Biochemistry
Enzymes
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ENZYMES

PROPERTIES OF ENZYMES

- Are organic catalyst with controllable activity. Under optimal conditions most of the enzymatic reactions proceed 10^8-10^{11} faster than non-enzymatic reactions
- Being proteinacious they are thermolabile and less stable
- They do not alter thermodynamic properties of the reaction but alter kinetic properties; increasing only the rate at which equilibrium is reached
- Increases the rate of a reaction by lowering the free energy of activation of the reaction
- Enzymes are neither consumed or destroyed by

NAMING & CLASSIFICATION OF ENZYMES

- A living cell contain as many as 10^4 enzyme molecules catalysing nearly 2000 odd kind of reactions

- Commission on enzyme has recognised six classes of enzymes

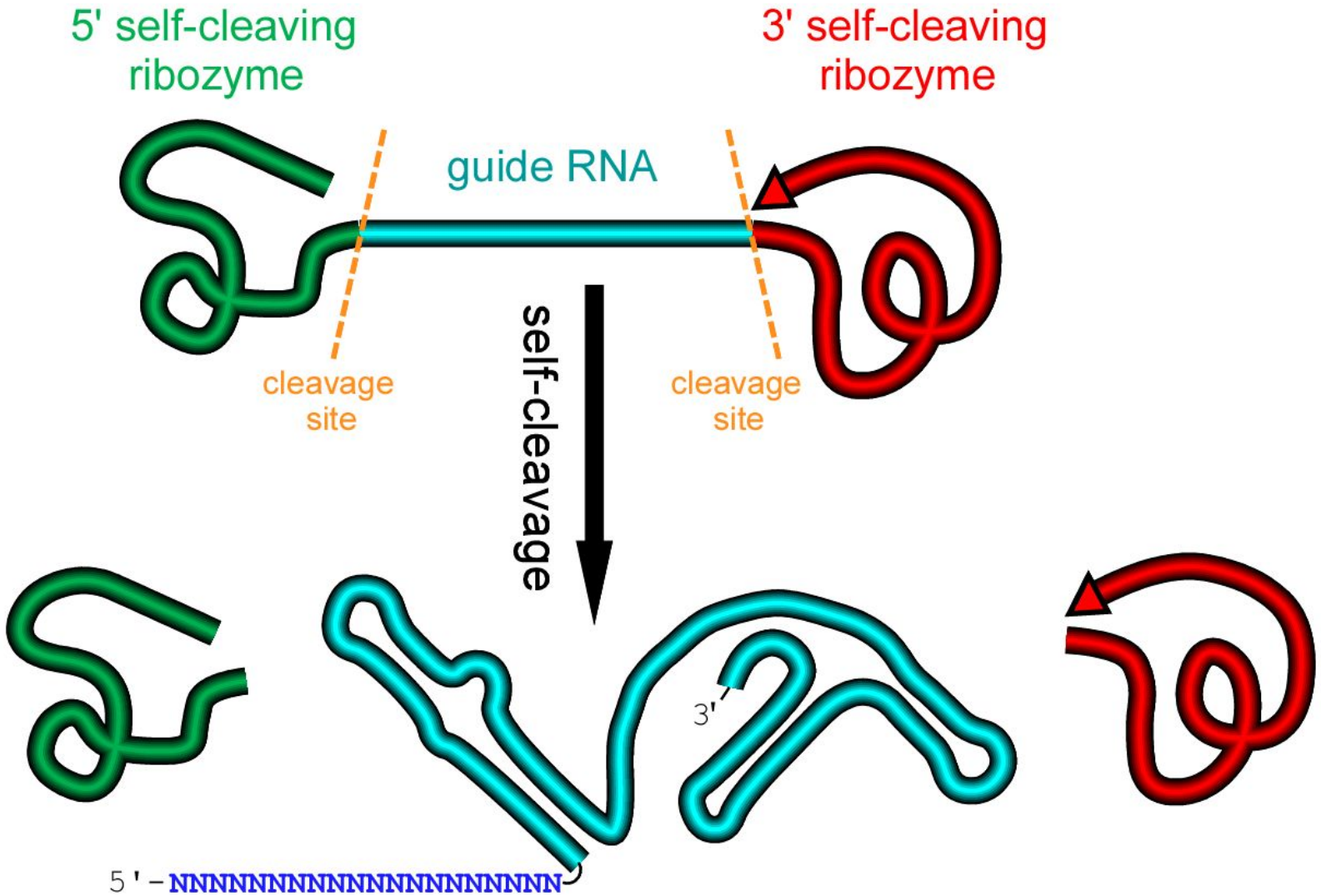
- Oxidoreductase: Oxidases, peroxidases and dehydrogenases
- Transferases: Phosphoryl transferase, transaminases, transpeptidases
- Hydrolases: Peptidases, glycosidases, esterases
- Lyases: Anhydrases, Decarboxylases etc.
- Isomerases: Epimerases, ,mutases

TYPES OF ENZYMES

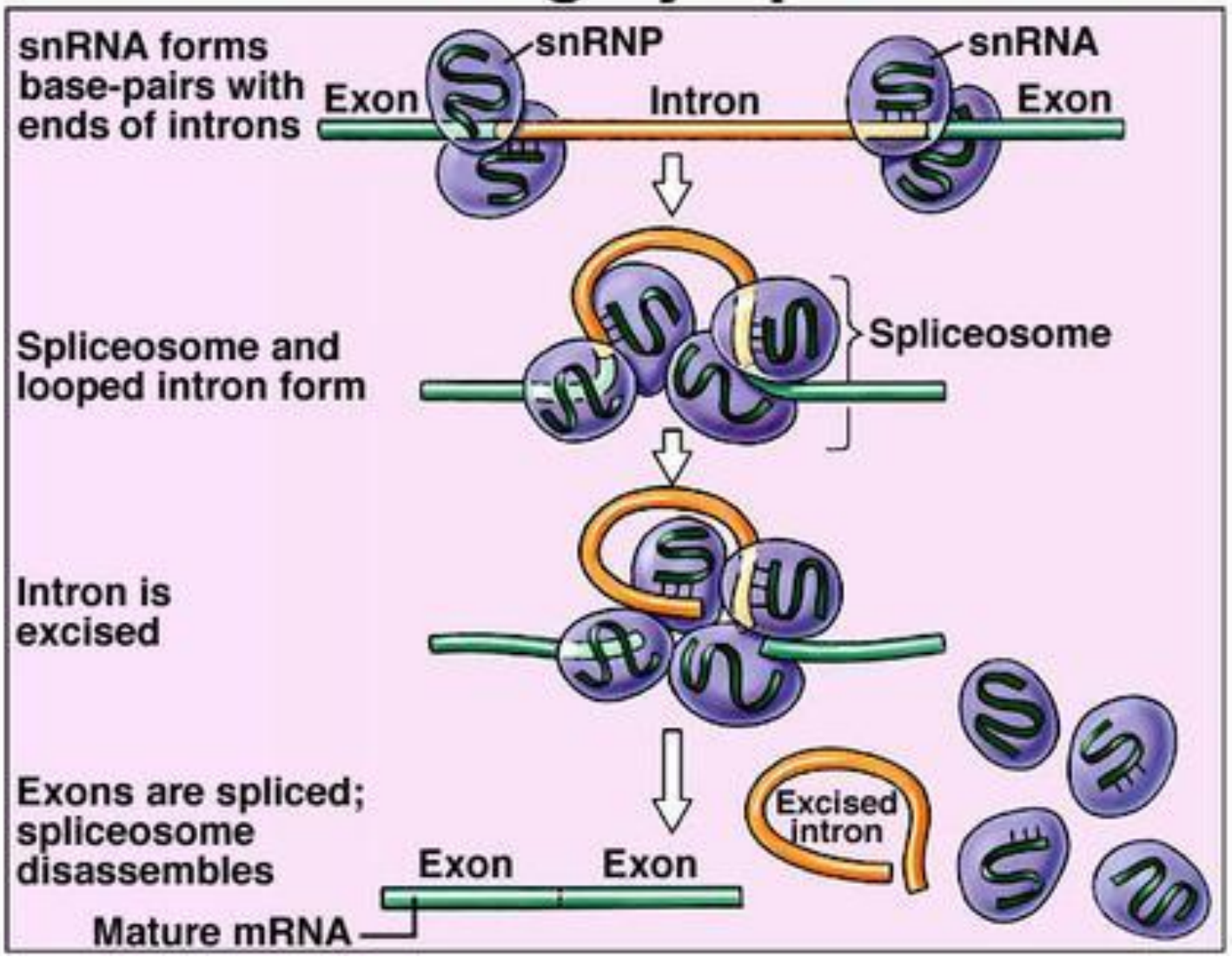
- ***Multienzymes*** :Enzymes of metabolic pathway which brings about chains of interrelated and sequential reactions eg: Pyruvic acid dehydrogenase complex
- ***Exoenzymes:*** Enzymes of alimentary canal
- ***Endoenzymes*** : Enzymes of respiratory system
- ***Constitutive enzyme*** : Found as normal constituents of a cell
- ***Inducible enzyme***: Produced only when substrate is available
- ***Extremozymes***: which function at extreme temperature and pH
- ***Abzymes***: Catalytic antibodies
- ***Metallo enzymes***: Which require metallic

RIBOZYMES or RNA enzymes

- Are autocatalytic RNA molecules with sequence specific cleavage activity
- It mediate the splicing of RNA molecules by acting as ***"RNA-cutting enzymes"*** eg: Many Spliceosomes , Ribonuclease P etc.
- Ribozymes that split other RNAs is called 'hammer headed robozymes' because of its shape
- First reported by Altman, Cech, Zaug and Grabowski (1982)
- Two categories
  - Self-splicing Ribozymes
  - Self-cleaving Ribozymes


5' self-cleaving ribozyme
3' self-cleaving ribozyme
guide RNA
cleavage site
cleavage site
self-cleavage
3'
5' – NNNNNNNNNNNNNNNNNNNN

RNA Processing by Spliceosomes



ISOENZYMES

- Are molecular variants or polymorphic forms of an enzyme with same or similar biological function but differing in molecular structure
  Eg: Lactic acid dehydrogenase (LDH, Pyruvic acid Lactic acid, Hexokinase, Acid-alkaline phosphatase etc.

- Homologous: with almost similar molecular structure and catalytic properties

  Analogous: with similar reaction properties but different in molecular organisation

LDH isoforms

Isoenzymes of lactate dehydrogenase	Highest levels found in the following:	Isoenzymes of lactate dehydrogenase	Highest levels found in the following:
		 H_2M_2 (LDH_3)	Brain, lung, white blood cells
 H_4 (LDH_1)	Heart, kidneys	 HM_3 (LDH_4)	Lung, skeletal muscle
 H_3M (LDH_2)	Red blood cells, heart, kidney, brain	 M_4 (LDH_5)	Skeletal muscle, liver

MOLECULAR ORGANISATION OF ENZYMES

- Simple enzymes
- Complex enzymes : Are conjugated proteins known as ***holoenzymes***

  which has a

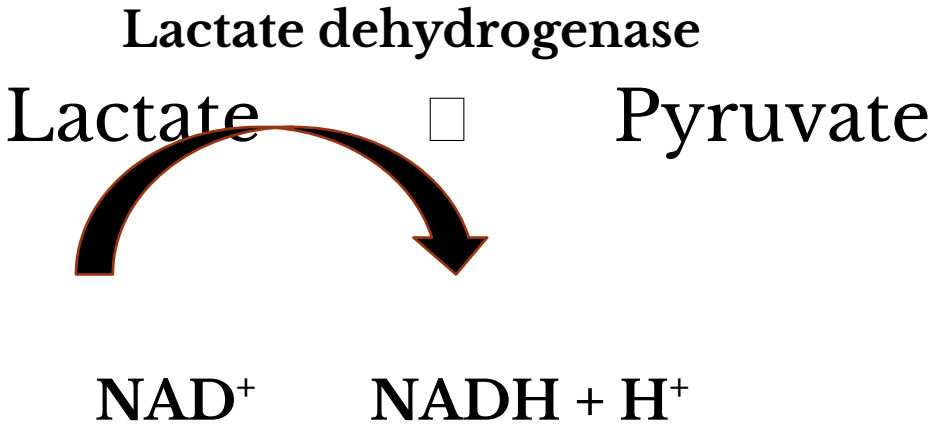
1. Protein part called ***apoenzyme***
2. Non-protein part ***co-factors***

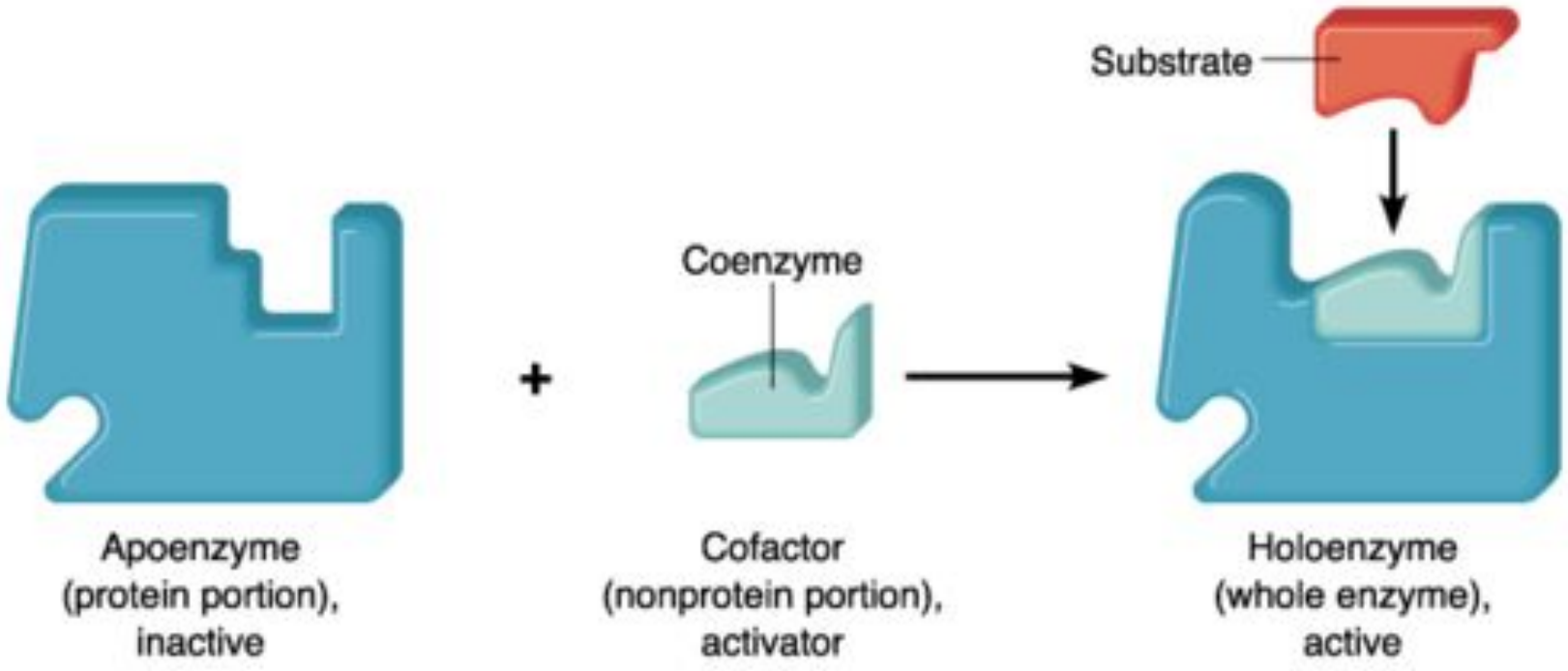
- When the cofactor is tightly and covalently bound to their apoenzyme it is called ***Prosthetic group*** eg: Fe containing part of cytochromes and haemoglobin
- ***Co factors*** are either ***inorganic ions*** (Na, K, Mg, Mn,Fe,Zn,Co etc) or non-proteinaceous organic molecules generally called

- ***Co-enzymes*** are of two major groups

i. Those participating in redox reactions which involve the transfer of hydrogen atoms or electrons (NAD, NADP, FAD, FMN)

ii. Those taking part in reactions which involve the transfer of chemical groups (CoA – transfer of acetyl group, TPP, biotin)



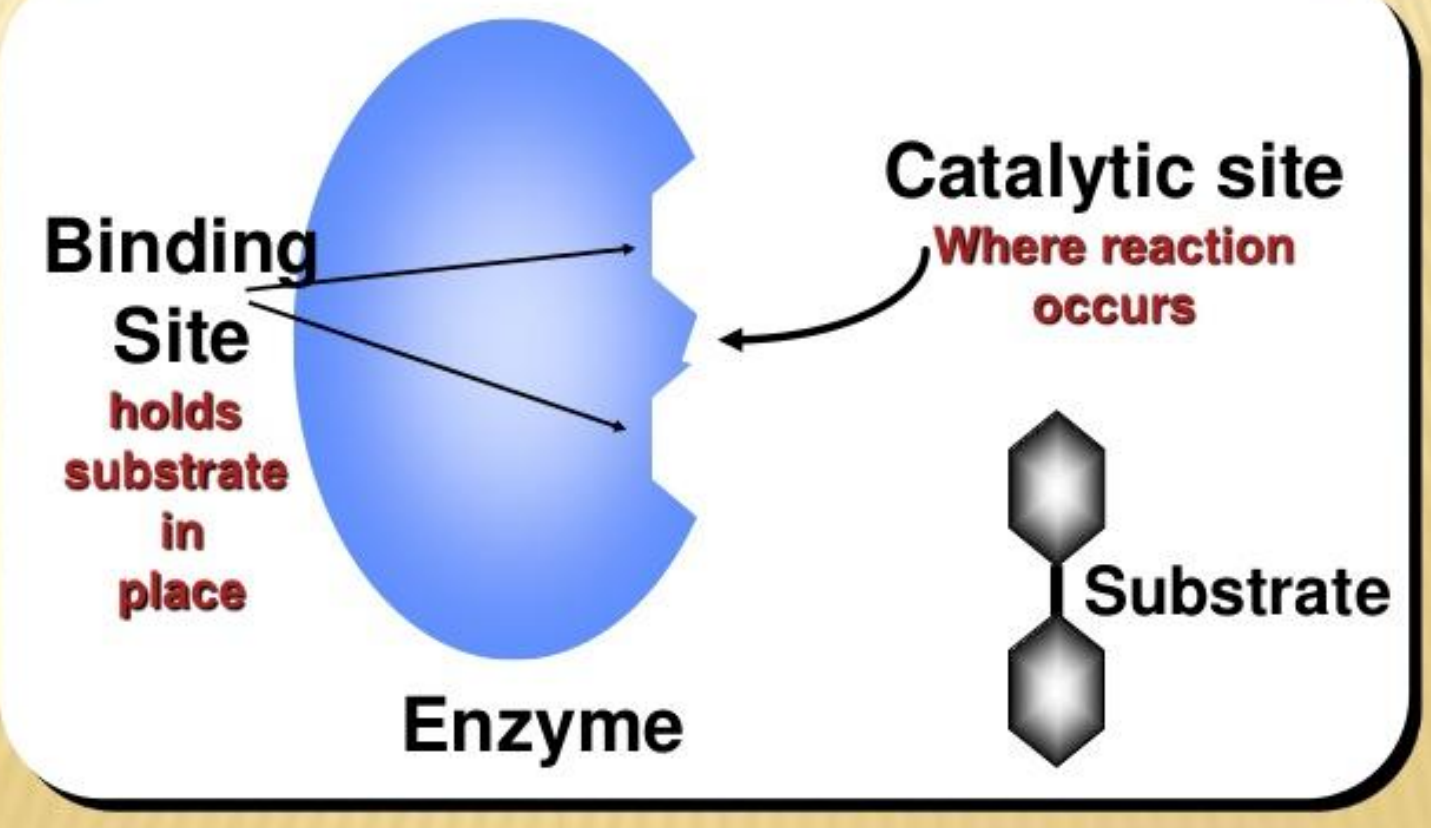

Substrate
Coenzyme
+
Apoenzyme
(protein portion),
inactive
Cofactor
(nonprotein portion),
activator
Holoenzyme
(whole enzyme),
active

FUNCTIONAL ORGANISATION OF ENZYMES

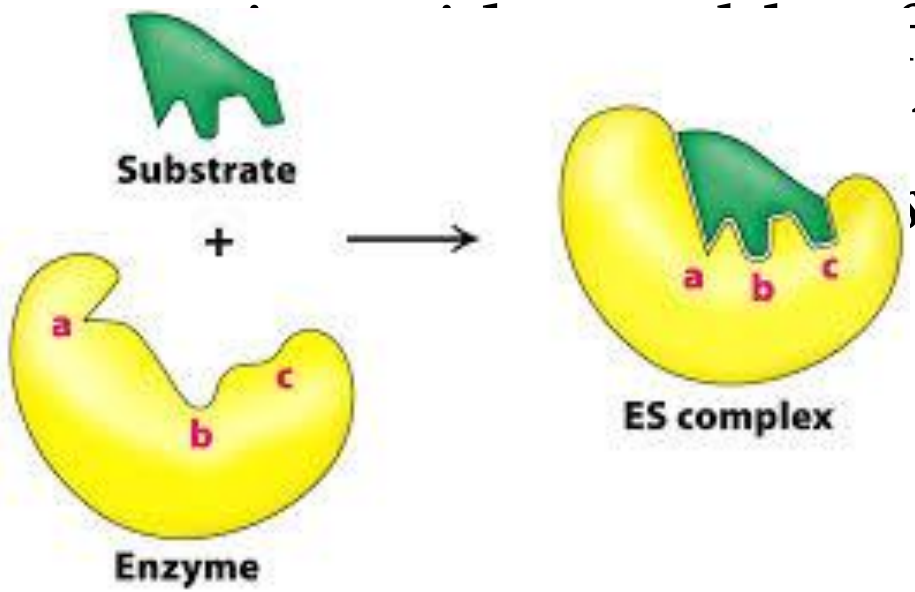
- An enzyme molecule has several functional regions, each with a specific function

1. ***ACTIVE SITE*** - a small portion of an enzyme which serves as the specific site for binding with the substrate and also to covert it to product. It has two portions namely contact site and catalytic site. The contact site mediates the binding while catalytic site mediates the conversion of substrate to product
   - Binding of a substrate with active site occurs mainly through non-covalent hydrophobic interactions
   - The active site has no rigid shape since

THE ACTIVE SITE



- These aminoacids may be located at distant points often at opposite ends. The specific folding of the polypeptide chain brings them to close proximity
- Those aminoacids seen close to the active site capable of influencing the reactivity of functional groups are called *accessory groups* and other rem
  influencin tion of
  enzymes a



The Mechanism of Enzymatic Action

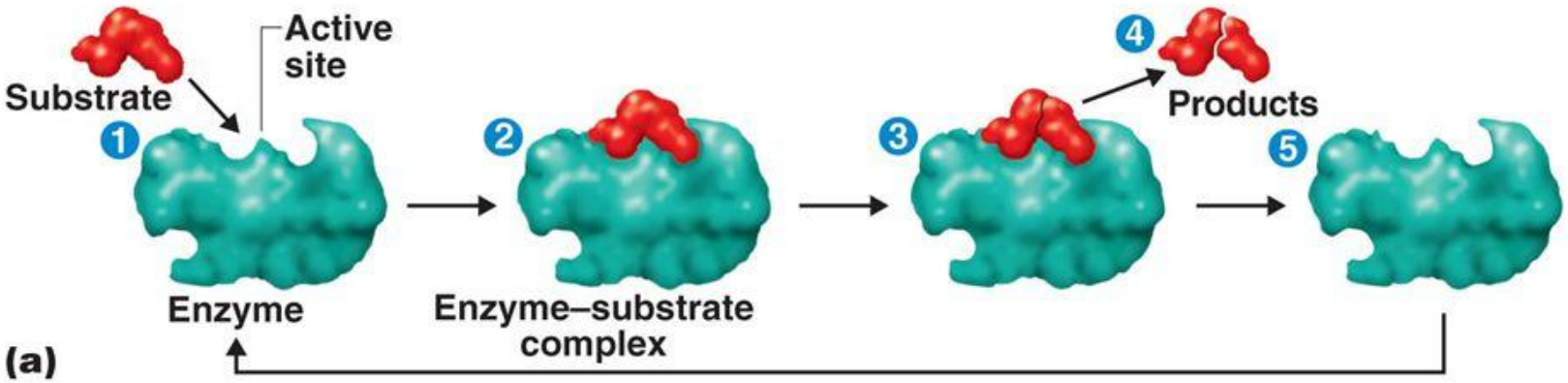
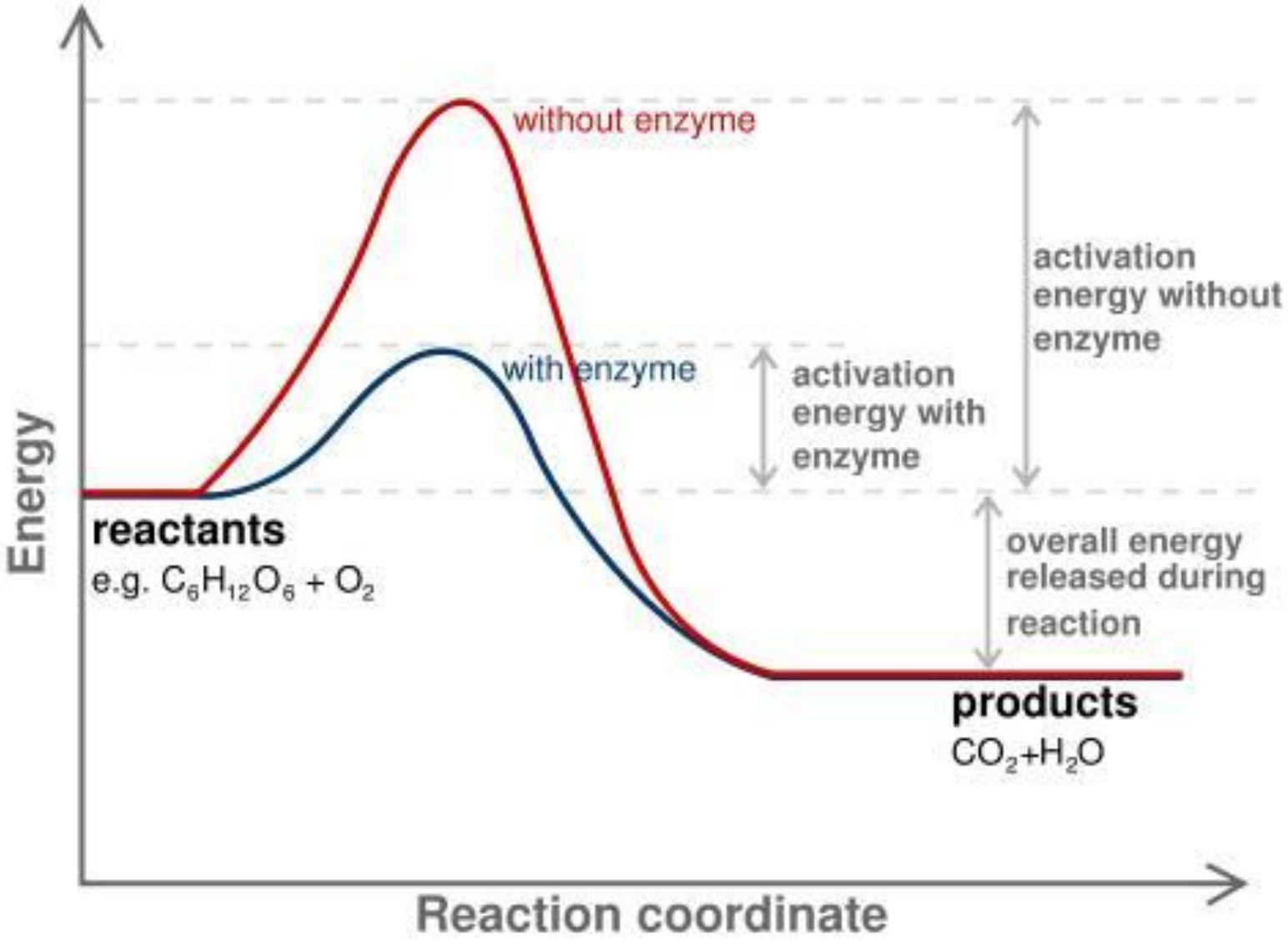


Figure 5.4a

MECHANISM OF ENZYME ACTION

- Enzymes function as catalysts reducing the energy barrier ie, free energy of activation and thereby enhancing the overall rate of a reaction without altering its temperature level

- Activation energy [Ea] or free energy of activation [$\Delta G^{\pm}$] is the energy required to make a substrate reactive for its transformation to a product. So higher the activation energy, slower would be the reaction


Energy
without enzyme
with enzyme
activation energy without enzyme
activation energy with enzyme
overall energy released during reaction
reactants
e.g. $C_6H_{12}O_6 + O_2$
products
CO_2+H_2O
Reaction coordinate

THEORIES OF ENZYME ACTION

1) *The Enzyme – substrate complexing hypothesis*

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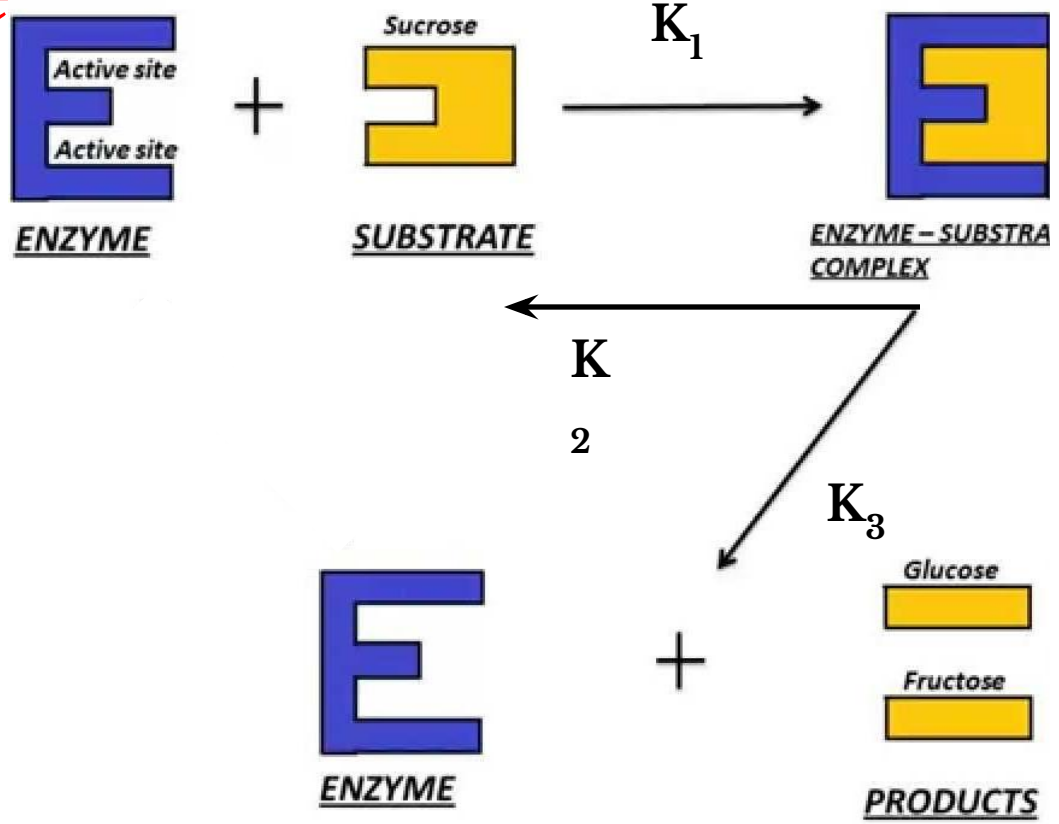
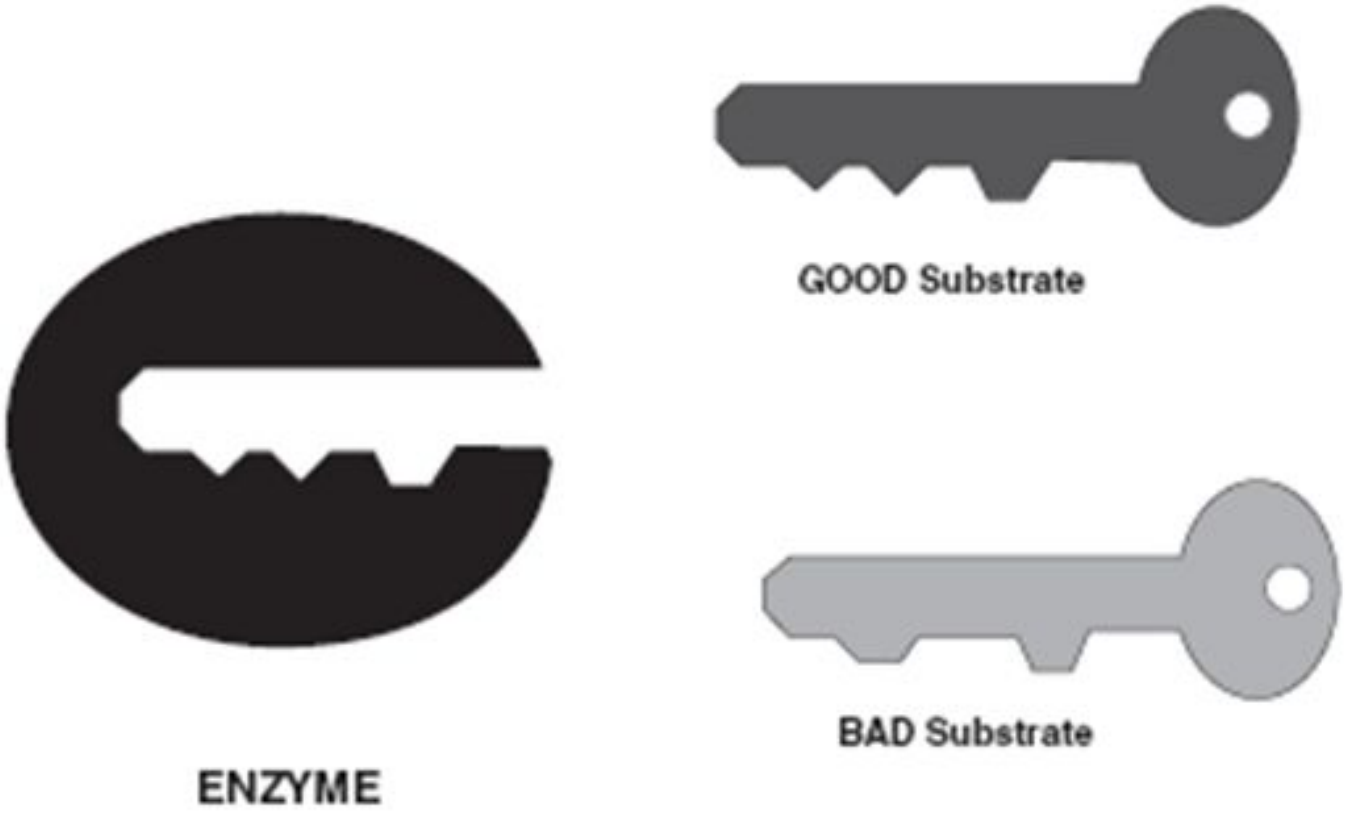
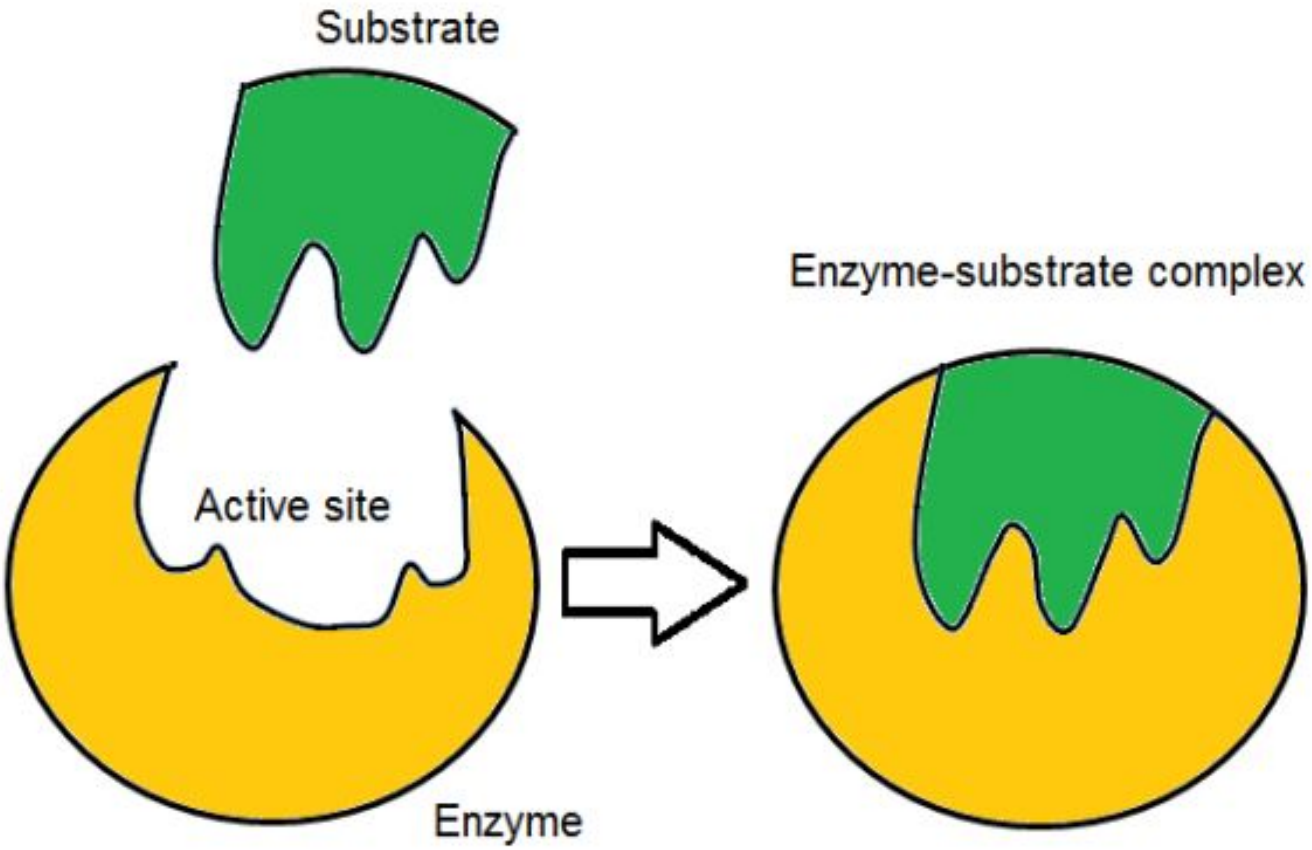
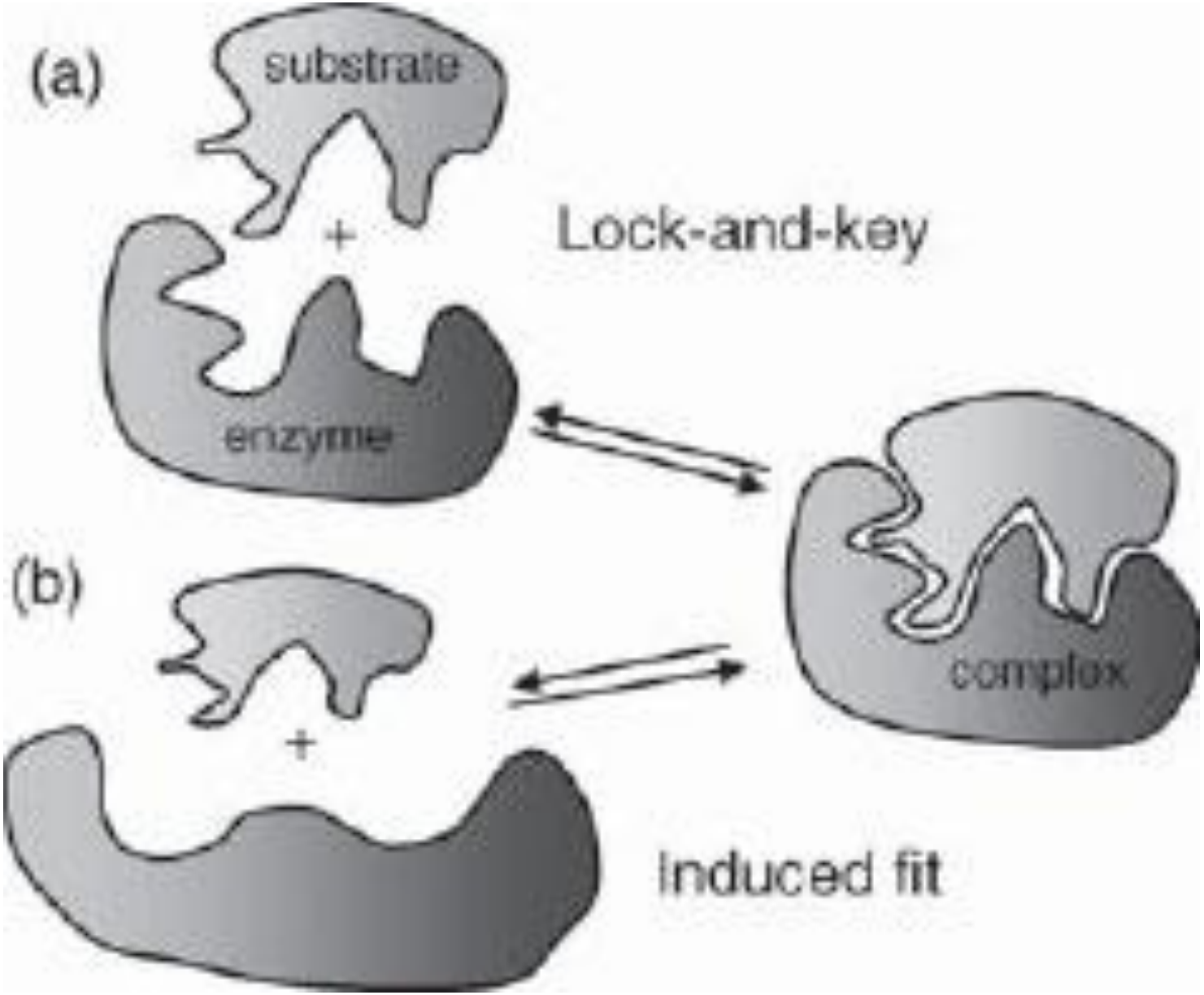


2) *Lock and Key hypothesis*



3) *Induced fit hypothesis*




(a)
substrate
+
enzyme
Lock-and-key
complex
(b)
+
Induced fit

INHIBITION