Biochemistry Module For Medical Students
Lecture 8: Enzymes I
Introduction to Enzymology

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Learning Objectives:

The main objectives of this lecture are :

- **Identify nomenclature of Enzymes and their Classification.**
- **Define Co-enzymes, Isoenzymes and holoenzymes**
- **Describe the active site.**
- **Outline enzyme specificity and properties**

Enzymes:

Are biocatalysts, which are soluble proteins produced by living cells and are specific in their reaction.
It increases the rate of the reaction without being changed in the overall process.

Among the many biologic reactions that are energetically possible, enzymes selectively channel reactants (called substrates) into useful pathways.

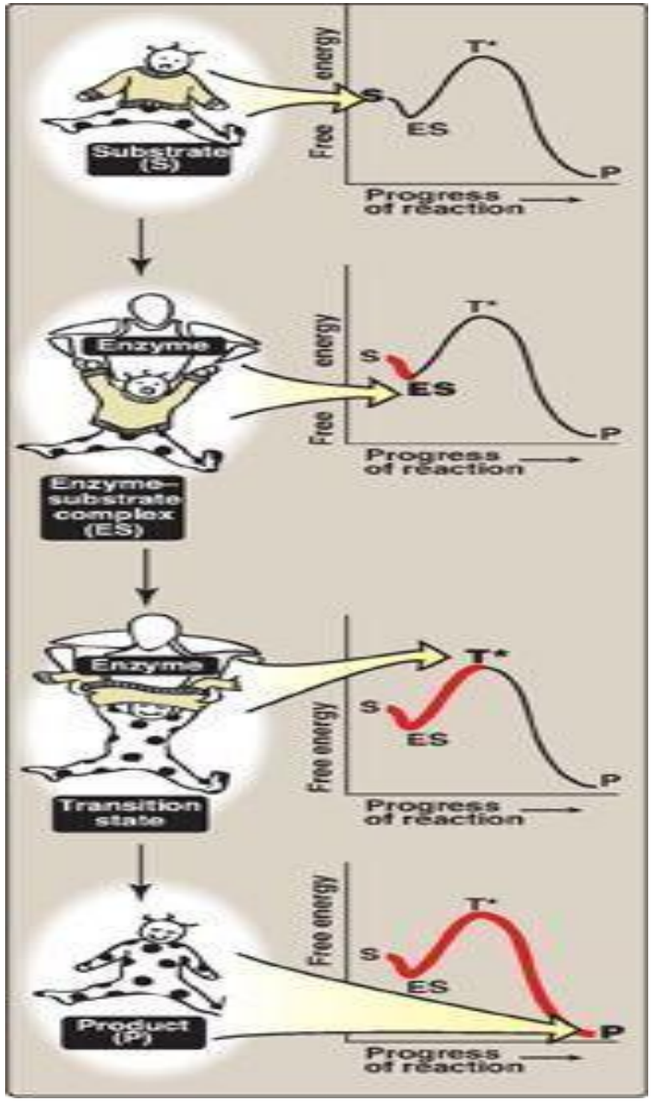


Figure 1: Schematic representation of energy changes accompanying formation of an enzyme-substrate complex and subsequent formation of transition state complex.

Nomenclature and Classifying of Enzyme:

A. Recommended names:

The compound on which an enzyme acts is called its substrate.

- **Many enzymes are naming by adding the suffix "-ase" to the name of the substrate. For the example (urease is the enzyme that catalyzed the hydrolysis of urea).**
- **Other enzymes have been named for the type of reaction they catalyzed. For example (lactate dehydrogenase catalyzed the oxidation of lactate to pyruvate.**
- **Some enzymes that have been known for a long time carry the names that were given by their discoverers. Trypsin and Pepsin are two examples.**

- **Some types of RNA can act like enzymes, usually catalyzing the cleavage and synthesis of phosphodiester bonds. RNAs with catalytic activity are called ribozymes.**

B. Systematic Name:

The International Union of Biochemistry and Molecular Biology (IUBMB) developed a system of naming in which enzymes are divided into six major classes according to the type of reaction catalyzed.

The EC numbers; each enzyme is described by a sequence of four numbers preceded by "EC", which stands for "Enzyme Commission".

The first number broadly classifies the enzyme based on its mechanism.

EC 1: Oxidoreductases: catalyze oxidation/reduction reactions.

EC 2: Transferases: transfer a functional group (e.g. a methyl or phosphate group)

EC 3: Hydrolases: catalyze the hydrolysis of various bonds.

EC 4: Lyases: cleave various bonds by means other than hydrolysis and oxidation

EC 5: Isomerases: catalyze isomerization changes within a single molecule

EC 6: Ligases: join two molecules with covalent bonds.

For example, hexokinase (EC 2.7.1.1) is a transferase (EC 2) that adds a phosphate group (EC 2.7) to a hexose sugar, a molecule containing an alcohol group (EC 2.7.1).

Properties of Enzymes:

A. Active sites:

Enzyme molecules contain a special pocket or cleft called the active site. The active site contains amino acid side chains that create a three-dimensional surface complementary to the substrate (Figure 2).

The active site binds the substrate, forming an enzyme - substrate (ES) complex. ES is converted to enzyme-product (EP), which subsequently dissociates to enzyme and product.

- **There are two models to explain how the binding of enzyme and substrate occurs:**
- **"lock and key" model**
- **"induced fit model " .**

Lock and key hypothesis:

This is the simplest model to represent how an enzyme works. The substrate simply fits into the active site to form a reaction intermediate.

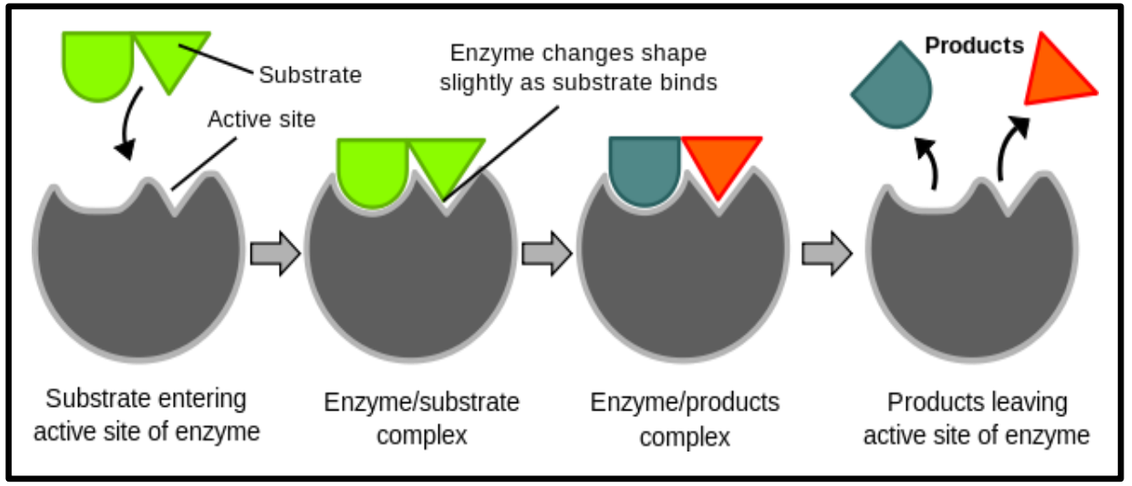


Figure 2: The active site of the enzyme.

Induced fit hypothesis:

In this model the enzyme molecule changes shape as the substrate molecules gets close. The change in shape is 'induced' by the approaching substrate molecule. This more model relies on the fact that enzyme molecules are flexible because single covalent bonds are free to rotate, Binding is thought to cause a conformational change in the enzyme (induced fit model) that allows catalysis.

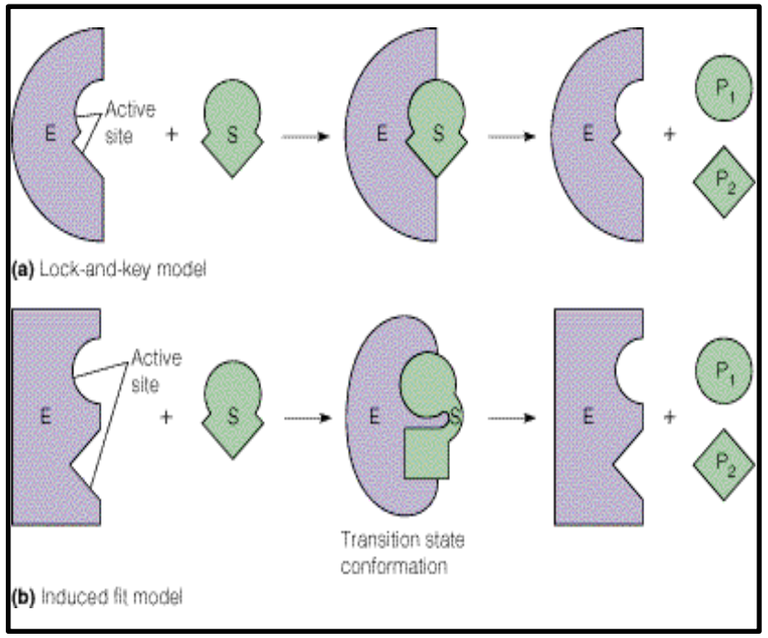


Figure 3: b- induce fit theory

B. Catalytic Efficiency:

Most enzyme-catalyzed reactions are highly efficient proceeding from 10^3 to 10^8 times faster than uncatalyzed reactions. Typically, each enzyme molecule is capable of transforming 100 to 1000 substrate molecules into product each second.

The number of molecules of substrate converted to product per enzyme molecule per second is called the turnover number.

C. Specificity:

Enzymes are highly specific, interacting with one or a few substrates and catalyzing only one type of chemical reaction.

D. Holoenzymes:

Some enzymes require molecules other than proteins for enzyme activity.

Holoenzyme refers to the active enzyme with its nonprotein component.

- **Whereas the enzyme without its nonprotein moiety (part) is termed an apoenzyme and is inactive.**
- **If the nonprotein moiety is a metal ion such as Zn^{2+} or Fe^{2+} it is called a cofactor.**
- **If it is a small organic molecule, it is termed a coenzyme. Coenzymes commonly are derived from vitamins. For example, NAD^{+} contains niacin (B3), and FAD contains riboflavin (B2), and coenzyme A contains pantothenic acid (B5).**
- **Cofactor and Coenzymes: are non-protein chemical species required by inactive apoenzymes (protein only) to convert themselves to active holoenzymes.**
- **In the absence of the appropriate cofactor, coenzyme the apoenzyme typically does not show biologic activity.**

Remember

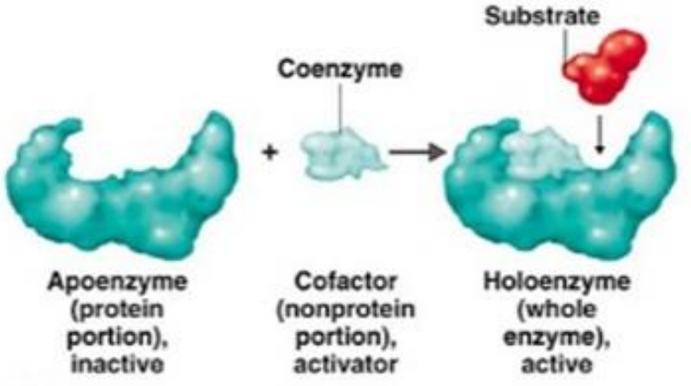
Holoenzymes

- Some enzymes require molecules other than proteins for enzymatic activity.
- The term **holoenzyme** refers to the **active** enzyme with its **nonprotein** component.
- The term **apoenzyme** is **inactive** enzyme without its **nonprotein** part.
- If the **nonprotein part** is a **metal ion** such as Zn 2+ or Fe2+, it is called a **cofactor**.
- If it is a **small organic molecule**, it is termed a **coenzyme.**

7

COENZYMES

- Coenzymes = organic (non-protein) molecule required for proper functioning of enzyme
- e.g. NAD^+, FAD^+, vitamin complexes
- Coenzymes often remove electrons from the substrate and pass them to other molecules



COFACTORS

- Cofactors = inorganic molecule required by enzyme for proper functioning of enzyme
- e.g. copper (Cu^+), zinc (Zn^{++}), iron (Fe^{++}), magnesium (Mg^{++}), potassium (K^+), and calcium (Ca^{++}) ions
- The cofactors bind to the enzyme and participate in the reaction by removing electrons, protons , or chemical groups from the substrate.

- **ApoEnzyme = Inactive Enzyme**
- **HoloEnzyme = Active Enzyme**

CoENZYMES and CoFactors function

A coEnzyme/coFactor prepares the active site for catalytic activity.

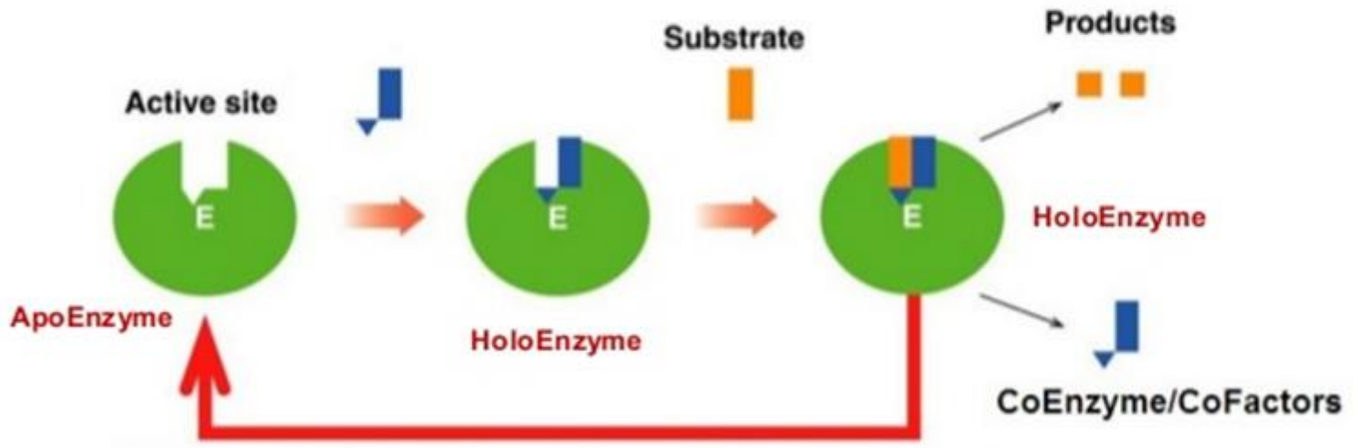


Figure 4:Coenzymes & cofactors

- **Prosthetic group and coenzyme are two types of helper molecules of enzymes. The key difference between prosthetic group and coenzyme is that prosthetic group tightly binds with the enzyme to assist enzyme while coenzyme loosely binds with an enzyme to support its catalytic function. Prosthetic groups can be organic molecules or metal ions while coenzymes are totally organic molecules.**

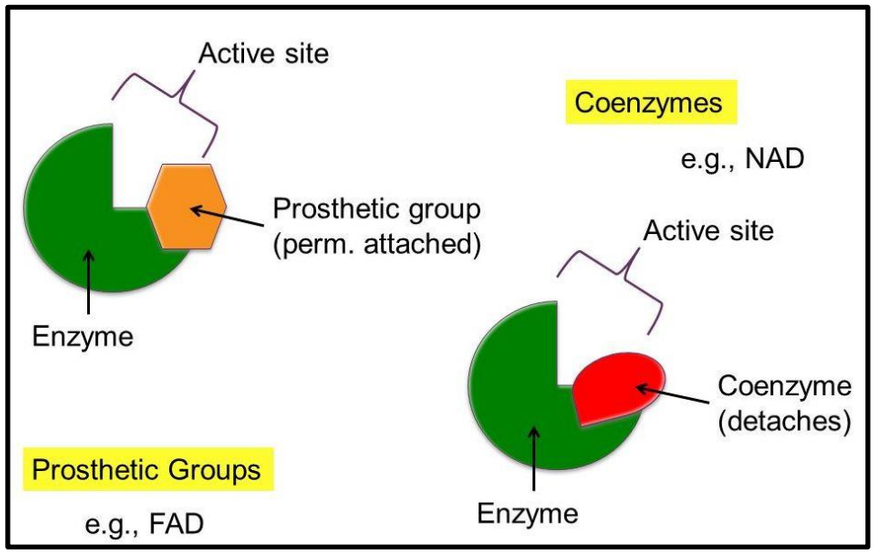


Figure 5

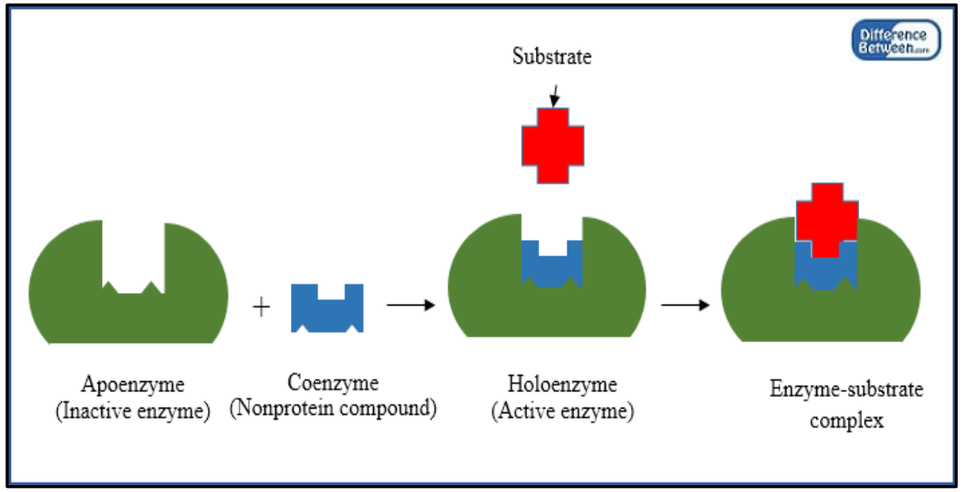
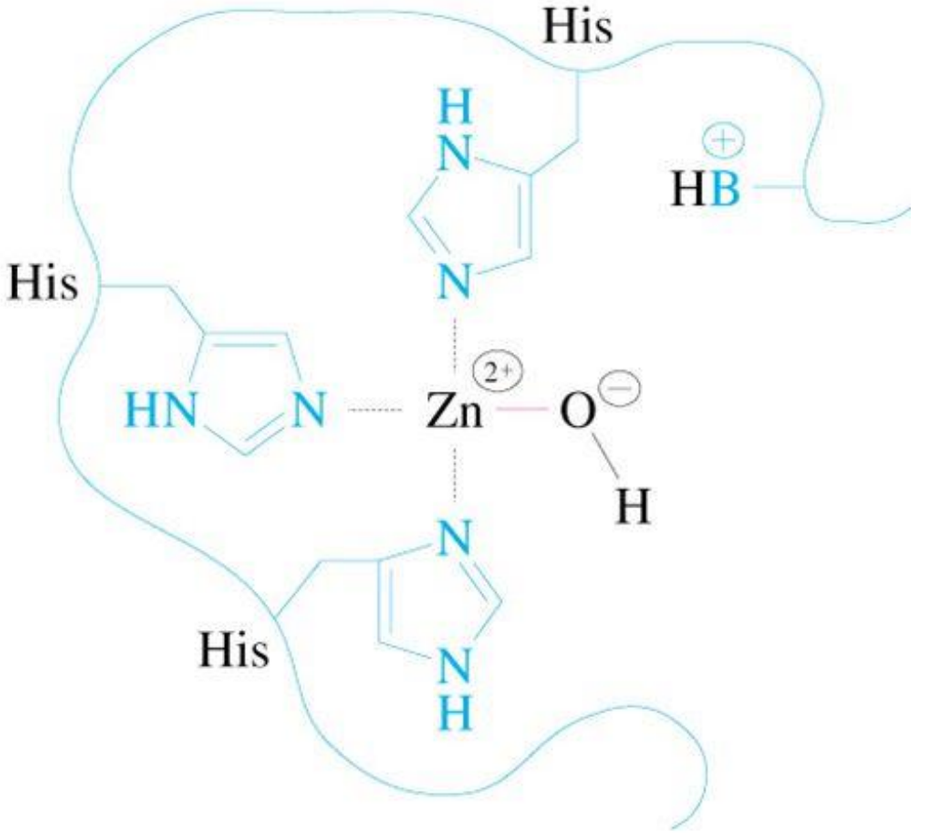


Figure 6

Example of prosthetic group

Metalloenzymes contain firmly bound metal ions at the enzyme active sites (examples: iron, zinc, copper, cobalt).



Example of metalloenzyme: **carbonic anhydrase contains zinc**

E. Isoform (Isoenzymes):

A group of enzymes that catalyze the same reaction but differ from each other in their structure, substrate affinity, and regulatory properties. Present in different tissues of the same system, or subcellular components of the same cell.

For e.g. : there are five isoenzymes for lactate dehydrogenase (LDH1 – LDH5, figure 5). It is Tetramer consist from [M subunits (M for muscle)] and [H subunits (H for heart)]. It has different catalytic activities. Used as the marker for disease diagnosis.

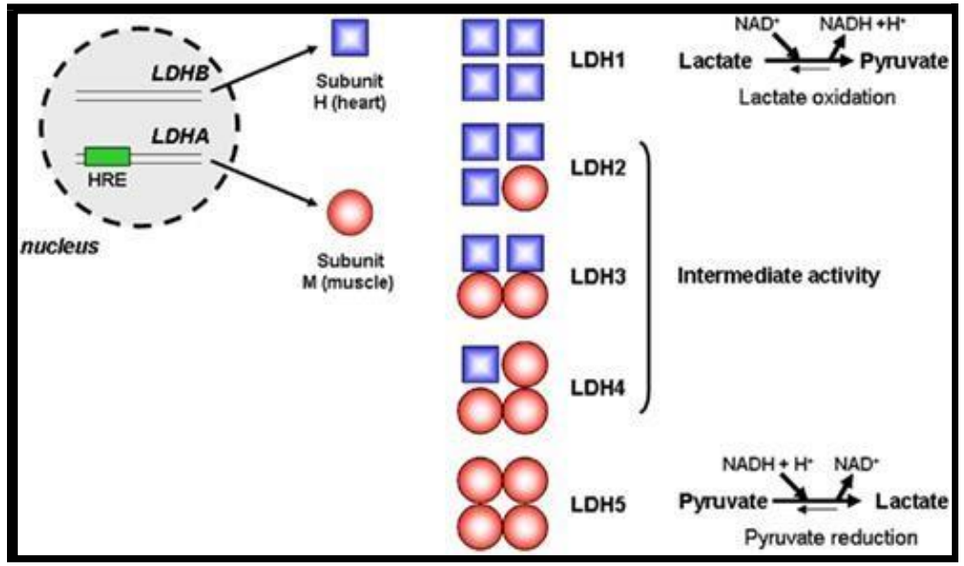


Figure 7: Isoforms of LDH.

G. Intracellular and Extracellular Enzymes (Endoenzymes and Exoenzymes):

Enzymes which are used in the cells which produce them are called as intracellular enzymes.eg: all metabolic enzymes.

Enzymes which are produced by cells and are used to the other part of the body are called as extracellular enzymes. E.g.: enzymes of digestive juices.

F. Regulation:

Enzyme activity can be regulated, that is, enzymes can be activated or inhibited, so that the rate of product formation responds to the needs of the cell.

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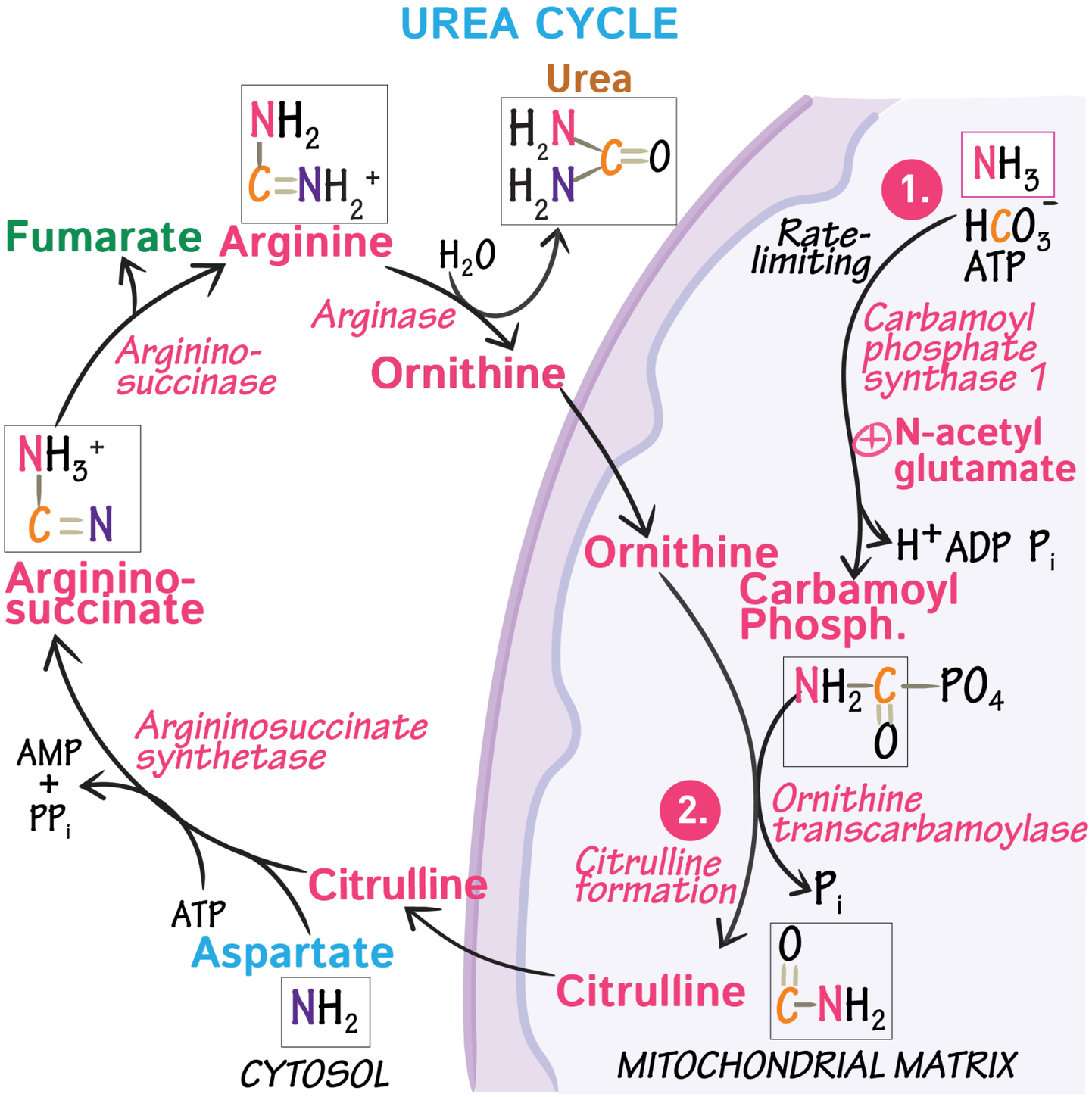
UREA CYCLE
Urea
Fumarate
Arginine
Arginase
Ornithine
Arginino-succinase
Arginino-succinate
Argininosuccinate synthetase
AMP + PPi
ATP
Aspartate
Citrulline
CYTOSOL
1.
Rate-limiting
NH3
HCO3−
ATP
Carbamoyl phosphate synthase 1
⊕N-acetyl glutamate
H+ ADP Pi
Carbamoyl Phosph.
Ornithine
2.
Citrulline formation
Ornithine transcarbamoylase
Pi
Citrulline
MITOCHONDRIAL MATRIX

H. Zymogen (proenzyme) :

There are extracellular enzymes secreted in an “inactivated” form (zymogen form) and activated by other agent secreted by other cells e.g. Pepsinogen (inactive form), it is activated to form active pepsin. Trypsinogen (inactive form), it is activated to form active trypsin.

I. Zymase reaction:

The extracellular enzyme when secreted and ready for action is called zymase reaction. e.g. : salivary α-amylase.

Evaluation and Assessment:

After reading your lecture try to answer these questions:

1- Define Enzymes?

2- Explain Holoenzyme , Apoenzyme , Cofactors and coenzymes.

3- What are Isoenzymes?

4- What is active site of enzyme and the theories that involved in binding substrate with enzyme?

5- What are intracellular and extracellular Enzymes?

GOOD LUCK