ENZYMES (1)

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Topics of the lecture

General properties of proteins

- Affinity: the strength of binding between a protein (or any molecule) and other molecule
- Specificity: the ability of a protein to bind one molecule in preference to other molecules, the ability to bind to more different molecules is inversely related with the Specificity

Applications of enzymes

-Human body
-Black tea
-Candy
-Chocolate
-Amoxicillin
-Meat
-Others

The biological catalysts; enzymes

Enzymes: Biological catalysts that are made mostly of proteins, they accelerate the reaction without being change at the end of it, and they are found in small amounts in the living organism.

Enzymes are the most efficient catalysts known in the nature.

express an enzymatic reaction

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

Or

$$E + S \leftrightarrows ES \leftrightarrows E + P$$

Active sites of enzymes

Active site: specific three-dimensional shape which includes a region where the biochemical reaction takes place.

Features:
1. look like canals, clefts or crevices
2. made of multiple secondary structures
3. small compared to the whole enzyme
4. Binding occurs at least at three points
5. The active site contains two sub-sites: the <u>binding site</u> and the <u>catalytic site</u>
6. Water is removed after binding unless it participates in the reaction

How do enzymes work

1) Lock and key model (old): this model adopt the idea of having 100% complementarity between the active site and the substrate

2) The induced fit model (new): this model adopt the idea of having 100% complementarity between the active site and the substrate **<u>that is induced after binding</u>**

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 (or any molecule) and other molecule

Specificity: the ability of a protein to bind one molecule in preference to other molecules, the ability to bind to more different molecules is inversely related with the Specificity

- The more the Specificity toward a certain molecule, the more the affinity usually

applications of enzymes

- Human body: almost every metabolic process involves the use of enzymes (s0 we can't live without enzymes).
- Black tea: it's derived from green tea by the enzyme polyphenoloxidase which breaks the polyphenol molecule into tannis in the presence of oxygen
- Candy: we add on candy a substance that's called "corn syrup" which is cheap and made by enzymes, it gives the candy it's sweat taste and cohesive structure
- Chocolate: we make it softer for sandwich by adding "sucrase" which breaks "sucrose" sugar into smaller sugars.
- Amoxicillin: The most famous antibiotic in the world, it's made by enzymes
- Meat: we add "pectinases" and "proteases" to break the proteins and make smaller molecules more soluble, so the meat become softer
- Others: The solution of contact lenses / labs / laundry detergents

The biological catalysts; enzymes

- Enzymes: **Biological catalysts** that are **made mostly of proteins**, they accelerate the reaction **without being change at the end of it**, and they are **found in small amounts** in the living organism.

Biological: they're found in living organisms, so they aren't chemical catalysts
catalysts: They speed the reaction, so they increase products per unit of time
made mostly of proteins: We said "mostly" because there are some enzymes that are made of RNA, we call them "Ribozymes"
without being change at the end of it: we said "at the end" because the enzyme change inside the reaction as they bind strongly to the substrate, but at the end of the reaction, the enzyme will be the same as the beginning in all it's characteristics such as shape, amount ..etc.
found in small amounts: Because they aren't consumed (hormones are also found in small amounts)

The biological catalysts; enzymes

- Enzymes are the most efficient catalysts known in the nature

$$2\,H_2O_2 \xrightleftharpoons{\text{Catalase}} 2\,H_2O + O_2(g) \qquad CO_2 + H_2O \xleftrightarrow{\text{Carbonic anhydrase}} H_2CO_3$$

↑ (10^8) ↑ (10^7)

- If we compare enzymatic and non-enzymatic catalysts:
  - Enzymatic catalysts Usually in the range of **10^6** to **10^{14}**
  - Non-Enzymatic catalysts Usually in the range of **10^2** to **10^4**

E.g. →

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

How to express an enzymatic reaction?

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

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

Or

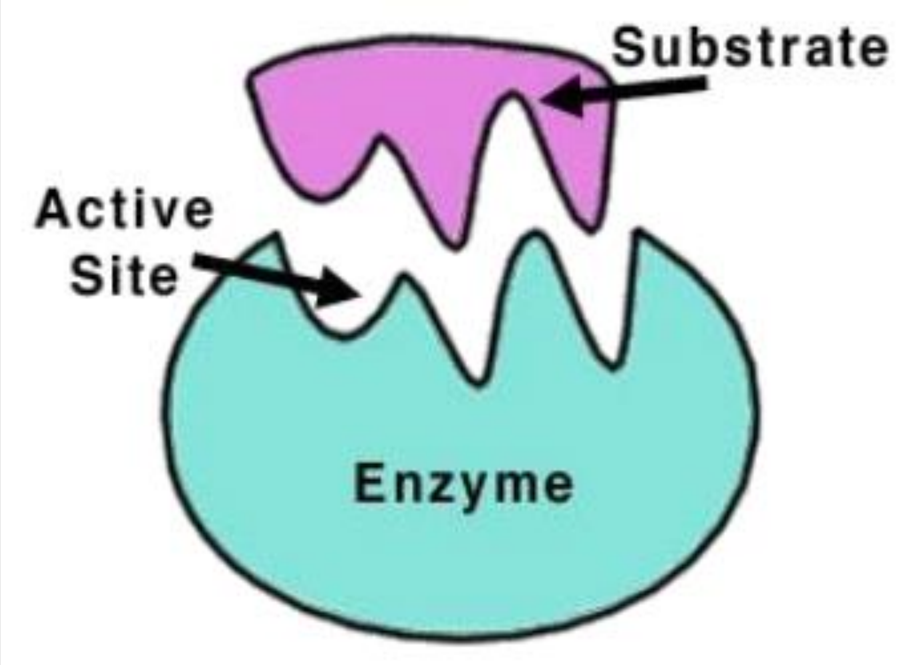
$$E + S \leftrightarrows ES \leftrightarrows E + P$$

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

Note: when the affinity (strength of binding) between the enzyme and the reactant increases, the reaction become faster

Active sites of enzymes

- specific three-dimensional shape which includes a region where the biochemical reaction takes place.



Active sites of enzymes

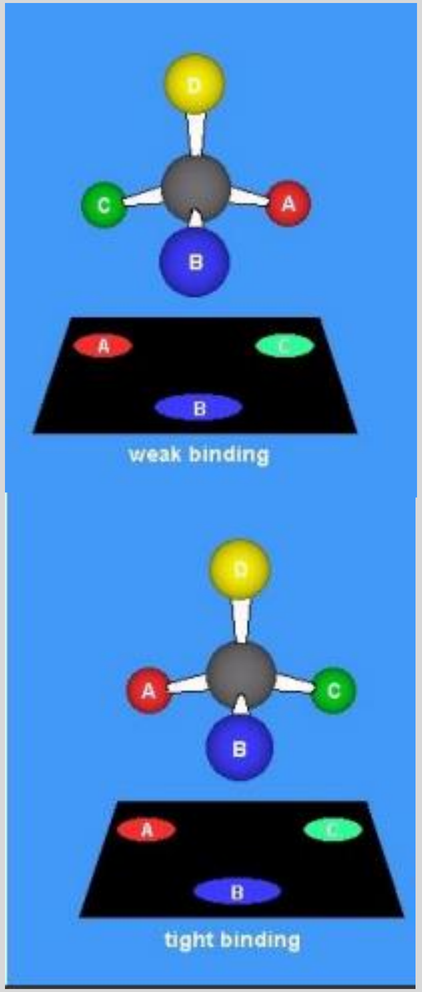
- Features of the active site:
  1. they look like canals, clefts or crevices, they're not flat surfaces, so when the substrate attach to the active site, the active site enclose on and does it's function better
  2. Formed by groups from different parts of the amino acid sequence usually forming a domain made of multiple secondary structures
  3. Takes up a relatively small part of the total volume of the enzyme (why?)
  Answer: you need to know first that the active site can change it's conformation easily as it's a protein and this is important for it's function (that's why it's neither a carbohydrate nor a lipid)
  We need to change the conformation in **a specific way** when we the reaction is going on only not all the time , and this is achieved and regulated by the rest of the enzyme which support the active site at the reaction
  Note: it can also be a regulatory site where an inhibitor or an activator binds, they work by changing the conformation also

Active sites of enzymes

4. Binding occurs at least at three points (chirality), this shows that enzymes are greatly specific to their substrates
- Enzymes differentiate between different isomers, so if it catalyzes the reaction for D- isomer it won’t catalyze the reaction for L- isomer (it won’t catalyze the reaction for both enantiomers)

- Enzymes have different degrees of this specificity (certain enzymes only accept one certain reactant, other enzymes can take 2 or 3 different substrates at the same time and others can take them at different times)

e.g. catalase only react with H_2O_2 as a reactant while glucokinase reacts with glucose and ATP at the same time, and in a different sets it can reacts with fructose and ATP.

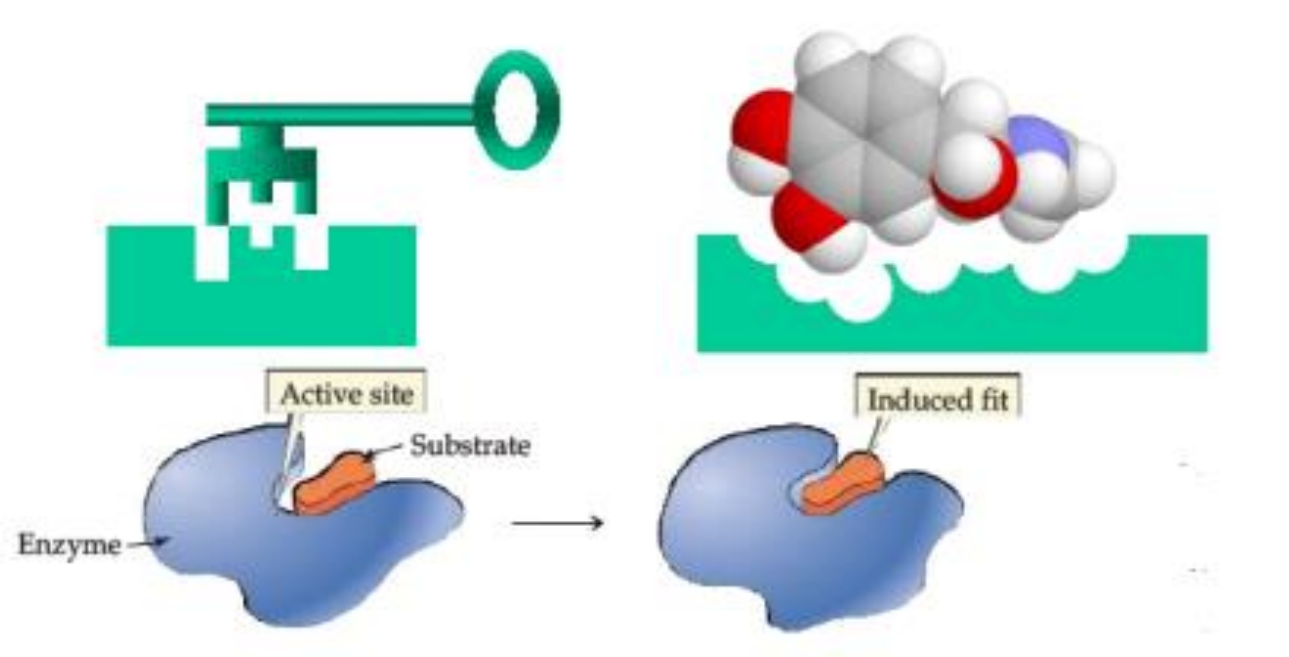


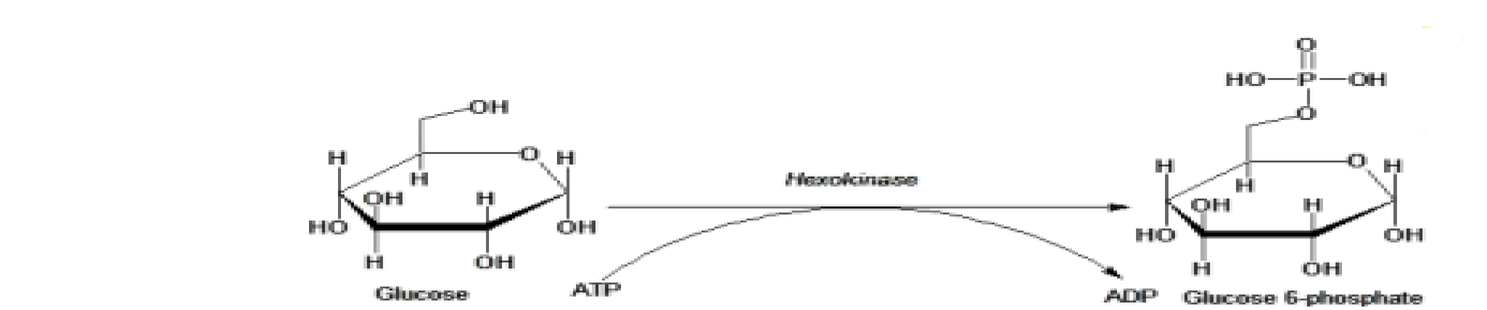
Active sites of enzymes

5. The active site contains two sub-sites: the binding site and the catalytic site (They may be one domain if the active site is small)
Catalytic site: contains the catalytic groups (e.g. Asp-Ser: polar ï they interact as H/electrons donor or acceptor ï responsible of catalysis)
Binding site: binds substrate through multiple weak bonds (such as ionic, H-bonding , electrostatic, van der Waals, & hydrophobic bonds), but not covalent bonds (e.g. Phe: hydrophobic ï responsible of binding)
Any material binds initially the active site covalently, it will be either a toxin, poison, nerve gas or drug act as a covalent inhibitor, and it is not physiological. Why? Because if the interaction is covalent, the substrate can't leave the enzyme, so I can't use the enzyme again

6. Water is usually excluded after binding unless it participates in the reaction

How do enzymes work? (from a theoretical point of view)





How do enzymes work? (from a theoretical point of view)

- 1) Lock and key model (old): this model adopt the idea of having 100% complementarity between the active site and the substrate
  it’s not accepted any more because:
  a. enzymes are proteins and proteins are not static in solutions
  b. enzymes can have more than one substrate (e.g. glucokinase binds glucose and binds ATP, and in different conditions it binds fructose with ATP)
- 2) The induced fit model (new): this model adopt the idea of having 100% complementarity between the active site and the substrate **<u>that is induced after binding</u>**