5.111 Lecture Summary # 34 **Monday, December 8, 2014**

Reading for Today: 14.14 & 14.16 in 5th ed and 13.14 & 13.16 in 4th ed

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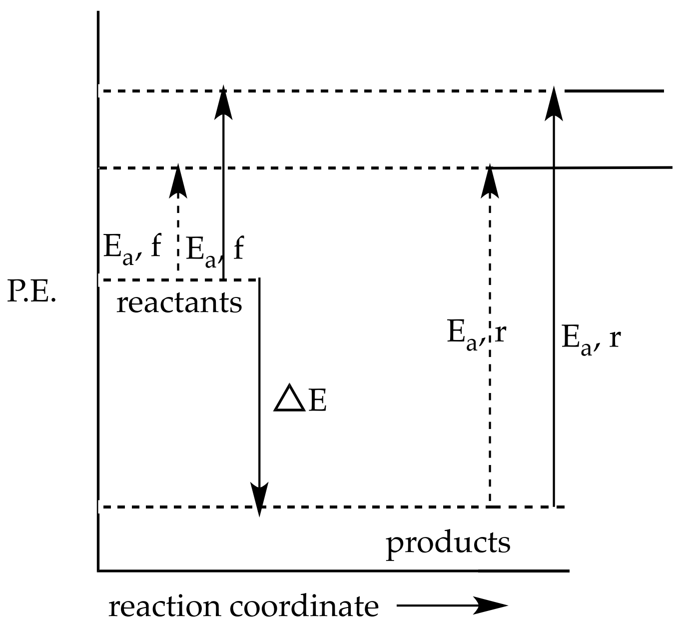
Topics: Kinetics
- I. Introduction to Catalysis
- II. Types of Catalysts
- III. Catalysts of Life and Enzyme Catalysis

I. Introduction to Catalysis

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

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



Activation energy barrier without a catalyst

Activation energy barrier with a catalyst

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

Catalysts stabilize the ________________ also known as the activated complex.

Catalysts have _______________ 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.

II. Types of Catalysts

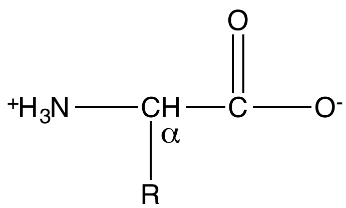
Homogeneous catalysts: reactants and catalysts are in the same phase
Example: chlorofluocarbons catalyze the depletion of O_3 (all gas phase)

Heterogeneous catalysts: different phase
Example: catalytic converters reduce pollution by using solid metals (platinum, palladium, and rhodium) to catalyze the oxidation of hydrocarbons and CO gases, and the reduction of nitrogen oxide gases.

III. Catalysts of Life: Enzymes

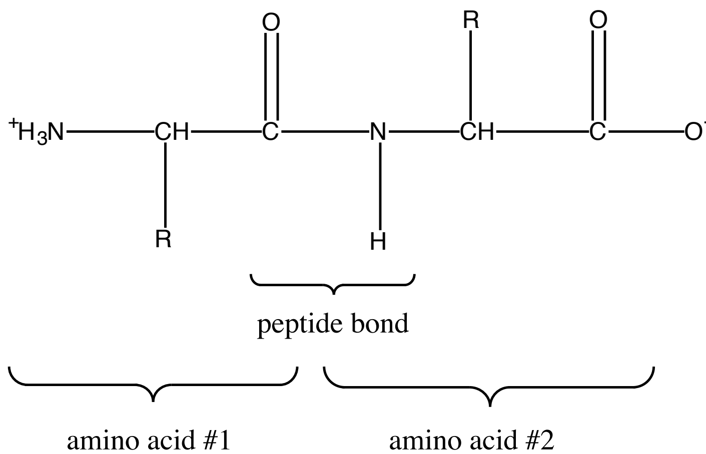
An enzyme is a large protein molecule (typically 20,000 g/mol or more) that is capable of carrying out a specific reaction or series of reactions.

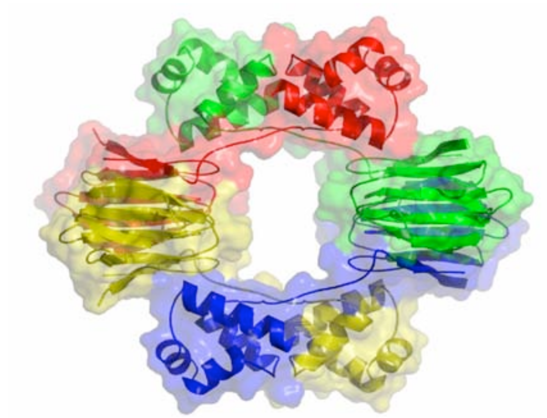
Proteins are made up of amino acids



R= sidechain
20 different sidechains
20 different amino acids

Amino acids are connected by peptide bonds to form polypeptide chains (or proteins).
A long chain of amino acids folds up into a compact structure.





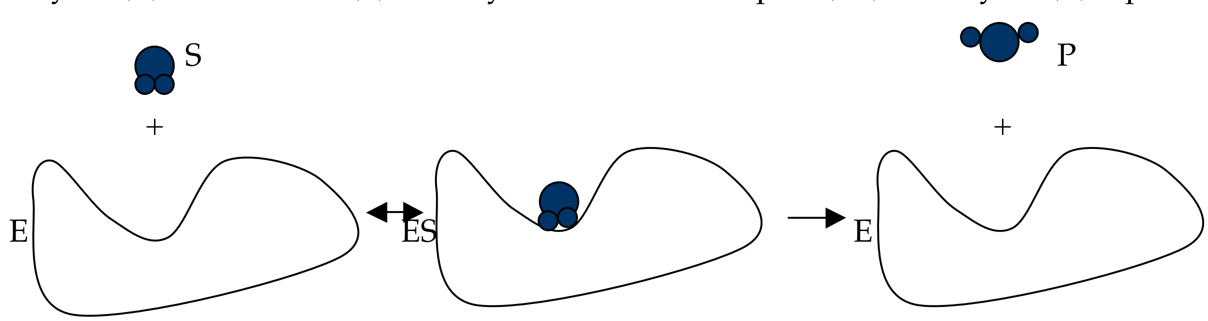
Four polypeptide chains with 198 amino acids each fold to form this enzyme structure.
Ribbons drawn through the alpha (α) carbons.   Dimensions are ~90 Å x 70 Å x 50 Å.
This Fe-dependent enzyme catalyzes the final step in making the antibiotic fosfomycin.

<u>**Enzyme Catalysis**</u>

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

Substrates bind to an ____________________ 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 $\quad E + S \underset{k_{-1}}{\overset{k_1}{\Leftrightarrow}} ES$ $\qquad$ $rate_f =$

$rate_r =$

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

$[E]_0$	=	[E]	+	[ES]
total enzyme		free enzyme		bound enzyme

replace [E] with ($\mathbf{[E]_0 - [ES]}$)

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

rearrange [ES] terms to one side of the equation, and then solve for [ES]

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

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

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

Introduce new term K_m (Michaelis-Menten constant) $\qquad K_m = \dfrac{k_{-1} + k_2}{k_1}$

Substitute K_m into [ES] expression

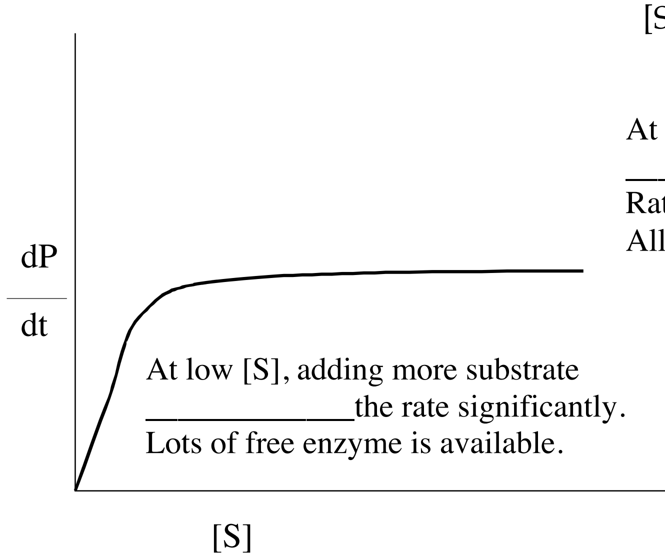
$$[ES] = \frac{k_1 [E]_0 [S]}{k_1 [S] + k_{-1} + k_2} \qquad K_m = \frac{k_{-1} + k_2}{k_1}$$

divide by k_1

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

Substitute [ES] into the rate expression

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



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

When [S] >> K_m, then

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

small

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

When [S] = K_m, then

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

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

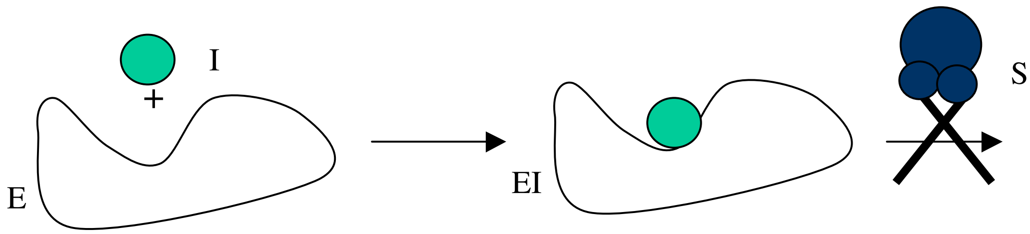
Example: The conversion of CO_2 in blood to HCO_3^- and H_3O^+ is catalyzed by the enzyme carbonic anhydrase. The Michaelis-Menten constants for this enzyme and substrate are $K_m = 8 \times 10^{-5}$ M and $k_2 = 6 \times 10^5$ s^{-1}.

Calculate the maximum reaction rate if the enzyme concentration is 5×10^{-6} M?

At which concentration of substrate will the rate be 1.5 M/s?

An <u>inhibitor</u> is the opposite of a catalyst. It ________________ the rate of a reaction, typically by increasing the activation energy.

<u>Enzyme Inhibition</u>. If an inhibitor is bound in the active site of an enzyme forming an enzyme-inhibitor complex (EI), then substrate can't bind.



Many pharmaceutical drugs work by blocking the action of enzymes.

Given that enzymes catalyze reactions by lowering the energy of the "transition state," compounds that resemble the __________________________ can bind tightly to the enzyme, and thereby block substrate binding.

IN THEIR OWN WORDS

Jingnan Lu, a graduate student in the Sinskey laboratory in the Biology Department, discusses the kinetic considerations in her research on the development of biofuels.