
بسم الله الرحمن الرحيم
"سنريهم آياتنا فى الآفاق وفى أنفسهم حتى
يتبين لهم انه الحق "
صدق الله العظيم

Enzymology

(BIOC306)

For

Undergraduate Biochemistry Students

By

Dr. Hisham Ismail

Assistant Professor of Biochemistry

Chemistry Dept., Minia University , Egypt

Today

Enzymology

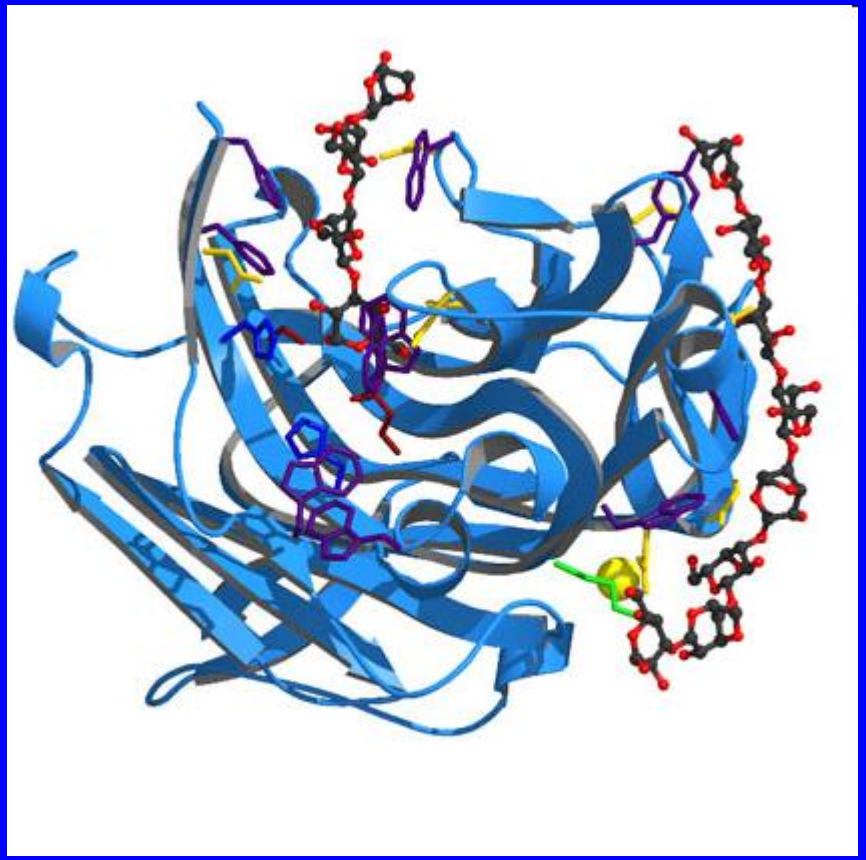
2. Structural Components of Enzymes.

What are enzymes?

- **Biological catalysts made up of proteins**

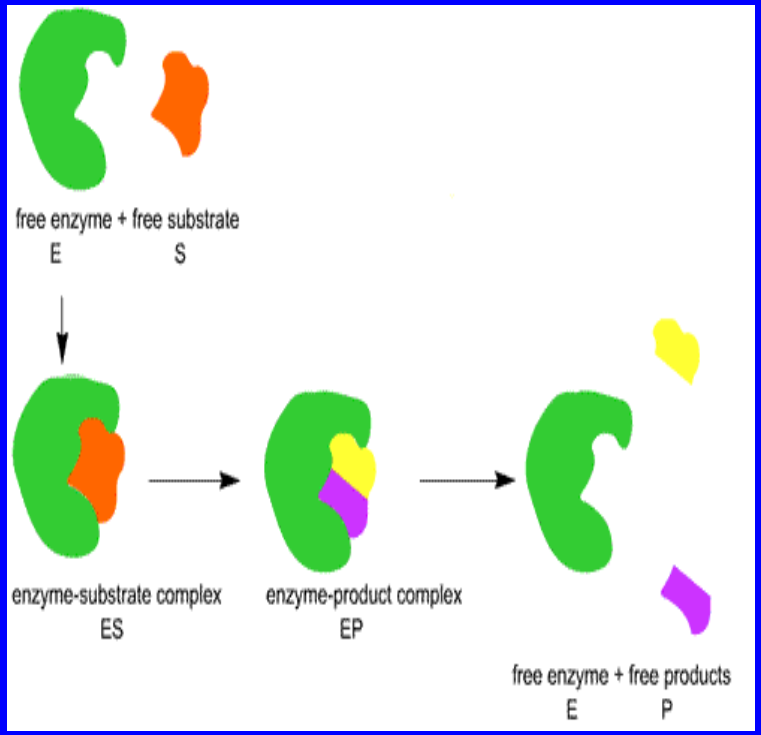
Substrate

Product



What are enzymes?

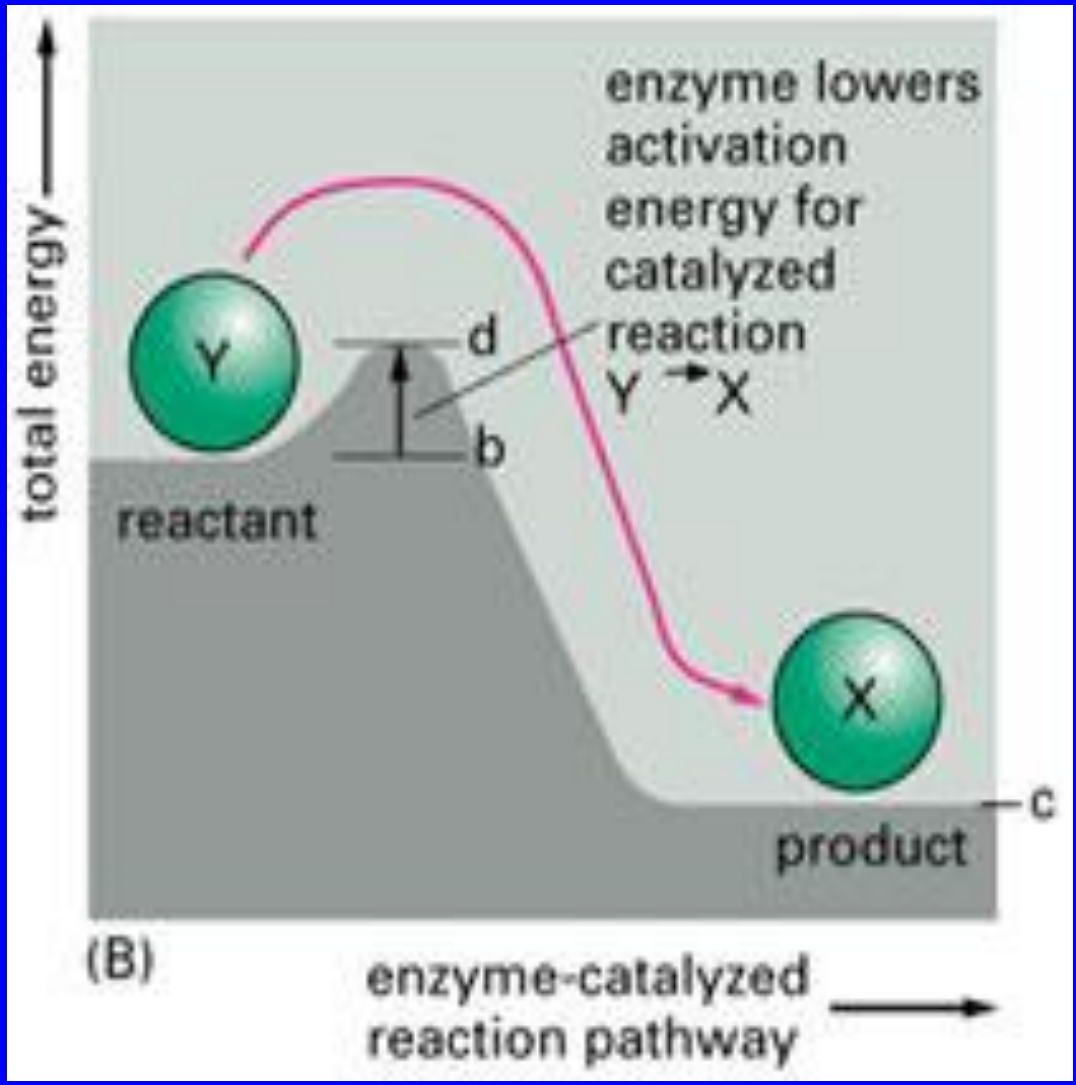
*. Enzymes speed up the rate of chemical reactions in the body; both breaking down reactions (e.g.: starch into maltose) building up reactions (e.g: amino acids into proteins).



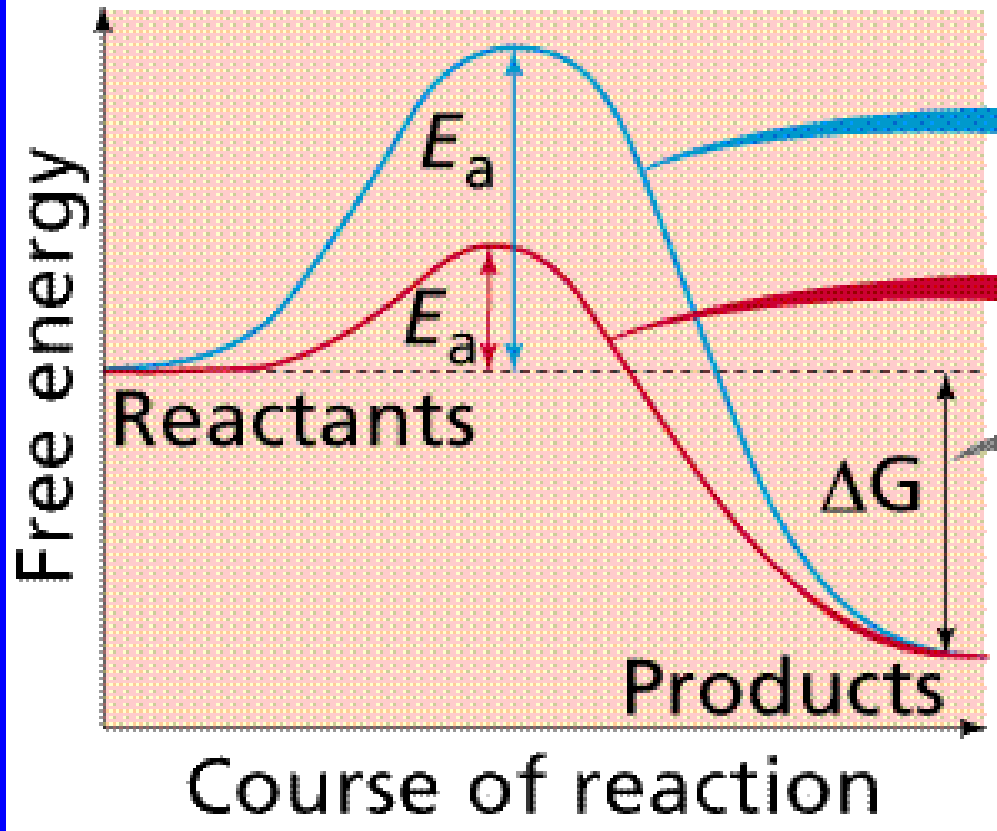
*. Enzymes lower the activation energy required to start a chemical reaction.

How do enzymes work?

Enzymes work by weakening bonds which lowers activation energy



How do enzymes increase the rate of the reaction ?



An uncatalyzed reaction requires a higher activation energy than does a catalyzed reaction

There is no difference in free energy between catalyzed and uncatalyzed reactions

1. STRUCTURAL COMPONENTS OF ENZYMES

Like all proteins, enzymes are composed mainly of the 20 naturally occurring amino acids.

In addition to the amino acids, many enzymes utilize non-protein *cofactors* to add additional chemical reactivities to their repertoire.

We shall describe some of the more common cofactors found in enzymes, and discuss how they are utilized in catalysis.

STRUCTURAL COMPONENTS OF ENZYMES

Physicochemical properties of the natural amino acids

Amino Acid	Three-Letter Code	One-Letter Code	Mass of Residue in Proteins[a]	Accessible Surface Area (Å²)[b]	Hydrophobicity[c]	pK_a of Ionizable Side Chain	Occurrence in Proteins (%)[d]	Relative Mutability[e]	Van der Waals Volume (Å³)
Alanine	Ala	A	71.08	115	+1.8		9.0	100	67
Arginine	Arg	R	156.20	225	−4.5	12.5	4.7	65	148
Asparagine	Asn	N	114.11	160	−3.5		4.4	134	96
Aspartate	Asp	D	115.09	150	−3.5	3.9	5.5	106	91
Cysteine	Cys	C	103.14	135	+2.5	8.4	2.8	20	86
Glutamate	Glu	E	128.14	180	−3.5	4.1	3.9	102	109
Glutamine	Gln	Q	129.12	190	−3.5		6.2	93	114
Glycine	Gly	G	57.06	75	−0.4		7.5	49	48
Histidine	His	H	137.15	195	−3.2	6.0	2.1	66	118
Isoleucine	Ile	I	113.17	175	+4.5		4.6	96	124
Leucine	Leu	L	113.17	170	+3.8		7.5	40	124
Lysine	Lys	K	128.18	200	−3.9	10.8	7.0	56	135
Methionine	Met	M	131.21	185	+1.9		1.7	94	124
Phenylalanine	Phe	F	147.18	210	+2.8		3.5	41	135
Proline	Pro	P	97.12	145	−1.6		4.6	56	90
Serine	Ser	S	87.08	115	−0.8		7.1	120	73
Threonine	Thr	T	101.11	140	−0.7		6.0	97	93
Tryptophan	Trp	W	186.21	255	−0.9		1.1	18	163
Tyrosine	Tyr	Y	163.18	230	−1.3	10.1	3.5	41	141
Valine	Val	V	99.14	155	+4.2		6.9	74	105

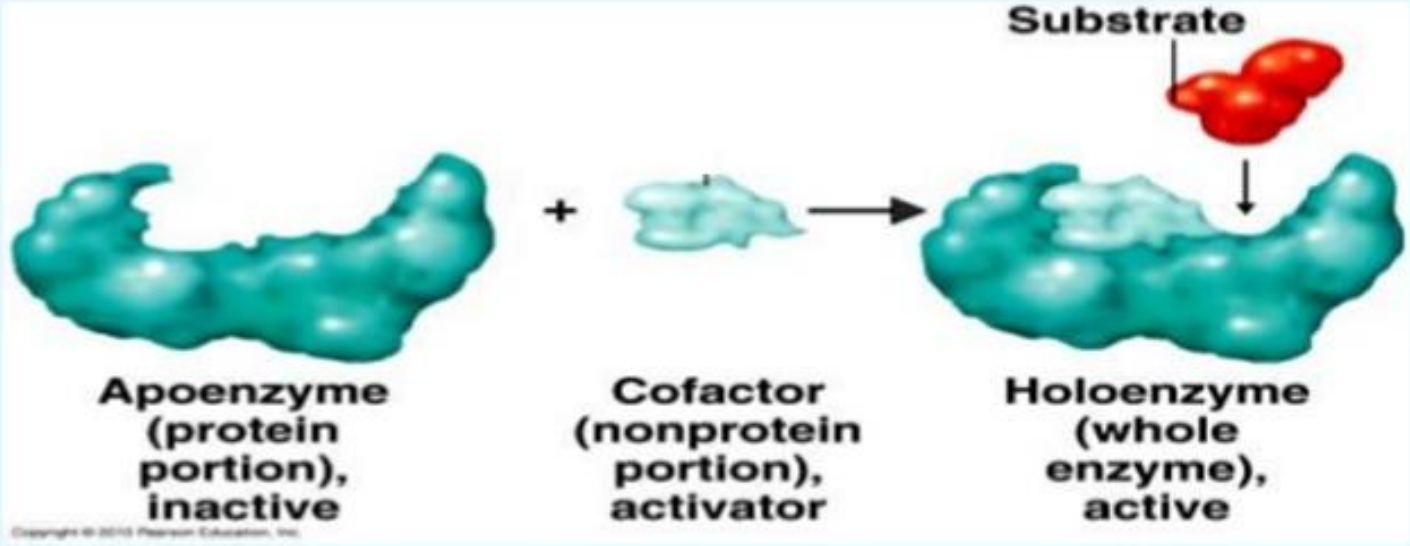
STRUCTURAL COMPONENTS OF ENZYMES

*. **Many** enzymes incorporate **Non-protein chemical portion** into the structures of their active sites **to facilitate rapid reaction**.

*. These non-protein chemical portions are collectively referred to as ***Cofactors or Coenzymes*** which **mostly bind non-covalently** to enzyme.

*. In enzymes requiring a cofactor or Coenzyme for activity, the **Protein portion** of the active species is referred to as the ***apoenzyme***, and the active complex between the **Protein** and **Non-protein portion** is called the ***holoenzyme***.

STRUCTURAL COMPONENTS OF ENZYMES



Enzymes

Inactive Enzymes

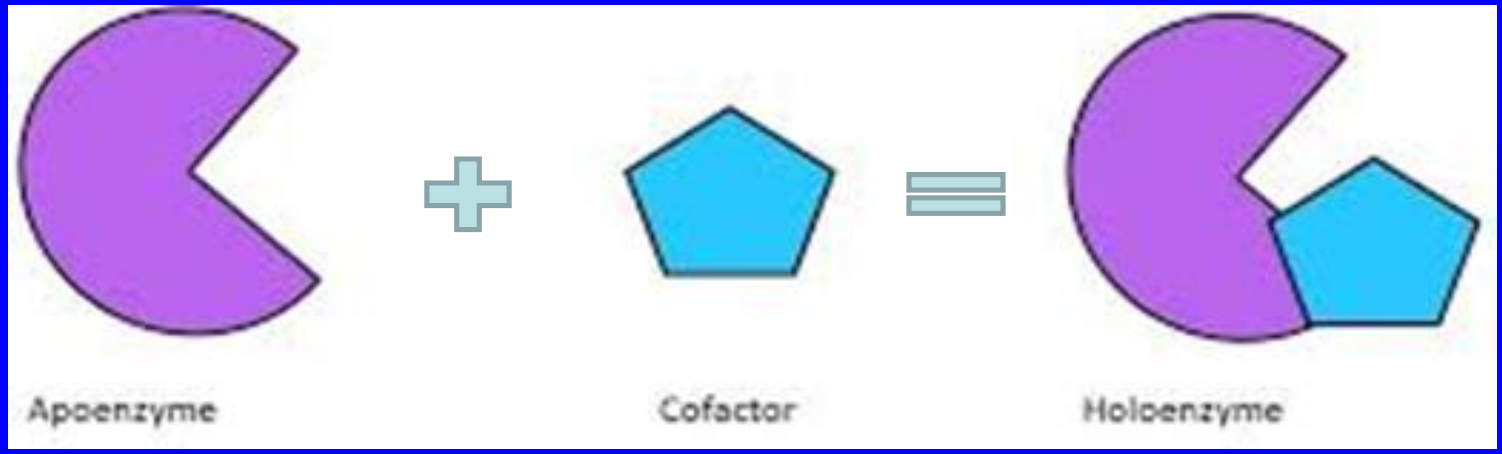
Apoenzymes:

Need cofactors but don't have any

Active Enzymes

Holoenzymes:

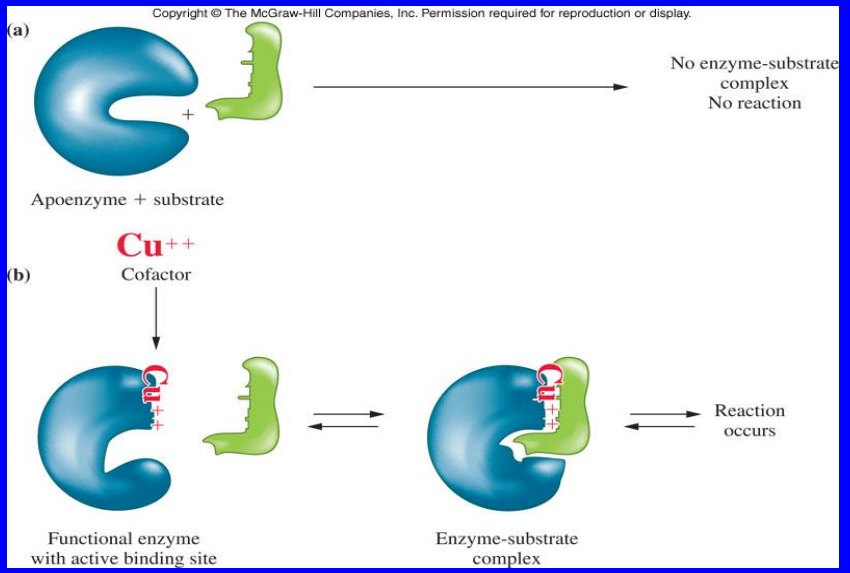
Apoenzyme + **Cofactor**



Cofactors & Coenzymes

- **Active enzyme / Holoenzyme:**
  - **Polypeptide portion of enzyme (Apoenzyme)**
  - **Non-protein portion (Cofactor or Coenzyme)**

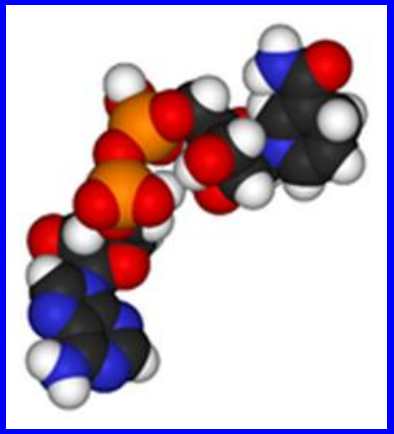
- **Non-protein portions are bound to the enzyme for it to maintain the correct configuration of the active site:**
  - **Metal ions or Cofactors (Mg, Cu,..)**
  - **Organic compounds or Coenzymes (NAD, FAD, ….).**



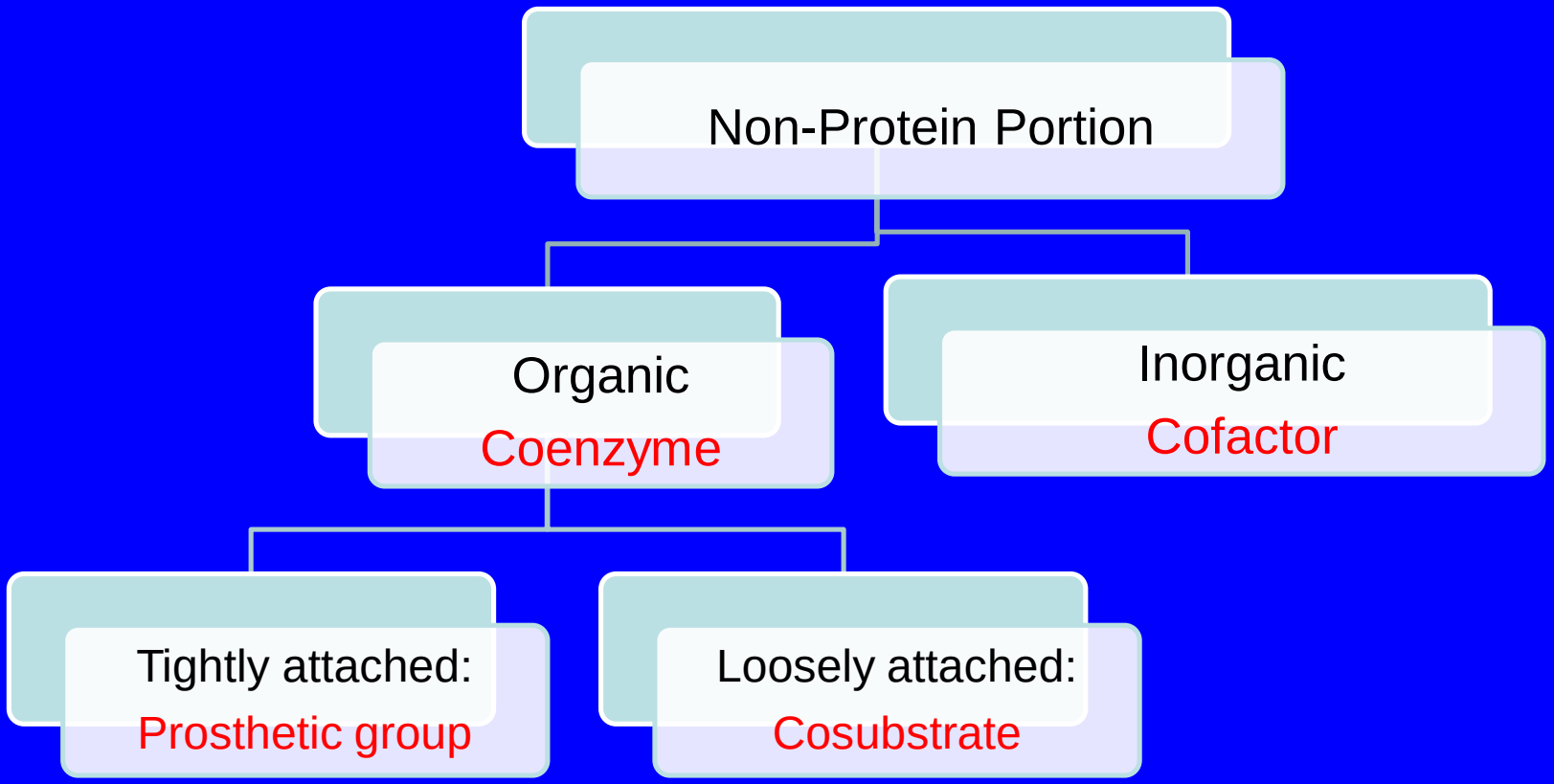
STRUCTURAL COMPONENTS OF ENZYMES

*. if Coenzyme is tightly bound to the enzyme protein, the coenzyme is called a prosthetic group.

*. if Coenzyme is loosely bound to enzyme protein, the coenzyme is called a Cosubstrate.



STRUCTURAL COMPONENTS OF ENZYMES



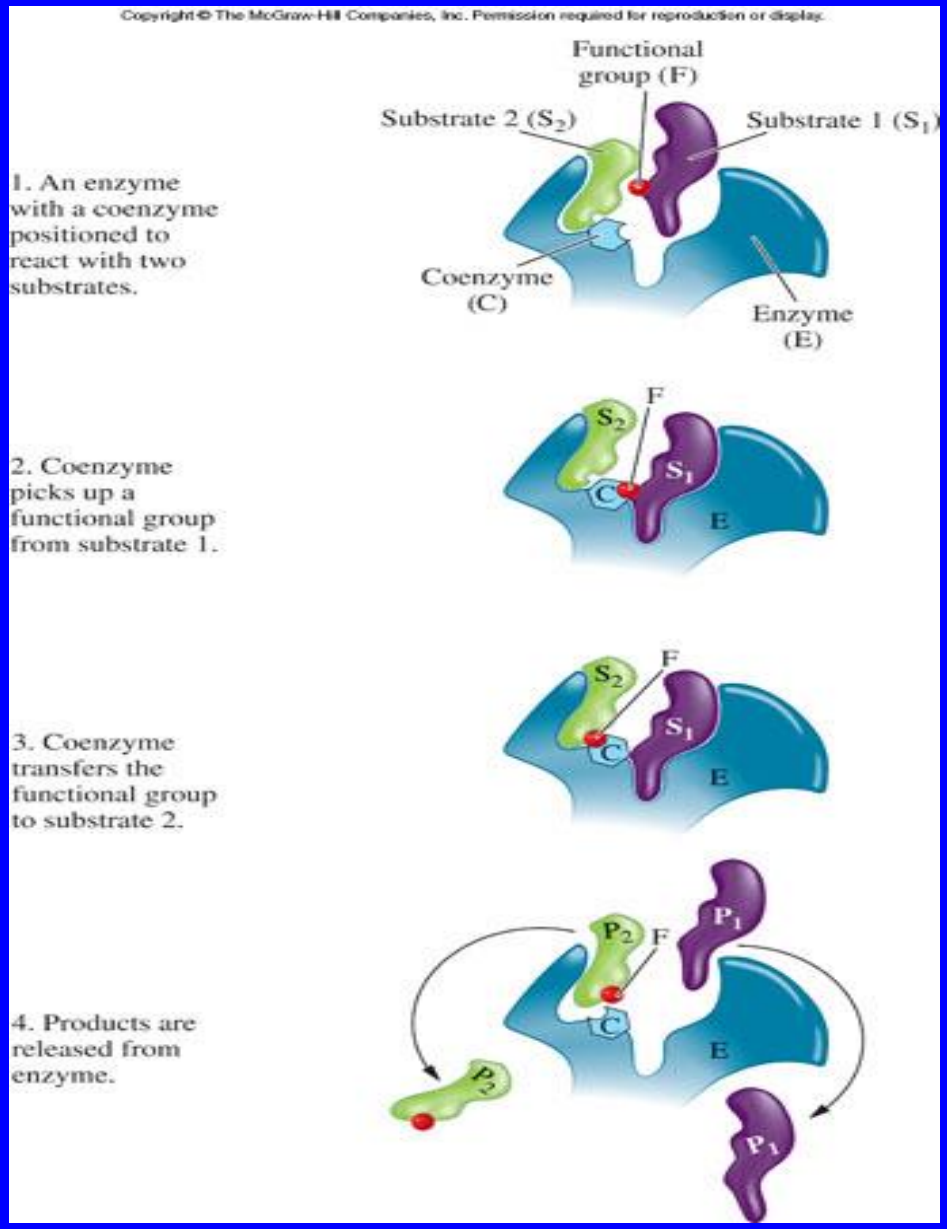
Cofactors can be considered "helper molecules" that assist in biochemical transformations.

Metals as Cofactors for Enzymes

Metals	Enzymes
Fe++ or Fe++	Catalase, Peroxidase
Cu++	Cytochrome oxidase
Zn++	Carbonic anhydrase, Alcohol dehydrogenase
Mg++	Hexokinase, (all kinases), G-6-phosphatase
Mn++	Arginase, Ribonucleotide reductase
K+	Pyruvate kinase
Ni++	Urease
Mo++	Dinitrogenase
Se	Glutathione perioxidase

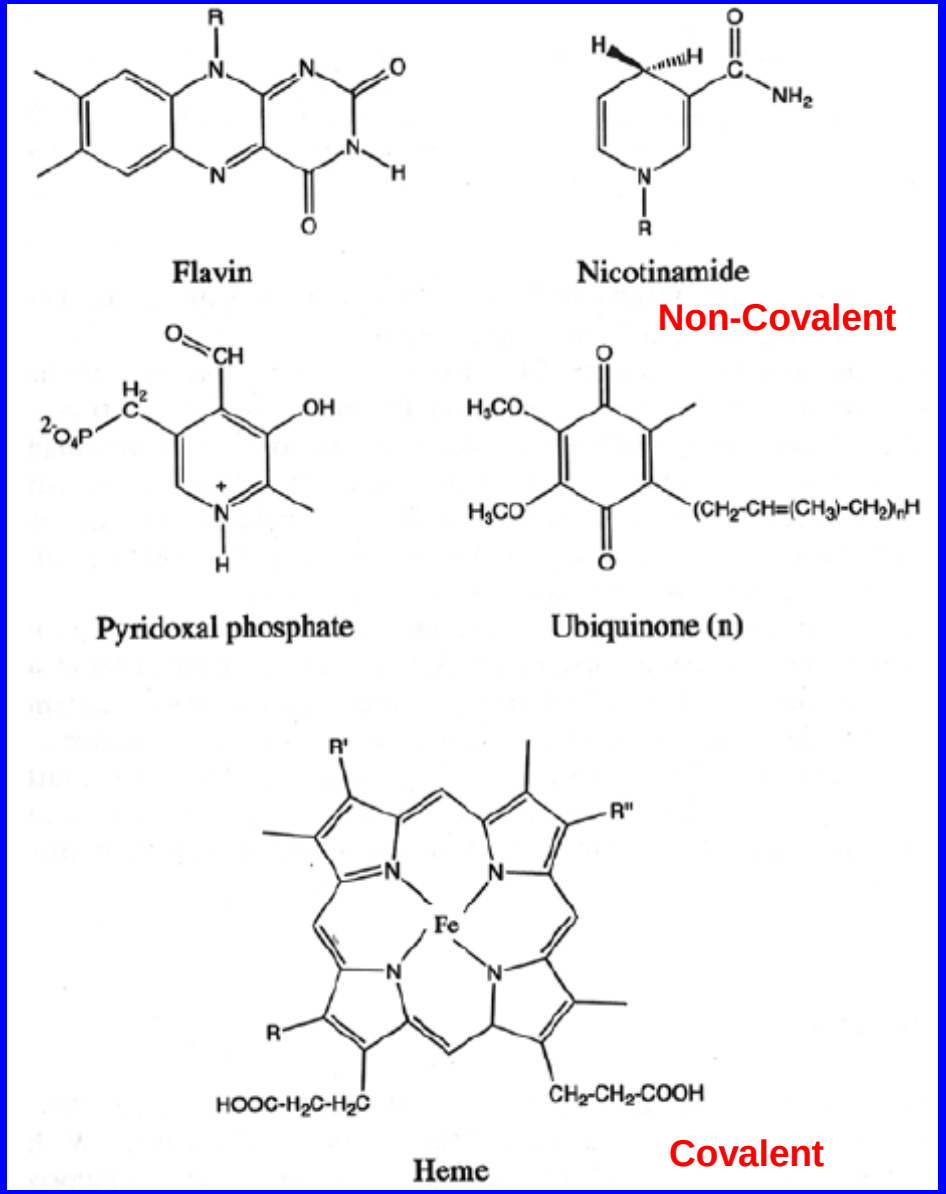
Coenzymes

- Organic molecule bound to the enzyme by weak interactions / Hydrogen bonds.
- Most coenzymes carry electrons or small groups.
- Many have modified vitamins in their structure.



Coenzymes

Structures of some common coenzymes found in enzymes.

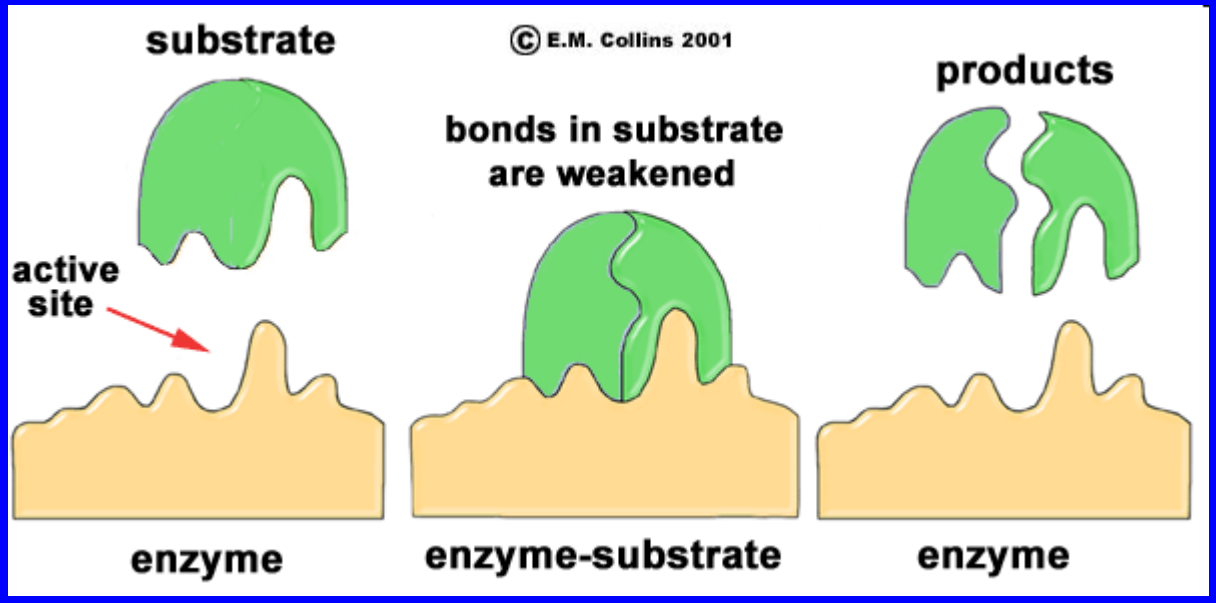


STRUCTURAL COMPONENTS OF ENZYMES

Some examples of Cofactors and Coenzymes found in enzymes

Cofactor	Enzymatic Use	Examples of Enzyme
Copper ion	Redox center–ligand binding	Cytochrome oxidase, superoxide dismutase phosphodiesterases, ATP synthases
Magnesium ion	Active site electrophile–phosphate binding	
Zinc ion	Active site electrophile	Matrix metalloproteases, carboxypeptidase A
Flavins	Redox center–proton transfer	Glucose oxidase, succinate dehydrogenase
Hemes	Redox center–ligand binding	Cytochrome oxidase, cytochrome P450s
NAD and NADP	Redox center–proton transfer	Alcohol dehydrogenase, ornithine cyclase
Pyridoxal phosphate	Amino group transfer–stabilizer of intermediate carbanions	Aspartate transaminase, arginine racemase
Quinones	Redox center–hydrogen transfer	Cytochrome b_o, dihydroorotate dehydrogenase
Coenzyme A	Acyl group transfer	Pyruvate dehydrogenase,

Mode of Action



Substrate fits in the enzyme active site,
just like a key fits into a lock.

An enzyme-substrate complex is formed.

Chemical reactions occur at the active site and products are formed.

Specificity of the Enzyme-Substrate Complex

- For enzyme and substrate to react, surfaces of each must be complementary

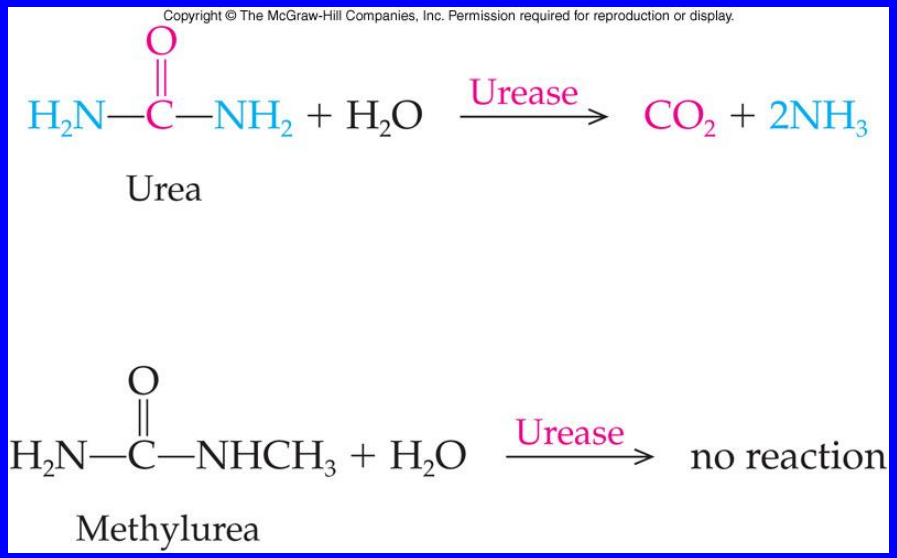
- Enzyme specificity: the ability of an enzyme to bind only one, or a very few, substrates thereby catalyzing only a single reaction.

- Compare these 2 reactions:
- Urease is

  VERY Specific or

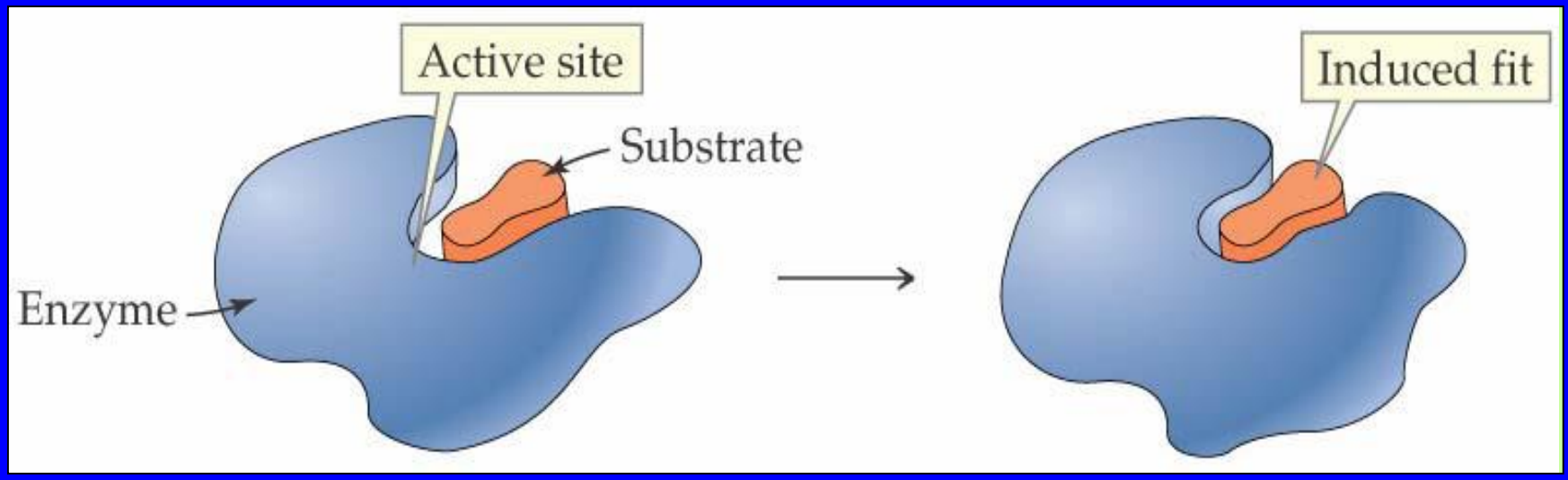
  has a HIGH DEGREE

  of Specificity.



How Enzyme Work ?

In enzyme catalyzed reactions, substrates are drawn into the active site to form enzyme-substrate complex. Within the enzyme-substrate complex, the enzyme promoted reactions takes place. Once the chemical reaction is over, enzyme separates from the substrate and restores its original conditions, becomes available for another reaction.



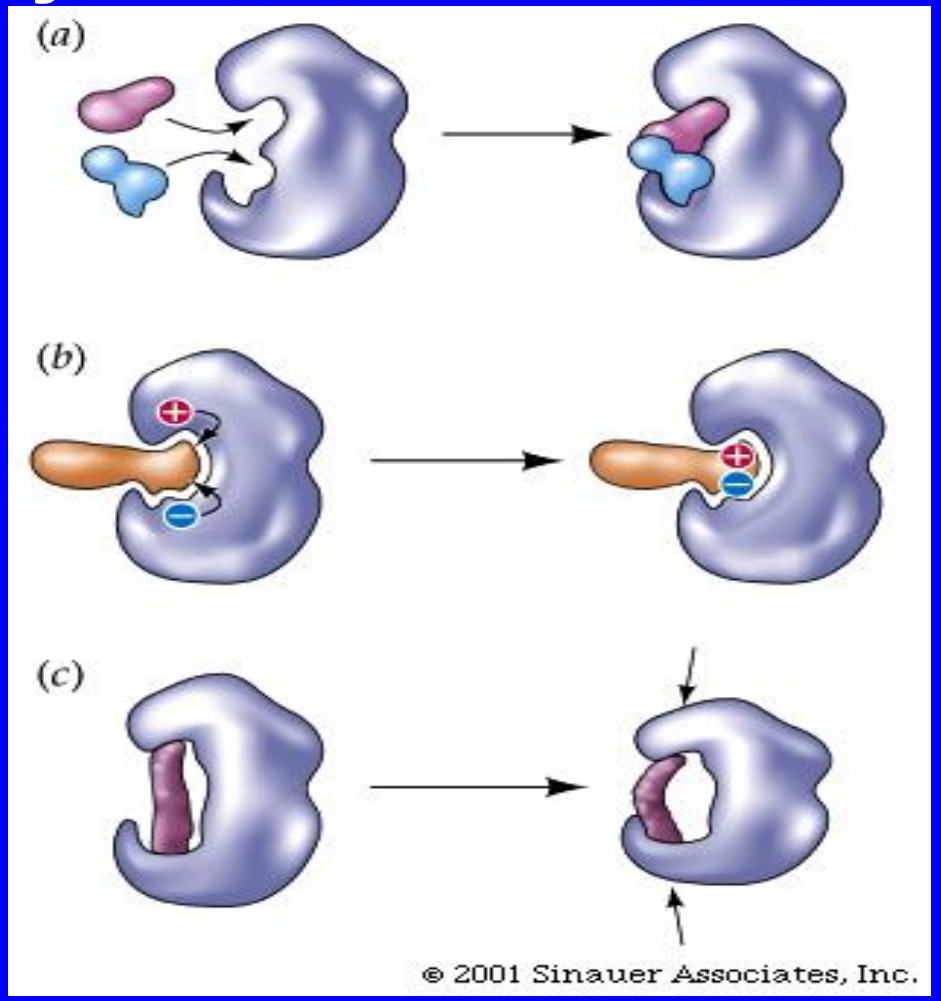
Lock-and-key model: The substrate is described as fitting into the active site as a key fit into a lock.

Induced-fit-model : The enzyme has a flexible active site that changes shape to accommodate the substrate and facilitate the reaction

Theories to explain specificity of enzyme action

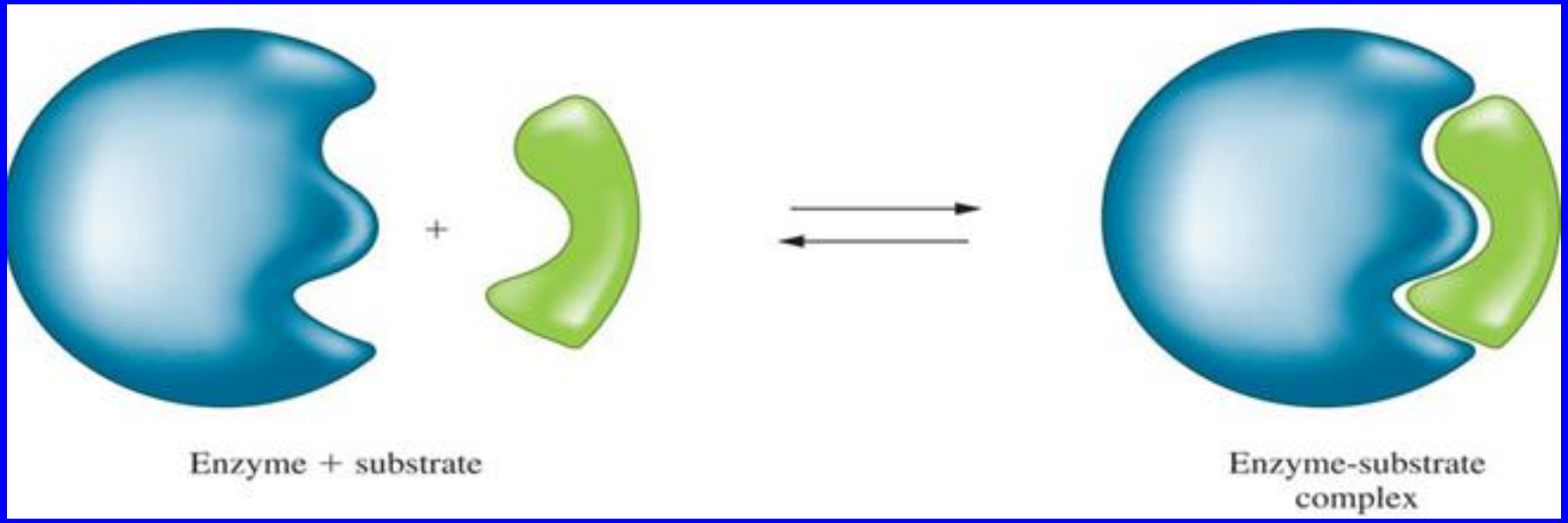
Lock and Key Theory:

The enzyme active site is complementary in conformation to the substrate, so that enzyme and substrate recognize each other.



Lock and Key Enzyme Model

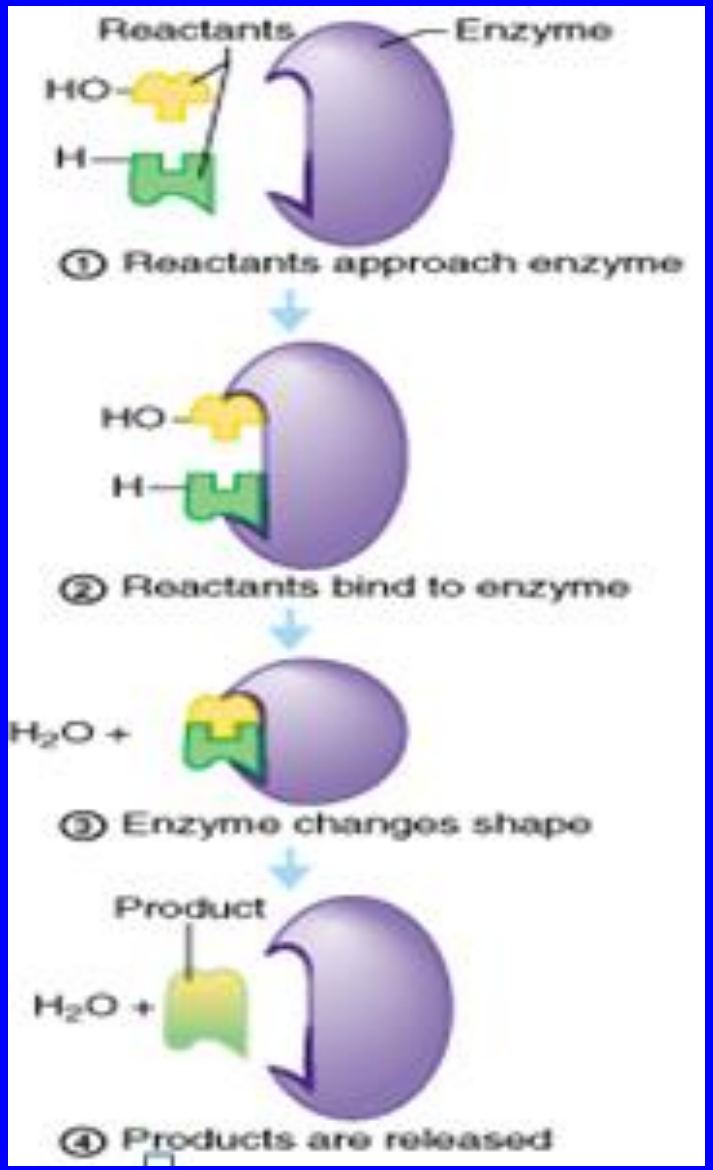
- In this model, the enzyme is assumed to be the key and the substrate the lock
  - The enzyme and substrate are made to fit exactly
  - This model fails to take into account proteins conformational changes to accommodate a substrate molecule



Theories to explain specificity of enzyme action

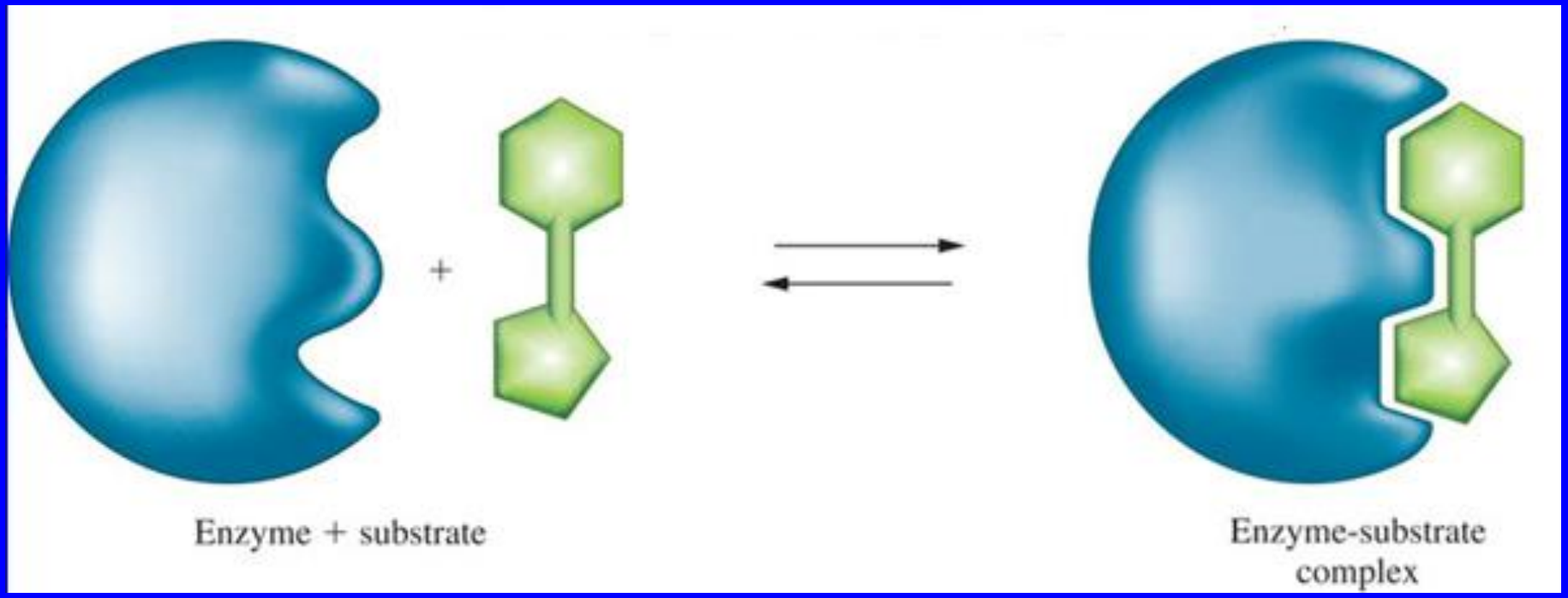
Induced-Fit Theory:

The enzyme changes shape on binding to the substrate, so that the conformation of Substrate & Enzyme active site is complementary only after binding.



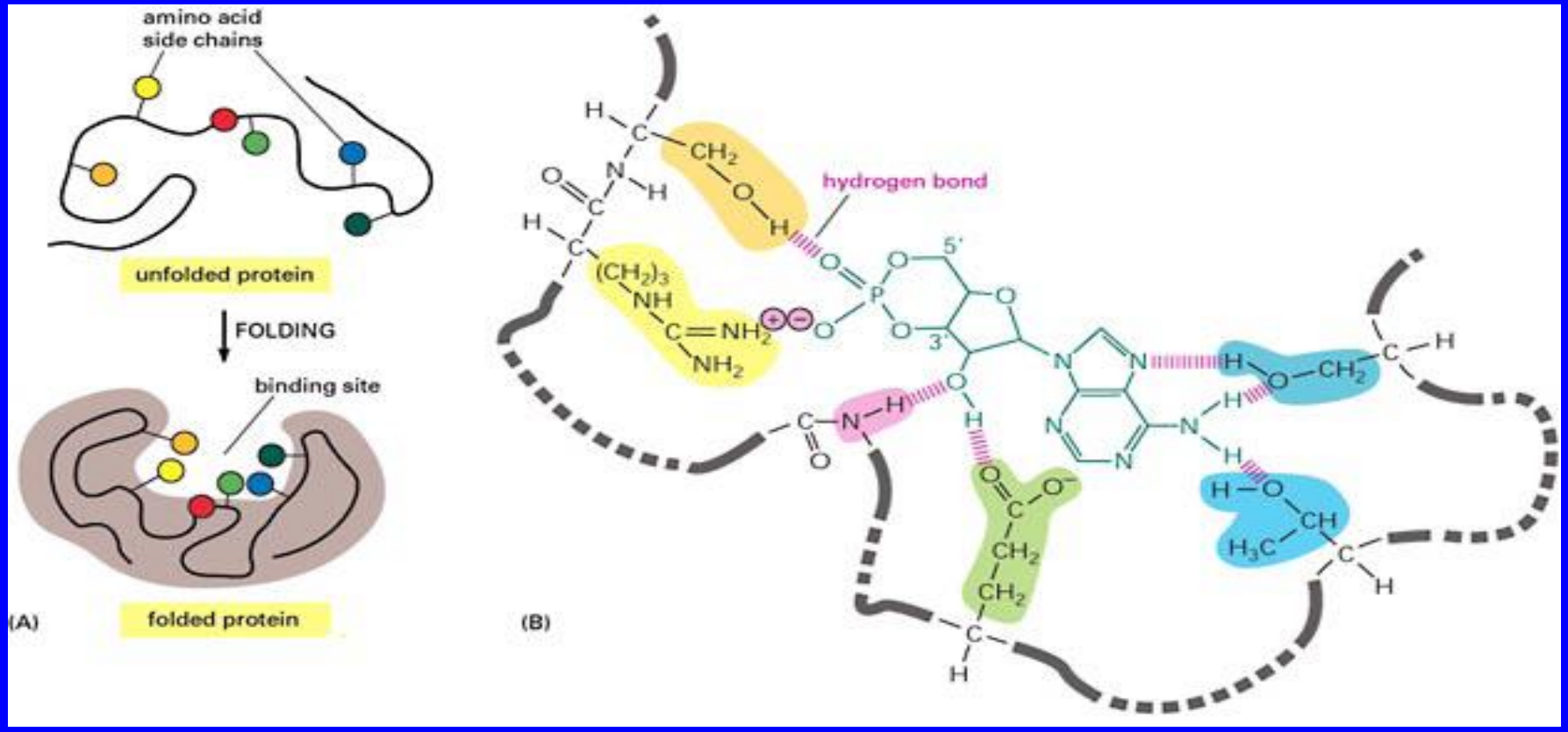
Induced-Fit Enzyme Model

- This model of enzyme action assumes that the enzyme active site is more a flexible pocket whose conformation changes to accommodate the substrate molecule



Theories to explain specificity of enzyme action

Induced- fit theory:



The enzyme change shape on the substrate binding

Next Week

Enzymology

3. Nomenclature and Classification of Enzymes.


Good Bye