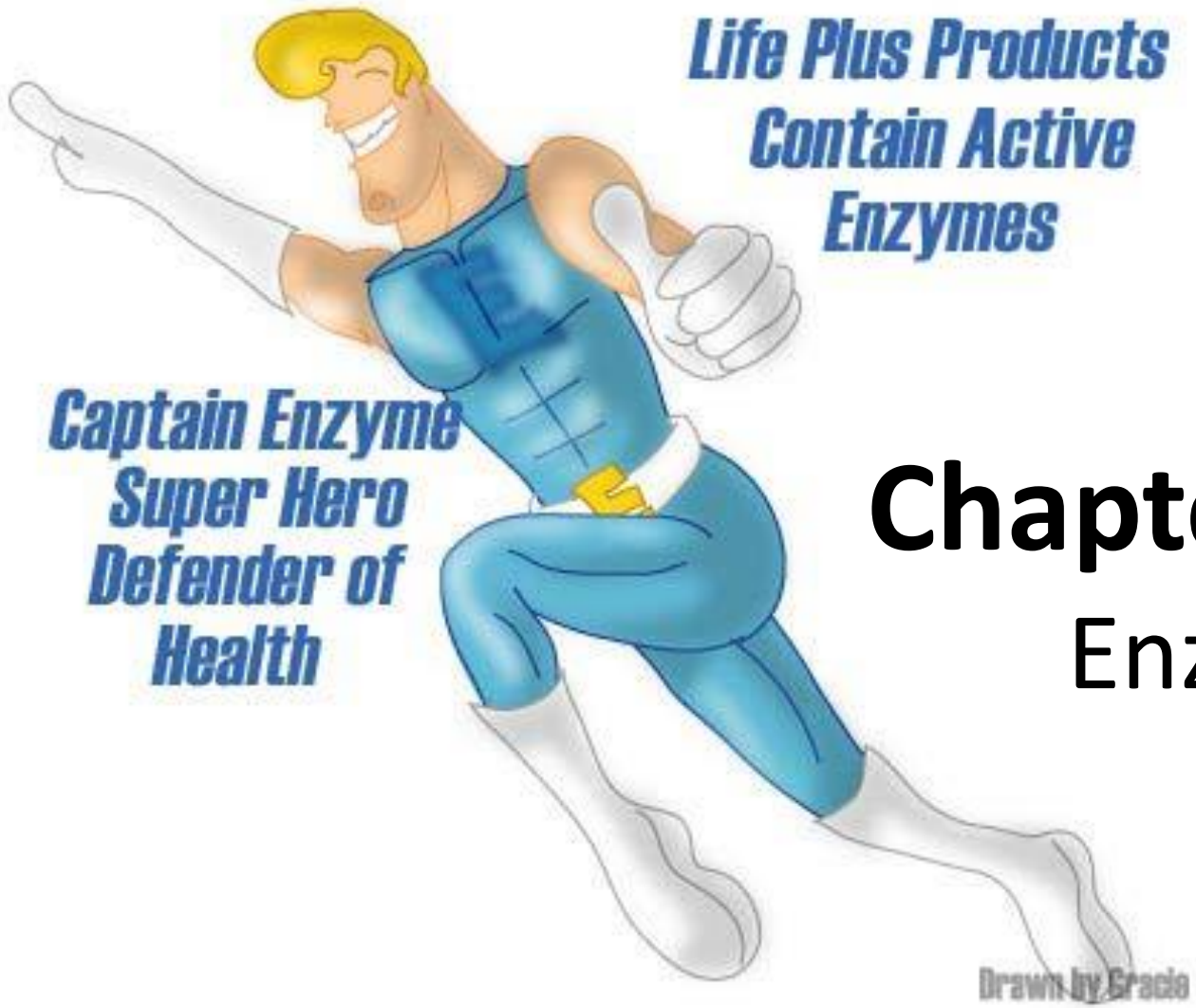


Chapter 10

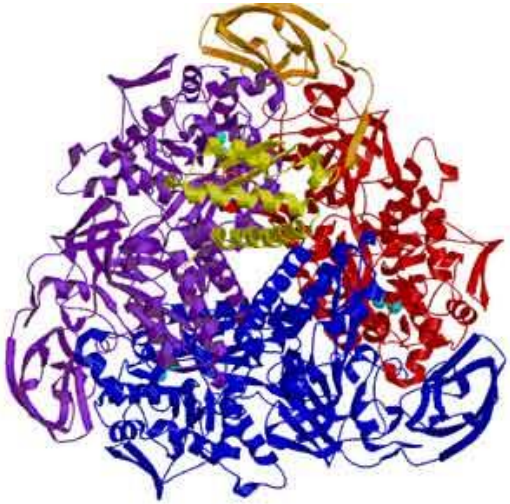
Enzymes

Enzymes

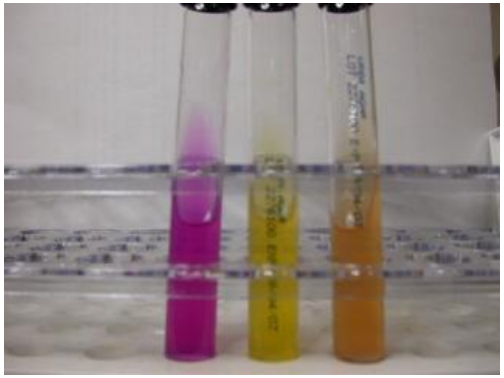
Most known enzymes are large “globular proteins”.

There are 27,383 proteins in the human genome. 12,000 have unknown functions and 6,000 behave as enzymes.

Enzymes are necessary for nearly all reactions in the human body.



Urease

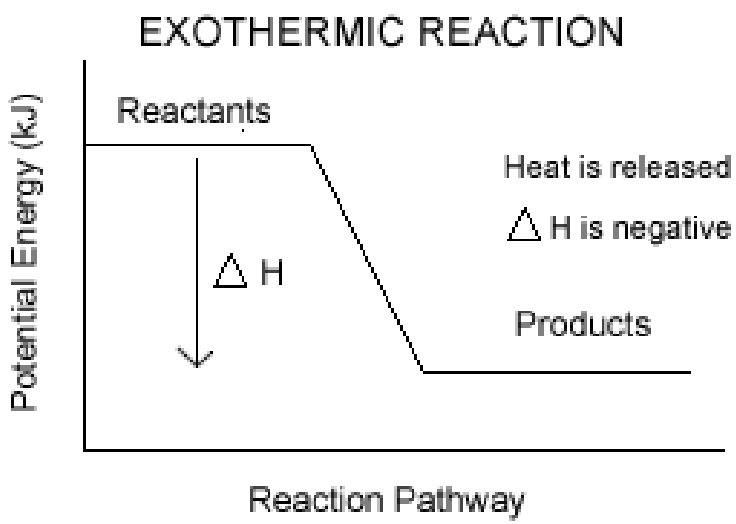


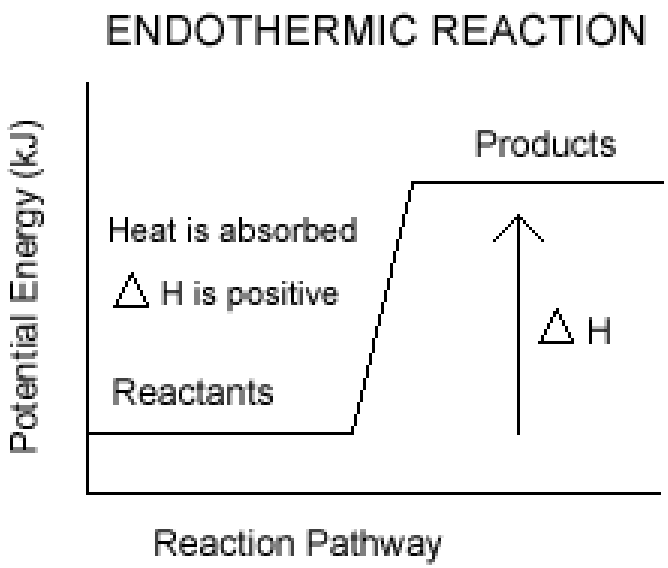
Urease: enzyme responsible for catalyzing the hydrolysis of urea to ammonia and carbon dioxide. The presence of ammonia gives a pink color with a pH indicator.

Functions of Enzymes

Enzymes are primarily catalysts.

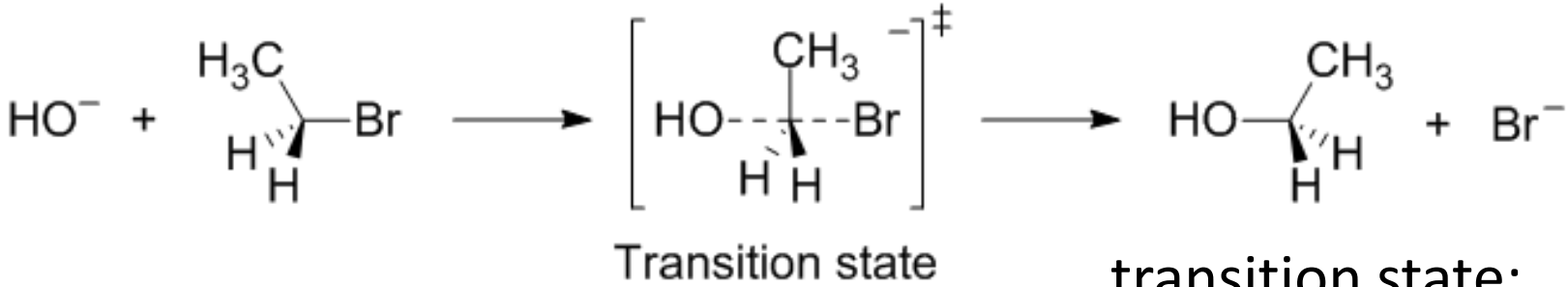
<u>catalyst</u>: **speeds** up a chemical reaction and is **regenerated**.

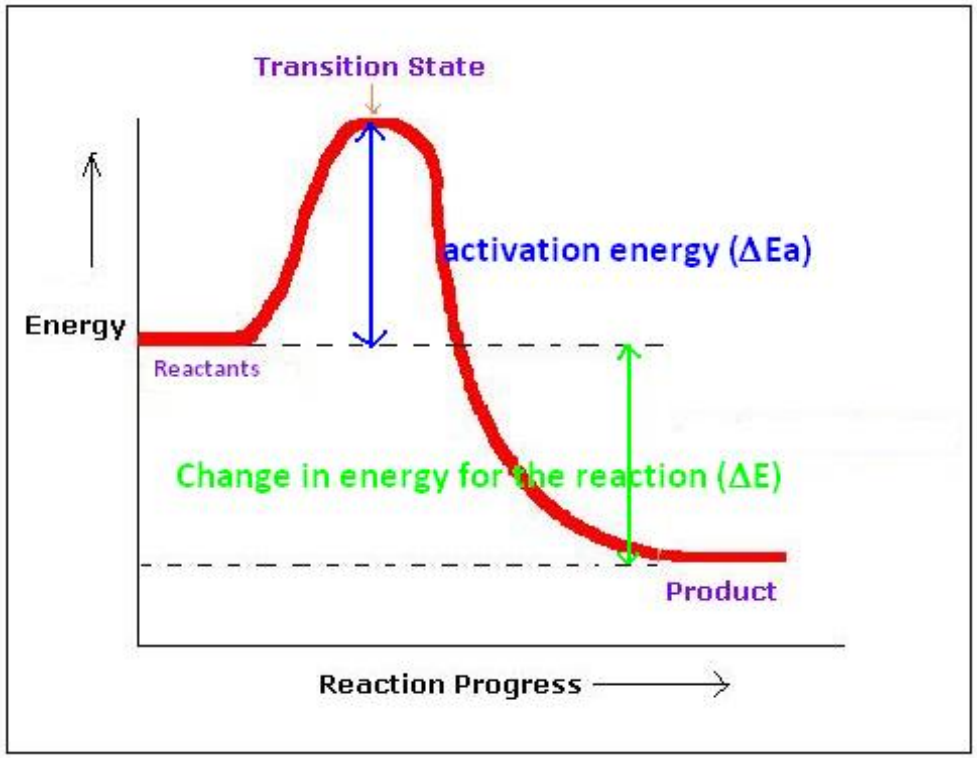




Reaction Coordinate Diagrams

reactants → transition state→ products

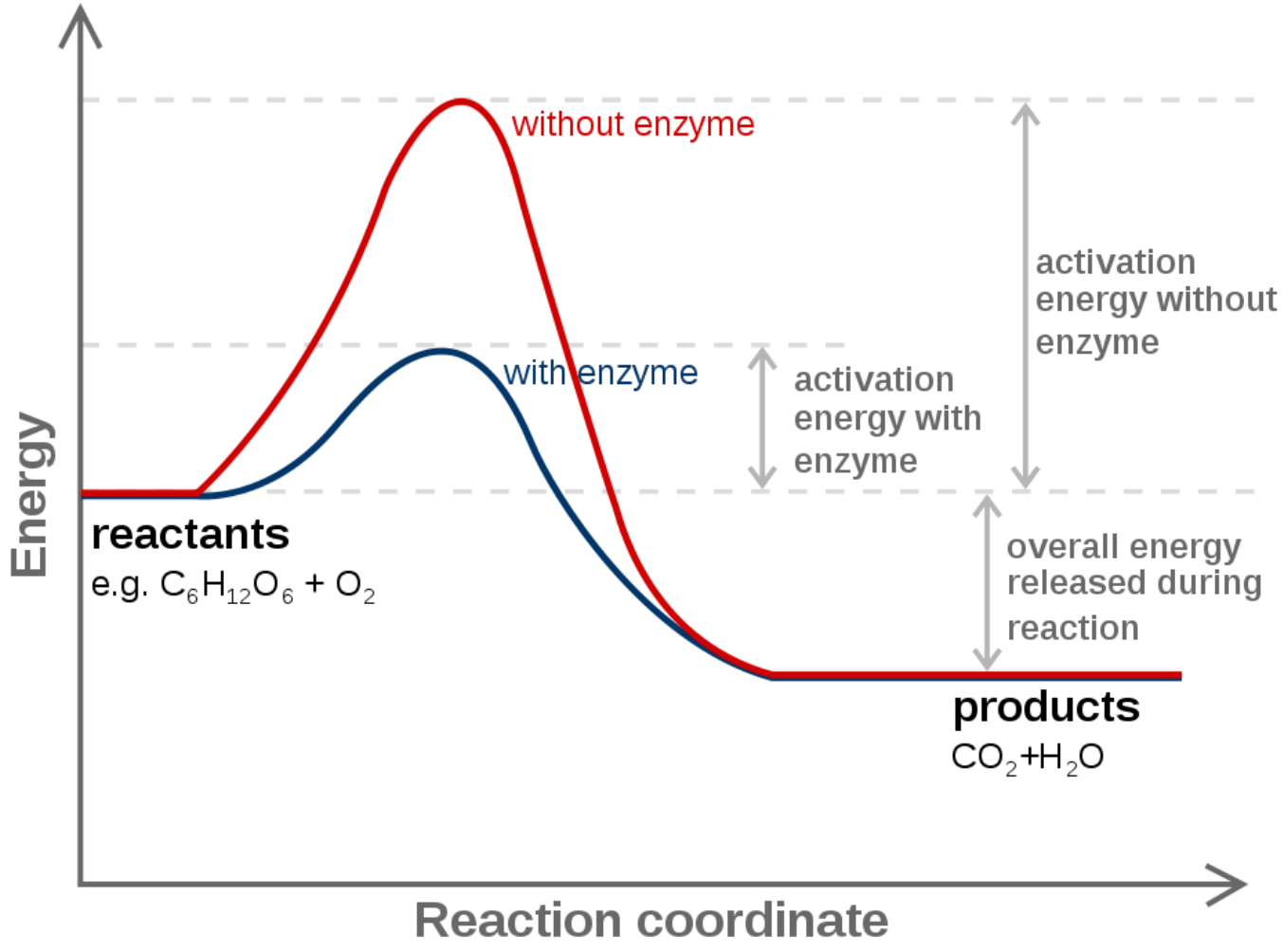




<u>transition state</u>: intermediary state of bonds being broken or formed that requires the highest amount of energy to reach.

<u>activation energy</u>: the energy required to convert the reactants to the transition state.

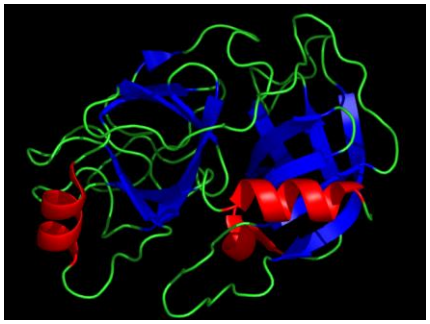
Function of Catalysts



Classifications of Enzymes

Enzymes are named based on the types of reactions that they catalyze.

Example: “serine proteases” cut peptide bonds at the serine active site

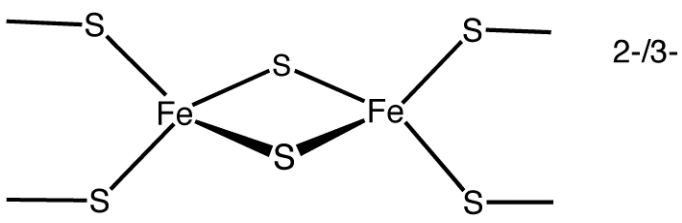


The six major classifications are:

- Oxidoreductases: redox reactions
- Transferases: transfer of atoms
- Hydrolases: hydrolysis reactions
- Lyases: addition of two groups to a double bond, or removal of 2 groups from adjacent atoms to form a double bond
- Isomerases: isomerization reactions
- Ligases/Synthetases: joining of two molecules

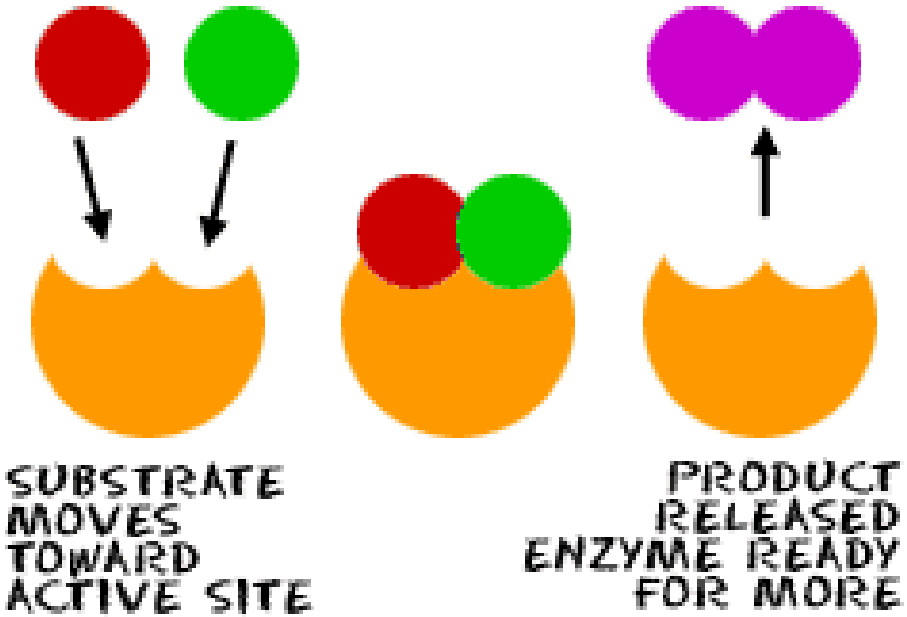
Terminology

Enzymes can contain polypeptides, organic compounds, or metallic ions.



- <u>apoenzyme</u>: polypeptide portion of an enzyme
- <u>cofactor</u>: non-polypeptide portion of an enzyme
- <u>coenzymes</u>: organic cofactors
- <u>substrate</u>: compound which binds to the enzyme and whose reaction is sped up as a result
- <u>active site</u>: area on the substrate that binds to a specific portion of the enzyme during the reaction
- <u>activation</u>: any process that initiates or increases an enzyme's activity
- <u>inhibition</u>: any process that makes an active enzyme less active

Enzyme Activity



1. Substrate binds at the enzyme's active site.
2. The intermediary complex changes bonds in the substrate.
3. The intermediary complex breaks apart.
4. The enzyme is released in its original form; the substrate is now product.

Enzyme Binding

The more tightly bound,
the higher the enzyme's activity.

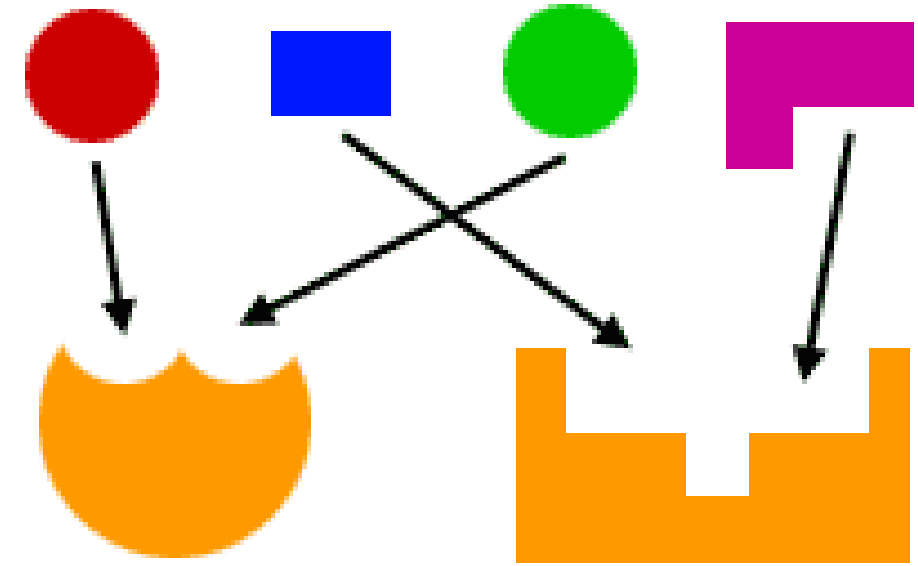
Substrates are **specific**; they will only bind to one type of enzyme.

Lock and Key Model assumes the enzyme is a rigid, 3D body.

Induced-Fit Model assumes the substrate can change shape when bound to the enzyme.

The Lock and Key Model

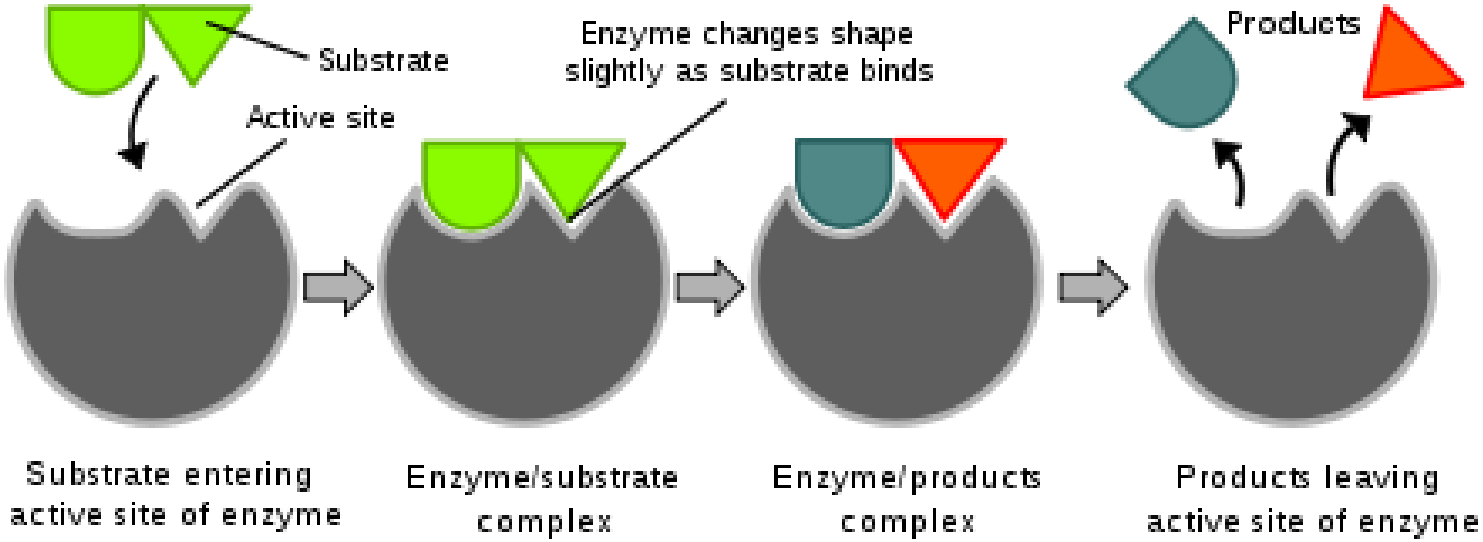
The enzyme is assumed to be a *rigid object*. Its active site is a specially-shaped structure to create a hole in which only one particular substrate can fit.



ENZYMES ARE VERY SPECIFIC AND ONLY WORK WITH CERTAIN SUBSTRATES

The Induced-Fit Model

While the active site has mostly the right shape, the substrate-enzyme intermediate changes slightly after binding to accommodate each other.



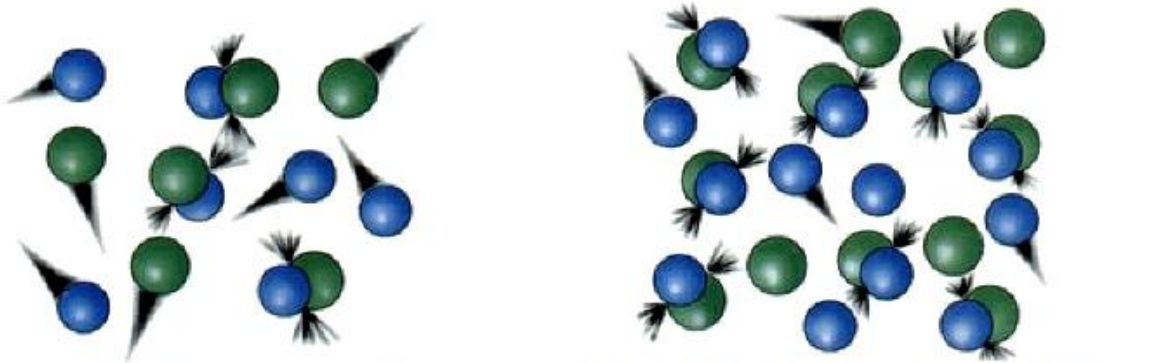
Activity of Enzymes

Enzyme activity is measured by how much the enzyme increases reaction rate.

- <u>kinetics:</u> branch of chemistry that studies reaction rates to derive relationships between them and factors that affect them.

The activity of an enzyme is dependent on:

- the relative concentrations of substrate and enzyme
- temperature
- pH
- inhibitors



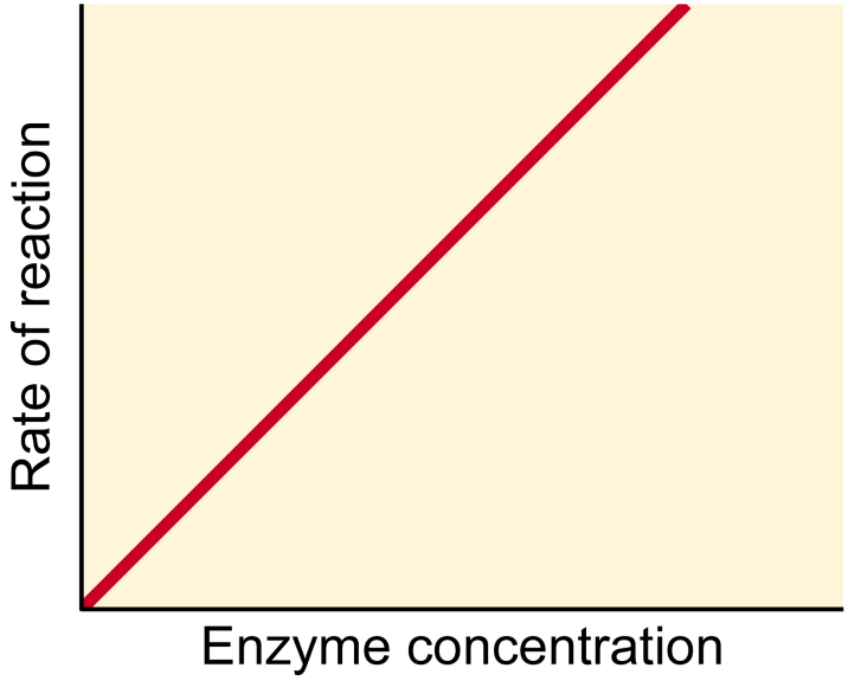
Low concentration = Few collisions

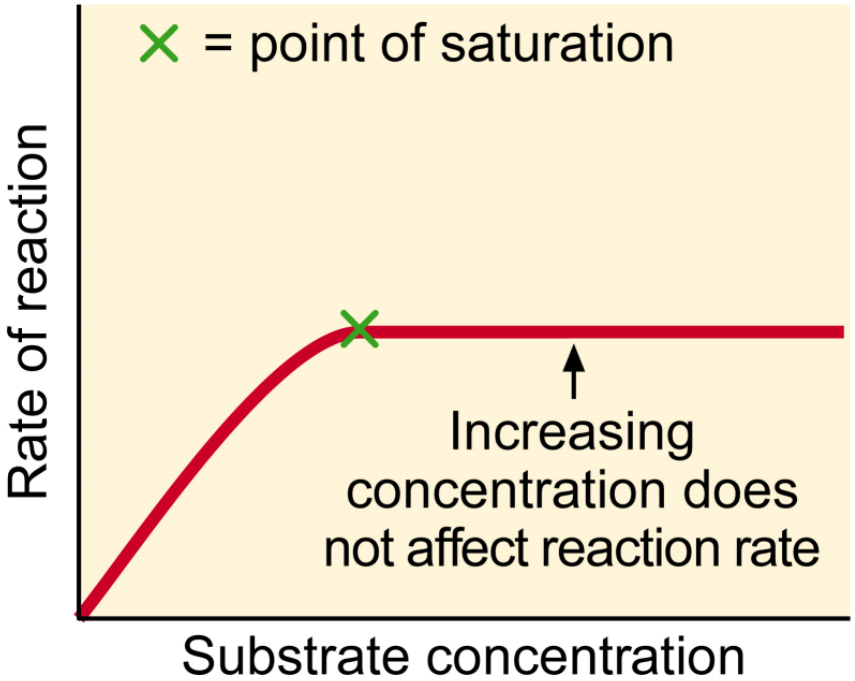
High concentration = More collisions

Concentration Dependency

The concentration of the substrate is assumed to be much, much higher than the concentration of the enzyme.

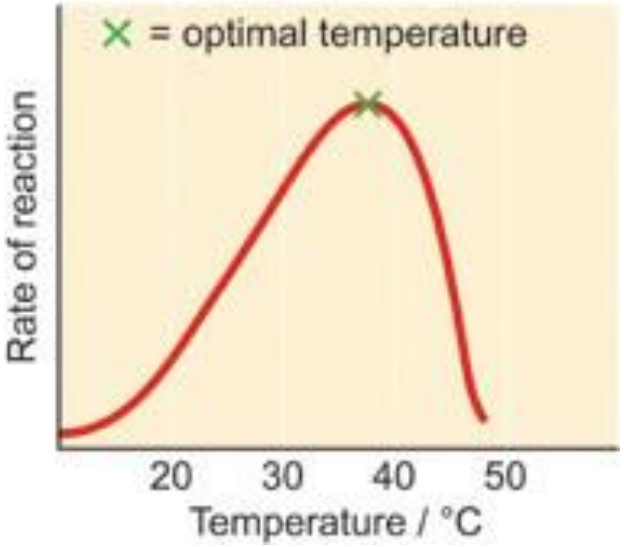
(Remember: enzymes are produced solely by need)

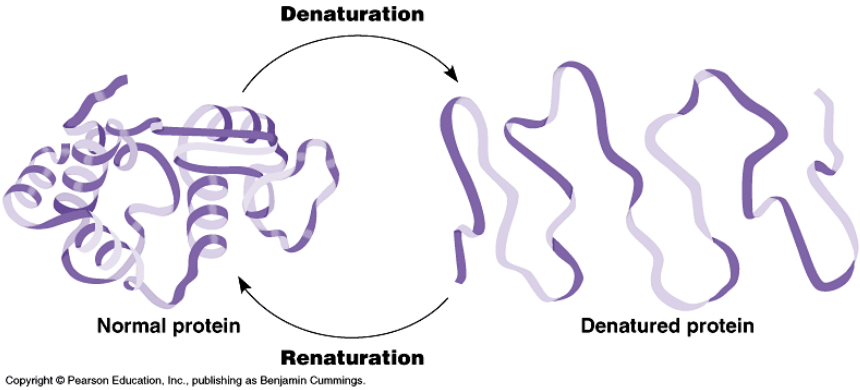




Temperature Dependency

Increasing the temperature increases the kinetic activity of the molecules, thus making them move faster.



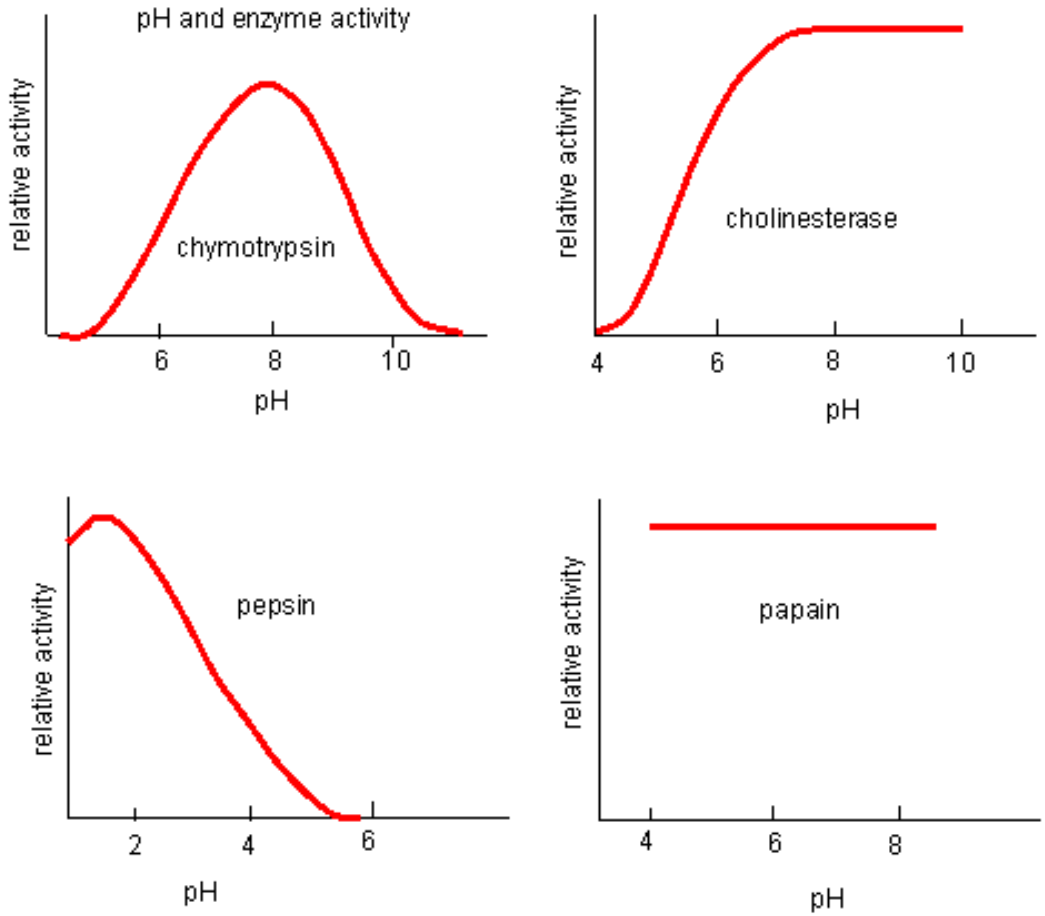


Too extreme temperature can **denature** enzymes.

pH Dependency

The pH of the surroundings changes both the side chains (acidic/basic) and the backbone.

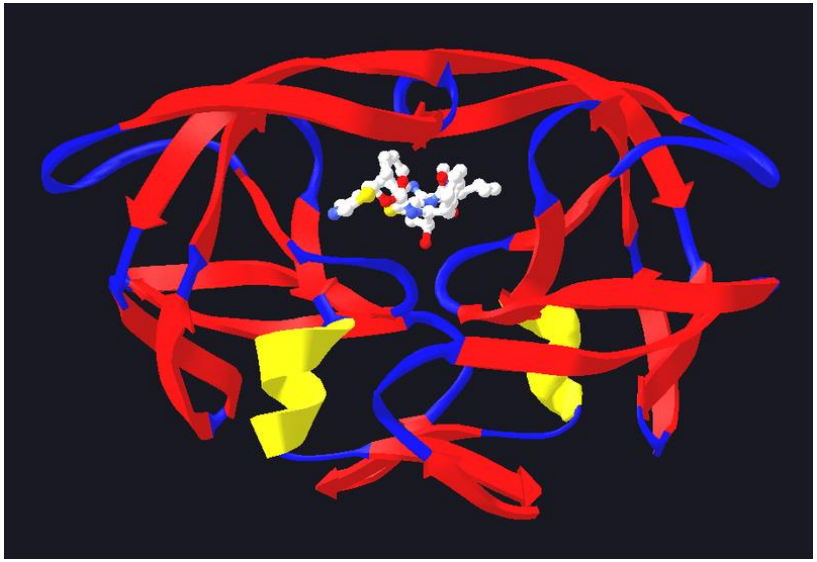
Each enzyme has a particular optimal pH at which it will have the highest activity.



Inhibition

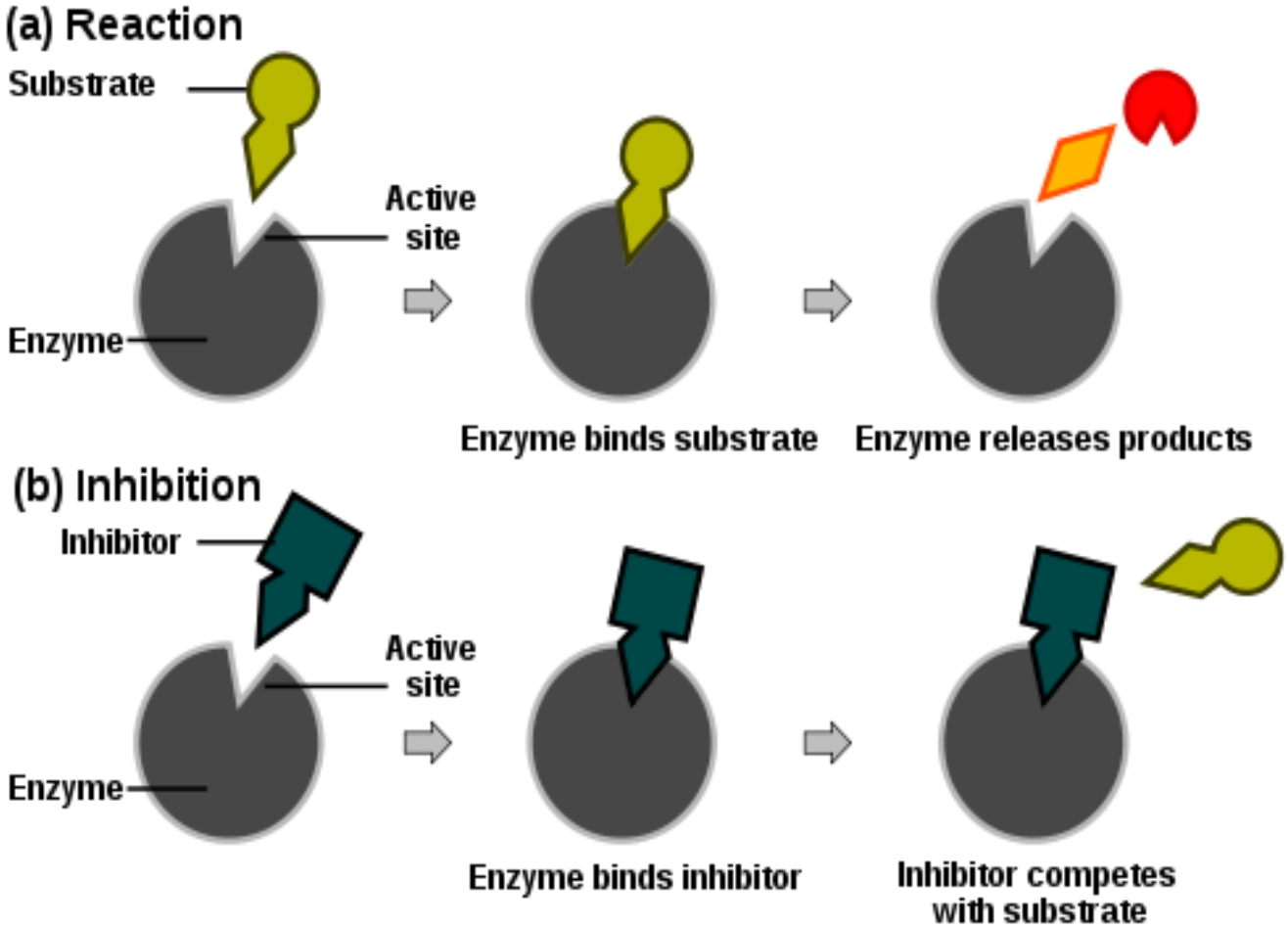
Inhibitors are molecules that negatively impact an enzyme's activity by reducing its ability to bind with the substrate.

Inhibitors are most commonly used as drugs to fully stop enzyme activity.



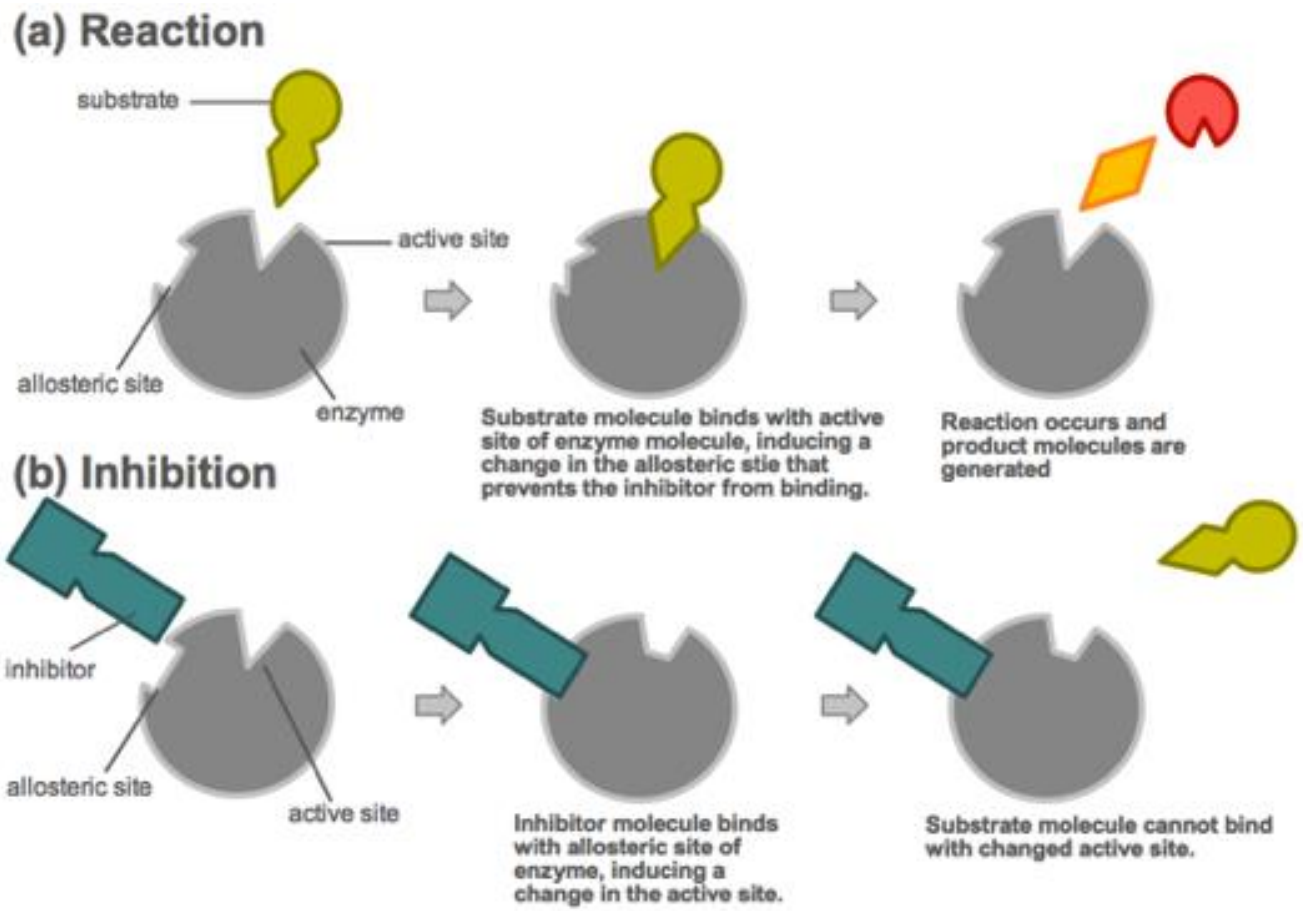
Ritonavir: A "booster" inhibitor that, by binding to proteases, prevents the metabolism of other protease inhibitors, thus allowing other drugs to have longer and more profound effects at lower concentrations.

Competitive Inhibitors



Competitive inhibitors directly bind to the active site of the enzyme.

Noncompetitive Inhibitors



Noncompetitive inhibitors also bind to the enzyme, but NOT at the active site.

Kinetics of Competitive

Competitive:

- The inhibitor-substrate complex is in equilibrium with the unbound substrate.
- At low [substrate], it is mostly inhibited.
- At high [substrate], the free substrate, forces the inhibitor out and can then form the substrate-enzyme complex that can go on to product.

In Normal Conditions:

$$E + S \rightleftharpoons E\text{-}S \rightleftharpoons E + P$$

With Inhibitor:

$$E + I \rightleftharpoons E\text{-}I \underset{S \curvearrowright I}{\rightleftharpoons} E\text{-}S \rightleftharpoons E + P$$

Kinetics of Noncompetitive

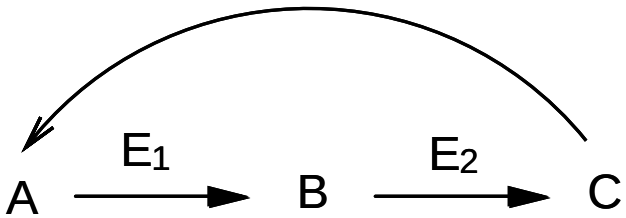
Noncompetitive:

- Increasing [substrate] will have absolutely no effect on the enzyme-inhibitor complex.

Therefore:

- For **competitive** inhibition, increasing [substrate] enough will allow the reaction to eventually reach its maximum rate.
- For **noncompetitive** inhibition, increasing [substrate] will have no effect on reaction rate at all.

Enzyme Regulation



- Feedback Control: A product from subsequent reactions inhibits a previous reaction from producing.
- Proenzymes: Precursors to enzymes that are "inactive" and require a subsequent alteration to become active
- Allosterism: An outside molecule binds to the enzyme to have an indirect affect on its activity (noncompetitive inhibition).
- Protein Modification: Changes the structure of the enzyme.
- Isoenzymes: Isomers of the same enzyme in different locations
- Transition State Analogs: outside molecule that mimics the transition state of a reaction

Seed Inhibitors: genetic modifications add inhibitors to seeds to discourage animals