Chapter 10 Lecture

General, Organic, and Biological Chemistry: An Integrated Approach

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Chapter 10

Enzymes—Nature's Chemists

Chapter Outline

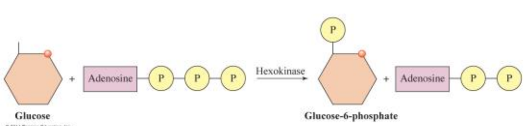
Introduction

- ***Enzymes*** are biologically active proteins that accelerate the breakdown of food that is eaten.
- Enzymes are biological ***catalysts***. They accelerate reactions, but are not consumed or changed in reactions.
- Discussions on the production or consumption of energy, specifically heat, during chemical reactions is called ***thermodynamics***.

10.1 Enzymes and Their Substrates

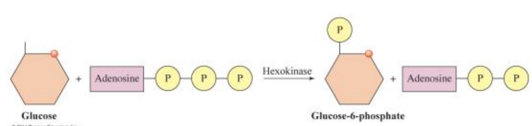
- Enzymes are large proteins with complex, three-dimensional structures.
- Enzymes work in an aqueous environment in our body so that the protein chain folds such that the polar amino acids are on the surface.
- Consider hexokinase, an enzyme whose job is to transfer a phosphate group from the high energy molecule, adenosine triphosphate, ATP, to D-glucose.

10.1 Enzymes and Their Substrates, Continued



- In this equation, the enzyme name is written above or below the reaction arrow.
- The phosphate group is represented by a P in a circle.

10.1 Enzymes and Their Substrates, Continued



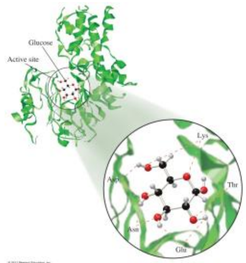
- Increase reaction speed (temp, pressure, pH)
- Specific for one type of reaction
- Often specific for one substrate
- Names end in "ase"

10.1 Enzymes and Their Substrates, Continued

The Active Site

Active site animation

The folded structure for hexokinase is shown here.



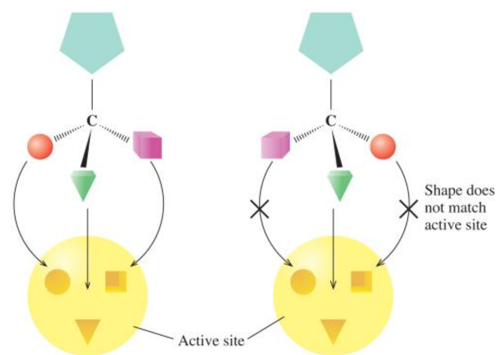
10.1 Enzymes and Their Substrates, Continued

- When in its proper three-dimensional shape, hexokinase has an indentation on one side of the structure.
- This indentation is known as the ***active site***, and it is lined with amino acid side chains.
- The active site is the functional part of an enzyme where catalysis occurs.

10.1 Enzymes and Their Substrates, Continued

- Glucose, the reactant for hexokinase, fits snugly in the active site. In an enzyme reaction, the reactant is called the ***substrate***.
- Enzymes have specific substrates, a property known as ***substrate specificity***. For example, the active site of hexokinase reacts with D-glucose, but will not react with L-glucose.
- Enzymes are specific for one enantiomer of the substrate. *Not L-glucose*

10.1 Enzymes and Their Substrates, Continued



10.1 Enzymes and Their Substrates, Continued

Some enzymes, like hexokinase, have non-protein helpers. Two categories of helpers are as follows:

1. ***Cofactors*** are inorganic substances like magnesium ions (minerals)
2. ***Coenzymes*** are small organic molecules derived from vitamins. Riboflavin found in the coenzyme flavin adenine dinucleotide (FAD) is a coenzyme.

10.1 Enzymes and Their Substrates, Continued

Enzyme–Substrate Models

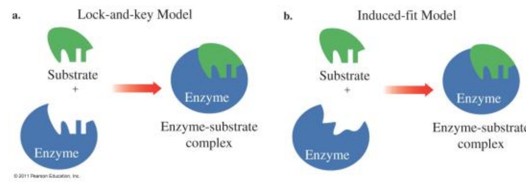
- A substrate is drawn into the active site by intermolecular attractions like hydrogen bonding.
- Hydrogen bonding orients the substrate properly within the active site.
- The initial interaction of the enzyme with the substrate is called the ***enzyme–substrate complex (ES).*** This complex forms prior to catalysis.

10.1 Enzymes and Their Substrates, Continued

There are two enzyme–substrate models:

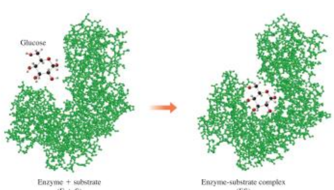
1. In the ***Lock-and-key model***, the active site is thought to be a rigid, inflexible shape that is an exact complement to the shape of the substrate. The substrate fits in the active site much like a key fits in a lock.
2. In the ***induced-fit model***, the active site is flexible, has a shape roughly complementary to the shape of its substrate, and undergoes a conformational change, adjusting to the shape of the substrate when the substrate interacts with the enzyme.

10.1 Enzymes and Their Substrates, Continued



10.1 Enzymes and Their Substrates, Continued

A good example of an induced-fit model is when hexokinase and glucose form an enzyme–substrate complex as shown.



10.2 Thermodynamics of Chemical Reactions

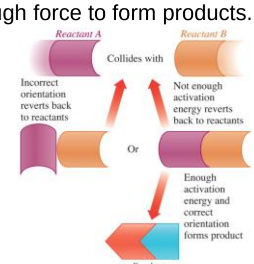
- As chemical reactions occur, some bonds are formed and some are broken, and in the process, the amount of energy changes.
- Some reactions release energy as heat (***exothermic reactions***), and some absorb energy as heat (***endothermic reactions***).

10.2 Thermodynamics of Chemical Reactions, Continued

- A collision of reactant molecules must occur for a chemical reaction to occur. Energy is required to cause reactant molecules to collide. (temp)
- Reactant molecules must be aligned properly in order for a reaction to occur.
- ***Activation energy*** is required to properly align reactant molecules and to cause them to collide to produce products.

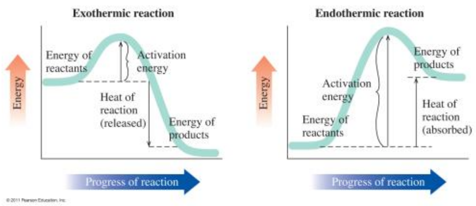
10.2 Thermodynamics of Chemical Reactions, Continued

If the energy that is available is lower than the activation energy, the molecules will not collide with enough force to form products.



10.2 Thermodynamics of Chemical Reactions, Continued

- The activation energy that must be overcome before products are formed is shown as:



- The ***heat of reaction*** is the difference between the energy of reactants and the energy of products.

10.2 Thermodynamics of Chemical Reactions, Continued

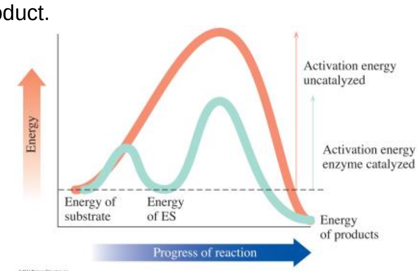
- Reactions with a low activation energy will proceed at a faster rate than reactions with a high activation energy.
- Activation energy can be lowered with a catalyst, which will cause the reaction to proceed at a faster rate.

10.3 Enzymes and Catalysis

- Enzymes lower the activation energy by forming ES complex.
- ES is formed through the interactions between the enzyme and substrate. Each interaction releases a small amount of energy to stabilize the complex.
- These interactions combine to lower the activation energy of the reaction.
- Some interactions that help lower the activation energy are discussed in the next several slides.

10.2 Thermodynamics of Chemical Reactions, Continued

An enzyme-catalyzed reaction increases the rate of a reaction by forming ES before forming a product.



10.3 Enzymes and Catalysis, Continued

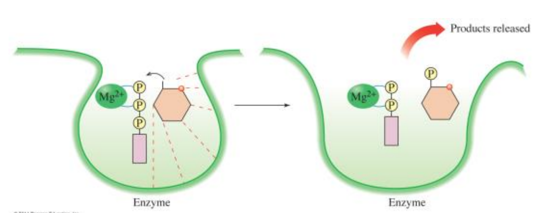
Proper orientation is shown as:

In the absence of an enzyme, it is more difficult for substrates to get close enough and orient themselves to react.

In the presence of an enzyme, it is easier for substrates to get close enough and orient themselves to react.

10.3 Enzymes and Catalysis, Continued

This figure shows the formation of glucose-6-phosphate by hexokinase.



10.4 Factors That Affect Enzyme Activity

- If allowed to sit untouched, the flesh of sliced apples will turn brown by a process known as ***oxidation***, caused by an enzyme.
- If lemon juice is sprinkled on the sliced apple, the vitamin C in the lemon juice will inhibit the formation of this brown color by changing the pH of the environment of the enzyme.

10.4 Factors That Affect Enzyme Activity

- Enzyme reactions are affected by reaction conditions such as
  - Substrate concentration
  - pH
  - Temperature
  - The presence of inhibitors

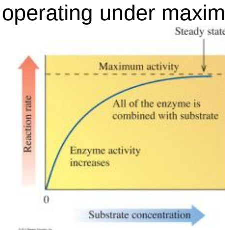
10.4 Factors That Affect Enzyme Activity, Continued

Substrate Concentration

- Recall that the first step in an enzyme-catalyzed reaction is the formation of ES.
- At a constant concentration of enzyme, an increase in substrate concentration will cause an increase in the enzyme activity up to the point where the enzyme becomes saturated with substrate.

10.4 Factors That Affect Enzyme Activity, Continued

- Increasing substrate concentration will not affect the rate of the reaction.
- A condition known as ***steady state*** is when an enzyme is operating under maximum activity.



10.4 Factors That Affect Enzyme Activity, Continued

pH

- When the enzyme environment is changed by pH, its tertiary structure is disrupted, altering the active site and causing the enzyme's activity to decrease.
- Enzymes are most active at a pH known as their ***optimum pH***.
- At optimum pH, the enzyme maintains its tertiary structure and its active site.

10.4 Factors That Affect Enzyme Activity, Continued

- Changes in pH will also affect the nature of the amino acid side chains in the active site.
- The optimum pH for enzymes is based on the location of the enzymes as shown:

TABLE 10.1 OPTIMUM pH FOR SELECTED ENZYMES

Enzyme	Location	Substrate	Optimum pH
Pepsin	Stomach	Peptide bonds	2
Sucrase	Small intestine	Sucrose	6.2
Urease	Liver	Urea	7.4
Hexokinase	All tissues	Glucose	7.5
Trypsin	Small intestine	Peptide bonds	8
Arginase	Liver	Arginine	9.7

10.4 Factors That Affect Enzyme Activity, Continued

Temperature

- Enzymes have an ***optimum temperature*** at which they are most active.
- The optimum temperature for most human enzymes is normal body temperature, 37 ºC.
- Above optimum temperature, enzymes lose activity due to disruption of intermolecular forces stabilizing the tertiary structure

10.4 Factors That Affect Enzyme Activity, Continued

- At high temperatures, enzymes denature, which modifies the active site.
- At low temperatures, enzyme activity is low due to a lack of energy for the reaction to occur.
- Food is stored in a refrigerator or freezer to slow spoilage brought on by enzymes.
- Boiling contaminated water will destroy enzymes in bacteria that are present in the water.

10.4 Factors That Affect Enzyme Activity, Continued

Inhibitors

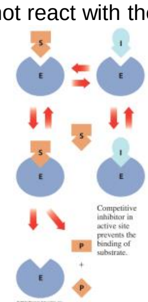
- ***Inhibitors*** are types of molecules that will cause enzymes to lose activity.
- Enzyme inhibitors prevent the active site from interacting with substrate to form ES.
- Some inhibitors cause temporary loss of activity, while others cause permanent loss of activity.

10.4 Factors That Affect Enzyme Activity, Continued

- ***Reversible inhibition*** occurs when the inhibitor causes a temporary loss of activity. However, activity is regained if the inhibitor is removed.
- Reversible inhibitors can be competitive or noncompetitive.
- ***Competitive inhibitors*** are molecules that compete with a substrate for the active site, and have a structure similar to the substrate.

10.4 Factors That Affect Enzyme Activity, Continued

As long as an inhibitor remains in the active site, the enzyme cannot react with the substrate to form product.



10.4 Factors That Affect Enzyme Activity, Continued

- An example of a medical therapy that involves a competitive inhibitor involves liver alcohol dehydrogenase (LAD). This enzyme oxidizes ethanol, the alcohol found in alcoholic beverages.
- This enzyme will also react with ethylene glycol and methanol, which are found in antifreeze, and will compete with ethanol for the active site.
- If a pet is poisoned by drinking antifreeze, a slow intravenous infusion of ethanol is administrated.

10.4 Factors That Affect Enzyme Activity, Continued

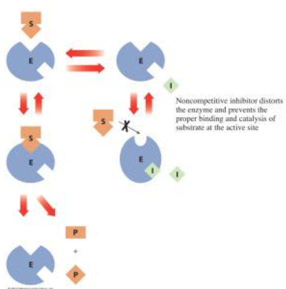
- Administration of ethanol slows the production of the toxic metabolites of ethylene glycol and methanol, giving the kidneys time to eliminate these two substrates.
- ***Noncompetitive inhibitors*** do not resemble the substrate. They do not compete for the enzyme's active site.
- Noncompetitive inhibitors bind at a site on the enzyme that is usually remote to the active site.

10.4 Factors That Affect Enzyme Activity, Continued

- When a noncompetitive inhibitor binds to an enzyme, it causes a conformational change in the enzyme. This change in shape causes the active site to no longer interact with the substrate.
- As long as this type of inhibitor is bound to the enzyme, it will no longer function effectively.

10.4 Factors That Affect Enzyme Activity, Continued

This figure diagrams how a noncompetitive inhibitor functions.



10.4 Factors That Affect Enzyme Activity, Continued

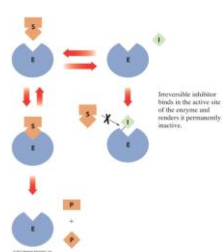
- Inhibitions caused by competitive and noncompetitive inhibitors can be reversed.
- Inhibition by competitive inhibitors can be reversed by adding more substrate. The higher the concentration of substrate, the more likely it will overcome the competition for the active site.
- Adding more substrate with noncompetitive inhibitors has no effect on overcoming inhibition.

10.4 Factors That Affect Enzyme Activity, Continued

- Reversing a noncompetitive inhibitor requires a special chemical reagent to remove the inhibitor and restore catalytic activity.
- An <u>***irreversible inhibitor***</u> forms a covalent bond with an amino acid side chain in the enzyme's active site.
- Irreversible inhibition causes the substrate to be excluded from the active site.
- Irreversible inhibition is a <u>permanent</u> inhibition.

10.4 Factors That Affect Enzyme Activity, Continued

- Irreversible inhibition is demonstrated in this figure.



- Heavy metals like silver, mercury, and lead are examples of irreversible inhibitors.

10.4 Factors That Affect Enzyme Activity, Continued

Antibiotics Inhibit Bacterial Enzymes

- Enzyme inhibitors are used to fight bacterial infections.
- Penicillin is an example of an irreversible inhibitor. It binds to the enzyme that bacteria use to synthesize cell walls, and slows the growth of cell walls.
- Without a cell wall, bacteria cannot survive and the infection stops.