بسم الله الرحمن الرحيم

BioChemistry | FINAL 9

Enzymes pt.1

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ENZYMES

Enzymes are involved in all chemical reactions in our body; their appearance has many advantages such as speeding up the reactions.

General properties of proteins

- The function of nearly all proteins depends on their ability to bind other molecules (ligands)
- Two properties of a protein characterize its interaction with ligands:

  - **Affinity: the strength of binding between a protein and other molecule**

    Higher Affinity = Higher binding Strength
    Lower Affinity = Lower binding Strength

  - **Specificity: the ability of a protein to bind one molecule in preference to other molecules**

    It is a scale of binding; this means how much are the two molecules prefer to make bonds between each other. So, if we have 2 materials (A+B) , if A binds with a lot of molecules other than B this means we have a low specificity, but if it binds with only B molecules here, we will have a high specificity case.

Important Note :
If material A has a high specificity to material B, that doesn't mean that they have a high affinity or a high strength of binding between each other. However, usually the materials that have a high specificity they also have a high affinity, but IT IS NOT A MUST.

Are enzymes important?

Enzymes must undergo configurational changes to perform their job.

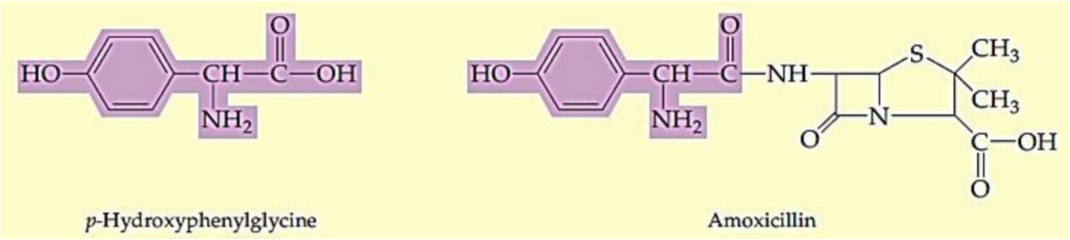
- In the human body, almost every metabolic process involve the use of enzymes

Sucrase : An enzyme is responsible for breaking down sucrose in the chocolate which gives its texture.

Tea leaves are rich with polyphenols, when we expose them to oxygen, the enzyme polyphenoloxidase will reacts with polyphenol to give us tannins, which have the black color and the special taste of the black tea.

crushed leaves are exposed to the oxygen in air, a polyphenoloxidase breaks up polyphenols into tannins which impart the darker color and characteristic flavors

Sucrose (table sugar), yeast enzyme breaks sucrose into its two smaller sugar quantities



Amoxicillin is the most famous antibiotic.

The Biological Catalysts; Enzymes

They are not only proteins, but RNA can also be an Enzyme

- **What are enzymes? (specialized proteins, small amounts, acceleration, no change). Ribozymes are the exception**
- **Enzymes are the most efficient catalysts known**
  - **Usually in the range of 10^6 to 10^{14}**
  - **Non-enzymatic catalysts (10^2 to 10^4)**
  - **The actions of enzymes are fine-tuned by regulatory processes**
- **Examples: catalase (10^8) & carbonic anhydrase (10^7)**

Enzymes can catalyze so many reactions in our body, which means they are not consumed in the reactions

	Activation Free Energy		
Reaction Conditions	**kJmol^{-1}**	**kcal mol^{-1}**	**Relative Rate**
No catalyst	75.2	18.0	1
Platinum surface	48.9	11.7	2.77×10^4
Catalase	23.0	5.5	6.51×10^8

$$CO_2 + H_2O \xrightleftharpoons{\text{Carbonic anhydrase}} H_2CO_3$$

$$2\,H_2O_2 \xrightleftharpoons{\text{Catalase}} 2\,H_2O + O_2(g)$$

We can see the huge difference in the rate; catalase can speed up the reaction by 100 million times by that the activation energy will decrease

The Biological Catalysts; Enzymes

➢ **Enzymes are everywhere in our body; they have so many special things :**

1 – Specialized Proteins, but not all enzymes are proteins, why ? Researchers found that we have RNA molecules that can function like enzymes.

2 – They are biological molecules that are found in low and stable concentrations, they are useable after the reaction is over. During the reaction, enzymes must undergo configurational changes to perform the job, otherwise if they stay without any changes their existence is useless.

3- They are biological catalysts that accelerate chemical reactions by reducing activation energy, "biological" means that their function will only be found in living things.

4- Enzymes can accelerate and catalyze so many reactions, this means they will not be consumed during the reactions, but their function as we said requires a configurational changes (binding between the enzyme and molecules).

5 – All chemical reactions happens to be stable and to start the reaction collisions between reactant's molecules must occur.

How to express an enzymatic reaction?

- In enzymatic reactions, reactants are known as substrates
- We can simply express an enzymatic reaction using this formula

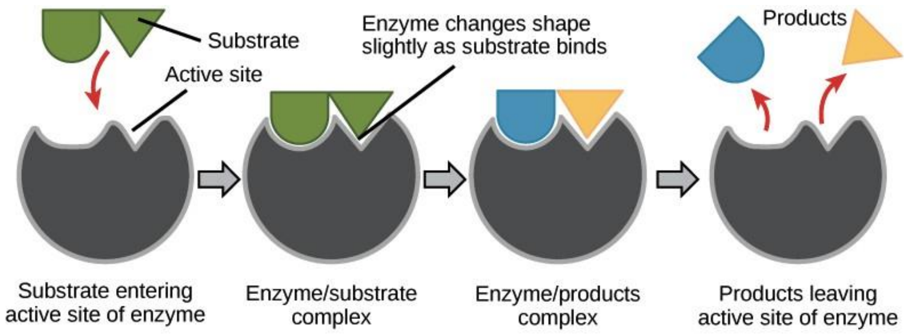
$$E + S \rightleftharpoons ES \rightleftharpoons EP \rightleftharpoons E + P$$

Or

$$E + S \rightleftharpoons ES \rightleftharpoons E + P$$

In the complexes ES & EP there are no free enzymes

where E is the free enzyme; S is the free substrate, ES is the enzyme-substrate complex; P is the product of the reaction; and EP is the enzyme-product complex before the product is released



Enzymes and Chemical Reactions

Chemical reactions can be classified as either exergonic (energy-releasing) or endergonic (energy-consuming).

To illustrate this: imagine standing on a table and then moving down to the ground. On the table, your energy level is higher, while on the ground, it is lower. Moving down releases energy. However, you cannot simply jump from the ground back onto the table without additional effort—this is because you are dealing with materials that are already stable.

Even stable molecules still tend to move toward an even more stable state. If all exergonic reactions had only one spontaneous direction to follow, then every reaction would already be completed, and all substances would already exist in their final, most stable form (the product stage).

The energy barrier is the amount of energy required to push a stable molecule into an unstable, high-energy condition known as the transition state. From this transition state, the molecule can either proceed forward to form products or fall back into the stable reactants.

Reactions occur through the breaking and formation of chemical bonds, which requires energy input to the reactants. Without enzymes, this energy comes from kinetic energy generated by molecular collisions. These collisions are random, and in most cases, they do not provide enough energy to reach the transition state—therefore, products are not formed. In the absence of enzymes, to accumulate a noticeable amount of products, the only factor available is time.

It is important to note that enzymes do not cause reactions to occur; reactions can still happen without them. Instead, enzymes decrease the activation energy needed for the reaction to proceed. Thus, the main difference is the rate of the reaction. For example, if a reaction in the absence of enzymes requires 10,000 years to fully consume all reactants (as is the case with many biochemical reactions in the body), the presence of enzymes can speed it up dramatically to occur within seconds or less.

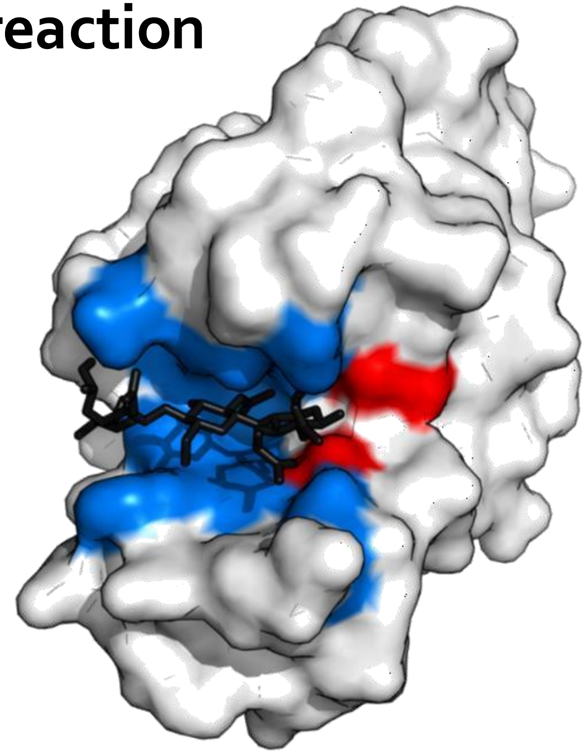
To measure the energy levels of substrates and products, we use units such as Joules or kilojoules per mole (J/kJ per mol), or calories/kilocalories per mole (cal/kcal per mol).

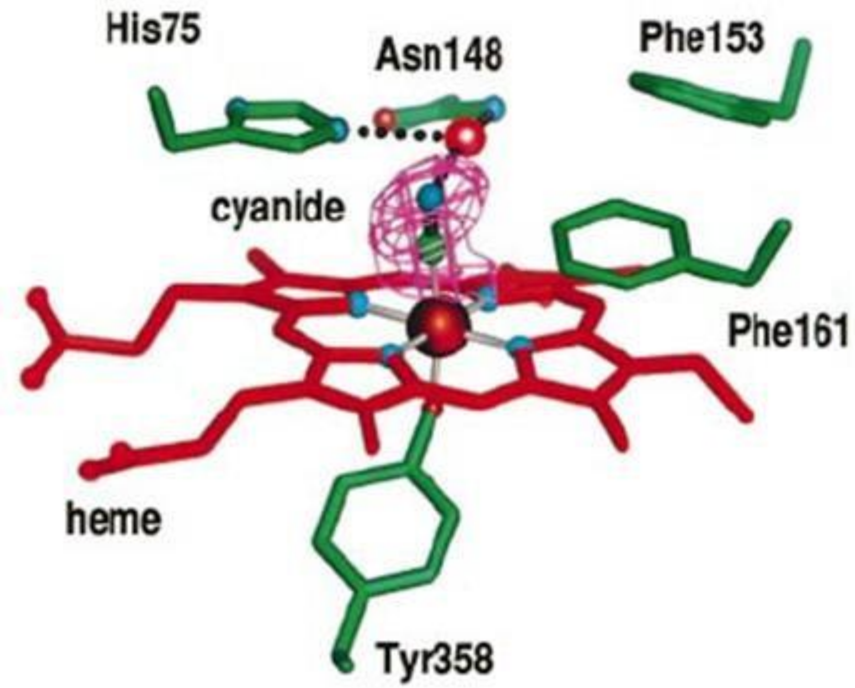
For instance, if a reaction has a $\Delta G = -60$ kcal/mol at 25°C, the value of ΔG remains unchanged whether or not an enzyme is present. Enzymes do not alter the energy difference between reactants and products; they only affect the pathway by lowering the activation energy.

In kinetics, if we assign a relative rate of "1" to an uncatalyzed reaction and we can compare it to a catalyzed one we notice that the rate is hugely increased. For example, the enzyme catalase can convert about 10^8 molecules of hydrogen peroxide (H_2O_2) into water and oxygen per second, showing how powerfully enzymes can accelerate reactions.

Active sites of enzymes

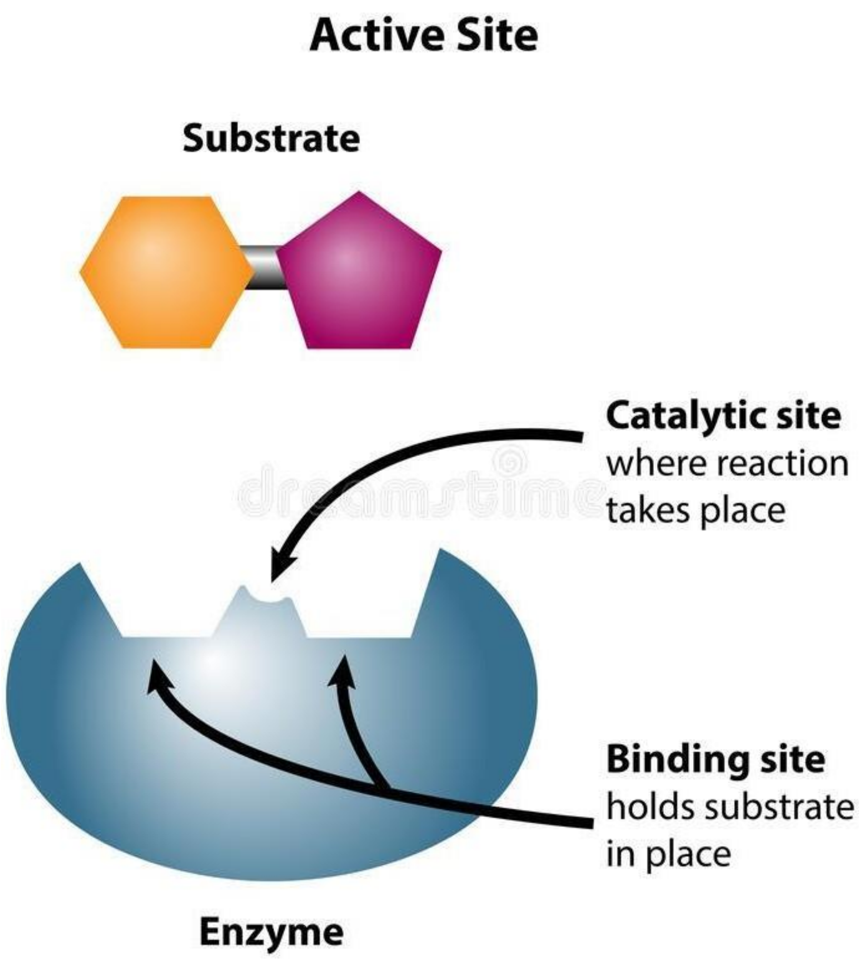
- A specific <u>three-dimensional shape</u> which includes a region where the biochemical reaction takes place
- Contains a <u>specialized amino acid sequence</u> that facilitates the reaction





Active sites of enzymes

- Within the active site are two sub-sites, the binding site and the catalytic site, The binding & catalytic site may be the same
- Binding site: binds substrate through ionic, H-bonding or other electrostatic forces, or hydrophobic interactions
- Catalytic site: contains the catalytic groups



Not all proteins act as enzymes.
Why?? Because many proteins lack an active site.

The Active Site: The specific region of an enzyme where the substrate binds.

Example:

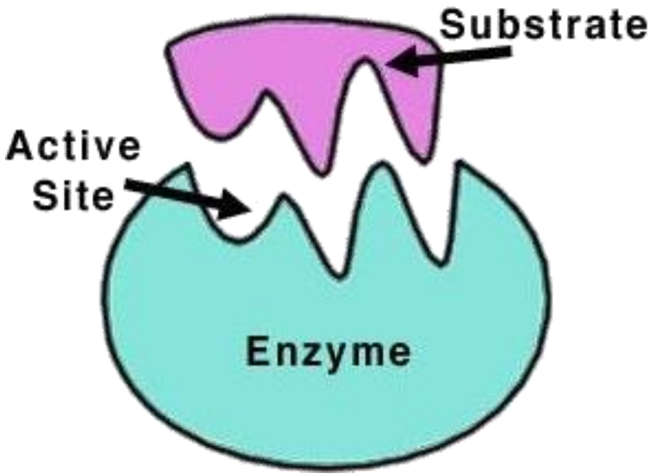
Hemoglobin and Myoglobin VS Catalase

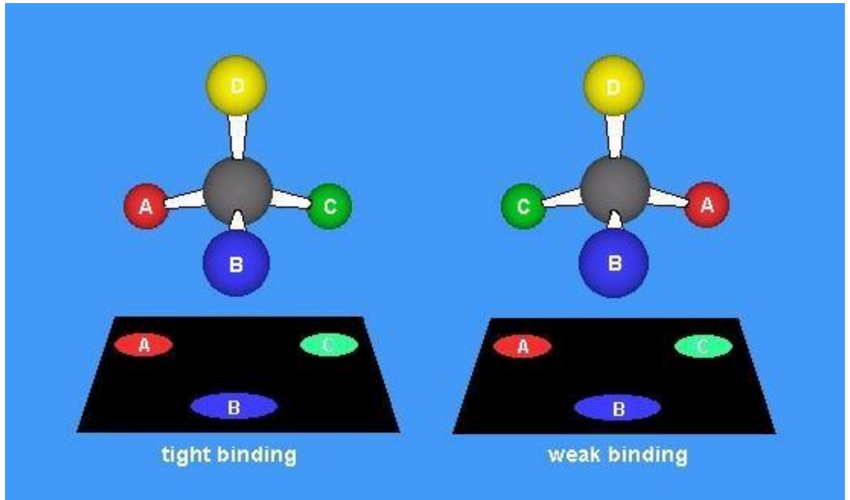
Hemoglobin and Myoglobin	Catalase
•Both contain heme groups.	•Also contains a heme group.
•In these proteins, the heme binds and releases oxygen as it is.	•In this case, the heme binds hydrogen peroxide (H_2O_2).
•No chemical reaction is catalyzed.	•Here, the heme catalyzes a reaction, converting H_2O_2 into water and oxygen.

Why does the heme function differently in these cases?
- For a protein to act as an enzyme, its active site must have specific properties.
- These properties of the active site are what allow the protein to function as an enzyme.

Features of active site

- Active sites; structures that look like <u>canals, clefts or crevices</u>
- <u>Water is usually excluded</u> after binding unless it participates in the reaction
- Substrates are bound to enzymes by <u>multiple weak attractions</u> (electrostatic, hydrogen, van der Waals, & hydrophobic)
- Binding occurs at least at <u>three points (chirality)</u>





Features of active site

Location and Structure:

- The **active site** is usually embedded within the protein, not on the surface.
- It forms a canal, crevice, or pocket-like structure, providing space for substrate binding.

- This pocket is lined by amino acids, with their side chains projecting into the space.

- The amino acids appear in a random sequence, not ordered by type.

- The active site is very small compared to the overall size of the enzyme.

Features of active site

Specificity of Binding:

•Substrate binding occurs at at least three contact points between the substrate and the active site.

•This multi-point recognition allows enzymes to distinguish between different isomers (e.g., D vs. L forms).

•If two substrates only matched at two points, they would be considered isomers of each other.

Chemical Nature of Active Site Amino Acids:

- Amino acids in the active site are mainly hydrophilic (polar), which allows them to form hydrogen bonds and ionic interactions with the substrate, facilitating binding and catalysis. However, nonpolar residues can also be present; they interact with hydrophobic parts of the substrate through van der Waals forces and help maintain the structural stability of the active site.

Features of active site

Functional Regions:

•If the active site is large enough, it may have two distinct regions:

1. Binding site → holds the substrate
2. Catalytic site → performs the chemical transformation

Nature of Substrate–Enzyme Binding:

•Binding between substrate and active site must be weak (noncovalent interactions).

•This ensures that the product can be released after the reaction.

•If binding is covalent, the material is usually a toxin, poison, or inhibitor, not a normal physiological substrate.

Why is the overall three-dimensional structure of an enzyme necessary for its catalytic activity, even though substrate binding occurs at the active site?

Role of the Rest of the Protein Structure:

- The protein's structure stabilizes the active site.

- Stability is important because the specific shape and affinity of the active site must be maintained.

- Without this support, small changes could reduce specificity, although not enough to destroy enzyme identity.

- The overall structure also allows the enzyme to recognize other molecules that bind outside the active site and cause conformational changes:

- Positive change → activation
- Negative change → inhibition

For any feedback, scan the code or click on it.

Corrections from previous versions:

Versions	Slide # and Place of Error	Before Correction	After Correction
V0 → V1			
V1 → V2			

رسالة من الفريق العلمي:

أَحبابُنا في جِنانِ اللهِ قد نعموا

لقد شقينا بهم لكنَّهم سَعِدوا

تألَّقوا في سماءِ المجدِ ما خَمَدَتْ

رغم العواصفِ ذِكراهُم وما خَمَدوا

رُوحُ الشَّهيدِ بنورِ اللهِ ما هَمَدتْ

لَبِّثْ قليلاً تَرَ الظُّلَّامَ قد هَمَدوا...

خُصُّوا أهلَنا في القطاعِ وفي سائرِ بلادِ الإسلامِ بحثيثِ الدُّعاءِ