

Anatomy and Physiology

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OUTLINE

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AT THE CONCLUSION OF THIS CHAPTER, STUDENTS WILL BE ABLE TO:

- Define *anatomy* and *physiology* and explain why they are important to biomedical engineering.
- Define important anatomical terms.
- Describe the cell theory.
- List the major types of organic compounds and other elements found in cells.
- Explain how the plasma membrane maintains the volume and internal concentrations of a cell.
- Calculate the internal osmolarity and ionic concentrations of a model cell at equilibrium.
- List and describe the functions of the major organelles found within mammalian cells.
- Describe the similarities, differences, and purposes of replication, transcription, and translation.
- List and describe the major components and functions of five organ systems: cardiovascular, respiratory, nervous, skeletal, and muscular.
- Define *homeostasis* and describe how feedback mechanisms help maintain it.

3.1 INTRODUCTION

Since biomedical engineering is an interdisciplinary field based in both engineering and the life sciences, it is important for biomedical engineers to have knowledge about and be able to communicate in both areas. Biomedical engineers must understand the basic components of the body and how they function well enough to exchange ideas and information with physicians and life scientists. Two of the most basic terms and areas of study in the life sciences are anatomy and physiology. *Anatomy* refers to the internal and external structures of the body and their physical relationships, whereas *physiology* refers to the study of the functions of those structures.

Figure 3.1a shows a male body in anatomical position. In this position, the body is erect and facing forward, with the arms hanging at the sides and the palms facing outward. This particular view shows the anterior (ventral) side of the body, whereas Figure 3.1c illustrates the posterior (dorsal) view of another male body that is also in anatomical position, and Figure 3.1b presents the lateral view of the female body. In clinical practice, directional terms are used to describe the relative positions of various parts of the body. Proximal parts are nearer to the trunk of the body or to the attached end of a limb than are distal parts (Figure 3.1a). Parts of the body that are located closer to the head than other parts when the body is in anatomical position are said to be *superior* (Figure 3.1b), whereas those located closer to the feet than other parts are termed *inferior*. *Medial* implies that a part is toward the midline of the body, whereas *lateral* means away from the midline (Figure 3.1c). Parts of the body that lie in the direction of the head are said to be in the cranial direction,

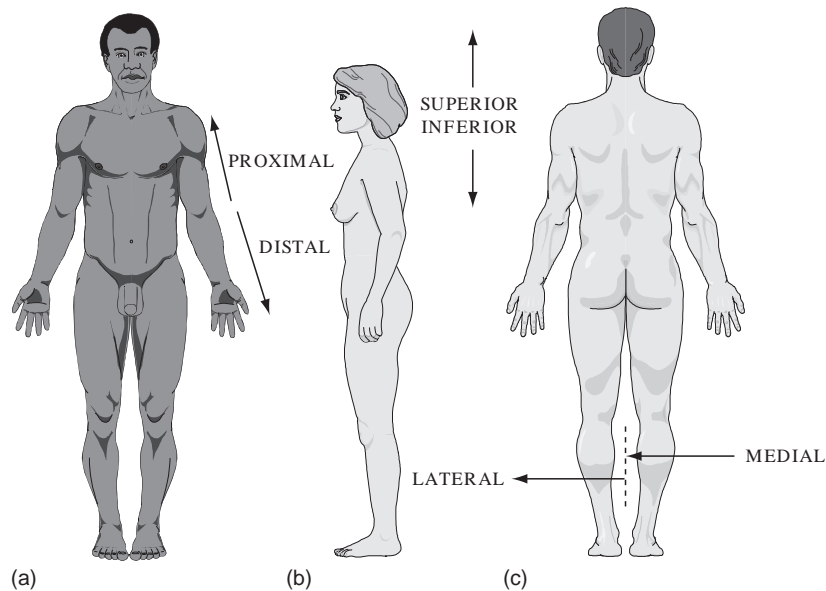


FIGURE 3.1 (a) Anterior view of male body in anatomical position. (b) Lateral view of female body. (c) Posterior view of male body in anatomical position. Relative directions (proximal and distal, superior and inferior, and medial and lateral) are also shown.

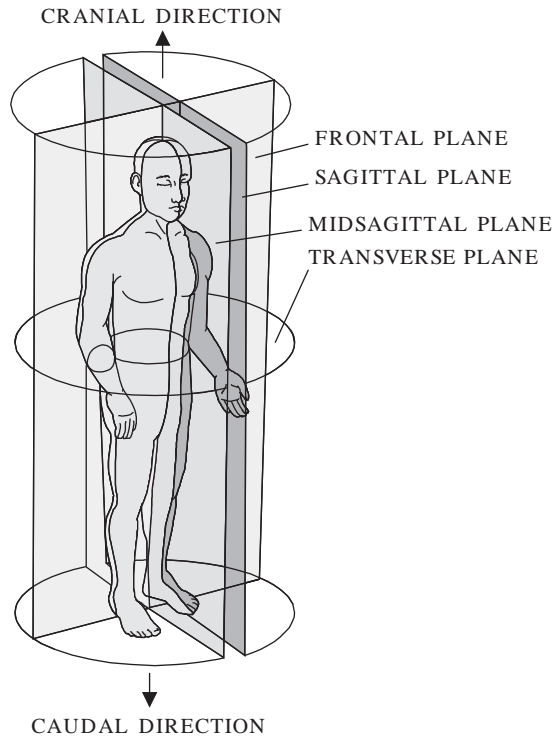


FIGURE 3.2 The body can be divided into sections by the frontal, sagittal, and transverse planes. The midsagittal plane goes through the midline of the body.

whereas those parts that lie in the direction of the feet are said to be in the caudal direction (Figure 3.2).

Anatomical locations can also be described in terms of planes. The plane that divides the body into two symmetric halves along its midline is called the midsagittal plane (Figure 3.2). Planes that are parallel to the midsagittal plane but do not divide the body into symmetric halves are called sagittal planes. The frontal plane is perpendicular to the midsagittal plane and divides the body into asymmetric anterior and posterior portions. Planes that cut across the body and are perpendicular to the midsagittal and frontal planes are called transverse planes.

Human bodies are divided into two main regions: axial and appendicular. The axial part consists of the head, neck, thorax (chest), abdomen, and pelvis, while the appendicular part consists of the upper and lower extremities. The upper extremities, or limbs, include the shoulders, upper arms, forearms, wrists, and hands, while the lower extremities include the hips, thighs, lower legs, ankles, and feet. The abdominal region can be further divided into nine regions or four quadrants.

The cavities of the body hold the internal organs. The major cavities are the dorsal and ventral body cavities, while smaller ones include the nasal, oral, orbital (eye), tympanic (middle ear), and synovial (movable joint) cavities. The dorsal body cavity includes the

cranial cavity that holds the brain and the spinal cavity that contains the spinal cord. The ventral body cavity contains the thoracic and abdominopelvic cavities that are separated by the diaphragm. The thoracic cavity contains the lungs and the mediastinum, which contains the heart and its attached blood vessels, the trachea, the esophagus, and all other organs in this region except for the lungs. The abdominopelvic cavity is divided by an imaginary line into the abdominal and pelvic cavities. The former is the largest cavity in the body and holds the stomach, small and large intestines, liver, spleen, pancreas, kidneys, and gallbladder. The latter contains the urinary bladder, the rectum, and the internal portions of the reproductive system.

The anatomical terms described previously are used by physicians, life scientists, and biomedical engineers when discussing the whole human body or its major parts. Correct use of these terms is vital for biomedical engineers to communicate with health care professionals and to understand the medical problem of concern or interest. While it is important to be able to use the general terms that describe the human body, it is also important for biomedical engineers to have a basic understanding of some of the more detailed aspects of human anatomy and physiology.

3.2 CELLULAR ORGANIZATION

Although there are many smaller units such as enzymes and organelles that perform physiological tasks or have definable structures, the smallest anatomical and physiological unit in the human body that can, under appropriate conditions, live and reproduce on its own is the cell. Cells were first discovered more than 300 years ago shortly after Antony van Leeuwenhoek, a Dutch optician, invented the microscope. With his microscope, van Leeuwenhoek was able to observe “many very small animalcules, the motions of which were very pleasing to behold” in tartar scrapings from his teeth. Following the efforts of van Leeuwenhoek, Robert Hooke, a Curator of Instruments for the Royal Society of England, in the late 1600s further described cells when he used one of the earliest microscopes to look at the plant cell walls that remain in cork. These observations and others led to the cell theory developed by Theodor Schwann and Matthias Jakob Schleiden and formalized by Rudolf Virchow in the mid-1800s. The cell theory states that (1) all organisms are composed of one or more cells, (2) the cell is the smallest unit of life, and (3) all cells come from previously existing cells. Thus, cells are the basic building blocks of life.

Cells are composed mostly of organic compounds and water, with more than 60 percent of the weight in a human body coming from water. The organic compounds—carbohydrates, lipids, proteins, and nucleic acids—that cells synthesize are the molecules that are fundamental to sustaining life. These molecules function as energy packets, storehouses of energy and hereditary information, structural materials, and metabolic workers. The most common elements found in humans (in descending order based on percent of body weight) are oxygen, carbon, hydrogen, nitrogen, calcium, phosphorus, potassium, sodium, chlorine, magnesium, sulfur, iron, and iodine. Carbon, hydrogen, oxygen, and nitrogen contribute more than 99 percent of all the atoms in the body. Most of these elements are incorporated into organic compounds, but some exist in other forms, such as phosphate groups and ions.

Carbohydrates are used by cells not only as structural materials but also to transport and store energy. The three classes of carbohydrates are monosaccharides (e.g., glucose),

oligosaccharides (e.g., lactose, sucrose, maltose), and polysaccharides (e.g., glycogen). Lipids are greasy or oily compounds that will dissolve in each other but not in water. They form structural materials in cells and are the main reservoirs of stored energy. Proteins are the most diverse form of biological molecules. Specialized proteins, called enzymes, make metabolic reactions proceed at a faster rate than would occur if the enzymes were not available and enable cells to produce the organic compounds of life. Other proteins provide structural elements in the body, act as transport channels across plasma membranes, function as signals for changing activities, and provide chemical weapons against disease-carrying bacteria. These diverse proteins are built from a small number (20) of essential amino acids.

Nucleotides and nucleic acids make up the last category of important biological molecules. Nucleotides are small organic compounds that contain a five-carbon sugar (ribose or deoxyribose), a phosphate group, and a nitrogen-containing base that has a single or double carbon ring structure. Adenosine triphosphate (ATP) is the energy currency of the cell and plays a central role in metabolism. Other nucleotides are subunits of coenzymes that are enzyme helpers. The two nucleic acids are deoxyribonucleic acid (DNA) and ribonucleic acid (RNA). DNA (Figure 3.3) is a unique, helical molecule that contains chains of paired nucleotides that run in opposite directions. Each nucleotide contains either a pyrimidine base—thymine (T) or cytosine (C)—with a single ring structure or a purine base—adenine (A) or guanine (G)—with a double ring. In the double helix of DNA, thymine always pairs with adenine (T-A) and cytosine always pairs with guanine (C-G). RNA is similar to DNA except that it consists of a single helical strand, contains ribose instead of deoxyribose, and has uracil (U) instead of thymine.

All cells are surrounded by a plasma membrane that separates, but does not isolate, the cell's interior from its environment. Animal cells, such as those found in humans, are eukaryotic cells. A generalized animal cell is shown in Figure 3.4. In addition to the plasma membrane, eukaryotic cells contain membrane-bound organelles and a membrane-bound nucleus. Prokaryotic cells, such as bacteria, lack membrane-bound structures other than the plasma membrane. In addition to a plasma membrane, all cells have a region that contains DNA (which carries the hereditary instructions for the cell) and cytoplasm (which is a semifluid substance that includes everything inside the plasma membrane except for the DNA).

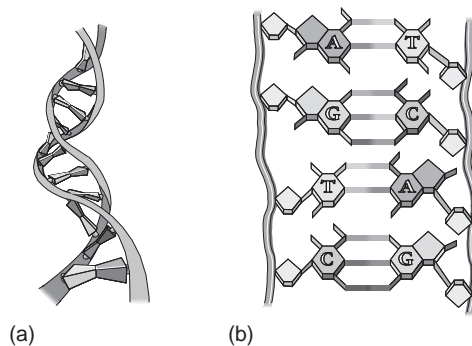


FIGURE 3.3 (a) DNA consists of two chains of paired nucleotides that run in opposite directions and form a helical structure. (b) Thymine pairs with adenine (T-A) and cytosine pairs with guanine (C-G) due to hydrogen bonding between the bases.

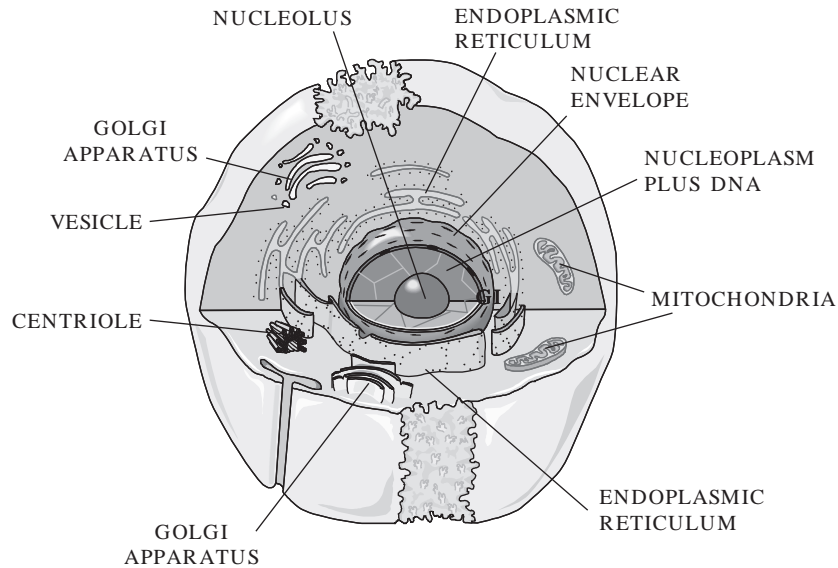


FIGURE 3.4 Animal cells are surrounded by a plasma membrane. They contain a membrane-bound region, the nucleus, which contains DNA. The cytoplasm lies outside of the nucleus and contains several types of organelles that perform specialized functions.

3.2.1 Plasma Membrane

The plasma membrane performs several functions for the cell. It gives mechanical strength, provides structure, helps with movement, and controls the cell's volume and its activities by regulating the movement of chemicals in and out of the cell. The plasma membrane is composed of two layers of phospholipids interspersed with proteins and cholesterol (Figure 3.5). The proteins in the plasma membranes of mammalian cells provide

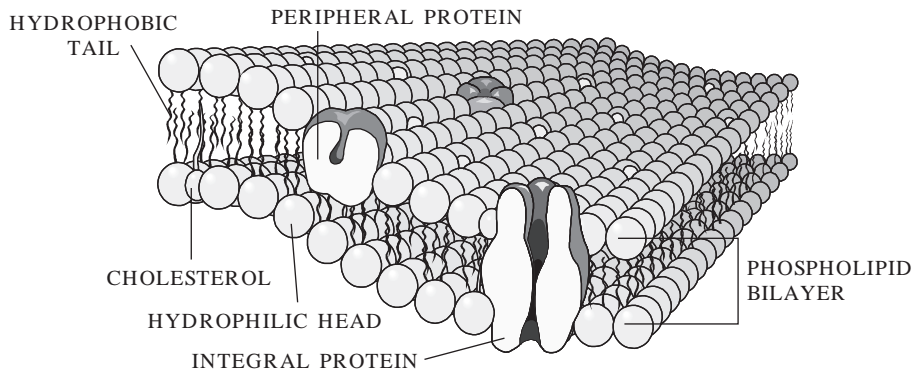


FIGURE 3.5 The plasma membrane surrounds all cells. It consists of a double layer of phospholipids interspersed with proteins and cholesterol.

binding sites for hormones, recognition markers for identifying cells as one type or another, adhesive mechanisms for binding adjacent cells to each other, and channels for transporting materials across the plasma membrane. The phospholipids are arranged with their “water loving” (hydrophilic) heads pointing outward and their “water fearing” (hydrophobic) tails pointing inward. This double-layer arrangement of phospholipids interspersed with protein channels helps maintain the internal environment of a cell by controlling the substances that move across the membrane, whereas the cholesterol molecules act as stabilizers to prevent extensive lateral movement of the lipid molecules.

Some molecules, such as oxygen, carbon dioxide, and water, can easily cross the plasma membrane, whereas other substances, such as large molecules and ions, must move through the protein channels. *Osmosis* is the process by which substances move across a selectively permeable membrane such as a cell’s plasma membrane, whereas *diffusion* refers to the movement of molecules from an area of relatively high concentration to an area of relatively low concentration. Substances that can easily cross the plasma membrane achieve diffusion equilibrium when there is no net movement of these substances across the membrane; that is, the concentration of the substance inside the cell equals the concentration of the substance outside of the cell. Active transport, which requires an input of energy usually in the form of ATP, can be used to move ions and molecules across the plasma membrane and is often used to move them from areas of low concentration to areas of high concentration. This mechanism helps maintain concentrations of ions and molecules inside a cell that are different from the concentrations outside the cell. A typical mammalian cell has internal sodium ion (Na^+) concentrations of 12 mM (12 moles of Na^+ per 1,000 liters of solution) and extracellular Na^+ concentrations of 120 mM, whereas intracellular and extracellular potassium ion (K^+) concentrations are on the order of 125 mM and 5 mM, respectively. In addition to positively charged ions (cations), cells also contain negatively charged ions (anions). A typical mammalian cell has intracellular and extracellular chloride ion (Cl^-) concentrations of 5 mM and 125 mM and internal anion (e.g., proteins, charged amino acids, sulfate ions, and phosphate ions) concentrations of 108 mM. These transmembrane ion gradients are used to make ATP, to drive various transport processes, and to generate electrical signals.

EXAMPLE PROBLEM 3.1

How many molecules of sodium and potassium ions would a cell that has a volume of 2 nl contain?

Solution

Assuming that the intracellular concentrations of Na^+ and K^+ are 12 mM and 125 mM, respectively, the number of molecules for each can be determined by using the volume of the cell and Avadro’s number.

$$\text{Na}^+ : 12 \frac{\text{moles}}{1,000 \text{ liters}} \times 6.023 \times 10^{23} \frac{\text{molecules}}{\text{mole}} \times 2 \times 10^{-9} \text{ liters} = 1.45 \times 10^{13} \text{ molecules}$$

$$\text{K}^+ : 125 \frac{\text{moles}}{1,000 \text{ liters}} \times 6.023 \times 10^{23} \frac{\text{molecules}}{\text{mole}} \times 2 \times 10^{-9} \text{ liters} = 1.51 \times 10^{14} \text{ molecules}$$

The plasma membrane plays an important role in regulating cell volume by controlling the internal osmolarity of the cell. Osmolarity is defined in terms of concentration of dissolved substances. A 1 osmolar (1 Osm) solution contains 1 mole of dissolved particles per liter of solution, while a 1 milliosmolar (1 mOsm) solution has 1 mole of dissolved particles per 1,000 liters of solution. Thus, solutions with high osmolarity have low concentrations of water or other solvents. For biological purposes, solutions with 0.1 Osm glucose and 0.1 Osm urea have essentially the same concentrations of water. It is important to note that a 0.1 M solution of sodium chloride (NaCl) will form a 0.2 Osm solution, since NaCl dissociates into Na^+ and Cl^- ions and thus has twice as many dissolved particles as a solution of a substance—for example, glucose—that does not dissociate into smaller units. Two solutions are isotonic if they have the same osmolarity. One solution is hypotonic to another if it has a lower osmolarity and hypertonic to another if it has a higher osmolarity. It is important to note that tonicity (isotonic, hypotonic, or hypertonic) is only determined by those molecules that cannot cross the plasma membrane, since molecules that can freely cross will eventually reach equilibrium with the same concentration inside and outside of the cell.

Consider a simple model cell that consists of a plasma membrane and cytoplasm. The cytoplasm in this model cell contains proteins that cannot cross the plasma membrane and water that can. At equilibrium, the total osmolarity inside the cell must equal the total osmolarity outside the cell. If the osmolarity inside and the osmolarity outside of the cell are out of balance, there will be a net movement of water from the side of the plasma membrane where it is more highly concentrated to the other until equilibrium is achieved. For example, assume that a model cell (Figure 3.6) contains 0.2 M protein and is placed in a hypotonic solution that contains 0.1 M sucrose. The plasma membrane of this model cell is impermeable to proteins and sucrose but freely permeable to water. The volume of the

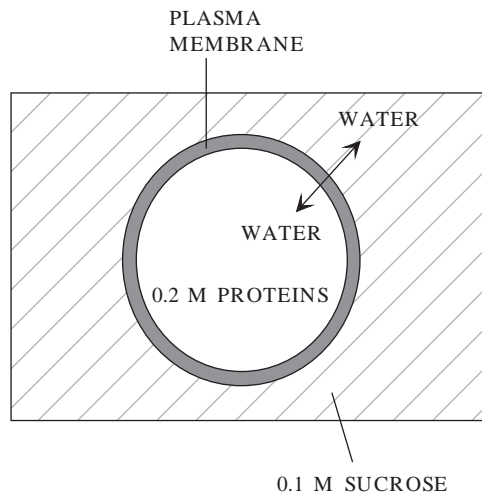


FIGURE 3.6 A simple model cell that consists of cytoplasm, containing 0.2 M proteins, and a plasma membrane is placed in a solution of 0.1 M sucrose. The plasma membrane is insoluble to proteins and sucrose but allows water to pass freely in either direction. The full extent of the extracellular volume is not shown and is much larger than the cell's volume of 1 nl.

cell, 1 nl, is very small relative to the volume of the solution. In other words, changes in the cell's volume have no measurable effect on the volume of the external solution. What will happen to the volume of the cell as it achieves equilibrium?

At equilibrium, the osmolarity inside the cell must equal the osmolarity outside the cell. The initial osmolarity inside the cell is 0.2 Osm, since the proteins do not dissociate into smaller units. The osmolarity outside the cell is 0.1 Osm due to the sucrose solution. A 0.2 Osm solution has 0.2 moles of dissolved particles per liter of solution, while a 0.1 Osm solution has half as many moles of dissolved particles per liter. The osmolarity inside the cell must decrease by a factor of 2 in order to achieve equilibrium. Since the plasma membrane will not allow any of the protein molecules to leave the cell, this can only be achieved by doubling the cell's volume. Thus, there will be a net movement of water across the plasma membrane until the cell's volume increases to 2 nl and the cell's internal osmolarity is reduced to 0.1 Osm—the same as the osmolarity of the external solution. The water moves down its concentration gradient by diffusing from where it is more highly concentrated in the 0.1 M sucrose solution to where it is less concentrated in the 0.2 M protein solution in the cell.

EXAMPLE PROBLEM 3.2

What would happen to the model cell in Figure 3.6 if it were placed in pure water?

Solution

Water can pass through the plasma membrane and would flow down its concentration gradient from where it is more concentrated (outside of the cell) to where it is less concentrated (inside of the cell). Eventually, enough water would move into the cell to rupture the plasma membrane, since the concentration of water outside the cell would be higher than the concentration of water inside the cell as long as there were proteins trapped within the cell.

EXAMPLE PROBLEM 3.3

Assume that the model cell in Figure 3.6 has an initial volume of 2 nl and contains 0.2 M protein. The cell is placed in a large volume of 0.2 M NaCl. In this model, neither Na^+ nor Cl^- can cross the plasma membrane and enter the cell. Is the 0.2 M NaCl solution hypotonic, isotonic, or hypertonic relative to the osmolarity inside the cell? Describe what happens to the cell as it achieves equilibrium in this new environment. What will be the final osmolarity of the cell? What will be its final volume?

Solution

The osmolarity inside the cell is 0.2 Osm. The osmolarity of the 0.2 M NaCl solution is 0.4 Osm ($0.2 \text{ Osm Na}^+ + 0.2 \text{ Osm Cl}^-$). Thus, the NaCl solution is hypertonic relative to the osmolarity inside the cell ($\text{osmolarity}_{\text{outside}} > \text{osmolarity}_{\text{inside}}$). Since none of the particles (protein, Na^+ , and Cl^-) can cross the membrane, water will move out of the cell until the osmolarity inside

Continued

the cell is 0.4 Osm. This will be achieved when the volume inside the cell has been reduced from 2 nl to 1 nl.

$$C_1V_1 = C_2V_2$$

$$\frac{0.2 \text{ Osm}}{0.4 \text{ Osm}} \times 2\text{nl} = V_2$$

$$1\text{nl} = V_2$$

Real cells are much more complex than the simple model just described. In addition to achieving osmotic balance at equilibrium, real cells must also achieve electrical balance with regard to the ions that are present in the cytoplasm. The principle of electrical neutrality requires that the overall concentration of cations in a biological compartment—for example, a cell—must equal the overall concentration of anions in that compartment. Consider another model cell (Figure 3.7) with internal and external cation and anion concentrations similar to those of a typical mammalian cell. Is the cell at equilibrium if the plasma membrane is freely permeable to K^+ and Cl^- but impermeable to Na^+ and the internal anions? The total osmolarity inside the cell is 250 mOsm (12 mM Na^+ , 125 mM K^+ , 5 mM Cl^- , 108 mM anions), while the total osmolarity outside the cell is also 250 mOsm (120 mM Na^+ , 5 mM K^+ , 125 mM Cl^-), so the cell is in osmotic balance—that is, there will be no net movement of water across the plasma membrane. If the average charge per molecule of the anions inside the cell is considered to be -1.2 , then the cell is also approximately in electrical equilibrium (12 + 125 positive charges for Na^+ and K^+ ; 5 + 1.2 * 108 negative charges for Cl^- and the other anions). Real cells, however, cannot maintain this equilibrium without expending energy, since real cells are slightly permeable to Na^+ . In order to maintain equilibrium and keep Na^+ from accumulating intracellularly, mammalian cells must actively pump Na^+ out of the cell against its diffusion and electrical gradients. Since Na^+

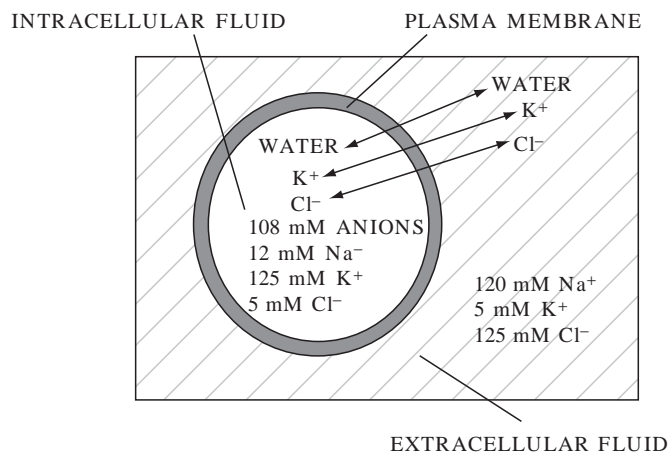


FIGURE 3.7 A model cell with internal and external concentrations similar to those of a typical mammalian cell. The full extent of the extracellular volume is not shown and is much larger than the cell's volume.

is pumped out through specialized protein channels at a rate equivalent to the rate at which it leaks in through other channels, it behaves osmotically as if it cannot cross the plasma membrane. Thus, mammalian cells exist in a steady state, rather than at equilibrium, since energy in the form of ATP must be used to prevent a net movement of ions across the plasma membrane.

EXAMPLE PROBLEM 3.4

Consider a simple model cell, such as the one in Figure 3.7, that has the following ion concentrations. Is the cell at equilibrium? Explain your answer.

Ion	Intracellular Concentration (mM)	Extracellular Concentration (mM)
K ⁺	158	4
Na ⁺	20	163
Cl ⁻	52	167
A ⁻	104	—

Solution

Yes. The cell is both electrically and osmotically at equilibrium because the charges within the inside and outside compartments are equal, and the osmolarity inside the cell equals the osmolarity outside of the cell.

	Inside	Outside
Positive	$158 + 20 = 178 \text{ mM}$	$4 + 163 = 167 \text{ mM}$
Negative	$52 + 1.2 * 104 = 177 \text{ mM}$ $178 \text{ mM}_{\text{pos}} \approx 177 \text{ mM}_{\text{neg}}$	167 mM $167 \text{ mM}_{\text{pos}} = 167 \text{ mM}_{\text{neg}}$
Osmolarity	$158 + 20 + 52 + 104 = 334 \text{ mM}$ $334 \text{ mM}_{\text{inside}} = 334 \text{ mM}_{\text{outside}}$	$4 + 163 + 167 = 334 \text{ mM}$

One of the consequences of the distribution of charged particles in the intracellular and extracellular fluids is that an electrical potential exists across the plasma membrane. The value of this electrical potential depends on the intracellular and extracellular concentrations of ions that can cross the membrane and will be described more fully in Chapter 11.

In addition to controlling the cell's volume, the plasma membrane also provides a route for moving large molecules and other materials into and out of the cell. Substances can be moved into the cell by means of endocytosis (Figure 3.8a) and out of the cell by means of exocytosis (Figure 3.8b). In endocytosis, material—for example, a bacterium—outside of the cell is engulfed by a portion of the plasma membrane that encircles it to form a vesicle. The vesicle then pinches off from the plasma membrane and moves its contents to the inside of the cell. In exocytosis, material within the cell is surrounded by a membrane to form a vesicle. The vesicle then moves to the edge of the cell, where its membrane fuses with the plasma membrane and its contents are released to the exterior of the cell.

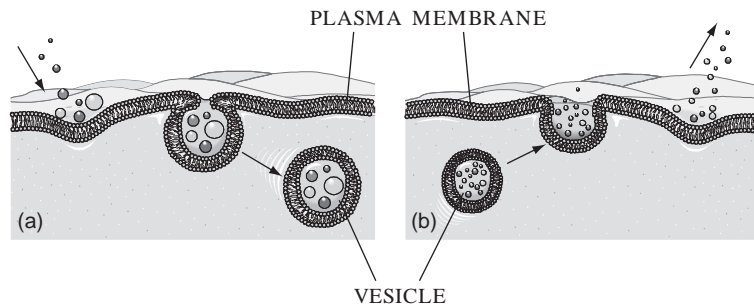


FIGURE 3.8 Substances that are too large to pass through the integral proteins in the plasma membrane can be moved into the cell by means of endocytosis (a) and out of the cell by means of exocytosis (b).

3.2.2 Cytoplasm and Organelles

The cytoplasm contains fluid (cytosol) and organelles. Ions (such as Na^+ , K^+ , and Cl^-) and molecules (such as glucose) are distributed through the cytosol via diffusion. Membrane-bound organelles include the nucleus, rough and smooth endoplasmic reticulum, the Golgi apparatus, lysosomes, and mitochondria. Nonmembranous organelles include nucleoli, ribosomes, centrioles, microvilli, cilia, flagella, and the microtubules, intermediate filaments, and microfilaments of the cytoskeleton.

The nucleus (see Figure 3.4) consists of the nuclear envelope (a double membrane) and the nucleoplasm (a fluid that contains ions, enzymes, nucleotides, proteins, DNA, and small amounts of RNA). Within its DNA, the nucleus contains the instructions for life's processes. Nuclear pores are protein channels that act as connections for ions and RNA, but not proteins or DNA, to leave the nucleus and enter the cytoplasm and for some proteins to enter the nucleoplasm. Most nuclei contain one or more nucleoli. Each nucleolus contains DNA, RNA, and proteins and synthesizes the components of the ribosomes that cells use to make proteins.

The smooth and rough endoplasmic reticulum (ER), Golgi apparatus, and assorted vesicles (Figures 3.4, 3.9a, and 3.9b) make up the cytomembrane system, which delivers proteins and lipids for manufacturing membranes and accumulates and stores proteins and lipids for specific uses. The ER also acts as a storage site for calcium ions. The rough ER differs from the smooth ER in that it has ribosomes attached to its exterior surface. Ribosomes provide the platforms for synthesizing proteins. Those that are synthesized on the rough ER are passed into its interior, where nonproteinaceous side chains are attached to them. These modified proteins move to the smooth ER, where they are packaged in vesicles. The smooth ER also manufactures and packages lipids into vesicles and is responsible for releasing stored calcium ions. The vesicles leave the smooth ER and become attached to the Golgi apparatus, where their contents are released, modified, and repackaged into new vesicles. Some of these vesicles, called lysosomes, contain digestive enzymes that are used to break down materials that move into the cells via endocytosis. Other vesicles contain proteins, such as hormones and neurotransmitters, that are secreted from the cells by means of exocytosis.

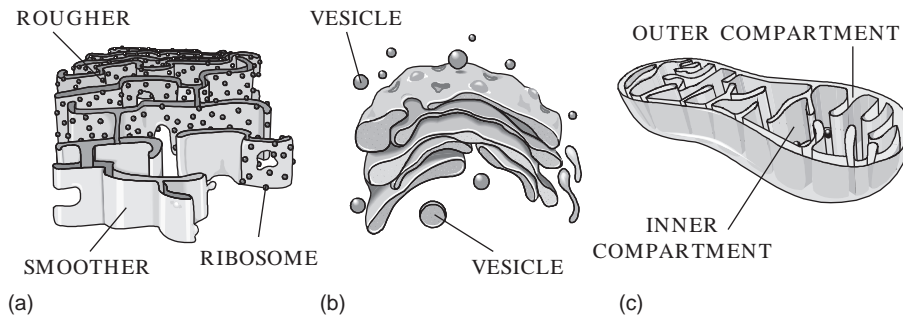


FIGURE 3.9 Subcellular organelles. The endoplasmic reticulum (a), the Golgi apparatus (b), and vesicles (b) make up the cytomembrane system in the cell. The small circles on the endoplasmic reticulum (ER) represent ribosomes. The area containing ribosomes is called the rough ER, while the area that lacks ribosomes is called the smooth ER. The mitochondria (c) have a double membrane system that divides the interior into two compartments that contain different concentrations of enzymes, substrates, and hydrogen ions (H^+). Electrical and chemical gradients between the inner and outer compartments provide the energy needed to generate ATP.

The mitochondria (Figures 3.9c and 3.10) contain two membranes: an outer membrane that surrounds the organelle and an inner membrane that divides the organelle's interior into two compartments. Approximately 95 percent of the ATP required by the cell is produced in the mitochondria in a series of oxygen-requiring reactions that produce carbon dioxide as a by-product. Mitochondria are different from most other organelles in that they contain their own DNA. The majority of the mitochondria in sexually reproducing organisms, such

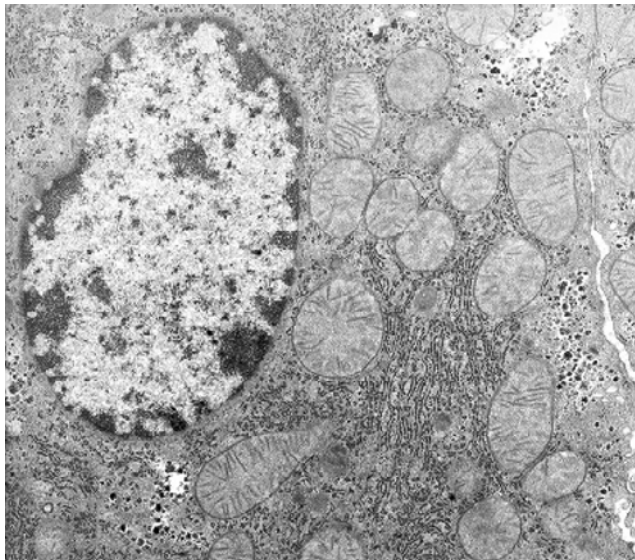


FIGURE 3.10 Scanning electron micrograph of a normal mouse liver at 8,000X magnification. The large round organelle on the left is the nucleus. The smaller round and oblong organelles are mitochondria that have been sliced at different angles. The narrow membranes in parallel rows are endoplasmic reticula. The small black dots on the ERs are ribosomes. *Photo courtesy of Valerie Knowlton, Center for Electron Microscopy, North Carolina State University.*

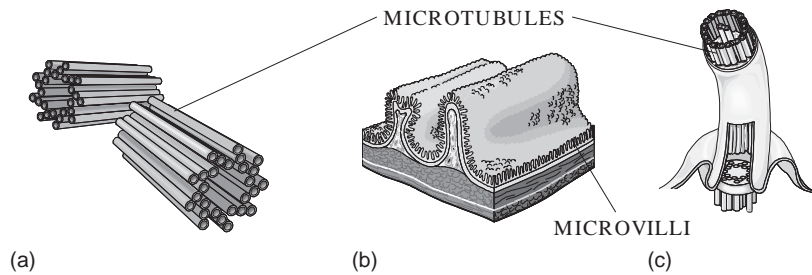


FIGURE 3.11 Centrioles (a) contain microtubules and are located at right angles to each other in the cell's centrosome. These organelles play an important part in cell division by anchoring the microtubules that are used to divide the cell's genetic material. Microvilli (b), which are extensions of the plasma membrane, line the villi, tiny fingerlike protrusions in the mucosa of the small intestine, and help increase the area available for the absorption of nutrients. Cilia (c) line the respiratory tract. The beating of these organelles helps move bacteria and particles trapped in mucus out of the lungs.

as humans, come from the mother's egg cell, since the father's sperm contributes little more than the DNA in a haploid (half) set of chromosomes to the developing offspring.

Microtubules, intermediate filaments, and microfilaments provide structural support and assist with movement. Microtubules are long, hollow, cylindrical structures that radiate from microtubule organizing centers and, during cell division, from centrosomes, a specialized region of the cytoplasm that is located near the nucleus and contains two centrioles (Figures 3.4 and 3.11a) oriented at right angles to each other. Microtubules consist of spiraling subunits of a protein called tubulin, whereas centrioles consist of nine triplet microtubules that radiate from their centers like the spokes of a wheel. Intermediate filaments are hollow and provide structure to the plasma membrane and nuclear envelope. They also aid in cell-to-cell junctions and in maintaining the spatial organization of organelles. Myofilaments are found in most cells and are composed of strings of protein molecules. Cell movement can occur when actin and myosin, protein subunits of myofilaments, interact. Microvilli (Figure 3.11b) are extensions of the plasma membrane that contain microfilaments. They increase the surface area of a cell to facilitate absorption of extracellular materials.

Cilia (Figure 3.11c) and flagella are parts of the cytoskeleton that have shafts composed of nine pairs of outer microtubules and two single microtubules in the center. Both types of shafts are anchored by a basal body that has the same structure as a centriole. Flagella function as whiplike tails that propel cells such as sperm. Cilia are generally shorter and more profuse than flagella and can be found on specialized cells such as those that line the respiratory tract. The beating of the cilia helps move mucus-trapped bacteria and particles out of the lungs.

3.2.3 DNA and Gene Expression

DNA (see Figure 3.3) is found in the nucleus and mitochondria of eukaryotic cells. In organisms that reproduce sexually, the DNA in the nucleus contains information from both parents, while that in the mitochondria comes from the organism's mother. In the nucleus, the DNA is wrapped around protein spools, called nucleosomes, and is organized into pairs of chromosomes. Humans have 22 pairs of autosomal chromosomes and two sex

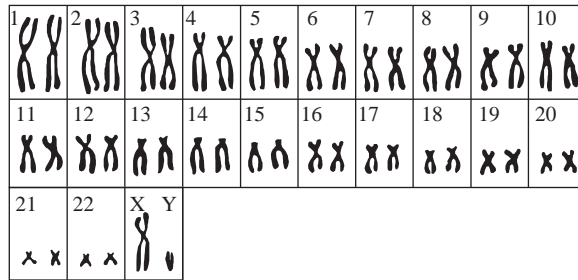


FIGURE 3.12 This karyotype of a normal human male shows the 22 pairs of autosomal chromosomes in descending order based on size, as well as the X and Y sex chromosomes.

chromosomes, XX for females and XY for males (Figure 3.12). If the DNA from all 46 chromosomes in a human somatic cell—that is, any cell that does not become an egg or sperm cell—was stretched out end to end, it would be about 2 nm wide and 2 m long. Each chromosome contains thousands of individual genes that are the units of information about heritable traits. Each gene has a particular location in a specific chromosome and contains the code for producing one of the three forms of RNA (ribosomal RNA, messenger RNA, and transfer RNA). The Human Genome Project was begun in 1990 and had as its goal to first identify the location of at least 3,000 specific human genes and then to determine the sequence of nucleotides (about 3 billion!) in a complete set of haploid human chromosomes (one chromosome from each of the 23 pairs). See Chapter 13 for more information about the Human Genome Project.

DNA replication occurs during cell division (Figure 3.13). During this semiconservative process, enzymes unzip the double helix, deliver complementary bases to the nucleotides, and bind the delivered nucleotides into the developing complementary strands. Following replication, each strand of DNA is duplicated so two double helices now exist, each consisting of one strand of the original DNA and one new strand. In this way, each daughter cell gets the same hereditary information that was contained in the original dividing cell. During replication, some enzymes check for accuracy, while others repair pairing mistakes so the error rate is reduced to approximately one per billion.

Since DNA remains in the nucleus, where it is protected from the action of the cell's enzymes, and proteins are made on ribosomes outside of the nucleus, a method (transcription) exists for transferring information from the DNA to the cytoplasm. During transcription (Figure 3.14), the sequence of nucleotides in a gene that codes for a protein is transferred to messenger RNA (mRNA) through complementary base pairing of the nucleotide sequence in the gene. For example, a DNA sequence of TACGCTCCGATA would become AUGCGAGGCUAU in the mRNA. The process is somewhat more complicated, since the transcript produced directly from the DNA contains sequences of nucleotides, called introns, that are removed before the final mRNA is produced. The mRNA also has a tail, called a poly-A tail, of about 100–200 adenine nucleotides attached to one end. A cap with a nucleotide that has a methyl group and phosphate groups bonded to it is attached at the other end of the mRNA. Transcription differs from replication in that (1) only a certain stretch of DNA acts as the template and not the whole strand, (2) different enzymes are used, and (3) only a single strand is produced.

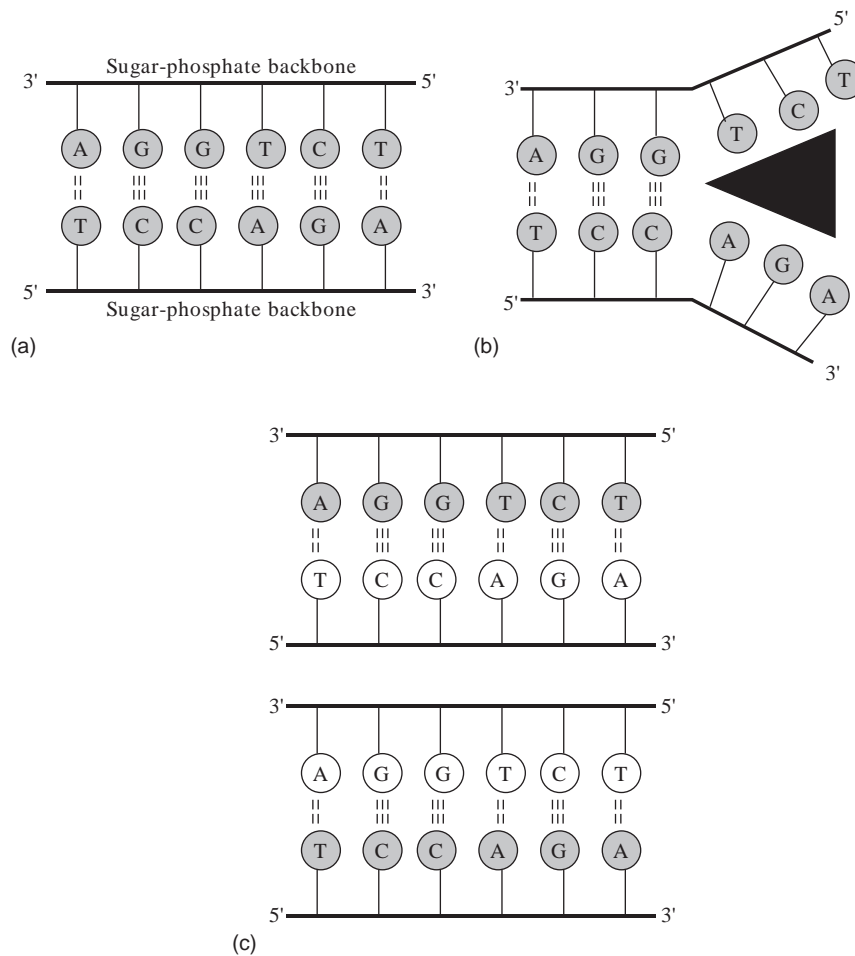


FIGURE 3.13 During replication, DNA helicase shown as a black wedge in (b) unzips the double helix (a). Another enzyme, DNA polymerase, then copies each side of the unzipped chain in the 5' to 3' direction. One side of the chain (5' to 3') can be copied continuously, while the opposite side (3' to 5') is copied in small chunks in the 5' to 3' direction that are bound together by another enzyme, DNA ligase. Two identical double strands of DNA are produced as a result of replication.

After being transcribed, the mRNA moves out into the cytoplasm through the nuclear pores and binds to specific sites on the surface of the two subunits that make up a ribosome (Figure 3.15). In addition to the ribosomes, the cytoplasm contains amino acids and another form of RNA: transfer RNA (tRNA). Each tRNA contains a triplet of bases, called an anticodon, and binds at an area away from the triplet to an amino acid that is specific for that particular anticodon. The mRNA that was produced from the gene in the nucleus also contains bases in sets of three. Each triplet in the mRNA is called a codon. The four

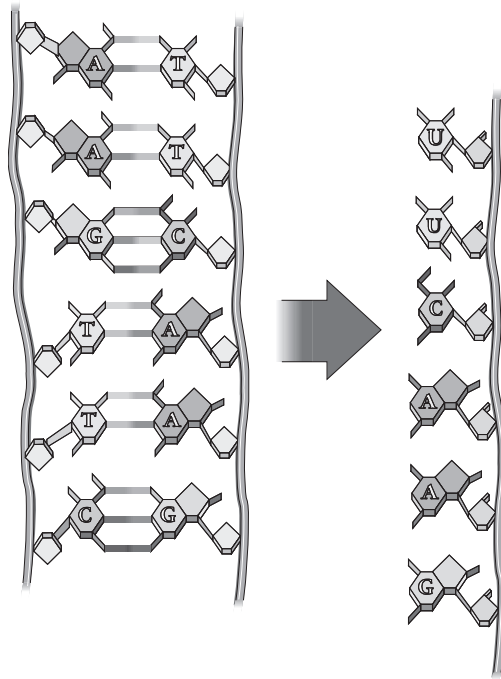


FIGURE 3.14 During transcription, RNA is formed from genes in the cell's DNA by complementary base pairing to one of the strands. RNA contains uracil (U) rather than thymine (T), so the Ts in the first two pairs of the DNA become Us in the single-stranded RNA.

possibilities for nucleotides (A, U, C, G) in each of the three places give rise to 64 (4^3) possible codons. These 64 codons make up the genetic code. Each codon codes for a specific amino acid, but some amino acids are specified by more than one codon (Table 3.1). For example, AUG is the only mRNA codon for methionine (the amino acid that always signals the starting place for translation—the process by which the information from a gene is used to produce a protein), while UUA, UUG, CUU, CUC, CUA, and CUG are all codons for leucine. The anticodon on the tRNA that delivers the methionine to the ribosome is UAC, whereas tRNAs with anticodons of AAU, AAC, GAA, GAG, GAU, and GAC deliver leucine.

During translation, the mRNA binds to a ribosome and tRNA delivers amino acids to the growing polypeptide chain in accordance with the codons specified by the mRNA. Peptide bonds are formed between each newly delivered amino acid and the previously delivered one. When the amino acid is bound to the growing chain, it is released from the tRNA, and the tRNA moves off into the cytoplasm, where it joins with another amino acid that is specified by its anticodon. This process continues until a stop codon (UAA, UAG, or UGA) is reached on the mRNA. The protein is then released into the cytoplasm or into the rough ER for further modifications.

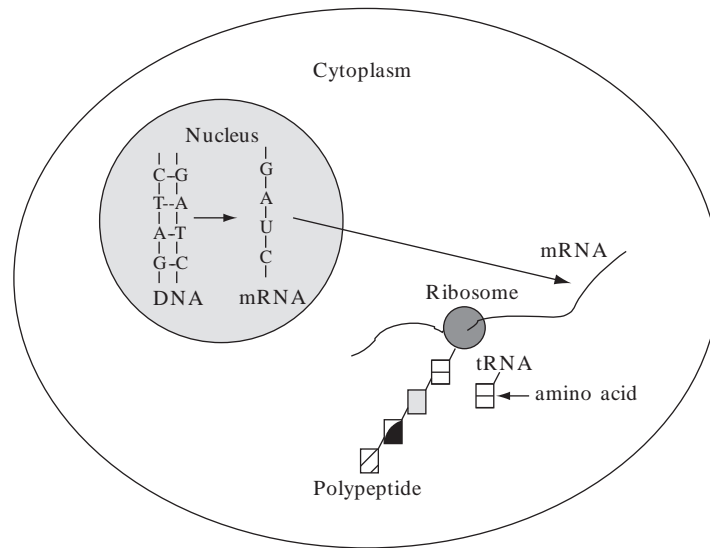


FIGURE 3.15 Following transcription from DNA and processing in the nucleus, mRNA moves from the nucleus to the cytoplasm. In the cytoplasm, the mRNA joins with a ribosome to begin the process of translation. During translation, tRNA delivers amino acids to the growing polypeptide chain. Which amino acid is delivered depends on the three-base codon specified by the mRNA. Each codon is complementary to the anticodon of a specific tRNA. Each tRNA binds to a particular amino acid at a site that is opposite the location of the anticodon. For example, the codon CUG in mRNA is complementary to the anticodon GAC in the tRNA that carries leucine and will result in adding the amino acid leucine to the polypeptide chain.

EXAMPLE PROBLEM 3.5

Consider a protein that contains the amino acids asparagine, phenylalanine, histidine, and serine in sequence. Which nucleotide sequences on DNA (assuming that there were no introns) would result in this series of amino acids? What would be the anticodons for the tRNAs that delivered these amino acids to the ribosomes during translation?

Solution

The genetic code (see Table 3.1) provides the sequence for the mRNA codons that specify these amino acids. The mRNA codons can be used to determine the sequence in the original DNA and the anticodons of the tRNA, since the mRNA bases must pair with the bases in both DNA and tRNA. Note that DNA contains thymine (T) but no uracil (U) and that both mRNA and tRNA contain U and not T. See Figures 3.3 and 3.14 for examples of base pairing.

	Asparagine (Asn)	Phenylalanine (Phe)	Histidine (His)	Serine (Ser)
mRNA codon	AAU or AAC	UUU or UUC	CAU or CAC	UC(A, G, U, or C)
DNA	TTA or TTG	AAA or AAG	GTA or GTG	AG(T, C, A, or G)
tRNA anticodon	UUA or UUG	AAA or AAG	GUA or GUG	AG(U, C, A, or G)

TABLE 3.1 The Genetic Code

First Base	Second Base				Third Base
	A	U	G	C	
A	Lys	Ile	Arg	Thr	A
	Lys	Met - Start	Arg	Thr	G
	Asn	Ile	Ser	Thr	U
	Asn	Ile	Ser	Thr	C
U	Stop	Leu	Stop	Ser	A
	Stop	Leu	Trp	Ser	G
	Tyr	Phe	Cys	Ser	U
	Tyr	Phe	Cys	Ser	C
G	Glu	Val	Gly	Ala	A
	Glu	Val	Gly	Ala	G
	Asp	Val	Gly	Ala	U
	Asp	Val	Gly	Ala	C
C	Gln	Leu	Arg	Pro	A
	Gln	Leu	Arg	Pro	G
	His	Leu	Arg	Pro	U
	His	Leu	Arg	Pro	C

Amino acid 3-letter and 1-letter codes: Ala (A) = Alanine; Arg (R) = Arginine; Asn (N) = Asparagine; Asp (D) = Aspartic acid; Cys (C) = Cysteine; Glu (E) = Glutamic acid; Gln (Q) = Glutamine; Gly (G) = Glycine; His (H) = Histidine; Ile (I) = Isoleucine; Leu (L) = Leucine; Lys (K) = Lysine; Met (M) = Methionine; Phe (F) = Phenylalanine; Pro (P) = Proline; Ser (S) = Serine; Thr (T) = Threonine; Trp (W) = Tryptophan; Tyr (Y) = Tyrosine; Val (V) = Valine.

3.3 TISSUES

Groups of cells and surrounding substances that function together to perform one or more specialized activities are called tissues (Figure 3.16). The four primary types of tissue in the human body are epithelial, connective, muscle, and nervous. Epithelial tissues are either composed of cells arranged in sheets that are one or more layers thick or are organized into glands that are adapted for secretion. They are also characterized by having a free surface—for example, the inside surface of the intestines or the outside of the skin—and a basilar membrane. Typical functions of epithelial tissue include absorption (lining of the small intestine), secretion (glands), transport (kidney tubules), excretion (sweat glands), protection (skin, Figure 3.16a), and sensory reception (taste buds). Connective tissues are the most abundant and widely distributed. Connective tissue proper can be loose (loosely woven fibers found around and between organs), irregularly dense (protective capsules around organs), and regularly dense (ligaments and tendons), whereas specialized connective tissue includes blood

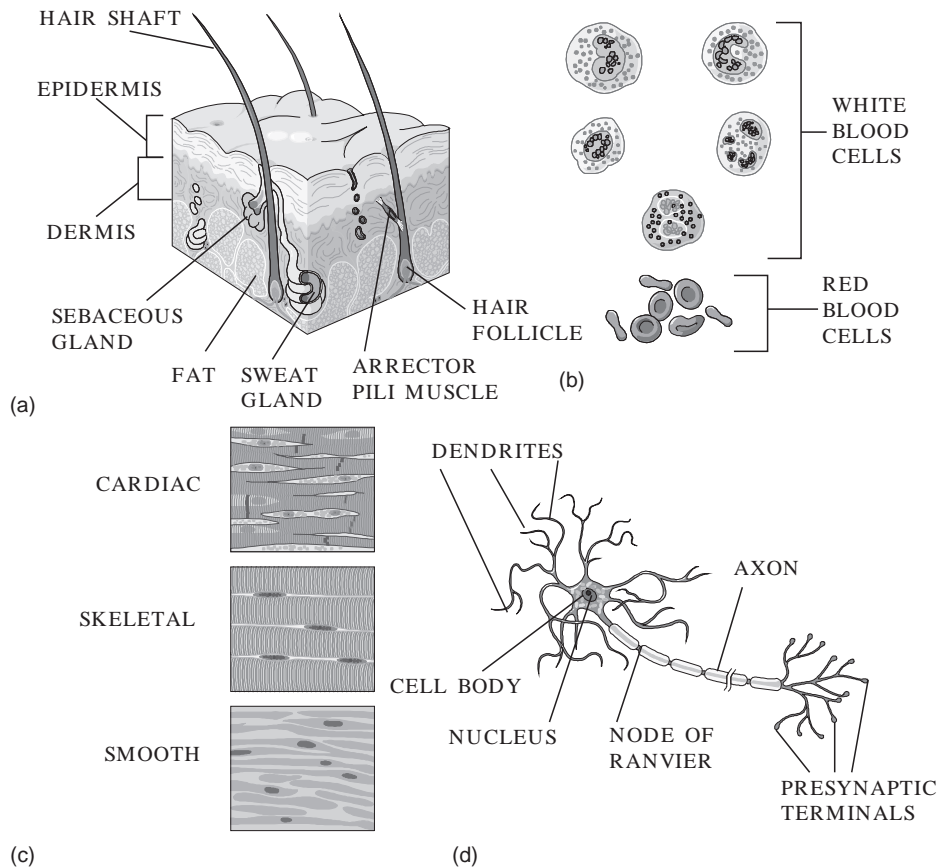


FIGURE 3.16 Four tissue types. Skin (a) is a type of epithelial tissue that helps protect the body. Blood (b) is a specialized connective tissue. The three types of muscle tissue (c) are cardiac, skeletal, and smooth. Motor neurons (d) are a type of nervous tissue that conducts electrical impulses from the central nervous system to effector organs such as muscles.

(Figure 3.16b), bone, cartilage, and adipose tissue. Muscle tissue provides movement for the body through its specialized cells that can shorten in response to stimulation and then return to their uncontracted state. Figure 3.16c shows the three types of muscle tissue: skeletal (attached to bones), smooth (found in the walls of blood vessels), and cardiac (found only in the heart). Nervous tissue consists of neurons (Figure 3.16d) that conduct electrical impulses and glial cells that protect, support, and nourish neurons.

3.4 MAJOR ORGAN SYSTEMS

Combinations of tissues that perform complex tasks are called organs, and organs that function together form organ systems. The human body has 11 major organ systems: integumentary, endocrine, lymphatic, digestive, urinary, reproductive, circulatory, respiratory, nervous, skeletal, and muscular. The integumentary system (skin, hair, nails, and various

glands) provides protection for the body. The endocrine system (ductless glands such as the thyroid and adrenals) secretes hormones that regulate many chemical actions within cells. The lymphatic system (glands, lymph nodes, lymph, lymphatic vessels) returns excess fluid and protein to the blood and helps defend the body against infection and tissue damage. The digestive system (stomach, intestines, and other structures) ingests food and water, breaks food down into small molecules that can be absorbed and used by cells, and removes solid wastes. The urinary system (kidneys, ureters, urinary bladder, and urethra) maintains the fluid volume of the body, eliminates metabolic wastes, and helps regulate blood pressure and acid-base and water-salt balances. The reproductive system (ovaries, testes, reproductive cells, and accessory glands and ducts) produces eggs or sperm and provides a mechanism for the production and nourishment of offspring. The circulatory system (heart, blood, and blood vessels) serves as a distribution system for the body. The respiratory system (airways and lungs) delivers oxygen to the blood from the air and carries away carbon dioxide. The nervous system (brain, spinal cord, peripheral nerves, and sensory organs) regulates most of the body's activities by detecting and responding to internal and external stimuli. The skeletal system (bones and cartilage) provides protection and support as well as sites for muscle attachments, the production of blood cells, and calcium and phosphorus storage. The muscular system (skeletal muscle) moves the body and its internal parts, maintains posture, and produces heat. Although biomedical engineers have made major contributions to understanding, maintaining, and/or replacing components in each of the 11 major organ systems, only the last 5 listed will be examined in greater detail.

3.4.1 Circulatory System

The circulatory system (Figure 3.17) delivers nutrients and hormones throughout the body, removes waste products from tissues, and provides a mechanism for regulating temperature and removing the heat generated by the metabolic activities of the body's internal organs. Every living cell in the body is no more than 10–100 μm from a capillary (small blood vessels with walls only one cell thick that are 8 μm in diameter, approximately the same size as a red blood cell). This close proximity allows oxygen, carbon dioxide, and most other small solutes to diffuse from the cells into the capillary or from the capillary into the cells, with the direction of diffusion determined by concentration and partial pressure gradients.

Accounting for about 8 \pm 1 percent of total body weight, averaging 5,200 ml, blood is a complex, heterogeneous suspension of formed elements—the *blood cells*, or *hematocytes*—suspended in a continuous, straw-colored fluid called *plasma*. Nominally, the composite fluid has a mass density of 1.057 \pm 0.007 g/cm^3 , and it is six times as viscous as water. The hematocytes include three basic types of cells: red blood cells (erythrocytes, totaling nearly 95 percent of the formed elements), white blood cells (leukocytes, averaging less than .15 percent of all hematocytes), and platelets (thrombocytes, on the order of 5 percent of all blood cells). Hematocytes are all derived in the active (“red”) bone marrow (about 1,500 g) of adults from undifferentiated stem cells called *hemocytoblasts*, and all reach ultimate maturity via a process called *hematocytopoiesis*.

The primary function of erythrocytes is to aid in the transport of blood gases—about 30 to 34 percent (by weight) of each cell consisting of the oxygen- and carbon dioxide-carrying protein hemoglobin (64,000 MW \leq 68,000) and a small portion of the cell containing the

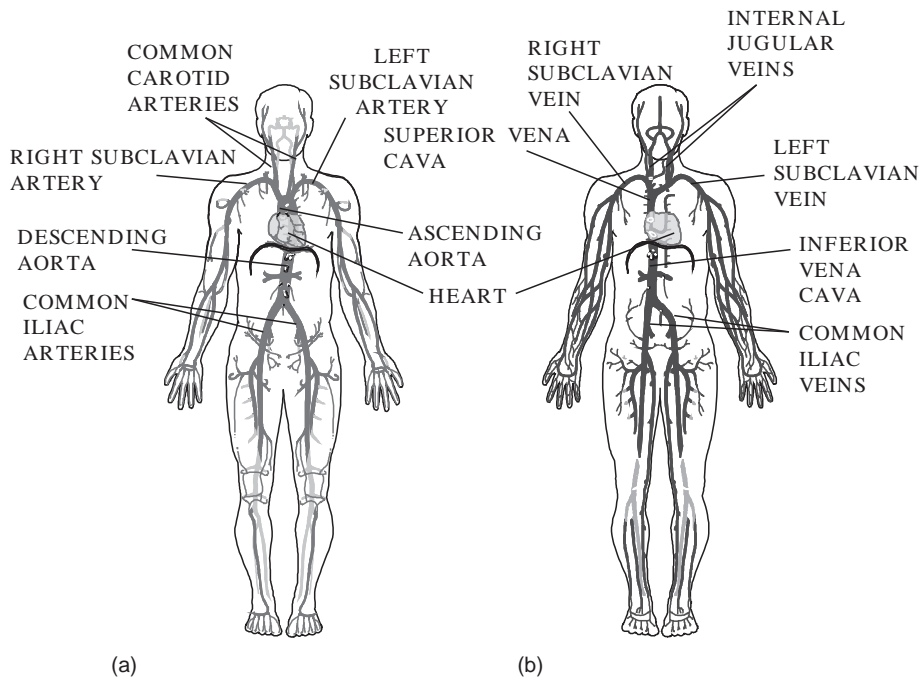


FIGURE 3.17 (a) The distribution of the main arteries in the body that carry blood away from the heart. (b) The distribution of the main veins in the body that return the blood to the heart.

enzyme carbonic anhydrase, which catalyzes the reversible formation of carbonic acid from carbon dioxide and water. The primary function of leukocytes is to endow the human body with the ability to identify and dispose of foreign substances (such as infectious organisms) that do not belong there—agranulocytes (lymphocytes and monocytes) essentially doing the “identifying” and granulocytes (neutrophils, basophils, and eosinophils) essentially doing the “disposing.” The primary function of platelets is to participate in the blood-clotting process.

Removal of all hematocytes from blood centrifugation or other separating techniques leaves behind the aqueous (91 percent water by weight, 94.8 percent water by volume), saline (0.15N) suspending medium called *plasma*—which has an average mass density of $1.035 \pm 0.005 \text{ g/cm}^3$ and a viscosity $1\frac{1}{2}$ to 2 times that of water. Some 6.5 to 8 percent by weight of plasma consists of the plasma proteins, of which there are three major types—albumin, the globulins, and fibrinogen—and several of lesser prominence.

The primary functions of albumin are to help maintain the osmotic (oncotic) transmembrane pressure differential that ensures proper mass exchange between blood and interstitial fluid at the capillary level and to serve as a transport carrier molecule for several hormones and other small biochemical constituents (such as some metal ions). The primary function of the globulin class of proteins is to act as transport carrier molecules (mostly of the α and β) for large biochemical substances, such as fats (lipoproteins) and certain carbohydrates (mucopolysaccharides and glycoproteins) and heavy metals (mineraloproteins), and to work together with leukocytes in the body’s immune system. The latter function is primarily the responsibility

of the γ class of immunoglobulins, which have antibody activity. The primary function of fibrinogen is to work with thrombocytes in the formation of a blood clot—a process also aided by one of the most abundant of the lesser proteins, prothrombin.

Of the remaining 2 percent or so (by weight) of plasma, just under half consists of minerals (inorganic ash), trace elements, and electrolytes, mostly the cations sodium, potassium, calcium, and magnesium and the anions chlorine, bicarbonate, phosphate, and sulfate—the latter three helping as buffers to maintain the fluid at a slightly alkaline pH between 7.35 and 7.45 (average 7.4). What is left, about 1,087 mg materials per deciliter of plasma, includes (1) mainly three major types of fat—cholesterol (in a free and esterified form), phospholipids (a major ingredient of cell membranes), and triglyceride—with lesser amounts of the fat-soluble vitamins (A, D, E, and K), free fatty acids, and other lipids, and (2) “extractives” (0.25 percent by weight), of which about two-thirds include glucose and other forms of carbohydrate, the remainder consisting of the water-soluble vitamins (B-complex and C), certain enzymes, nonnitrogenous and nitrogenous waste products of metabolism (including urea, creatine, and creatinine), and many smaller amounts of other biochemical constituents—the list seeming virtuously endless. It is easy to understand why blood is often referred to as the “river of life.” This river is made to flow through the vascular piping network by two central pumping stations arranged in series: the left and right sides of the human heart.

The heart (Figure 3.18), the pumping station that moves blood through the blood vessels, consists of two pumps: the right side and the left side. Each side has one chamber (the atrium) that receives blood and another chamber (the ventricle) that pumps the blood away from the heart. The right side moves deoxygenated blood that is loaded with carbon dioxide from the body to the lungs, and the left side receives oxygenated blood that has had most of its carbon dioxide removed from the lungs and pumps it to the body. The vessels that lead to and from the lungs make up the pulmonary circulation, and those that lead to and from the rest of the tissues in the body make up the systemic circulation (Figure 3.19).

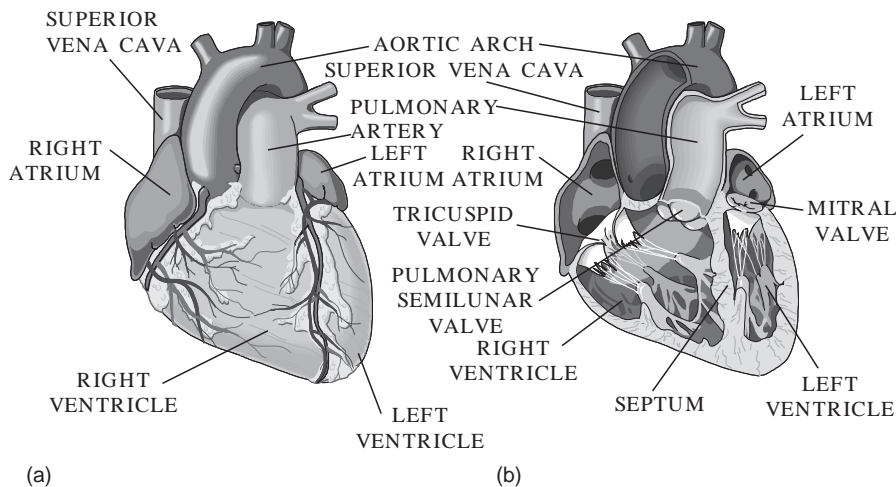


FIGURE 3.18 (a) The outside of the heart as seen from its anterior side. (b) The same view after the exterior surface of the heart has been removed. The four interior chambers—right and left atria and right and left ventricles—as well as several valves are visible.

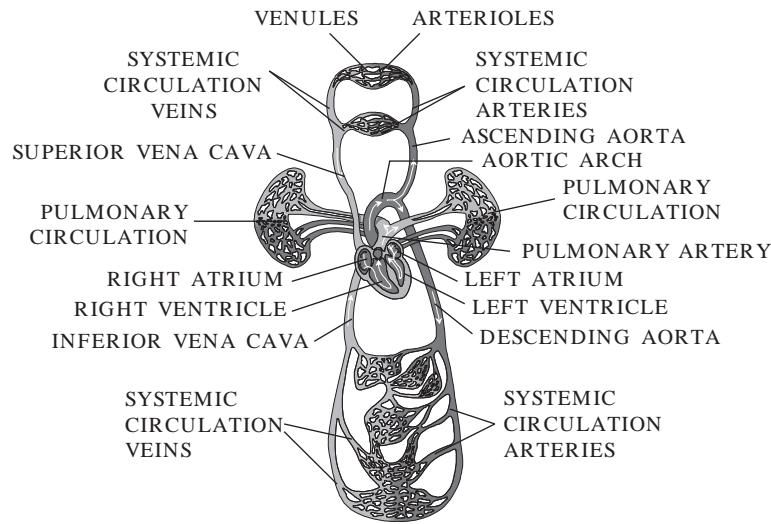


FIGURE 3.19 Oxygenated blood leaves the heart through the aorta. Some of the blood is sent to the head and upper extremities and torso, whereas the remainder goes to the lower torso and extremities. The blood leaves the aorta and moves into other arteries, then into smaller arterioles, and finally into capillary beds, where nutrients, hormones, gases, and waste products are exchanged between the nearby cells and the blood. The blood moves from the capillary beds into venules and then into veins. Blood from the upper part of the body returns to the right atrium of the heart through the superior vena cava, whereas blood from the lower part of the body returns through the inferior vena cava. The blood then moves from the right atrium to the right ventricle and into the pulmonary system through the pulmonary artery. After passing through capillaries in the lungs, the oxygenated blood returns to the left atrium of the heart through the pulmonary vein. It moves from the left atrium to the left ventricle and then out to the systemic circulation through the aorta to begin the same trip over again.

Blood vessels that carry blood away from the heart are called arteries, while those that carry blood toward the heart are called veins. The pulmonary artery is the only artery that carries deoxygenated blood, and the pulmonary vein is the only vein that carries oxygenated blood. The average adult has about 5 L of blood with 80 to 90 percent in the systemic circulation at any one time; 75 percent of the blood is in the systemic circulation in the veins, 20 percent is in the arteries, and 5 percent is in the capillaries.

Because of the anatomic proximity of the heart to the lungs, the right side of the heart does not have to work very hard to drive blood through the pulmonary circulation, so it functions as a low-pressure ($P \leq 40$ mmHg gauge) pump compared with the left side of the heart, which does most of its work at a high pressure (up to 140 mmHg gauge or more) to drive blood through the entire systemic circulation to the furthest extremes of the organism.

In order of size, the somewhat spherically shaped left atrium is the smallest chamber—holding about 45 ml of blood (at rest). The pouch-shaped right atrium is next (63 ml of blood), followed by the conical/cylindrically shaped left ventricle (100 ml of blood) and the crescent-shaped right ventricle (about 130 ml of blood). Altogether, then, the heart chambers collectively have a capacity of some 325 to 350 ml, or about 6.5 percent of the total blood volume in a “typical” individual—but these values are nominal, since the organ alternately fills and expands, contracts, and then empties.

During the 480-ms or so filling phase—diastole—of the average 750-ms cardiac cycle, the inlet valves of the two ventricles (3.8-cm-diameter tricuspid valve from right atrium to right ventricle; 3.1-cm-diameter bicuspid or mitral valve from left atrium to left ventricle) are open, and the outlet valves (2.4-cm-diameter pulmonary valve and 2.25-cm-diameter aortic semilunar valve, respectively) are closed—the heart ultimately expanding to its end-diastolic-volume (EDV), which is on the order of 140 ml of blood for the left ventricle. During the 270-ms emptying phase—systole—electrically induced vigorous contraction of cardiac muscle drives the intraventricular pressure up, forcing the one-way inlet valves closed and the unidirectional outlet valves open as the heart contracts to its end-systolic-volume (ESV), which is typically on the order to 70 ml of blood for the left ventricle. Thus, the ventricles normally empty about half their contained volume with each heartbeat, the remainder being termed the *cardiac reserve volume*. More generally, the difference between the actual EDV and the actual ESV, called the *stroke volume* (SV), is the volume of blood expelled from the heart during each systolic interval, and the ratio of SV to EDV is called the *cardiac ejection fraction*, or *ejection ratio* (0.5 to 0.75 is normal, 0.4 to 0.5 signifies mild cardiac damage, 0.25 to 0.40 implies moderate heart damage, and less than 0.25 warns of severe damage to the heart's pumping ability). If the stroke volume is multiplied by the number of systolic intervals per minute, or heart rate (HR), one obtains the total cardiac output (CO):

$$\text{CO} = \text{HR} \times (\text{EDV} - \text{ESV})$$

where EDV-ESV is the stroke volume.

Several investigations have suggested that the cardiac output (in milliliters per minute) is proportional to the weight W (in kilograms) of an individual according to the equation

$$\text{CO} = 224W^{3/4}$$

and that “normal” heart rate obeys very closely the relation

$$\text{HR} = 229W^{-1/4}$$

For a “typical” 68.7-kg individual (blood volume = 5,200 ml), these equations yield $\text{CO} = 5,345$ ml/min, $\text{HR} = 80$ beats/min (cardiac cycle period = 754 ms) and $\text{SV} = \text{CO}/\text{HR} = 229W^{-1/4}/\text{CO} = 224W^{3/4}/\text{CO} = 0.978W = 67.2$ ml/beat, which are very reasonable values. Furthermore, assuming this individual lives to be about 75 years old, his or her heart will have cycled over 3.1536 billion times, pumping a total of 0.2107 billion liters of blood (55.665 million gallons, or 8,134 quarts per day) within their lifetime.

In the normal heart, the cardiac cycle, which refers to the repeating pattern of contraction (systole) and relaxation (diastole) of the chambers of the heart, begins with a self-generating electrical pulse in the pacemaker cells of the sinoatrial node (Figure 3.20). This rapid electrical change in the cells is the result of the movement of ions across their plasma membranes. The permeability of the plasma membrane to Na^+ changes dramatically and allows these ions to rush into the cell. This change in the electrical potential across the plasma membrane from one in which the interior of the cell is more negative than the extracellular fluid (approximately -90 mV) to one in which the interior of the cell is more positive than the extracellular fluid (approximately 20 mV) is called depolarization. After a very short period of time (<0.3 s), changes in the membrane and activation of the sodium-potassium pumps result in repolarization, the restoration of the original ionic balance in the cells. The entire electrical event in which the polarity of the potential across the plasma membrane rapidly

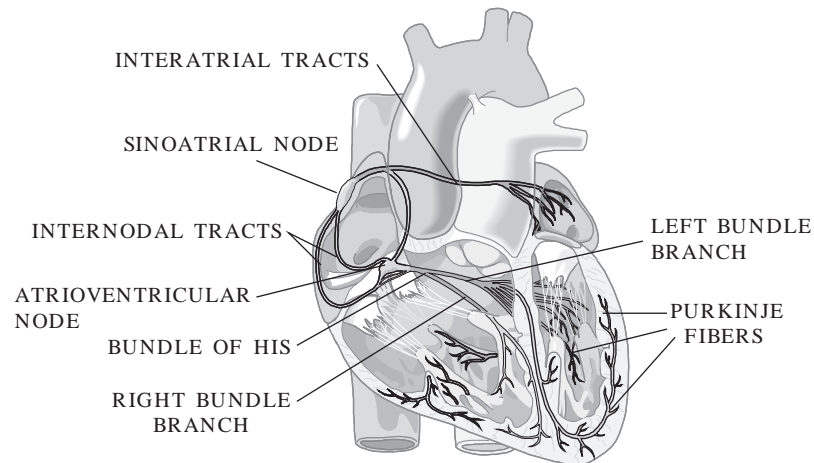


FIGURE 3.20 Pacemaker cells in the sinoatrial node (SA node) depolarize first and send an activation wavefront through the atria. The propagating action potential slows down as it passes through the atrioventricular node (AV node), then moves through the bundle of His and Purkinje system very rapidly until it reaches the cells of the ventricles.

reverses and then becomes reestablished is called an action potential. The cells in the sinoatrial node depolarize on the average of every 0.83 s in a typical adult at rest. This gives a resting heart rate of 72 beats per minute, with about $\frac{5}{8}$ of each beat spent in diastole and $\frac{3}{8}$ in systole.

Cardiac cells are linked and tightly coupled so action potentials spread from one cell to the next. Activation wavefronts move across the atria at a rate of about 1 m/s. When cardiac cells depolarize, they also contract. The contraction process in the atria (atrial systole) moves blood from the right atrium to the right ventricle and from the left atrium to the left ventricle (Figure 3.21). The activation wavefront then moves to the atrioventricular

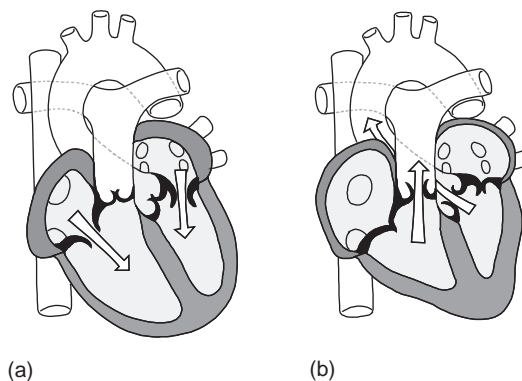


FIGURE 3.21 (a) During the first part of the cardiac cycle, the atria contract (atrial systole) and move blood into the ventricles. (b) During the second part of the cardiac cycle, the atria relax (diastole), and the ventricles contract (ventricular systole) and move blood to the lungs (pulmonary circulation) and to the rest of the body (systemic circulation).

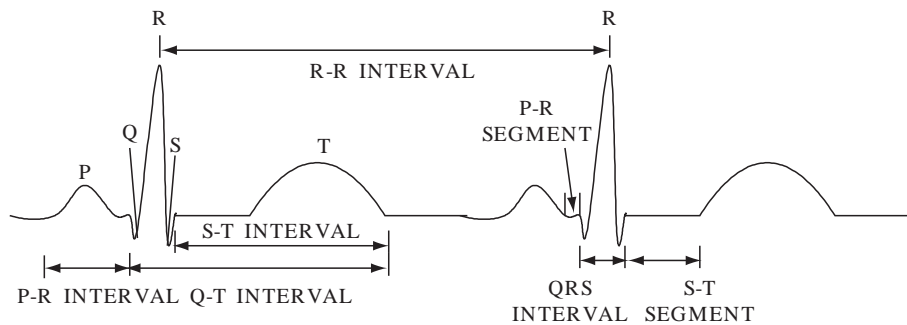


FIGURE 3.22 Typical lead II ECG. This electrocardiogram is typical of one that would be recorded from the body's surface by having a positive electrode on the left leg and a negative electrode on the right arm. The vertical direction represents voltage, and the horizontal direction represents time. The P, R, and T waves are easily identified and are the result of the movement of ions in cells in different parts of the heart. Different intervals and segments have been identified that provide information about the health of the heart and its conduction system. The R-R interval can be used to determine heart rate.

(AV) node, where it slows to a rate of about 0.05 m/s to allow time for the ventricles to completely fill with the blood from the atria. After leaving the AV node, the activation wavefront moves to specialized conduction tissue, the Purkinje system, which spreads the wavefront very rapidly (at about 3 m/s) to many cells in both ventricles. The activation wavefront spreads through ventricular tissue at about 0.5 m/s. This results in the simultaneous contraction of both ventricles (ventricular systole) so blood is forced from the heart into the pulmonary artery from the right ventricle and into the aorta from the left ventricle.

The electrocardiogram (ECG; Figure 3.22) is an electrical measure of the sum of these ionic changes within the heart. The P wave represents the depolarization of the atria, while the QRS represents the depolarization of the ventricles. Ventricular repolarization shows up as the T wave, while atrial repolarization is masked by ventricular depolarization. Changes in the amplitude and duration of the different parts of the ECG provide diagnostic information for physicians. Many biomedical engineers have worked on methods for recording and analyzing ECGs.

EXAMPLE PROBLEM 3.6

What would be the heart rate given by an ECG in which 10 R-waves occurred in 6.4 s?

Solution

A sequence of 10 R-waves represents 9 R-R intervals (see Figure 3.22) or beats of the heart.

$$\left(\frac{9 \text{ beats}}{6.4 \text{ s}}\right) \left(\frac{60 \text{ s}}{1 \text{ min}}\right) = 84 \text{ bpm}$$

EXAMPLE PROBLEM 3.7

What would be the cardiac output of the heart in Example Problem 3.6 if the stroke volume is 75 ml?

Solution

The cardiac output (given in liters per minute) is the product of the heart rate and the stroke volume.

$$CO = 84 \frac{\text{beats}}{\text{min}} \times 75 \frac{\text{ml}}{\text{beat}} = 6300 \frac{\text{ml}}{\text{min}} = 6.3 \frac{\text{liters}}{\text{min}}$$

During atrial and ventricular systole, special one-way valves (Figure 3.23a) keep the blood moving in the correct direction. When the atria contract, the atrioventricular valves (tricuspid and mitral) open to allow blood to pass into the ventricles. During ventricular systole, the semilunar valves (aortic and pulmonary) open to allow blood to leave the heart, while the atrioventricular valves close and prevent blood from flowing backward from the ventricles to the atria. The aortic and pulmonary valves prevent blood from flowing back from the pulmonary artery and aorta into the right and left ventricles, respectively. If a valve becomes calcified or diseased or is not properly formed during embryonic development, it can be replaced by an artificial valve (Figure 3.23b), a device that has been developed by cooperative work between biomedical engineers and physicians.

Blood pressure can be measured directly or indirectly (noninvasively). Direct blood pressure measurements are made by introducing a catheter or needle that is coupled to a pressure transducer into a vein or artery. Indirect methods include sphygmomanometry,

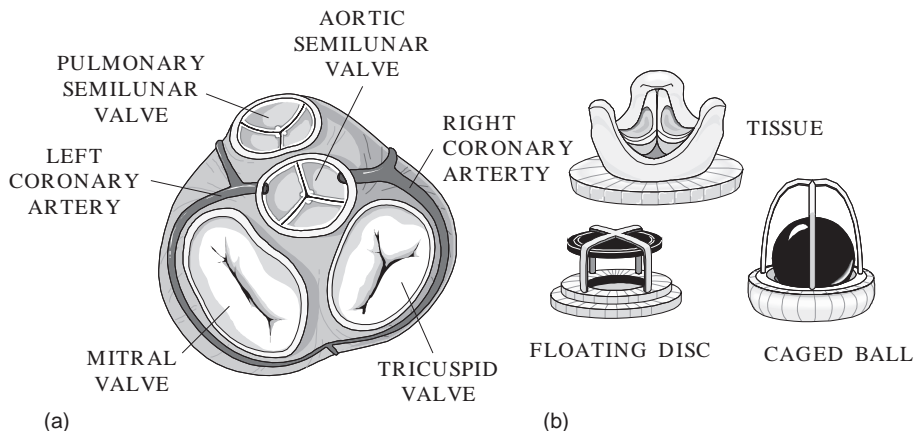


FIGURE 3.23 (a) The atrioventricular (tricuspid and mitral) and semilunar (pulmonary and aortic) valves. (b) Three types of artificial valves—tissue, floating disc, and caged ball—that can be used to replace diseased or malformed human valves.

in which a cuff is used to apply sufficient pressure to an artery, usually in the arm, to prevent the flow of blood through the artery, and a stethoscope is used to listen to the change in sounds as the cuff is slowly deflated. The first Korotkoff sounds occur when the systolic pressure, the highest pressure reached when the ventricles contract and eject blood, first exceeds the pressure in the cuff so blood once again flows through the artery beneath the stethoscope. The Korotkoff sounds become muffled and disappear when the pressure in the cuff drops below the diastolic pressure, the minimum pressure that occurs at the end of ventricular relaxation. Another indirect measurement is the oscillometric method, which uses a microprocessor to periodically inflate and slowly deflate a cuff. When blood breaks through the occlusion caused by the cuff, the walls of the artery begin to vibrate slightly due to the turbulent nature of the blood flow. The onset of these oscillations in pressure correlates with the systolic pressure. The oscillations decrease in amplitude over time with the diastolic pressure event corresponding to the point at which the rate of amplitude decrease suddenly changes slope. A third indirect measurement, the ultrasonic method, depends on the Doppler shift of sound waves that hit red blood cells that are flowing with the blood.

Blood in the systemic circulation leaves the heart through the aorta with an average internal pressure of about 100 mmHg (maximum systolic pressure of about 120 mm Hg, with a diastolic pressure of about 80 mm Hg in a normal adult) and moves to medium-sized arteries (see Figure 3.17a) and arterioles. Arterioles lead to capillaries (average internal pressure of about 30 mm Hg), which are followed by venules. Venules lead to medium-sized veins, then to large veins, and finally to the venae cavae (average internal pressure of about 10 mm Hg), which return blood to the heart at the right atrium. Blood in the pulmonary circulation (see Figure 3.19) leaves the pulmonary artery and moves to arterioles and then the capillary beds within the lungs. It returns to the heart through the left atrium. Blood flow is highest in the large arteries and veins (30–40 cm/s in the aorta; 5 cm/s in the vena cavae) and slowest in the capillary beds (1 mm/s), where the exchange of nutrients, metabolic wastes, gases, and hormones takes place. Pressures in the pulmonary circulation are lower (25 mm Hg/10 mm Hg) than in the systemic circulation due to the decreased pumping power of the smaller right ventricle as compared to the left and to the lower resistance of blood vessels in the lungs.

EXAMPLE PROBLEM 3.8

What would be the pulse pressure and the mean arterial pressure for a person with a blood pressure reading of 118 mmHg/79 mmHg?

Solution

The pulse pressure is defined as the difference between the systolic (118 mmHg) and diastolic (79 mmHg) pressures, which would be 39 mmHg in this case.

Mean arterial pressure is the average blood pressure in the arteries and is estimated as the diastolic pressure plus one-third of the pulse pressure, which would be 92 mmHg in this example.

3.4.2 Respiratory System

The respiratory system (Figure 3.24a) moves air to and from the gas exchange surfaces in the body where diffusion can occur between air and the circulating blood. It includes the conduction zone and the respiratory zone. In the conduction zone (mouth, nose, sinuses, pharynx, trachea, bronchi, and bronchioles), the air that enters the body is warmed, humidified, filtered, and cleaned. Mucus is secreted by cells in the conduction zone and traps small particles ($>6\ \mu\text{m}$) before they can reach the respiratory zone. Epithelial cells that line the trachea and bronchi have cilia that beat in a coordinated fashion to move mucus toward the pharynx, where it can be swallowed or expectorated. The respiratory zone, consisting of respiratory bronchioles with outpouchings of alveoli and terminal clusters of alveolar sacs, is where gas exchange between air and blood occurs (Figure 3.24b). The respiratory zone comprises most of the mass of the lungs.

Conduction of air begins at the larynx, or voice box, at the entrance to the trachea, which is a fibromuscular tube 10 to 12 cm in length and 1.4 to 2.0 cm in diameter. At a location called the *carina*, the trachea terminates and divides in the left and right bronchi. Each bronchus has a discontinuous cartilaginous support in its wall. Muscle fibers capable of controlling airway diameter are incorporated into the walls of the bronchi, as well as in those of air passages closer to the alveoli. Smooth muscle is present throughout the respiratory bronchiolus and alveolar ducts but is absent in the last alveolar duct, which terminates in one to several alveoli. The alveolar walls are shared by other alveoli and are composed of highly pliable and collapsible squamous epithelium cells. The bronchi subdivide into subbronchi, which further subdivide into bronchioli, which further subdivide, and so on, until finally reaching the alveolar level.

Movement of gases in the respiratory airways occurs mainly by bulk flow (convection) throughout the region from the mouth to the nose to the fifteenth generation. Beyond the

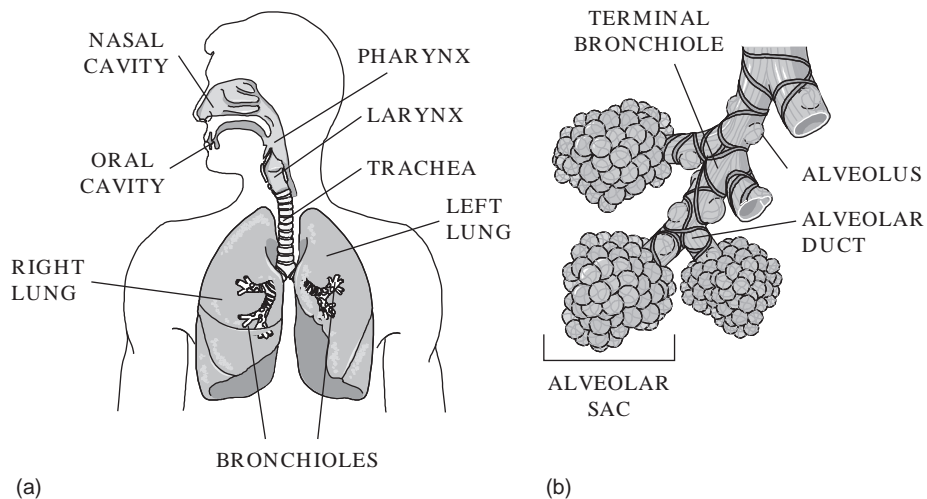


FIGURE 3.24 (a) The respiratory system consists of the passageways that are used to move air into and out of the body and the lungs. (b) The terminal bronchioles and alveolar sacs within the lungs have alveoli where gas exchange occurs between the lungs and the blood in the surrounding capillaries.

fifteenth generation, gas diffusion is relatively more important. With the low gas velocities that occur in diffusion, dimensions of the space over which diffusion occurs (alveolar space) must be small for adequate oxygen delivery into the walls; smaller alveoli are more efficient in transfer of gas than are larger ones. Thus, animals with high levels of oxygen consumption are found to have smaller-diameter alveoli compared with animals with low levels of oxygen consumption.

Alveoli are the structures through which gases diffuse to and from the body. To ensure that gas exchange occurs efficiently, alveolar walls are extremely thin. For example, the total tissue thickness between the inside of the alveolus to pulmonary capillary blood plasma is only about 0.4×10^{-6} m. Consequently, the principal barrier to diffusion occurs at the plasma and red blood cell level, not at the alveolar membrane.

Molecular diffusion within the alveolar volume is responsible for mixing of the enclosed gas. Due to small alveolar dimensions, complete mixing probably occurs in less than 10 ms, fast enough that alveolar mixing time does not limit gaseous diffusion to or from the blood.

Of particular importance to proper alveolar operation is a thin surface coating of surfactant. Without this material, large alveoli would tend to enlarge and small alveoli would collapse. It is the present view that surfactant acts like a detergent, changing the stress-strain relationship of the alveolar wall and thereby stabilizing the lung.

Certain physical properties, such as compliance, elasticity, and surface tension, are characteristic of lungs. Compliance refers to the ease with which lungs can expand under pressure. A normal lung is about 100 times more distensible than a toy balloon. Elasticity refers to the ease with which the lungs and other thoracic structures return to their initial sizes after being distended. This aids in pushing air out of the lungs during expiration. Surface tension is exerted by the thin film of fluid in the alveoli and acts to resist distention. It creates a force that is directed inward and creates pressure in the alveolus, which is directly proportional to the surface tension and inversely proportional to the radius of the alveolus (Law of Laplace). Thus, the pressure inside an alveolus with a small radius would be higher than the pressure inside an adjacent alveolus with a larger radius and would result in air flowing from the smaller alveolus into the larger one. This could cause the smaller alveolus to collapse. This does not happen in normal lungs because the fluid inside the alveoli contains a phospholipid that acts as a surfactant. The surfactant lowers the surface tension in the alveoli and allows them to get smaller during expiration without collapsing. Premature babies often suffer from respiratory distress syndrome because their lungs lack sufficient surfactant to prevent their alveoli from collapsing. These babies can be kept alive with mechanical ventilators or surfactant sprays until their lungs mature enough to produce surfactant.

Breathing, or ventilation, is the mechanical process by which air is moved into (inspiration) and out of (expiration) the lungs. A normal adult takes about 15 to 20 breaths per minute. During inspiration, the inspiratory muscles contract and enlarge the thoracic cavity, the portion of the body where the lungs are located. This causes the alveoli to enlarge and the alveolar gas to expand. As the alveolar gas expands, the partial pressure within the respiratory system drops below atmospheric pressure by about 3 mmHg so air easily flows in (Boyle's Law). During expiration, the inspiratory muscles relax and return the thoracic cavity to its original volume. Since the volume of the gas inside the respiratory system

has decreased, its pressure increases to a value that is about 3 mmHg above atmospheric pressure. Air now moves out of the lungs and into the atmosphere.

The primary purpose of the respiratory system is gas exchange. In the gas-exchange process, gas must diffuse through the alveolar space, across tissue, and through plasma into the red blood cell, where it finally chemically joins to hemoglobin. A similar process occurs for carbon dioxide elimination.

As long as intermolecular interactions are small, most gases of physiologic significance can be considered to obey the ideal gas law:

$$pV = nRT$$

where

p = pressure, N/m²

V = volume of gas, m³

n = number of moles, mol

R = gas constant, (N × m)/(mol × K)

T = absolute temperature, K

The ideal gas law can be applied without error up to atmospheric pressure; it can be applied to a mixture of gases, such as air, or to its constituents, such as oxygen or nitrogen. All individual gases in a mixture are considered to fill the total volume and have the same temperature but reduced pressures. The pressure exerted by each individual gas is called the *partial pressure* of the gas.

Dalton's law states that the total pressure is the sum of the partial pressures of the constituents of a mixture:

$$P = \sum_{i=1}^N p_i$$

where

p_i = partial pressure of the i th constituent, N/m²

N = total number of constituents

Dividing the ideal gas law for a constituent by that for the mixture gives

$$\frac{P_i V}{P V} = \frac{n_i R_i T}{n R T}$$

so that

$$\frac{p_i}{p} = \frac{n_i R_i}{n R}$$

which states that the partial pressure of a gas may be found if the total pressure, mole fraction, and ratio of gas constants are known. For most respiratory calculations, p will be considered to be the pressure of 1 atmosphere, 101 kN/m². Avogadro's principle states that different gases at the same temperature and pressure contain equal numbers of molecules:

$$\frac{V_1}{V_2} = \frac{n R_1}{n R_2} = \frac{R_1}{R_2}$$

Thus,

$$\frac{p_i}{p} = \frac{V_i}{V}$$

where V_i/V is the volume fraction of a constituent in air and is therefore dimensionless. Table 3.2 provides individual gas constants, as well as volume fractions of constituent gases of air.

Lung mechanics refers to the study of the mechanical properties of the lung and chest wall, whereas lung statics refers to the mechanical properties of a lung in which the volume is held constant over time. Understanding lung mechanics requires knowledge about the volumes within the lungs. Lung capacities contain two or more volumes. The tidal volume (TV) is the amount of air that moves in and out of the lungs during normal breathing (Figure 3.25). The total lung capacity (TLC) is the amount of gas contained within the lungs at the end of a maximum inspiration. The vital capacity (VC) is the maximum amount of air that can be exhaled from the lungs after inspiration to TLC. The residual volume (RV) is the amount of gas remaining in the lungs after maximum exhalation. The amount of gas that can be inhaled after inhaling during tidal breathing is called the inspiratory reserve volume (IRV). The amount of gas that can be expelled by a maximal exhalation after exhaling during tidal breathing is called the expiratory reserve volume (ERV). The inspiratory capacity (IC) is the maximum amount of gas that can be inspired after a normal exhalation during tidal breathing, and the functional residual capacity (FRC) is the amount of gas that remains in the lungs at this time (Table 3.3).

All of the volumes and capacities except those that include the residual volume can be measured with a spirometer. The classic spirometer is an air-filled container that is constructed from two drums of different sizes. One drum contains water, and the other air-filled drum is inverted over an air-filled tube and floats in the water. The tube is connected to a mouthpiece used by the patient. When the patient inhales, the level of the

TABLE 3.2 Molecular Masses, Gas Constants, and Volume Fractions for Air and Constituents

Constituent	Molecular Mass kg/mol	Gas Constant N m/(mol K)	Volume Fraction in Air m ³ /m ³
Air	29.0	286.7	1.0000
Ammonia	17.0	489.1	0.0000
Argon	39.9	208.4	0.0093
Carbon Dioxide	44.0	189.0	0.0003
Carbon Monoxide	28.0	296.9	0.0000
Helium	4.0	2,078.6	0.0000
Hydrogen	2.0	4,157.2	0.0000
Nitrogen	28.0	296.9	0.7808
Oxygen	32.0	259.8	0.2095

Note: Universal gas constant is 8314.43 N m/kg K.

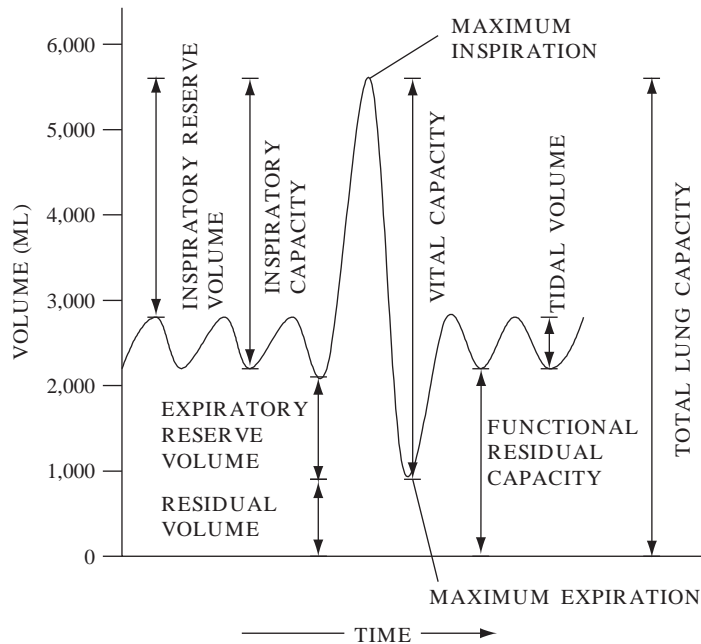


FIGURE 3.25 Lung volumes and capacities, except for residual volume, functional residual capacity, and total lung capacity, can be measured using spirometry.

floating drum drops. When the patient exhales, the level of the floating drum rises. These changes in floating drum position can be recorded and used to measure lung volumes.

EXAMPLE PROBLEM 3.9

The total lung capacity of a patient is 5.9 liters. If the patient's inspiratory capacity was found to be 3.3 liters using spirometry, what would be the patient's functional residual capacity? What would you need to measure in order to determine the patient's residual volume?

Solution

From Figure 3.25, total lung capacity (TLC) is equal to the sum of inspiratory capacity (IC) and functional residual capacity (FRC).

$$TLC = IC + FRC$$

$$5.9\text{ l} = 3.3\text{ l} + FRC$$

$$FRC = 2.6\text{ l}$$

TLC, which cannot be determined by means of spirometry, and vital capacity (VC), which can be measured using spirometry, must be known in order to determine residual volume (RV), since

$$TLC - VC = RV$$

TABLE 3.3 Typical Lung Volumes for a Normal, Healthy Male

Lung Volume	Normal Values	
Total lung capacity (TLC)	$6.0 \times 10^{-3} \text{m}^3$	(6,000 cm ³)
Residual volume (RV)	$1.2 \times 10^{-3} \text{m}^3$	(1,200 cm ³)
Vital capacity (VC)	$4.8 \times 10^{-3} \text{m}^3$	(4,800 cm ³)
Inspiratory reserve volume (IRV)	$3.6 \times 10^{-3} \text{m}^3$	(3,600 cm ³)
Expiratory reserve volume (ERV)	$1.2 \times 10^{-3} \text{m}^3$	(1,200 cm ³)
Functional residual capacity (FRC)	$2.4 \times 10^{-3} \text{m}^3$	(2,400 cm ³)
Anatomic dead volume (V_D)	$1.5 \times 10^{-4} \text{m}^3$	(150 cm ³)
Upper airways volume	$8.0 \times 10^{-5} \text{m}^3$	(80 cm ³)
Lower airways volume	$7.0 \times 10^{-5} \text{m}^3$	(70 cm ³)
Physiologic dead volume (V_D)	$1.8 \times 10^{-4} \text{m}^3$	(180 cm ³)
Minute volume (V_e) at rest	$1.0 \times 10^{-4} \text{m}^3/\text{s}$	(6,000 cm ³ /m)
Respiratory period (T) at rest	4s	
Tidal volume (V_T) at rest	$4.0 \times 10^{-4} \text{m}^3$	(400 cm ³)
Alveolar ventilation volume (V_A) at rest	$2.5 \times 10^{-4} \text{m}^3$	(250 cm ³)
Minute volume during heavy exercise	$1.7 \times 10^{-3} \text{m}^3/\text{s}$	(10,000 m ³ /m)
Respiratory period during heavy exercise	1.2s	
Tidal volume during heavy exercise	$2.0 \times 10^{-3} \text{m}^3$	(2,000 cm ³)
Alveolar ventilation during heavy exercise	$1.8 \times 10^{-3} \text{m}^3$	(1,820 cm ³)

Since spirometers record changes in volume over time, flow rates can be determined for different maneuvers. For example, if a patient exhales as forcefully as possible to residual volume following inspiration to TLC, then the forced expiratory volume (FEV_{1.0}) is the total volume exhaled at the end of 1 s. The FEV_{1.0} is normally about 80 percent of the vital capacity. Restrictive diseases, in which inspiration is limited by reduced compliance of the lung or chest wall or by weakness of the inspiratory muscles, result in reduced values for FEV_{1.0} and vital capacity, but their ratio remains about the same. In obstructive diseases, such as asthma, the FEV_{1.0} is reduced much more than the vital capacity. In these diseases, the TLC is abnormally large, but expiration ends prematurely. Another useful measurement is the forced expiratory flow rate (FEF₂₅₋₇₅ percent), which is the average flow rate measured over the middle half of the expiration—that is, from 25 to 75 percent of the vital capacity. Flow-volume loops provide another method for analyzing lung function by relating the rate of inspiration and expiration to the volume of air that is moved during each process.

The TLC can be measured using the gas dilution technique. In this method, patients inspire to TLC from a gas mixture containing a known amount of an inert tracer gas, such as helium, and hold their breath for 10 s. During this time, the inert gas becomes evenly distributed throughout the lungs and airways. Due to conservation of mass, the product of initial tracer gas concentration (which is known) times the amount inhaled (which is measured) equals the product of final tracer gas concentration (which is measured during expiration) times the TLC. Body plethysmography, which provides the most accurate method for measuring lung volumes, uses an airtight chamber in which the patient sits and breathes through a mouthpiece. This method uses Boyle's Law, which states that the product of pressure and volume for gas in a chamber is constant under isothermal conditions. Changes in lung volume and pressure at the mouth when the patient pants against a closed shutter can be used to calculate the functional residual capacity. Since the expiratory reserve volume can be measured, the residual volume can be calculated by subtracting it from the functional residual capacity.

EXAMPLE PROBLEM 3.10

A patient is allowed to breathe a mixture from a 2-liter reservoir that contains 10 percent of an inert gas—that is, a gas that will not cross from the lungs into the circulatory system. At the end of a period that is sufficient for the contents of the reservoir and the lungs to equilibrate, the concentration of the inert gas is measured and is found to be 2.7 percent. What is the patient's total lung capacity?

Solution

The total amount of inert gas is the same at the beginning and end of the measurement, but its concentration has changed from 10 percent (C_1) to 2.7 percent (C_2). At the beginning, it is confined to a 2-liter reservoir (V_1). At the end, it is in both the reservoir and the patient's lungs ($V_2 = V_1 + TLC$).

$$\begin{aligned} C_1 V_1 &= C_2 V_2 \\ (0.1)(2\text{ l}) &= (0.027)(2\text{ l} + TLC) \\ 0.2\text{ l} - 0.054\text{ l} &= 0.027\text{ TLC} \\ 5.4\text{ l} &= TLC \end{aligned}$$

External respiration occurs in the lungs when gases are exchanged between the blood and the alveoli (Figure 3.26). Each adult lung contains about 3.5×10^8 alveoli, which results in a large surface area (60–70 m²) for gas exchange to occur. Each alveolus is only one cell layer thick, so the air-blood barrier is only two cells thick (an alveolar cell and a capillary endothelial cell), which is about 2 μm. The partial pressure of oxygen in the alveoli is higher than the partial pressure of oxygen in the blood, so oxygen moves from the alveoli into the blood. The partial pressure of carbon dioxide in the alveoli is lower than the partial pressure of carbon dioxide in the blood, so carbon dioxide moves from the blood into the alveoli. During internal respiration, carbon dioxide and oxygen move between the blood and the extracellular fluid surrounding the body's cells. The direction and rate of

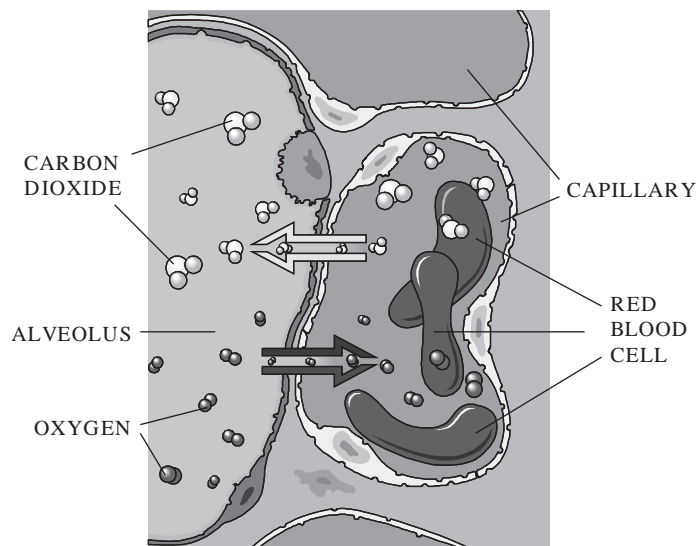


FIGURE 3.26 During external respiration, oxygen moves from the alveoli to the blood, and carbon dioxide moves from the blood to the air within the alveoli.

movement of a gas depends on the partial pressures of the gas in the blood and the extracellular fluid, the surface area available for diffusion, the thickness of the membrane that the gas must pass through, and a diffusion constant that is related to the solubility and molecular weight of the gas (Fick's Law).

Mechanical ventilators can be used to deliver air or oxygen to a patient. They can be electrically or pneumatically powered and can be controlled by microprocessors. Negative pressure ventilators, such as iron lungs, surround the thoracic cavity and force air into the lungs by creating a negative pressure around the chest. This type of ventilator greatly limits access to the patient. Positive pressure ventilators apply high-pressure gas at the entrance to the patient's lungs so air or oxygen flows down a pressure gradient and into the patient. These ventilators can be operated in control mode to breathe for the patient at all times or in assist mode to help with ventilation when the patient initiates the breathing cycle. This type of ventilation changes the pressure within the thoracic cavity to positive during inspiration, which affects venous return to the heart and cardiac output (the amount of blood the heart moves with each beat). High-frequency jet ventilators deliver very rapid (60–90 breaths per minute) low-volume bursts of air to the lungs. Oxygen and carbon dioxide are exchanged by molecular diffusion rather than by the mass movement of air. This method causes less interference with cardiac output than does positive pressure ventilation. Extracorporeal membrane oxygenation (ECMO) uses the technology that was developed for cardiopulmonary bypass machines. Blood is removed from the patient and passed through an artificial lung, where oxygen and carbon dioxide are exchanged. It is warmed to body temperature before being returned to the patient. This technique allows the patient's lungs to rest and heal themselves and has been used successfully on some cold water drowning victims and on infants with reversible pulmonary disease.

3.4.3 The Nervous System

The most exciting and mysterious part of the human body is the magical 3½ pounds of tissue we carry around inside our skulls: the brain. For centuries, the brain has frustrated those daring enough to explore its secrets. Encased not only in its bony protective covering but also in a shroud of mysticism, it has been an extremely difficult structure to study. Even with the invention of the microscope and the discovery of electricity, generations of Western scientists refrained from investigating the activity of the human brain out of respect for it as the seat of a human's immortal soul.

In recent years, this convoluted mass, the source of all thought and emotion, has been the focal point of intense scientific investigation. There has been a great flurry of activity in assembling interdisciplinary teams consisting of physiologists, psychologists, biochemists, and engineers in order to gain a better understanding of brain function. To many of these individuals, the brain represents a symbolic Mt. Everest, an obstacle to be scaled and conquered before it will be better understood. And yet, in spite of all the efforts to date, we are still only in the foothills of such a climb. The mechanisms and processes that enable the brain to convert the variety of electrical and chemical activity occurring within it into thoughts, feeling, dreams, and memories—the fundamental awareness of self—are still beyond our understanding.

However, in spite of the difficulties encountered and the frustrations experienced by explorers in this world of the mind, significant progress has been made in deciphering the cryptic flow of electrical energy coming from the brain. In reviewing these electrical signals, it has been possible to detect the presence of certain patterns or rhythms that occur in the brain that represent a "language" that can be recognized and understood by neural circuits in the brain itself. The fundamental building block of this neuronal communication network is the individual nerve cell: the neuron. Figure 3.16d is a schematic drawing of just such a cell. It consists of three major components: the cell body itself, or *soma*; the receptor zone, or *dendrites*; and a long fiber called the *axon*, which carries electrical signals from the main body of the cell to the muscles, glands, or other neurons. Numbering approximately 20 billion in each human being, these tiny cells come in a variety of sizes and shapes. However, nowhere is more variety displayed than in the length of the axonal terminating fiber. In the human body, it ranges from a few thousandths of an inch up to three feet or more, depending on the type of neuron involved. Consider, for example, the long pathways from the extremities to the brain. In these communication channels between the periphery and the "central data processor" that we call the brain, only a few neurons may be connected to one another. As a result, the axon of these nerve cells may be as long as 2 or 3 feet, even though the cell body is quite small. Some axons are surrounded by sheaths of myelin that are formed by specialized nonneural cells called Schwann cells. Gaps, called "Nodes of Ranvier," in the myelin sheath allow the action potential generated by the neuron to travel more rapidly by essentially jumping from one node to the next.

Neurons are anatomically distinct units with no physical continuity between them. The transmitting portion of a neuron, its axon, ends in a series of synapses, thereby making contact with other neurons (see Figure 3.28). Under the microscope this often stands out as a spherical enlargement at the end of the axon to which various names have been given, for example, boutons, end-feet, or synaptic terminals. This ending does not actually make contact with the soma or the dendrite but is separated by a narrow cleft (gap) that is, on

average, 100 to 200 Angstroms (10^{-9} meters) wide. This is known as the *synaptic cleft*. Each of these synaptic endings contains a large number of submicroscopic spherical structures (*synaptic vesicles*) that can be detected only under the electron microscope. These synaptic vesicles, in turn, are essentially “chemical carriers” containing transmitter substance that is released into the synaptic clefts on excitation. With this information in hand, let us consider the sequence of events that enables one neuron to communicate with another.

When an individual neuron is excited, an electrical signal is transmitted along its axon to many tiny branches, diverging fibers near its far end. These axonal terminals end or synapse close to the “input terminals” (the dendrites and cell body) of a large number of other neurons. When an electrical pulse arrives at the synapse, it triggers the release of a tiny amount of transmitter substance. This chemical carrier floats across the synaptic cleft between the axonal fiber and the cell body, thereby altering the status of the receiving neuron. For example, the chemical emissions may urge the receiving neuron into a state whereby this second cell is activated and conducts a similar electrical pulse to its axon. In this way, the initial electrical signal may be propagated to a still more remote part of the other hand. If the surfaces of muscle cells lie close enough to a number of such terminals to receive a substantial supply of these chemical carriers, the muscle will experience a resulting electrochemical reaction of its own that will cause it to contract and thereby perform some mechanical chore. In a similar manner, a gland can be stimulated to secrete the chemical characteristic to its activity. Neurons with the ability to cause a muscular or glandular reaction are known as effector neurons or motoneurons.

For most of us, the most pleasurable sensations come from our perception of the world around us. This sense of awareness is made possible by still another group of specialized neurons known as *receptor cells*. Acting as input devices, these neurons accept and convert various sensory information into appropriate electrical impulses that can then be properly processed within the nervous system. These receptors measure such quantities as pressure, warmth, cold, and displacement, as well as the presence of specific chemicals. Considering that every minute of one’s life the brain is virtually bombarded by such a voluminous amount of incoming information, it is astounding that it can function at all.

So as we have seen, nerve cells are responsible for the following variety of essential functions:

1. Accepting and converting sensory information into a form that can be processed with the nervous system by other neurons.
2. Processing and analyzing this information so an “integrated portrait” of the incoming data can be obtained.
3. Translating the final outcome or “decision” of this analysis process into an appropriate electrical or chemical form needed to stimulate glands or activate muscles.

The nervous system, which is responsible for the integration and control of all the body’s functions, has been divided by neuroscientists into the central nervous system (CNS) and the peripheral nervous system (PNS) (Figure 3.27). The former consists of all nervous tissue enclosed by bone (e.g., the brain and spinal cord), and the latter consists of all nervous tissue not enclosed by bone, which enables the body to detect and respond to both internal and external stimuli. The peripheral nervous system consists of the 12 pairs of cranial and 31 pairs of spinal nerves with afferent (sensory) and efferent (motor) neurons.

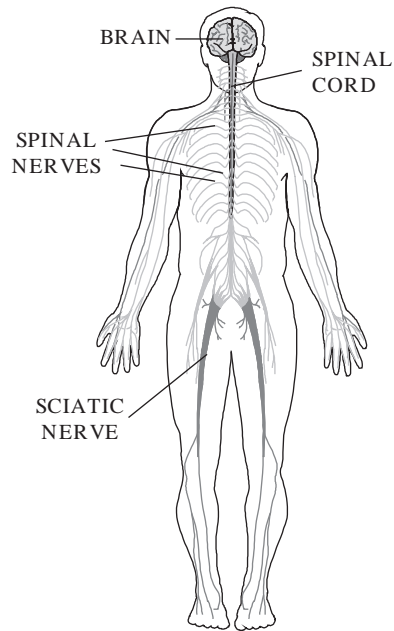


FIGURE 3.27 The central nervous system (CNS) consists of all nervous tissue that is enclosed by bone—that is, the brain and spinal cord—whereas the peripheral nervous system (PNS) consists of the nervous tissue that is not encased by bone.

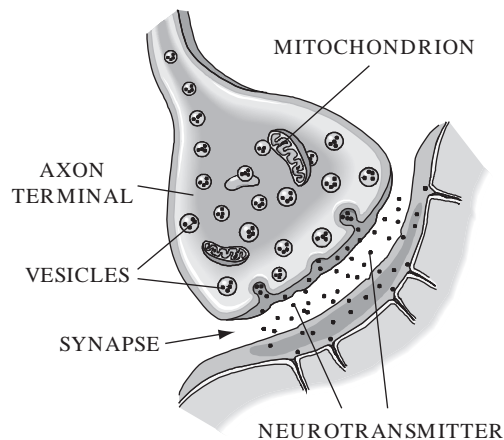


FIGURE 3.28 Following stimulation, vesicles in the axon terminal move to the synapse by means of exocytosis and release neurotransmitters into the space between the axon and the next cell, which could be the dendrite of another neuron, a muscle fiber, or a gland. The neurotransmitters diffuse across the synapse and elicit a response from the adjacent cell.

Clusters of nerve cells located in the CNS are called nuclei, and clusters of nerve cells in the PNS are called ganglion. On the other hand, nucleons located in the PNS have been designated as nerves, while those in the CNS are called tracts.

The nervous system has also been divided into the somatic and autonomic nervous systems. Each of these systems consists of components from both the central and peripheral nervous systems. For example, the somatic peripheral nervous system consists of the sensory neurons, which convey information from receptors for pain, temperature, and mechanical stimuli in the skin, muscles, and joints to the central nervous system, and the motor neurons, which return impulses from the central nervous system to these same areas of the body.

The autonomic nervous system is concerned with the internal meter of the body, including involuntary regulation of smooth muscle, cardiac muscle, and glands and is further divided into the sympathetic and parasympathetic divisions. The sympathetic division causes blood vessels in the viscera and skin to constrict, vessels in the skeletal muscles to dilate, and the heart rate to increase, whereas the parasympathetic division has the opposite effect on the vessels in the viscera and skin, provides no innervation to the skeletal muscles, and causes the heart rate to decrease. Thus, the sympathetic division prepares the body for “fight or flight,” while the parasympathetic division returns the body to normal operating conditions.

Brain function is dependent on neuronal circuits. Neurons interconnect in several different types of circuits. In a divergent circuit, each branch in the axon of the presynaptic neuron connects with the dendrite of a different postsynaptic neuron. In a convergent circuit, axons from several presynaptic neurons meet at the dendrite(s) of a single postsynaptic neuron. In a simple feedback circuit, the axon of a neuron connects with the dendrite of an interneuron that connects back with the dendrites of the first neuron. A two-neuron circuit is one in which a sensory neuron synapses directly with a motor neuron, whereas a three-neuron circuit consists of a sensory neuron, an interneuron in the spinal cord, and a motor neuron. Both of these circuits can be found in reflex arcs (Figure 3.29). The reflex arc is a special type of neural circuit that begins with a sensory neuron at a receptor (e.g., a pain receptor in the fingertip) and ends with a motor neuron at an effector (e.g., a skeletal muscle).

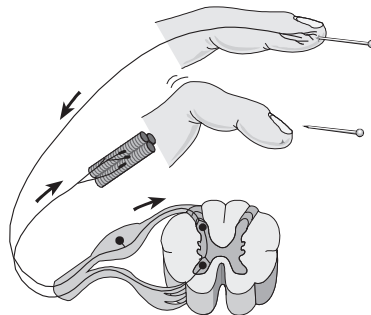


FIGURE 3.29 This reflex arc begins with a sensory neuron in the finger that senses pain when the fingertip is pricked by the pin. An action potential travels from the sensory neuron to an interneuron and then to a motor neuron that synapses with muscle fibers in the finger. The muscle fibers respond to the stimulus by contracting and removing the fingertip from the pin.

Withdrawal reflexes are elicited primarily by stimuli for pain and heat great enough to be painful and are also known as protective or escape reflexes. They allow the body to respond quickly to dangerous situations without taking additional time to send signals to and from the brain and to process the information.

The brain is a large, soft mass of nervous tissue and consists of the cerebrum, the diencephalon, the mesencephalon (midbrain), and the brain stem and cerebellum. The cerebrum (Figure 3.30a), which is divided into two hemispheres, is the largest and most obvious portion of the brain and consists of many convoluted ridges (gyri), narrow grooves (sulci), and deep fissures, which result in a total surface area of about 2.25 m². The outer layer of the cerebrum, the cerebral cortex, is composed of gray matter (neurons with unmyelinated

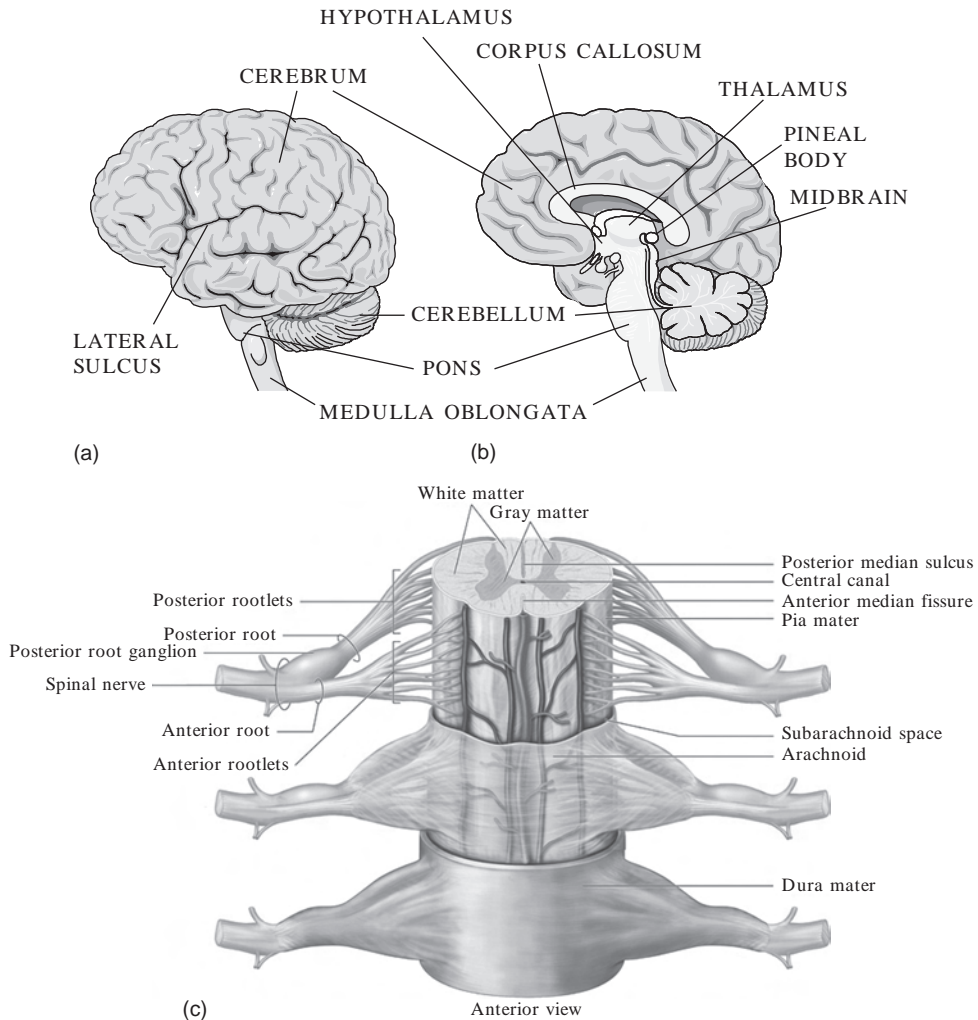


FIGURE 3.30 (a) The exterior surface of the brain. (b) A midsagittal section through the brain. (c) Structure of the spinal cord.

axons) that is 2–4 mm thick and contains over 50 billion neurons and 250 billion glial cells called neuroglia. The thicker inner layer is the white matter that consists of interconnecting groups of myelinated axons that project from the cortex to other cortical areas or from the thalamus (part of the diencephalon) to the cortex. The connection between the two cerebral hemispheres takes place via the corpus callosum (Figure 3.30b). The left side of the cortex controls motor and sensory functions from the right side of the body, whereas the right side controls the left side of the body. Association areas that interpret incoming data or coordinate a motor response are connected to the sensory and motor regions of the cortex.

Fissures divide each cerebral hemisphere into a series of lobes that include the frontal lobe, the parietal lobe, the temporal lobe, and the occipital lobe. Each of these lobes has different functions. The functions of the frontal lobe include initiating voluntary movement of the skeletal muscles, analyzing sensory experiences, providing responses relating to personality, and mediating responses related to memory, emotions, reasoning, judgment, planning, and speaking. The parietal lobe responds to stimuli from cutaneous (skin) and muscle receptors throughout the body. The temporal lobes interpret some sensory experiences, store memories of auditory and visual experiences, and contain auditory centers that receive sensory neurons from the cochlea of the ear. The occipital lobes integrate eye movements by directing and focusing the eye and are responsible for correlating visual images with previous visual experiences and other sensory stimuli. The insula is a deep portion of the cerebrum that lies under the parietal, frontal, and temporal lobes. Little is known about its function, but it seems to be associated with gastrointestinal and other visceral activities.

The diencephalon is the deep part of the brain that connects the midbrain of the brain stem with the cerebral hemispheres. Its main parts include the thalamus, hypothalamus, and epithalamus (Figure 3.30b). The thalamus, the major switchboard of the brain, is involved with sensory and motor systems, general neural background activity, and the expression of emotion and uniquely human behaviors. Due to its two-way communication with areas of the cortex, it is linked with thought, creativity, interpretation and understanding of spoken and written words, and identification of objects sensed by touch. The hypothalamus is involved with integration within the autonomic nervous system, temperature regulation, water and electrolyte balance, sleep-wake patterns, food intake, behavioral responses associated with emotion, endocrine control, and sexual responses. The epithalamus contains the pineal body that is thought to have a neuroendocrine function.

The brain stem connects the brain with the spinal cord and automatically controls vital functions such as breathing. Its principal regions include the midbrain, pons, and medulla oblongata (Figure 3.30b). The midbrain connects the pons and cerebellum with the cerebrum and is located at the upper end of the brain stem. It is involved with visual reflexes, the movement of eyes, focusing of the lenses, and the dilation of the pupils. The pons is a rounded bulge between the midbrain and medulla oblongata that functions with the medulla oblongata to control respiratory functions, acts as a relay station from the medulla oblongata to higher structures in the brain, and is the site of emergence of cranial nerve V. The medulla oblongata is the lowermost portion of the brain stem and connects the pons to the spinal cord. It contains vital centers that regulate heart rate, respiratory rate, constriction and dilation of blood vessels, blood pressure, swallowing, vomiting, sneezing, and coughing.

The cerebellum is located behind the pons and is the second largest part of the brain. It processes sensory information that is used by the motor systems and is involved with

coordinating skeletal muscle contractions and impulses for voluntary muscular movement that originate in the cerebral cortex. The cerebellum is a processing center that is involved with coordination of balance, body positions, and the precision and timing of movements.

The gray matter of the spinal cord is divided into the dorsal and ventral horns. In a human, standing upright, the “dorsal” horn is posterior and the “ventral” horn is anterior. Dorsal horn neurons receive and process sensory information from the skin, while ventral horn neurons participate in the control of skeletal muscle contraction. The gray matter is surrounded by columns (funiculi) of white matter containing ascending and descending axons. The spinal cord communicates with the periphery via the dorsal and ventral root fibers that exit between the bony vertebra. Dorsal root fibers bring information to the spinal cord, and ventral root fibers carry information away from the spinal cord (Figure 3.30c).

3.4.4 The Skeletal System

The average adult skeleton contains 206 bones, but the actual number varies from person to person and decreases with age as some bones become fused. Like the body, the skeletal system is divided into two parts: the axial skeleton and the appendicular skeleton (Figure 3.31). The axial skeleton contains 80 bones (skull, hyoid bone, vertebral column, and thoracic cage), whereas the appendicular skeleton contains 126 (pectoral and pelvic girdles and upper and lower extremities). The skeletal system protects and supports the

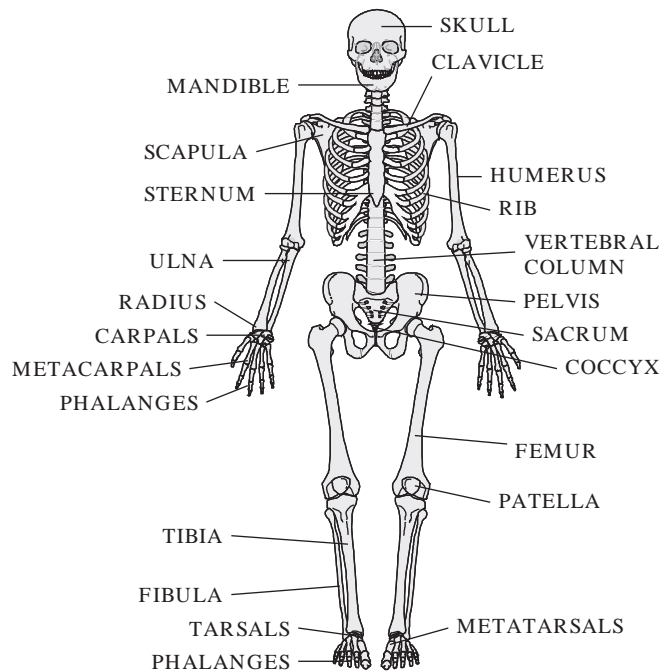


FIGURE 3.31 The skull, hyoid bone (not shown), vertebral column, and thoracic cage (ribs, cartilage, and sternum) make up the axial skeleton, whereas the pectoral (scapula and clavicle) and pelvic girdles and upper and lower extremities make up the appendicular skeleton.

body, helps with movement, produces blood cells, and stores important minerals. It is made up of strong, rigid bones that are composed of specialized connective tissue, bear weight, and form the major supporting elements of the body. Some support also comes from cartilage that is a smooth, firm, resilient, nonvascular type of connective tissue. Since the bones of the skeleton are hard, they protect the organs, such as the brain and abdominal organs, that they surround.

There are 8 cranial bones that support, surround, and protect the brain. Fourteen facial bones form the face and serve as attachments for the facial muscles that primarily move skin rather than bone. The facial bones, except for the lower jaw (mandible), are joined with each other and with the cranial bones. There are 6 auditory ossicles, 3 in each ear, that transmit sound waves from the external environment to the inner ear. The hyoid bone, which is near the skull but is not part of it, is a small U-shaped bone that is located in the neck just below the lower jaw. It is attached to the skull and larynx (voice box) by muscles and ligaments and serves as the attachment for several important neck and tongue muscles.

The vertebral column starts out with approximately 34 bones, but only 26 independent ones are left in the average human adult. There are 7 cervical bones including the axis, which acts as a pivot around which the head rotates, and the atlas, which sits on the axis and supports the “globe” of the head. These are followed by 5 cervical, 12 thoracic, and 5 lumbar vertebrae and then the sacrum and the coccyx. The last two consist of 5 fused vertebrae. The vertebral column supports the weight of and allows movement of the head and trunk, protects the spinal cord, and provides places for the spinal nerves to exit from the spinal cord. There are four major curves (cervical, thoracic, lumbar, and sacral/coccygeal) in the adult vertebral column that allow it to flex and absorb shock. While movement between any two adjacent vertebrae is generally quite limited, the total amount of movement provided by the vertebral column can be extensive. The thoracic cage consists of 12 thoracic vertebrae (which are counted as part of the vertebral column), 12 pairs of ribs and their associated cartilage, and the sternum (breastbone). It protects vital organs and prevents the collapse of the thorax during ventilation.

Bones are classified as long, short, flat, or irregular, according to their shape. Long bones, such as the femur and humerus, are longer than they are wide. Short bones, such as those found in the ankle and wrist, are as broad as they are long. Flat bones, such as the sternum and the bones of the skull, have a relatively thin and flattened shape. Irregular bones do not fit into the other categories and include the bones of the vertebral column and the pelvis.

Bones make up about 18 percent of the mass of the body and have a density of 1.9 g/cm^3 . The two types of bone are spongy and compact (cortical). Spongy bone forms the ends (epiphyses) of the long bones and the interior of other bones and is quite porous. Compact bone forms the shaft (diaphysis) and outer covering of bones and has a tensile strength of 120 N/mm^2 , compressive strength of 170 N/mm^2 , and Young's modulus of $1.8 \times 10^4 \text{ N/mm}^2$. The medullary cavity, a hollow space inside the diaphysis, is filled with fatty yellow marrow or red marrow that contains blood-forming cells.

Bone is a living organ that is constantly being remodeled. Old bone is removed by special cells, osteoclasts, and new bone is deposited by osteoblasts. Bone remodeling occurs during bone growth and in order to regulate calcium availability. The average skeleton is totally remodeled about three times during a person's lifetime. Osteoporosis is a disorder in which old bone is broken down faster than new bone is produced so the resulting bones are weak and brittle.

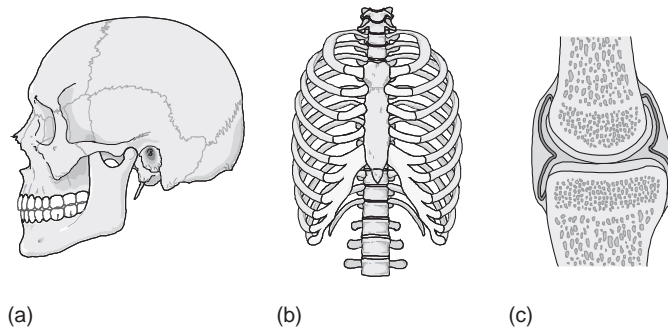


FIGURE 3.32 Bones of the skeletal system are attached to each other at (a) fibrous, (b) cartilaginous, or (c) synovial joints.

The bones of the skeletal system are attached to one another at fibrous, cartilaginous, or synovial joints (Figure 3.32). The articulating bones of fibrous joints are bound tightly together by fibrous connective tissue. These joints can be rigid and relatively immovable to slightly movable. This type of joint includes the suture joints in the skull. Cartilage holds together the bones in cartilaginous joints. These joints allow limited motion in response to twisting or compression and include the joints of the vertebral system and the joints that attach the ribs to the vertebral column and to the sternum. Synovial joints, such as the knee, are the most complex and varied and have fluid-filled joint cavities, cartilage that covers the articulating bones, and ligaments that help hold the joints together.

Synovial joints are classified into six types, depending on their structure and the type of motion they permit. Gliding joints (Figure 3.33) are the simplest type of synovial joint, allow

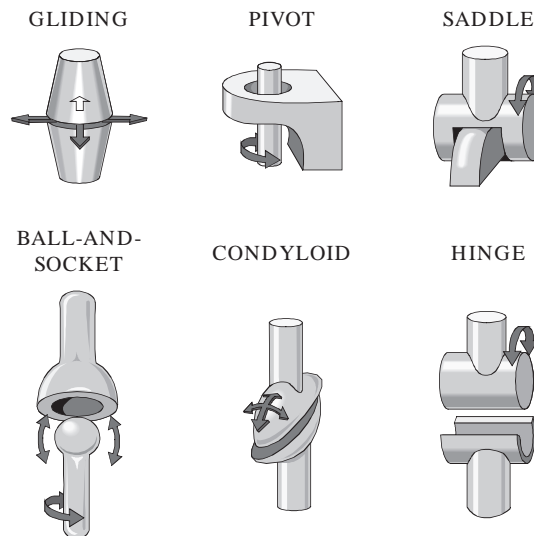


FIGURE 3.33 Synovial joints have fluid-filled cavities and are the most complex and varied types of joints. Each synovial joint is classified into one of six types, depending on its structure and type of motion.

back-and-forth or side-to-side movement, and include the intercarpal articulations in the wrist. Hinge joints, such as the elbow, permit bending in only one plane and are the most common type of synovial joint. The atlas and axis provide an example of a pivot joint that permits rotation. In condyloid articulations, an oval, convex surface of one bone fits into a concave depression on another bone. Condyloid joints, which include the metacarpophalangeal joints (knuckles) of the fingers, permit flexion-extension and rotation and are considered to be biaxial because rotation is limited to two axes of movement. The saddle joint, represented by the joint at the base of the thumb, is a modified condyloid joint that permits movement in several directions (multiaxial). Ball-and-socket joints allow motion in many directions around a fixed center. In these joints, the ball-shaped head of one bone fits into a cuplike concavity of another bone. This multiaxial joint is the most freely movable of all and includes the shoulder and hip joints. Biomedical engineers have helped develop artificial joints that are routinely used as replacements in diseased or injured hips, shoulders, and knees (Figure 3.34).

3.4.5 Muscular System

The muscular system (Figure 3.35) is composed of 600–700 skeletal muscles, depending on whether certain muscles are counted as separate or as pairs, and makes up 40 percent of the body's mass. The axial musculature makes up about 60 percent of the skeletal muscles in the body and arises from the axial skeleton (see Figure 3.31). It positions the head and spinal column and moves the rib cage during breathing. The appendicular musculature moves or stabilizes components of the appendicular skeleton.

The skeletal muscles in the muscular system maintain posture, generate heat to maintain the body's temperature, and provide the driving force that is used to move the bones and joints of the body and the skin of the face. Muscles that play a major role in accomplishing a movement are called prime movers, or agonists. Muscles that act in opposition to a prime

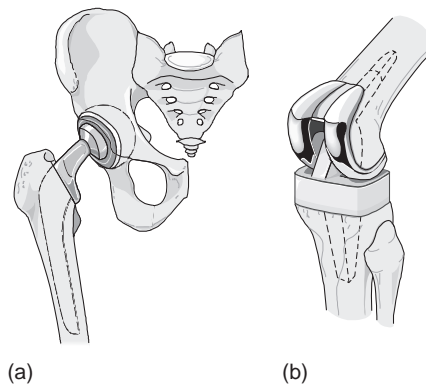


FIGURE 3.34 Diseased or damaged hip (a) and knee (b) joints that are nonfunctional or extremely painful can be replaced by prostheses. Artificial joints can be held in place by a special cement (polymethylmethacrylate [PMMA]) and by bone ingrowth. Special problems occur at the interfaces due to the different elastic moduli of the materials (110 GPa for titanium, 2.2 GPa for PMMA, and 20 GPa for bone).

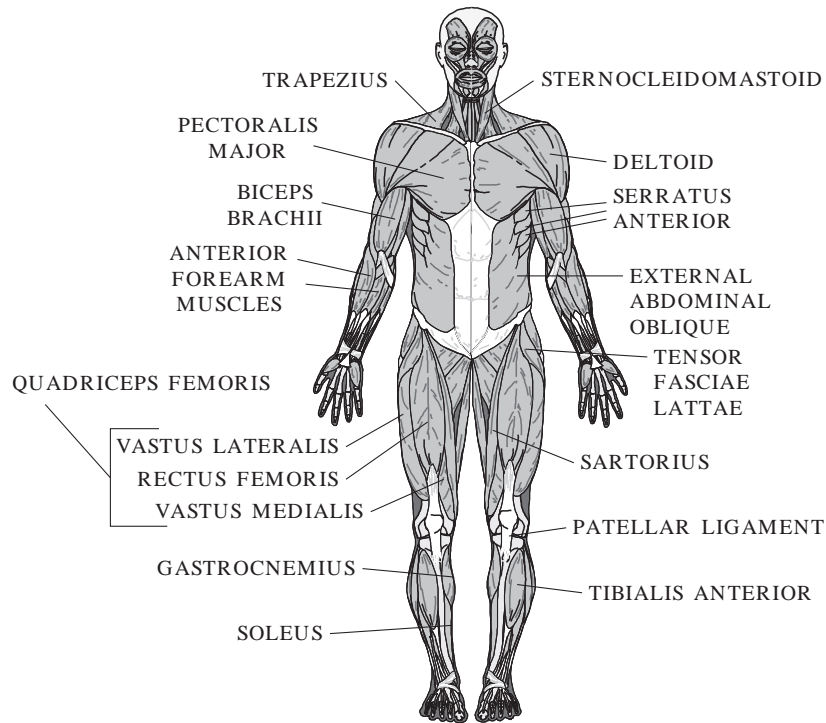


FIGURE 3.35 Some of the major skeletal muscles on the anterior side of the body.

mover are called antagonists, whereas muscles that assist a prime mover in producing a movement are called synergists. The continual contraction of some skeletal muscles helps maintain the body's posture. If all of these muscles relax, which happens when a person faints, the person collapses.

A system of levers, which consists of rigid lever arms that pivot around fixed points, is used to move skeletal muscle (Figure 3.36). Two different forces act on every lever: the weight to be moved—that is, the resistance to be overcome—and the pull or effort applied—that is, the applied force. Bones act as lever arms, and joints provide a fulcrum. The resistance to be overcome is the weight of the body part that is moved, and the applied force is generated by the contraction of a muscle or muscles at the insertion, the point of attachment of a muscle to the bone it moves. An example of a first-class lever, one in which the fulcrum is between the force and the weight, is the movement of the facial portion of the head when the face is tilted upward. The fulcrum is formed by the joint between the atlas and the occipital bone of the skull, and the vertebral muscles inserted at the back of the head generate the applied force that moves the weight, the facial portion of the head. A second-class lever is one in which the weight is between the force and the fulcrum. This can be found in the body when a person stands on "tip toe." The ball of the foot is the fulcrum, and the applied force is generated by the calf muscles on the back of the leg. The weight that is moved is that of the whole body. A third-class lever is one in which the force is between the weight and the fulcrum. When a person has a bent elbow and holds

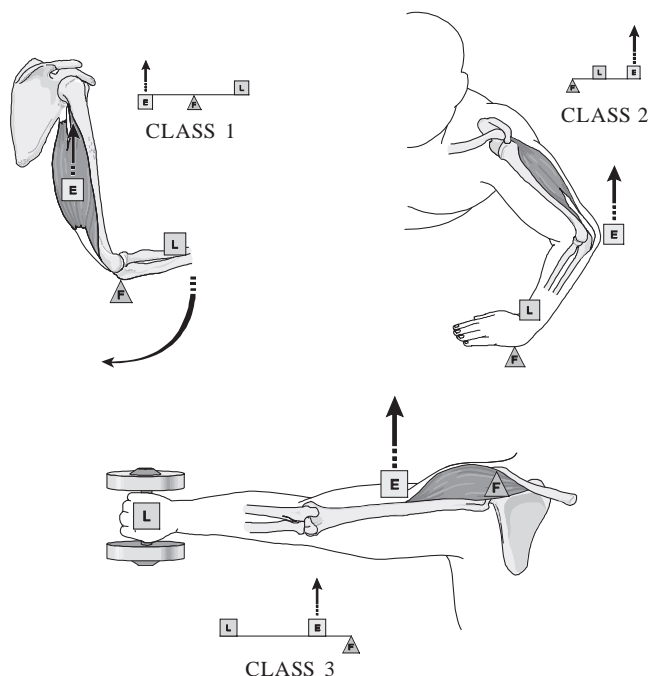


FIGURE 3.36 Depending on the muscle in use, the location of the load, and the location of the fulcrum, the humerus can act as a class 1 lever, a class 2 lever, or a class 3 lever.

a ball in front of the body, the applied force is generated by the contraction of the biceps brachii muscle. The weight to be moved includes the ball and the weight of the forearm and hand, and the elbow acts as the fulcrum.

The three types of muscle tissue—cardiac, skeletal, and smooth—share four important characteristics: *contractility*, the ability to shorten; *excitability*, the capacity to receive and respond to a stimulus; *extensibility*, the ability to be stretched; and *elasticity*, the ability to return to the original shape after being stretched or contracted. Cardiac muscle tissue is found only in the heart, whereas smooth muscle tissue is found within almost every other organ, where it forms sheets, bundles, or sheaths around other tissues. Skeletal muscles are composed of skeletal muscle tissue, connective tissue, blood vessels, and nervous tissue.

Each skeletal muscle is surrounded by a layer of connective tissue (collagen fibers) that separates the muscle from surrounding tissues and organs. These fibers come together at the end of the muscle to form tendons, which connect the skeletal muscle to bone, to skin (face), or to the tendons of other muscles (hand). Other connective tissue fibers divide the skeletal muscles into compartments called fascicles that contain bundles of muscle fibers. Within each fascicle, additional connective tissue surrounds each skeletal muscle fiber and ties adjacent ones together. Each skeletal muscle fiber has hundreds of nuclei just beneath the cell membrane. Multiple nuclei provide multiple copies of the genes that direct the production of enzymes and structural proteins needed for normal contraction so contraction can occur faster.

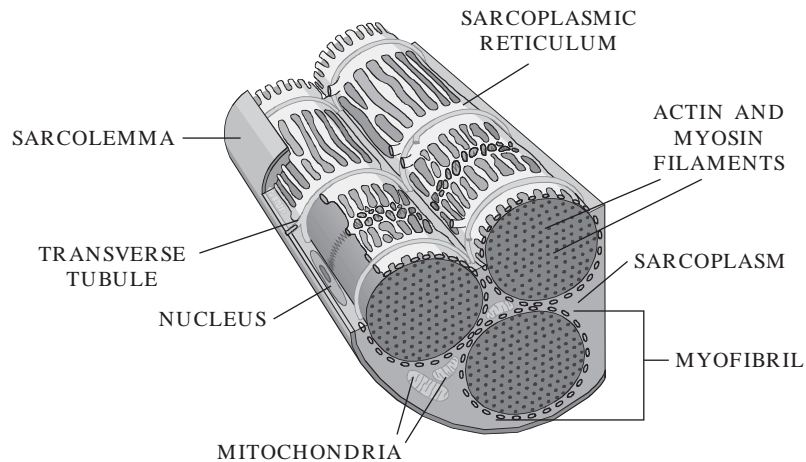


FIGURE 3.37 Skeletal muscles are composed of muscle fascicles that are composed of muscle fibers such as the one shown here. Muscle fibers have hundreds of nuclei just below the plasma membrane—the sarcolemma. Transverse tubules extend into the sarcoplasm, the cytoplasm of the muscle fiber, and are important in the contraction process because they deliver action potentials that result in the release of stored calcium ions. Calcium ions are needed to create active sites on actin filaments so cross-bridges can be formed between actin and myosin and the muscle can contract.

In muscle fibers, the plasma membrane is called the sarcolemma, and the cytoplasm is called the sarcoplasm (Figure 3.37). Transverse tubules (T tubules) begin at the sarcolemma and extend into the sarcoplasm at right angles to the surface of the sarcolemma. The T tubules, which play a role in coordinating contraction, are filled with extracellular fluid and form passageways through the muscle fiber. They make close contact with expanded chambers, cisternae, of the sarcoplasmic reticulum, a specialized form of the ER. The cisternae contain high concentrations of calcium ions that are needed for contraction to occur.

The sarcoplasm contains cylinders 1 or 2 μm in diameter that are as long as the entire muscle fiber and are called myofibrils. The myofibrils are attached to the sarcolemma at each end of the cell and are responsible for muscle fiber contraction. Myofilaments—protein filaments consisting of thin filaments (primarily actin) and thick filaments (mostly myosin)—are bundled together to make up myofibrils. Repeating functional units of myofilaments are called sarcomeres (Figure 3.38). The sarcomere is the smallest functional unit of the muscle fiber and has a resting length of about 2.6 μm . The thin filaments are attached to dark bands, called Z lines, which form the ends of each sarcomere. Thick filaments containing double-headed myosin molecules lie between the thin ones. It is this overlap of thin and thick filaments that gives skeletal muscle its banded, striated appearance. The I band is the area in a relaxed muscle fiber that just contains actin filaments, and the H zone is the area that just contains myosin filaments. The H zone and the area in which the actin and myosin overlap form the A band.

When a muscle contracts, myosin molecules in the thick filaments form cross-bridges at active sites in the actin of the thin filaments and pull the thin filaments toward the center of

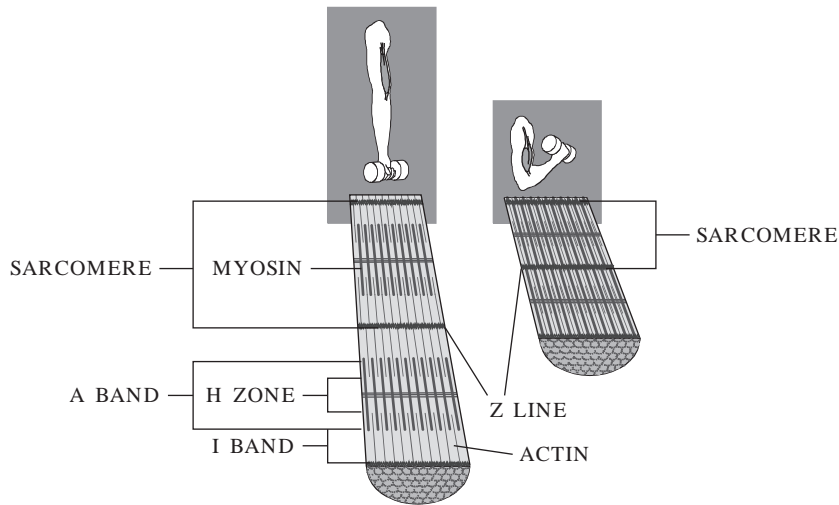


FIGURE 3.38 The sarcomere is the basic functional unit of skeletal muscles and extends from one Z line to the next. Actin filaments are attached to the Z lines and extend into the A band, where they overlap with the thicker myosin filaments. The H zone is the portion of the A band that contains no overlapping actin filaments. When the muscle changes from its extended, relaxed position (left panel) to its contracted state (right panel), the myosin filaments use cross-bridges to slide past the actin filaments and bring the Z lines closer together. This results in shorter sarcomeres and a contracted muscle.

the sarcomere. The cross-bridges are then released and reformed at a different active site further along the thin filament. This results in a motion that is similar to the hand-over-hand motion that is used to pull in a rope. This action, the sliding filament mechanism, is driven by ATP energy and results in shortening of the muscle. Shortening of the muscle components (contraction) results in bringing the muscle's attachments (e.g., bones) closer together (Figure 3.38).

Muscle fibers have connections with nerves. Sensory nerve endings are sensitive to length, tension, and pain in the muscle and send impulses to the brain via the spinal cord, whereas motor nerve endings receive impulses from the brain and spinal cord that lead to excitation and contraction of the muscle. Each motor axon branches and supplies several muscle fibers. Each of these axon branches loses its myelin sheath and splits up into a number of terminals that make contact with the surface of the muscle. When the nerve is stimulated, vesicles in the axon terminals release a neurotransmitter, acetylcholine, into the synapse between the neuron and the muscle. Acetylcholine diffuses across the synapse and binds to receptors in a special area, the motor end plate, of the sarcolemma. This causes the sodium channels in the sarcolemma to open up, and an action potential is produced in the muscle fiber. The resulting action potential spreads over the entire sarcolemmal surface and travels down all of the T tubules, where it triggers a sudden massive release of calcium by the cisternae. Calcium triggers the production of active sites on the thin filaments so cross-bridges with myosin can form and contraction occurs. Acetylcholinesterase breaks down the acetylcholine while the contraction process is under way so the original relatively low permeability of the sarcolemma to sodium is restored.

A motor unit consists of a motor neuron and the muscle fibers that it innervates. All the muscle fibers in a single motor unit contract at the same time, whereas muscle fibers in the same muscle but belonging to different motor units may contract at different times. When a contracted muscle relaxes, it returns to its original (resting) length if another contracting muscle moves it or if it is acted upon by gravity. During relaxation, ATP is expended to move calcium back to the cisternae. The active sites that were needed for cross-bridge formation become covered so actin and myosin can no longer interact. When the cross-bridges disappear, the muscle returns to its resting length—that is, it relaxes.

The human body contains two different types of skeletal muscle fibers: fast and slow. Fast fibers can contract in 10 ms or less following stimulation and make up most of the skeletal muscle fibers in the body. They are large in diameter and contain densely packed myofibrils, large glycogen reserves (used to produce ATP), and relatively few mitochondria. These fibers produce powerful contractions that use up massive amounts of ATP and fatigue (can no longer contract in spite of continued neural stimulation) rapidly. Slow fibers take about three times as long to contract as fast fibers. They can continue to contract for extended periods of time because they contain (1) a more extensive network of capillaries, so they can receive more oxygen; (2) a special oxygen-binding molecule called myoglobin; and (3) more mitochondria, which can produce more ATP than fast fibers. Muscles contain different amounts of slow and fast fibers. Those that are dominated by fast fibers (e.g., chicken breast muscles) appear white, while those that are dominated by slow fibers (e.g., chicken legs) appear red. Most human muscles appear pink because they contain a mixture of both. Genes determine the percentage of fast and slow fibers in each muscle, but the ability of fast muscle fibers to resist fatigue can be increased through athletic training.

3.5 HOMEOSTASIS

Organ systems work together to maintain a constant internal environment within the body. Homeostasis is the process by which physical and chemical conditions within the internal environment of the body are maintained within tolerable ranges even when the external environment changes. Body temperature, blood pressure, and breathing and heart rates are some of the functions that are controlled by homeostatic mechanisms that involve several organ systems working together.

Extracellular fluid—the fluid that surrounds and bathes the body's cells—plays an important role in maintaining homeostasis. It circulates throughout the body and carries materials to and from the cells. It also provides a mechanism for maintaining optimal temperature and pressure levels, the proper balance between acids and bases, and concentrations of oxygen, carbon dioxide, water, nutrients, and many of the chemicals that are found in the blood.

Three components—sensory receptors, integrators, and effectors—interact to maintain homeostasis (Figure 3.39). Sensory receptors, which may be cells or cell parts, detect stimuli—that is, changes to their environment—and send information about the stimuli to integrators. Integrators are control points that pull together information from one or more sensory receptors. Integrators then elicit a response from effectors. The brain is an

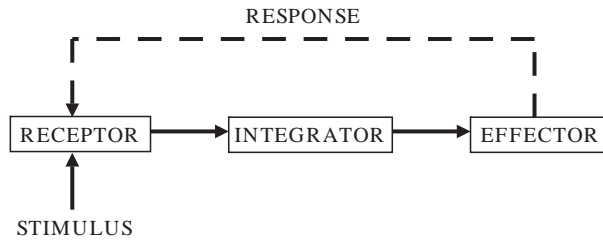


FIGURE 3.39 Feedback mechanisms are used to help maintain homeostasis. A stimulus is received by a receptor that sends a signal (messenger) to an effector or to an integrator that sends a signal to an effector. The effector responds to the signal. The response feeds back to the receptor and modifies the effect of the stimulus. In negative feedback, the response subtracts from the effect of the stimulus on the receptor. In positive feedback, the response adds to the effect of the stimulus on the receptor.

integrator that can send messages to muscles or glands or both. The messages result in some type of response from the effectors. The brain receives information about how parts of the body are operating and can compare this to information about how parts of the body should be operating.

Positive feedback mechanisms are those in which the initial stimulus is reinforced by the response. There are very few examples of this in the human body, since it disrupts homeostasis. Childbirth provides one example. Pressure from the baby's head in the birth canal stimulates receptors in the cervix, which send signals to the hypothalamus. The hypothalamus responds to the stimulus by releasing oxytocin, which enhances uterine contractions. Uterine contractions increase in intensity and force the baby further into the birth canal, which causes additional stretching of the receptors in the cervix. The process continues until the baby is born, the pressure on the cervical stretch receptors ends, and the hypothalamus is no longer stimulated to release oxytocin.

Negative feedback mechanisms result in a response that is opposite in direction to the initiating stimulus. For example, receptors in the skin and elsewhere in the body detect the body's temperature. Temperature information is forwarded to the hypothalamus in the brain, which compares the body's current temperature to what the temperature should be (approximately 37°C). If the body's temperature is too low, messages are sent to contract the smooth muscles in blood vessels near the skin (reducing the diameter of the blood vessels and the heat transferred through the skin), to skeletal muscles to start contracting rapidly (shivering), and to the arrector pili muscles (see Figure 3.16a) to erect the hairs and form "goose bumps." The metabolic activity of the muscle contractions generates heat and warms the body. If the body's temperature is too high, messages are sent to relax the smooth muscles in the blood vessels near the skin (increasing the diameter of the blood vessels and the amount of heat transferred through the skin) and to sweat glands to release moisture and thus increase evaporative cooling of the skin. When the temperature of circulating blood changes to such an extent in the appropriate direction that it reaches the set point of the system, the hypothalamus stops sending signals to the effector muscles and glands.

Another example of a negative feedback mechanism in the body involves the regulation of glucose in the bloodstream by clusters of cells, the pancreatic islets (Figure 3.40). There are between 2×10^5 and 2×10^6 pancreatic islets scattered throughout the adult

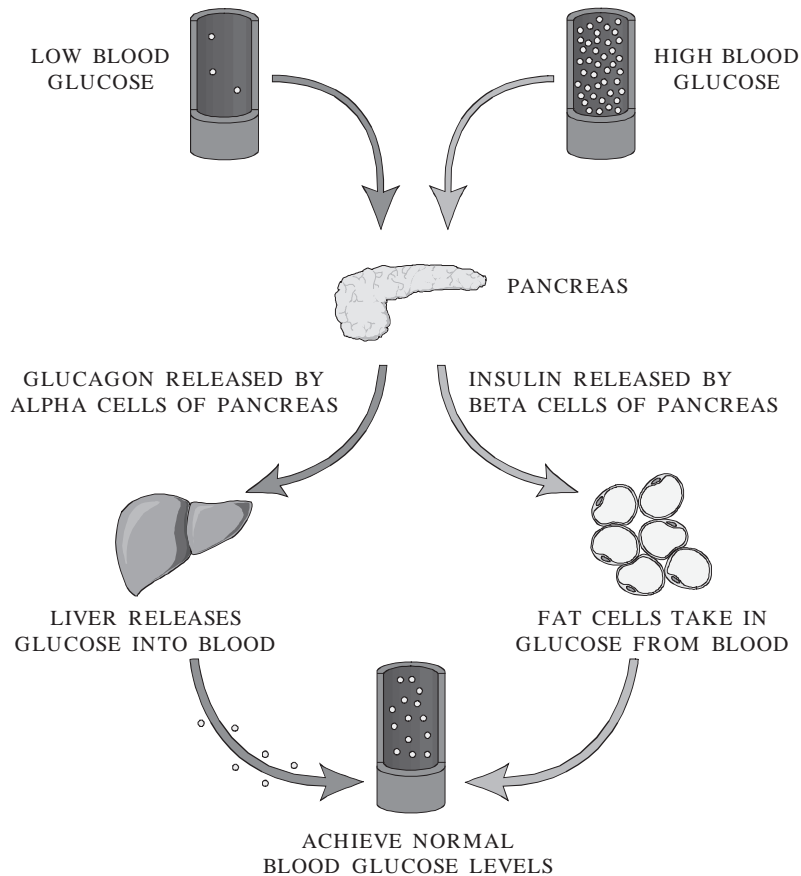


FIGURE 3.40 Two negative feedback mechanisms help control the level of glucose in the blood. When blood glucose levels are higher than the body's set point (stimulus), beta cells (receptors) in the pancreatic islets produce insulin (messenger), which facilitates glucose transport across plasma membranes and enhances the conversion of glucose into glycogen for storage in the liver (effector). This causes the level of glucose in the blood to drop. When the level equals the body's set point, the beta cells stop producing insulin. When blood glucose levels are lower than the body's set point (stimulus), alpha cells (receptors) in the pancreatic islets produce glucagon (messenger), which stimulates the liver (effector) to convert glycogen into glucose. This causes the level of glucose in the blood to increase. When the level equals the body's set point, the alpha cells stop producing glucagon.

pancreas. When glucose levels are high, beta cells in the islets produce insulin, which facilitates glucose transport across plasma membranes and into cells and enhances the conversion of glucose into glycogen that is stored in the liver. During periods of fasting, or whenever the concentration of blood glucose drops below normal (70–110 mg/dl), alpha cells produce glucagon, which stimulates the liver to convert glycogen into glucose and the formation of glucose from noncarbohydrate sources such as amino acids and lactic acid. When glucose levels return to normal, the effector cells in the pancreatic islets stop producing their respective hormone—that is, insulin or glucagon. Some biomedical

engineers are working on controlled drug delivery systems that can sense blood glucose levels and emulate the responses of the pancreatic islet cells, whereas other biomedical engineers are trying to develop an artificial pancreas that would effectively maintain appropriate blood glucose levels.

3.6 EXERCISES

1. Using as many appropriate anatomical terms as apply, write sentences that describe the positional relationship between your mouth and (a) your left ear, (b) your nose, and (c) the big toe on your right foot.
2. Using as many appropriate anatomical terms as apply, describe the position of the stomach in the body and its position relative to the heart.
3. Search the Internet to find a transverse section of the body that was imaged using computerized tomography (CT) or magnetic resonance imaging (MRI). Print the image and indicate its web address.
4. Search the Internet to find a frontal section of the body that was imaged using CT or MRI. Print the image and indicate its web address.
5. Name and give examples of the four classes of biologically important organic compounds. What are the major functions of each of these groups?
6. What are the molarity and osmolarity of a 1-liter solution that contains half a mole of calcium chloride? How many molecules of chloride would the solution contain?
7. Consider a simple model cell, such as the one in Figure 3.6, that consists of cytoplasm and a plasma membrane. The cell's initial volume is 2 nl and contains 0.2 M protein. The cell is placed in a large volume of 0.05 M CaCl_2 . Neither Ca^{++} nor Cl^- can cross the plasma membrane and enter the cell. Is the 0.05 M CaCl_2 solution hypotonic, isotonic, or hypertonic relative to the osmolarity inside the cell? Describe what happens to the cell as it achieves equilibrium in this new environment. What will be the final osmolarity of the cell? What will be its final volume?
8. What does the principle of electrical neutrality mean in terms of the concentration of ions within a cell?
9. Consider the same model cell that was used in problem 7, but instead of being placed in 0.05 M CaCl_2 , the cell is placed in 0.2 M urea. Unlike Ca^{++} and Cl^- , urea can cross the plasma membrane and enter the cell. Describe what happens to the cell as it achieves equilibrium in this environment. What will be the final osmolarity of the cell? What will be its final volume?
10. Briefly describe the path that a protein, such as a hormone, that is manufactured on the rough ER would take in order to leave the cell.
11. What major role do mitochondria have in the cell? Why might it be important to have this process contained within an organelle?
12. List and briefly describe three organelles that provide structural support and assist with cell movement.
13. Find a location on the Internet that describes the Human Genome Project. Print its home page and indicate its web address. Find and print an ideogram of a chromosome that shows a gene that causes cystic fibrosis.

Continued

14. Briefly describe the major differences between replication and transcription.
15. Describe how the hereditary information contained in genes within the cell's DNA is expressed as proteins that direct the cell's activities.
16. Six different codons code for leucine, while only one codes for methionine. Why might this be important for regulating translation and producing proteins?
17. Insulin (Figure 3.41) was the first protein to be sequenced biochemically. Assuming that there were no introns involved in the process, what are the possible DNA sequences that produced the last four amino acids in the molecule?

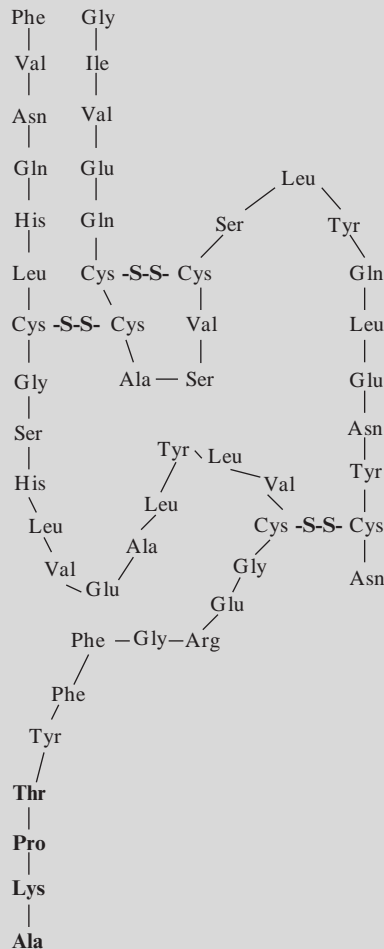


FIGURE 3.41 Bovine insulin consists of two polypeptide chains that are joined by two disulfide bonds (-S-S-). Hydrogen bonds also exist between the chains and between segments of the same chain. The three-letter names stand for different amino acids (see Table 3.1).

18. Copy the title page and abstract of five peer-reviewed journal articles that discuss engineering applications for five different organ systems in the body (one article per organ system). Review articles, conference proceeding papers, copies of keynote addresses and other speeches, book chapters, articles from the popular press and newspapers, and editorials are not acceptable. Good places to look are the *Annals of Biomedical Engineering*, the *IEEE Transactions on Biomedical Engineering*, the *IEEE Engineering in Medicine and Biology Magazine*, and *Medical and Biological Engineering and Computing*. What information in the article indicates that it was peer-reviewed?
19. Trace the path of a single red blood cell from a capillary bed in your right hand to the capillary beds of your right lung and back. What gases are exchanged? Where are they exchanged during this process?
20. Draw and label a block diagram of pulmonary and systemic blood flow that includes the chambers of the heart, valves, major veins and arteries that enter and leave the heart, the lungs, and the capillary bed of the body. Use arrows to indicate the direction of flow through each component.
21. Find an example of an ECG representing normal sinus rhythm on the Internet and use it to demonstrate how heart rate is determined.
22. Why are R waves (Figure 3.22) used to determine heart rate rather than T waves?
23. How could the stroke volume be determined if a thermal dilution technique is used to determine cardiac output?
24. What would be the pulse pressure and mean arterial pressure for a hypertensive person with a systolic pressure of 145 mmHg and a diastolic pressure of 98 mmHg?
25. The total lung capacity of a patient is 5.5 liters. Find the patient's inspiratory reserve volume if the patient's vital capacity was 4.2 liters, the tidal volume was 500 ml, and the expiratory reserve volume was 1.2 liters.
26. What would you need to know or measure in order to determine the residual volume of the patient described in Example Problem 3.10?
27. Briefly describe the functions and major components of the central, peripheral, somatic, automatic, sympathetic, and parasympathetic nervous systems. Which ones are subsets of others?
28. Explain how sarcomeres shorten and how that results in muscle contraction.
29. How do the muscular and skeletal systems interact to produce movement?
30. Draw a block diagram to show the negative feedback mechanisms that help regulate glucose levels in the blood. Label the inputs, sensors, integrators, effectors, and outputs.

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