Enzymes

1. The chemistry of life is organized into metabolic pathways.
   a. The total of all the chemical reactions occurring in an organism is called **metabolism**.
   b. All metabolic pathways consist of a series of reactions which convert one molecule (the reactant) into another (the product).
   c. A specific enzyme catalyzes each step of the pathway.
   d. **Catabolic pathways** release energy by breaking down complex molecules to simpler compounds.
      i. A major catabolic pathway is cellular respiration, in which the sugar glucose is broken down in the presence of oxygen to carbon dioxide and water.
   e. **Anabolic pathways** consume energy to build complicated molecules from simpler compounds.
      i. The synthesis of protein from amino acids is an example of an anabolic pathway.
   f. The energy released by catabolic pathways can be stored and then used to drive anabolic pathways.

2. Organisms transform energy
   a. **Energy** is the capacity to do work.
      i. Energy exists in various forms, and cells transform energy from one type into another.
      ii. Organisms absorb energy—light or chemical energy in the form of organic molecules—and release heat and metabolic waste products such as CO_2 to their surroundings.
   b. During every transfer or transformation of energy, some energy is converted to heat, which is the energy associated with the random movement of atoms and molecules.
   c. Chemical reactions can be classified as either **exergonic** or **endergonic** based on the change in energy that occurs because of the reaction.
      i. An exergonic reaction is one that releases energy.
      ii. An endergonic reaction is one that absorbs energy.

3. Enzymes speed up metabolic reactions by lowering energy barriers.
   a. Many chemical reactions occur spontaneously in cells but at very slow rates.
   b. A **catalyst** is a chemical agent that speeds up the rate of a reaction without being consumed by the reaction. An **enzyme** is a catalytic protein.
   c. The initial investment of energy for starting a reaction is the **free energy of activation** or **activation energy** (E_A).
   d. Activation energy is the amount of energy necessary to push the reactants over an energy barrier so that the reaction can proceed.
   e. There is not enough energy at the temperatures typical of the cell for most organic molecules to make it over the hump of activation energy. Heat would speed up reactions, but it would also denature proteins and kill cells.
   f. Enzymes speed reactions by lowering E_A.

4. Enzymes are substrate specific
    a. The reactant that an enzyme acts on is the **substrate.**
    b. The enzyme binds to the substrate and while they are bound, the catalytic action of the enzyme converts the substrate(s) to the product or products.
    c. Enzymes are often named for the substrate with the suffix "ase." *e.g.,* an enzyme which digests protein is a protease; one that digests lipids is a lipase.
    d. The reaction catalyzed by each enzyme is very specific.
    e. The **active site** is the area of the enzyme where the reaction actually occurs. The active site is like a pocket into which the substrate fits. There is specificity between the enzyme and substrate because of the shape of the active site.
        i. As the substrate enters the active site, interactions between the substrate and the amino acids of the enzyme causes the enzyme to change shape slightly, leading to a tighter **induced fit** that improves the fit between the substrate and the enzyme.
        ii. In most cases, substrates are held in the active site by weak interactions, such as hydrogen bonds and ionic bonds.
        iii. R groups of a few amino acids on the active site catalyze the conversion of substrate to product.
        iv. The product then leaves the active site.
    f. Enzymes are unaffected by the reaction and are reusable.
    g. A single enzyme molecule can catalyze thousands of reactions a second.

5. Factors affecting the rate of enzyme-catalyzed reactions:
    a. Temperature
        i. As with non-catalyzed reactions, the reaction rate increases with increasing temperature because the kinetic energy of the molecules is greater and closer to the activation energy. Also, the increased molecular movement means more frequent collisions between molecules.
        ii. For enzyme-catalyzed reactions, as temperature increases, collisions between substrates and active sites occur more frequently so reaction rate increases.
        iii. This is advantageous for homeotherms because they can maintain body temperature close to the optimum temperature for enzymes.
        iv. If temperature increases too much, the protein denatures and the reaction slows down or stops.
    b. pH
        i. A change in pH (*i.e.*, $[H^+]$ or $[OH^-]$) can affect the tertiary structure of proteins.
        ii. Because there is such high specificity between the active site and the substrate, if the shape of the active site changes, it will no longer match the substrate as well.
    c. Substrate concentration
        i. At low [S], an increase in [S] speeds binding to available active sites. With increasing [S], the enzyme spends less time "waiting" for substrate and more time catalyzing reactions.
        ii. At high substrate concentrations, the active sites on all enzymes are busy and we say the enzyme is **saturated**.
    d. Enzyme concentration
        i. When an enzyme is saturated, the only way to increase productivity is to add more enzyme molecules.

e. Many enzymes require nonprotein helpers, called **cofactors,** for catalytic activity.
    i. Cofactors bind permanently or reversibly to the enzyme.
    ii. Some inorganic cofactors include zinc, iron, and copper. This is partly why it is important to get these minerals in our diet.
f. Organic cofactors are called **coenzymes.**
    i. Many vitamins are coenzymes.

6. Enzyme regulation - to be efficient, the cell must be able to control enzyme activity.
    a. Inhibition - enzyme activity is slowed
        i. **Competitive inhibition**
            (1) Some inhibitors resemble the substrate and compete for binding to the active site, preventing the binding of substrate.
            (2) Competitive inhibition can be partially overcome by increasing the concentration of the substrate.
        ii. **Non-competitive inhibition**
            (1) Noncompetitive inhibitors slow enzymatic reactions by binding to another part of the molecule.
            (2) The inhibitor binds to a site other than the active site and causes a conformational change in the enzyme so the active site shape no longer matches that of the substrate.
            (3) Toxins and poisons are often irreversible enzyme inhibitors.
        iii. A**llosteric Inhibition**
            (1) Some inhibitors bind to an allosteric site, a specific site away from the active site.
            (2) Some enzymes are constructed of two or more polypeptide chains. Each chain has its own active site.
            (3) Allosteric site are often where two polypeptides join.
            (4) Binding of an inhibitor to the allosteric site, causes a conformational change in all the active sites of that enzyme molecule.
        iv. **Feedback inhibition**
            (1) Most reactions occur as part of a metabolic pathway.
            (2) By controlling an early step in the pathway, the entire path can be controlled.
            (3) In feedback inhibition, an end-product from a chain of reactions is an inhibitor of an enzyme in the chain.
            (4) Feedback inhibition is an especially efficient way of regulating enzyme activity.
                (a) It is self-regulating.
                (b) The cell does not waste chemical resources by synthesizing more product than is needed.

b. Activation - enzyme activity is increased

i. **Allosteric**

(1) Binding of an activator to the allosteric site improves the fit between substrate and active site.

ii. **Cooperativity**

(1) In enzymes with multiple active sites, binding by a substrate to one active site induces a favorable change in the shape of other active sites of that enzyme molecule.

(2) Think of this as similar to allosteric activation.

iii. **Precursor activity**

(1) In a metabolic pathway, a precursor might be an activator of an enzyme later in the chain

(2) Think of this as a means of priming an enzyme to function more quickly when the substrate is about to be present.