a threshold energy (the activation energy E_a) for reactants gives

$$k = Z^0 e^{-E_a/RT}$$

- Transition state theory:
 - It explains the progress of the reaction in “thermodynamic terms”.
 - This is the preferred approach in biology



Transition State theory

- TST considers the formation of an intermediate AB^\ddagger
- AB^\ddagger is an activated complex in thermal equilibrium with A and B.
- Now, the reaction is divided in two steps
 - The formation of AB^\ddagger considered as an equilibrium process
 - The decomposition of AB^\ddagger to form products.
- $[AB^\ddagger]$ decomposition rate (k_d) depends on vibrational state of AB. It comes from kinetic quantum theory.
- Classic Thermodynamics is are used to deal with AB^\ddagger

$$k_d = q \frac{k_B T}{h}$$

q: progress probability (~ 1)
h: Plank constant

$$\Delta G^\ddagger = -RT \ln K^\ddagger$$

$$K^\ddagger = \frac{[AB^\ddagger]}{[A][B]}$$

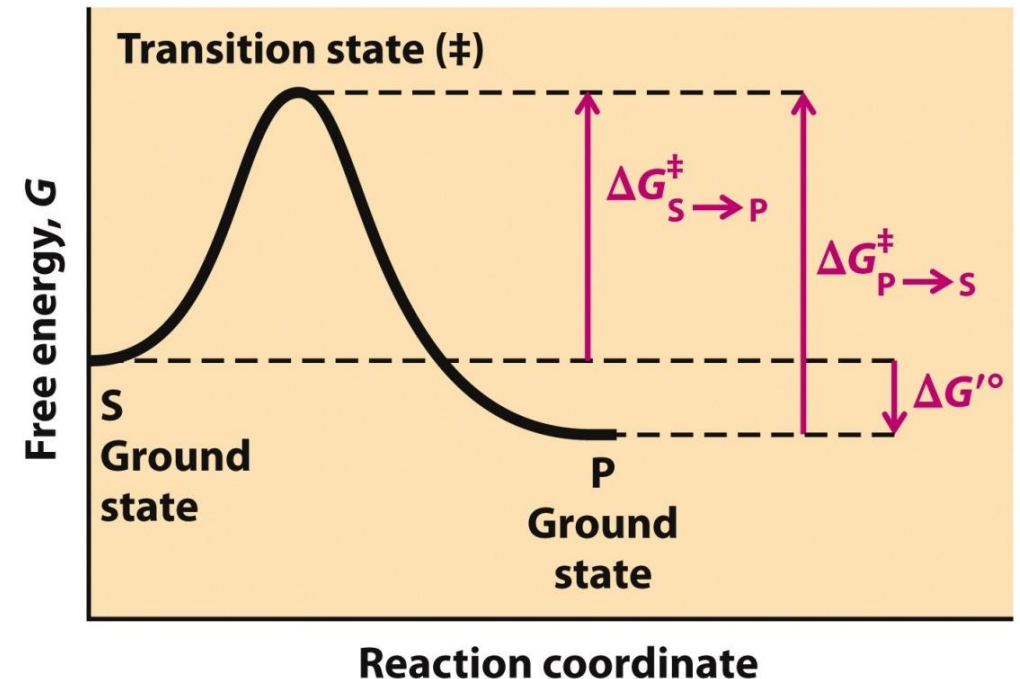
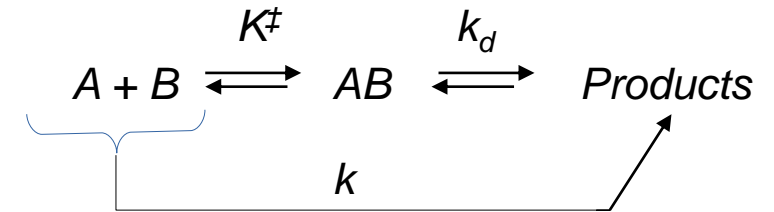


Figure 6-2
Lehninger Principles of Biochemistry, Fifth Edition
© 2008 W. H. Freeman and Company

Transition State theory

Macroscopic law

Microscopic law

using $K^\ddagger = \frac{[AB^\ddagger]}{[A][B]}$

using $k_d = q \frac{k_B T}{h}$
 $\Delta G^\ddagger = -RT \ln K^\ddagger$

using $\Delta G^\ddagger = \Delta H^\ddagger - T \Delta S^\ddagger$

$$v = k [A][B]$$

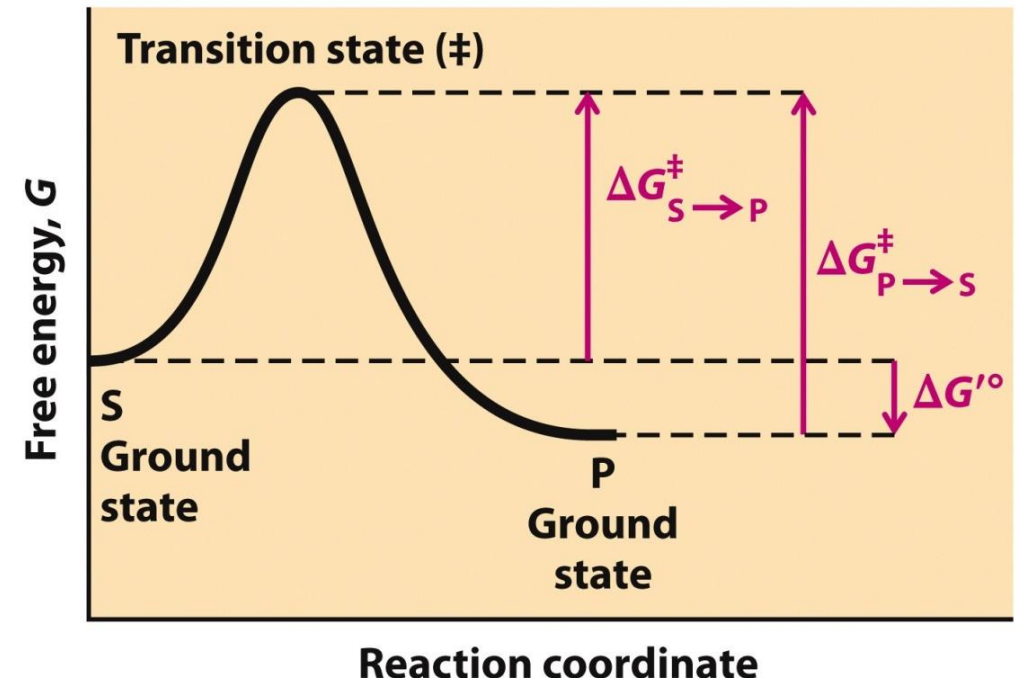
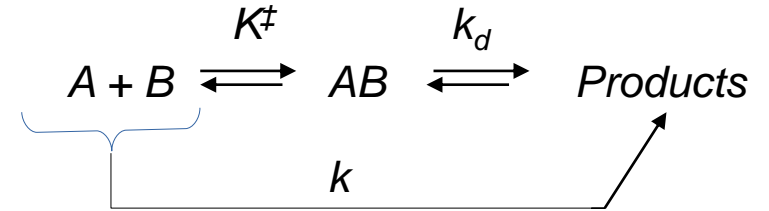
$$v = k_d [AB^\ddagger]$$

$$v = k_d K^\ddagger [A][B]$$

$$k = k_d K^\ddagger$$

$$k = q \frac{k_B T}{h} e^{-\frac{\Delta G^\ddagger}{RT}}$$

$$k = q \frac{k_B T}{h} e^{\frac{\Delta S^\ddagger}{R}} e^{-\frac{\Delta H^\ddagger}{RT}}$$



ΔS^\ddagger has a large influence independent on T

Catalysis

- A catalyst is a substance that changes the velocity of a chemical reaction. Catalysts doesn't appear in the stoichometric equation.
- It modifies the reaction mechanism to decrease the energy of activation
- A small quantity of catalysts is enough to produce a considerable effect. They can increase the reaction rate from 10 to 10^{12} times. The catalysts is not destroyed, it is regenerated.
- It does not affect the position of the equilibrium (it works on both directions of the reaction)
- Most biological processes have negligible rates without catalysis.
 - Biological catalysts are mostly proteins (Enzymes), but also RNAs (Ribozymes)
 - Control of catalytic effect is key to control biological processes

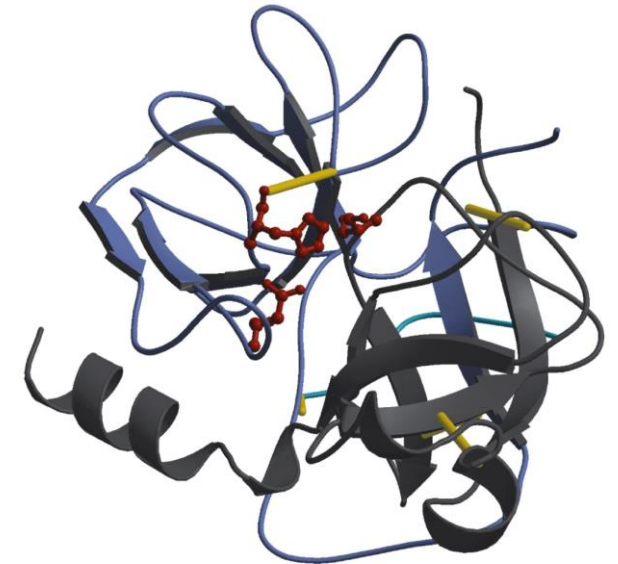
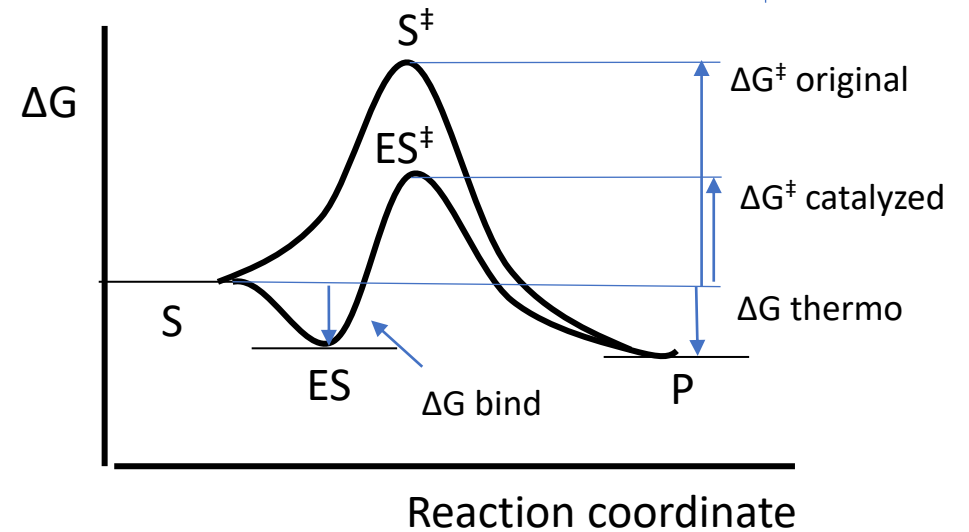
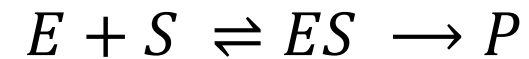


Figure 6-18c
Lehninger Principles of Biochemistry, Fifth Edition
© 2008 W. H. Freeman and Company

Enzymes use binding energy to decrease activation barriers

- First step is the formation of ES
 - The binding energy ($\Delta G < 0$) is invested in decreasing the original activation energy
- Binding decreases the degrees of freedom of S and reduces ΔS^\ddagger ($ES \rightarrow ES^\ddagger$)
 - Effects of "approximation" and "orientation"
- Residues in the protein can, additionally, provide acid-base or electrostatic catalysis



Summary

- (Chemical) Kinetics tries to understand how the velocity of (chemical) processes
- Reaction rates are proportional to the concentration of reactants powered to some exponent (reaction order).
 - For elementary reactions reaction order correspond to the number of molecules involved
- Temperature affects rate constants following Arrhenius law
 - From the microscopic point of view, another consequence of Boltzmann distribution
- Transition State theory provides a way to understand energies involved on kinetics
- Catalysis allows otherwise slow reactions to take place in reasonable times.
 - Biological processes are always controlled by regulation of enzyme activity