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Biochemistry

Lecture 6

Enzymes

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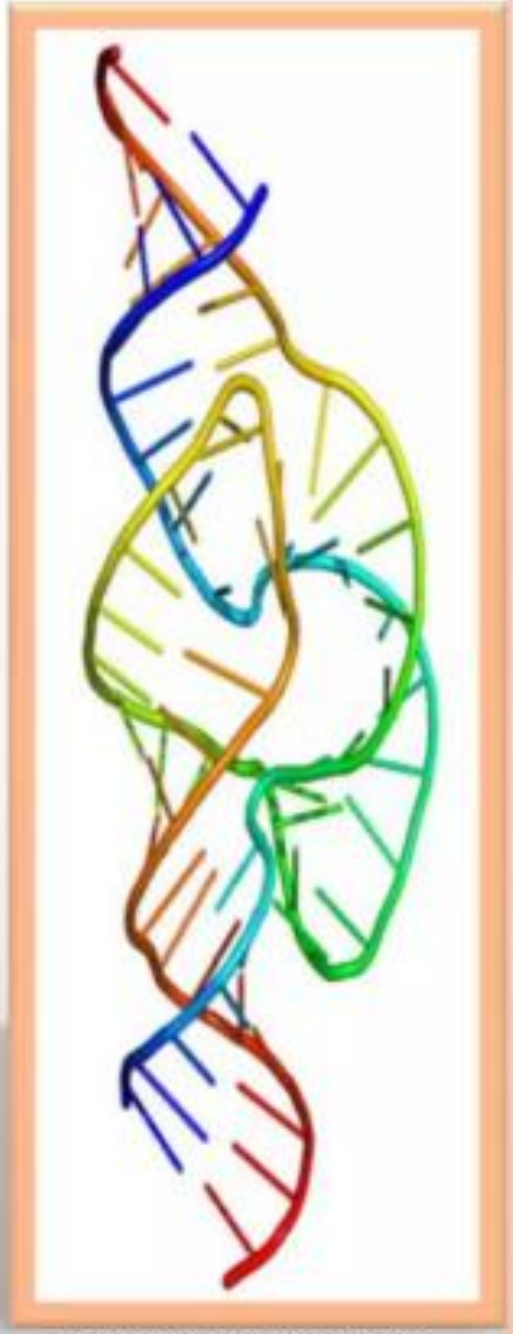
Contents

- Chemistry
- Classification
- Mechanism of Enzyme Action
- Enzyme Kinetics
- Inhibition
- Activation
- Specificity

Introduction

- Enzymes are *biological catalysts* that speed up the rate of the biochemical reaction.
- Most enzymes are three dimensional *globular proteins* (tertiary and quaternary structure).
- Some special RNA species also act as enzymes and are called *Ribozymes* e.g. hammerhead ribozyme.



Hammerhead enzyme

Structure of Enzymes

- The *active site* of an enzyme is the region that binds substrates, co-factors and prosthetic groups and contains residue that helps to hold the substrate.
- Active sites generally occupy less than 5% of the total surface area of enzyme.
- Active site has a *specific shape* due to tertiary structure of protein.
- A change in the shape of protein affects the shape of active site and function of the enzyme.

ACTIVE SITE

- Active site can be further divided into:

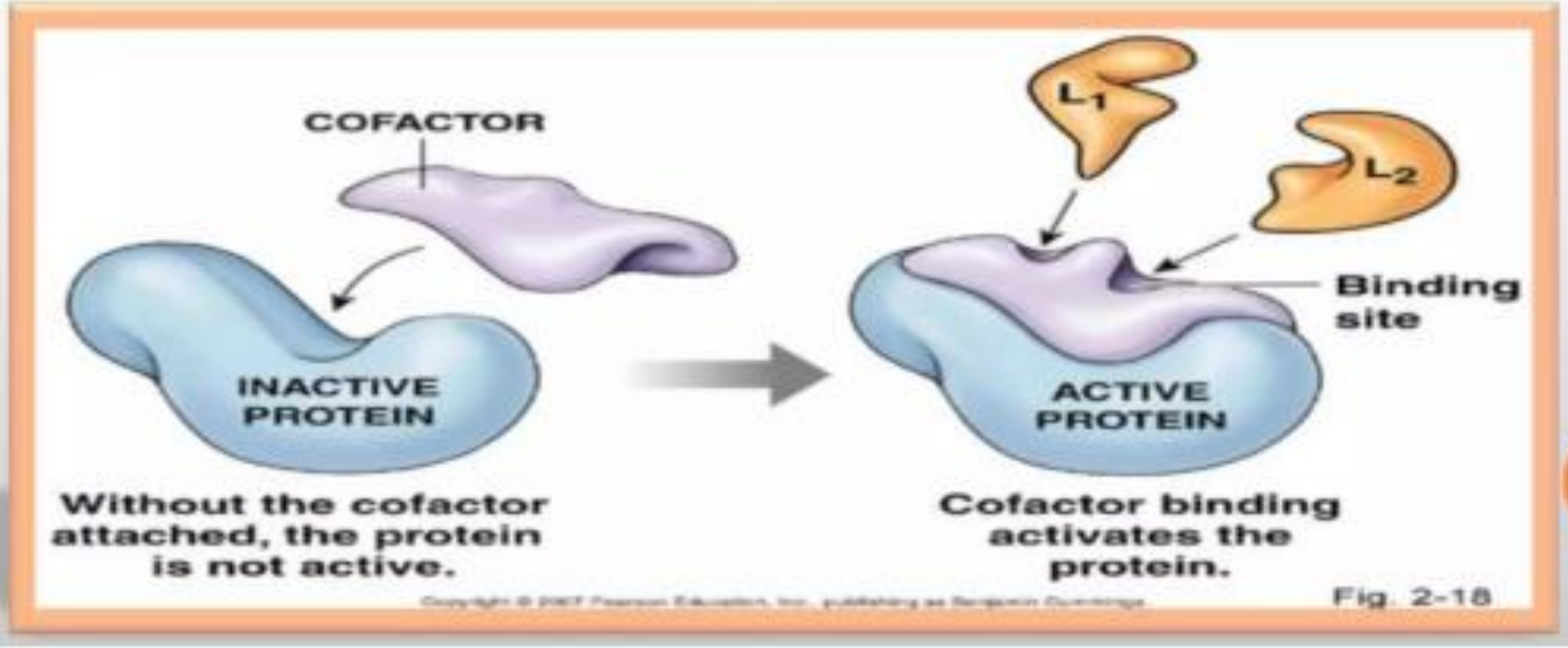
It chooses the substrate and binds it to active site.

It performs the catalytic action of enzyme.

CO-FACTORS

- Co-factor is the non protein molecule which carries out chemical reactions that can not be performed by standard 20 amino acids.

- Co-factors are of two types:
  - Organic co-factors
  - Inorganic cofactors



INORGANIC CO-FACTORS

- These are the inorganic molecules required for the proper activity of enzymes.

Examples:

- Enzyme carbonic anhydrase requires Zn^{++} for it's activity.
- Hexokinase has co-factor Mg^{++}

ORGANIC CO-FACTORS

- These are the organic molecules required for the proper activity of enzymes.

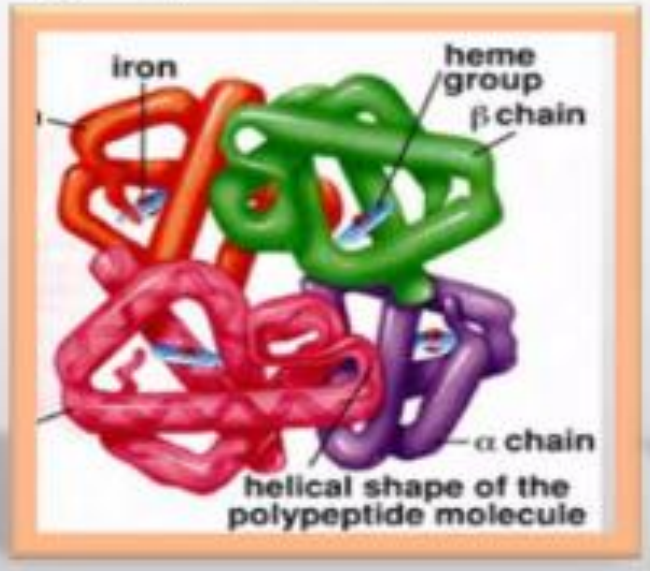
Example:

- Glycogen phosphorylase requires the small organic molecule pyridoxal phosphate.

Types of Organic co-factors

Prosthetic Group

- A prosthetic group is a tightly bound organic co-factor e.g. Flavins, heme groups and biotin.

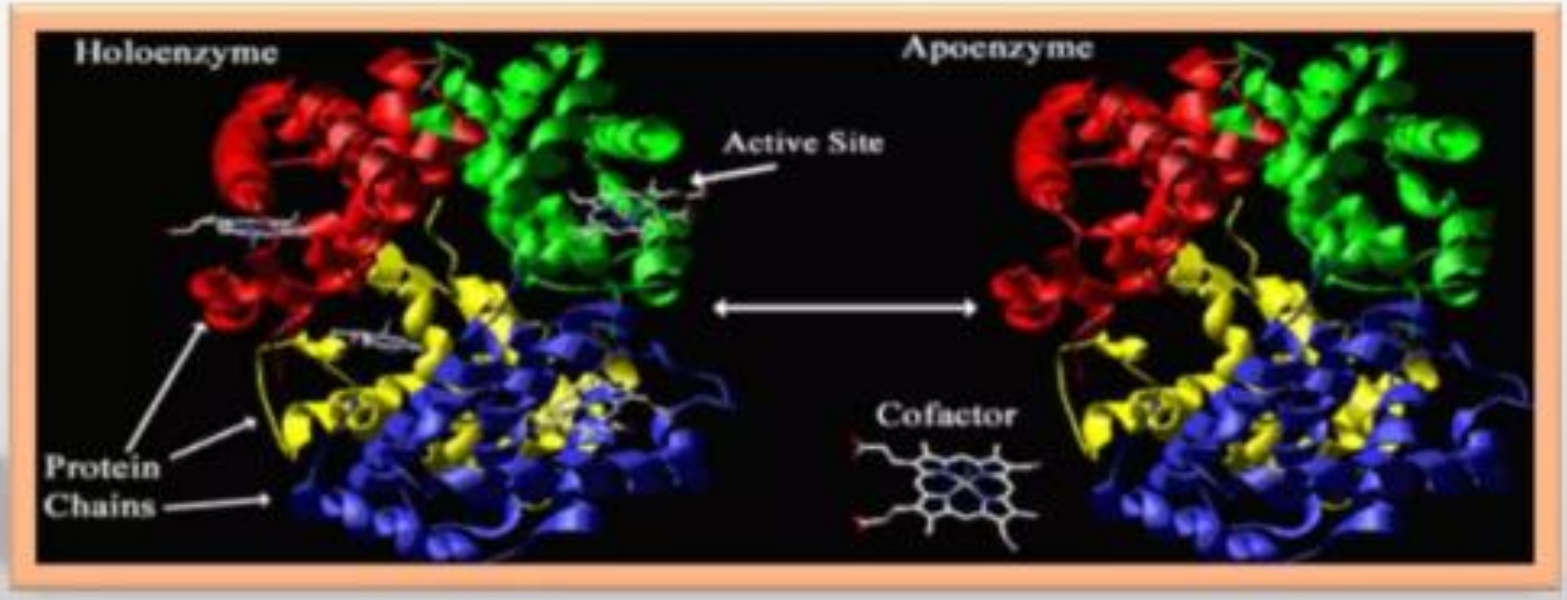


Coenzyme

- A coenzyme is loosely bound organic co-factor. E.g. NAD^+

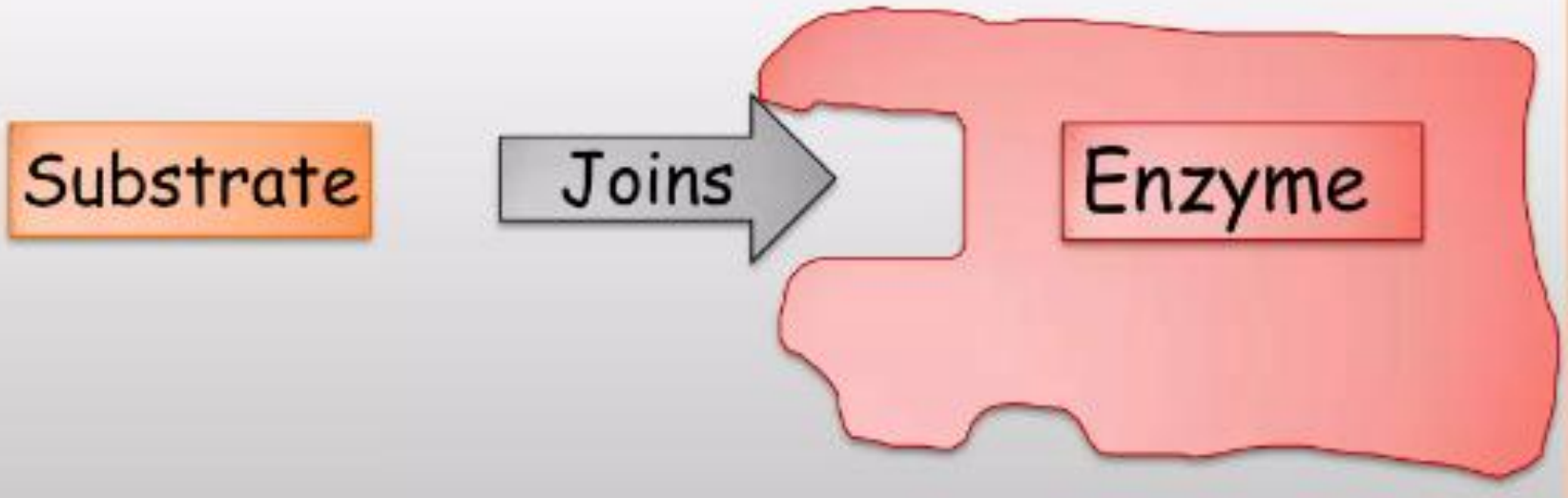
Types of co-factors Continued…

- An enzyme with it's co-factor removed is designated as *apoenzyme*.
- The complete complex of a protein with all necessary small organic molecules, metal ions and other components is termed as *holoenzyme* of *holoprotein*.



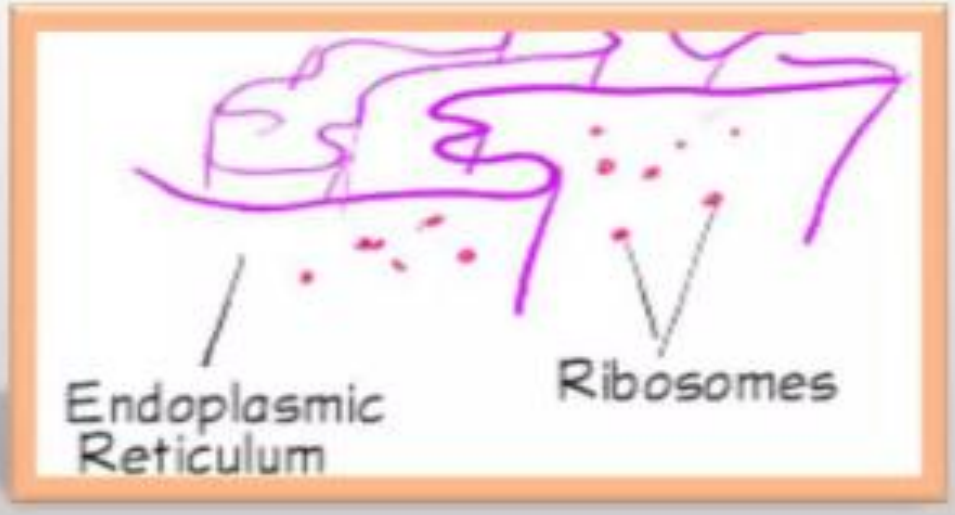
SUBSTRATE

- The reactant in biochemical reaction is termed as substrate.
- When a substrate binds to an enzyme it forms an enzyme-substrate complex.



SITES OF ENZYME SYNTHESIS

- Enzymes are synthesized by *ribosomes* which are attached to the rough endoplasmic reticulum.
- Information for the synthesis of enzyme is *carried by DNA.*
- Amino acids are bonded together to form specific enzyme according to the DNA's codes.



INTRACELLULAR AND EXTRACELLULAR ENZYMES

- **Intracellular** enzymes are *synthesized and retained in the cell for the use of cell itself.*
- They are found in the cytoplasm, nucleus, mitochondria and chloroplast.

Example :

- Oxydoreductase catalyses biological oxidation.
- Enzymes involved in reduction in the mitochondria.

- **Extracellular** enzymes are *synthesized in the cell but secreted from the cell to work externally.*

Example :

- Digestive enzyme produced by the pancreas, are not used by the cells in the pancreas but are transported to the duodenum.

CHARACTERISTICS

- Enzymes *speed up* the reaction by lowering the activation energy of the reaction.
- Their presence *does not effect* the nature and properties of *end product*.
- They are *highly specific* in their action that is each enzyme can catalyze one kind of substrate.
- Small amount of enzymes can accelerate chemical reactions.
- Enzymes are *sensitive* to change in pH, temperature and substrate concentration.
- *Turnover number* is defined as the number of substrate molecules transformed per minute by one enzyme molecule.

Catalase turnover number = 6 x106/min

NOMENCLATURE OF ENZYMES

- An enzyme is named according to the name of the substrate it catalyses.
- Some enzymes were named before a systematic way of naming enzyme was formed.

  Example: pepsin, trypsin and rennin
- By adding suffix **-ase** at the end of the name of the substrate, enzymes are named.
- Enzyme for catalyzing the hydrolysis is termed as hydrolase.

  Example :

maltose + water $\xrightarrow{\text{maltase}}$ glucose + glucose

EXAMPLES

substrate	enzymes	products
lactose	lactase	glucose + galactose
maltose	maltase	Glucose
cellulose	cellulase	Glucose
lipid	lipase	Glycerol + fatty acid
starch	amylase	Maltose
protein	protease	Peptides + polypeptide

Classification

Classification of enzymes

- A systematic classification of enzymes has been developed by *International Enzyme Commission*.
- This classification is based on the type of reactions catalyzed by enzymes.
- There are *six* major classes.
- Each class is further divided into sub classes, sub sub-classes and so on, to describe the huge number of different enzyme-catalyzed reactions.

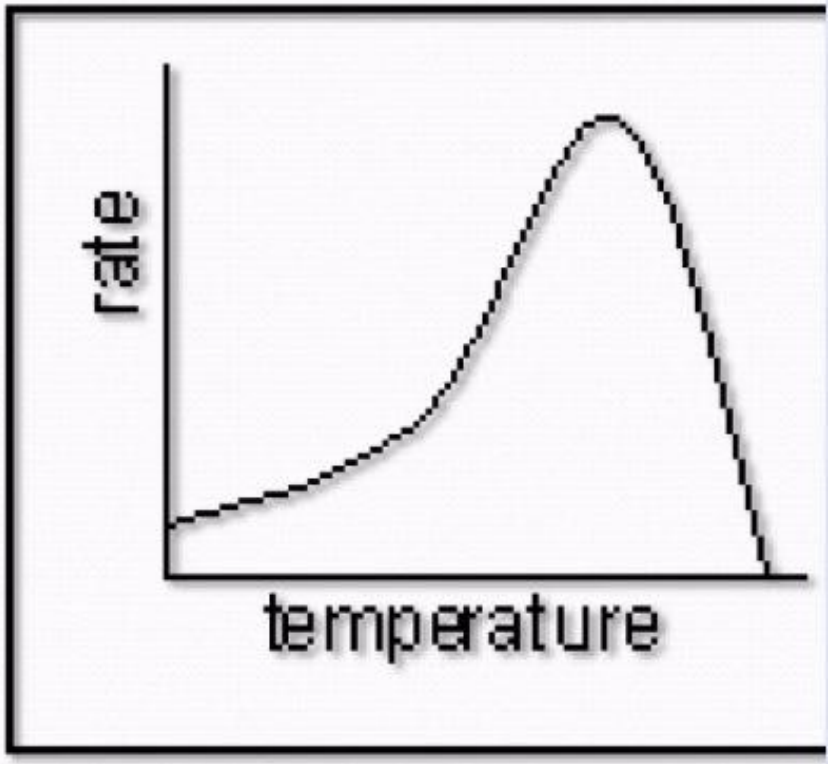
Classification of enzymes

Continued……..

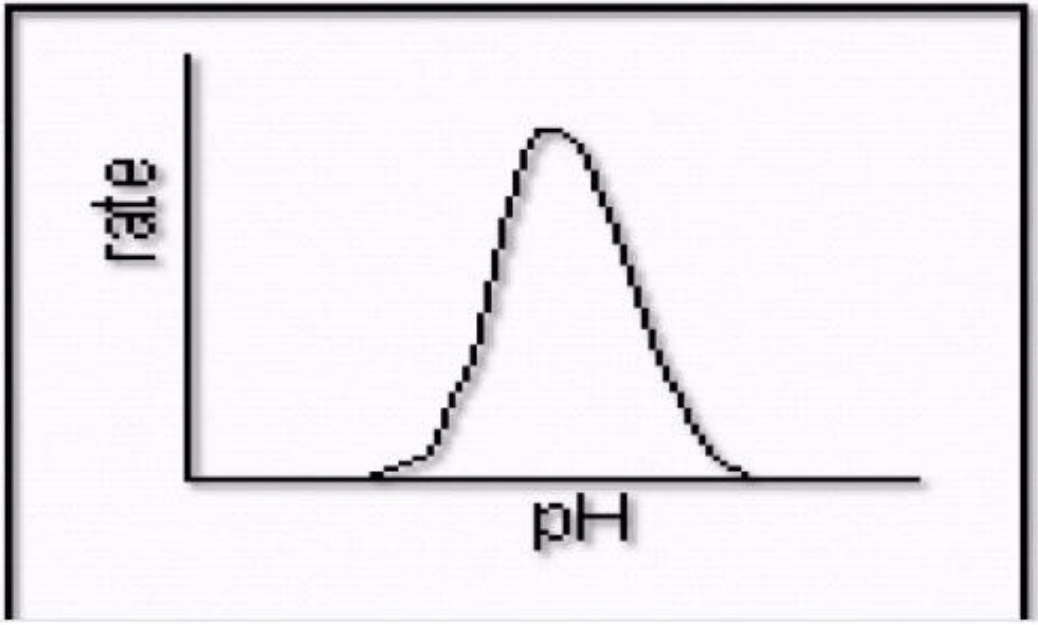
ENZYME CLASS	REACTION TYPE	EXAMPLES
Oxidoreductases	Reduction-oxidation (redox)	Lactate dehydrogenase
Transferases	Move chemical group	Hexokinase
Hydrolases	Hydrolysis; bond cleavage with transfer of functional group of water	Lysozyme
Lysases	Non-hydrolytic bond cleavage	Fumarase
Isomerases	Intramolecular group transfer (isomerization)	Triose phosphate isomerase
Ligases	Synthesis of new covalent bond between substrates, using ATP hydrolysis	RNA polymerase

FACTORS AFFECTING THE RATE OF ENZYME ACTIONS

- **1. TEMPERATURE**
- Enzymes have an optimum temperature at which they work fastest.
- Up to the optimum temperature the rate increases
- Above the optimum temperature the rate decreases

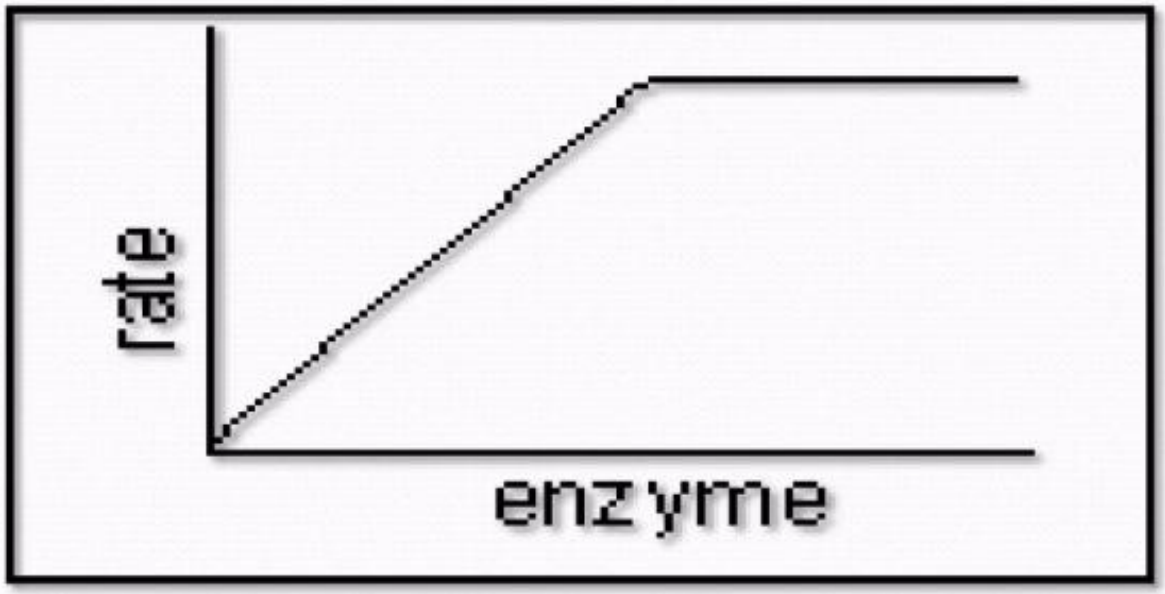


- **2. pH**
- Enzymes have an optimum pH at which they work fastest.
- For most enzymes this is about pH 7-8
- but a few enzymes can work at extreme pH, such as protease enzymes in animal stomachs, which have an optimum of pH 1.



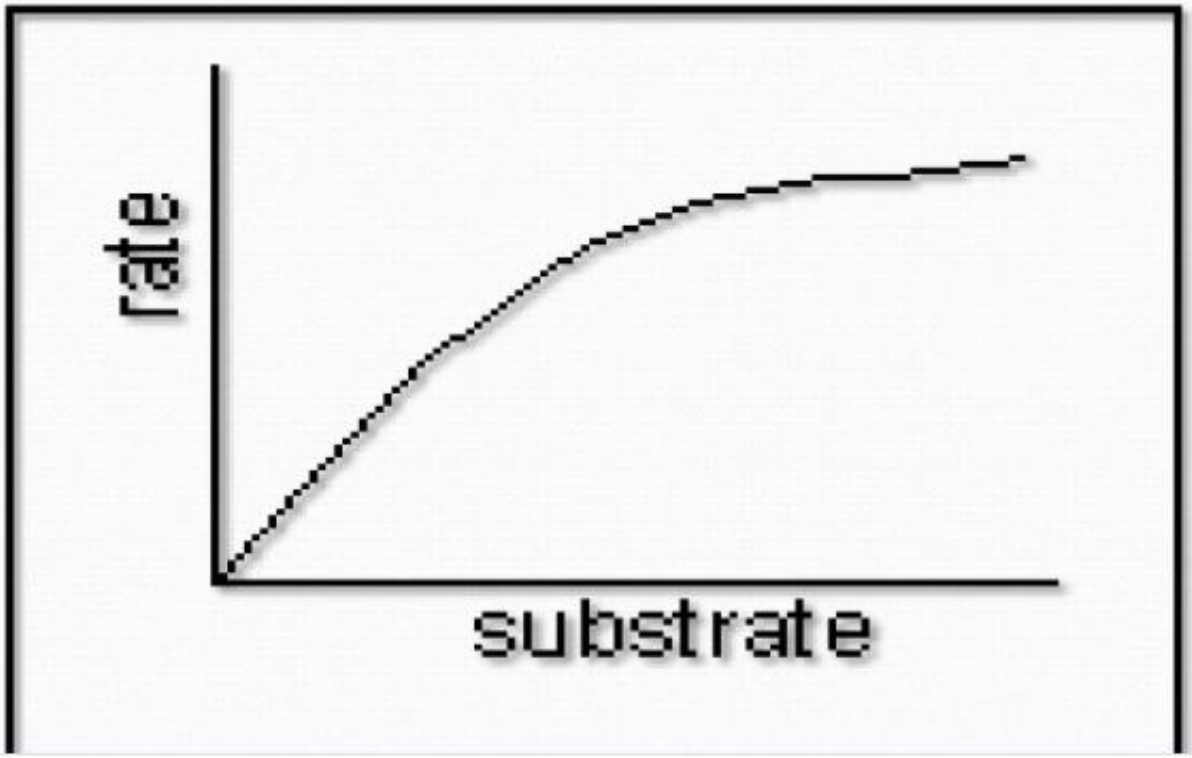
3. ENZYME CONCENTRATION

- As the enzyme concentration increases the rate of the reaction increases linearly
- At very high enzyme concentration the substrate concentration may become rate-limiting



4. SUBSTRATE CONCENTRATION

- As the substrate concentration increases, the rate increases because more substrate molecules can collide with enzyme molecules, so more reactions will take place



Mechanism of enzyme action

Mechanism of enzyme action

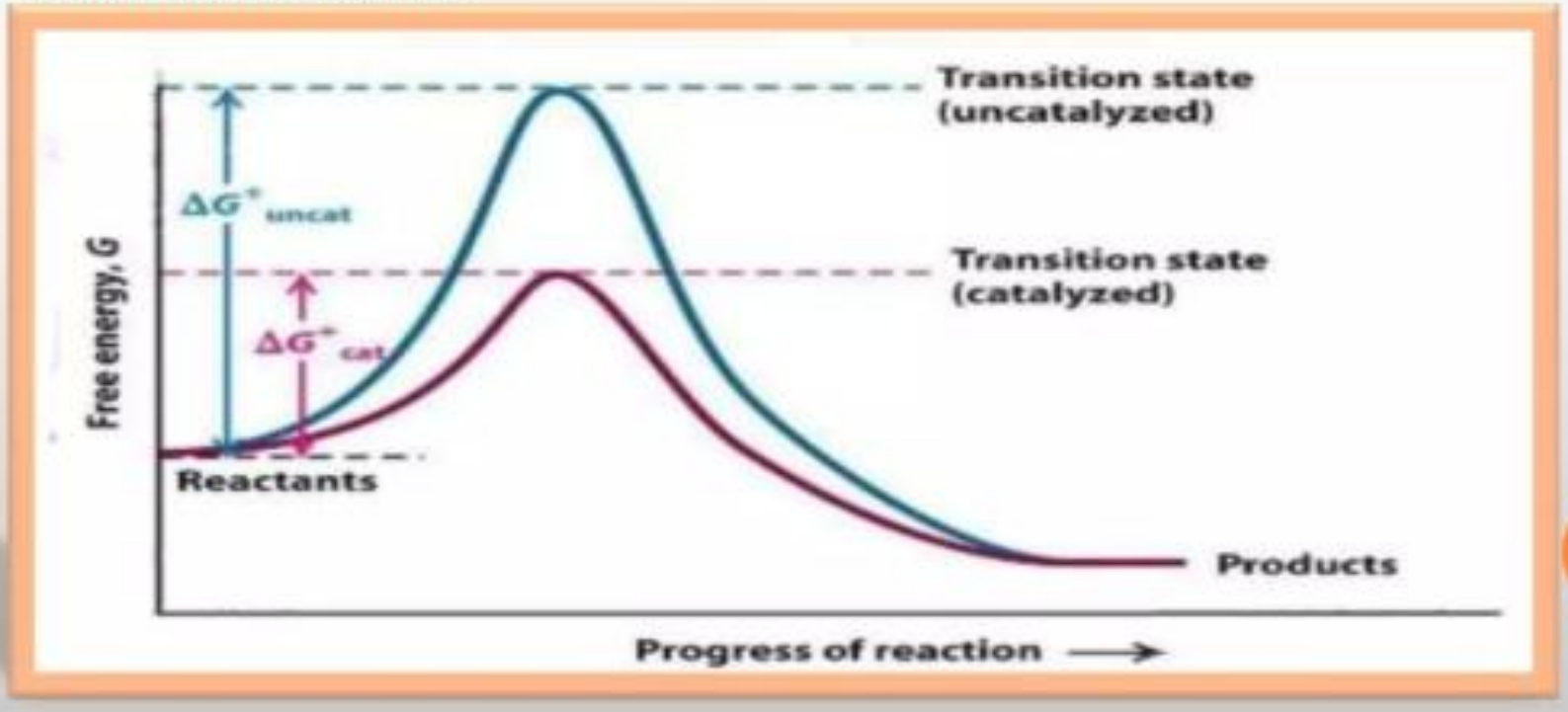
- The catalytic efficiency of enzymes is explained by two perspectives:

Thermodynamic changes

Processes at the active site

THERMODYNAMIC CHANGES

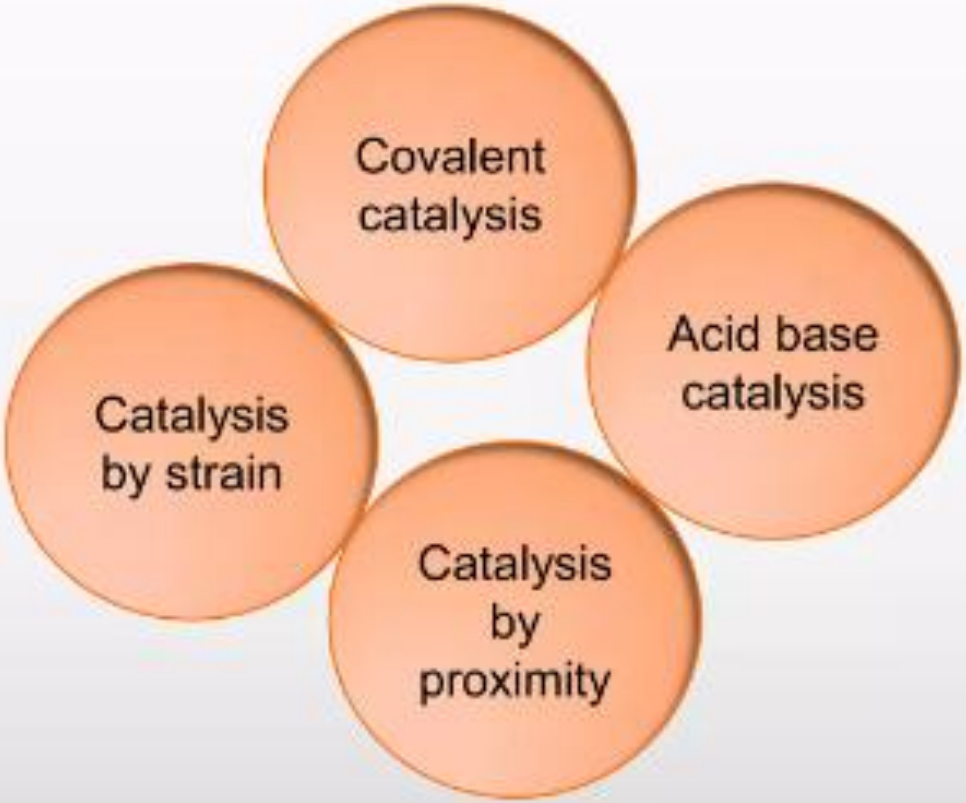
- All chemical reactions have energy barriers between reactants and products.
- The difference in transitional state and substrate is called *activational barrier*.



THERMODYNAMIC CHANGES

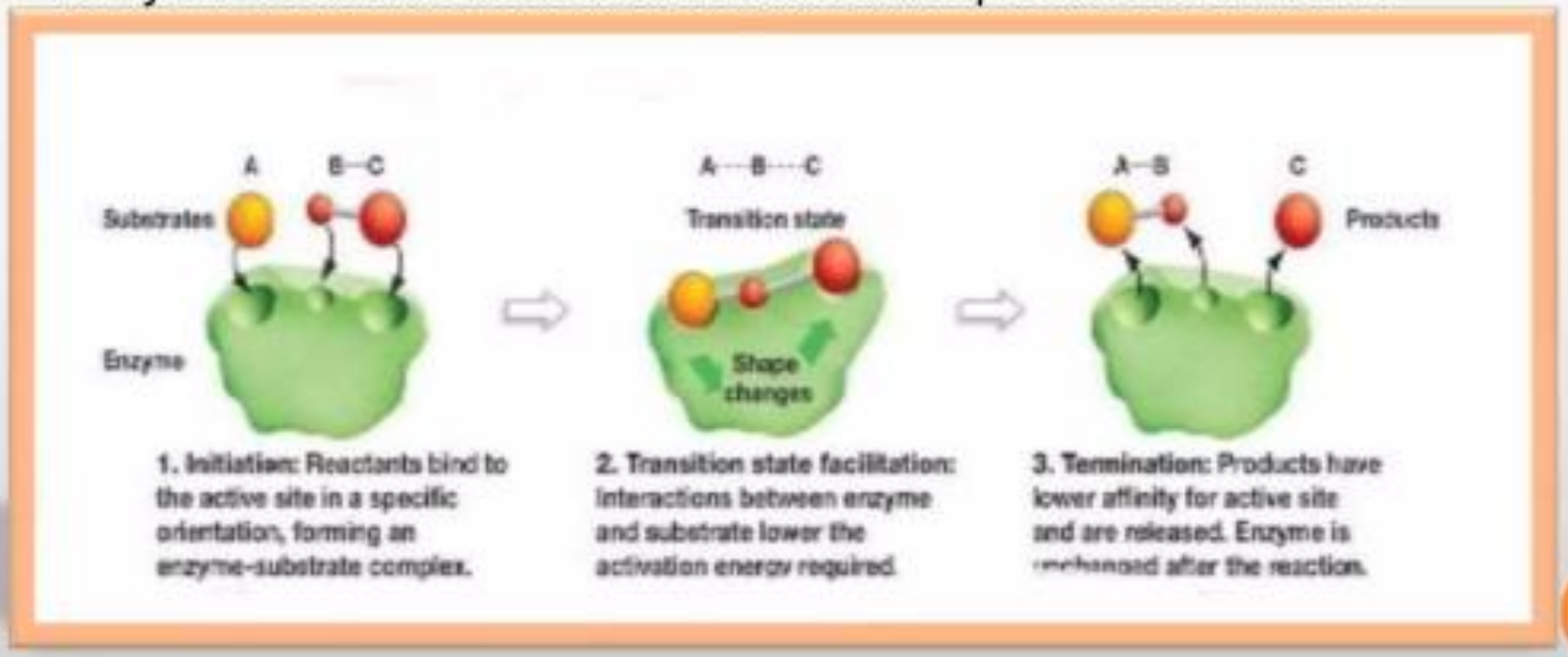
- Only a few substances cross the activation barrier and change into products.
- That is why rate of uncatalyzed reactions is much slow.
- Enzymes provide an alternate pathway for conversion of substrate into products.
- Enzymes accelerate reaction rates by forming transitional state having low activational energy.
- Hence, the reaction rate is increased many folds in the presence of enzymes.
- The total energy of the system remains the same and equilibrium state is not disturbed.

PROCESSES AT THE ACTIVE SITE



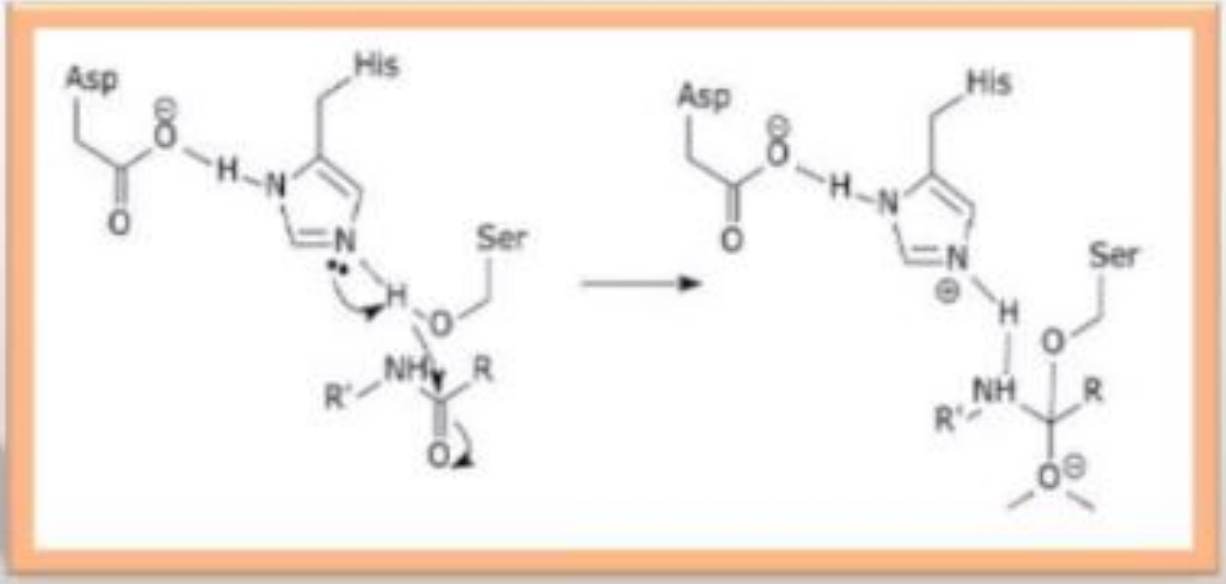
COVALENT CATALYSIS

- Enzymes form covalent linkages with substrate forming transient enzyme-substrate complex with very low activation energy.
- Enzyme is released unaltered after completion of reaction.



ACID-BASE CATALYSIS

- Mostly undertaken by oxido- reductases enzyme.
- Mostly at the active site, histdine is present which act as both proton donor and proton acceptor.



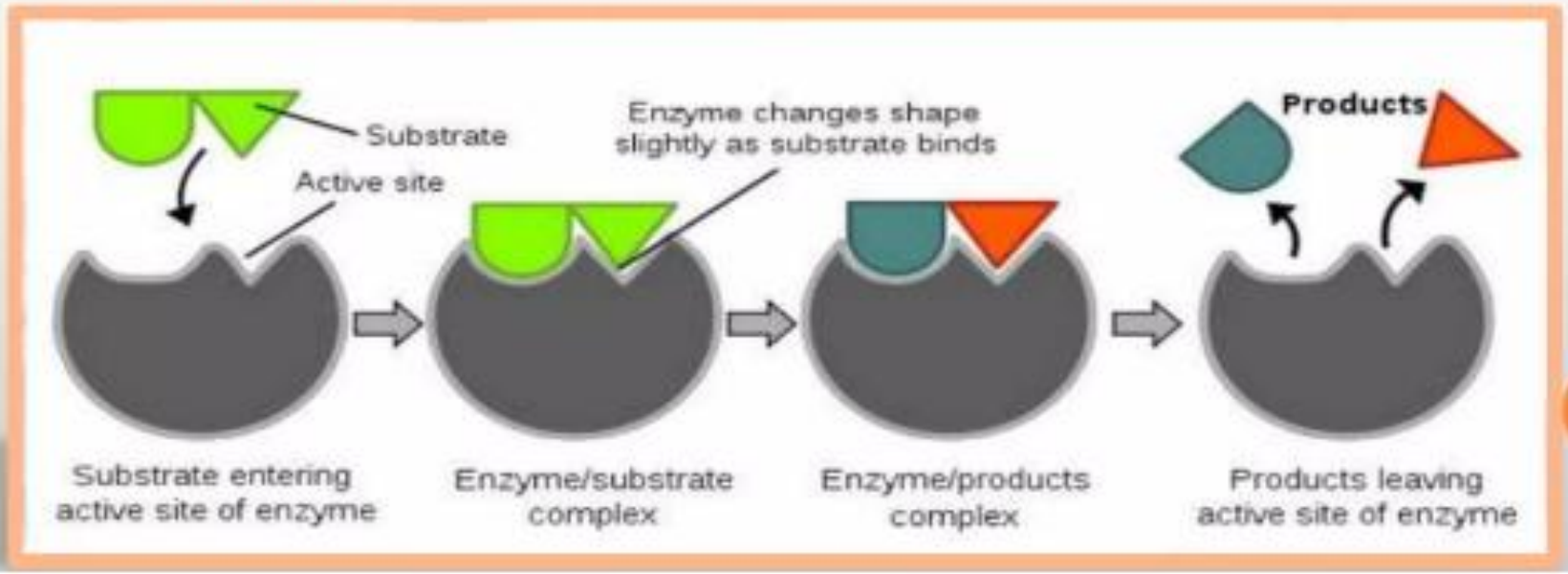
CATALYSIS BY PROXIMITY

- In this catalysis molecules must come in bond forming distance.

- When enzyme binds:
  - A region of high substrate concentration is produced at active site.
  - This will orient substrate molecules especially in a position ideal for them.

CATALYSIS BY BOND STRAIN

- Mostly undertaken by *lyases*.
- The enzyme-substrate binding causes *reorientation* of the structure of site due to in a strain condition.
- Thus *transitional state* is required and here bond is unstable and eventually broken.
- In this way bond between substrate is *broken* and converted into *products*.



Thank you