UNIT 3: CHEMICAL REACTIONS AND GENERATION OF METABOLIC ENERGY

Introduction:

We shall begin this unit with the study of the energetics of chemical reactions and the role of enzymes as catalysts. We shall then go on to consider where the energy required to drive the chemical reactions that maintains life comes from. Both basic and specialized cell functions require a continuous supply of energy that is almost always supplied to the cell in the form of adenosine triphosphate (ATP). The ways in which this energy-rich ATP is generated will be the main subject of this unit.

Glycolysis is a process for generating ATP found in all living things. The citric acid cycle, while absent from a few organisms, is the primary means of ATP generation in almost all plants, animals, and prokaryotes.

Next we look at an overview of metabolism. On the one hand, we will see that organic molecules other than glucose can serve as starting points for respiration. In addition, we will see how the aerobic metabolic pathway serves as a metabolic headquarters for the acquisition and deposition of chemical intermediates needed for or produced by other metabolic pathways.

Readings: Chapters 8 and 9
Chapter 40 (pages 860-872)
"Energy and Chemical Bonds" and "The Metabolic Effects of Starvation (or 'Crash-dieting')" at the end of this unit

To Do This Unit:

1. Read through the concepts and objectives.
2. Read the text assignment and readings at the end of this unit, examine the demonstration materials (online and in the Study Center), and write out the answers to the objectives. The chemiosmosis movie available on the course website will be helpful for some objectives as well.
3. Attend the scheduled Flock Session. If you feel prepared to test on the unit before the flock session, please feel free to do so.
4. Take a written quiz and an oral test on this unit.

CONCEPTS AND OBJECTIVES:

After you have studied the material in this unit you should understand the following concepts and you should be able to carry out the objectives listed for each.

All chemical reactions proceed so as to use up free energy (increase entropy).

1. a) State the First and Second Laws of Thermodynamics and explain how they govern chemical reactions. According to the Second Law, in general what is happening to the amount of free energy in the universe? What is the relationship between free energy and entropy?

b) Define the term free energy and explain how ΔG is derived. Differentiate between exergonic and endergonic reactions (Fig. 8.6, p. 147) and give the relationship between ΔG and whether a reaction is exergonic or endergonic.

c) Explain what is meant by the term "energy coupling." Explain how cells are able to maintain a lack of metabolic equilibrium. How are the two concepts related? What happens when a cell reaches metabolic equilibrium? (Figs. 8.7, p. 148, and 8.10, p. 150 may be helpful.)

Breaking and forming chemical bonds go hand-in-hand. In any net reaction, chemical bonds are broken and formed. The breaking of a bond <u>always</u> requires energy, whereas the formation of a bond is <u>always</u> accompanied by a release of energy. Whether such a chemical reaction is endergonic or exergonic depends on the <u>net</u> result of the breaking and formation of bonds. If the energy released in forming bonds exceeds the energy used to break bonds, then the reaction will be exergonic.

2. Using the information in the section, "Energy and Chemical Bonds" found at the end of this unit, explain how the free energy change (ΔG) of a reaction is related to the breaking and forming of chemical bonds in the reactants and products.

Biological oxidation-reduction reactions frequently involve the coenzyme NAD as an energy or electron intermediary. However, the eventual repository for released energy is generally ATP. Similarly, ATP is generally the immediate source whenever energy is needed in the cell.

3. a) Draw a diagram of an ATP molecule in the space below (see Fig. 8.8, p. 149). Circle the parts of the molecule representing the nitrogen-containing base adenine, the ribose sugar, and the phosphate groups. (You do not need to memorize the structure of this molecule.)

   b) Explain the role of ATP as the immediate source of energy in performing the two different kinds of cellular work diagrammed in Fig. 8.11 (p. 151).

   c) Describe the difference between adenosine monophosphate (AMP), adenosine diphosphate (ADP), and adenosine triphosphate (ATP). (Not sure? See the diagram in the **demo**.)

d) Is the hydrolysis of ATP to ADP and Ⓟ$_i$ an exergonic or endergonic reaction? What is the ΔG for this reaction? __________ Is this bond between the terminal phosphate and the rest of the ATP molecule a strong or weak bond? Why?

e) Using Fig. 8.10 (p. 150) and the information in "Energy and Chemical Bonds" of this manual, explain how ATP hydrolysis can be used to drive an endergonic reaction. Where does the ATP come from?

Enzymes are extraordinarily effective catalysts, speeding up reactions as much as 10 million times. Like other catalysts, enzymes lower the activation energy for reactions.

Enzymes speed up chemical reactions but cannot alter the reaction equilibrium.

4. a) Using the diagram in Fig. 8.14 (p. 152) point out the free energy of reactants, the free energy of products, and the free energy change, Δ*G*, in going from reactants to products. Compare this diagram to the diagrams shown in Fig. 8.6 (p. 147). Which diagram is the more accurate one? Why?

b) Explain whether the graph in Fig. 8.14 (p. 152) describes an endergonic or an exergonic reaction. Using the figure as a model, draw a graph that represents the other type of reaction.

c) Explain which of these reactions may proceed spontaneously. Which of these two reactions requires a net input of free energy in order to proceed? (Refer to pp. 147-148).

d) What does the term "activation energy" (abbreviated E_A) mean? Explain how the activation-energy barrier provides stability for high-energy molecules. See Fig. 8.14 (p. 152).

e) What is a chemical catalyst? What is an enzyme? What is the significance of the active site? What is the significance of the term "induced fit"? See Figs. 8.16-8.17 (pp. 153-154) and the online **demo**.

f) Use Fig. 8.15 (p. 153) to illustrate the role that an enzyme plays in speeding up a reaction. How does the enzyme affect ΔG for this reaction? How would it affect an endergonic reaction?

g) Briefly describe two mechanisms by which enzymes lower activation energy and speed up reactions. See Fig 8.17 (p. 154).

Most enzymes are highly specific; each enzyme can interact only with those substrates that fit chemically and spatially into its active site.

5. a) Use Fig. 8.17 (p. 154) and the information on carboxypeptidase in the online **demo** to describe the mechanism(s) by which the enzyme carboxypeptidase speeds up the rate of removal of amino acids from one end of a polypeptide chain. Include the role of the enzyme in concentrating and orienting substrates in your description.

b) Using Fig. 8.17 (p. 154), explain why enzymes show great specificity. On the carboxypeptidase diagram in the **demo**, find the important amino acids that form the active site of the enzyme. Which positions do these amino acids occupy in the amino acid sequence of this enzyme? Are the amino acids in the active site necessarily next to each other in the primary structure of the polypeptide?

c) On the carboxypeptidase diagram in the **demo**, point out the substrate in the active site in Fig. 2. What kind of molecule is it (polysaccharide, polypeptide, or lipid)?

d) Find the electrostatic and hydrogen bonds that bind the substrate to the enzyme in Fig. 2 in the **demo**. Compared with covalent bonds, are these strong bonds or weak bonds?

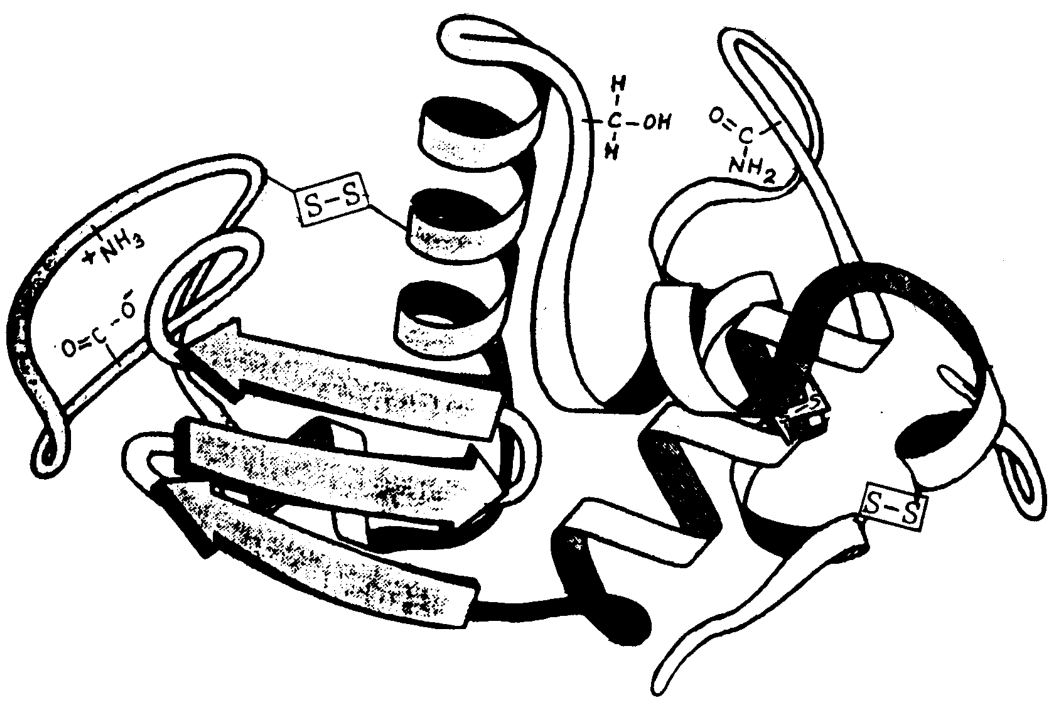
e) Is the zinc atom a cofactor or coenzyme? What is the difference?

f) Given the kind of enzyme-substrate interaction that is illustrated in Fig. 2 of the **demo**, can you account for the specificity of carboxypeptidase?

Anything that alters the shape of an enzyme alters its activity. Secondary, tertiary, and quaternary structures of proteins are determined by weak bonds and interactions. This means that changes in temperature and pH may disrupt such bonds and have marked effects upon the shape and activities of enzymes.

6. a) Explain the fact that changes in temperature may affect the overall structure of enzymes and their active sites. Why is this important to living organisms?

b) Explain how changes in pH alter enzyme activity (Fig. 8.18, p. 155). Using the protein diagram below, explain in detail how changes in pH affect protein structure and therefore enzyme activity.



c) Explain what an inhibitor is and distinguish between competitive and noncompetitive inhibition (Fig. 8.19, p. 156). How could you determine whether an inhibitor is competitive or noncompetitive?

d) Describe how allosteric enzymes can be regulated and give the role of allosteric activator and allosteric inhibitor molecules. Are all enzymes allosteric?

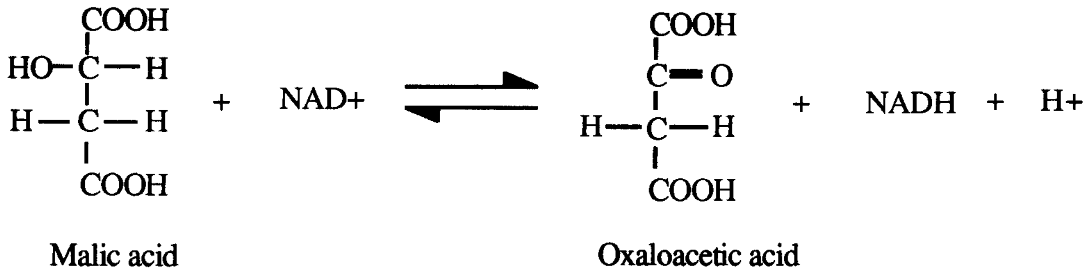
e) How are allosteric enzymes related to feedback inhibition (see Fig. 8.22, p. 159) and explain how cooperativity differs from other types of allosteric activation (see Fig. 8.20b, p. 157)?

Oxidation is the loss of electrons and reduction is the gain of electrons. During chemical reactions, if one atom is oxidized, then another must be reduced. This is the essential feature of an oxidation-reduction (redox) reaction.

Most biologically important redox reactions occur through the addition or removal of hydrogen atoms rather than by the transfer of isolated electrons. An organic compound generally acquires energy when reduced and releases energy when it is oxidized. Oxidation-reduction is the essential feature of respiration.

7. a) Define oxidation and reduction in terms of gain or loss of electrons.

b) Given reactions such as the following:



point out:

- the molecule on the left side of the equation that is oxidized when the reaction proceeds to the right. Circle the atoms that are removed from that molecule during the reaction.

- the molecule on the left side of the equation that is reduced when the reaction proceeds to the right.

- which of the two molecules on the left side donates electrons and which receives electrons.

- which of the two molecules on the left side will gain energy and which will lose energy.

c) Write a **balanced** chemical equation for aerobic respiration. Explain why this is a redox reaction. What molecule is oxidized? What is reduced?

d) Describe the general role of the electron transport chain during cellular respiration.

All living cells obtain energy for immediate use from the breakdown of sugars via glycolysis. This pathway consists of a series of reactions in which the product of one reaction becomes the substrate of the next. Each endergonic reaction in the series can proceed by being coupled to an exergonic reaction.

Note: The term **pathway** as used by biochemists refers to a set of consecutive reactions in which the product of one reaction becomes the reactant for the next. A separate enzyme catalyzes each reaction.

8. a) Given a flow chart of the reactions in glycolysis, such as in Fig. 9.9 (pp. 168-169)[1], point out:

- reactions in which a phosphate from ATP is transferred to a sugar (energy-investment phase)

- the reaction in which a hexose sugar is converted to trioses.

- the single oxidation-reduction reaction in glycolysis. [Note that the addition (or removal) of a phosphate group to a carboxyl group does not involve oxidation or reduction.] Point out glyceraldehyde-3-phosphate (G3P).

- the role of NAD^+ in glycolysis.

- the two reactions in which ATP is synthesized directly, by **substrate-level phosphorylation**. (See also Fig. 9.7, p. 167.)

b) List the main products of glycolysis. What is the <u>net</u> synthesis of ATP for each molecule of glucose converted to products during the reactions of glycolysis? See Fig. 9.8, p. 167.

c) Do the reactions of glycolysis take place in the cytosol or in the mitochondrial matrix (inner compartment)? See Fig. 9.6, p. 166.

The amount of energy that can be conserved if glucose is broken down when oxygen is present is considerably greater than when it is absent; consequently, a plentiful supply of oxygen is essential for most organisms if their energy demands are to be met.

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[1] Please note: You need not memorize the names or the structures of the various molecules, but you do need to explain, given a diagram, what is taking place during catabolism.

Aerobic (oxygen-using) organisms get most of their energy from the complete oxidation of pyruvate and the subsequent oxidation of the reduced electron carriers (NADH and FADH2) formed during pyruvate catabolism.

9. Write an equation, in words, representing the conversion of pyruvate into acetyl CoA. Include the three products made. Does this conversion involve oxidation-reduction?

10. Viewing the chemiosmosis movie in the online **demo** may help with the following objectives:

a) Where in the cell do the reactions of the citric acid cycle take place?

b) Given a diagram of the citric acid cycle such as the one in Fig. 9.12 (p. 171), point out:

(1) the four oxidation-reduction reactions and the compounds (carriers) that accept electrons during oxidation of organic acids.

(2) the reactions in which CO_2 is liberated.

(3) the number of turns of the citric acid cycle necessary to complete the oxidation of one molecule of glucose. Account for the fate of all six carbon atoms in the glucose molecule.

(4) the one reaction where a phosphate group is transferred from an energy-rich compound to ADP, to form ATP (i.e., substrate-level phosphorylation).

Most of the energy released in the complete oxidation of glucose is temporarily stored in the reduced carriers NADH and $FADH_2$.

11. Complete the following chart and relate this information to Figs. 9.9-9.12 (pp. 168-171) and 9.18 (p. 178):

	Reactants	Products	Specific Steps Where ATP is Formed or Hydrolyzed	Specific Steps Where CO_2 is Released	Specific Steps Where e^- Carriers are Oxidized or Reduced
glycolysis					
conversion of pyruvate to acetyl CoA					
citric acid cycle					
muscle | fermentation | yeast					

Electrons and hydrogen ions are passed from reduced NADH and $FADH_2$ to oxygen <u>indirectly</u> via a number of membrane-bound electron carriers.

The energy released in transferring electrons from reduced NADH and $FADH_2$ to oxygen is used to pump H^+ ions across the inner mitochondrial membranes, establishing a H^+ ion gradient across the membrane. ATP is synthesized when the hydrogen ions flow back down the electrochemical gradient through the ATP synthase complex.

12. Using the information in the chemiosmosis handout available in the online **demo** and Fig. 9.16 (p. 175):

a) trace the flow of electrons from the citric acid cycle, through NAD^+, FAD, and the electron transport molecules, to oxygen.

b) point out the three sites where hydrogen ions are pumped across the inner mitochondrial membrane as a consequence of the flow of electrons along the electron transport chain. Indicate where the H^+ ion concentration is the highest in the mitochondrion, and explain how the H^+ ion gradient is storing energy by generating a proton motive force.

c) observe the F_1 complex of the ATP synthase protein in the on-line **demo** and/or view Fig. 9.14 (p. 174). The bottom portion of the molecule is the F_1 complex; note also the rod anchoring the F_1 in the membrane.

d) show where H^+ ions return to the inner compartment of the mitochondrion. What is produced as the H^+ ions move back across the membrane? What would happen to ATP synthesis if the inner mitochondrial membrane were suddenly made permeable to H^+ ions? Could the citric acid cycle continue?

Cells living temporarily or permanently in the absence of oxygen must possess, in addition to the reactions of glycolysis, another set of reactions for regenerating NAD+ from NADH. The purpose of fermentation is to regenerate NAD+.

The flow of electrons from each NADH produced within the mitochondrion establishes enough of a proton-motive force to generate approximately 3 ATP. But, the electrons from NADH produced by glycolysis in the cytosol and the $FADH_2$ produced in the citric acid cycle enter the electron transport chain at a lower level, and therefore only about 2 ATP are generated per molecule.

13. a) Explain why a continuous supply of NAD^+ is required for glycolysis to continue. How is NAD^+ regenerated from NADH when there is no oxygen available? Point out on Fig. 9.9 (pp. 168-169) the reaction where NAD^+ is used. What then is the primary role of fermentation?

b) In Fig. 9.18 (p. 178), point out the reactions by which NAD^+ is regenerated in yeast growing anaerobically. Do the same for muscle cells. What roles do ethanol and lactic acid play in the cells producing them?

c) What is the total number of ATP molecules (net) gained in the glycolysis and fermentation to lactic acid or ethanol? What is the answer if one starts with 2 glyceraldehyde-3-phosphate molecules instead of glucose?

d) On the diagram provided in the online **demo** with the chemiosmosis movie, point out the place where the electrons from the NADH produced in glycolysis enter the electron transport chain. Is it the same site where the electrons from NADH produced in the mitochondrion enter? Are as many H^+ ions pumped across the membrane? Would the proton-motive force resulting from the glycolysis NADHs result in as many ATPs being produced? How would the number of ATPs produced from the glycolysis NADHs compare with the number of ATPs produced by $FADH_2$? (See Fig. 9.17 p. 176 and text on pp. 176-177.)

e) What is the total number of ATPs (net) gained from glycolysis alone under aerobic conditions. (Figure it out; assume chemiosmosis occurs.) __________

f) What is the total number of ATP molecules (net) that can be gained when a molecule of glucose is oxidized completely in the presence of oxygen?[2] __________ How many of these are formed by the chemiosmotic synthesis of ATP? __________

g) Is oxygen used directly in the reaction of the citric acid cycle? Can the citric acid cycle operate in the absence of oxygen? Explain why or why not. **Hint**: think about the sources of the various reactants used in the citric acid cycle.

Metabolism has two aspects: Reactions by which molecules are broken down (catabolism) and reactions leading to the synthesis of new cellular components (anabolism). Energy and intermediates produced during catabolism or anabolism are used in other aspects of metabolism.

A wide variety of compounds in addition to glucose are used as carbon sources by many organisms. The oxidative state of an organic compound relates to the amount of energy that the compound could be used to produce. The more reduced the compound, the more ATP energy can be produced from it.

14. a) For many types of organisms or cells, the starting point for catabolism is not glucose but some other substance, usually a lipid, polysaccharide, or protein. Using a diagram such as Fig. 9.20 (p. 180), explain how the products of protein, carbohydrate, and fat breakdown can be oxidized to yield energy.

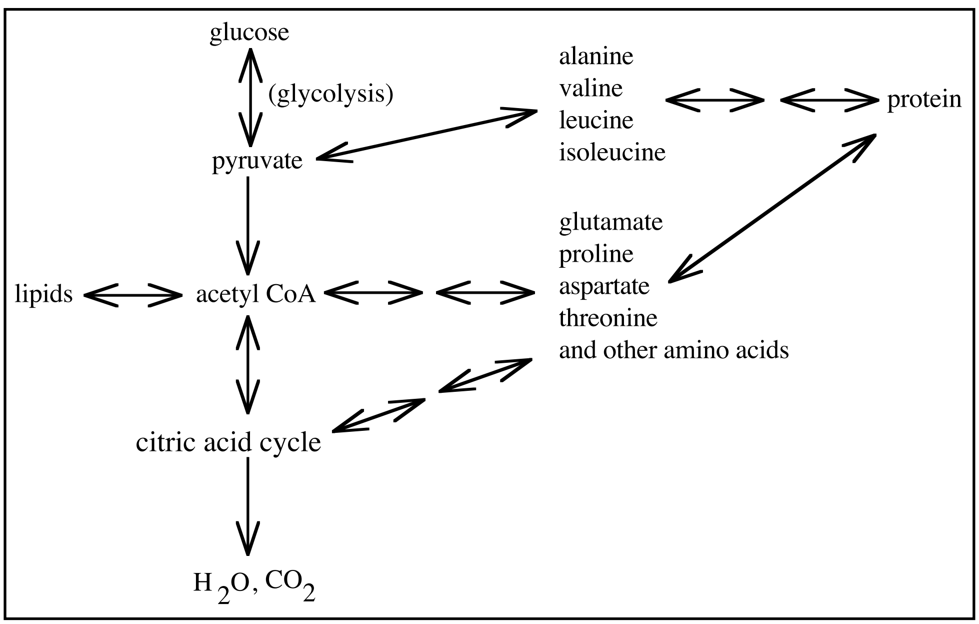
[2]**Note**: the information given in the online movie says that a total of 30 ATP are produced by the complete oxidation of one glucose molecule, whereas your text gives the number about 36-38. The reason for this discrepancy is: Your text rounds off the number of ATP to 3 per NADH (the movie uses the minimum value of 2.5) and 2 per $FADH_2$ (rather than 1.5) to simplify bookkeeping. The important thing to understand is that all these ATP counts are "soft" estimates that vary, but that, regardless of what calculations you use, chemiosmotic synthesis yields a far greater number of ATP than substrate-level phosphorylation. See pp. 176-177 in your text for a nice discussion of "an accounting of ATP production by cellular respiration".

b) Which would produce more ATP: glucose or six-carbon fatty acid? Explain your answer. The online **demo** has information to help you answer this question.

Glycolysis and the citric acid cycle play important roles not only in generation of ATP, but also in providing building blocks for the large number of anabolic reactions that go on in cells.

15. Your textbook focuses on glycolysis and the citric acid cycle mainly in terms of their role in generating ATP. Less attention is paid to the role of these pathways in generating intermediates for anabolic pathways, but you should be aware of this role as well. The following scheme will illustrate the relationship of glycolysis and the citric acid cycle to anabolism.

Compare the diagram below with Fig. 9.20 (p. 180). How can Fig. 9.20 be modified to show anabolism as well as catabolism as in the diagram below? For a discussion of the implications of this diagram, read the section "The Metabolic Effects of Starvation" at the end of this unit. Can lipids be used to synthesize glucose?



The metabolic breakdown of high-energy compounds is an inefficient process; more than half the available energy is lost as heat. Some animals have evolved mechanisms for retaining this heat and can thus maintain a uniformly high body temperature and metabolic rate.

16. a) Using the information in your text on pages 862-868 and the **demo**, explain the terms endothermic and ectothermic, and describe some of the behaviors and physiological processes used by organisms to heat and cool themselves.

b) Give some advantages and disadvantages of being endothermic. ...ectothermic. Figure 40.20 (p. 871) may be useful.

c) Using the information in the **demo**, explain the terms homeothermic and heterothermic. Using the information on pp. 871-872, give examples of some of the patterns of daily and seasonal hibernation and torpor.[3]

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[3]Hibernation should be distinguished from winter sleep. During hibernation, an animal's basal metabolic rate falls to extremely low levels during certain parts of its life cycle. This results in a decrease in body temperature, often as low as 2 to 4^{o}C, resulting in an enormous saving of metabolic energy. The hibernation season is controlled by an internal biological clock. In winter sleep, however, the basal metabolic rate of an animal does not change markedly from the metabolic rate during sleep. Animals must have enough energy stored in their bodies to meet the sleeping metabolic rate. Bears, for instance, are winter sleepers, **not** hibernators.

d) Place representative organisms in each of the four boxes in the chart below.

	endothermic	ectothermic
homeothermic		
heterothermic		

17. a) What is the general relationship between body temperature and metabolic rate? Among mammals, what is the relationship between body size and metabolic rate? Differentiate between BMR and SMR. See pp. 869-871.

b) Contrast the energy budgets of endotherms and ectotherms (Fig. 40.20, p. 871) and contrast the energy budgets of three different endotherms. What is the largest portion of the budget used for in humans? ...penguins? ...deer mice?

c) Why is energy expenditure per unit mass is so much higher in a deer mouse than in a penguin or human?

d) Explain how an organism's metabolic rate influences its oxygen needs.

Below are summary questions relating to important concepts in this unit. The TA may use these questions in his or her oral test or you may see them as essay questions on the final exam. Take a few moments now to formulate answers.

The two most striking features of enzymes are their specificity and their catalytic effectiveness. Discuss these two features with respect to the structure of the enzyme, organization of an active site, the kinds of interactions occurring between a substrate and an active site, and the enzymes catalytic effectiveness.

Summarize the complete metabolic breakdown of one molecule of glucose to CO_2 and H_2O by outlining the main stages of the process. Discuss the energy relationships between degradative pathways (e.g., breakdown of glucose to CO_2 and water) and biosynthesis reactions (e.g., biosynthesis of carbohydrates, fats, and proteins). What role does ATP play in these processes?

Describe the principal events in chemiosmotic synthesis of ATP in mitochondria.

Energy and Chemical Bonds

The many forms of energy fall into two major classes: kinetic (the energy associated with motion) and potential (the energy of position). The latter category is also called "stored energy" and includes such forms as nuclear energy, electrical potential, and chemical energy. The last of these is particularly important for living organisms because it is the immediate source of energy for the work done by cells. To mention an obvious example, the carbohydrates, proteins, and fats found in the food we eat are all used--at least in part--to meet our energy requirements. Since the oxidation of an organic molecule such as a fat releases energy, it seems natural to refer to such substances as "energy-rich." One might then ask, if a fat molecule is rich in energy, where in the molecule is the energy stored? Since the chemical bonds within the molecule are broken during the oxidation process, we might assume that the energy is released when the bonds are broken.

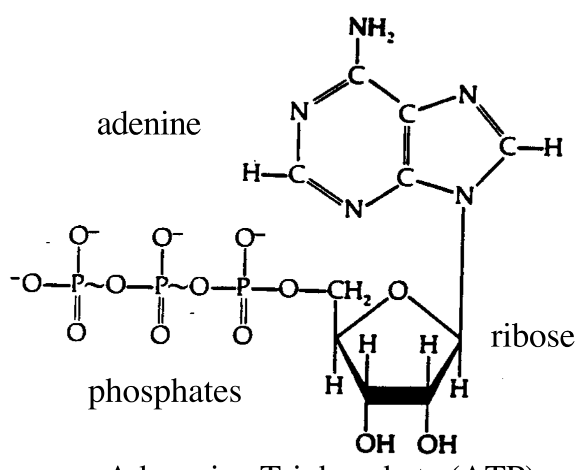
A moment's thought will convince you, however, that there is something wrong with this reasoning. You learned in Unit 1 that covalent bonds require energy to break (50-110 kcal/mole). How can a process that requires an *investment* of energy simultaneously be a *source* of energy? Of course the answer is that it can't; therefore the idea that chemical bonds store energy must be mistaken.

Where, then, does the energy released in an exergonic reaction such as the oxidation of fat come from? And how is energy stored in an endergonic reaction? The basic concept to remember is that **energy is invested as existing bonds are broken, whereas it is given off as new bonds are formed**. If in a particular reaction, the total amount of energy released by the formation of new bonds exceeds the amount required to break the old ones, then the reaction is exergonic; conversely, if forming the new bonds releases less energy than is invested in breaking the old ones, the reaction is endergonic.

Let's apply this principle to the reaction by which ATP is hydrolyzed:

$$ATP + H_2O \longleftrightarrow ADP + Ⓟ_i$$

This exergonic reaction (ΔG = -7.3 kcal/mole) provides the energy for the vast majority of energy-requiring functions of cells. Its importance was first recognized by the biochemist and Nobel-laureate Fritz Lipmann in 1941. If you look at the structure of ATP shown below, you will notice that the bond that is broken during the hydrolysis of this molecule is located between the last two phosphate groups and is indicated by a "squiggle."



Adenosine Triphosphate (ATP)

It was Lipmann who introduced this way of designating the bond and who first described it as a "high-energy bond." As we have seen, this phrase is nonsensical. The reason the reaction is exergonic is that this covalent bond is unusually *weak* (in part because of the electrostatic repulsion of the negatively-charged phosphate groups) and therefore requires only a small investment of energy to break. By contrast, the newly created bonds are relatively strong and stable; hence a large amount of energy is released as they are formed, and the reaction as a whole is exergonic. In fact, we can draw the general conclusion from this example that reactions that involve breaking weak bonds to form stronger ones tend to be exergonic, whereas reactions that require the breaking of strong bonds to form weaker, less stable ones tend to be endergonic.

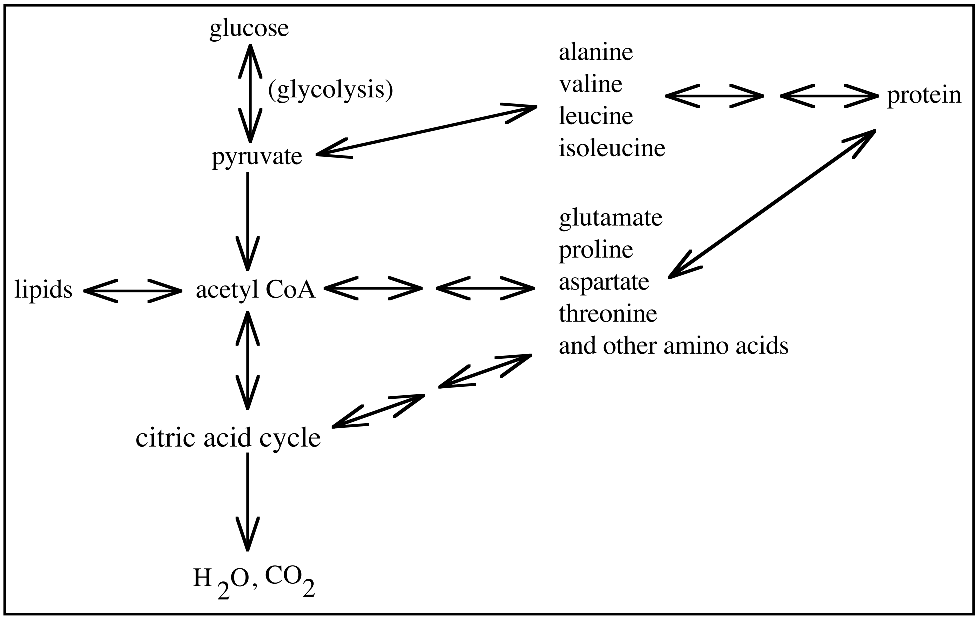
How is the energy released by the hydrolysis of ATP used by the cell? One very important function is to facilitate reactions that would otherwise be endergonic and hence thermodynamically unfavorable. We can get a sense of how this process works by considering a specific example: the first step of glycolysis. In this reaction a phosphate group is attached to glucose, creating glucose-6-phosphate (G-6-P). If the enzyme that catalyzes this reaction were attaching a free phosphate group directly to glucose, the reaction would be endergonic and little of the product would be formed. But in fact the enzyme **couples** this reaction with another, exergonic one: the removal of phosphate from ATP by hydrolysis. Considered together the two reactions result in a negative free energy change, as shown below:

ATP + H_20	<-->	ADP + Ⓟ$_i$	ΔG = -33 kJ/mole
glucose + Ⓟ$_i$	<-->	G-6-P + H_20	ΔG = 12 kJ/mole
glucose + ATP	<-->	G-6-P + ADP	ΔG = -21 kJ/mole

Thus the inclusion of the hydrolysis of ATP as part of the reaction makes the formation of G-6-P thermodynamically favorable.

This example illustrates how ATP is used in the cell in **coupled reactions,** in which free energy derived from a thermodynamically favorable (exergonic) reaction is used to drive a thermodynamically unfavorable (endergonic) one. More information about this extremely important biochemical principle is provided in your textbook. Bearing in mind the second law of thermodynamics, do you think that an endergonic reaction requiring 10 kcal/mole could be driven by an exergonic reaction releasing the same quantity of free energy, or would more be required?

The Metabolic Effects of Starvation (or 'Crash-dieting')



Objective 15 asks you to compare the diagram above with Figure 9.20 on page 180 of the text. An obvious difference between them is that the diagram here has double-headed arrows in it to show that, in general, the catabolic pathways by which carbohydrates, lipids and proteins are broken down are reversible. Note especially that pyruvate can be used as the starting point for anabolic pathways leading to the formation of glucose, of certain amino acids, and (via acetyl CoA) of lipids.

But the diagram shows one irreversible reaction: the oxidation of pyruvate to acetyl CoA. As a consequence, *it is impossible to create glucose from acetyl CoA*. And since lipids (except for glycerol) are broken down into acetyl CoA, it follows that it is impossible to make glucose from lipids. This limitation on the manufacture of glucose is significant because of the importance of this sugar as a nutrient for the cells of the nervous system. A severe drop in the blood glucose level (**hypoglycemia**) can lead to coma and death due to impaired brain function.

In view of the dire consequences of severe hypoglycemia, it is not surprising that there are a number of homeostatic mechanisms in our bodies that tend to stabilize the blood glucose level. Among these are hormones that determine the rates at which the anabolic and catabolic pathways shown in the diagram take place. For example, suppose that a person does not eat for a period of several days. As the level of blood glucose begins to drop, the body's reserves of stored glycogen are hydrolyzed to create glucose monomers, which are secreted into the blood. Once the glycogen reserves are exhausted (in less than 24 hours), other sources of glucose must be drawn upon. But as we have seen, the body's stored fat cannot be utilized for this purpose. Instead the body's proteins begin to be broken down into their constituent amino acids. Then, in a process called **gluconeogenesis**, some amino acids are converted into pyruvate and others into various compounds of the citric acid cycle, such as oxaloacetic acid, from which glucose is made.

Gluconeogenesis is a mixed blessing. The good news about it is that 18 of the 20 amino acids found in proteins can be converted (minus their amino groups) into glucose. The bad news is that the person is losing lean body mass during the period of fasting as well as fat stored in adipose tissue. During prolonged fasting (starvation), proteins of the liver, muscles, and spleen are used for gluconeogenesis, largely sparing those of the heart and brain. The brain also begins to use products of fat metabolism as a source of energy and thus slows the loss of protein. But once the body's fat stores are used up, the catabolism of protein accelerates and death follows quickly. The average time from the start of a fast till death is about 60 days.

In recent decades we have witnessed the tragic consequences of these metabolic events in the form of the starving victims of societal disintegration in parts of Africa. We have seen the children with swollen bellies that indicate a severe dietary deficiency of protein and calories. As you will learn in Unit 7, proteins in the blood normally make the plasma hypertonic to the surrounding tissue fluid. As blood proteins are broken down, fluid accumulates in the tissues instead of being returned to the blood--a condition called **edema**. The excess tissue fluid tends to pool in the abdomen of the child, who is probably too weak to stand.

From a metabolic standpoint, voluntary fasting and "crash-dieting" are the same as involuntary starvation because they all result in the breakdown of the body's protein. To prevent this from happening, it is important to eat a balanced diet--including carbohydrate and protein--during any weight-reduction effort. Because a certain amount of degradation of proteins continually occurs, at least 20 to 30 grams of protein should be eaten daily, and 60 to 75 grams is recommended to be on the safe side. Nutritional studies also show that a reducing diet should include a minimum of about 1000 kilocalories per day to prevent loss of lean body mass.

Unit 3 Evaluation: PLEASE FILL OUT THIS EVALUATION SHEET AFTER YOU HAVE COMPLETED THE UNIT, AND PLACE IT IN THE WOODEN BOX IN THE STUDY CENTER. THESE FORMS WILL PROVIDE FEEDBACK NECESSARY FOR IMPROVING THE UNITS.

How many hours did you spend studying for this unit? _________

Do you consider the time you spent studying for this unit to be:
A. too little? B. about right? C. excessive?

Was the majority of the material in this unit:
A. new to you? B. somewhat familiar? C. very familiar?

How many times have you taken this unit test? _________

How effective were the objectives in organizing your study?
A. ineffective B. effective C. very effective

Did the objectives clearly indicate what you were expected to know about the unit material?
A. Yes B. No

What objectives did you have the most problems with? ___________________________

Was the demo helpful in learning the unit material?
A. not at all B. moderately C. very helpful; essential

The amount of information in this unit is:
A. too little B. about right C. excessive

The level of difficulty of this unit is:
A. too easy B. about right C. too hard

How crowded was the Study Center when you took your test?
A. not crowded B. crowded, but OK C. very crowded; a long wait

Indicate day of the week and time of day that you took this exam: __________________

Did you receive any tutoring from TAs in learning this unit material?
A. Yes B. No

If you needed help from a staff member, was he/she willing and able to provide the help you needed?
A. unwilling/unable B. satisfactory C. very helpful

Name of TA who tested you on this unit: ______________________________________

Did you feel the TA who tested you was well prepared?
A. poorly prepared B. satisfactorily prepared C. very well prepared

Do you feel the TA who tested you gave you a fair and impartial test?
A. Yes B. No

Any comments or suggestions?