CHAPTER 6

How Cells Harvest Chemical Energy

Objectives

Introduction Compare the structure of slow and fast muscle fibers. Note how these adaptations relate to the properties of these muscle fibers.

Introduction to Cellular Respiration

6.1 Define and compare the processes of breathing and cellular respiration.
6.2 Describe the overall chemical equation for cellular respiration. Compare the efficiency of this process in cells to the efficiency of a gasoline engine.
6.3 Explain how the human body uses its daily supply of ATP.

Basic Mechanisms of Energy Release and Storage

6.4 Explain how the energy in a glucose molecule is released during cellular respiration.
6.5 Explain how redox reactions are used in cellular respiration.
6.6–6.7 Describe the roles of the electron transport chain and chemiosmosis in cellular respiration.
6.7 Compare the process of substrate-level phosphorylation to chemiosmosis.

Stages of Cellular Respiration and Fermentation

6.8 Describe the cellular regions where glycolysis, the Krebs cycle, and the electron transport chain occur.
6.8–6.14 Compare the reactants, products, and energy yield of the three stages of respiration. Also indicate where each process occurs in the cell.
6.15 Compare the reactants, products, and energy yield of alcoholic and lactic acid fermentation. Distinguish between strict anaerobes and facultative anaerobes.

Interconnections Between Molecular Breakdown and Synthesis

6.16 Explain how polysaccharides, proteins, and fats are broken down to yield ATP.
6.17 Explain how food molecules are used in biosynthesis.
6.18 Describe the fundamental relationship between respiration and photosynthesis.

Key Terms

cellular respiration
redox reaction
oxidation
reduction
dehydrogenase
NAD^+
electron carrier
electron transport chain
chemiosmosis
ATP synthase
substrate-level phosphorylation
glycolysis
Krebs cycle
intermediate
acetyl CoA (acetyl coenzyme A)
alcoholic fermentation
lactic acid fermentation
strict anaerobe
facultative anaerobe

Word Roots

glyco- = sweet; **-lysis** = split (*glycolysis:* the splitting of glucose into pyruvate)

Lecture Outline

Introduction *How Is a Marathoner Different from a Sprinter?*

A. *Review:* The definition of metabolism and what it entails (Chapter 5).

B. Harvesting chemical energy from food molecules is one side of a cycle that, in eukaryotes, often involves mitochondria and chloroplasts (Figure 5.21).

C. Muscles in our legs are of two types, slow-twitch and fast-twitch muscle. The difference between the muscle types is determined by the type of work they do and the type of metabolic processes they perform. Sprinters have proportionally more fast-twitch muscle, while distance runners have a larger portion of slow-twitch muscle.

D. Slow-twitch muscles metabolize glucose in the presence of O_2 (aerobic respiration), producing large amounts of ATP, and can therefore work for a long period of time. Fast-twitch muscles metabolize glucose in the absence of O_2 (anaerobic), producing very little ATP, and therefore can only work for a short amount of time, albeit furiously.

E. This chapter covers the various metabolic pathways by which energy is released from food molecules, particularly glucose, in the presence and absence of oxygen.

I. Introduction to Cellular Respiration

Module 6.1 Breathing supplies oxygen to our cells and removes carbon dioxide.

A. The oxygen needed to burn food by the process of **cellular respiration** is outside the bodies of organisms and is obtained by breathing (respiration).

B. ATP is needed by cells to perform work.

C. Mitochondria use O_2 in the process of cellular respiration.

D. The muscular, respiratory, and circulatory systems combine forces to bring reactants (food molecules and O_2) to cells and remove waste products (CO_2 and H_2O) from cells (Figure 6.1).

Module 6.2 Cellular respiration banks energy in ATP molecules.

A. Overall equation:

$C_6H_{12}O_6 + 6\ O_2 \rightarrow 6\ CO_2 + 6\ H_2O$ + energy in the form of ATP and heat (Figure 6.2A).

B. *Review:* The second law of thermodynamics. Remind students that the wasted energy is lost to each system as random kinetic energy (heat).

C. Compare the efficiency of the overall process in cells (about 40%) to the efficiency of energy use by an automobile (about 25%) (Figure 6.2B).

Module 6.3 Connection: The human body uses energy from ATP for all its activities.

A. Energy is used for body maintenance, for example, breathing, digesting food, temperature regulation, and blood circulation.

B. Voluntary activities require additional energy input and utilize calories at a faster rate than simple body maintenance (Table 6.3).

C. A general estimate for an adult human of average weight for both types of energy expenditure is 2200 kcal per day.

II. Basic Mechanisms of Energy Release and Storage

Module 6.4 Cells tap energy from electrons transferred from organic fuels to oxygen.

A. One glucose molecule contains more energy than a cell needs to use for a single job.

B. Discuss the rearrangements that have occurred in the locations of bonds in the reactants and products of cellular respiration.

C. The movement of hydrogens represents transfer of electrons (Figure 6.4).

D. Cellular respiration involves a gradual series of steps, each coupling an exergonic with an endergonic reaction.

E. Some of the energy that is released is stored in the phosphate bonds of ATP.
Review: The coupling of the release of energy from ATP, an exergonic reaction, to provide energy to drive endergonic reactions is discussed in Module 5.4.

F. At each step, electrons move from a chemical bond in a molecule where they have more energy to a bond where they have less energy.

G. Oxygen atoms (from molecular oxygen, O_2) are the ultimate electron acceptors. When these oxygen atoms bind with the hydrogen atoms carrying the electrons, they form water molecules with relatively low-energy covalent bonds.
NOTE: The majority of energy is released as heat. However, this should not be considered "wasted" energy because this heat is used to maintain body temperature and thus facilitate biochemical reactions (the optimal temperature for enzymes in humans is approximately 37°C).

Module 6.5 Hydrogen carriers such as NAD^+ shuttle electrons in redox reactions.

A. The paired endergonic-exergonic reactions at each step in the transfer of energy are known as **redox (reduction-oxidation) reactions.**

B. **Oxidation** reactions involve electron loss and are the exergonic half (Figure 6.5 top half).

C. **Reduction** reactions involve electron gain and are the endergonic half (Figure 6.5 bottom half).
NOTE: A mnemonic for this is LEO-GER: Loss of Electrons, Oxidation; Gain of Electrons, Reduction.

D. At each step in the breakdown of glucose, small redox reactions occur, involving an enzyme, **dehydrogenase,** and its coenzyme, **NAD^+,** that functions as an electron shuttle.

E. During each step, the breakdown portion (glucose being stripped of its electrons) is oxidized while the NAD^+ is reduced, forming NADH.

Module 6.6 Redox reactions release energy when electrons "fall" from a hydrogen carrier to oxygen.

A. At the beginning of a different set of reactions, all the NADH generated as above gives up its energetic electrons and NAD^+ is regenerated (Figure 6.6A).

B. These energetic electrons then pass from molecule to molecule in an "energy cascade," or **electron transport chain.** Each molecule is temporarily reduced by the oxidation of the previous molecule and, in turn, is oxidized when it reduces the next.
NOTE: This gradual release of energy can be analogized to a slinky going down a flight of steps one step at a time.

C. The ultimate electron acceptor in this part of the overall process is oxygen.

D. During the cascade, small amounts of energy are released that can build ATP.

E. Contrast the stepwise transfer of energy to oxygen to the direct reaction of hydrogen and oxygen and the explosive release of energy (Figure 6.6B).

Module 6.7 Two mechanisms generate ATP.

A. **Chemiosmosis** is a process involving the electron transport chain and ATP synthases (protein clusters extending through the mitochondrial membrane). The electron transport chain temporarily produces potential energy in the form of an increase in H^+ concentration on one side of a membrane; the **ATP synthases** use the potential energy to generate ATP (from ADP and inorganic phosphate) by H^+ flow through them—down the concentration gradient (Figure 6.7A).

B. **Substrate-level phosphorylation** involves neither the electron transport chain nor membranes. This process occurs when a phosphorylated reactant gives up its covalently bonded phosphate to ADP with the aid of an enzyme and produces an ATP (Figure 6.7B).

III. Stages of Cellular Respiration and Fermentation

Module 6.8 Overview: Respiration occurs in three main stages.

A. Summarizing and previewing the overall process, cellular respiration is composed of three major steps:

1. **Glycolysis** (in the cytoplasm)
2. The **Krebs cycle** (in the mitochondrial matrix)
3. The electron transport chain (on the inner mitochondrial membrane)

B. These three parts are interconnected, as shown in Figure 6.8, which also shows the location of ATP synthesis (Figure 6.8).

Module 6.9 Glycolysis harvests chemical energy by oxidizing glucose to pyruvic acid.

A. This process occurs in the cytoplasm.

B. Overall there are nine chemical steps, the net result of which is to split one six-carbon sugar molecule into two three-carbon pyruvic acid molecules (Figure 6.9A).

C. Each of the nine intermediate steps involves a separate enzyme (Figure 6.9B).

D. In addition to glucose, ADP, phosphate, and NAD^+ are required as reactants. ATP is also required because in order to get some intermediates formed, energy must be expended.

E. Glycolysis can be broken into two phases: Steps 1–4 are preparatory and require ATP input (Figure 6.9B; "preparatory phase"); Steps 5–9 are energy releasing, producing ATP and NADH (Figure 6.9B; "energy payoff phase").

F. Net energy production for glycolysis: 2 ATP (immediately usable for cellular work) and 2 NADH molecules for each glucose molecule entering the process.

Module 6.10 Pyruvic acid is chemically groomed for the Krebs cycle.

A. This process occurs in the mitochondrial matrix (the fluid within the inner mitochondrial membrane) (Figure 6.10).

B. It is oxidized, reducing NAD^+ to NADH.

C. It is stripped of a carbon, releasing CO_2.

D. It is complexed with coenzyme A, resulting in the molecule, acetyl coenzyme A **(acetyl CoA),** the high-energy (but not as high as glucose) fuel for the Krebs cycle.

E. Net energy production for this step: 2 NADH molecules per glucose molecule entering the process.

Module 6.11 The Krebs cycle completes the oxidation of organic fuel, generating many NADH and $FADH_2$ molecules.

A. This process occurs in the mitochondrial matrix.

B. Overall there are five chemical steps, the net result of which is to disassemble one two-carbon acetyl CoA into two CO_2 molecules while reducing one FAD molecule and three NAD^+ molecules (Figure 6.11A).

C. Each of the five intermediate steps involves a separate enzyme (Figure 6.11B).

D. In addition to acetyl CoA, ADP, phosphate, NAD^+, FAD (another energy shuttle molecule), and oxaloacetic acid are required as reactants.

E. The five intermediate reactions regenerate oxaloacetic acid. This molecule is required at the beginning, and thus the cycle can start again.

F. Coenzyme A is released at the first step and goes back to groom more pyruvic acid.

G. Net energy production for the Krebs cycle: 2 ATP (immediately usable), 6 NADH (not immediately usable), and 2 $FADH_2$ (not immediately usable) for each glucose molecule entering the whole cellular respiration process.

Module 6.12 Chemiosmosis powers most ATP production.

A. The electron transport chain is a series of protein complexes built into the cristae (inner mitochondrial membrane) (Figure 6.12).

B. Each protein in the chain oscillates between reduced and oxidized states as the energetic electrons from NADH and $FADH_2$ pass through their region.

C. As redox occurs, H^+ ions are actively transported from inside the cristae to the intermembrane space.

D. The resulting H^+ ions' gradient drives the production of ATP in the matrix, as the H^+ ions are transported through the ATP synthase.

E. Net energy production for the electron transport chain: 32 ATP (immediately usable) for each glucose molecule entering the whole cellular respiration process.

F. These ATPs are only produced if O_2 is available as the terminal electron acceptor.

Module 6.13 Connection: Certain poisons interrupt critical events in cellular respiration (Figure 6.13).

A. Rotenone (a plant product commonly used to kill fish and insect pests), cyanide, and carbon monoxide block various parts of the electron transport chain.
Preview: Biological magnification can be a consequence of the use of such biocides (Module 38.3).

B. The antifungal oligomycin blocks passage of H^+ ions through the ATP synthase molecule.

C. "Uncouplers," such as dinitrophenol, cause the cristae to leak H^+ ions so that the H^+ ions' gradient is not maintained and chemiosmosis cannot occur.

Module 6.14 Review: Each molecule of glucose yields many molecules of ATP.

A. Glycolysis in cytoplasm yields some ATP in the absence of O_2 but mostly prepares for further steps in the mitochondria that require O_2.

B. The Krebs cycle in mitochondrial matrix yields some ATP directly but strips out CO_2, producing energy shuttles.

C. The electron transport chain produces lots of ATP, but only in the presence of O_2.

D. Three ATP are produced for each NADH and 2 ATP are produced for each $FADH_2$ introduced into the electron transport chain.

E. However, these are maximums. In some cells, ATP is required to shuttle NADH from the cytoplasm into the mitochondrion. Thus, the estimate of the total yield of ATP generated by the aerobic respiration of glucose has a theoretical maximum of 38 (Figure 6.14).
NOTE: This is a good time to discuss the meaning behind the diagrammatic representations of metabolism and how the processes are studied. Reactions proceed from one "pool" of a compound to the next, depending on concentration gradients and the presence of the correct enzymes. The reactions are all happening in many places at the same time. Research into these pathways involves the introduction of radioactive isotope-labeled reactants followed by the recovery of the labeled products (Modules 2.5 and 7.3).

Module 6.15 Fermentation is an anaerobic alternative to aerobic respiration.

NOTE: Fermentation refers to energy-releasing molecular rearrangements in the absence of oxygen.
NOTE: In the two cases reviewed in this module, the role of fermentation is to recharge NAD^+ so that glycolysis can continue to proceed in the absence of O_2. In addition, products are produced that are reduced and still energy rich.

A. **Alcoholic fermentation,** characteristic of some yeasts and bacteria, results in one two-carbon ethanol. This product is toxic, and high concentrations will ultimately kill the cells that produce it (Figure 6.15A).
NOTE: Different strains of yeast are killed by concentrations of up to 20%.
NOTE: You might want to tell the story of the individual who never drank alcohol and yet got drunk whenever he ate. What happened is that outpouchings in his intestines (an anaerobic environment) contained yeast that produced ethanol by fermentation whenever he ate. A fun way to finish this story is to ask the students to picture him getting arrested for driving under the influence of food.

B. **Lactic acid fermentation,** characteristic of many organisms including animals and bacteria, results in one three-carbon lactic acid molecule. Although the accumulation of lactic acid causes muscle fatigue in animals, it is less toxic than alcohol and can be removed from the affected cells and detoxified by the liver with the Cori cycle (Figure 6.15B).

C. Organisms that can only live in environments that lack oxygen are known as **strict anaerobes.** These organisms lack the necessary molecular and cellular equipment with which to carry out cellular respiration.
NOTE: Since aerobic photosynthesis evolved earlier than aerobic respiration, the oxygen that was produced was a toxin.

D. Organisms that can live in environments lacking or containing oxygen are known as facultative anaerobes.

IV. Interconnections Between Molecular Breakdown and Synthesis

Module 6.16 Cells use many kinds of organic molecules as fuel for cellular respiration.

A. Free glucose is not the most common source of fuel in most animal diets, including the human diet. Each of the basic food types can be used as a source of energy (Figure 6.16).

B. Polysaccharides such as starch and glycogen are usually hydrolyzed by digestive enzymes (or liver enzymes) to glucose, which enters glycolysis.

C. Proteins must first be digested to their constituent amino acids. The amino acids are then transformed into various compounds, which enter the middle of glycolysis or the Krebs cycle. Toxic parts of amino acids are stripped off and eliminated in urine (urea) or used to synthesize other compounds.

D. Lipids contain almost twice as much energy per unit weight as carbohydrates. They must first be digested to glycerol and free fatty acids. Glycerol enters in the middle of glycolysis and the free fatty acids are converted into multiple copies of acetyl CoA and enter the Krebs cycle.

E. *Preview:* Human nutrition and the fate, following digestion, of many of the types of basic foods introduced here (and in the next module) are the subjects of Chapter 21.

Module 6.17 Food molecules provide raw materials for biosynthesis.

A. Cells and organisms obtain some raw materials directly from the digestion of the macromolecules in food (Figure 6.17).

B. The processes that produce new molecules often appear to be the reverse of processes that break down the same class of molecules. However, there are differences in the details, as discussed in Module 6.16.

C. ATP is required in biosynthetic pathways and produced by degradative pathways.

Module 6.18 The fuel for respiration ultimately comes from photosynthesis.

A. Cells of all living things can harvest molecular energy (by either cellular respiration or fermentation).

B. The ability to convert light energy into stored molecular energy is a process limited to plants (photosynthesis, the subject of Chapter 7).

Class Activities

1. The production of CO_2 as a by-product of cellular respiration can be demonstrated by using a straw to blow bubbles into a pH indicator solution. CO_2 will make the solution acidic.
2. When looking at food labels, all fats are treated as though they contain the same number of calories. Ask your students if, based on what they learned about the structure of fats in Chapter 3 and cellular respiration in this chapter, this is strictly true. Recall that fats are energy-rich molecules because they contain many hydrogens; however, fats vary in the number of fatty acids they contain as well as in the length and degree of saturation of these fatty acids.

Transparency Acetates

Figure 6.1	The connection between breathing and cellular respiration
Figure 6.2A	Summary equation for cellular respiration
Figure 6.2B	The efficiency of cellular respiration (and comparison with an auto engine) *(combined with Figure 6.2A)*
Table 6.3	Energy consumed by various activities (in kcal)
Figure 6.4	Rearrangement of hydrogen atoms (with their electrons) in cellular respiration
Figure 6.5	A pair of redox reactions, which occur simultaneously

Figure 6.6A	In cellular respiration, cascading electrons release energy in small increments and finally reduce O_2
Figure 6.7A	Chemiosmosis
Figure 6.7B	Substrate-level phosphorylation
Figure 6.8	An overview of cellular respiration
Figure 6.9A	An overview of glycolysis
Figure 6.9B	Details of glycolysis (Layer 1)
Figure 6.9B	Details of glycolysis (Layer 2)
Figure 6.9B	Details of glycolysis (Layer 3)
Figure 6.10	The conversion of pyruvic acid to acetyl CoA
Figure 6.11A	An overview of the Krebs cycle
Figure 6.11B	Details of the Krebs cycle (Layer 1)
Figure 6.11B	Details of the Krebs cycle (Layer 2)
Figure 6.11B	Details of the Krebs cycle (Layer 3)
Figure 6.12	Chemiosmosis in the mitochondrion
Figure 6.13	The effects of five poisons on the electron transport chain and chemiosmosis
Figure 6.14	A tally of the ATP yield from cellular respiration
Figure 6.15A	Alcoholic fermentation
Figure 6.15B	Lactic acid fermentation
Figure 6.16	Pathways of molecular breakdown
Figure 6.17	Biosynthesis of macromolecules from intermediates in cellular respiration

Thinking as a Scientist Question 4: Succinic acid experiment

Media

See the beginning of this book for a complete description of all media available for instructors and students. Animations and videos are available in the Campbell Image Presentation Library. Media Activities and Thinking as a Scientist investigations are available on the student CD-ROM and web site.

Animations and Videos	File Name
Glycolysis Animation	06-09B-GlycolysisAnim.mov
Krebs Cycle Animation	06-11A-KrebsCycleAnim.mov
Electron Transport Animation	06-12-ElectronTransportAnim.mov

Activities and Thinking as a Scientist	Module Number
Web/CD Activity 6A: *Overview of Cellular Respiration*	6.8
Web/CD Activity 6B: *Glycolysis*	6.9
Web/CD Activity 6C: *The Krebs Cycle*	6.11
Web/CD Activity 6D: *Electron Transport and Chemiosmosis*	6.12
Web/CD Thinking as a Scientist: *How Is the Rate of Cellular Respiration Measured?*	6.14
Biology Labs On-Line: *MitochondriaLab*	6.14
Web/CD Activity 6E: *Fermentation*	6.15