An Introduction to Metabolism
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Slide 1
A biochemical pathway is a series of chemical reactions in which the product of each reaction serves as the reactant for the next reaction. In nearly all biochemical pathways, each reaction is catalyzed by a specific enzyme.

Slide 2
Energy can be classified into two major categories:
- Potential energy can be thought of as stored energy. It is energy that can be used to do some kind of work, but it is not being used at the moment.
- Kinetic energy is energy that is currently being used to do some kind of work.

Energy can readily be converted from potential energy to kinetic energy, and vice versa. In the picture, a person climbing the diving platform is converting kinetic energy into potential energy, whereas a person falling off the platform is converting potential energy into kinetic energy.

Slide 3
Thermodynamics is the branch of chemistry concerned with changes in energy. Though there are four laws of thermodynamics, only two are discussed in this course:
- The first law of thermodynamics (also called the law of conservation of energy) states that energy cannot be created or destroyed, but it can be transformed (changed from one form to another) and transferred (moved from one object to another).
- The second law of thermodynamics deals with entropy, which can roughly be described as disorder. The law states that entropy in the universe is continuously increasing. For a system (some subset of the universe, like a chemical reaction or an organism) to become more highly ordered (i.e., to decrease in entropy) there must be an even greater increase in entropy in the surroundings (to more than offset the decrease occurring in the system).

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The free energy (or Gibbs free energy, symbolized as G) is a system's potential energy available to perform work. There is a correlation between G and the degree of stability of a system. In general, a more highly ordered system exhibits lower stability (highly ordered systems are more unstable, so they tend to become less ordered to increase stability). When a system changes from being more highly ordered to being less highly ordered, the value of G (the amount of free energy) decreases. The symbol used to denote the change in free energy is ΔG. For a system that loses free energy (by becoming more stable) the value for ΔG is negative. A negative value for ΔG is an indication of a spontaneous process (one that will happen on its own). Spontaneous processes occur on their own, because systems tend to become less ordered and more stable. A nonspontaneous process (positive ΔG) will not happen on its own, because it requires input of energy to force a system to become more ordered and less stable.

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A spontaneous reaction (one with negative ΔG) is called an exergonic reaction, because it releases energy. Since the free energy (G) of the products is less than the free energy of the reactants, the value of ΔG ($\Delta G = G_{final} - G_{initial}$) is negative. But that decrease in energy does not mean that energy is destroyed; rather, that energy is released by the reaction. Some of the energy released by an exergonic reaction can be harnessed to perform some kind of work. A nonspontaneous reaction (one with positive ΔG) is called an endergonic reaction because it requires energy to be put into the reaction if the reaction is to proceed. For a nonspontaneous reaction, the free energy of the products is greater than the free energy of the reactants.

Slide 6
A thermodynamic system is some arbitrary subset of the universe. Choosing a system divides the universe into the system and its surroundings. An isolated system is one that does not exchange any energy or matter with the surroundings, whereas an open system can exchange energy and matter with the surroundings. All organisms are open systems. No organism can be an isolated system, because the chemical reactions occurring in a living cell require exchange of energy and matter with the surroundings. The energy processing that occurs in cells is similar to an open, multistep hydroelectric plant, because the energy obtained from incoming nutrients is released little-by-little in biochemical pathways (as opposed to all at once by a single reaction), allowing cells to use some of the released energy to perform cellular work.

Slide 7
An adenosine triphosphate (ATP) molecule is an example of a nucleoside triphosphate. The nucleoside, adenosine, consists of ribose and adenine. Attached to adenosine are three phosphate groups. ATP is the most abundant energy-carrying molecule found in cells. Chemical energy stored as the bonds linking the phosphates can be released and used to power endergonic processes in cells.

Slide 8
Some of the energy in an ATP molecule can be made available by removing the terminal phosphate from ATP. This is a hydrolysis reaction that converts ATP into ADP (adenosine diphosphate) and inorganic phosphate.

Slide 9
An endergonic reaction is possible in a cell if the endergonic reaction is coupled to an exergonic reaction, and further if the energy released by the exergonic reaction (which includes some waste heat) is greater than the energy required for the endergonic reaction. Usually, the exergonic reaction that supplies the energy is the hydrolysis of ATP.

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ATP can be used to perform two classes of cellular work:

- Active transmembrane transport moves particles against their gradient through a membrane.
- Mechanical work involves moving particles from place to place within a cell or causing structures to move.

Slide 11
ATP serves as an energetic intermediary that links catabolic, exergonic reactions (the breakdown of nutrients) with endergonic processes (anabolic reactions and cellular work). The catabolism of nutrients fuels the formation of ATP from ADP and inorganic phosphate. That ATP then powers either the formation of larger molecules from smaller ones (anabolism) or one of the two kinds of cellular work (active transport or mechanical work).

Slide 12
Nearly every biochemical reaction, including those that are spontaneous (like the one shown in this slide), requires the catalytic assistance of a specific enzyme that allows that reaction to occur quickly and at a low enough temperature to be tolerable to the cell. Most enzymes are named either for their function or for the substrate on which they can act. Sucrase, for example, is an enzyme that catalyzes the hydrolysis of the disaccharide, sucrose, into its constituent monosaccharides, glucose and fructose.

Slide 13
Any chemical reaction involves the breaking of bonds in the reactants and the formation of bonds in the products. The transformation of reactants into products involves a transition state that is highly unstable (and therefore features a higher free energy value that either the reactants or the products). The additional energy required to reach the free energy value for the transition state is known as the activation energy (E_A).

Slide 14
Catalysts (including enzymes) are able to speed up reactions, because they reduce the activation energy. Reducing the activation energy does not affect ΔG (which depends only on the reactants and products involved in the reaction), and enzymes never change the value of ΔG. A typical enzyme speeds up a reaction at least a million-fold.

Slide 15
Enzymes are specific in that each enzyme has an active site that is properly shaped to receive just one kind or a very few kinds of particles having a corresponding shape. The reactants of enzyme-catalyzed reaction are called substrates. When a substrate binds to the active site of an enzyme (forming the enzyme-substrate complex), the slight conformational change that occurs in the enzyme is known as the induced fit. This improves the fit between the active site and the substrate.

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Enzymes (like all catalysts) are reusable, because they are not reactants in the reactions in which they are involved, so they don't get converted into products. An enzyme binds to a substrate or substrates, which then react to form a product or products released by the enzyme. After release of product, the enzyme returns to its unbound shape and is able to bind to any additional substrate that is available.

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For any given enzyme, there is an optimal temperature and an optimal pH. At these optimal conditions, the enzyme works best to convert substrate into product. Enzymes are proteins, and their function is based on their shape. Since changes in temperature and pH cause changes in protein conformation, if an enzyme is subjected to a change in either temperature or pH, its ability to function will be affected by the change in shape it undergoes.

Slide 18
If an enzyme and substrate come into contact, the enzyme will catalyze the conversion of substrate into product, whether that product is needed at the moment or not. Therefore, it is important for cells to be able to control enzymes. One way is to create enzymes when they are needed and destroy them as soon as they are no longer needed. A much more efficient mechanism is to regulate enzymes, which is much like turning them on or off. Turning an enzyme on is called activation, and turning one off is called inhibition. Inhibition can occur in either of two ways:

- Competitive inhibition occurs when an inhibitor particle binds to an enzyme's active site. This disallows any substrate particles that happen to be present from binding to the enzyme, because the active site is blocked.
- Noncompetitive inhibition occurs when an inhibitor particle binds to some part of the enzyme other than the active site. The binding of the inhibitor to the enzyme changes the enzyme's shape, so that the active site, though open, becomes deformed, and substrate is unable to fit into the active site.

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Regulating an enzyme by binding a regulator particle to somewhere other than the active site is called allosteric regulation. This includes noncompetitive inhibition. An enzyme can also be allosterically activated.

Slide 20
Allosteric regulation is useful for feedback inhibition, in which the final product of a biochemical pathway serves as an allosteric inhibitor for an enzyme in that pathway. That way, a buildup of product will cause the pathway to shut down, preventing additional unwanted product from being produced.