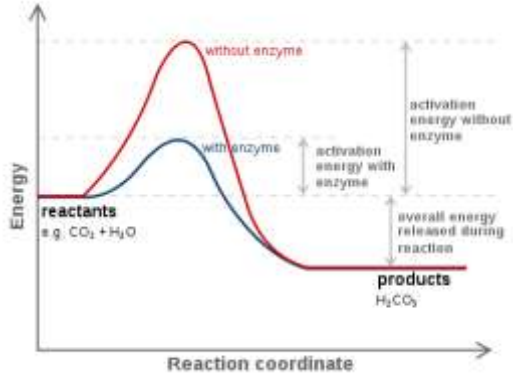
DEPARTMENT OF BIOTECHNOLOGY

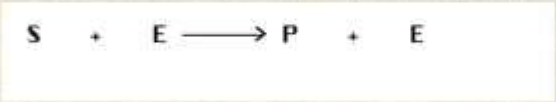
MECHANISM OF ENZYME ACTION



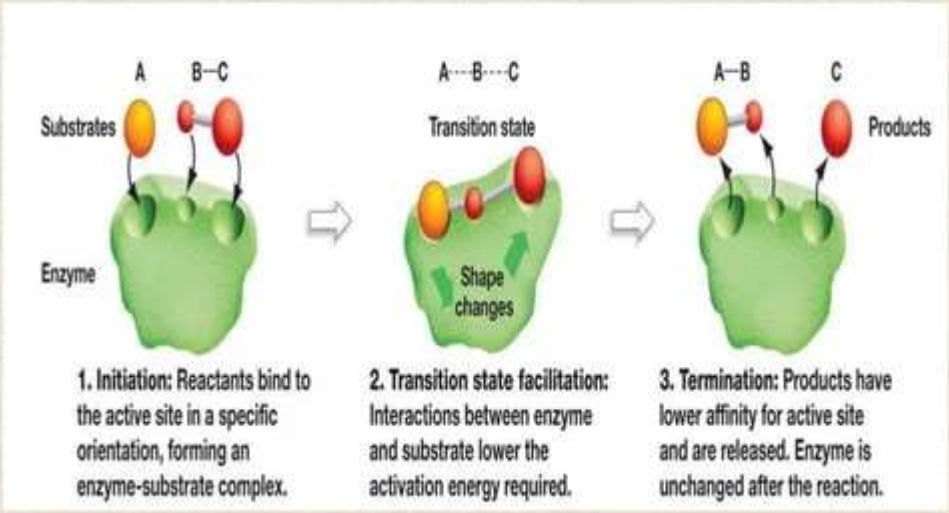
Ms. Payal Talekar

General Mechanism of Action of Enzymes

- Enzymes are catalysts and increase the speed of a chemical reaction without themselves undergoing any permanent chemical change.
- They are neither used up in the reaction nor do they appear as reaction products.
- The basic enzymatic reaction can be represented as follows



General Mechanism of Action of Enzymes



Mechanism of enzyme action

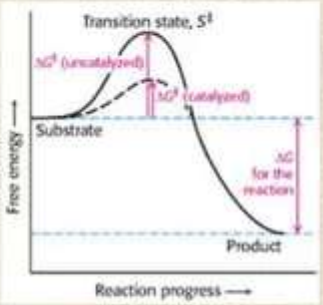
- Enzymes employ multiple mechanisms to facilitate catalysis. The mechanism of action of enzymes can be explained by two perspectives-

1) Thermodynamic changes

2) Processes at the active site

1) Thermodynamic changes

- A chemical reaction of substrate S to form product P goes through a *transition state* S‡ that has a higher free energy than does either S or P. (The double dagger denotes a thermodynamic property of the transition state).
- The difference in free energy between the transition state and the substrate is called the *Gibbs free energy of activation* or simply the *activation energy*, symbolized by $\Delta G‡$.



1) Thermodynamic changes

- All enzymes accelerate reaction rates by providing **transition states** with a lowered G for formation of the transition states. However, they may differ in the way this is achieved.
- The combination of substrate and enzyme creates a new reaction pathway whose transition-state energy is lower than that of the reaction in the absence of enzyme.
- The lower activation energy means that more molecules have the required energy to reach the transition state.

1) Thermodynamic changes

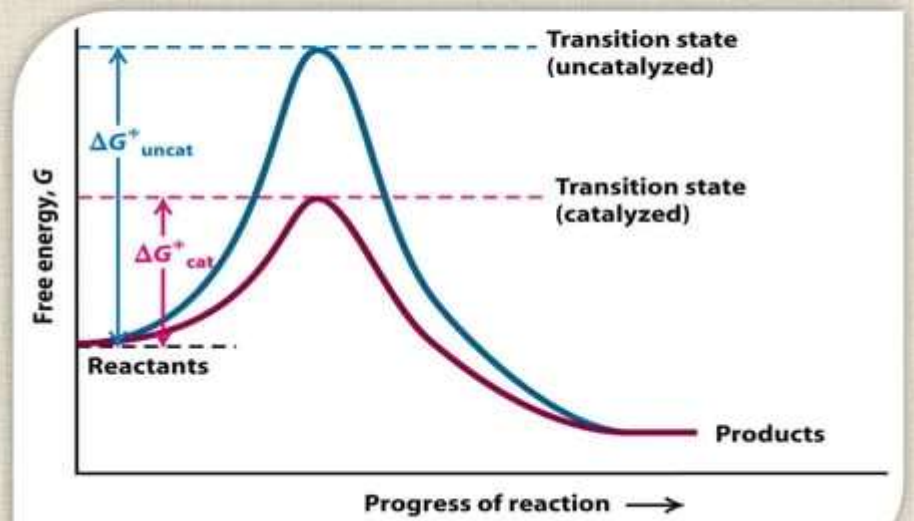


Figure 3-20
Molecular Cell Biology, Sixth Edition
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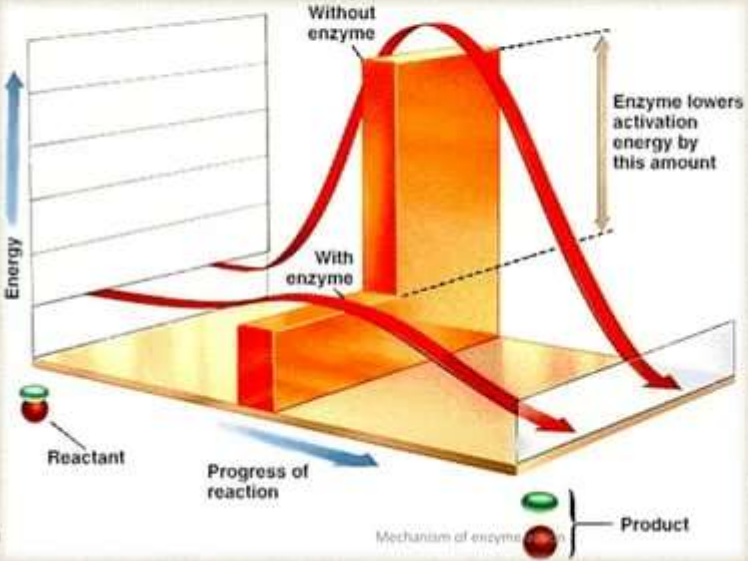
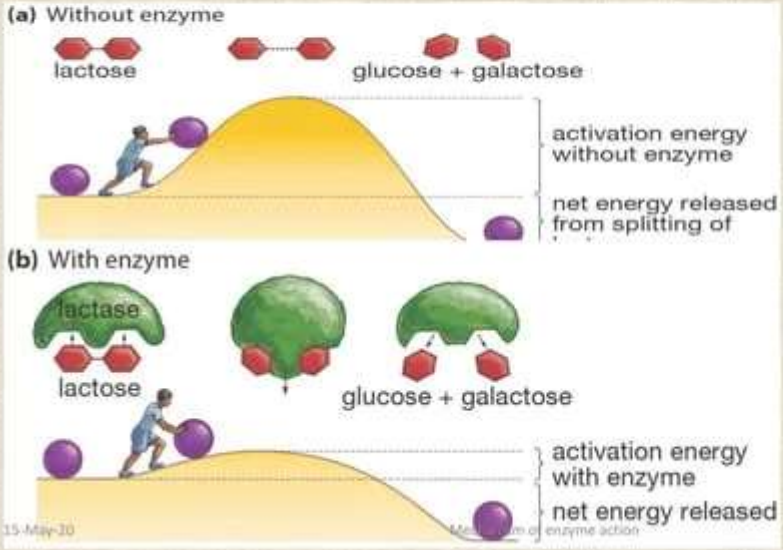
1) Thermodynamic changes



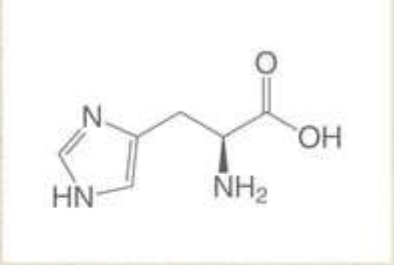
Thermodynamic changes-overview



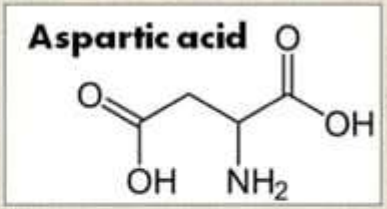
2) Processes at the active site

- Enzymes use various combinations of four general mechanisms to achieve dramatic catalytic enhancement of the rates of chemical reactions.
- These are as follows:
- Acid base catalysis
- Covalent catalysis
- Catalysis by proximity and orientation
- Catalysis by bond strain

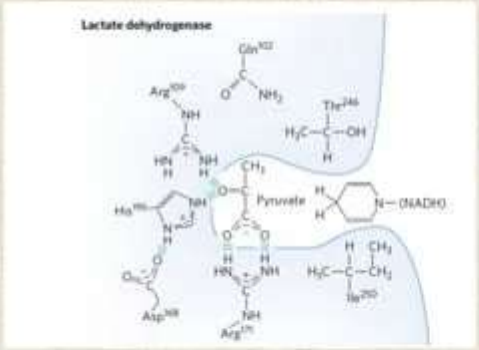
Acid- base catalysis



- Mostly undertaken by oxidoreductases. Usually, at the active site, either histidine is present which acts both as a proton donor and proton acceptor.
- At times aspartic acid, glutamic acid and cysteine residues are also present which participate in Hydrogen transfer reactions



Reaction catalyzed by Lactate dehydrogenase

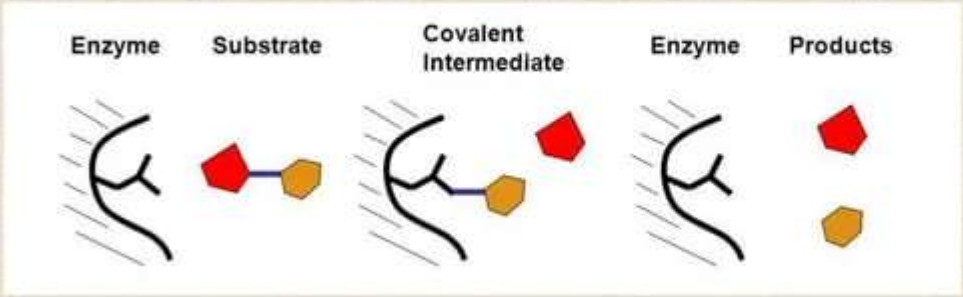


Covalent catalysis

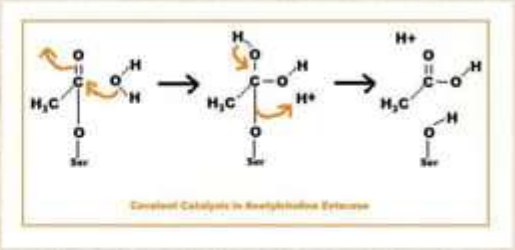
- In catalysis that takes place by covalent mechanisms, the substrate is oriented to active sites on the enzymes in such a way that a covalent intermediate forms between the enzyme or coenzyme and the substrate.
- Examples of this mechanism- digestive enzymes (trypsin, chymotrypsin, and elastase) and several enzymes of the blood clotting cascade.

Covalent catalysis

- Covalent catalysis introduces a new reaction pathway whose activation energy is lower—and therefore is faster—than the reaction pathway in homogeneous solution.
- The chemical modification of the enzyme is, however, transient.
- On completion of the reaction, the enzyme returns to its original unmodified state.
- Its role thus remains catalytic.
- Covalent catalysis is particularly common among enzymes that catalyze group transfer reactions.

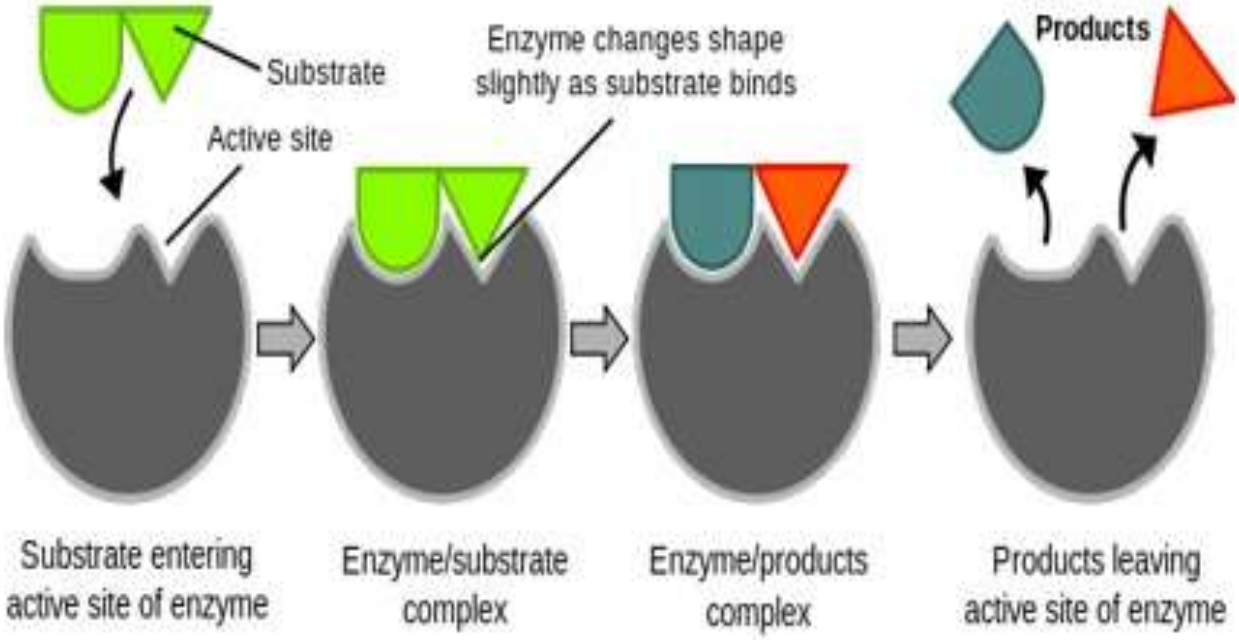

Enzyme
Substrate
Covalent Intermediate
Enzyme
Products


Subtilisin
Hydrolases
Cleavage with addition of water


Covalent Catalysis in Acetylcholine Esterase

Catalysis by proximity and orientation

- For molecules to react, they must come within bond-forming distance of one another.
- The higher their concentration, the more frequently they will encounter one -another and the greater will be the rate of their reaction.
- When an enzyme binds substrate molecules at its active site, it creates a region of high local substrate concentration.
- Enzyme-substrate interactions orient reactive groups and bring them into proximity with one another


Substrate
Active site
Enzyme changes shape slightly as substrate binds
Products
Substrate entering active site of enzyme
Enzyme/substrate complex
Enzyme/products complex
Products leaving active site of enzyme