The "effects" that are in play when the enzyme-substrate complex forms:

The proximity effect:	The enzyme has to join up with the substrate
The orientation effect:	The groups must connect close to one another
The catalytic effect:	The chains needed for catalysis are in the active site
The energy effect:	The activation energy is lowered

The Effect of Concentration on Enzymatic Activity

When the substrate concentration is low relative to that of the enzyme, then not all of the enzyme molecules are in use. The rate will increase as the substrate concentration goes up, but only to a certain point…the saturation point. As the saturation point nears, the rate begins to level off. Eventually the saturation point is reached…this is the point where no enzyme molecules are available. At this time the rate is constant. Now that the enzyme is saturated, adding more substrate will not cause the rate to go up. In the absence of a change in the concentration of an enzyme, the rate when the enzyme is saturated is determined by the efficiency of the enzyme, the pH and the temperature.

Usually an enzyme is not saturated, so typically the reaction rate is controlled by the amount of substrate added and the overall efficiency of the enzyme. Remember that the most efficient enzyme is catalase!

It is possible for the concentration of an enzyme to vary according to our body's needs. As long as the concentration of the substrate does not become a limiting factor, the reaction rate varies directly with the enzyme concentration…so if the enzyme concentration doubles, the rate doubles and so on.

Effect of Temperature and pH on Enzyme Activity

An enzyme's maximum catalytic activity is highly dependent on pH and temperature. Each enzyme's optimal conditions are pretty much the conditions (temp and pH) for the location in the body where that enzyme functions. For some enzymes, this is a pH of 7.4, and for others it's pH of 2.

Temperature

When temperature goes up most metabolic activity goes up and the same is true for enzymes. However, it is important to note that there is a point where the temperature is TOO HIGH and the enzyme denatures. For most enzymes this is about 50-60 degrees Celsius. Also, a drop in temperature causes a slowing of metabolic activity.

pH

Most enzymes have an optimal pH for catalytic activity…for example, pepsin has an optimal pH of 2 (it works in the stomach, which is highly acidic), while chymotripsin has

an optimal pH of 8 (it works in the slightly alkaline small intestine). Extreme pH will also denature a protein.

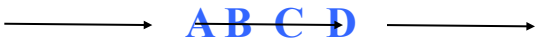
Enzyme Regulation

Enzymes don't just speed up reactions…they also turn some on, turn others off and even slow them down depending on the body's needs.

Activation: Any process that starts or increases the action of an enzyme

Inhibition: Any process that stops or slows the reaction rate of the enzyme

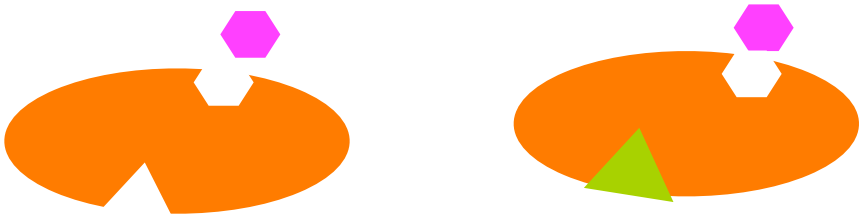
Feedback: Regulation of an enzyme's activity by the product of a reaction later on in the pathway. Think of positive and negative feedback.



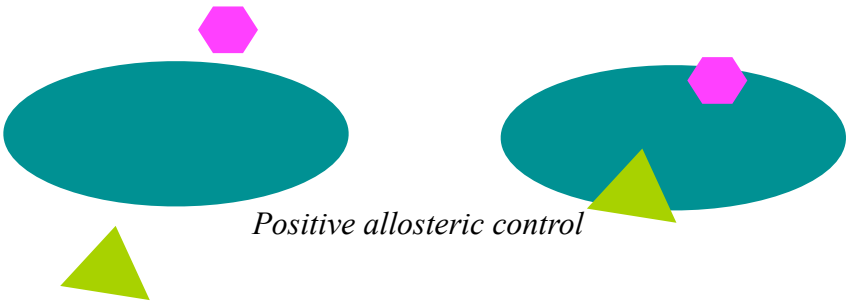
Allosteric Control

In this type of control, the regulator binds to the enzyme but not on the active site. This affects the protein's ability to bind to another molecule at its main active site. Most have two different types of binding sites…a site for substrate and a site for regulators. One advantage of allosteric enzyme control is that the regulators don't have to be structurally similar to the substrate because they have their own binding site separate from the active site.

Most of the regulators bind by noncovalent interactions.



Negative allosteric control



Positive allosteric control

Enzyme Regulation: Inhibition

Enzyme inhibition can be reversible or irreversible. When it is REVERSIBLE, the inhibitor binds to the substrate and then unbinds, allowing the enzyme to return to its normal state. When it is IRREVERSIBLE, then the inhibitor forms a covalent bond at the active site and stays there. The enzyme is completely inactivated. Most poisons work by irreversible inhibition.

Type of Inhibition	Where binding takes place	Type of bonding or control	Affect on Enzyme's Catalytic Rate
Reversible noncompetitive	Different place than substrate (not active site)	Allosteric control	With increased substrate rates increase more gradually with inhibitor than without. The max rate is lower. Once the max rate reached, no amount of substrate can increase it further.
Reversible competitive	Active site	Noncovalent bonds	Reaction rate increases more gradually with increasing substrate concentration than without. Maximum rate is unchanged. Eventually all of an enzyme's active sites can be occupied by substrate, you just need more substrate.
Irreversible	Active site	Covalent bonds	Stops all enzyme activity

Examples of some irreversible inhibitors are lead and mercury. Also, organophosphorus insecticides like parathion and malathion, also Sarin the nerve gas, are irreversible inhibitors. Nasty stuff…stay away from those guys!

Enzyme Regulation

COVALENT MODIFICATION is the removal of a covalently bonded portion OR the addition of a group. The biggie example of this is when the inactive form of an enzyme is activated…think of fibrinogen being activated to fibrin in blood clotting. The inactive form of the enzyme is called the zymogen or proenzyme. A chemical reaction cleaves off part of the molecule, making it the active form (active because now the active site is accessible to the substrate). This ensures that really powerful enzymes only "do their thing" when and where they are supposed to. For example, some of the digestive enzymes produced in the pancreas are produced as proenzymes (zymogens) because otherwise they would digest the pancreas. Ew!

The flip side of covalent modification is by adding a group. The book talks about the addition of phosphoryl groups to serine or threonine (remember, both of these have an -OH group, which is where this addition takes place). This occurs, for example, when glycogen stored in muscles must be hydrolyzed to glucose for energy needs. Two serine residues in glycogen phosphorylase (an enzyme that initiates glycogen breakdown) are phosphorylated…meaning the phosphoyrl group is added. The groups are then removed when the need to break down glycogen has passed.

GENETIC CONTROL is especially useful for enzymes that are only need at certain points in development.

Vitamins

A Vitamin is a small organic compound that is required in trace amounts but not at all synthesized in the body. We HAVE TO GET IT FROM DIET. If we don't then we get vitamin deficiencies which can lead to disease such as scurvy, rickets and pallegra.

Two classes of vitamins

1. Water soluble
2. Fat soluble

The water soluble vitamins are found in aqueous environments and most are needed as coenzymes inside cells. The best known are Vitamins C, B-6 and B-12. Structurally they all have an –OH, -COOH or other polar group of some kind. Remember…they need that polarity to be soluble in water!

Fat soluble vitamins (A,D,E,K) are stored in the body's fat deposits…so I guess I have a lot of these vitamins in my butt. Ha! Note that though the effects of deficiencies are well-documented, the mechanisms of action are not very well understood.

Vitamin	Class	Function	Deficiency	Excess
Vitamin C	Water-soluble	Antioxidant Hydroxylate proline	Scurvy	Kidney stones
B-6	Water-soluble	In coenzyme for AA and lipid metabolism	Retarded growth, anemia, convulsions, epithelial changes	CNS alterations, can be fatal
B-12	Water-soluble	In coenzyme for nucleic acid metab.	Pernicious anemia	Excess RBCs
Vitamin A	Fat-soluble	Maintains epithelia, night vision, healthy eyes	Retarded growth, night blindness, deterioration of epithelial membrane	Liver damage, skin peeling, CNS effects, nausea, anorexia
Vitamin D	Fat-soluble	Bone growth, Ca and P absorption at gut/ retention at kidneys	Rickets	Calcium deposits
Vitamin E	Fat-soluble	Antioxidant (prevents breakdown of Vit A and fatty acids)	Anemia	None reported
Vitamin K	Fat-soluble	Synthesis of blood-clotting factors	Bleeding disorders	Liver dysfunction, jaundice

Antioxidants

An antioxidant is a substance that prevents oxidation. In the body we need protection from oxidizing agents that are the by-product of normal metabolism. The principal dietary antioxidants are vitamin C, vitamin E, beta-carotene and selenium. They work to

diffuse the potentially harmful actions of free radicals, which are highly reactive molecular fragments with unpaired electrons. Free radicals gain stability when they bind to nearby molecules, causing damage.

The principal biochemical activity of Vitamin E is to give up its hydrogen from the –OH group to bond to the free radical, thereby rendering it ineffective. The hydrogen in the Vitamin E is then restored by a reaction with Vitamin C.

[O]