

Highlights of Enzymes III Lecture

1. Substrate binding to enzymes is relevant to catalysis that we will consider. The first is the category of Sequential Displacement. It has two subsets.

- a. Random binding - the order of binding multiple substrates is not rigidly set.
- b. Ordered binding - Simple ordered binding - one substrate binds first followed by another followed by release of product.

2. Note that the models of substrate binding above are both non-covalent.

3. Another non-covalent enzyme mechanism involving multiple substrates is called Double Displacement (or Ping-Pong kinetics). In this method, the enzyme only binds one substrate at a time, but switches back and forth between different states. In the exam given in class, transaminase flips back and forth between carrying an oxygen or carrying an amine group. This also affects what substrate it binds to.

4. Allosterism is a phenomenon in which a small molecule interacts with a protein and affects the protein's activity. Such an enzyme is an allosteric enzyme. I pointed out the similarity between the kinetics of allosterically acting enzymes and the cooperativity of binding of oxygen by hemoglobin.

5. Enzymatic reactions can be inhibited by reversible and irreversible processes. Reversible processes involve binding of an inhibitor and its subsequent release. Irreversible processes generally involve covalent attachment of a molecule to an enzyme followed by its inactivation.

a. Competitive Inhibition - This type of reversible inhibition occurs when the inhibitor competes with the substrate for the binding site on an enzyme. The greater the concentration of inhibitor, the greater the inhibition. However, competitive inhibition can be overcome by increasing amounts of substrate. The apparent V_{max} of competitive inhibition does not vary from the V_{max} of the same reaction when uninhibited. The apparent K_m , however, does vary, because it requires more substrate to get the same velocity as the uninhibited reaction.

b. Non-competitive inhibition - This type of reversible inhibition occurs when an inhibitor binds to an enzyme at a site unrelated to the substrate binding site. In this case, the inhibitor's binding to the enzyme is unrelated to the binding of the substrate and the inhibitor does not have to have a structure like that of the substrate. Thus, the inhibitor and substrate don't compete with each other. The inhibitor can inhibit the enzyme (during its binding) without interference from the substrate. Therefore, increasing substrate concentrations cannot eliminate the effect of the inhibitor. In this case, the V_{max} is lowered, but the K_m is unchanged.

6. You should be able to depict or understand graphically (V vs S , Lineweaver-Burk) what occurs in competitive and noncompetitive inhibition. You should also be able to describe precisely what is

involved in these types of inhibition, if asked. You will NOT be given a set of data and asked to plot it, however.

END EXAM I MATERIAL HERE