بسم الله الرحمن الرحيم

BIOCHEMISTRY

DOPAMINE
SCIENTIFIC TEAM

﴿ وَإِن تَتَوَلَّوۡاْ يَسۡتَبۡدِلۡ قَوۡمًا غَيۡرَكُمۡ ثُمَّ لَا يَكُونُوٓاْ أَمۡثَٰلَكُم ﴾

اللهم استعملنا لنصرة دينك

Lecture 24

Enzymes I - Introduction

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THE SCIENTIFIC TEAM OF DOPAMINE
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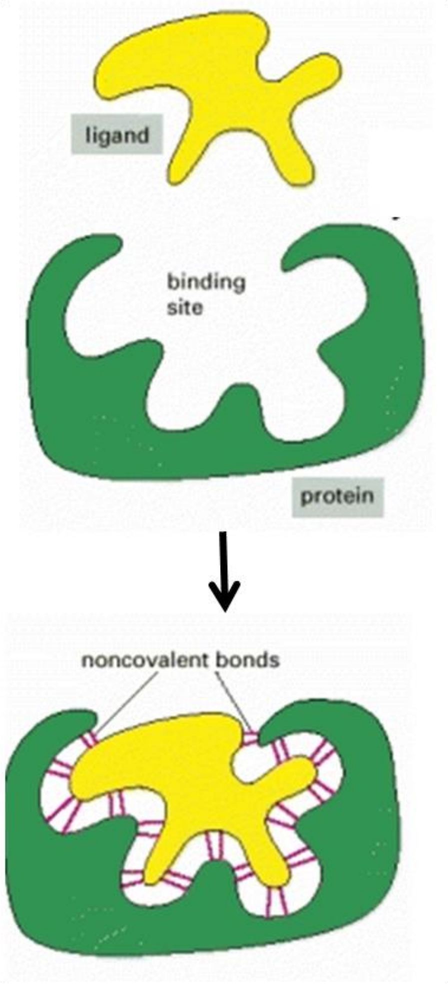
0501113-L24

General properties of proteins

- The function of proteins depends on their ability to bind other molecules (ligands).
  - Ligand: a substance that forms a complex with a biomolecule, usually via non-covalent interactions, to serve a biological purpose.



- Two properties of a protein characterize its interaction with ligands:
  - Affinity: the strength of binding between a protein and other molecules. Interactions are usually non-covalent. The higher the affinity the stronger the interaction and the stronger the effect.
  - Specificity: the ability of a protein to bind one molecule in preference to other molecules.

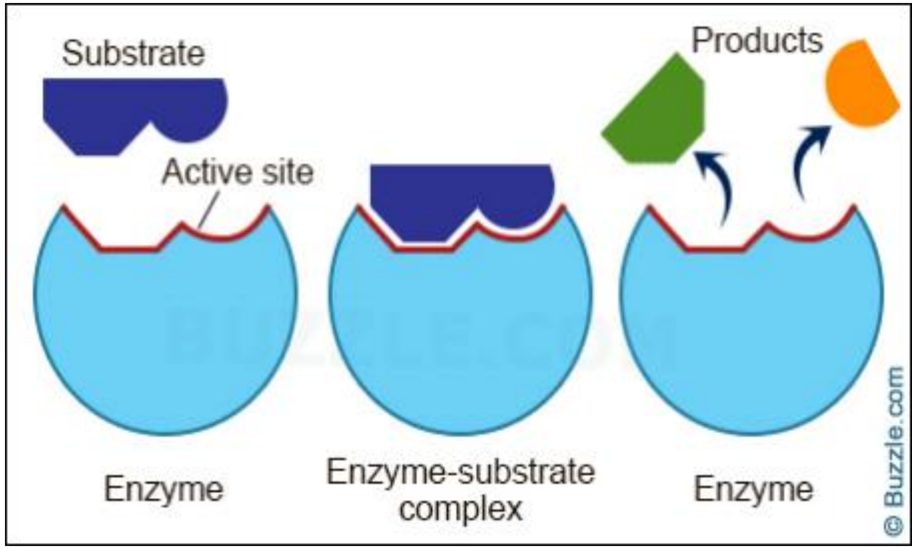
Albumin is an exception, as it interacts with many molecules.

What are enzymes?

- Enzymes: Specialized **proteins** that accelerate (catalyze) chemical reactions under biological conditions.
  - Exception: ribozymes (*to be discussed*) RNA Molecules
  - In enzymatic reactions, reactants are known as substrates.

- Most enzymes have very specific functions in converting specific substrates to products.
- Enzymes are catalysts.
  - They exist in small amounts relative to the reactants.
  - They increase the rate of a reaction.
  - At the end of the reaction, they do not change.

Hypothetically, if a cell produces few enzymes compared to normal, there'd be no disease symptoms because one enzyme molecule catalyzes a huge number of reactions per second.



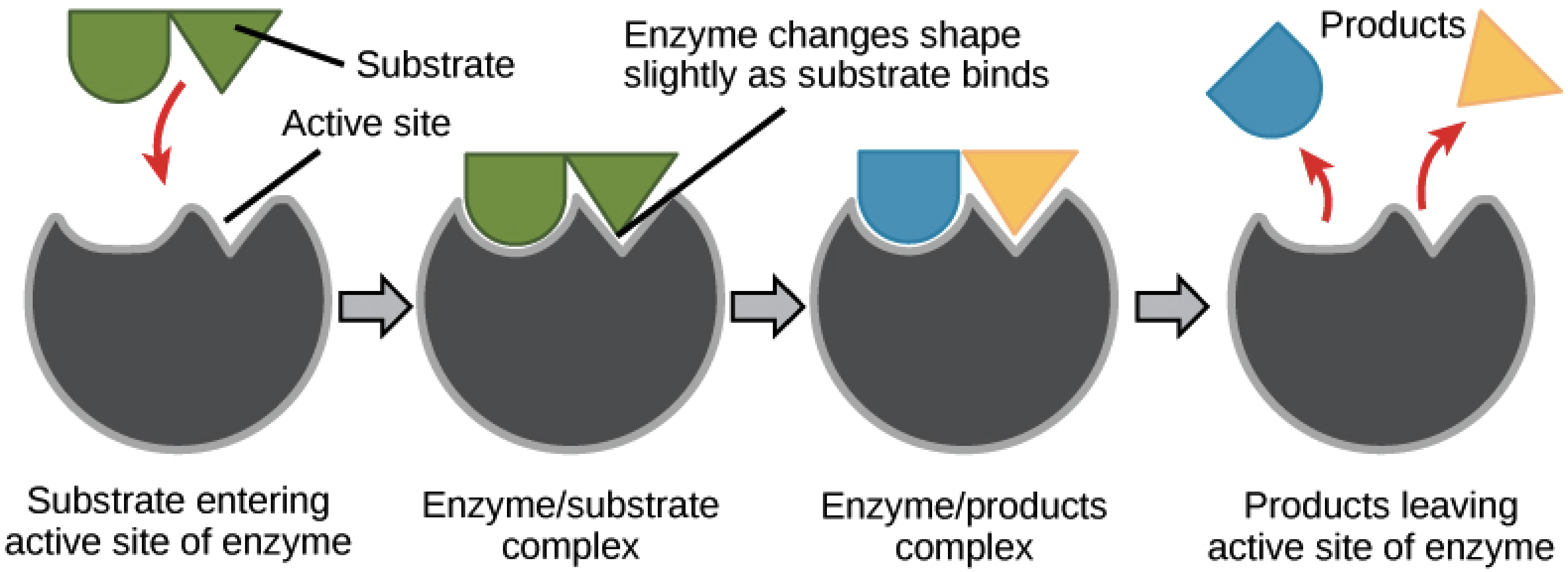
How can we express an enzymatic reaction?

- Simple expression of enzymatic reaction:

EP can be omitted, as the product gets instantly ejected from the enzyme complex after it is formed.

$E + S \leftrightarrows ES \leftrightarrows EP \leftrightarrows E + P$ For simplicity: $E + S \leftrightarrows ES \leftrightarrows E + P$

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



What do enzymes do?

- Enzymes accelerate reactions (usually within a range of 10^6 to 10^{14}).
  - Example: Catalase (10^8) & carbonic anhydrase (10^6)

Do not memorize

  - Carbonic anhydrase: $CO_2 + H_2O \xrightleftharpoons{\text{Carbonic anhydrase}} H_2CO_3$
  - One enzyme molecule hydrates 10^6 molecules of CO_2 per second (versus 1 per 10 seconds for uncatalyzed reactions)
  - Catalase: $2\,H_2O_2 \xrightleftharpoons{\text{Catalase}} 2\,H_2O + O_2\,(g)$

Reaction Conditions	Relative Rate
No catalyst	1
Platinum surface	2.77×10^4
Catalase	6.51×10^8

Do not memorize

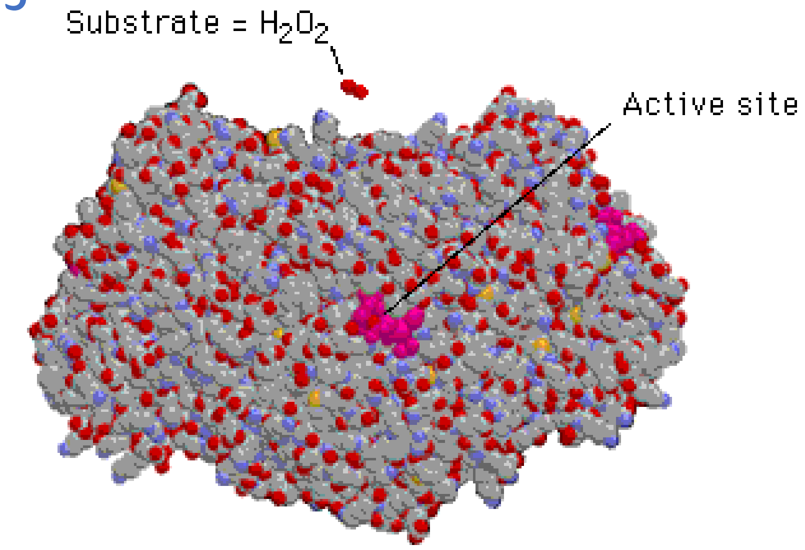
Platinum surfaces catalyze the reaction by altering the bonds of the H2O2 molecule, similar to how enzymes function.

Where does the reaction occur?

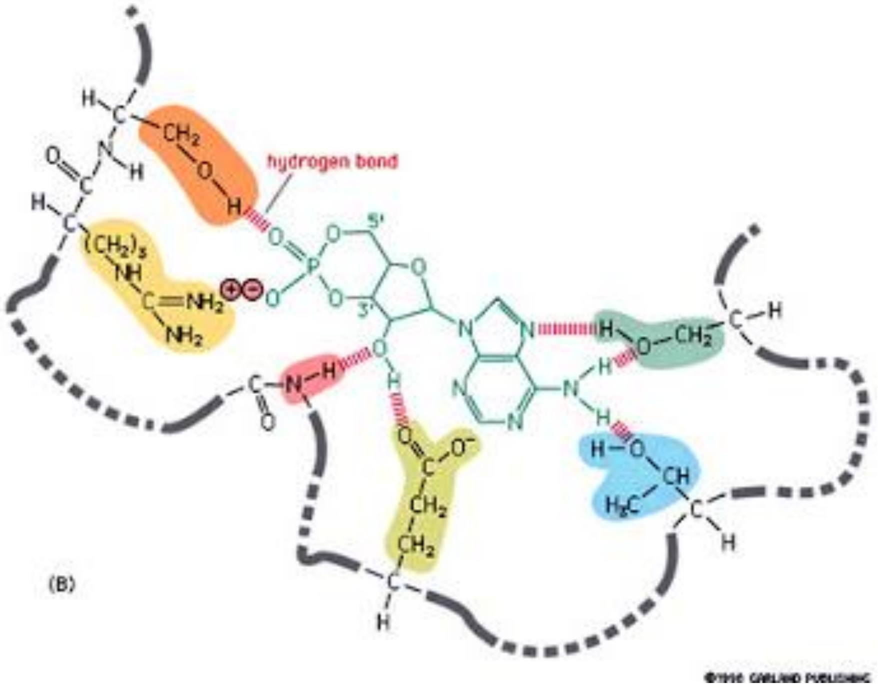
- Each enzyme has a specific three-dimensional shape called **the active site** (a region where the biochemical reaction takes place).

The amino acids in the active site facilitate non-covalent interactions with the substrate, enabling the enzyme to catalyze the reaction.

The active site contains a specialized amino acid sequence that facilitates the reaction.

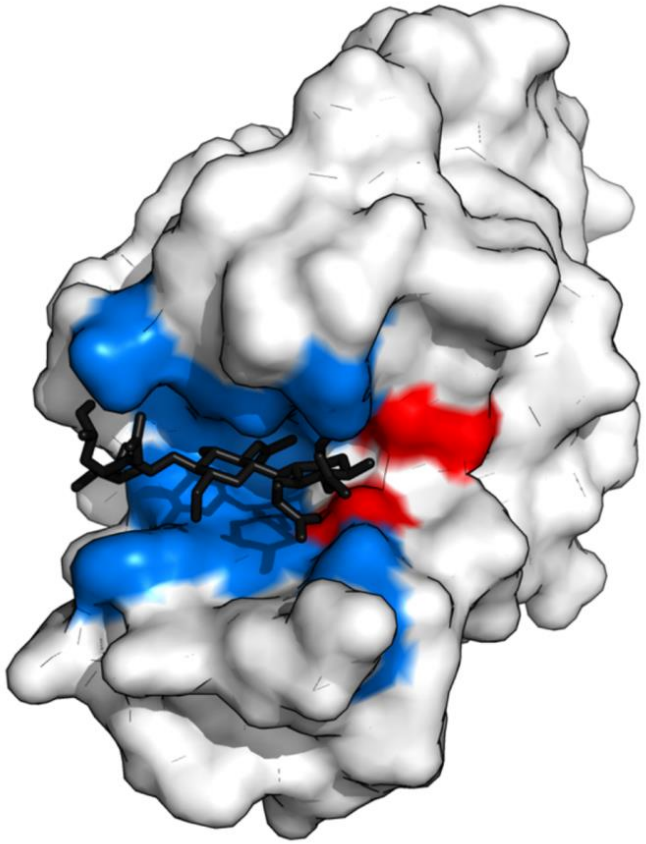


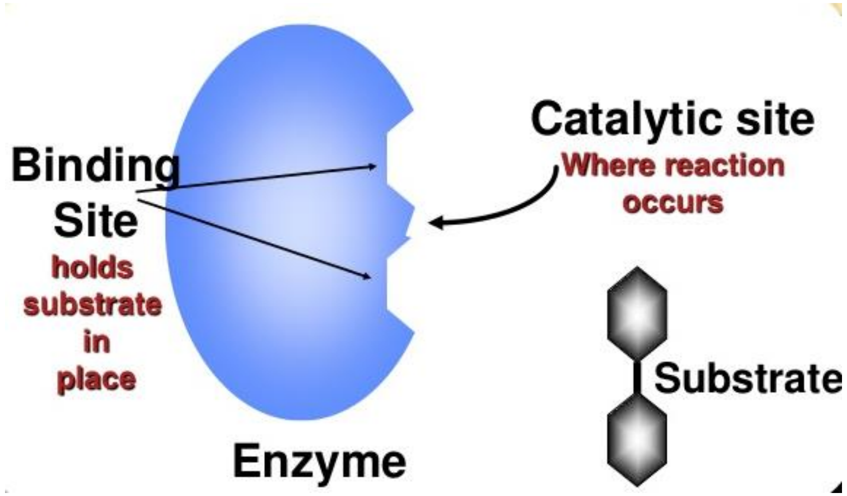
Molecular model of catalase

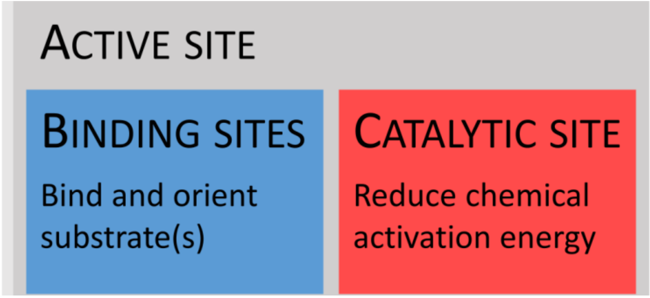


Catalytic and binding groups

- Within the active site there are two sub-sites: the binding and catalytic sites.
- The catalytic site contains amino acid residues (catalytic group) that carry out the actual reaction.
- The binding site contains amino acids that bind to the substrates.
- In some enzymes, the binding and catalytic sites are the same.



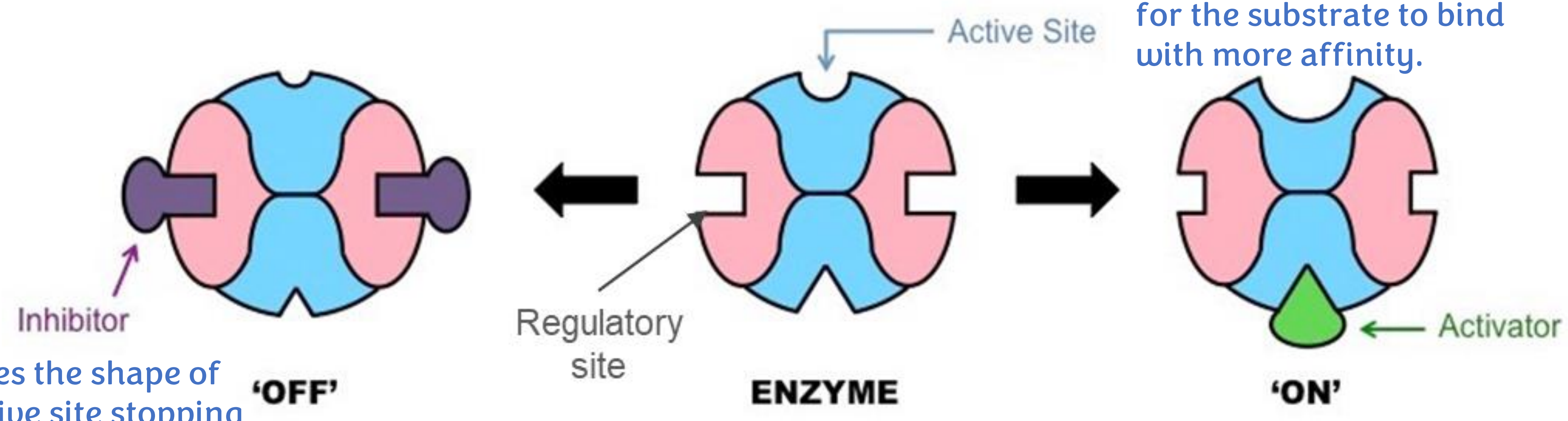




A regulatory site(s) can also be present.

- Binding of a substrate into the active site can be regulated by a *regulatory site*.

Changes the shape of the active site, making it easier for the substrate to bind with more affinity.



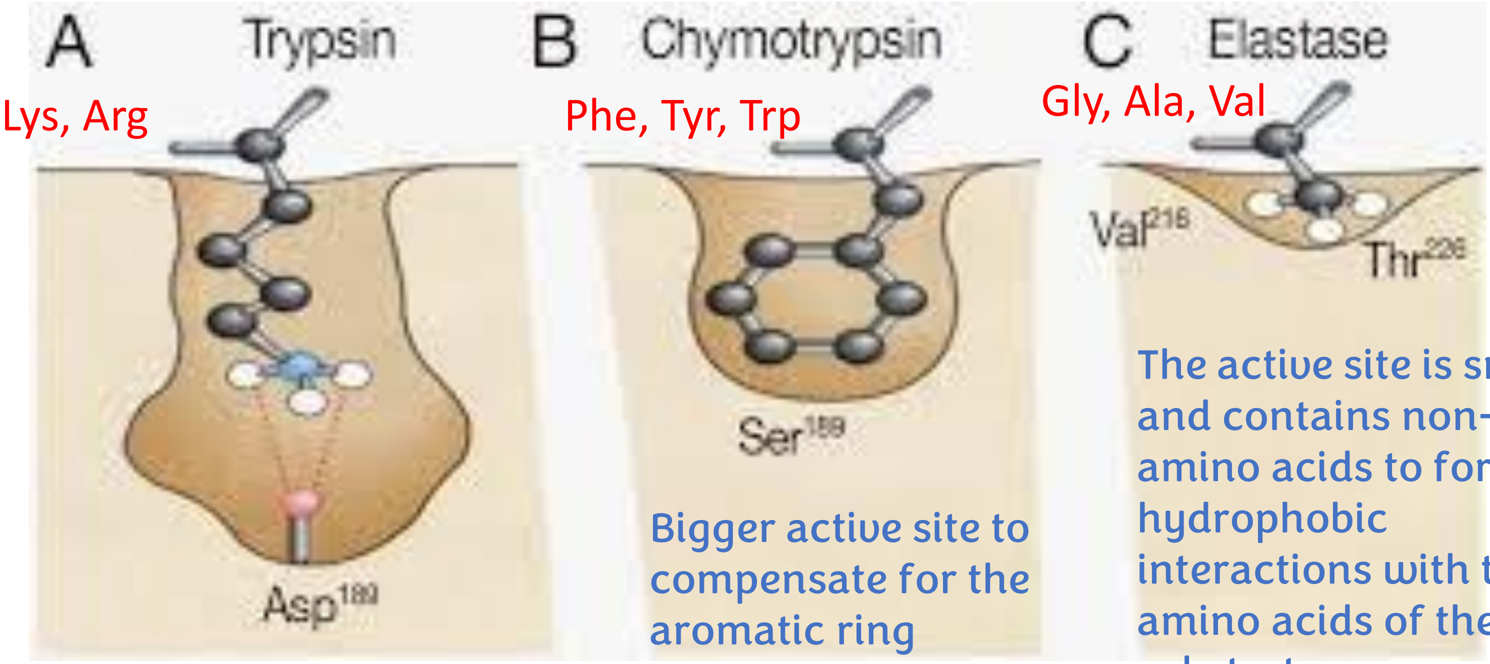
Changes the shape of the active site stopping the substrate from binding.

Binding specificity

Active sites must contain proper R groups and be of appropriate size to bind to the substrate and catalyze the reaction.

- The specificity and selectivity of enzymes are due to their precise interaction of active sites to their substrates.

Red = Amino acids present in the substrate.



These enzymes are proteases which's function is to degrade/cleave the peptides and proteins by breaking the peptide bonds in specific areas.

The active site will be thin and contain negatively charged amino acids, which enable it to bind to the aliphatic, positively charged amino acids present in the substrate.

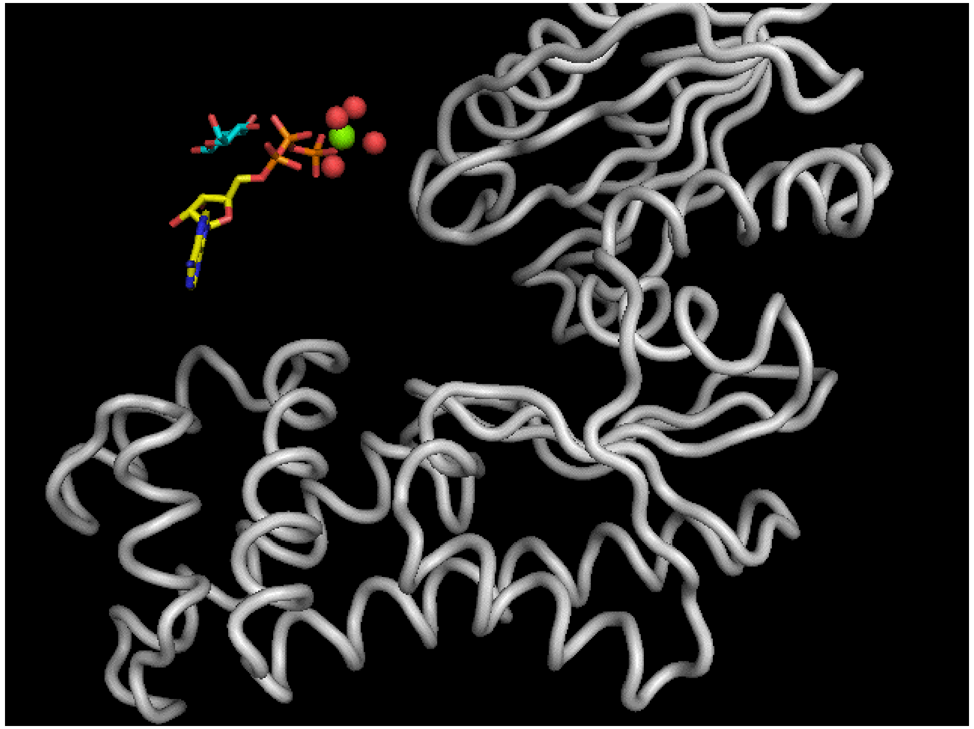
Bigger active site to compensate for the aromatic ring structures of the amino acids in the substrate.

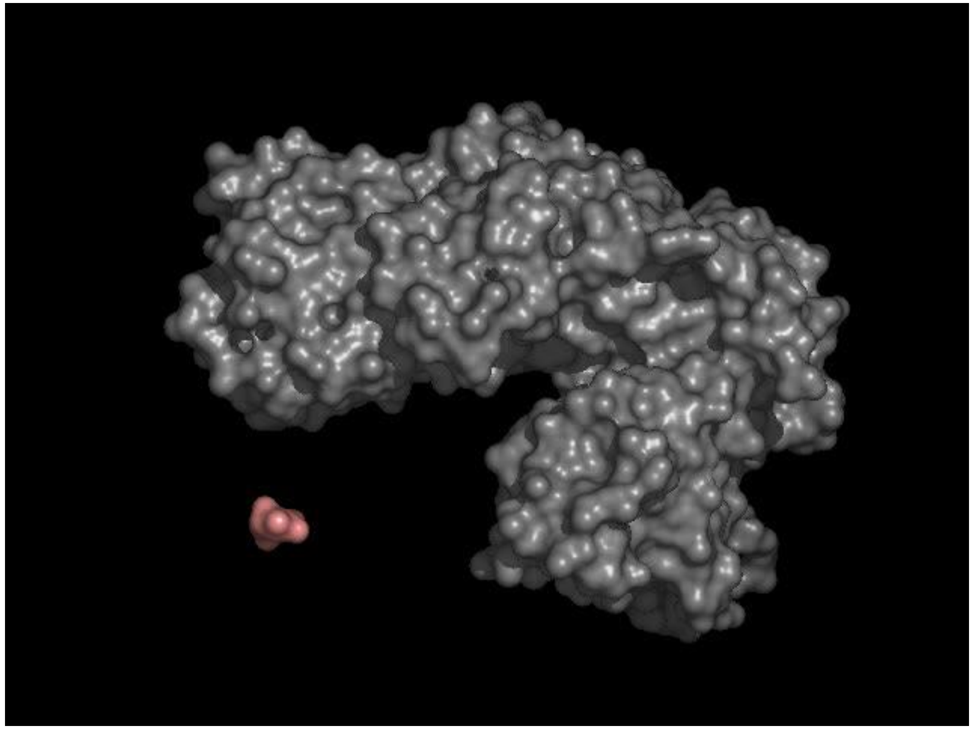
The active site is small and contains non-polar amino acids to form hydrophobic interactions with the amino acids of the substrate.

Features of active site 1

The active site must be canal-like to avoid non-specific interactions with the substrate. Furthermore, it must be designed to prevent water from reacting with the active site and disrupting the reaction.

- It is internal relative to the enzyme and looks like a canal

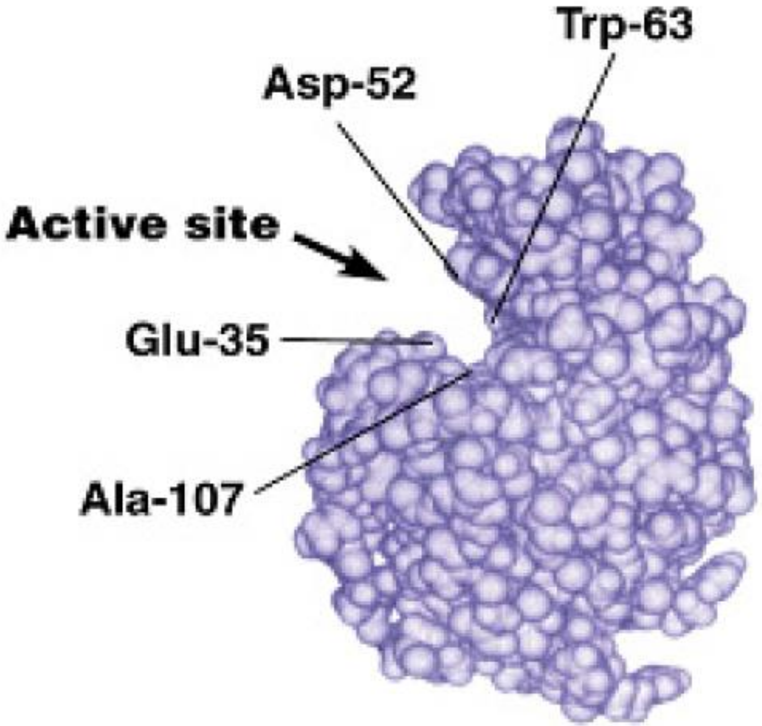




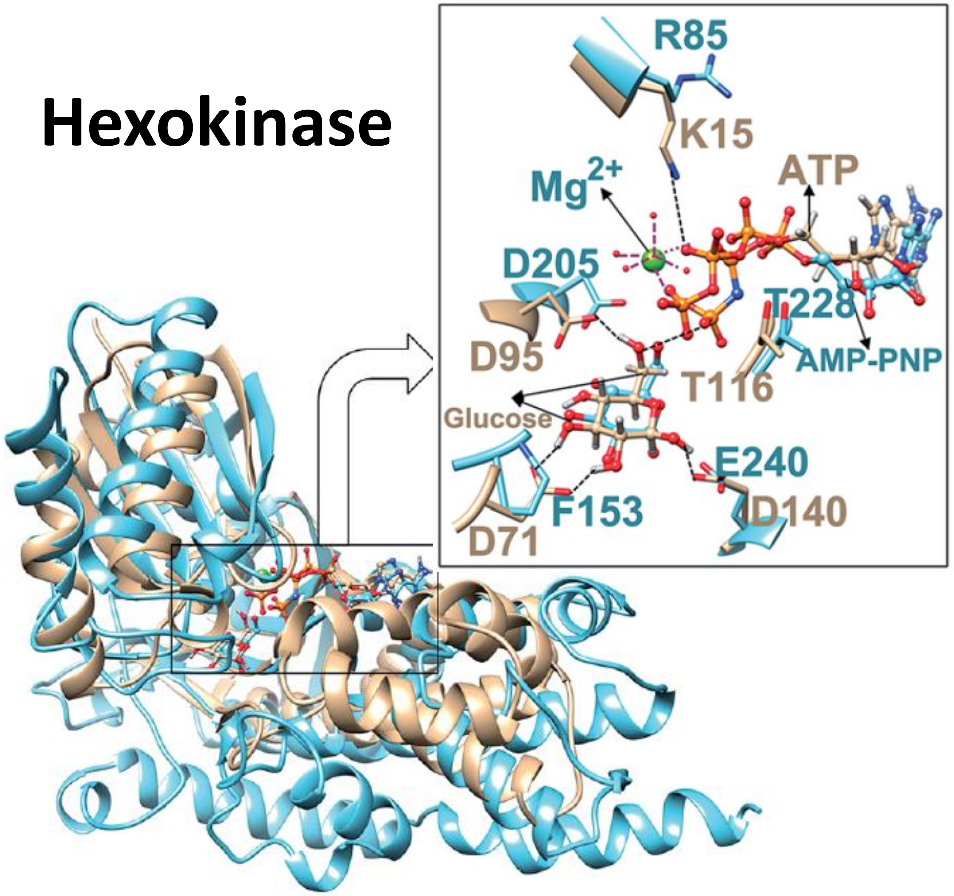
Features of active site 2

The amino acids that make up the active site are initially separated from each other in the primary structure. However, after protein folding, they come together to form the active site domain.

- It is a three-dimensional pocket formed by amino acid groups that come from different parts of the primary structure usually forming a domain.

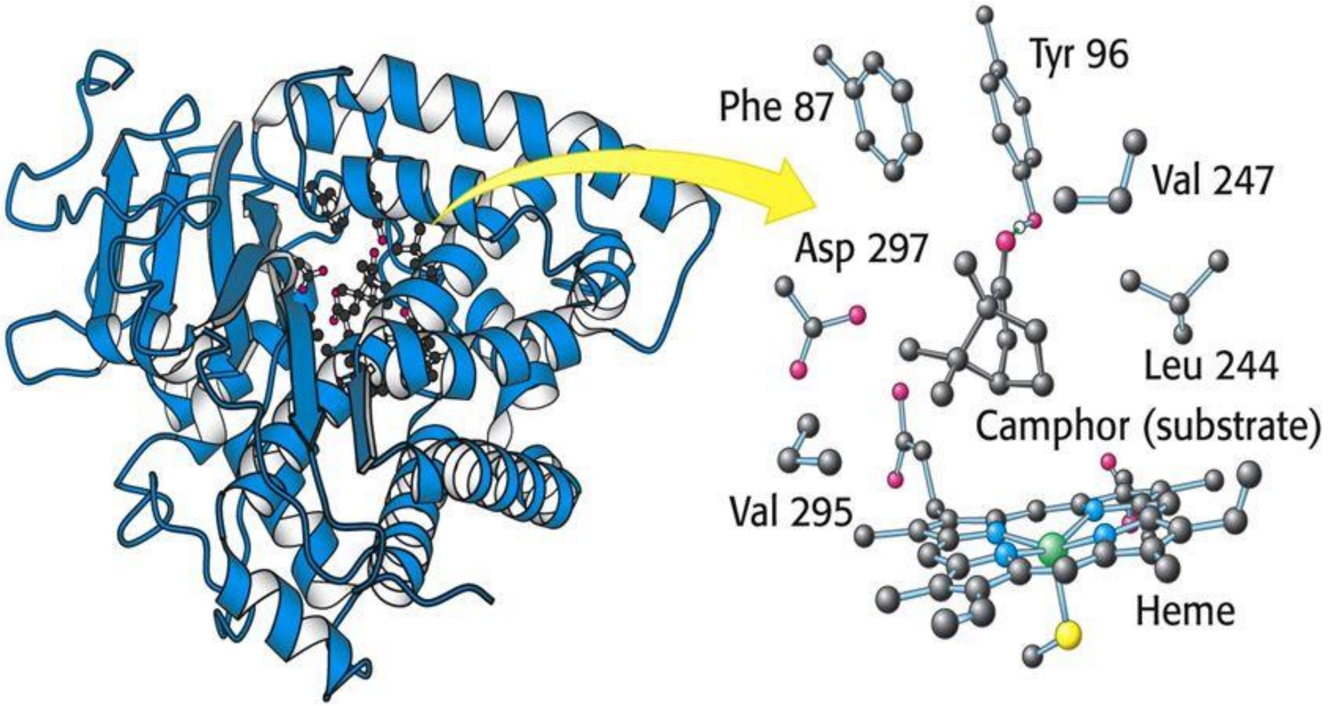


Hexokinase



Features of active site 3

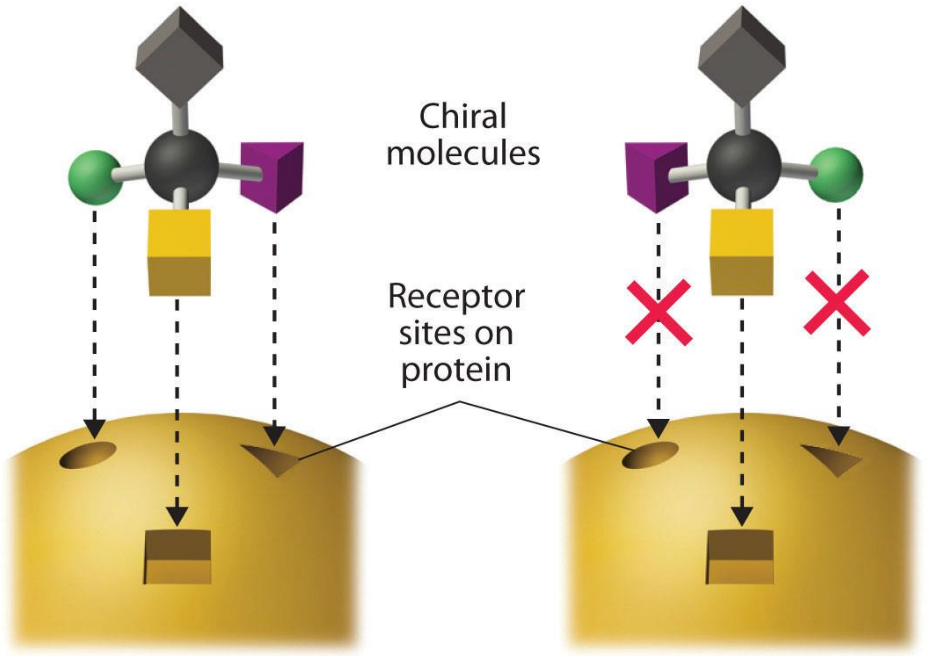
- The amino acid residues can be nonpolar and polar.
  - Water is usually excluded unless it is part of the reaction.
- Substrates bind to enzymes by multiple weak attractions.



Features of active site 4

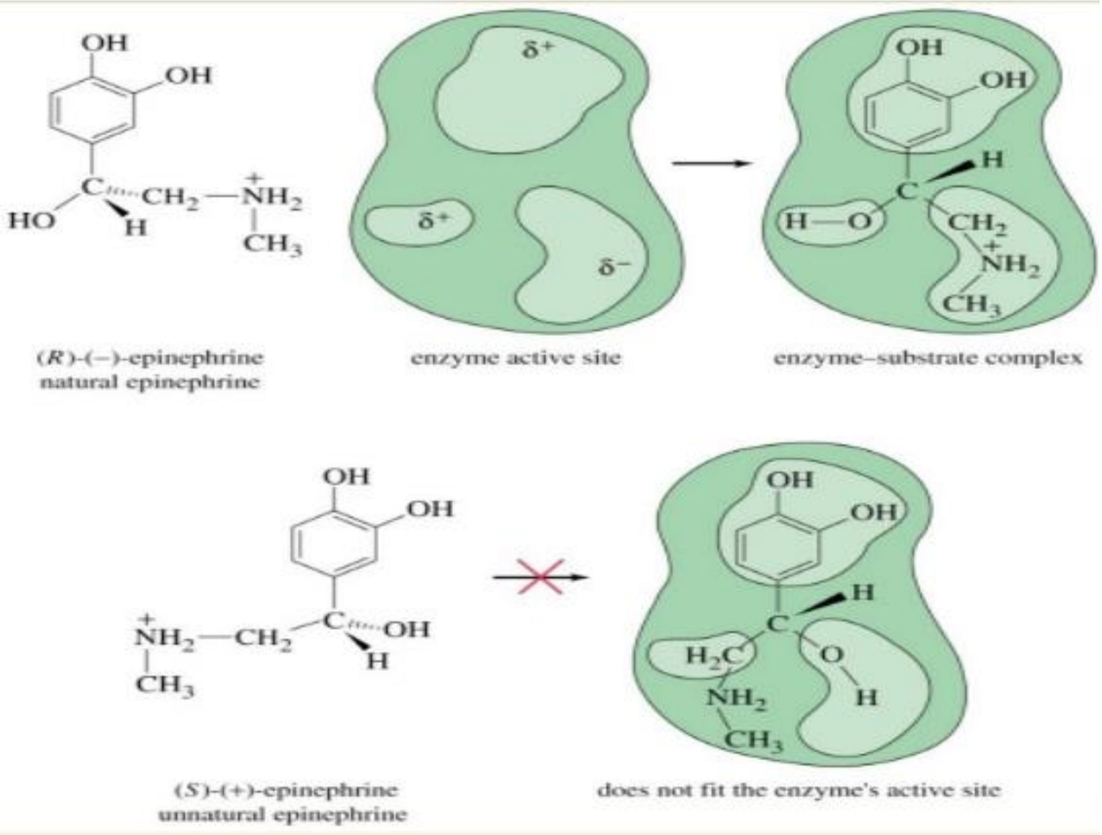
The interaction between the active sites and substrates must be between at least 3 points, because of chirality.

- Binding of substrates to active sites occurs at, at least, three points.
  - Chirality is important, hence specificity.



(a) Molecule fits receptor site, leading to a response

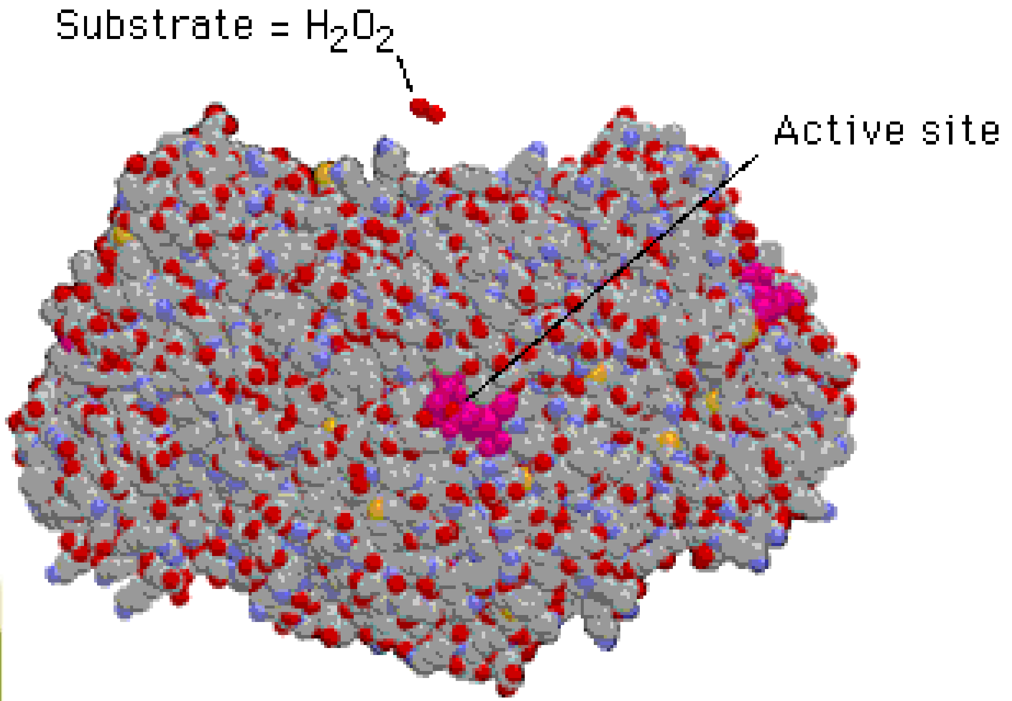
(b) Molecule does not fit receptor site; no response



Features of active site 5

- It is small relative to the total structure of an enzyme.
- The “extra” amino acids create the 3D active site.

The remaining amino acids may make up regulatory sites.

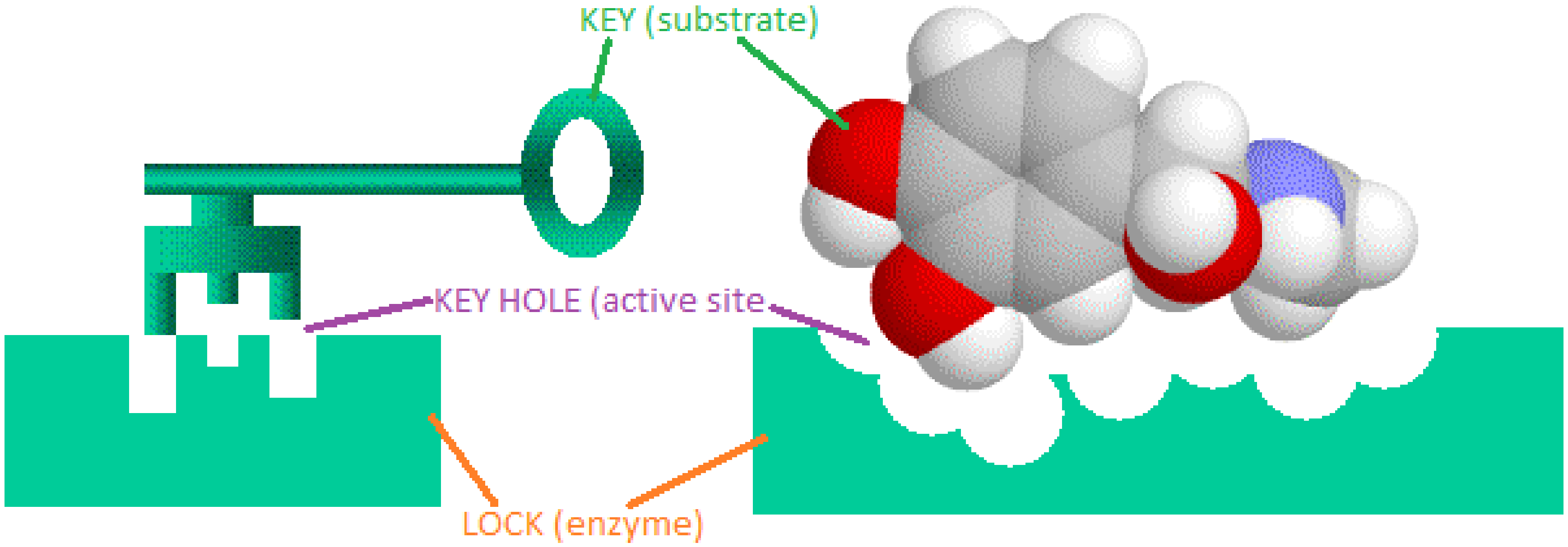


Molecular model of catalase

How do substrates fit into the active site of enzymes?

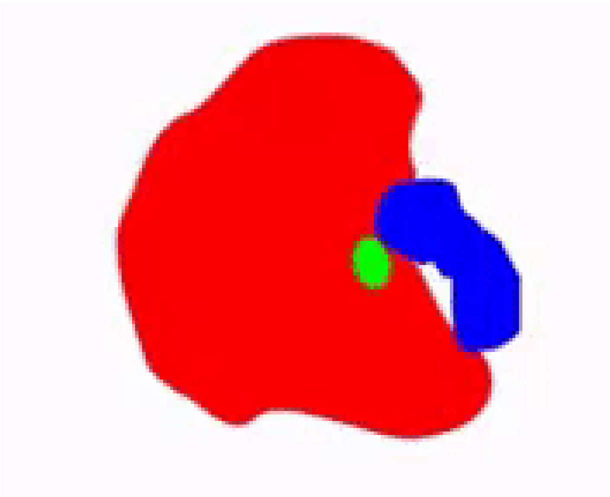
1. Lock-and-key model

- Here, the substrate fits directly into the active site.
- Neither the substrate nor the active site change their shape.



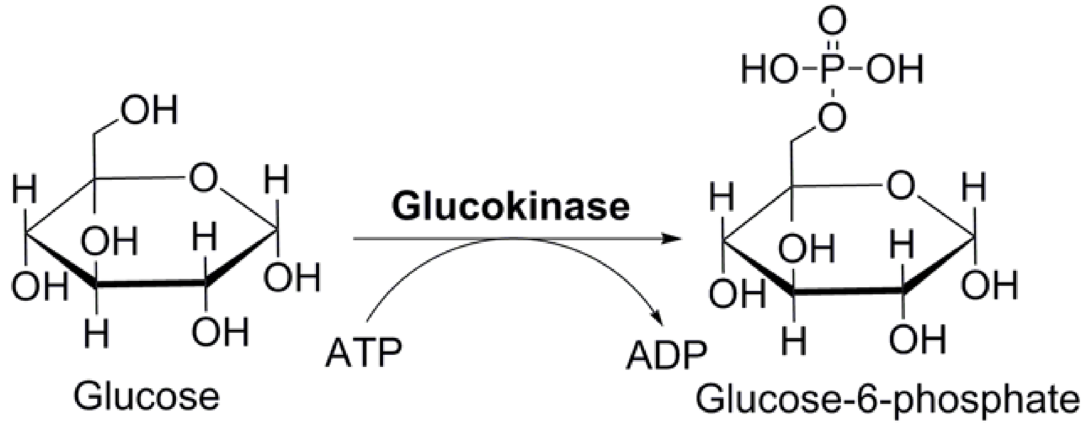
2. Induced fit model

- Enzymes are flexible and active sites can be modified by binding of substrate.
- As the substrate binds to the active site, non-covalent interactions such as hydrogen bonds, hydrophobic interactions, and electrostatic interactions cause conformational changes in the active site. These changes ensure that the substrate can perfectly fit into the active site.

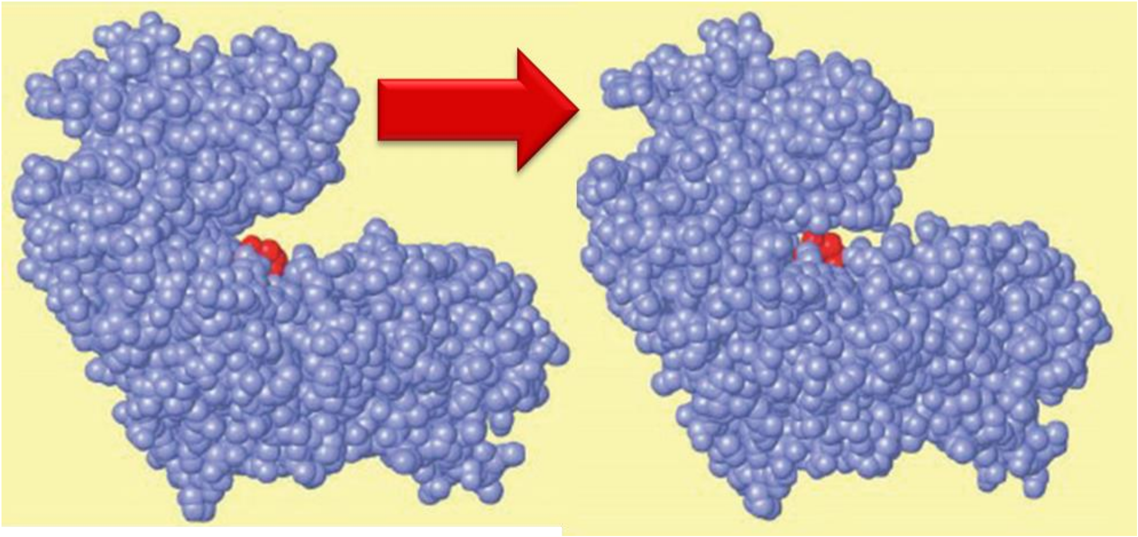


Glucokinase is the king of both!

- Glucose binds the active site of glucokinase as a lock and key resulting in the induced fit of the other substrate, ATP.



Glucokinase uses both mechanisms of binding:
1. Glucose binds by the lock-and-key model
2. ATP binds by the induced fit model



How do enzymes accelerate reactions?

Types of energy

- There are two forms of energy
  - potential - capacity to do work (stored in covalent bonds)
  - kinetic - energy of motion

- Potential energy is more important in the study of biological or chemical systems.
- Molecules have their own potential energy stored in the bonds connecting atoms in molecules.
  - It is known as free energy or G (for Josiah Gibbs).
  - It is the energy that is available for reactions to occur.

Free energy (G) and reaction types

- The difference between the free energy values between reactants and products (free-energy change ΔG):

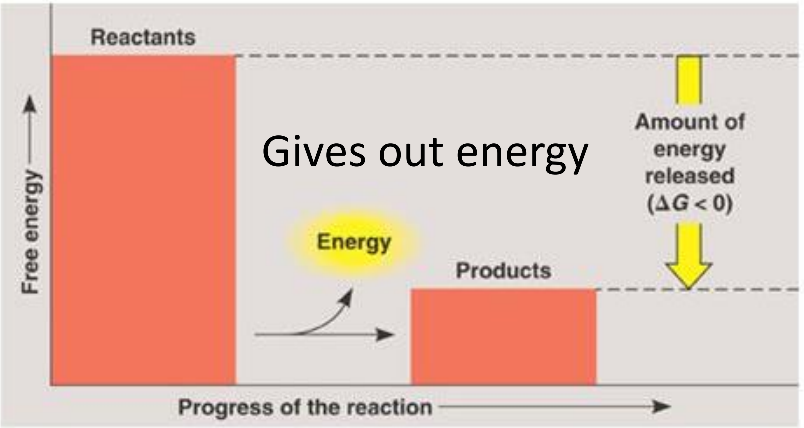
$$\Delta G = G_{products} - G_{reactants}$$

- Reactions are exergonic, endergonic, or at equilibrium.

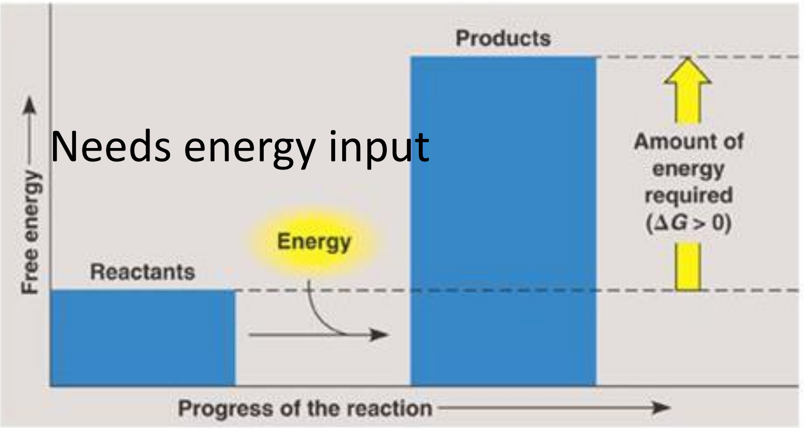
Equilibrium reactions exhibit no difference in the energies of the reactants and products.

*Bond Energies, D, (kJ/mol)	
C—H	414
C—C	348
C—N	293
C—O	351

Do not memorize



(a) Exergonic reaction: energy released



(b) Endergonic reaction: energy required

What does it mean?

$\Delta G = G_{products} - G_{reactants}$

- If ΔG is negative, $G_{products}$ is less than $G_{reactants}$, energy is not needed to drive the reaction, but is released, making the forward reaction (from left to right) spontaneous (the reaction is called exergonic).
- If ΔG is positive, $G_{products}$ is more than $G_{reactants}$, an input of energy is needed, making the reaction not spontaneous (the reaction is called endergonic).
  - The reverse reaction is exergonic and , thus, spontaneous.
- If ΔG is zero, both forward and reverse reactions occur at equal rates; the reaction is at equilibrium.

	Exergonic	Endergonic
What happens to the energy?	Released	Absorbed
ΔG	Negative	Positive
Energy of reactants	Higher than products	Lower than products
Input of energy	Not required	Required
Spontaneity	Spontaneous/favorable	Unspontaneous/unfavorable
Exothermic or endothermic	Exothermic	Endothermic

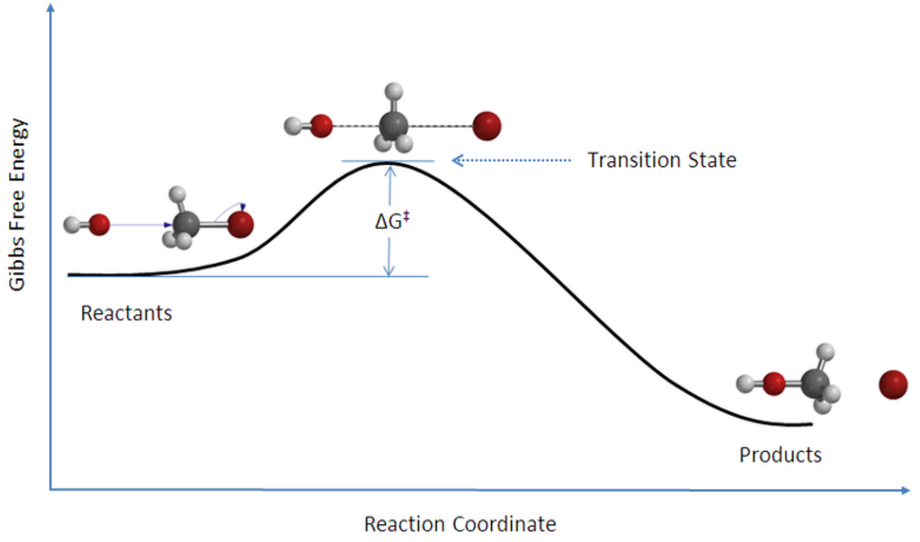
Important table

Transition state

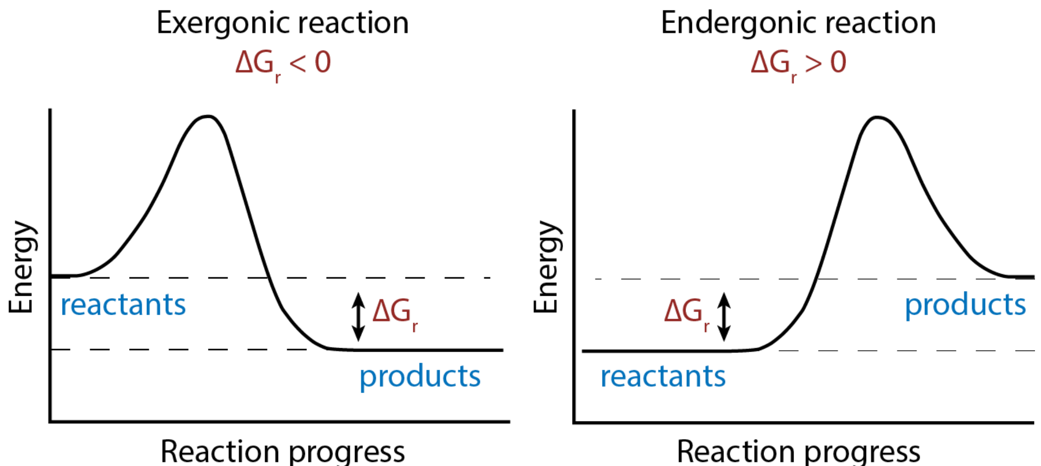
All reaction types require energy input to reach the transition state, which is referred to as "the energy of activation"

The transition state molecule is not stable, and its formation is not favorable.

- Any reaction goes through a transition state molecule (ES) that has a higher free energy than does either S or P.
- The difference in free energy of the transition state and the substrate is called the activation energy.
  - The configuration of the transition state molecule is most <u>unstable and</u> has the highest activation energy

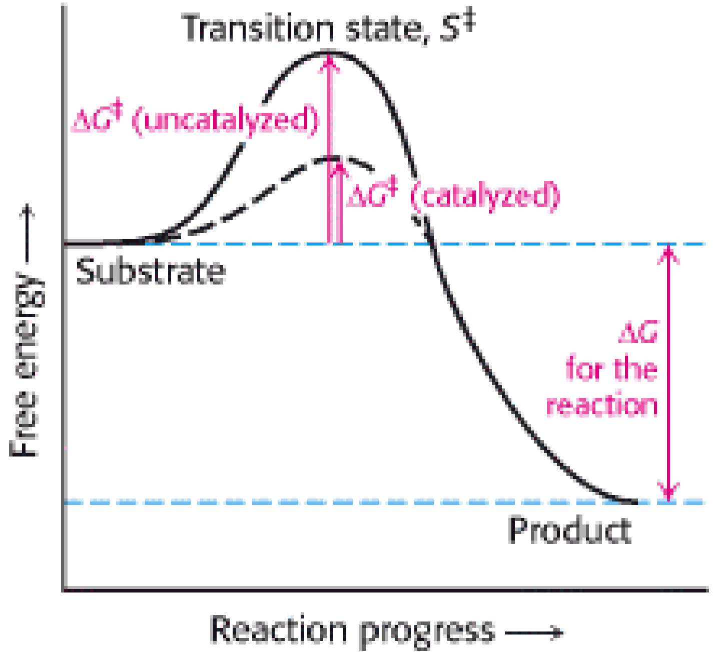


Reaction: $HO^- + CH_3Br \rightarrow [HO{-}{-}{-}CH_3{-}{-}{-}Br]^\ddagger \rightarrow CH_3OH + Br^-$



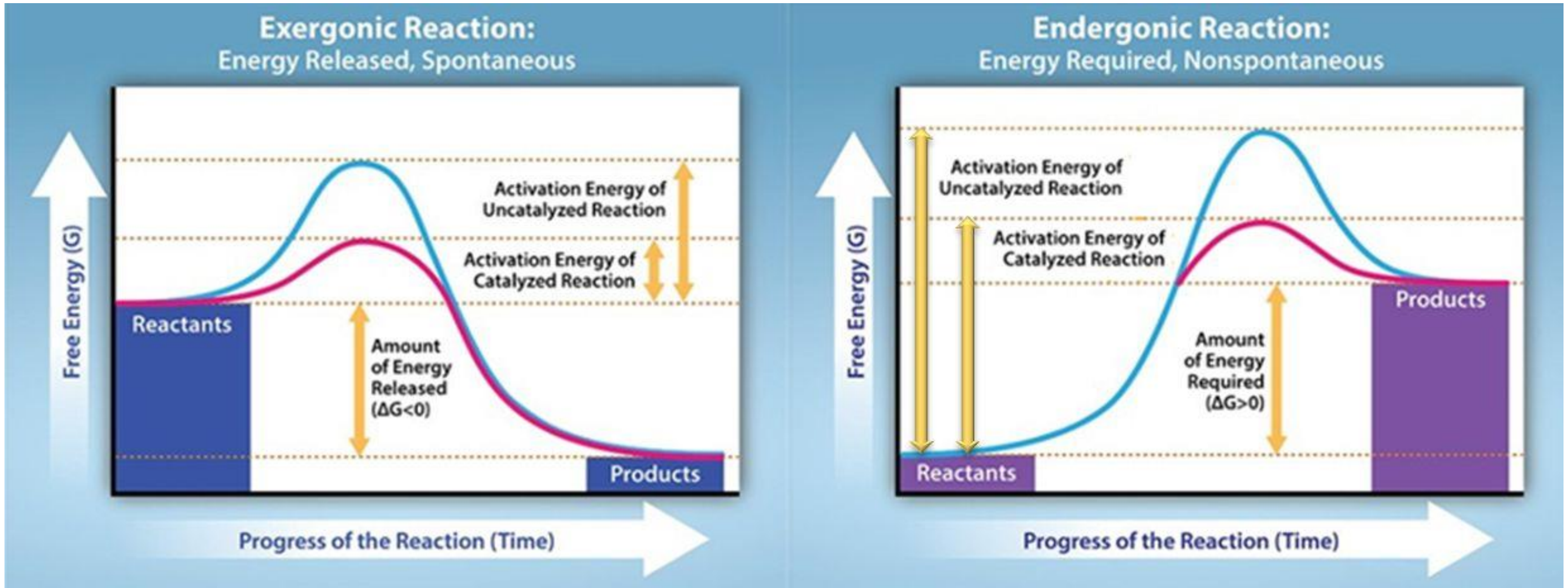
What do enzymes do?

- Enzymes lower the activation energy of the transition state, or in other words, enzymes facilitate the formation of a transition state at a lower energy.
  - *Still, the free energy of the transition state in still higher than those of the substrate or the product.*



Activation Energy = $E_{Transition\ State} - E_{substrate}$

Enzymes lower it by lowering the energy needed to reach the transition state.



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

Corrections from previous versions:

Versions	Slide # and Place of Error	Before Correction	After Correction
V1 → V2			
V2 → V3			

Additional Resources Used: رسالة من الفريق العلمي:

إياك نعبد، وإياك نستعين

مدارُ حياتنا