Metabolism: Chemical and energy transformations that occur in living organisms.

An organism's metabolism transforms (matters + energy) subject to the laws of thermodynamics.

2 Types of metabolic pathways

Catabolic Pathways.

Breakdown of: Complex molecules to simple molecules

Energy is release

Eg- Cellular respiration

Anabolic Pathways

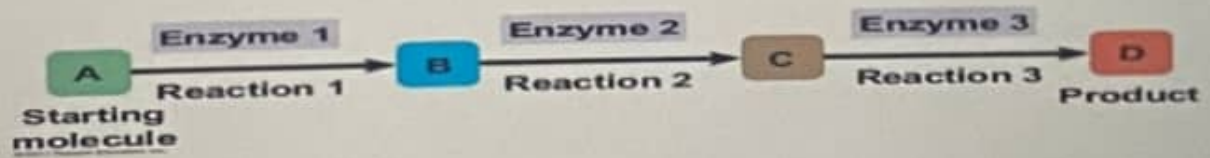
Build up complex molecules from simple molecules

Requires an input of energy

Eg- Photosynthesis // amino acisa to proteins

Reactions in the cell follows a metabolic pathway which begins with a specific molecule that's altered in a series of steps to form a specific product.

A specific enzymes catalyzes each step of the pathway.



Laws of thermodynamics:

First law of thermodynamics:

Energy can neither be created nor destroyed, only transferred or transformed from one from to another

Second law of thermodynamics:

Every energy alteration (transfer/transform) increases the entrophy of the universe.

What's entrophy???
When certain energy is lost during energy alteration, could be in the form of wasted heat.

Energy:
Ability to do work or cause change

Energy

Kinetic energy.	Potential energy.
Energy of an object in motion	Energy stored in an object.
Measured in joules.	Measured in Joules.
Eg-Thermal energy.	Eg-Chemical energy.

Free energy:
It's the portion of the system's energy available to do work when temp & pressure are uniform.

We can calculate the change in free energy between reactants and products
HOW???

Free energy of products – free energy of reactants

The concept of free energy can be applied to the chemistry of life's processes. Depending on the change in free energy (delta G)

A reaction can be

Exergonic.

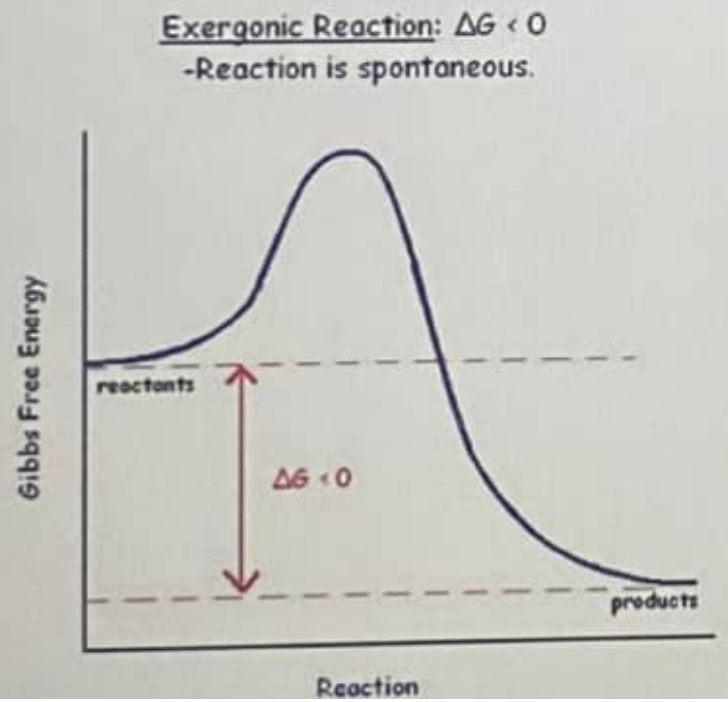
Proceeds with a net release of free energy.
Spontaneous. WHY???
(free energy of products < free energy of reactants)
reactants Delta G < 0
products)

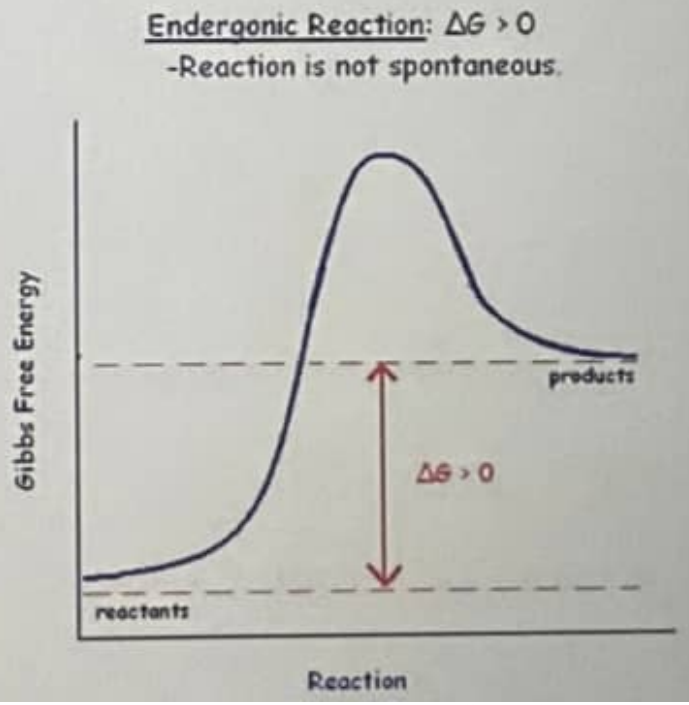
Eg-Respiration.

Endergonic

Absorbs free energy from its surroundings.
not spontaneous. WHY???
(free energy of
< free energy of

Delta G > 0
Eg-Photosynthesis





Question
Can delta G=0??

YES!
If reactants and products have the equal free energy (system is in equilibrium)
Where does this happen?
In closed systems.
(dead organisms for example)
What's a closed system?
Closed system: no exchange of matter/energy with its environment

Note
Cells in human body are in an open system.
(Constant flow of material in and out, preventing metabolic pathways ever reaching equilibrium)

Most cellular reaction are Endergonic which means they can't occur spontaneously. They require energy.

Energy Coupling
Since most of our bodies reactions are endergonic and require energy.
From where do our cells get this energy from??

Coupling Of Rxn's

We couple an endergonic reaction with an exergonic reaction through a coupler.

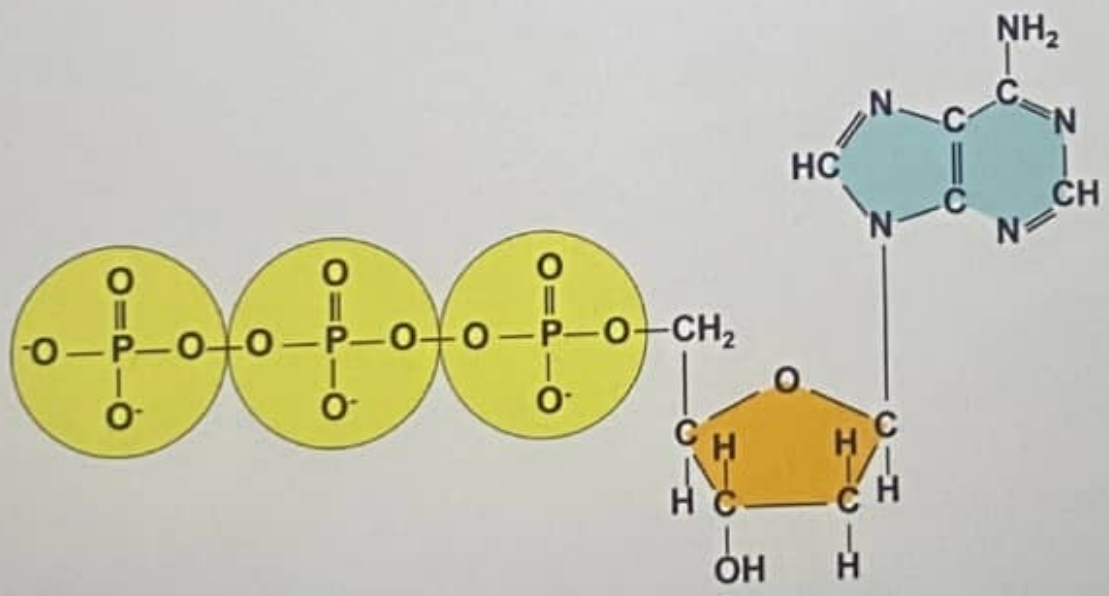
Eg- A + B → C + D + Energy (Exergonic rxn)

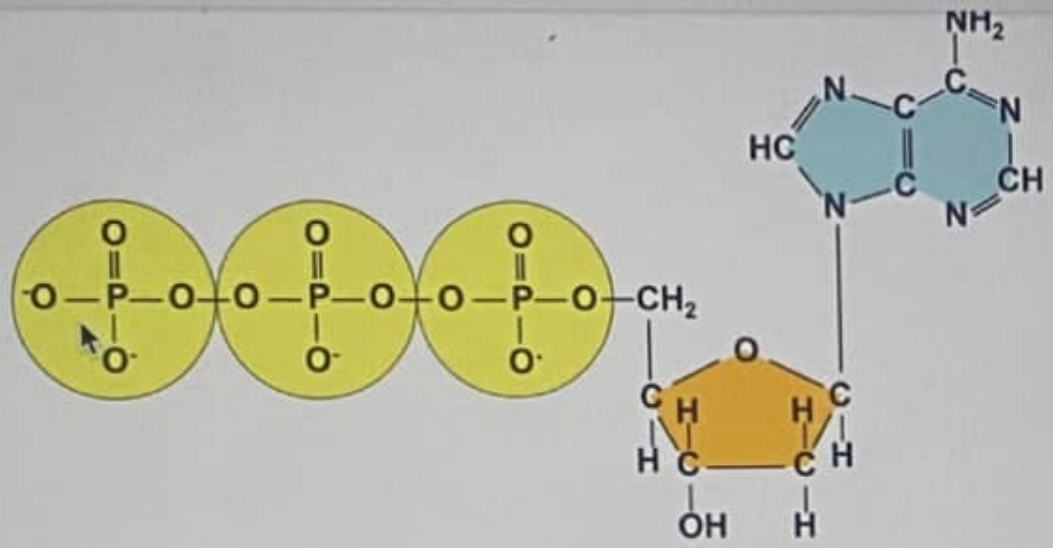
E + F + Energy. → G + H (Endergonic rxn)

Energy provided by catabolic (Exergonic rxn) is used to drive the anabolic rxn forward.

This couples reaction which revolves around a principle molecule (coupler) involved in providing the energy for endergonic cellular reaction.

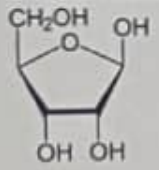
What's this coupler called??
ATP (Adenosine Triphosphate)



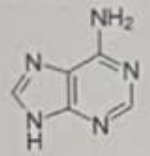


ATP is made of:

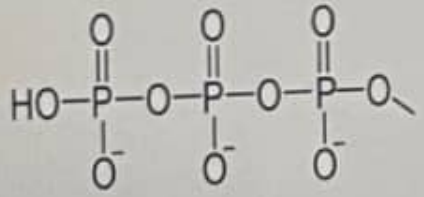
1-Ribose sugar



2-Adenine (nitrogenous base)



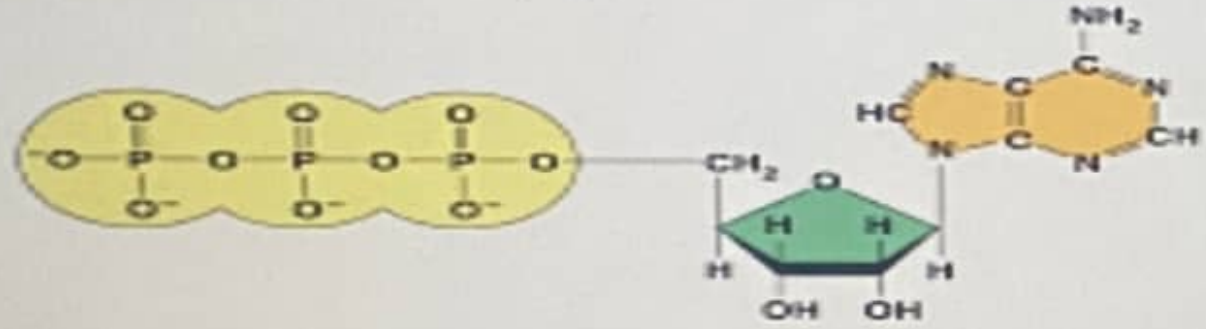
3- "3" Phosphate groups

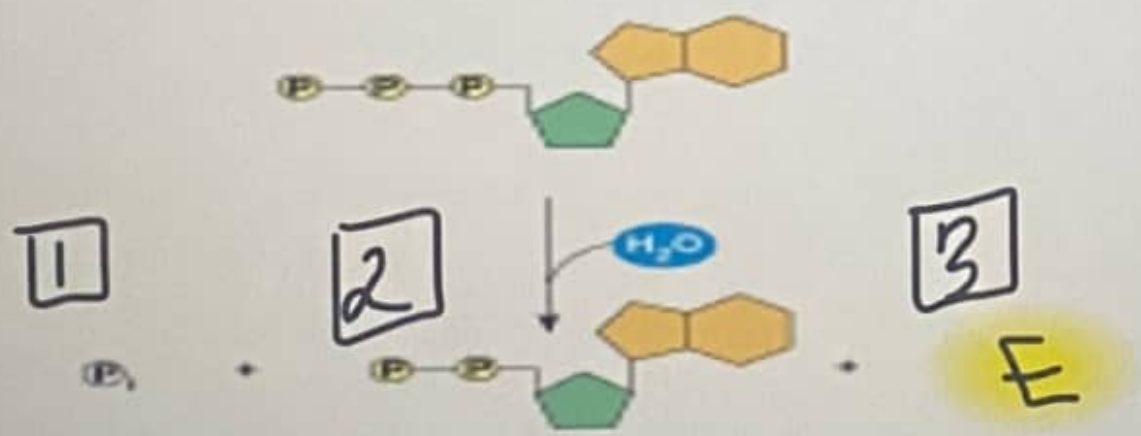


Note: In the 3 phosphate groups we have 3 O' (Oxygen with a –ve charge)
As we already know repulsion occurs between like charges (-ve, -ve) in this example
Which causes the molecule to become highly unstable with very high amounts of energy
(which means the bonds between phosphate can be broken down easily)

Let's take this example: if I take 1 mole of ATP and put it in a container with H20, hydrolysis takes place. What happens??

The bond between 2 phosphates breaks down froming ADP, inorganic phosphate and energy is released.





And the breakdown of every every bond between 2 phosphate molecules releases 7.3Kcal. Which means delta G= -7.3.

Knowing this lets organize our thoughts about ATP coupling

1- An exergonic reaction occurs, thus energy is released.
2- Energy produced is consumed by the addition of a third phosphate group to ADP forming ATP.
3- Due to the repulsion between the oxygen ions in every phosphate group ATP has a very high amount of energy. Therefore, ATP releases a phosphate group, becomes ADP and energy is released.
4- The energy released can be used to drive an endergonic reaction

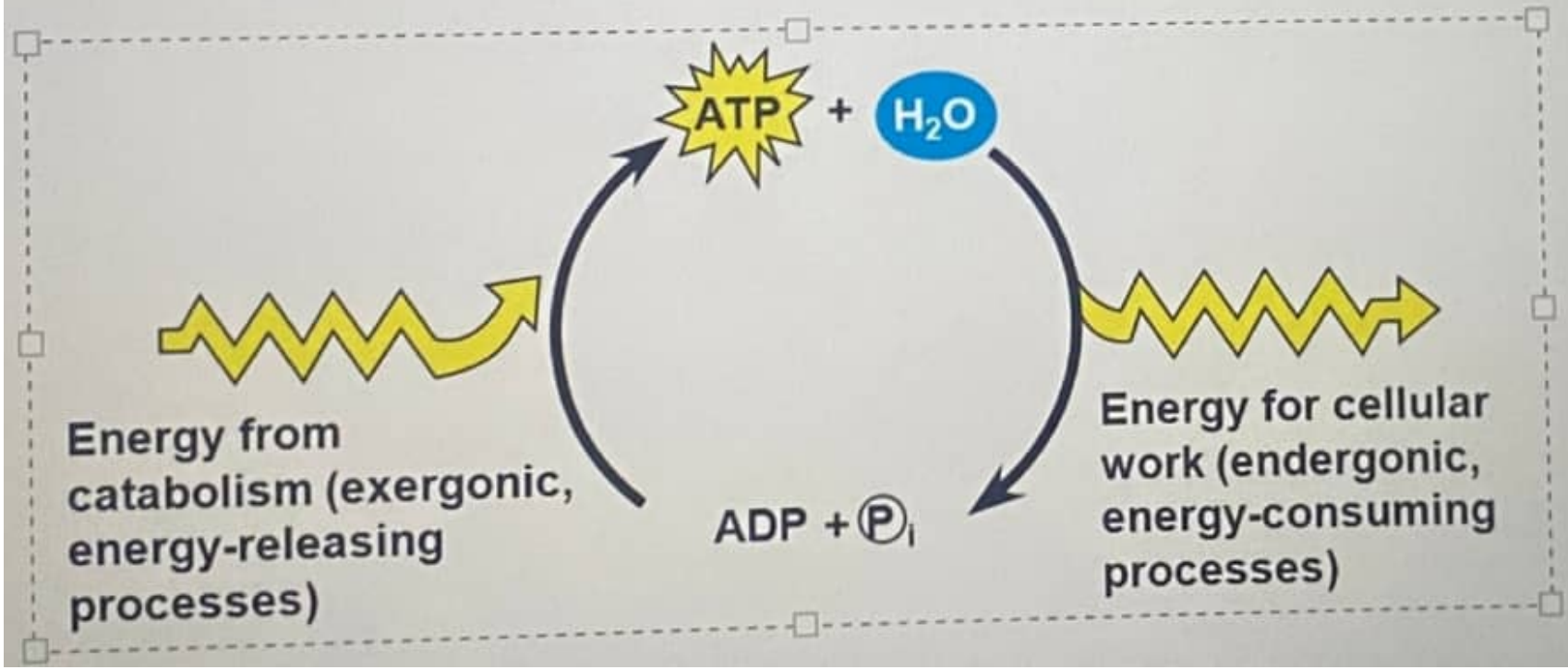
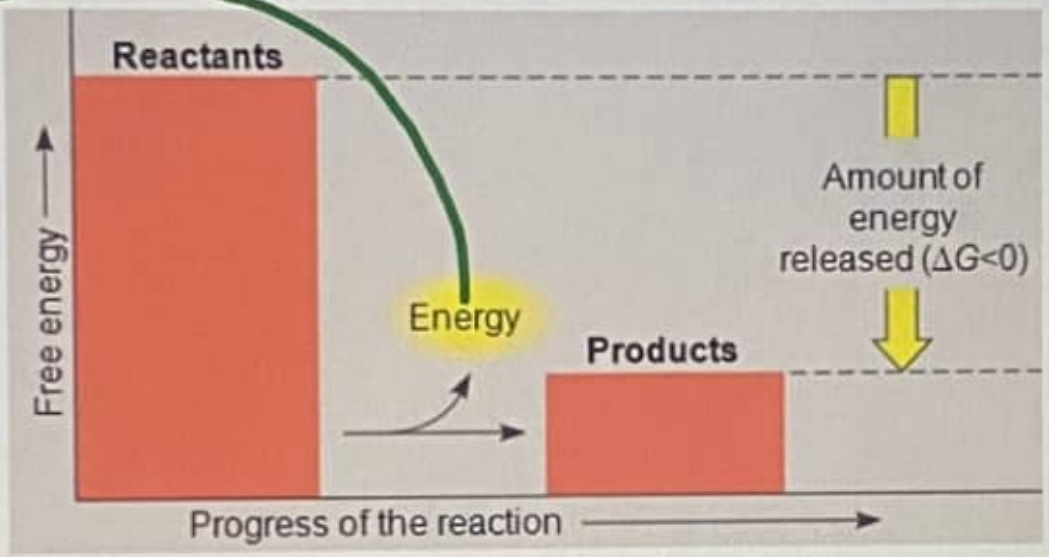
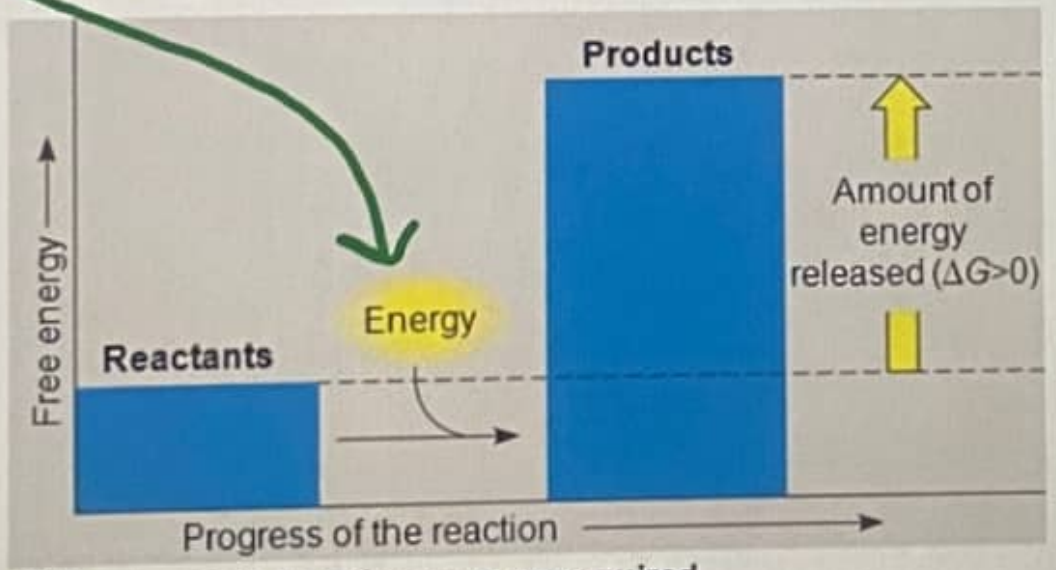


Figure 8.6 Free energy changes (ΔG) in exergonic and endergonic reactions



(a) Exergonic reaction: energy released



(b) Endergonic reaction: energy required

For a chemical reaction to occur:
1- reactants have to approach each other in the correct orientation.
2- Some of the existing bonds must break and new bonds must form.
3-Products are formed.

Since every reaction required the breaking of bonds → every reaction requires energy

the initial energy needed to start a chemical rxn is called THE ACTIVATION ENERGY.

Activation energy is often supplied in the form of thermal energy that the reactant molecules absorb from their surroundings to allow the reactants to get into their transition state.

Transition state is a phase where some of the reactant's bonds have been broken yet no new products have been formed.

Sometimes vital reactions require very high amounts of heat/pressure (activation energy) but having these condtitions may not be suitable since it'll lead to the death of the cell.

Therefor a catalyst is needed.

In biology we call this catalyst an enzyme

Enzyme:
A globular protein that functions as a biological catalyst, it speeds up the reaction by lowering the energy of activation without being affected by the reaction it catalyzes.

→ Therefore the energy of activation :
1- Can be reduced by enzymes
2- Varies from one reaction to another

Enzymes could be → Proteins (enzymes)
→ Composed of RNA (ribozymes)

Catalytic behavior depends on:
-primary –secondary –tertiary –quaternary Structures

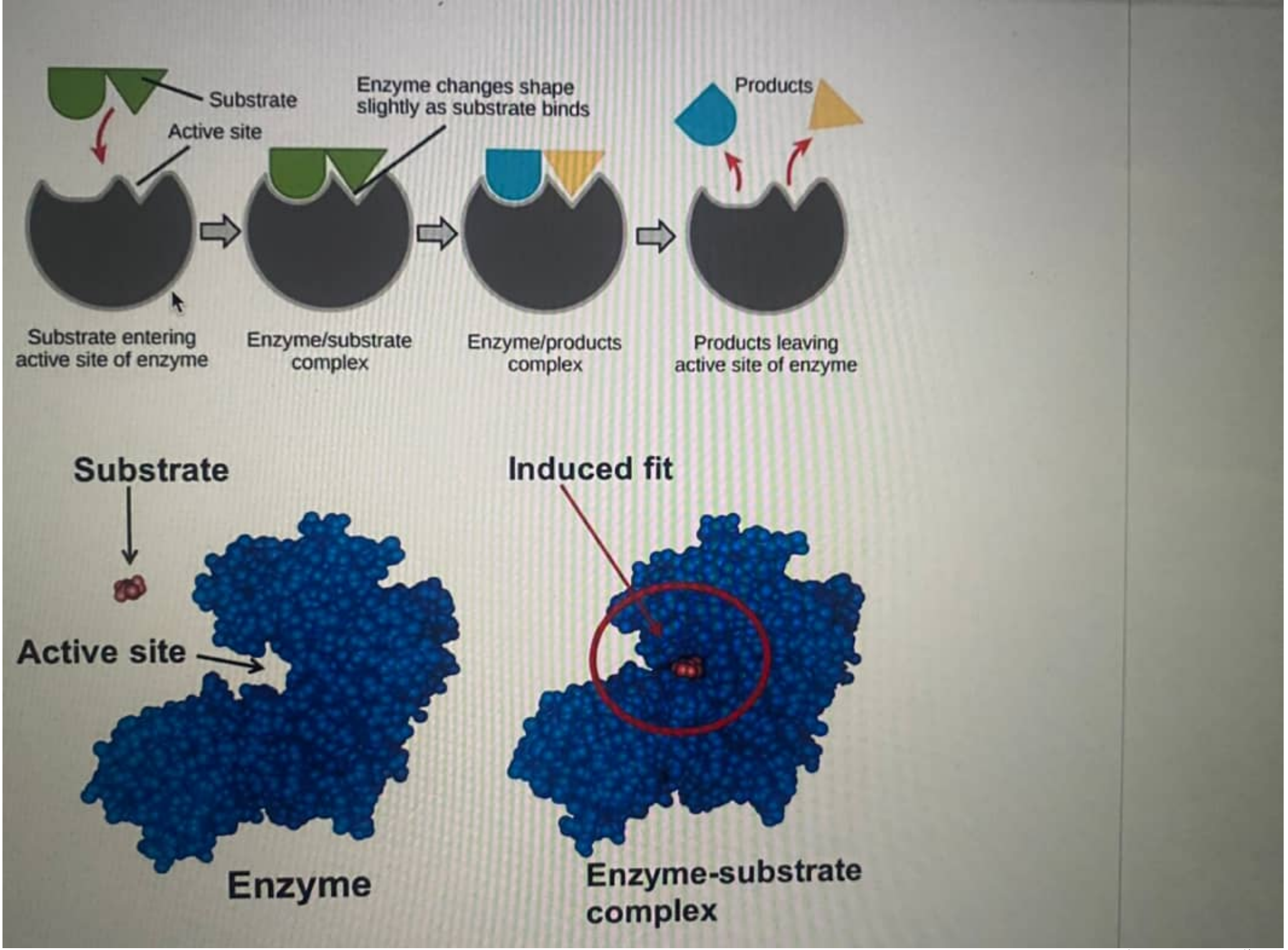
Note: Enzymes are substrate specific
WHY??
→ Presence of the active site(region where the substrate will bind)

The substrate is what gets catalyzed
Eg- gluecose, pyruvate etc...

How does the substrate bind to the active site??

→ Weak bonds. 1-Hydrogen bonds or 2-ionic bonds

Mechanism of enzyme action:
1- Substrate binds to active site via weak bonds (temporary bonds)
2- When substrate enters the active site the enzyme Is no longer loose and an induced fit is formed where the enzyme becomes tight around the substrate complex.
3- Formation of Enzyme Substrate Complex (ESC).
4- Substrate will be stressed. Where does this stress occur?? → Bonds between substrate. → Lower energy is required to break the bonds of the substrate → Energy of activation is reduced → Reactions can occur at body temperature.
5- New bonds form.
6- Reactants have been converted to products.
7- Since products have a different conformation that the reactants they are released and enzyme returns to its original conformation (loose and ready to accept the next substrate).



Enzymes can function alone but sometimes it requires activators (helpers) that are non-protein.

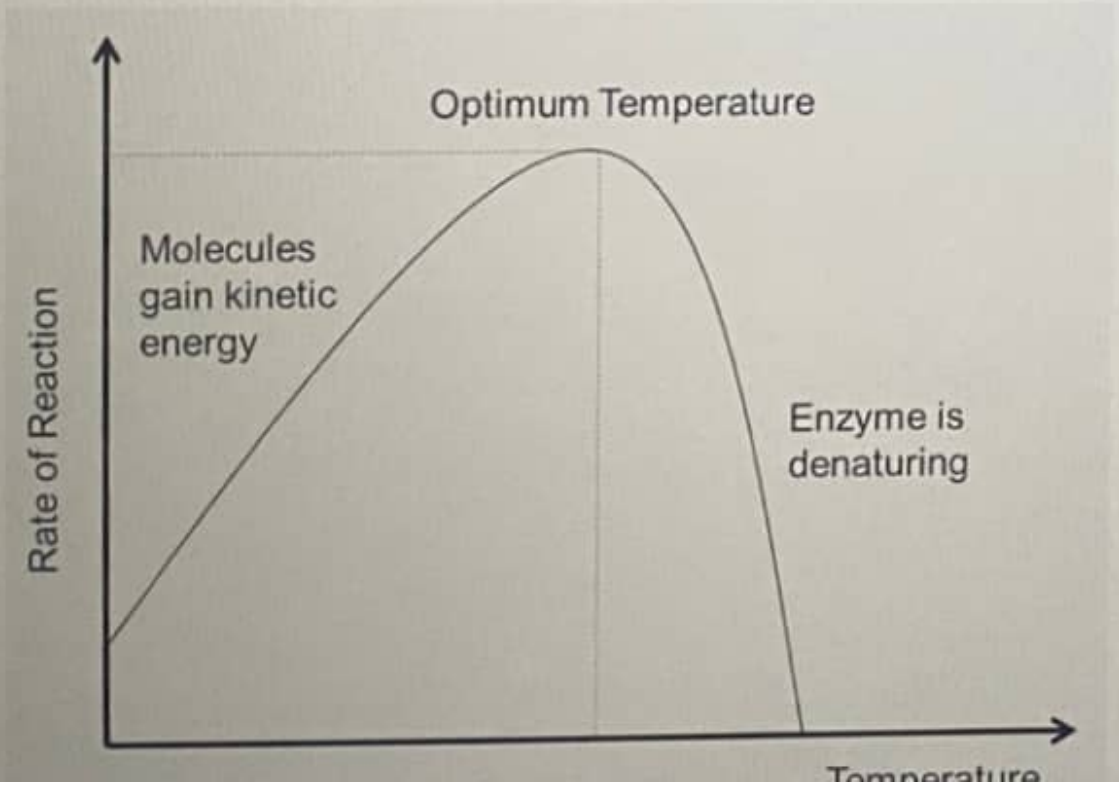
Activators: → 1- Cofactor (inorganic substance... eg- metal).

→ 2- Coenzyme (Organic substance... eg- Vitamins).

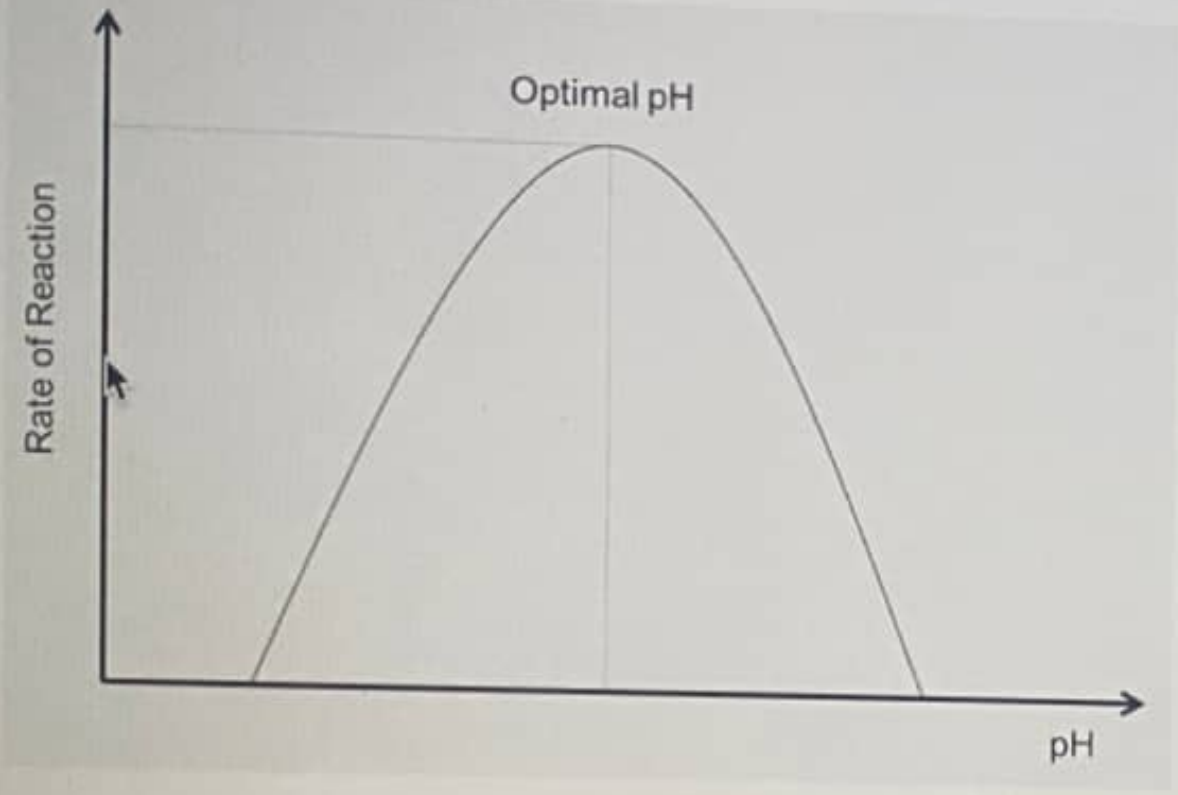
Factors that affect the rate of reaction:
1- Temperature
2- PH

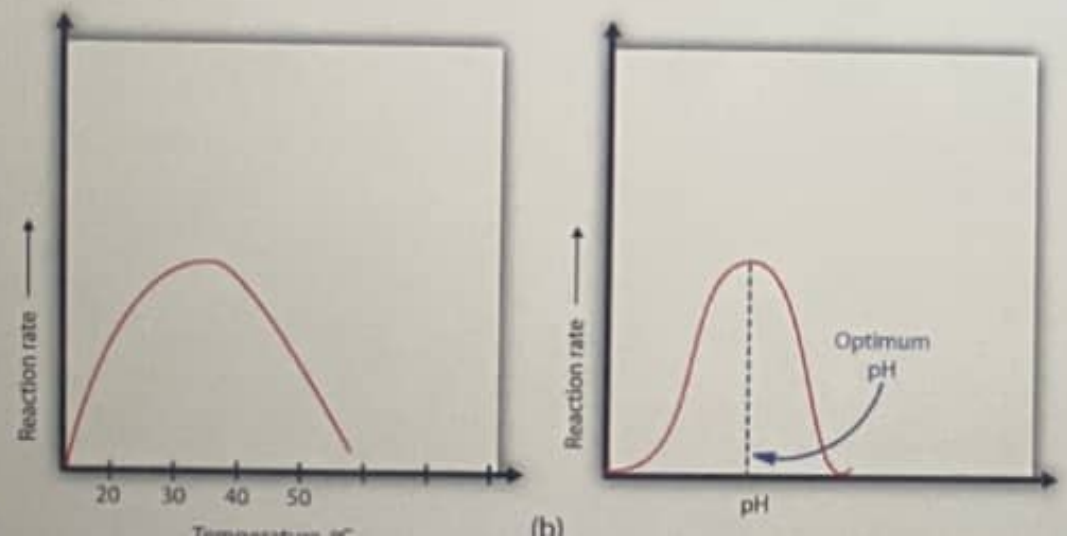
Effect of Temp on enzymatic activity.
In most human cells the optimum temp (enzyme activity is best) at 37 degrees Celcius.
If the temperature is >37 → Sharp reductivity in the rate → Denaturation.
Why does denaturation occur?

Heat changes the conformation of the enzyme, so the substrate can no longer fit into the active site, thus can no longer be converted to product.



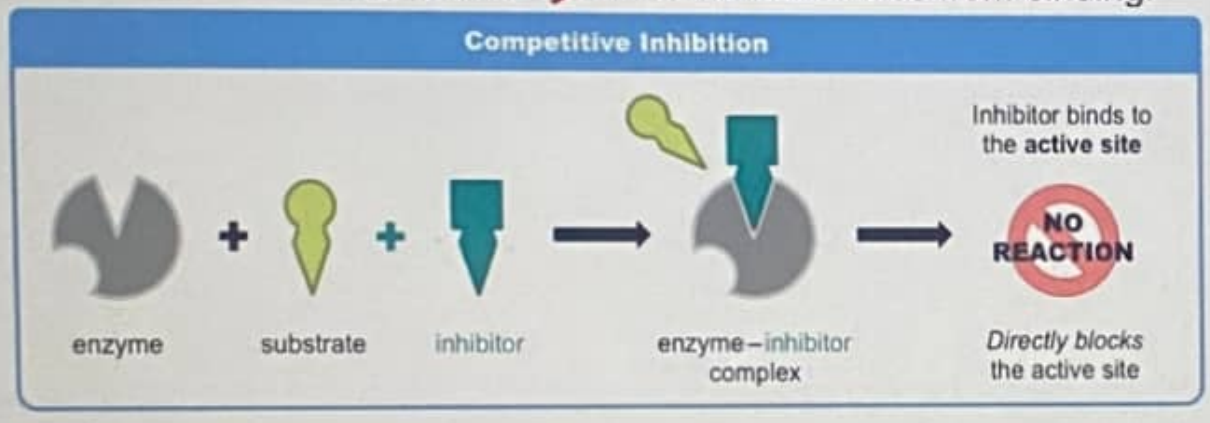
Effect of PH on enzymatic activity.
Most enzymes work best at PH near 7.4.
NOT ALL THOUGH
Eg- Pepsin: Optimum PH=2 (Acidic)
Eg- Trypsin: Optimum PH=8 (Basic) since its found in the intestines.



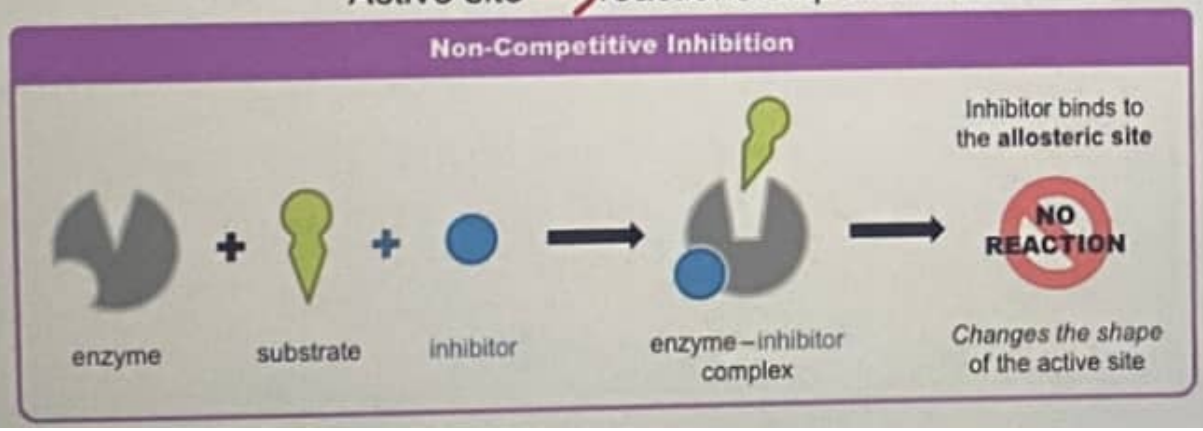


Enzyme Inhibitors:
Interfere with the ability of enzymes to do work.

Inhibitors: → Competitive inhibitor
Competitive inhibitors compete with the substrate. HOW??
Inhibitor and substrate have a similar shape → Tries to bind with the Active site → Prevents substrates from binding.



→ Non-Competitive inhibitor
Doest bind to the active site but binds to the lower end of the enzyme.
What happens??
→Changes the conformation of the enzyme → Changes Conformation of the active site → substrate can no longer fit into the Active site →reactions stop until it detaches.



Inhibitors could either be: Permanent or Temporary

How can I reduce the effect of competitive inhibitors?

→ By increasing the number of substrates.

Regulation of enzyme activity:

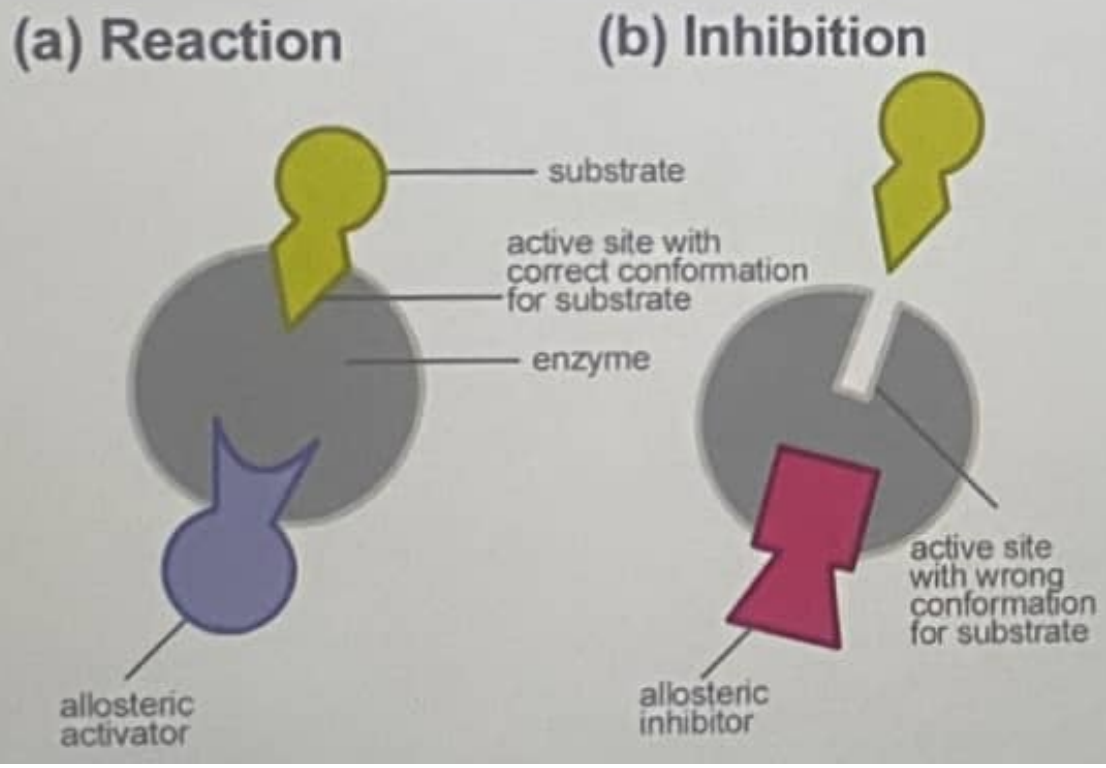
1- Inhibits or
2- stimulates

Enzymes activity

When does it occur?
When a regulatory molecule (regulator) binds to a protein at a different site that the active site. Although it doesn't bind to the active site It affects the protein's function at the active site (by changing the shape of the active site. It either:

Inhibits (deactivates) (negative). Allosteric inhibitor → change conformation of the active site. Stabilization of enzyme in inactive form.

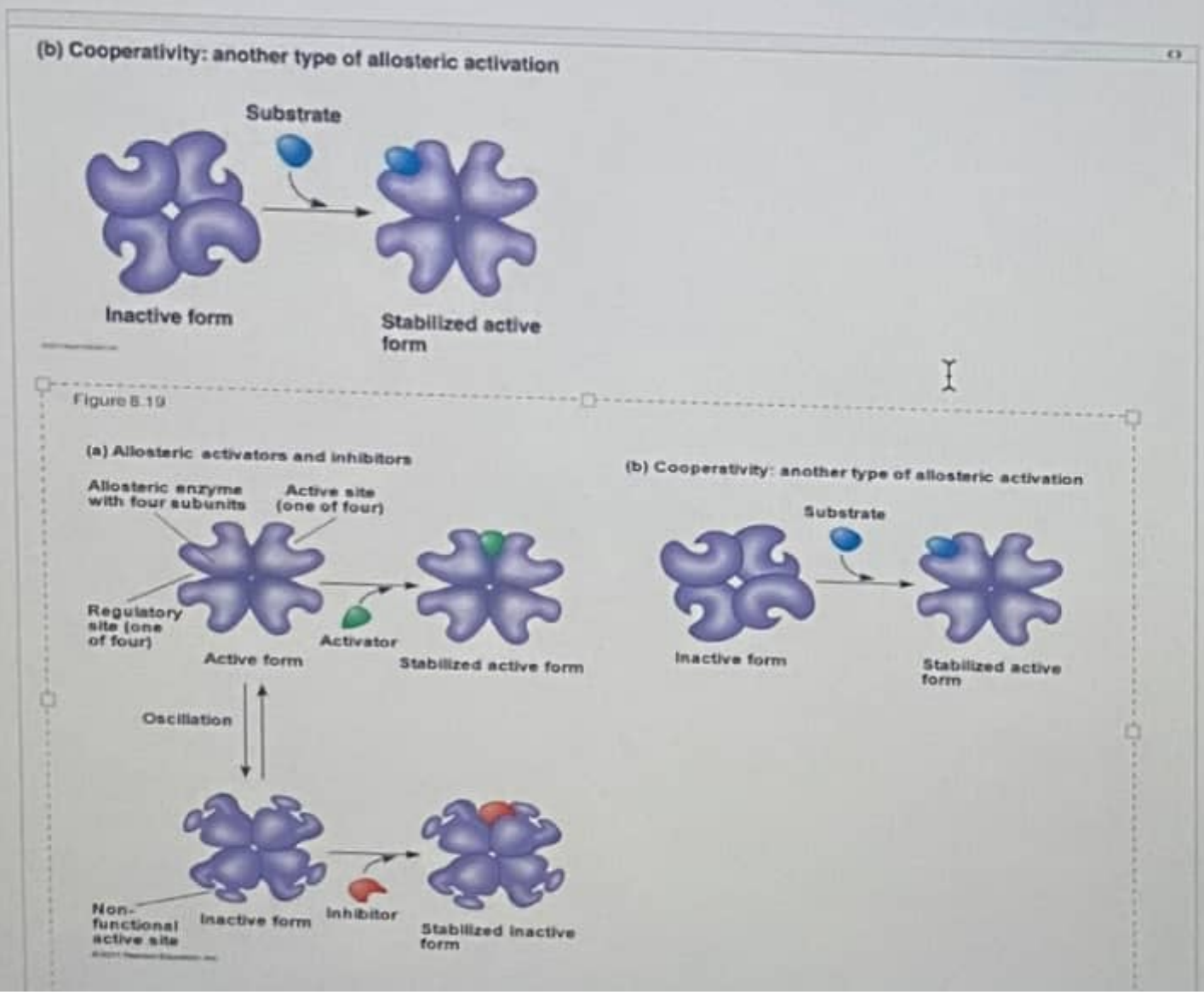
Stimulates (activates) (Positive).
Allosteric activators → Stabilization of enzyme in active form.



Allosteric Enzyme:
Consists of 4 subunits (4 Active sites)
Also contains regulatory site.

Cooperativity (Allosteric activation)
Inactive form → Stabilized active form

Substrate binds to one subunit (active site)



Regulation of metabolism.
(switch rxn's on/off)

→ Feedback mechanism.
→ Prevents accumulation of products. HOW??

1- Final product goes to primary/secondary enzyme
2- Product binds to regulatory site
→ Enzyme stabilizes in inactive form.
→ Inhibition. (feedback inhibition)
3- Once products is consumed and have a low conc it detaches from regulatory site and enzyme returns to its active form.