5.111 Principles of Chemical Science
Fall 2008

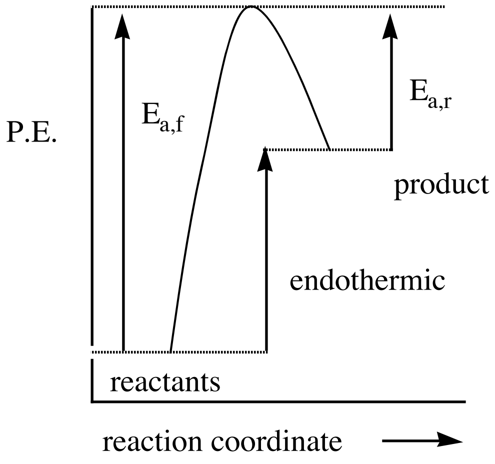
5.111 Lecture 35

Kinetics Topic: Catalysis
Chapter 13 (Section 13.14-13.15)

From Friday's material

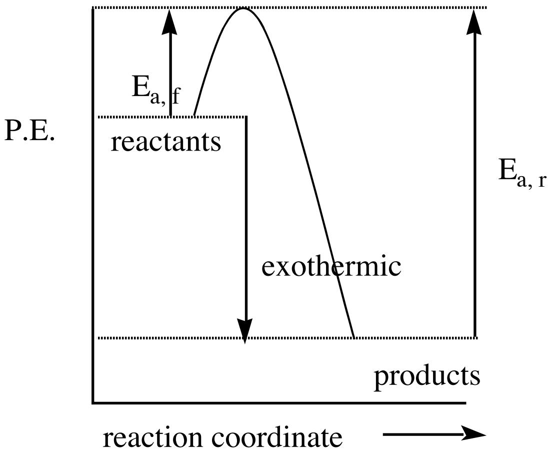
Le Chatelier's Principle - when a stress is applied to a system in equilibrium, the equilibrium tends to adjust to minimize the effect of the stress.

Increasing the temperature can cause reaction to shift in endothermic direction.



$\Delta E = E_{a,f} - E_{a,r}$
+ (endo) = big number - small number

increase temperature, easier to overcome $E_{a,f}$. Equilibrium shifts toward products for endothermic reaction.



$\Delta E = E_{a,f} - E_{a,r}$
- (exo) = small number - large number

increase temperature, easier to overcome $E_{a,r}$. Equilibrium shifts toward reactants in the exothermic reaction.

most molecules have enough energy to overcome small barriers
increasing temperature allows more molecules to overcome larger barriers

Recall, a large E_a means that the rate constant is very sensitive to changes in temperature.

Big E_a - increasing the temperature makes a _______ difference

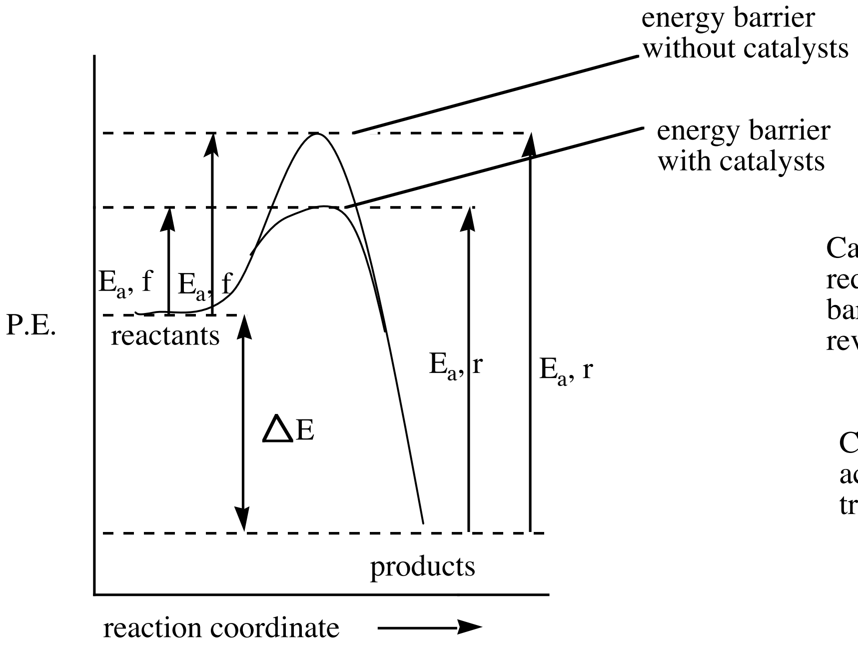
Small E_a - increasing the temperature does not make much of a difference.

End of Friday's material

Kinetics of Catalysis

A catalyst is a substance that takes part in a chemical reaction and speeds it up, but doesn't undergo any permanent change itself.

Catalysts, therefore, don't appear in the overall balanced equation.



Catalysts typically act by reducing the activation energy barrier, both for the forward and reverse reactions.

Catalysts stabilize the activated complex or the transition state.

Catalysts have no effect on the thermodynamics of the reaction.

Free energy, ΔG, is a state function, independent of path, therefore the equilibrium constant is ______________________ by the presence of a catalyst.

An inhibitor is the opposite of a catalyst. It slows the rate of a reaction, typically by increasing the activation energy.

Types of Catalysts

Homogeneous catalysts: reactants and catalysts are in the same phase

Example: chlorofluocarbons catalyze the depletion of O_3 (all gas phase)

Heterogeneous catalysts: different phase

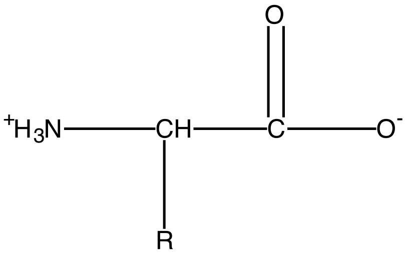
Example: catalytic converter

Solid metals (platinum, palladium, and rhodium) catalyze oxidation of hydrocarbons and CO gases and the reduction of nitrogen oxide gases to reduce pollution.

Catalysts of Life: enzymes

An enzyme is a large protein molecule (typically 20,000 g/mol or more) that is capable of carrying out a specific reaction or series of reactions.

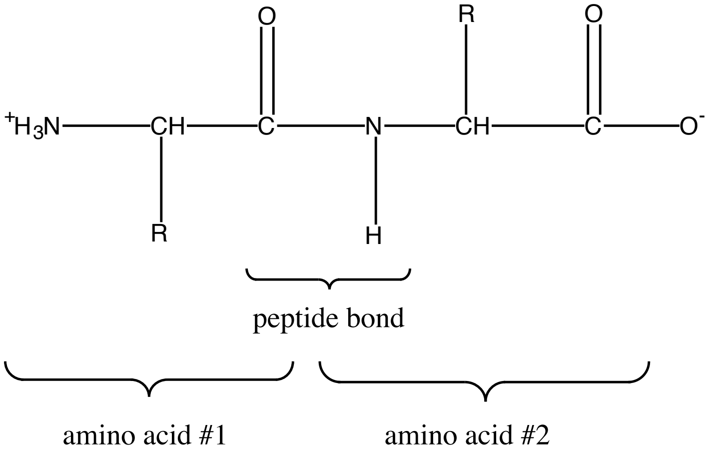
Proteins are made up of amino acids



$$^{+}H_3N-\underset{R}{CH}-\overset{O}{\overset{\|}{C}}-O^{-}$$

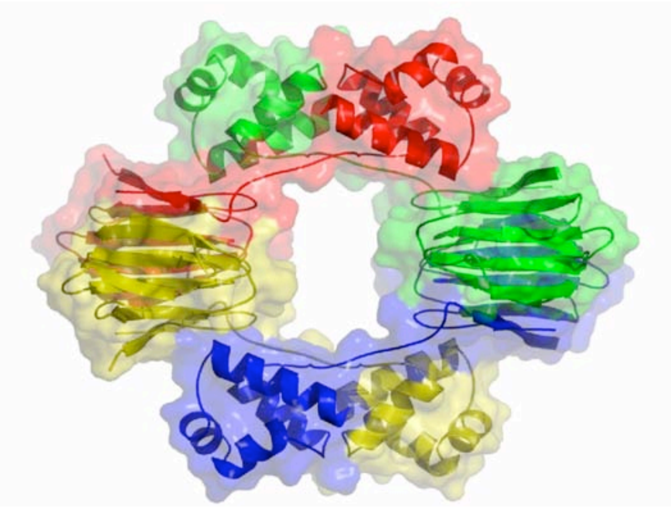
R= sidechain
20 different sidechains
20 different amino acids

Amino acids are connected by peptide bonds to form polypeptide chains (or proteins).



$$^{+}H_3N-\underset{R}{CH}-\overset{O}{\overset{\|}{C}}-\underset{H}{N}-\overset{R}{CH}-\overset{O}{\overset{\|}{C}}-O^{-}$$

A long chain of amino acids folds up into a compact structure.



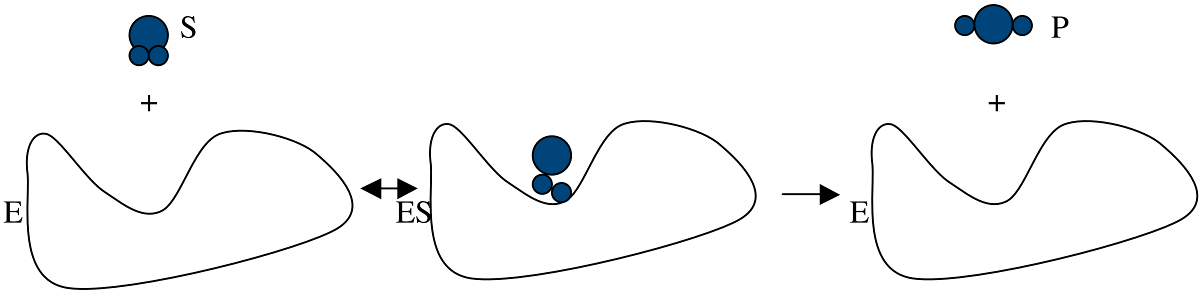
Four polypeptide chains with 198 amino acids each fold to form this enzyme.

Ribbons drawn through the alpha (α) carbons.

Dimensions are ~90 Å x 70 Å x 50 Å.
(1 Å equals 1×10^{-10} m)

<u>Enzyme catalysis</u>
Reactant molecules are called <u>substrates</u>.

Substrates bind to an <u>active site</u> on the enzyme.
enzyme (E) + substrate (S) ⇔ enzyme-substrate complex (ES) → enzyme (E) + product (P)



Derive rate expression for $E + S \Leftrightarrow ES \rightarrow E + P$:

Step 1 $$E + S \underset{k_{-1}}{\overset{k_1}{\Leftrightarrow}} ES$$

$\text{rate}_f =$

$\text{rate}_r =$

Step 2 $$ES \xrightarrow{k_2} E + P$$

rate =

Rate of product formation $= \dfrac{d[P]}{dt} = k_2[ES]$

Solve for intermediate [ES]

$$\frac{d[ES]}{dt} =$$

use steady-state approximation

$$0 = \frac{d[ES]}{dt} = k_1 [E][S] - k_{-1} [ES] - k_2 [ES]$$

Now a slight change. Instead of solving for [ES] in terms of [E], free enzyme, solve for [ES] in terms of $[E]_o$, total enzyme.

$$\begin{array}{lllll} [E]_0 & = & [E] & + & [ES] \\ \text{total} & & \text{free} & & \text{bound} \\ \text{enzyme} & & \text{enzyme} & & \text{enzyme} \end{array}$$

replace [E] with $([E]_0 - [ES])$

$$0 = \frac{d[ES]}{dt} = k_1 [E]_0 [S] - k_1 [ES][S] - k_{-1} [ES] - k_2 [ES]$$

rearrange [ES] terms to one side of the equation

$$k_1 [ES][S] + k_{-1} [ES] + k_2 [ES] = k_1 [E]_0 [S]$$

$$[ES] (k_1 [S] + k_{-1} + k_2) = k_1 [E]_0 [S]$$

$$[ES] = \frac{k_1 [E]_0 [S]}{k_1 [S] + k_{-1} + k_2}$$

Introduce new term K_m (michaelis-menten constant)

$$K_m = \frac{k_{-1} + k_2}{k_1}$$

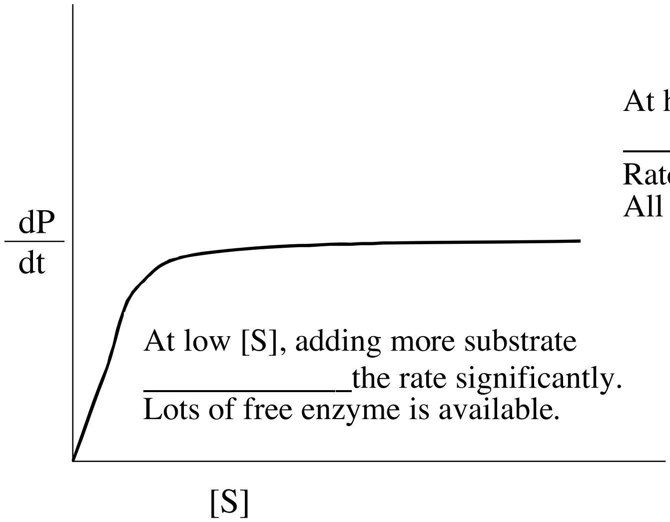
Substitute K_m into [ES] expression

$$[ES] = \frac{k_1 [E]_0 [S]}{k_1 [S] + k_{-1} + k_2} = \frac{k_1 [E]_0 [S]}{k_1 \left([S] + \frac{(k_{-1} + k_2)}{k_1}\right)} = \frac{\cancel{k_1} [E]_0 [S]}{\cancel{k_1} \left([S] + \frac{(k_{-1} + k_2)}{k_1}\right)} =$$

$$[ES] = \frac{[E]_0 [S]}{[S] + K_m}$$

Substitute [ES] into the rate expression

$$\text{rate of product formation} = k_2[ES] = \frac{k_2\,[E]_0\,[S]}{[S] + K_m}$$ Michaelis-Menten Equation



At high [S], adding more substrate _______________ change the rate much.
Rates level off. Enzyme is saturated.
All active sites on enzyme are filled.

At low [S], adding more substrate _____________the rate significantly.
Lots of free enzyme is available.

When $[S] >> K_m$, then

$$\text{rate of product formation} = \frac{k_2\,[E]_0\,\cancel{[S]}}{\cancel{[S]} + \underset{\text{small}}{\cancel{K_m}}} = k_2\,[E]_0$$ This is called V_{max}

Maximal rate = $V_{max} = k_2\,[E]_0$

When $[S] = K_m$, then

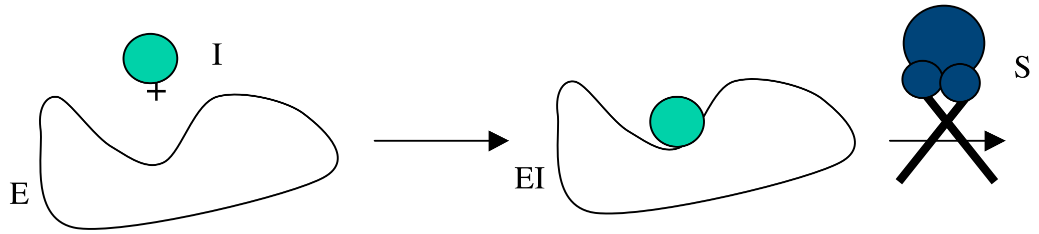
$$\text{rate of product formation} = \frac{k_2\,[E]_0\,[S]}{[S] + [S]} = \frac{1}{2}\,k_2\,[E]_0$$ half maximal rate

Definition of K_m ≡ concentration of [S] for which the rate is half-maximal.

Example: The conversion of CO_2 in blood to HCO_3^- and H_3O^+ is catalyzed by the enzyme carbonic anhydrase. The Michaelis-Menten constants for this enzyme and substrate are $K_m = 8 \times 10^{-5}$ M and $k_2 = 6 \times 10^5\ s^{-1}$. What is the maximum reaction rate if the enzyme concentration is 5×10^{-6} M?

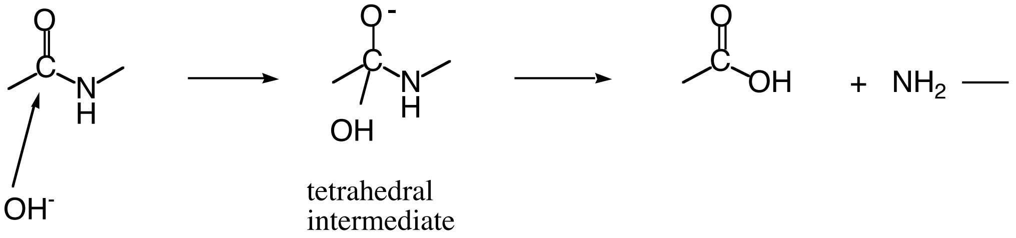
Enzyme Inhibition

If an inhibitor is bound in the active site, then substrate can't bind.



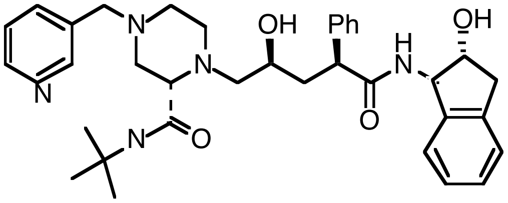
Many pharmaceutical drugs work by blocking the action of enzymes. Enzymes catalyze reactions by stabilizing the "transition state" of the reaction. Compounds that resemble the _______________ should bind more tightly to the enzyme than reactants or products. These compounds can therefore serve as enzyme inhibitors (drugs).

Example: Protease inhibitors are used in treatment of HIV. Enzymes that cleave peptide bonds are called proteases. Overall mechanism of peptide bond cleavage - a type of displacement reaction: Molecules with a stable tetrahedral atom at cleavage site will resemble the transition state and could bind more tightly to the enzyme than substrate does.



Examples of molecules with tetrahedral centers:

Approved drug for HIV, indinavir sulfate (The New England J. Med. 338, 1285 (1998)).



Ph=phenyl

Knowledge of reaction mechanism can lead to design of new therapeutic treatments. Interesting and important question - why doesn't this compound block all proteases? A second consideration is specificity. Tight binding is just one facet of drug design. Also must consider specificity and delivery.