MCB 150

Continue Energy & Enzymes

Today's Learning Catalytics Session ID is:
62062563

Announcements:

- Exam I is Thursday, February 8, from 7:00–9:00 PM
  - Check Canvas Announcements for Exam week details
  - Today is last material for Exam 1; Wednesday is optional review

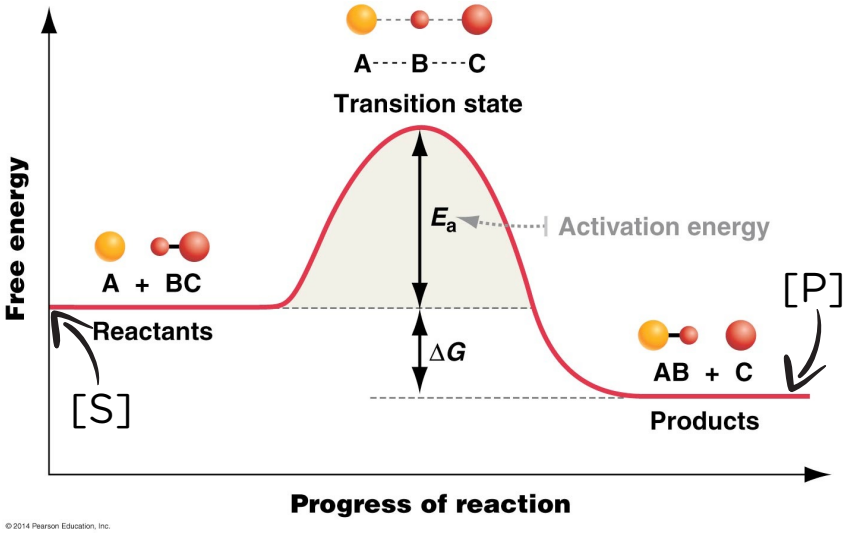
All reactions require energy to reach the transition state

- **Energy of Activation**, or E_a
- The E_a comes from Enzymes

Enzymes do not cause reactions to occur that would not eventually occur anyway; only speed up existing reactions by decreasing the E_a

Standard Activation Energy Diagram:

- [S] = energy level of substrate (reactants)
- [P] = energy level of products
- E_a = activation energy, which converts substrates into unstable transition states



ΔG = Free Energy of Reaction: difference in E between reactants & products

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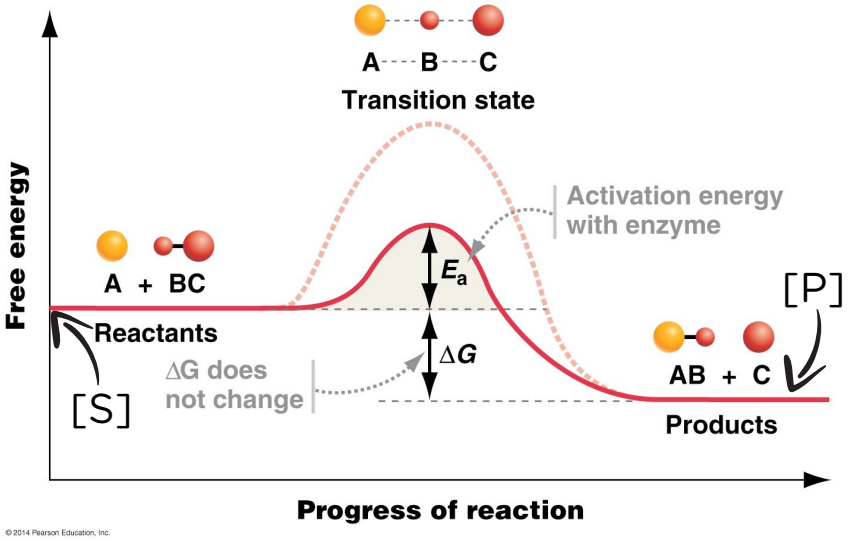
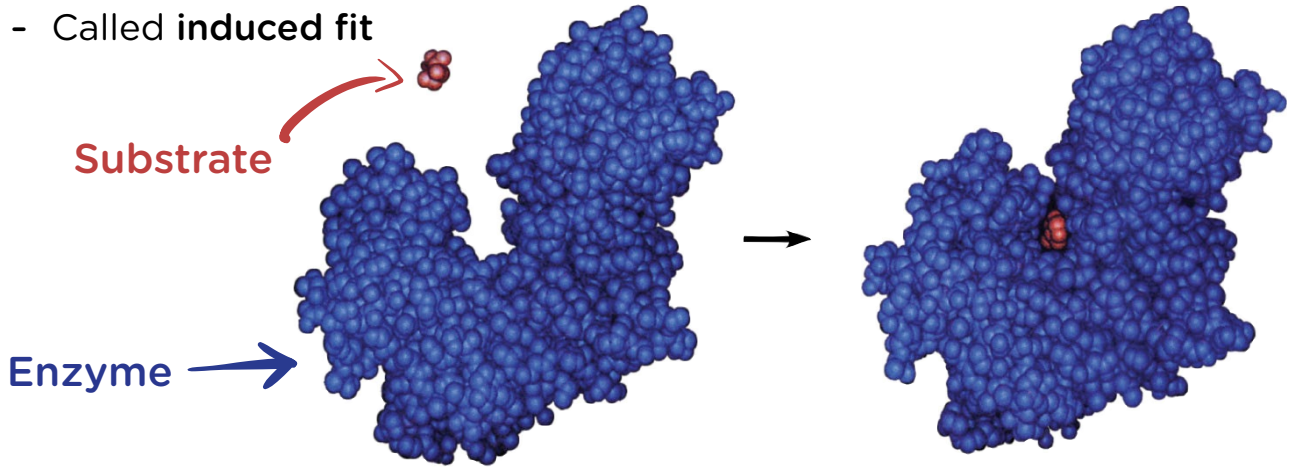


ΔG = Free Energy of Reaction: difference in E between reactants & products

Enzymes bind substrates with extremely high specificity into their **active sites** (usually just a few amino acids)

- Enzymes will most likely cause some conformational change in the substrate molecule(s), but they themselves usually change shape upon binding substrate
  - Called **induced fit**



How does substrate binding to active site decrease E_a?

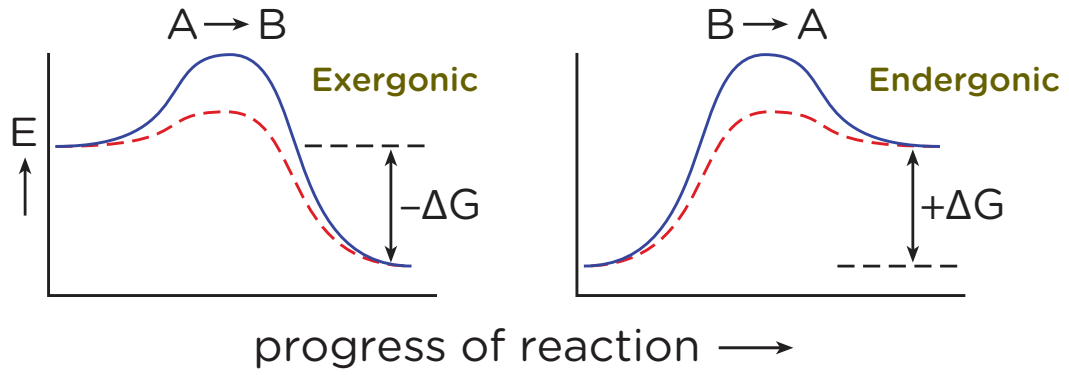
- Acting as a template for substrate orientation
- Stressing the substrate(s) and stabilizing the transition state
- Providing a favorable microenvironment
- Participating directly in the catalytic reaction

Very Important Point:

- If an enzyme accepts a group from a substrate, it must in turn donate that group to help form product
- ENZYMES ARE (ultimately) UNCHANGED BY THE REACTIONS THEY CATALYZE

Another Very Important Point:

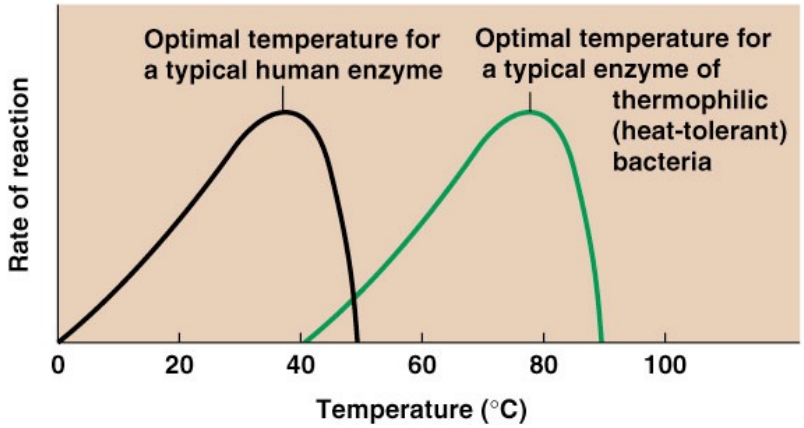
- ENZYMES DO NOT CHANGE THE EQUILIBRIUM OF REACTIONS, they only make it easier (and therefore faster) to reach that equilibrium



Enzymes decrease E_a by the same amount in both directions

Because most enzymes are proteins, it follows that conditions that affect protein stability also affect enzyme activity.

- Enzymes have temperature and pH optimums
- Most tend to be near body temperature (37 °C) and neutral pH (7.0)



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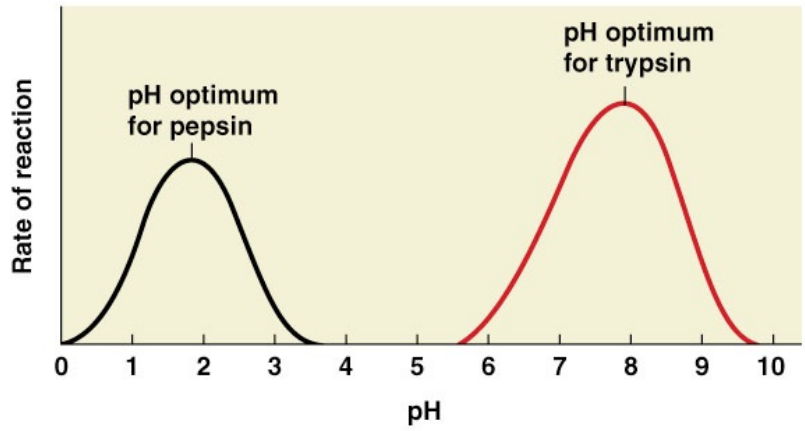
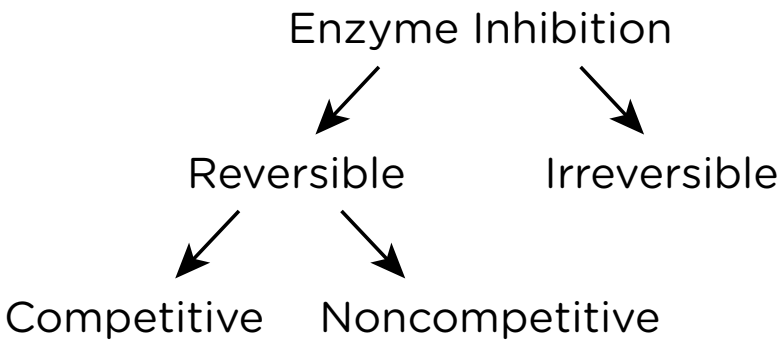


Enzyme Inhibition

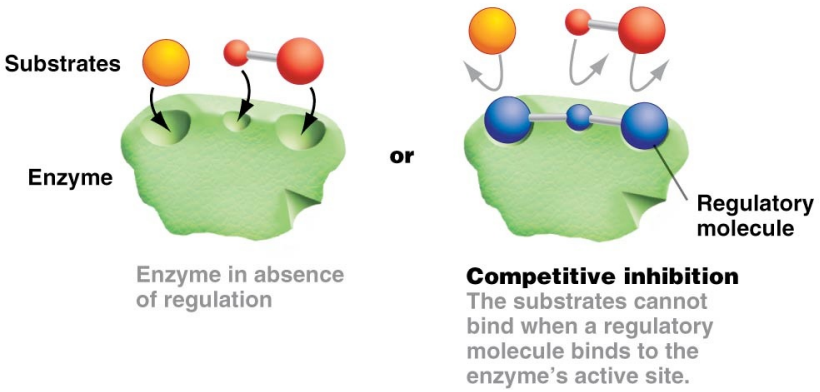
- E + S –> [ES] –> E + P
- E + I –> [EI] –//–>
- Can be either **reversible** or **irreversible**
- Reversible inhibition can be **competitive** or **noncompetitive**



Irreversible Inhibitors

- Permanently bind to or modify active site; changing concentration of natural substrate or inhibitor has no effect
  - Nerve agents like sarin gas are irreversible inhibitors of acetylcholinesterase, which catalyzes termination of nerve impulses
- Tend to be molecules not typically encountered by that particular cell
- Irreversible inhibition is a demonstration of the important point that enzymes must ultimately be unchanged if they are to be used over and over

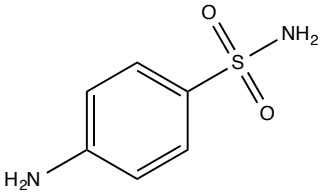
In **competitive** inhibition, the inhibitor molecule physically resembles the natural substrate, and occupies active site



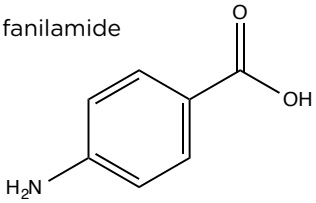
- enzyme can't use inhibitor as substrate - no products are formed
- can be "flooded out" by increasing concentration of natural substrate
- decreasing concentration of inhibitor also reduces probability of inhibitor finding active site

Example of competitive enzyme inhibitors:

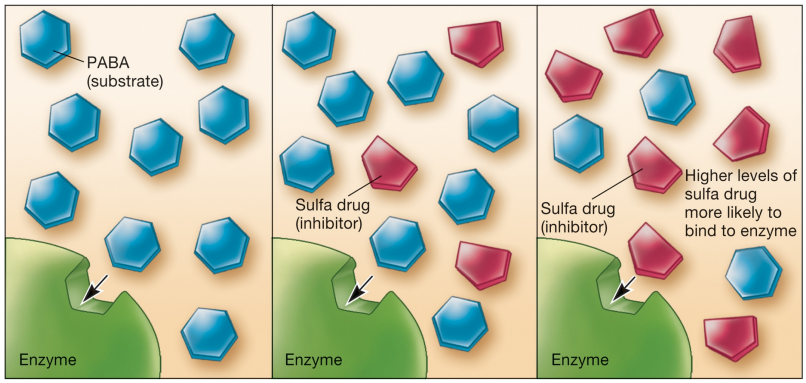
- In bacteria (but not humans), DHPS catalyzes the conversion of p-aminobenzoic acid into folic acid
  - sulfa drugs like sulfanilamide are inhibitors of DHPS; bacteria die, but humans are unaffected



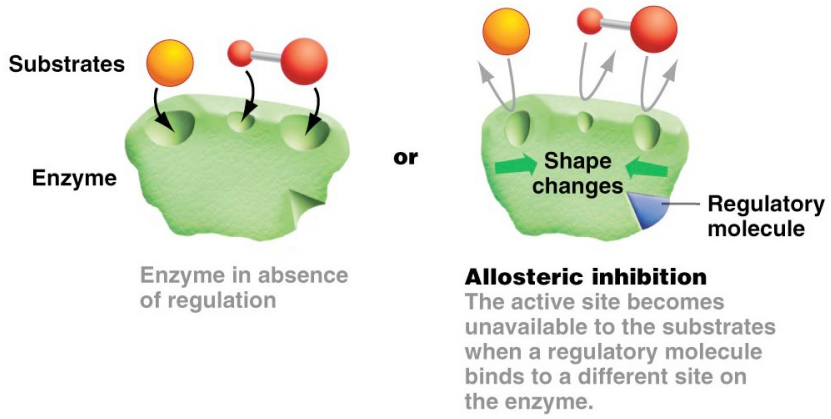
Sulfanilamide



Para-aminobenzoic acid (PABA)

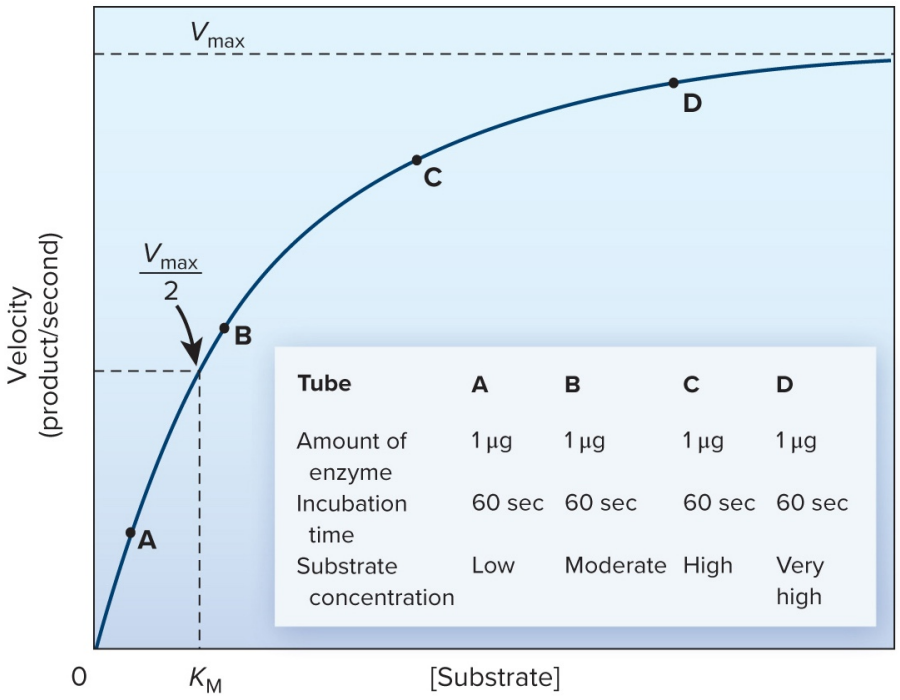


In **noncompetitive** inhibition, the inhibitor molecule binds to the enzyme in a place other than the active site



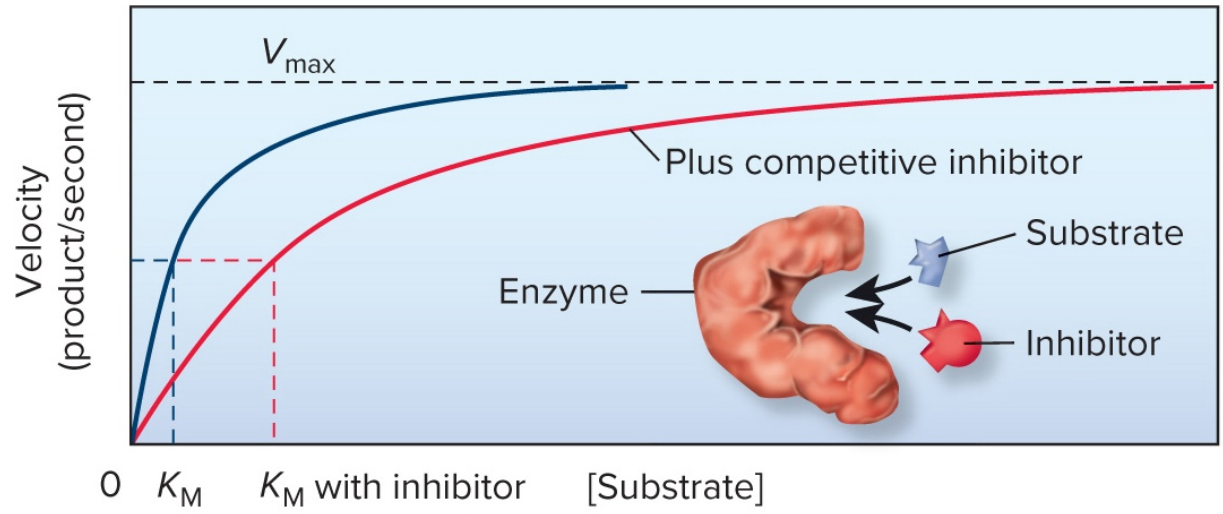
- if change in enzyme completely prevents substrate binding, increasing substrate concentration has no effect
- reversible because inhibitor can become unbound

Enzyme Biochemistry 101: V_{max} and K_M



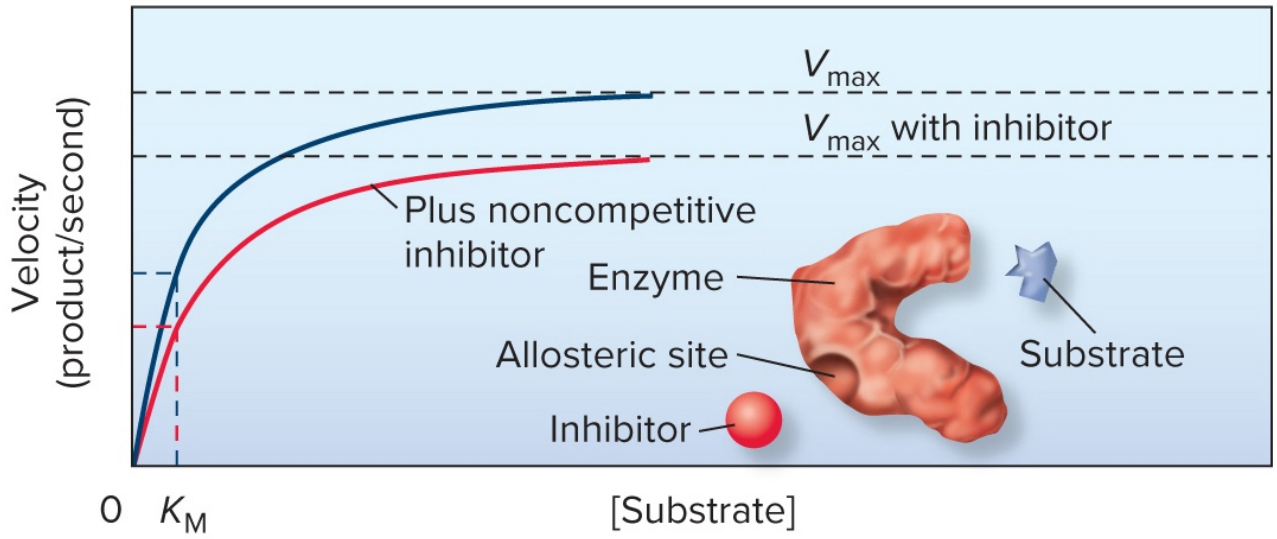
Tube	A	B	C	D
Amount of enzyme	1 µg	1 µg	1 µg	1 µg
Incubation time	60 sec	60 sec	60 sec	60 sec
Substrate concentration	Low	Moderate	High	Very high

Effect of Competitive Inhibitor on V_{max} and K_M



(b) Competitive inhibition

Effect of Noncompetitive Inhibitor on V_{max} and K_M



(c) Noncompetitive inhibition