◉Sheet ○Slides

Subject :	Enzymes
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Number :	11

Energy chart:

There is a huge relationship between enzymes chemical mechanism and the energy chart. But first, why do chemical reactions occur in the first place? It's to achieve a situation of higher stability (the reactants are stable, otherwise we won't be able to deal with them, but we want to achieve a situation of higher stability). Here in the chart (see the figure next page), the energy of the products is lower than the energy of the reactants, which means that products are more stable (Energy is inversely proportional to stability so the lower the energy the more the subject is stable). This also means that the reaction is spontaneous, favorable or exergonic . When we discuss the energy of a material we mean by that the bonds energy or the potential energy which can be measured by putting the material in a special container with a specific pressure and an energy meter, then a complete combustion reaction occurs, and finally we measure the amount of energy released. (remember there are 2 forms of energy: kinetic and potential)

We do measure the energy of the reactants and the products, if the value of the difference in energy (ΔG =G final-G initial) is negative it means that the reaction is spontaneous, otherwise the products will have more energy (less stable) and *(ΔG) will be positive and the reaction will be non spontaneous, unfavorable and undergone .if ΔG is zero the reaction is at equilibrium.*

In any reversible rxn if the forward rxn is exergonic the backward rxn will be endergonic.

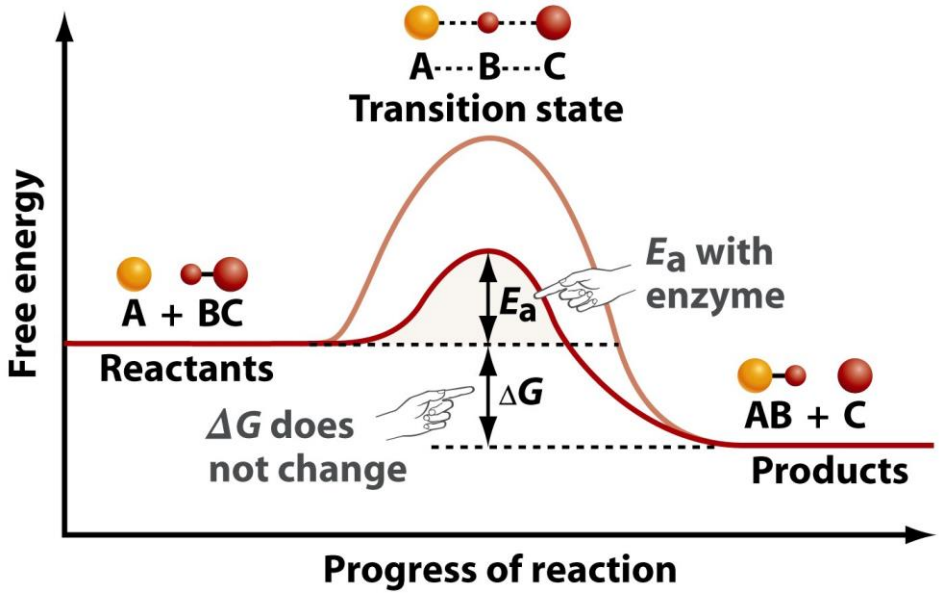

Figure 3-21 Biological Science, 2/e

There are no reactions in biological systems(whether they are exergonic or endergonic) that can occur without giving it an amount of energy first, so the total energy of reactants must be higher than the energy of the products and this is achieved in the transition state. so in endoergic reactions , an external extra amount of energy must be added using ATP for instance for the reaction to occur . But why do we give a little amount even if the reaction is exergonic where the products' energy are already lower than reactants? it's because the reactants are already stable , so we can't convert it to another product without converting it to an unstable condition first . This unstable condition is called the transition state , which is achieved by adding an amount of energy to the reactants .

We all know the activation energy , which is the energy needed to convert the reactants(which are originally stable) to the unstable transitional state , but why do we need it ? For regulation , because if every spontaneous reaction is going to

occur , there will be no reactants anymore and reactions will have no meaning , so the activation energy acts a barrier for the reactions .

So do all spontaneous reactions occur spontaneously? NO, you have to give it an amount of energy first which is the activation energy . This energy results from the random collisions , if the energy caused by the collisions equals at least the activation energy we will reach the transition state and the products will be formed(or we may go back to the reactants) .

What is the role of enzymes ?

Enzymes lower that amount of energy needed for the reaction to occur(lower the activation energy) so collisions that result in low amounts of energy will be enough to overcome the new energy barrier and this will give us big amounts of products . You have to understand that enzymes do not affect the potential energy or the (Delta G) , so they don't interfere with the initial and the final states , they only change the phase in between , In other words , they can't make an unfavorable reaction a favorable one , they can only help the favorable reactions to occur .

https www://.youtube.com/watch?v=YacsIU97OFc

Enzymes in industry:

Enzymes are very important in the industry as well , here are some examples " the doctor said you don't have to know all of them , you only have to know the importance of enzymes in the industry "

1-For example , green tea and black tea . Green tea has polyphenols(which act as antioxidants) and an enzyme called polyphenols oxidase which oxidizes them to tannins . but the enzyme needs oxygen first , in normal conditions(intact leaves) these enzymes won't be exposed to oxygen so they remain green . by breaking the leaves you expose the enzyme to the molecular oxygen of the atmosphere to oxidize polyphenols into tannins which have different color (black) and different taste .

2-Corn syrup is produced by enzymes .it's like honey but cheaper .

3-Chocolates that are hard from the outside and soft from the inside are made by putting sucrase enzymes inside the chocolate so it will hydrolyze sucrose to mono-saccharides which are more soluble so it becomes soft in the middle while remaining hard from the outside.

4-Proteases are used in meats to break the peptide bonds to make it softer.

5-Tide and other cleaning products have proteases and lipases to get rid of dirt and since different enzymes function in different conditions these cleaning products may function in different conditions(hot,cold water…etc).

6-contact lenses have proteases and lipases to break the molecules that attach to them so that they won't irritate the eye.

7-production of amoxicillin " the most common antibiotic used " depends on enzymes as well.

Expression of enzymatically catalyzed reactions:

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

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

*E=enzyme S=substrate ES=Enzyme-substrate complex

*EP=enzyme-product complex P=product

Note: we can easily notice from the equation that enzymes change during the reaction then it get back to its original state after the reaction.

Note:In enzymatic reactions , reactants are known as substrates.

Active site of enzymes:

Active site is a 3-D structure in the enzyme which is a region where biochemical reactions take place, it has a shape that looks like a cleft ,a canal, a pocket , so it's not a surface structure .the lining of this pocket consists of amino acids, these amino acids are not composed of continuous sequence of amino acids from one polypeptide chain rather they're composed of amino acids from different parts of the protein " multiple sec-structures form the active site " .

Some active sites have two sub-sites , a binding sub-site that has hydrophobic amino acids for binding , the other sub-site is the catalytic sub-site which is composed of hydrophilic amino

acids for lowering the activation energy .in many enzymes we only have one site ,so the one which does the binding also does the catalysis.

When a substrate binds to the active site , it binds to it through at least 3 points , because if it was 1 or 2 points the active site will not be able to differentiate between chiral compounds (D and L) , that's why enzymes usually react with **specific stereoisomers** .

The binding between the substrate and the active site is usually non-covalent (including hydrophobic interactions , hydrogen bonding , electrostatic interactions and van der waals)so that the enzyme can release the products . some molecules like toxins and poisons can bind covalently , for example sarine gas binds covalently and inhibits the acetylcholine esterase and causes respiratory arrest .

Size of the active site is very small compared to the full size of the enzyme , but why do we need the big size of the enzyme if the active site is only what matters to come up with the catalyzing job ? For stability of the active site , because the active site is a very small sequence of amino acids so its shape can't be stable and will change easily , The big structure of an enzyme preserves the shape of the active site . Another reason is that enzymes have allosteric(regulatory) sites which are not catalytic but have an activating or inhibiting effect on the active site .

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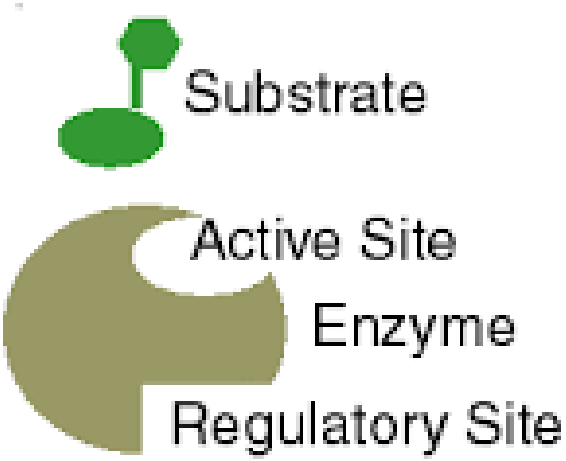
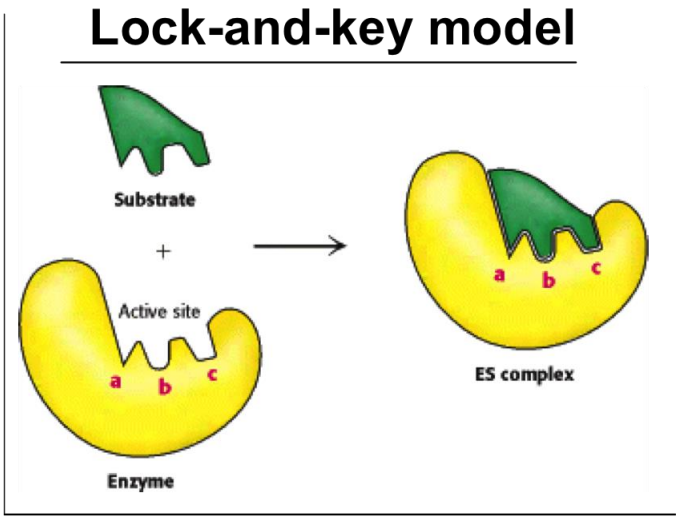
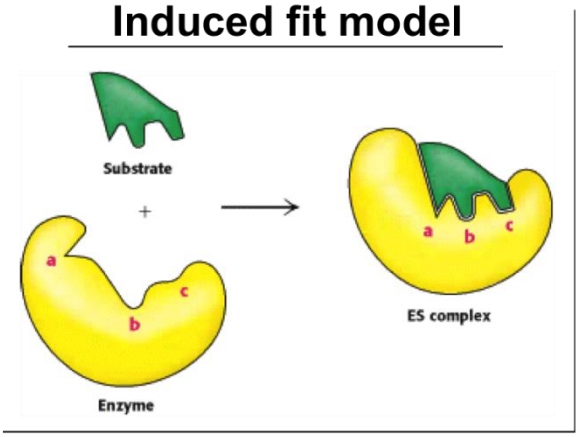


How do enzymes work:

1-Theory wise

First theory was the lock and key which is not 100% true since it doesn't fully explain the enzymatic action, but how is that? some enzymes work with more than one substrate like glucokinase that reacts with both glucose and fructose to add a phosphate group , this observation contradicts the 100% complementary fit of key and lock theory , another observation that canceled the key and lock theory is that this theory states that these molecules are static which is not true because everything is dynamic , proteins have many confirmations(at least one of them is active and is called the native conformation) , so they came up with the induced fit theory , which indicated that the 100% fit wasn't there from the start , however , binding of the substrate induces the active site to become 100% fit .





2-Eenergy wise

By lowering the activation energy which was explained before .many enzymes have more than one transition state , but the energy that is needed to reach the transition state with the highest energy (the most unstable) is the one defined to be the activation energy. An example is Adenosine Deaminize .

3-Mechanisim wise

A-Enzymes bring the reactive groups close to each other which is called the **"proximity effect " .**

B-The substrate after the initial binding and by the effect of the active site will direct(orient) itself in the active site for

the best fit and for the reaction to occur at best conditions which is called **" the orientation effect ".**

Note:- Enzyme-substrate interactions orient reactive groups and bring them into proximity with one another favoring their participation in catalysis, Such arrangements have been termed near-attack conformations (NACs), NACs are precursors to reaction transition states.

C-Active site will begin to interact(bind) with the substrate from the outside which wakens the bonds of the substrate itself (amino acids lining the active site interact with the substrate) this is called the **"catalytic effect "** which is followed by the energy effect.

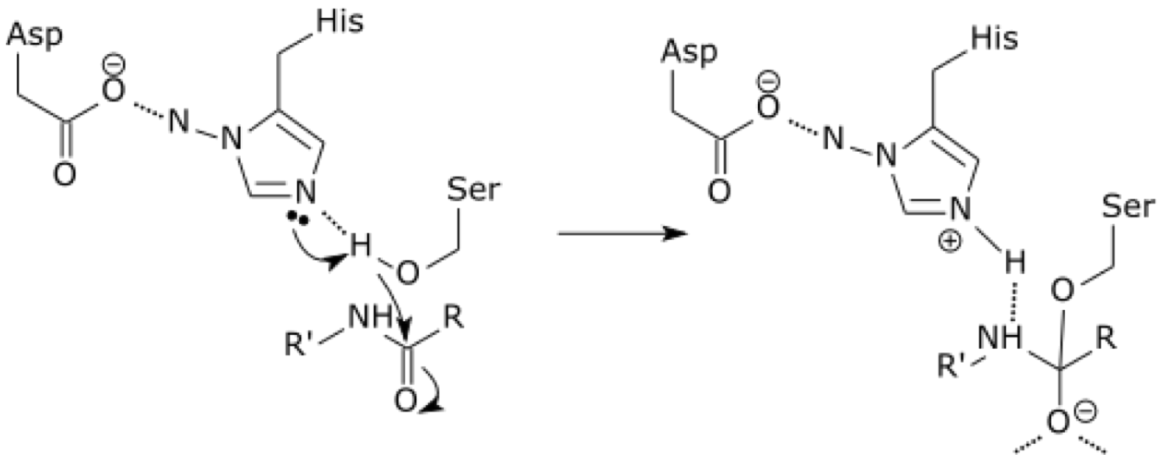
D-"The energy effect " where the energy of the substrate will change after the binding

Note :- all of these are done by all enzymes .

Some enzymes have special effects , for instance :-

*some enzymes produce strain on the substrate to change the orientation of the bonds within the substrate , for example lysozyme binds to a chair conformation substrate , by producing strain it changes it to a sofa confirmation which is similar in shape to the transition state (its more open and more reactive , the induced structural rearrangements produce strained substrate bonds reducing the activation energy)

*other enzymes work through acid-base catalysis where within the active site we have amino acids that have side chains with the ability of accepting or donating protons with the substrate .Histidine is an excellent proton donor and accepter , like in chymotrypsin . Histidine takes a proton of the OH group of serine , so serine will attack the substrate to compensate for the missing hydrogen . in the end the substrate will have deficiency in the electrons which will make it unstable , so it rearranges its bonds to become more stable which converts it to a product .



They mostly have histidine in the active site because the Pka is around 6 which is close to the physiological PH also they may have serine.

*some enzymes use an ionic catalysis pathways , where negative or positive charged substrates might react with the amino acids of the active site through ionic interactions that affect the bonds energy of the substrate. example:serine proteases.

*Covalent catalysis forms a covalent intermediate(during the mechanism) between the enzyme or coenzyme and the substrate ,these covalent bonds will be broken later. Examples of this mechanism is proteolysis by serine proteases, which include both digestive enzymes (trypsin, chymotrypsin, and elastase).

https://www.youtube.com/watch?v=0vvUIIulzMk

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