BIOLOGY 12 - ENZYMES & CELLULAR METABOLISM: CHAPTER NOTES

In order for cells to maintain homeostasis, they must constantly convert chemicals from one form to another, in order to produce necessary molecules, obtain usable molecules from food, and produce energy rich molecules.

- *These constantly occurring chemical reactions are collectively known as **metabolism**. In this chapter, you will learn about the molecules that control metabolism, **ENZYMES**.*

METABOLISM AND METABOLIC PATHWAYS

METABOLISM

- a term to collectively describe all the chemical reactions occurring constantly in the cell that maintain homeostasis.

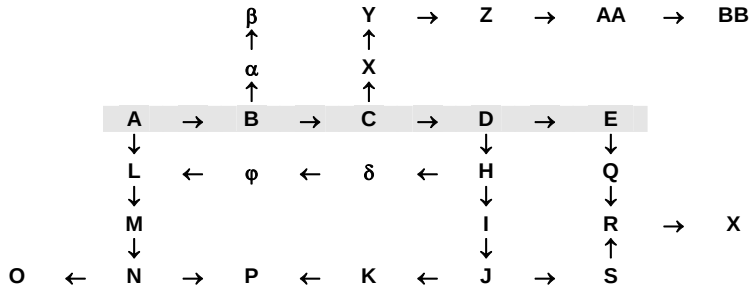
METABOLIC PATHWAYS

- the orderly step-wise series of chemical reactions from the initial **reactants** to the final **products**. One reaction leads to the next. Highly **structured**. Controlled by **enzymes**.
- each step (i.e. each chemical reaction) within the metabolic pathway requires **a SPECIFIC enzyme**.

	Step 1		Step 2		Step 3		Step 4		Step 5		Step 6	
A	⇨	**B**	⇨	**C**	⇨	**D**	⇨	**E**	⇨	**F**	⇨	**G**
reactant	Enz. 1		Enz. 2		Enz. 3		Enz. 4		Enz. 5		Enz. 6	Product

*There are **reasons** why metabolic pathways exist:*

1. it is **not possible in biological systems to have a single reaction that could produce complex molecules** from simple reactants. (e.g. $6CO_2 + 6H_2O \Rightarrow C_6H_{12}O_6 + 6O_2$ would **never** happen in a cell in one step). **Many** intermediate steps are needed.
2. one pathway **can lead to several others** (intermediate products of one pathway can be **starting reactant** for another pathway.
3. having more than one step means that there are more places where the overall reaction can be **controlled**.

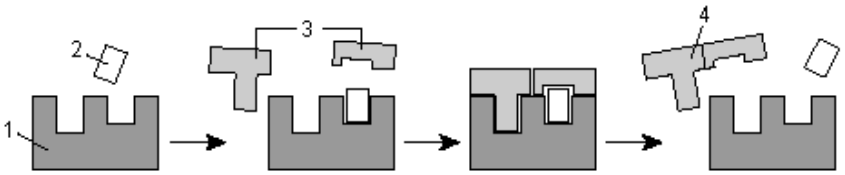


ENZYMES: Biological Catalysts

- **ENZYME** (abbr. = "E"): a **protein** that **can speed up a chemical reaction without being consumed**.
- Enzymes are the **sites** of chemical reactions, but **aren't used up in the reaction or permanently changed by the reaction.** They can, for example, hold reactant molecules together long enough for them to react.
- Enzymes are **Highly Specific**. Each enzyme speeds up only **one** reaction. Enzyme names usually end with the suffix "**ase**" (or sometimes "sin" e.g. trypsin, pepsin)
- **SUBSTRATE** ("S"): the **reactant**(s) in an enzyme's reaction.
- The equation for an enzyme-catalyzed reaction is always:

$$\mathbf{E + S \rightarrow ES \rightarrow E + P}$$

where "ES" = **ENZYME-SUBSTRATE COMPLEX** (the chemical reaction occurs when the ES complex exists). The place where the substrates actually bind on the enzyme is known as the **ACTIVE SITE**.

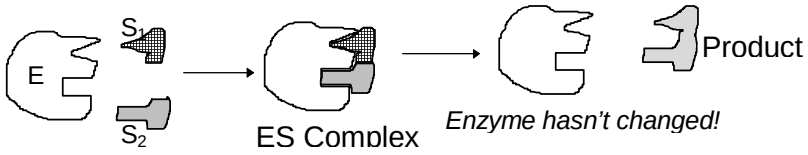


Please Label the parts of this diagram, and identify the ES complex.

How do Enzymes Work? The ***LOCK AND KEY THEORY*** vs. the ***Induced Fit Theory***

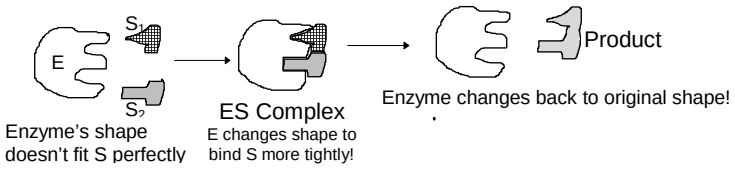
- Because the molecules in question are so *small* and the reaction happen so *fast*, we've never clearly seen how enzymes work. We do, however, have a *good model*. The original model, called the "**Lock and Key Theory**" has more recently been superseded by a slightly more sophisticated model called the "**Induced Fit Theory**."

Lock and Key Theory



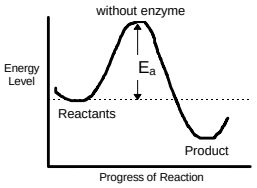
- *Mark in the active site on the above diagrams!*
- E and S meet during the reaction, and fit together perfectly from the very beginning, like a **lock and key**.
- While this model is basically correct, we now believe that instead of always remaining rigid, **the enzyme actually CHANGES SHAPE slightly** when it binds the substrates, in order to get a better tighter "grip" on the reactants. This modification of the Lock and Key theory is known as the **Induced Fit Theory**.

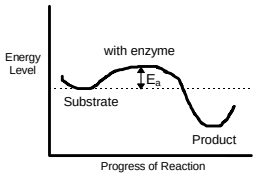
Induced Fit Theory



- Upon binding , the enzyme undergoes a slight **conformational change** to **more perfectly bind** the substrates.
- Then the reaction takes place, the ES complex separates, and **the enzyme re-assumes its original shape**. It is now free to catalyze another reaction.

How does an Enzyme work?





- **It LOWERS the ACTIVATION ENERGY** required for the reaction to proceed. Activation Energy is defined as **the energy that must be supplied to cause molecules to react with one another**. Enzymes do this **by bringing the substrate molecules together and holding them long enough for the reaction to take place**.

⇒ *You must be able to interpret the above graph!!*

FACTORS AFFECTING ENZYME ACTIVITY

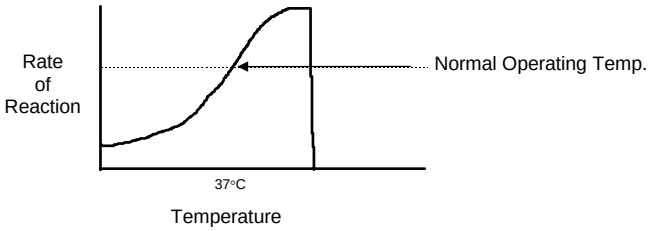
⇒ *As enzymes are proteins, they are affected by the same sorts of things that affect proteins. Since the **shape** of enzymes determines the shape of the active site, which determines their function, anything that changes the shape of an enzyme with affect the enymatic yield. Some factors are:*

1. pH:: most enzymes prefer pH's of 6 - 8 (some exceptions: **pepsin** in the stomach - pH ~ 2, **trypsin** in the small intestine - pH ~ 8)

- if the pH is too low **or** too high, the enzyme **DENATURES** (a denatured protein is one that **has lost its normal configuration**, and therefore its ability to form an enzyme-substrate complex).

2. TEMPERATURE

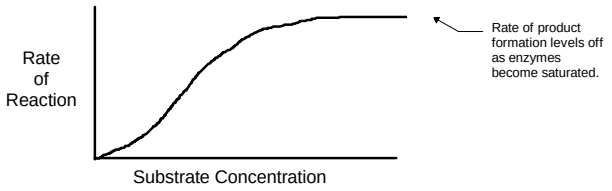
- **decreasing** temperature will **slow** rate of reaction. The lower the temperature, the lower the rate of reaction. Very low temperatures **don't** normally denature the enzyme, however.
- **increasing** the temperature slightly will, at first, **increase** the rate of reaction and product formation (as it speeds up the rate at which substrates bump into enzymes). i.e. within E's *operating range*, an *increase in Temp. will increase rate of reaction*.



- However, temperature too high (above about 45 °C) will **DENATURE** the enzyme.

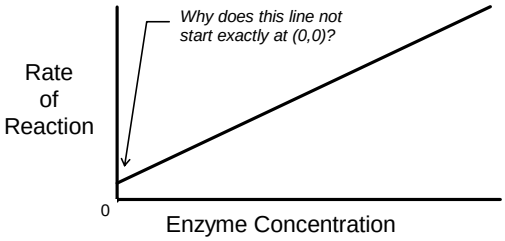
3. Concentrations of SUBSTRATES

- if the concentration (abbr. = "[ ]") of substrate increases, amount of product increases. The rate of product formation will usually increase too. However, after a certain [ ], the rate won't increase anymore, as all the enzymes are "saturated" with substrates and can't work any faster.
- if the concentration of substrate decreases, the rate of product formation will generally decrease as well.



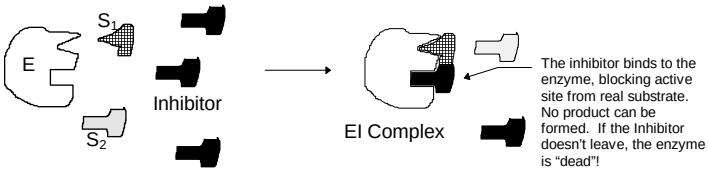
4. <u>Concentration of ENZYME</u>

- This is what **<u>limits the overall rate of reaction</u>**. Providing there is adequate substrate (and their is typically *millions* more substrate molecules than enzyme molecules**), <u>the</u> <u>more</u> <u>enzyme</u> <u>you</u> <u>add,</u> <u>the</u> <u>more</u> <u>product</u> <u>you</u> <u>get</u>**, and the **less enzyme you have, the less product you get**. In other words, if [enzyme] increases, rate of product formation increases. If amount of enzyme decreases, the rate of product formation decreases. The rate will only level off if you run out of substrate, which is usually not the case.



5. <u>Presence of INHIBITORS</u>

- inhibitors are molecules that **bind to the enzyme in some way to prevent or reduce the rate of substrate binding to enzyme**. There are several ways in which inhibition can work.

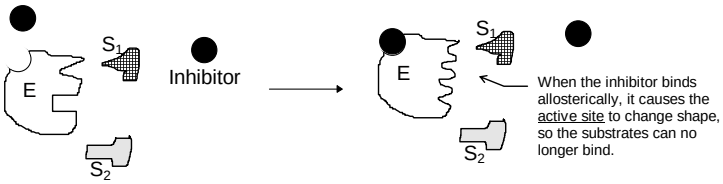


a) ***Competitive Inhibition***

- a molecule that **looks like the substrate** can **compete for space** at the active site (the place where the substrate binds to enzyme). This will **slow down** the reaction rate. The inhibitor binding to E can be **REVERSIBLE** or **IRREVERSIBLE**.

- Obviously, the more inhibitors are added, the lower the rate of reaction, and the less product is going to be made.

b) ***<u>NON-COMPETITIVE INHIBITION</u>***



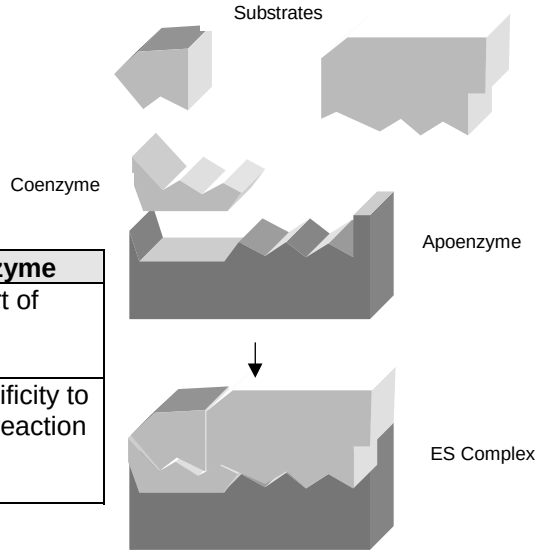
- in this case, the inhibitor binds to **another place** on enzyme (**<u>not</u>** the active site). The inhibitor may look completely different from the substrate.
- When the inhibitor binds, it cause the enzyme to change shape ***<u>at the active site</u>*** so S cannot bind.
- binding may, as it is for competitive inhibition, be reversible or non-reversible.
- This type of inhibition is also known as "*allosteric*" inhibition.

Examples of Inhibition:

- Reversible inhibition is often used as **a normal way of slowing down metabolic pathways** (e.g. an intermediate or final product may be a reversible inhibitor of another enzyme in the pathway e.g. threonine).
- Inhibitors can also be chemicals introduced into a system from the outside, and can act as medicines or poisons. e.g. **penicillin** is a medicine that kills bacteria. It works by binding **irreversibly** to the enzyme that makes bacterial cell walls.
- **HCN** (hydrogen cyanide) is a lethal **irreversible** inhibitor of enzyme action in human.
- **Lead** (Pb^{++}) and other **HEAVY METALS** (like **mercury** (Hg^{++}) and **cadmium**) are non-competitive inhibitors that cause poisoning when they bind irreversibly to enzymes and make them denature.

What are Enzymes Made of?

1) a **protein part** called an **<u>APOENZYME</u>** that gives it its ***specificity*** (i.e. exactly what reaction it will catalyze)
2) a **non-protein** group called a **<u>COENZYME</u>** which may help out the reaction by accepting or donating atoms (e.g. H^+). Label the diagram to the right.



To summarize...

Coenzyme	Apoenzyme
large non-protein molecules, many are **vitamins**. e.g. niacin (nicotinic acid) riboflavin (vitamin B_2), folic acid, biotin (vitamin H), thiamine (vitamin B_1)	protein part of enzyme
Helps reaction - may participate in reaction by accepting or giving atoms to the reaction. e.g. **<u>NAD cycle</u>** NAD (nicotinamide adenine dinucleotide) is a coenzyme of many oxidation-reduction reactions.	gives specificity to particular reaction