Enzymes
General

Enzymes:

- Proteins that catalyze biochemical reactions
- Eduard Buchner (1907) – Nobel prize – living cells not required for enzymes to function
- Accelerate chemical reactions 1-100 million times
- Enzyme Specificity
- Functionality is very specific (1 Enzyme catalyzes 1 Reaction)
- "-ase" ending

4 Common Features

- Speed up reactions
- Enzyme not altered in the reaction (reusable)
- Highly specific
- Reversible – One direction usually highly favored

Terms

Apoenzyme: protein part

Coenzyme: non-protein part

Holoenzyme = apoenzyme + coenzyme

Holoenzyme: enzyme requiring Apo + Co to function

Activator: Inorganic part (metal ions)

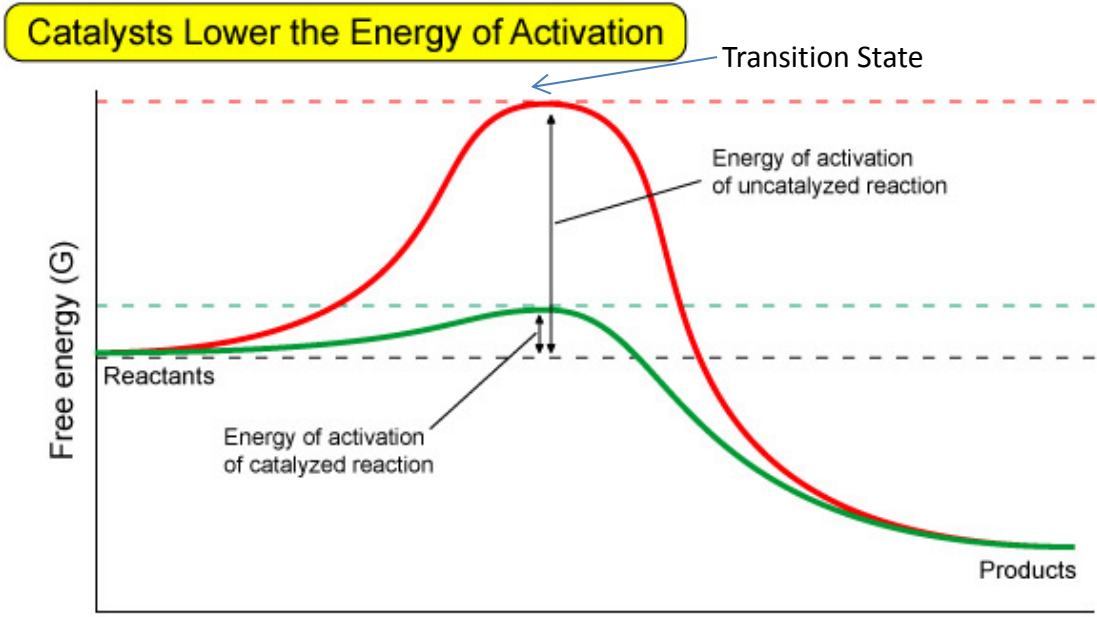
Substrate: substance acted on by enzyme

6 Classes of Enzymes

6 Main Classes of Enzymes

Class	Function
1. Oxidoreductases	Oxidation-Reduction reactions between 2 substrates
2. Transferases	Transfer of functional group between 2 substrates
3. Hydrolases	Hydrolysis of esters, carbohydrates and proteins
4. Lysases	Removal of functional groups (not by hydrolysis)
5. Isomerases	Interconversion of stereoisomers and structural isomers
6. Ligases	Linkage of 2 compounds via breaking a phosphate anhydride bond in ATP

Reaction-Energy Diagram


Catalysts Lower the Energy of Activation
Transition State
Energy of activation
of uncatalyzed reaction
Free energy (G)
Reactants
Energy of activation
of catalyzed reaction
Products

Reaction-Energy Terms

Activation Energy (Barrier):

- Energy required for a reaction to occur
- The larger the barrier the slower the rate

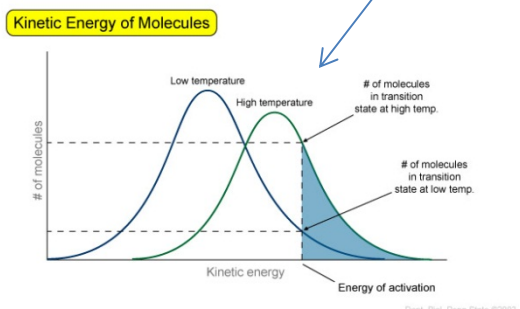
Transition State:

- Unstable intermediate state ½ way between reactants and products
- Catalysts work by altering the TS

Increasing Reaction Rates

3 Ways to Increase Reaction Rates

Method	Description
1. Increase Reactant concentration	Increases number of molecules with enough energy to be able to react
2. Increase Reaction Temperature	Increases number of energy of all molecules therefore increasing the number with E > AE
3. Catalysts	Changes AE, allowing more molecules to react



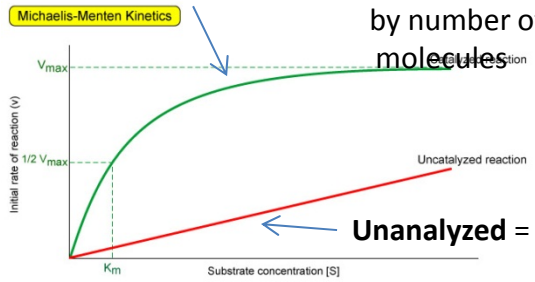
Enzyme Kinetics

Michaelis-Menton Plots:

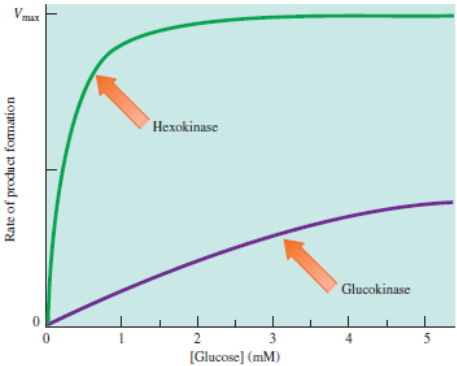
- Reaction Rate increases with increasing number of reactant molecules

- Enzymes tailored to meet specific metabolic needs

Enzyme Catalyzed = Maximum rate limited by number of catalyst molecules



Unanalyzed = linear response



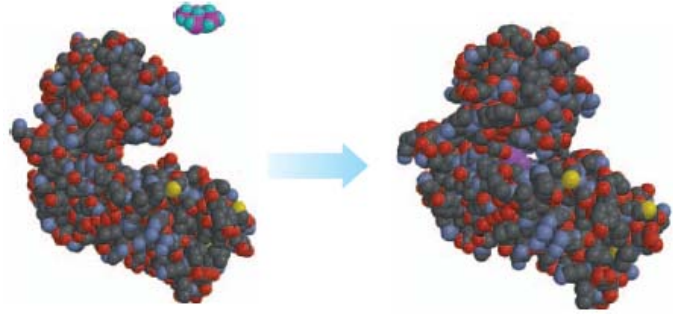
- Level of substrate concentration
  - Hexokinase = low [conc] = energy
  - Glucokinase = high [conc] = storage

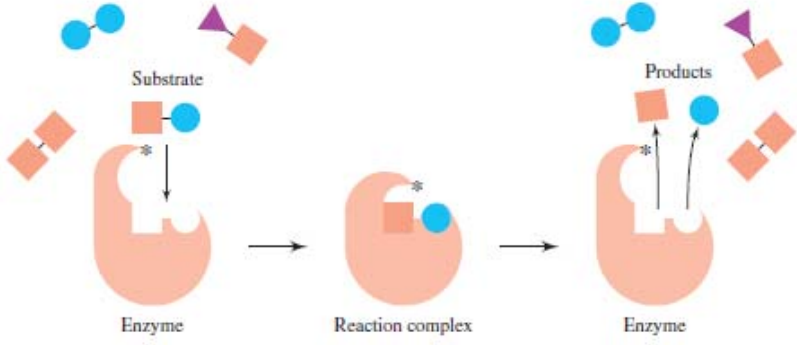
- Rate of reaction **(turnover number)**
  - Catalase = fast – destroys toxins
  - Chrymotrypsin = slow - digestion

Enzyme Active Site

Enzyme Active Site:

- Area where catalysis occurs
- Small (1-5%) of total surface area
- Very Specific: 1 enzyme = 1 reaction (Specificity)





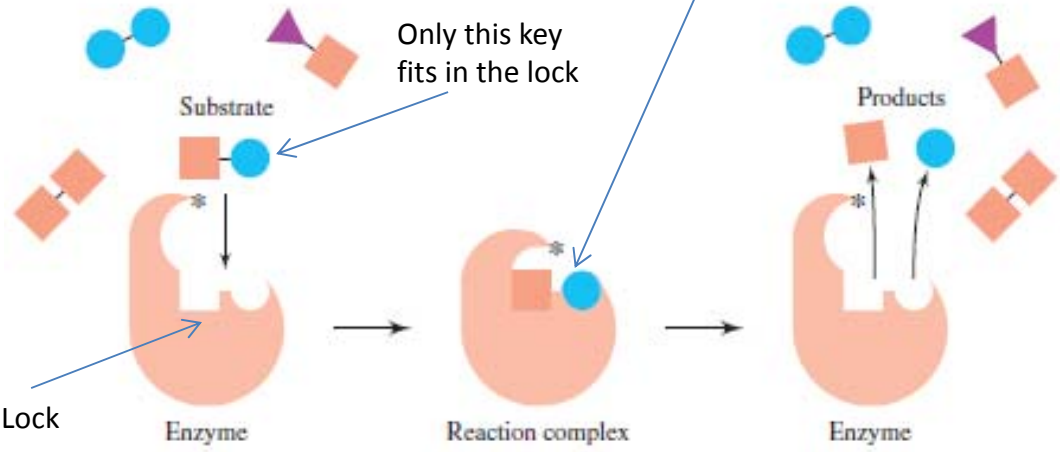
Lock-and-Key Hypothesis and Induced-Fit Model

Lock-and-Key Hypothesis:

- Substrate (Key) fits into the Enzyme (Lock)
- One key, One lock
- Flaw: not rigid → Induced Fit Model

Induced-Fit Model:

- Active site is flexible
- Enzyme can change state to bind/catalyze a reaction



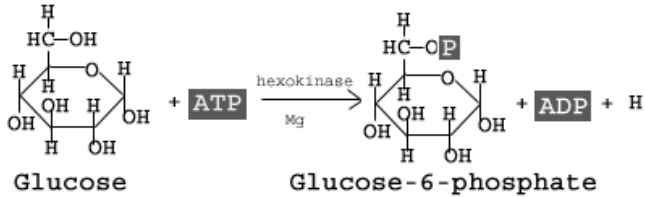
Proximity Catalysis and Productive Binding

Proximity Catalysis:

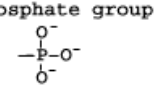
- Enzyme holds the reactants in close proximity

Productive Binding:

- Enzyme holds reactants in proper orientation for reaction to occur



P = phosphate group



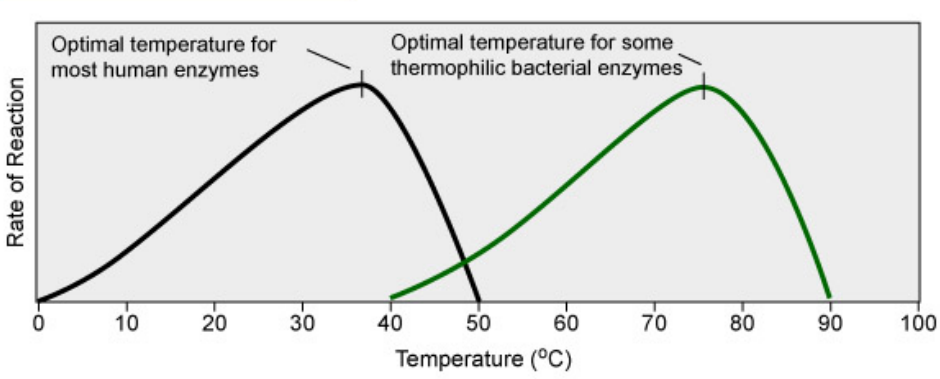
Example: Glucose → Glucose-6-Phosphate

- Many parts required (Substrate + ATP + Mg^{+2} ion. (Proximity Catalysis)
- Phosphate only added to #6 carbon (Productive Binding)

Temperature

Effect of Temperature on Catalysts:

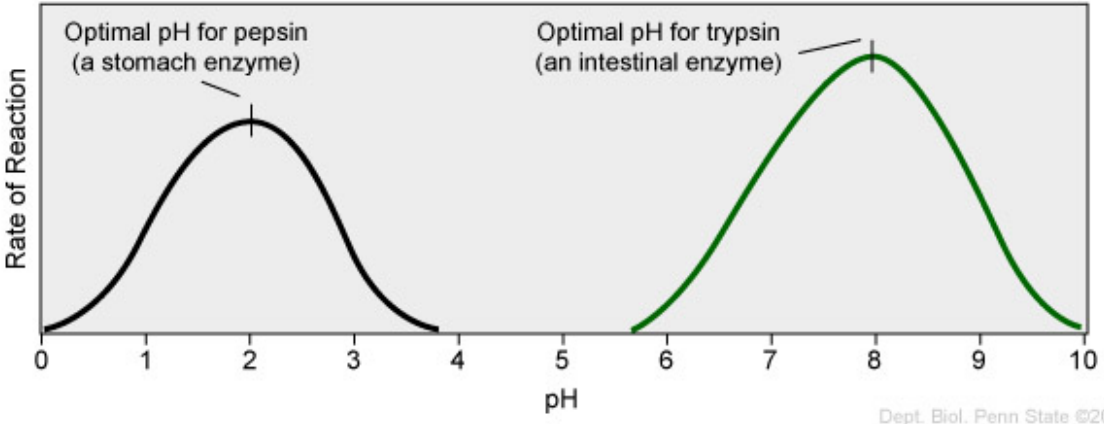
- Any change that effects protein structure effects an enzymes catalytic ability
- Low Temp = Few molecules have AE required to react (+ denaturation)
- High Temp = Enzymes denature



pH

Effect of pH on Catalysts:

- Any change that effects protein structure effects an enzymes catalytic ability
- Charge of –COOH and $–NH_2$ effected by pH → change in 2°/3°/4° structure



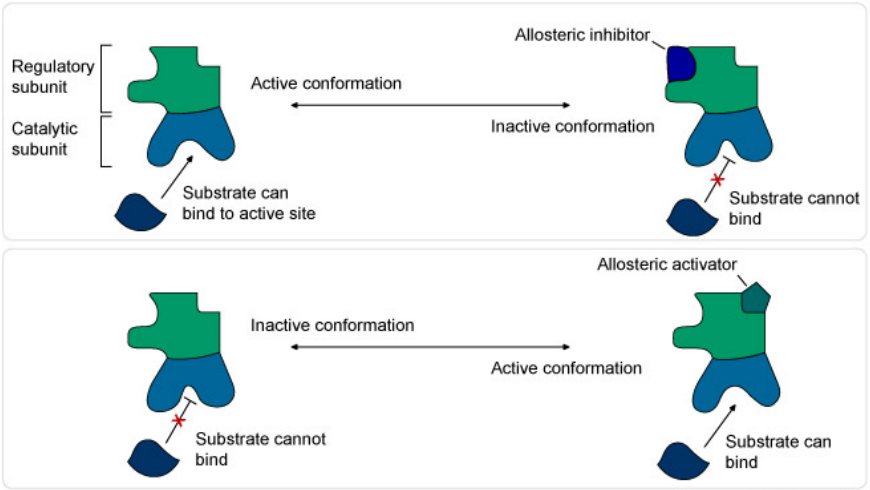
Enzyme Regulation

Allosteric Regulation:

- Active domain – catalyzes the reaction
- Regulatory domain – modulates activity
- Activator/inhibitors bind to Regulatory domain and change the catalytic ability of enzyme

Covalent Modification:

- Functional groups bonded to enzyme
- Ex: Phosphorylation



Feedback Inhibition
Feedforward Activation

Feedforward Activation

- Excess of beginning R/P increases the reaction rate of a later step

- **Feedback Inhibition**

Excess of final product decreases the reaction rate of an earlier step