The Cellular Level of Organization

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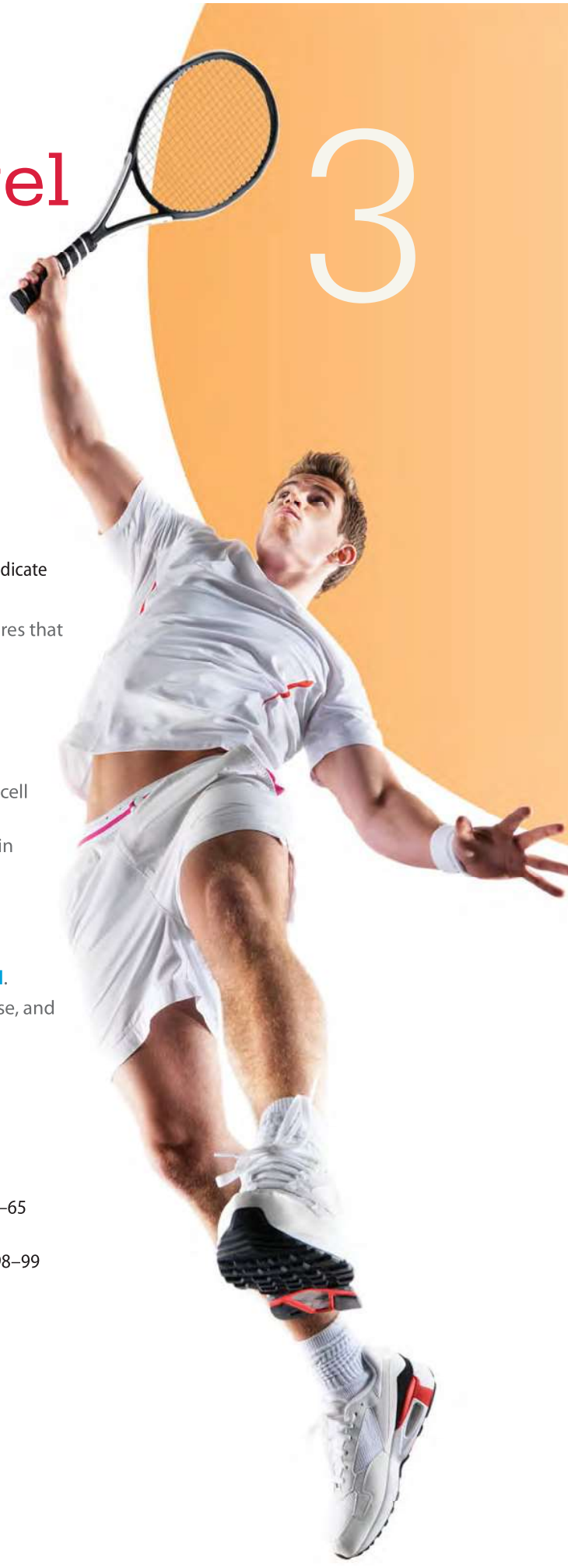


Learning Outcomes

These Learning Outcomes correspond by number to this chapter's sections and indicate what you should be able to do after completing the chapter.

- 3-1 List the functions of the **plasma membrane** and the structural features that enable it to perform those functions.
- 3-2 Describe the **organelles of a typical cell**, and indicate the specific functions of each.
- 3-3 Explain the functions of the **cell nucleus** and discuss the nature and importance of the **genetic code**.
- 3-4 Summarize the role of **DNA in protein synthesis**, cell structure, and cell function.
- 3-5 Describe the processes of cellular **diffusion and osmosis**, and explain their role in physiological systems.
- 3-6 Describe **carrier-mediated transport and vesicular transport mechanisms** used by cells to facilitate the absorption or removal of specific substances.
- 3-7 Explain the origin and significance of the **transmembrane potential**.
- 3-8 Describe the stages of the **cell life cycle**, including mitosis, interphase, and cytokinesis, and explain their significance.
- 3-9 Discuss the **regulation of the cell life cycle**.
- 3-10 Discuss the relationship between **cell division and cancer**.
- 3-11 Define **differentiation**, and explain its importance.

Clinical Notes

Spotlights

An Introduction to Cells

This chapter relates how combinations of chemicals form *cells*, the smallest living units in the human body. It also describes the chemical events that sustain life, which occur mostly inside cells.

Cells are very small—a typical cell is only about 0.1 mm in diameter. As a result, no one could actually examine the structure of a cell until effective microscopes were invented in the 17th century. In 1665, Robert Hooke inspected thin slices of cork and found that they consisted of millions of small, irregular units. In describing his observations, Hooke used the term *cell* because the many small, bare spaces he saw reminded him of the rooms, or cells, in a prison or monastery. Although Hooke saw only the outlines of the cells, and not the cells themselves, he stimulated broad interest in the microscopic world and in the nature of cellular life. The research that he began more than 345 years ago has, over time, produced the *cell theory* in its current form. The basic concepts of this theory can be summarized as follows:

- Cells are the building blocks of all plants and animals.
- All cells come from the division of preexisting cells.
- Cells are the smallest units that perform all vital physiological functions.
- Each cell maintains homeostasis at the cellular level. Homeostasis at the level of the tissue, organ, organ system, and organism reflects the combined and coordinated actions of many cells.

The human body contains trillions of cells, and all our activities—from running to thinking—result from the combined and coordinated responses of millions or even billions of cells. Many insights into human physiology arose from studies of the functioning of individual cells. What we have learned over the last 60 years has given us a new understanding of cellular physiology and the mechanisms of homeostatic control. Today, the study of cellular structure and function, or **cytology,** is part of the broader discipline of **cell biology,** which integrates aspects of biology, chemistry, and physics.

The human body contains two general classes of cells: sex cells and somatic cells. **Sex cells** (also called *germ cells* or *reproductive cells*) are either the *sperm* of males or the *oocytes* of females. The fusion of a sperm and an oocyte at fertilization is the first step in the creation of a new individual. **Somatic cells** (*soma*, body) include all the other cells in the human body. In this chapter, we focus on somatic cells; we will discuss sex cells in Chapters 28 and 29, which describe the reproductive system and development, respectively.

In the rest of this chapter, we describe the structure of a typical somatic cell, consider some of the ways in which cells interact with their environment, and discuss how somatic cells reproduce. It is important to keep in mind that the "typical" somatic cell is like the "average" person: Any description masks enormous individual variations. **Spotlight Figure 3–1** on p. 64 summarizes the structures and functions of a representative, or model, cell.

3-1 The plasma membrane separates the cell from its surrounding environment and performs various functions

We begin our look at the anatomy of cells by discussing the first structure you encounter when viewing cells through a microscope. The outer boundary of the cell is the **plasma membrane,** also called the **cell membrane.** Its general functions include the following:

- *Physical Isolation.* The plasma membrane is a physical barrier that separates the inside of the cell from the surrounding extracellular fluid. Conditions inside and outside the cell are very different, and those differences must be maintained to preserve homeostasis. For example, the plasma membrane keeps enzymes and structural proteins inside the cell.
- *Regulation of Exchange with the Environment.* The plasma membrane controls the entry of ions and nutrients, such as glucose; the elimination of wastes; and the release of secretions.
- *Sensitivity to the Environment.* The plasma membrane is the first part of the cell affected by changes in the composition, concentration, or pH of the extracellular fluid. It also contains a variety of receptors that allow the cell to recognize and respond to specific molecules in its environment. For instance, the plasma membrane may receive chemical signals from other cells. The binding of just one molecule may trigger the activation or deactivation of enzymes that affect many cellular activities.
- *Structural Support.* Specialized connections between plasma membranes, or between membranes and extracellular materials, give tissues stability. For example, the cells at the surface of the skin are tightly bound together, while those in the deepest layers are attached to extracellular protein fibers in underlying tissues.

The plasma membrane is extremely thin, ranging from 6 to 10 nm in thickness (**Figure 3–2**). This membrane contains lipids, proteins, and carbohydrates.

Membrane Lipids

Although lipids form most of the surface area of the plasma membrane, they make up only about 42 percent of its weight. The plasma membrane is called a **phospholipid bilayer,** because the phospholipid molecules in it form two layers. Recall from

Spotlight

Figure 3–1
Anatomy of a Model Cell

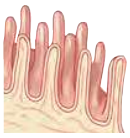
In our model cell, a *plasma membrane* separates the cell contents, callled the *cytoplasm*, from its surroundings. The cytoplasm can be subdivided into the *cytosol*, a liquid, and intracellular structures collectively known as *organelles (*or-ga-NELZ). Organelles are structures suspended within the cytosol that perform specific functions within the cell and can be further subdivided into membranous and nonmembranous organelles. Cells are surrounded by a watery medium known as the **extracellular fluid.** The extracellular fluid in most tissues is called **interstitial** (in-ter-STISH-ul) **fluid.**

= Plasma membrane
= Nonmembranous organelles
= Membranous organelles

Microvilli

Membrane extensions containing microfilaments

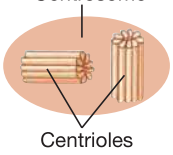
Function
Increase surface area to facilitate absorption of extracellular materials



Centrosome and Centrioles

Cytoplasm contains two centrioles at right angles; each centriole is composed of 9 microtubule triplets in a 9 + 0 array

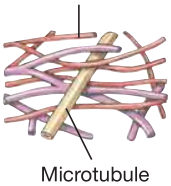
Functions
Essential for movement of chromosomes during cell division; organization of microtubules in cytoskeleton



Cytoskeleton

Proteins organized in fine filaments or slender tubes

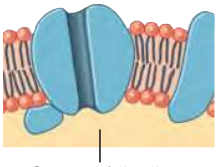
Functions
Strength and support; movement of cellular structures and materials

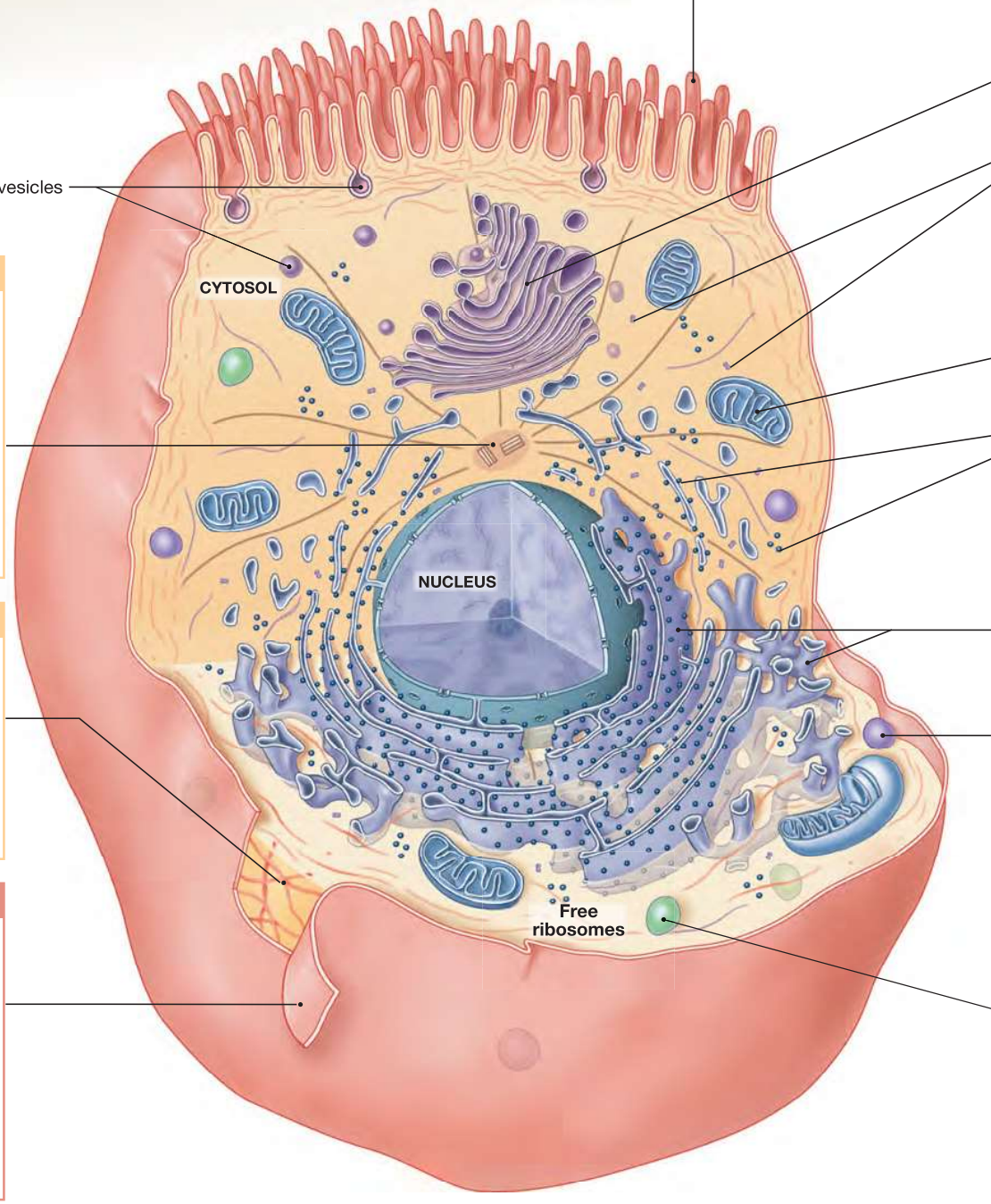


Plasma Membrane

Lipid bilayer containing phospholipids, steroids, proteins, and carbohydrates

Functions
Isolation; protection; sensitivity; support; controls entry and exit of materials

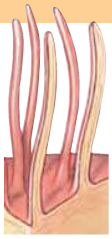




Cilia

Cilia are long extensions containing microtubule doublets in a 9 + 2 array (not shown in the model cell)

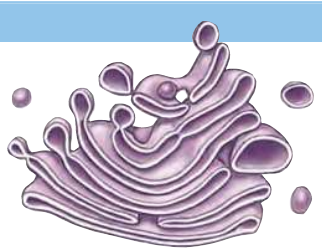
Function
Movement of material over cell surface



Golgi apparatus

Stacks of flattened membranes (cisternae) containing chambers

Functions
Storage, alteration, and packaging of secretory products and lysosomal enzymes



Proteasomes

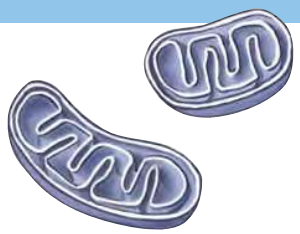
Hollow cylinders of proteolytic enzymes with regulatory proteins at their ends

Functions
Breakdown and recycling of damaged or abnormal intracellular proteins

Mitochondria

Double membrane, with inner membrane folds (cristae) enclosing important metabolic enzymes

Functions
Produce 95% of the ATP required by the cell



Ribosomes

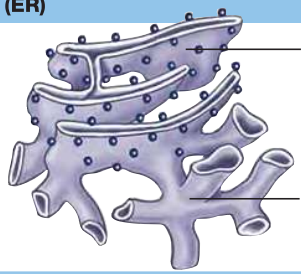
RNA + proteins; fixed ribosomes bound to rough endoplasmic reticulum, free ribosomes scattered in cytoplasm

Function
Protein synthesis

Endoplasmic reticulum (ER)

Network of membranous channels extending throughout the cytoplasm

Functions
Synthesis of secretory products; intracellular storage and transport



Rough ER modifies and packages newly synthesized proteins

Smooth ER synthesizes lipids and carbohydrates

Peroxisomes

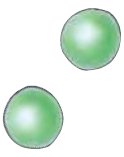
Vesicles containing degradative enzymes

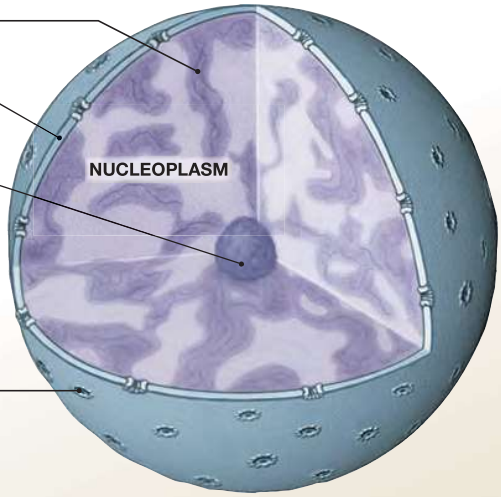
Functions
Catabolism of fats and other organic compounds, neutralization of toxic compounds generated in the process

Lysosomes

Vesicles containing digestive enzymes

Functions
Intracellular removal of damaged organelles or pathogens





NUCLEUS

Nucleoplasm containing nucleotides, enzymes, nucleoproteins, and chromatin; surrounded by a double membrane, the nuclear envelope

Functions:
Control of metabolism; storage and processing of genetic information; control of protein synthesis

Chapter 2 that a phospholipid has both a hydrophilic end (the phosphate portion) and a hydrophobic end (the lipid portion). p. 48 In each half of the bilayer, the phospholipids lie with their hydrophilic heads at the membrane surface and their hydrophobic tails on the inside. Thus, the hydrophilic heads of the two layers are in contact with the aqueous environments on either side of the membrane—the interstitial fluid on the outside and the cytosol on the inside—and the hydrophobic tails form the interior of the membrane. The lipid bilayer also contains cholesterol and small quantities of other lipids, but these have relatively little effect on the general properties of the plasma membrane.

Note the similarities in lipid organization between the plasma membrane and a micelle (**Figure 2–18c**, p. 49). Ions and water-soluble compounds cannot enter the interior of a micelle, because the lipid tails of the phospholipid molecules are hydrophobic and will not associate with water molecules. For the same reason, water and solutes cannot cross the lipid portion of the plasma membrane. Thus, the hydrophobic compounds in the center of the membrane isolate the cytoplasm from the surrounding fluid environment. Such isolation is important because the composition of cytoplasm is very different from that of extracellular fluid, and the cell cannot survive if the differences are eliminated.

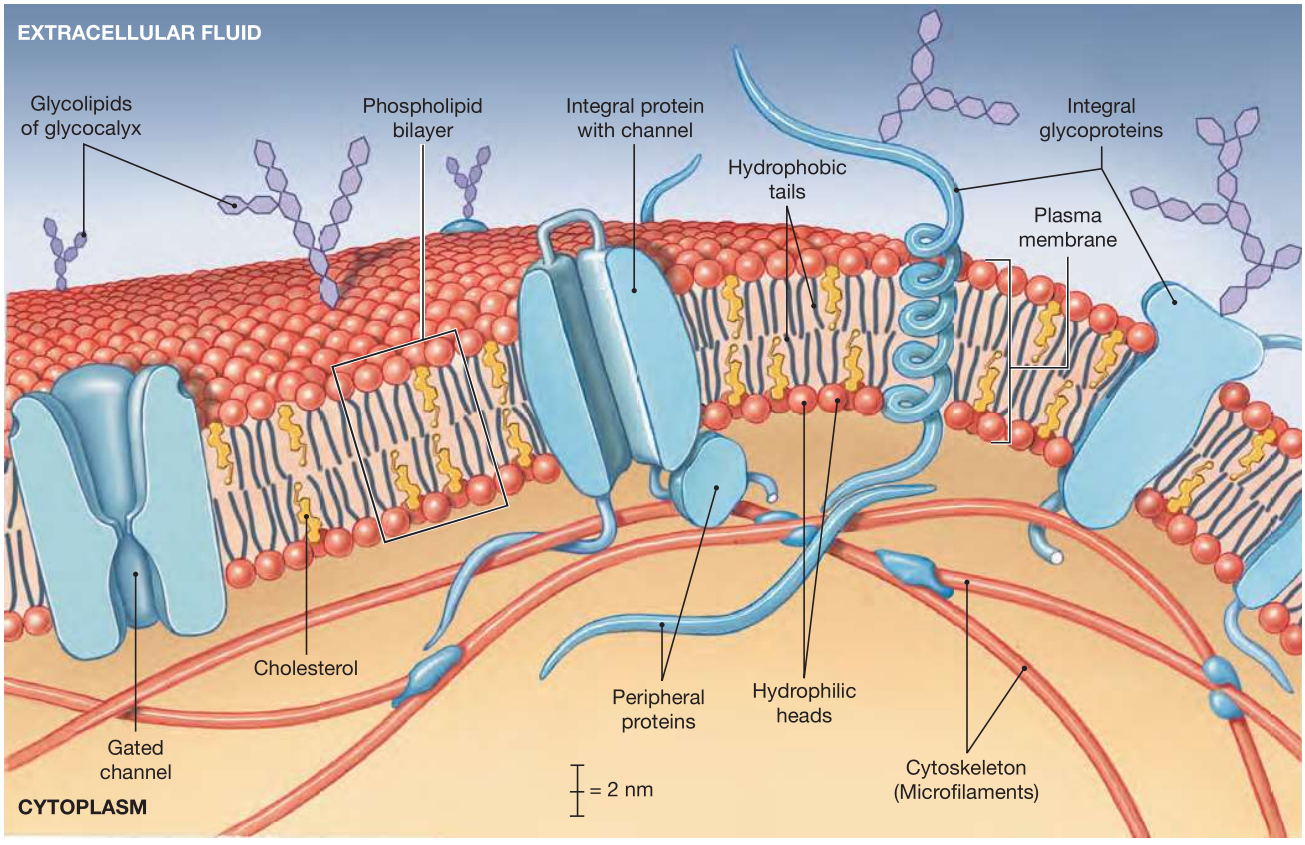
Membrane Proteins

Proteins, which are much denser than lipids, account for about 55 percent of the weight of a plasma membrane. There are two general structural classes of membrane proteins (**Figure 3–2**). **Integral proteins** are part of the membrane structure and cannot be removed without damaging or destroying the membrane. Most integral proteins span the width of the membrane one or more times, and are therefore known as *transmembrane proteins*. **Peripheral proteins** are bound to the inner or outer surface of the membrane and (like Post-it notes) are easily separated from it. Integral proteins greatly outnumber peripheral proteins.

Membrane proteins may have a variety of specialized functions. Examples of important types of functional proteins include the following:

1. *Anchoring Proteins.* **Anchoring proteins** attach the plasma membrane to other structures and stabilize its position. Inside the cell, membrane proteins are bound to the *cytoskeleton*, a network of supporting filaments in the cytoplasm. Outside the cell, other membrane proteins may attach the cell to extracellular protein fibers or to another cell.
2. *Recognition Proteins (Identifiers).* The cells of the immune system recognize other cells as normal or abnormal

Figure 3–2 The Plasma Membrane.



based on the presence or absence of characteristic **recognition proteins.** Many important recognition proteins are glycoproteins. ↩ p. 54 (We will discuss one group, the *MHC proteins* involved in the immune response, in Chapter 22.)

3. *Enzymes.* Enzymes in plasma membranes may be integral or peripheral proteins. They catalyze reactions in the extracellular fluid or in the cytosol, depending on the location of the protein and its active site. For example, dipeptides are broken down into amino acids by enzymes on the exposed membranes of cells that line the intestinal tract.
4. *Receptor Proteins.* **Receptor proteins** in the plasma membrane are sensitive to the presence of specific extracellular molecules called **ligands** (LĪ-gandz). A ligand can be anything from a small ion, like calcium, to a relatively large and complex hormone. An extracellular ligand will bind to the appropriate receptor, and that binding may trigger changes in the activity of the cell. For example, the binding of the hormone *insulin* to a specific membrane receptor protein is the key step that leads to an increase in the rate of glucose absorption by the cell. Plasma membranes differ in the type and number of receptor proteins they contain, and these differences account for a cell's sensitivity to specific hormones and other potential ligands.
5. *Carrier Proteins.* **Carrier proteins** bind solutes and transport them across the plasma membrane. Carrier proteins may require ATP as an energy source. ↩ p. 56 For example, virtually all cells have carrier proteins that bring glucose into the cytoplasm without expending ATP, but these cells must use ATP to transport ions such as sodium and calcium across the plasma membrane and out of the cytoplasm.
6. *Channels.* Some integral proteins contain a central pore, or **channel,** that forms a passageway completely across the plasma membrane. The channel permits the movement of water and small solutes across the plasma membrane. Ions do not dissolve in lipids, so they cannot cross the phospholipid bilayer. Thus, ions and other small water-soluble materials can cross the membrane only by passing through channels. Many channels are highly specific and permit the passage of only one particular ion. The movement of ions through channels is involved in a variety of physiological mechanisms. Although channels account for about 0.2 percent of the total surface area of the plasma membrane, they are extremely important in physiological processes like nerve impulse transmission and muscle contraction, described in Chapters 10 and 12.

Membranes are neither rigid nor uniform. At each location, the inner and outer surfaces of the plasma membrane may differ in important respects. For example, some cytoplasmic enzymes are found only on the inner surface of the membrane, and some receptors are found exclusively on its outer surface. Some embedded proteins are always confined to specific areas of the plasma membrane. These areas, called *rafts*, mark the location of anchoring proteins and some kinds of receptor proteins. Yet because membrane phospholipids are fluid at body temperature, many other integral proteins drift across the surface of the membrane like ice cubes in a bowl of punch. In addition, the composition of the entire plasma membrane can change over time, because large areas of the membrane surface are continually being removed and recycled in the process of metabolic turnover. ↩ p. 57

Membrane Carbohydrates

Carbohydrates account for about 3 percent of the weight of a plasma membrane. The carbohydrates in the plasma membrane are components of complex molecules such as *proteoglycans*, *glycoproteins*, and *glycolipids*. ↩ pp. 48, 54 The carbohydrate portions of these large molecules extend beyond the outer surface of the membrane, forming a layer known as the **glycocalyx** (glī-kō-KĀ-liks; *calyx*, cup). The glycocalyx has a variety of important functions, including the following:

- *Lubrication and Protection.* The glycoproteins and glycolipids form a viscous layer that lubricates and protects the plasma membrane.
- *Anchoring and Locomotion.* Because the components are sticky, the glycocalyx can help anchor the cell in place. It also takes part in the locomotion of specialized cells.
- *Specificity in Binding.* Glycoproteins and glycolipids can function as receptors, binding specific extracellular compounds. Such binding can alter the properties of the cell surface and indirectly affect the cell's behavior.
- *Recognition.* Cells involved with the immune response recognize glycoproteins and glycolipids as normal or abnormal. The characteristics of the glycocalyx are genetically determined. The body's immune system recognizes its own membrane glycoproteins and glycolipids as "self" rather than as "foreign." This recognition system keeps your immune system from attacking your cells, while still enabling it to recognize and destroy invading pathogens.

The plasma membrane serves as a barrier between the cytosol and the extracellular fluid. If the cell is to survive, dissolved substances and larger compounds must be permitted to move across this barrier. Metabolic wastes must be able to leave the cytosol, and nutrients must be able to enter the cell. The structure of the plasma membrane is ideally suited to this need for selective transport. We will discuss selective transport and other membrane functions further, after we have completed our overview of cellular anatomy.

3

Checkpoint

1. List the general functions of the plasma membrane.
2. Identify the components of the plasma membrane that allow it to perform its characteristic functions.
3. Which component of the plasma membrane is primarily responsible for the membrane's ability to form a physical barrier between the cell's internal and external environments?
4. Which type of integral protein allows water and small ions to pass through the plasma membrane?

See the blue Answers tab at the back of the book.

3-2 Organelles within the cytoplasm perform particular functions

Cytoplasm is a general term for the material located between the plasma membrane and the membrane surrounding the nucleus. A colloid with a consistency that varies between that of thin maple syrup and almost-set gelatin, cytoplasm contains many more proteins than does extracellular fluid. p. 40 As an indication of the importance of proteins to the cell, about 30 percent of a typical cell's weight is protein. The cytoplasm contains cytosol and organelles. **Cytosol,** or *intracellular fluid*, contains dissolved nutrients, ions, soluble and insoluble proteins, and waste products. **Organelles** are structures suspended within the cytosol that perform specific functions for the cell.

The Cytosol

The most important differences between cytosol and extracellular fluid are as follows:

1. The concentration of potassium ions is much higher in the cytosol than in the extracellular fluid. Conversely, the concentration of sodium ions is much lower in the cytosol than in the extracellular fluid.
2. The cytosol contains a much higher concentration of suspended proteins than does extracellular fluid. Many of the proteins are enzymes that regulate metabolic operations; others are associated with the various organelles. The consistency of the cytosol is determined in large part by the enzymes and cytoskeletal proteins.
3. The cytosol usually contains small quantities of carbohydrates, and small reserves of amino acids and lipids. The extracellular fluid is a transport medium only, and no reserves are stored there. The carbohydrates in the cytosol are broken down to provide energy, and the amino acids are used to manufacture proteins. Lipids, in particular triglycerides, are used primarily as a source of energy when carbohydrates are unavailable.

Both the cytosol and the extracellular fluid within tissues *(interstitial fluid)* may contain masses of insoluble materials. In the cytosol, these masses are known as **inclusions.** Among the most common inclusions are stored nutrients, such as glycogen granules in liver or in skeletal muscle cells, and lipid droplets in fat cells. Other common inclusions are pigment granules, such as the brown pigment *melanin* and the orange pigment *carotene*. Examples of insoluble materials in interstitial fluids include melanin in the skin and mineral deposits in bone.

The Organelles

Organelles are the internal structures that perform most of the tasks that keep a cell alive and functioning normally. Each organelle has specific functions related to cell structure, growth, maintenance, and metabolism. Cellular organelles can be divided into two broad categories, nonmembranous and membranous. **Nonmembranous organelles** are not completely enclosed by membranes, and all of their components are in direct contact with the cytosol. **Membranous organelles** are isolated from the cytosol by phospholipid membranes, just as the plasma membrane isolates the cytosol from the extracellular fluid.

The cell's nonmembranous organelles include the *cytoskeleton*, *microvilli*, *centrioles*, *cilia*, *ribosomes*, and *proteasomes*. Membranous organelles include the *endoplasmic reticulum*, the *Golgi apparatus*, *lysosomes*, *peroxisomes*, and *mitochondria*. The *nucleus*, also surrounded by a membranous envelope—and therefore, strictly speaking, a membranous organelle—has so many vital functions that we will consider it in a separate section.

The Cytoskeleton

The **cytoskeleton** functions as the cell's skeleton. It provides an internal protein framework that gives the cytoplasm strength and flexibility. The cytoskeleton of all cells includes *microfilaments*, *intermediate filaments*, and *microtubules*. Muscle cells contain these cytoskeletal parts plus *thick filaments*. The filaments of the cytoskeleton form a dynamic network. The organizational details remain poorly understood, because the network is extremely delicate and thus hard to study intact. **Figure 3–3a** is based on our current knowledge of cytoskeletal structure.

We will consider only a few of the many functions of the cytoskeleton in this section. In addition to the functions described here, the cytoskeleton plays a role in the metabolic organization of the cell by determining where in the cytoplasm key enzymatic reactions occur and where specific proteins are synthesized. For example, many intracellular enzymes—especially those involved with metabolism and energy production, and the ribosomes and RNA molecules responsible for the synthesis of proteins—are attached to the microfilaments and microtubules of the cytoskeleton. The varied metabolic functions of the cytoskeleton are now a subject of intensive research.

Microfilaments

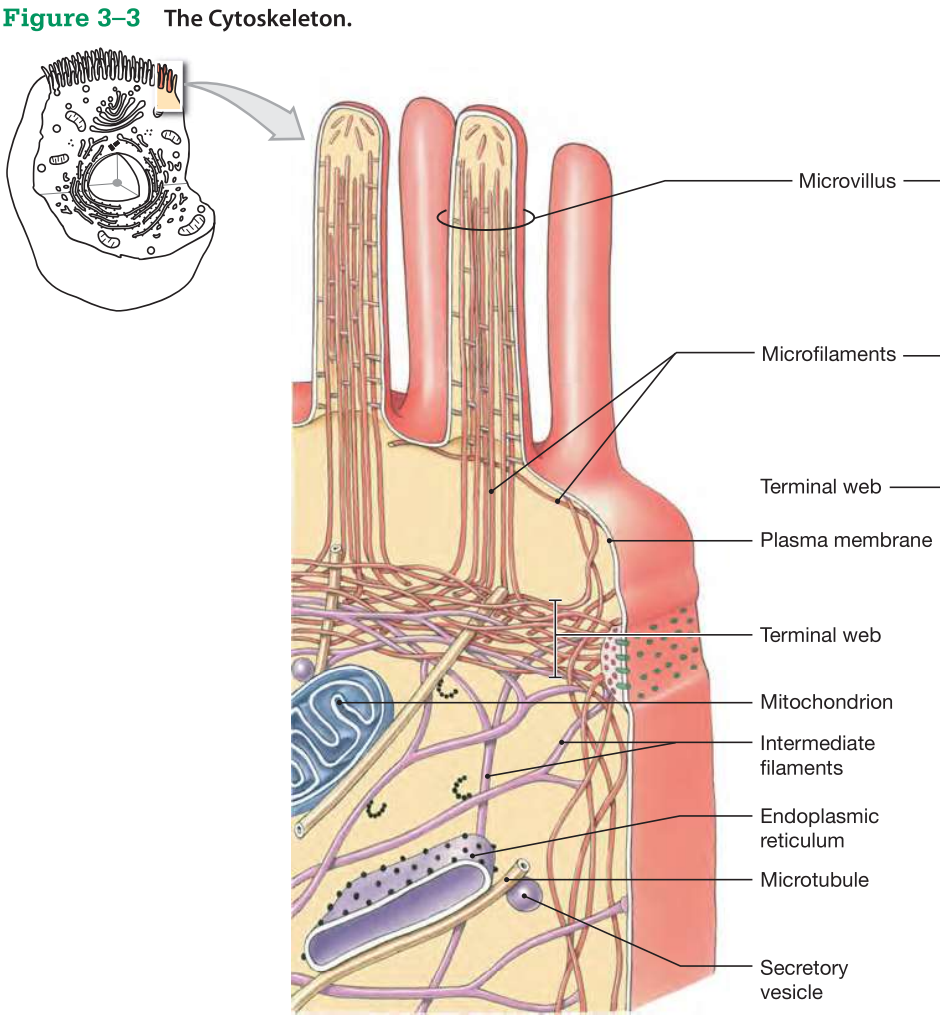
The smallest of the cytoskeletal elements are the **microfilaments.** These protein strands are generally less than 6 nm in diameter. Typical microfilaments are composed of the protein **actin.** In most cells, actin filaments are common in the periphery of the cell, but rare in the region immediately surrounding the nucleus. In cells that form a layer or lining, such as the lining of the intestinal tract, actin filaments also form a layer, called the *terminal web*, just inside the plasma membrane at the exposed surface of the cell (**Figure 3–3a**). Microfilaments have three major functions:

1. Microfilaments anchor the cytoskeleton to integral proteins of the plasma membrane. They give the cell additional mechanical strength and attach the plasma membrane to the enclosed cytoplasm.
2. Microfilaments, interacting with other proteins, determine the consistency of the cytoplasm. Where microfilaments form a dense, flexible network, the cytoplasm has a gelatinous consistency; where they are widely dispersed, the cytoplasm is more fluid.
3. Actin can interact with the protein *myosin* to produce movement of a portion of a cell or to change the shape of the entire cell.

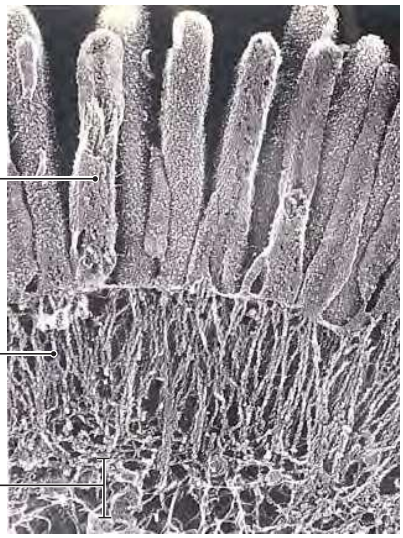
Intermediate Filaments

The protein composition of **intermediate filaments** varies among cell types. These filaments, which range from 7 to 11 nm in diameter, are intermediate in size between microfilaments and thick filaments. Intermediate filaments (1) strengthen the cell and help maintain its shape, (2) stabilize the positions of

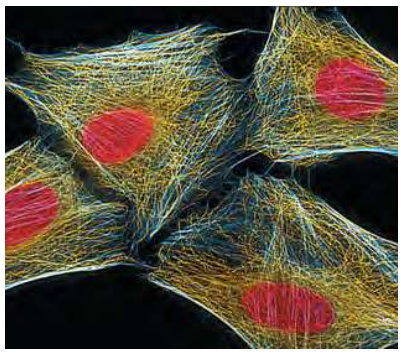
Figure 3–3 The Cytoskeleton.



a The cytoskeleton provides strength and structural support for the cell and its organelles. Interactions between cytoskeletal components are also important in moving organelles and in changing the shape of the cell.



b The microfilaments and microvilli of an intestinal cell. Such an image, produced by a scanning electron microscope, is called a scanning electron micrograph (SEM) (SEM × 30,000).



c Microtubules (yellow) in a living cell, as seen after special fluorescent labeling (LM × 3200).

organelles, and (3) stabilize the position of the cell with respect to surrounding cells through specialized attachment to the plasma membrane. Intermediate filaments, which are insoluble, are the most durable of the cytoskeletal elements. Many cells contain specialized intermediate filaments with unique functions. For example, the keratin fibers in superficial layers of the skin are intermediate filaments that make these layers strong and able to resist stretching.

Microtubules

Most cells contain **microtubules,** hollow tubes built from the globular protein **tubulin.** Microtubules are the largest components of the cytoskeleton, with diameters of about 25 nm. Microtubules extend outward into the periphery of the cell from a region near the nucleus called the *centrosome* (**Spotlight Figure 3–1**). The number and distribution of microtubules in the cell can change quickly over time. Each microtubule forms by the aggregation of tubulin molecules, growing out from its origin at the centrosome. The entire structure persists for a time and then disassembles into individual tubulin molecules again. Microtubules have the following functions:

1. Microtubules form the primary components of the cytoskeleton, giving the cell strength and rigidity and anchoring the position of major organelles.
2. The disassembly of microtubules provides a mechanism for changing the shape of the cell, perhaps assisting in cell movement.
3. Microtubules can serve as a kind of monorail system to move vesicles or other organelles within the cell. Proteins called *molecular motors* effect the movement. These proteins, which bind to the structure being moved, also bind to a microtubule and move along its length. The direction of movement depends on which of several known motor proteins is involved. For example, the molecular motors *kinesin* and *dynein* carry materials in opposite directions on a microtubule: Kinesin moves toward one end, dynein toward the other. Regardless of the direction of transport or the nature of the motor, the process requires ATP and is essential to normal cellular function.
4. During cell division, microtubules form the *spindle apparatus*, which distributes duplicated chromosomes to opposite ends of the dividing cell. We will consider this process in more detail in a later section.
5. Microtubules form structural components of organelles, such as *centrioles* and *cilia*.

Thick Filaments

Thick filaments are relatively massive bundles of subunits composed of the protein **myosin.** Thick filaments, which may reach 15 nm in diameter, appear only in muscle cells, where they interact with actin filaments to produce powerful contractions.

Microvilli

Many cells have small, finger-shaped projections of the plasma membrane on their exposed surfaces (**Figure 3–3b**). These projections, called **microvilli,** greatly increase the surface area of the cell exposed to the extracellular environment. Accordingly, they cover the surfaces of cells that are actively absorbing materials from the extracellular fluid, such as the cells lining the digestive tract. Microvilli have extensive connections with the cytoskeleton: A core of microfilaments stiffens each microvillus and anchors it to the cytoskeleton at the terminal web.

Centrioles

All animal cells capable of undergoing cell division contain a pair of **centrioles,** cylindrical structures composed of short microtubules (**Figure 3–4a**). The microtubules form nine groups, three in each group. Each of these nine "triplets" is connected to its nearest neighbors on either side. Because there are no central microtubules, this organization is called a *9 + 0 array*. (An axial structure with radial spokes leading toward the microtubular groups has also been observed, but its function is not known.)

During cell division, the centrioles form the spindle apparatus associated with the movement of DNA strands. Mature red blood cells, skeletal muscle cells, cardiac muscle cells, and typical neurons have no centrioles; as a result, these cells cannot divide.

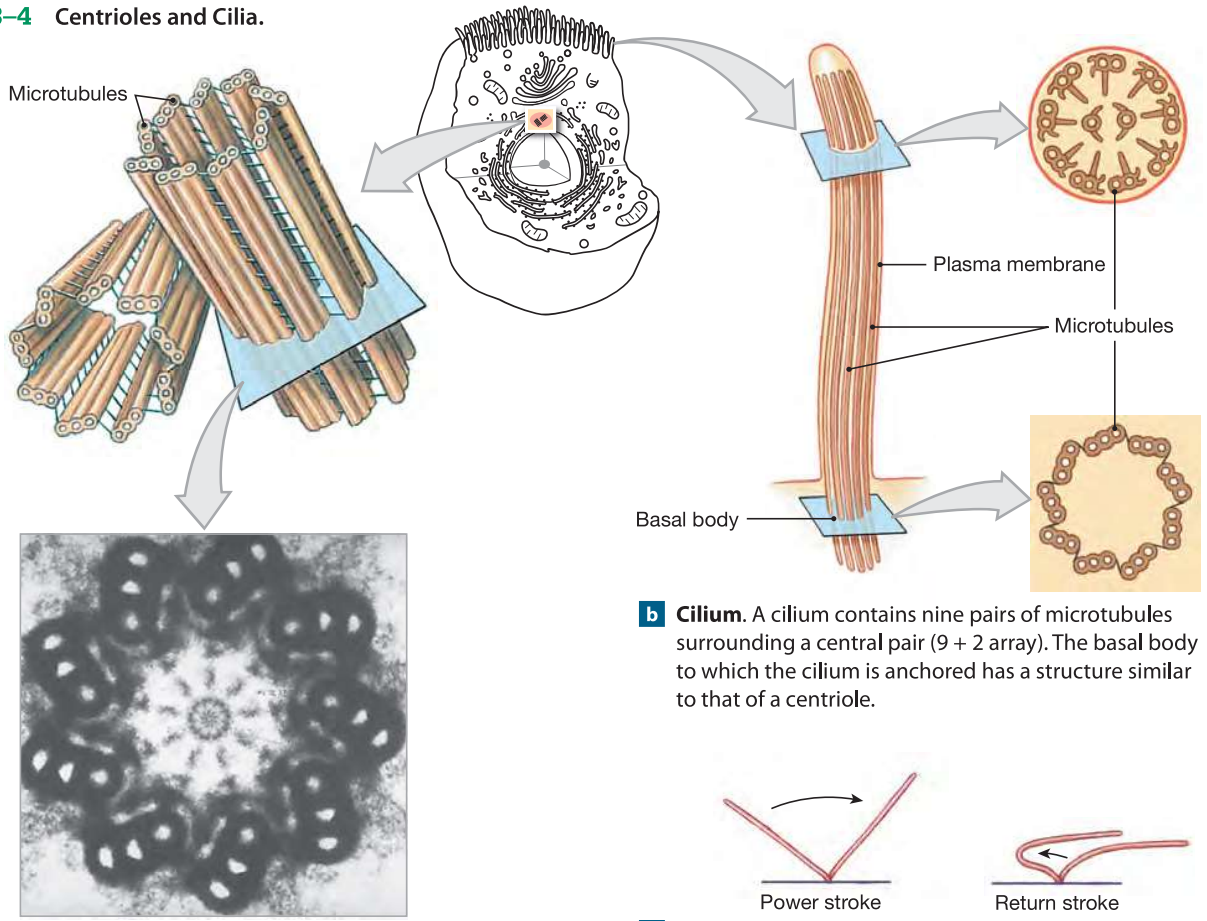
Centrioles are intimately associated with the cytoskeleton. The **centrosome,** the cytoplasm surrounding the centrioles, is the heart of the cytoskeletal system. Microtubules of the cytoskeleton generally begin at the centrosome and radiate through the cytoplasm.

Cilia

Cilia (singular, *cilium*) are fairly long, slender extensions of the plasma membrane. They are found on cells lining both the respiratory and reproductive tracts, and at various other locations in the body. Cilia have an internal arrangement similar to that of centrioles. However, in cilia, nine *pairs* of microtubules (rather than triplets) surround a central pair (**Figure 3–4b**)—an organization known as a *9 + 2 array*. The microtubules are anchored to a compact **basal body** situated just beneath the cell surface. The organization of microtubules in the basal body resembles the array of a centriole: nine triplets with no central pair.

Cilia are important because they can "beat" rhythmically to move fluids or secretions across the cell surface (**Figure 3–4c**). The cilium is relatively stiff during the effective *power stroke* and flexible during the *return stroke*. The ciliated cells along your trachea beat their cilia in synchronized waves to move sticky mucus and trapped dust particles toward the throat and away from delicate respiratory surfaces. If the cilia are damaged or immobilized by heavy smoking or a metabolic problem, the cleansing action is lost and the irritants will no longer be removed. As a result, a chronic cough and respiratory infections develop. Ciliated cells also move oocytes along the uterine tubes, and sperm from the testes into the male reproductive tract.

Figure 3–4 Centrioles and Cilia.



a **Centriole.** A centriole consists of nine microtubule triplets (known as a 9 + 0 array). A pair of centrioles orientated at right angles to one another occupies the centrosome. This micrograph, produced by a transmission electron microscope, is called a TEM.

b **Cilium.** A cilium contains nine pairs of microtubules surrounding a central pair (9 + 2 array). The basal body to which the cilium is anchored has a structure similar to that of a centriole.

c **Ciliary movement.** Action of a single cilium. During the power stroke, the cilium is relatively stiff; during the return stroke, it bends and returns to its original position.

Ribosomes

Proteins are produced within cells, using information provided by the DNA of the nucleus. The organelles responsible for protein synthesis are called **ribosomes.** The number of ribosomes in a particular cell varies with the type of cell and its demand for new proteins. For example, liver cells, which manufacture blood proteins, contain far more ribosomes than do fat cells (adipocytes), which primarily synthesize lipids.

Individual ribosomes are not visible with the light microscope. In an electron micrograph, they appear as dense granules approximately 25 nm in diameter. Each ribosome is about 60 percent RNA and 40 percent protein.

A functional ribosome consists of two subunits that are normally separate and distinct. One is called a **small ribosomal subunit** and the other a **large ribosomal subunit.** These subunits contain special proteins and **ribosomal RNA (rRNA),** one of the RNA types introduced in Chapter 2. Before protein synthesis can begin, a small and a large ribosomal subunit must join together with a strand of *messenger RNA* (*mRNA*, another type of RNA).

Two major types of functional ribosomes are found in cells: free ribosomes and fixed ribosomes. **Free ribosomes** are scattered throughout the cytoplasm. The proteins they manufacture enter the cytosol. **Fixed ribosomes** are attached to the *endoplasmic reticulum (ER)*, a membranous organelle. Proteins manufactured by fixed ribosomes enter the ER, where they are modified and packaged for secretion. We will examine ribosomal structure and functions in later sections, when we discuss the endoplasmic reticulum and protein synthesis.

Proteasomes

Free ribosomes produce proteins within the cytoplasm; the smaller proteasomes remove the proteins. **Proteasomes** are organelles that contain an assortment of protein-digesting (proteolytic)

enzymes, or *proteases*. Cytoplasmic enzymes attach chains of *ubiquitin*, a molecular "tag," to proteins destined for recycling. Tagged proteins are quickly transported into the proteasome. Once inside, they are rapidly disassembled into amino acids and small peptides, which are released into the cytoplasm.

Proteasomes are responsible for removing and recycling damaged or denatured proteins, and for breaking down abnormal proteins, such as those produced within cells infected by viruses. They also play a key role in the immune response, as we will see in Chapter 22.

Spotlight Figure 3–1 provides a review of the characteristics of nonmembranous organelles.

The Endoplasmic Reticulum

The **endoplasmic reticulum** (en-dō-PLAZ-mik re-TIK-ū-lum), or **ER,** is a network of intracellular membranes connected to the *nuclear envelope*, which surrounds the nucleus. The name *endoplasmic reticulum* is very descriptive. *Endo-* means "within," *plasm* refers to the cytoplasm, and a *reticulum* is a network. The ER has four major functions:

1. *Synthesis.* Specialized regions of the ER synthesize proteins, carbohydrates, and lipids.
2. *Storage.* The ER can store synthesized molecules or materials absorbed from the cytosol without affecting other cellular operations.
3. *Transport.* Materials can travel from place to place in the ER.
4. *Detoxification.* Drugs or toxins can be absorbed by the ER and neutralized by enzymes within it.

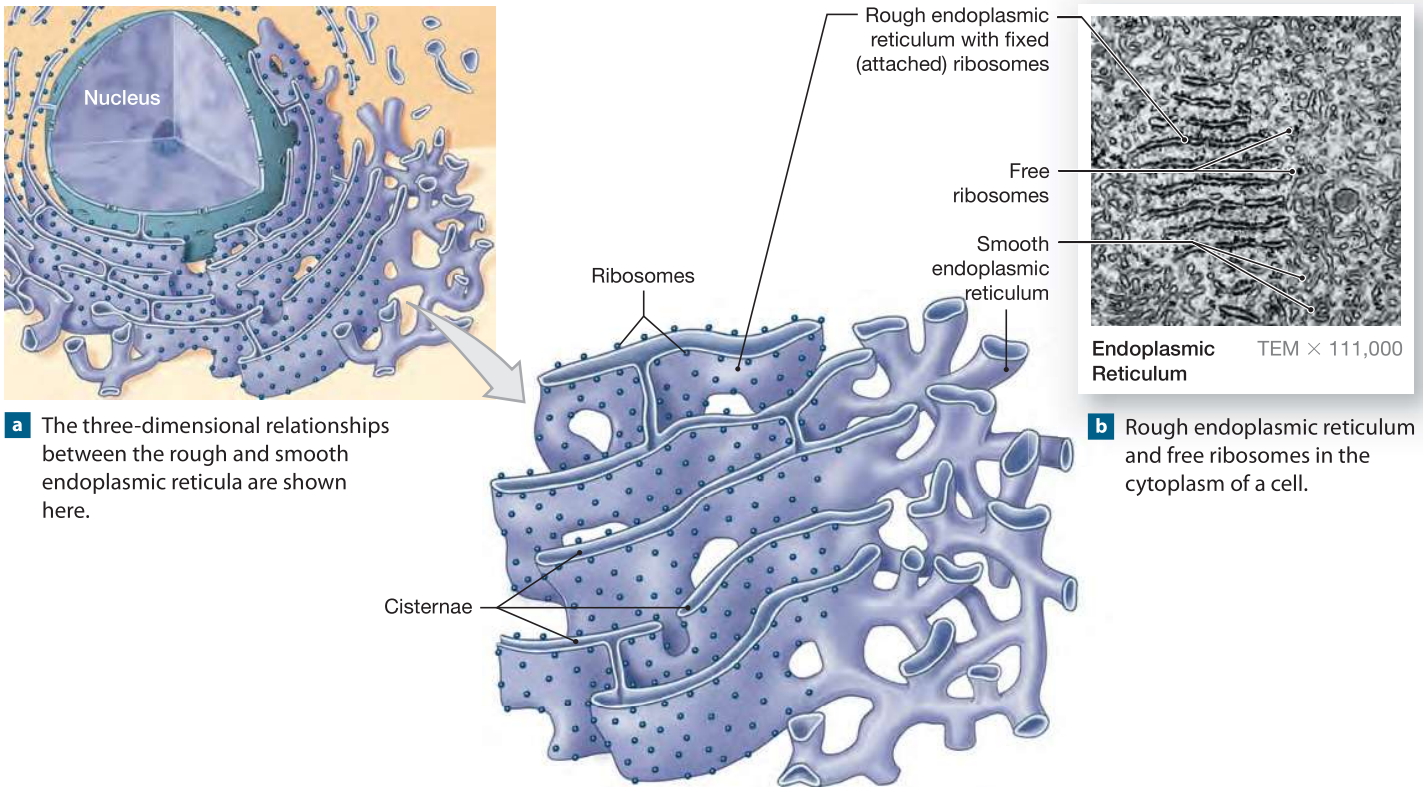
The ER forms hollow tubes, flattened sheets, and chambers called **cisternae** (sis-TUR-nē; singular, *cisterna*, a reservoir for water). Two types of ER exist: *smooth endoplasmic reticulum* and *rough endoplasmic reticulum* (**Figure 3–5**).

Smooth Endoplasmic Reticulum

The term "smooth" refers to the fact that no ribosomes are associated with the smooth endoplasmic reticulum (SER). The SER has the following functions, all associated with the synthesis of lipids and carbohydrates:

- Synthesis of the phospholipids and cholesterol needed for maintenance and growth of the plasma membrane, ER, nuclear membrane, and Golgi apparatus in all cells
- Synthesis of steroid hormones, such as *androgens* and *estrogens* (the dominant sex hormones in males and in females, respectively) in the reproductive organs
- Synthesis and storage of glycerides, especially triacylglycerides, in liver cells and adipocytes
- Synthesis and storage of glycogen in skeletal muscle and liver cells

Figure 3–5 The Endoplasmic Reticulum.



a The three-dimensional relationships between the rough and smooth endoplasmic reticula are shown here.

b Rough endoplasmic reticulum and free ribosomes in the cytoplasm of a cell.

In muscle cells, neurons, and many other types of cells, the SER also adjusts the composition of the cytosol by absorbing and storing ions, such as Ca^{2+} or larger molecules. In addition, the SER in liver and kidney cells is responsible for the detoxification or inactivation of drugs.

Rough Endoplasmic Reticulum

The rough endoplasmic reticulum (RER) functions as a combination workshop and shipping warehouse. It is where many newly synthesized proteins are chemically modified and packaged for export to their next destination, the *Golgi apparatus*.

The ribosomes on the outer surface of the rough endoplasmic reticulum are fixed ribosomes (**Figure 3–5**). Their presence gives the RER a beaded, grainy, or rough appearance. Both free and fixed ribosomes synthesize proteins using instructions provided by messenger RNA. The new polypeptide chains produced at fixed ribosomes are released into the cisternae of the RER. Inside the RER, each protein assumes its secondary and tertiary structures. ↩ p. 51 Some of the proteins are enzymes that will function inside the endoplasmic reticulum. Other proteins are chemically modified by the attachment of carbohydrates, creating glycoproteins. Most of the proteins and glycoproteins produced by the RER are packaged into small membranous sacs that pinch off from the tips of the cisternae. These **transport vesicles** subsequently deliver their contents to the Golgi apparatus.

The amount of endoplasmic reticulum and the proportion of RER to SER vary with the type of cell and its ongoing activities. For example, pancreatic cells that manufacture digestive enzymes contain an extensive RER, but the SER is relatively small. The situation is just the reverse in the cells of reproductive organs that synthesize steroid hormones.

The Golgi Apparatus

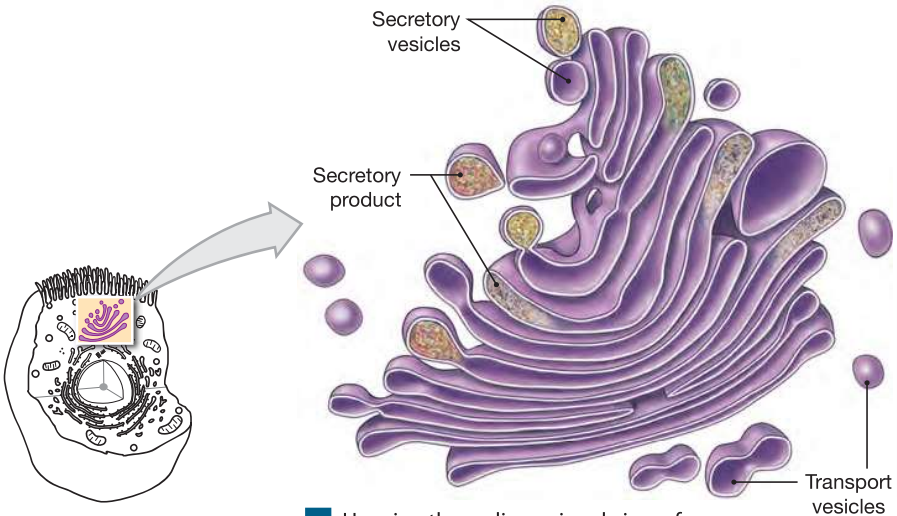
When a transport vesicle carries a newly synthesized protein or glycoprotein that is destined for export from the cell, it travels from the ER to an organelle that looks a bit like a stack of dinner plates. This organelle, the **Golgi** (GŌL-jē) **apparatus** (**Figure 3–6**), typically consists of five or six flattened membranous discs called *cisternae*. A single cell may contain several of these organelles, most often near the nucleus.

The Golgi apparatus has three major functions: It (1) modifies and packages secretions, such as hormones or enzymes, for release through exocytosis; (2) renews or modifies the plasma membrane; and (3) packages special enzymes within vesicles for use in the cytoplasm.

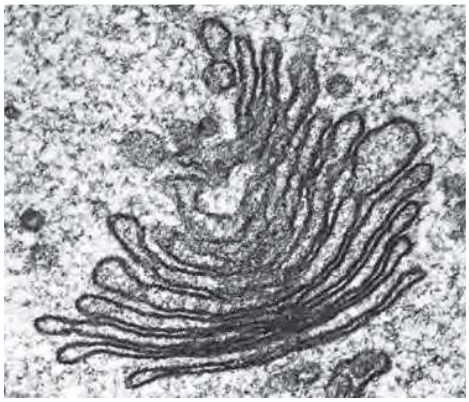
Lysosomes

Cells often need to break down and recycle large organic molecules and even complex structures like organelles. The breakdown process requires the use of powerful enzymes, and it often generates toxic chemicals that could damage or kill the cell. **Lysosomes** (LĪ-sō-sōmz; *lyso-*, a loosening + *soma*, body) are special vesicles that provide an isolated environment for potentially dangerous chemical reactions. These vesicles, produced at the Golgi apparatus, contain digestive enzymes. Lysosomes are small, often spherical bodies with contents that look dense and dark in electron micrographs (**Spotlight Figure 3–7**).

Figure 3–6 The Golgi Apparatus.



a Here is a three-dimensional view of the Golgi apparatus with a cut edge.



Golgi apparatus TEM × 42,000

b This is a sectional view of the Golgi apparatus of an active secretory cell.

Spotlight

Figure 3–7
Protein Synthesis

The Golgi apparatus plays a major role in modifying and packaging newly synthesized proteins. Some proteins and glycoproteins synthesized in the rough endoplasmic reticulum (RER) are delivered to the Golgi apparatus by transport vesicles. Here's a summary of the process, beginning with DNA.

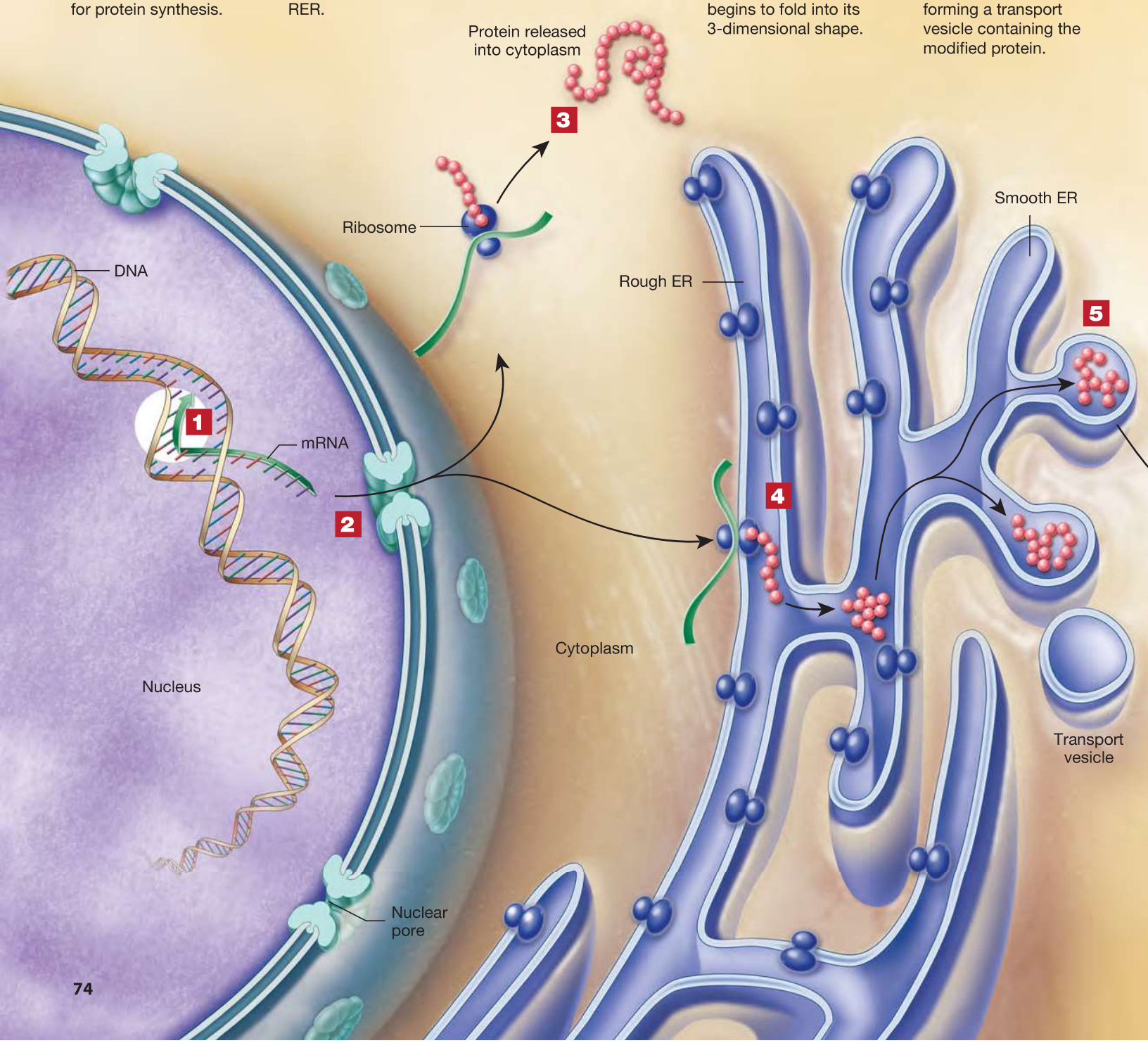
1 Protein synthesis begins when a gene on DNA produces messenger RNA (mRNA), the template for protein synthesis.

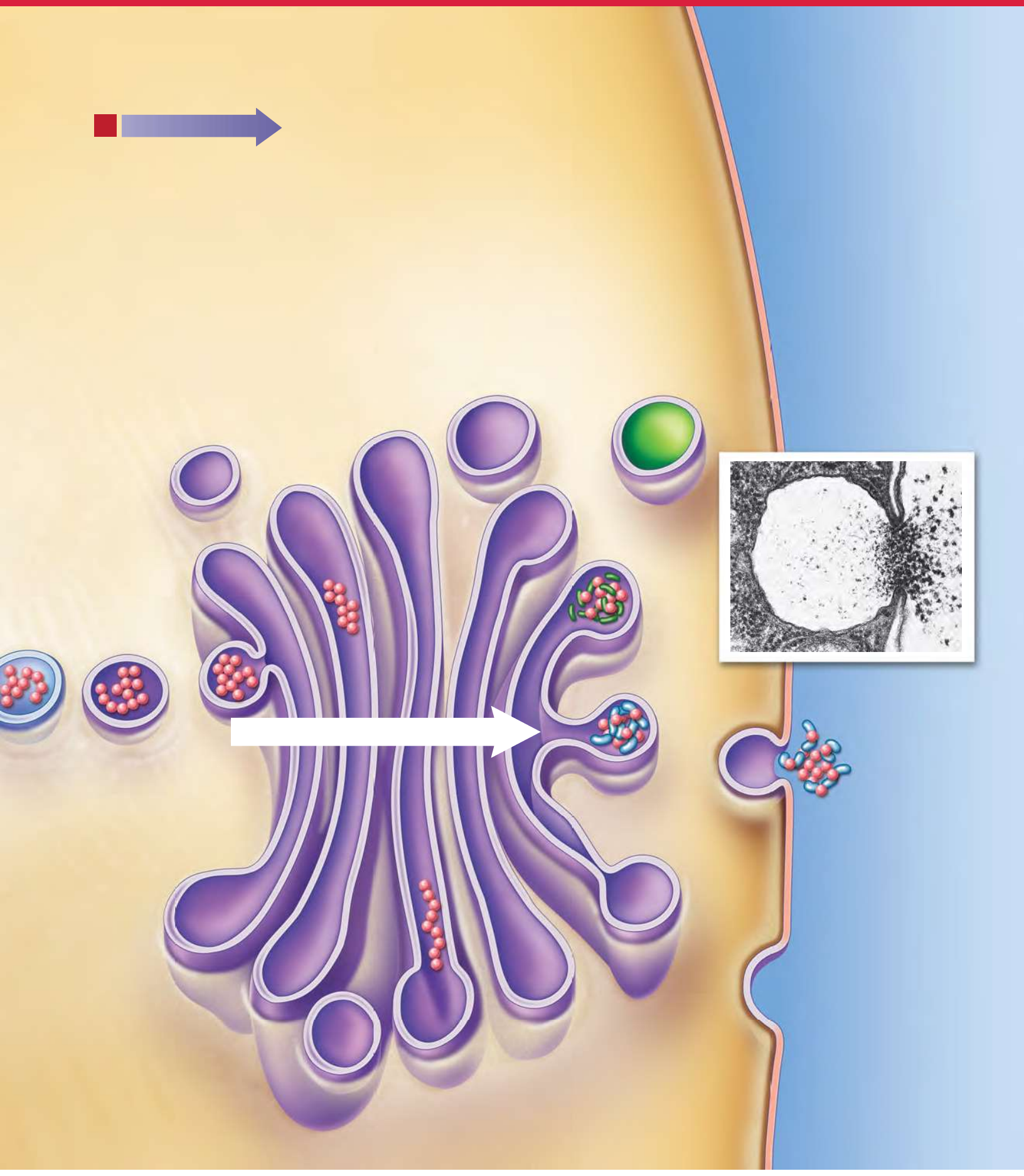
2 The mRNA leaves the nucleus and attaches to a free ribosome in the cytoplasm, or a fixed ribosome on the RER.

3 Proteins constructed on free ribosomes are released into the cytoplasm for use within the cell.

4 When a protein is synthesized on fixed ribosomes, it is threaded into the hollow tubes of the ER where it begins to fold into its 3-dimensional shape.

5 The proteins are then modified within the hollow tubes of the ER. A region of the ER then buds off, forming a transport vesicle containing the modified protein.





Lysosomes have several functions (**Figure 3–8**). *Primary lysosomes* contain inactive enzymes. When these lysosomes fuse with the membranes of damaged organelles (such as mitochondria or fragments of the ER), the enzymes are activated and *secondary lysosomes* are formed. These enzymes then break down the lysosomal contents. The cytosol reabsorbs released nutrients, and the remaining material is eliminated from the cell by exocytosis.

Lysosomes also function in the destruction of bacteria (as well as liquids and organic debris) that enter the cell from the extracellular fluid. The cell encloses these substances in a small portion of the plasma membrane, which is then pinched off to form a transport vesicle, or *endosome*, in the cytoplasm. (This method of transporting substances into the cell, called *endocytosis*, will be discussed later in this chapter.) When a primary lysosome fuses with the vesicle, activated enzymes in the secondary lysosome break down the contents and release usable substances, such as sugars or amino acids. In this way, the cell both protects itself against harmful substances and obtains valuable nutrients.

Lysosomes also perform essential cleanup and recycling functions inside the cell. For example, when muscle cells are inactive, lysosomes gradually break down their contractile proteins. (This mechanism accounts for the reduction in muscle mass that accompanies aging.) The process is usually precisely controlled, but in a damaged or dead cell, the regulatory mechanism fails. Lysosomes then disintegrate, releasing enzymes that become activated within the cytosol. These enzymes rapidly destroy the cell's proteins and organelles in a process called **autolysis** (aw-TOL-i-sis; *auto-*, self). We do not know how to control lysosomal activities or why the enclosed enzymes do not digest the lysosomal membranes unless the cell is damaged.

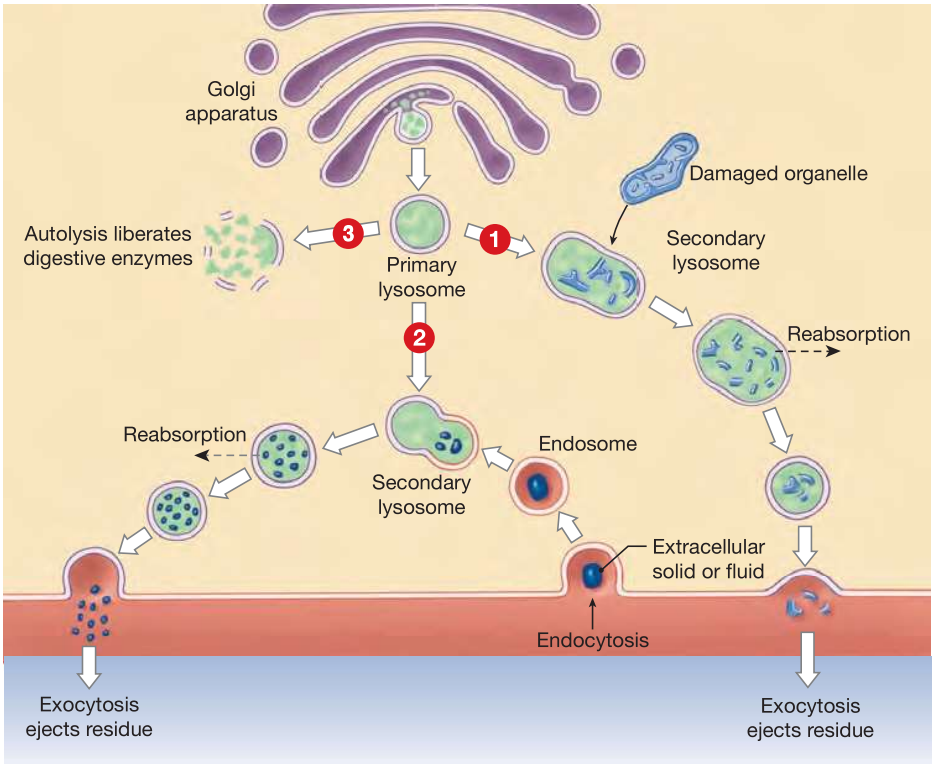
Problems with lysosomal enzyme production cause more than 30 serious diseases affecting children. In these conditions, called *lysosomal storage diseases*, the lack of a specific lysosomal enzyme results in the buildup of waste products and debris normally removed and recycled by lysosomes. Affected individuals may die when vital cells, such as those of the heart, can no longer function.

Peroxisomes

Peroxisomes are smaller than lysosomes and carry a different group of enzymes. In contrast to lysosomes, which are produced at the Golgi apparatus, new peroxisomes are produced by the growth and subdivision of existing peroxisomes. Their enzymes are produced at free ribosomes and transported from the cytosol into the peroxisomes by carrier proteins.

Peroxisomes absorb and break down fatty acids and other organic compounds. As they do so, peroxisomes generate hydrogen

Figure 3–8 **Lysosome Functions.** Primary lysosomes, formed at the Golgi apparatus, contain inactive enzymes. Activation may occur under any of the three basic conditions indicated here.



Activation of lysosomes occurs when:

1. A primary lysosome fuses with the membrane of another organelle, such as a mitochondrion
2. A primary lysosome fuses with an endosome containing fluid or solid materials from outside the cell
3. The lysosomal membrane breaks down during autolysis following injury to, or death of, the cell

peroxide (H_2O_2), a potentially dangerous free radical. p. 32 Catalase, the most abundant enzyme within the peroxisome, then breaks down the hydrogen peroxide to oxygen and water. Peroxisomes thus protect the cell from the potentially damaging effects of free radicals produced during catabolism. While these organelles are present in all cells, their numbers are highest in metabolically active cells, such as liver cells.

Membrane Flow

When the temperature changes markedly, you change your clothes. Similarly, when a cell's environment changes, it alters the structure and properties of its plasma membrane. With the exception of mitochondria, all membranous organelles in the cell are either interconnected or in communication through the movement of vesicles. The RER and SER are continuous and are connected to the nuclear envelope. Transport vesicles connect the ER with the Golgi apparatus, and secretory vesicles link the Golgi apparatus with the plasma membrane. Finally, vesicles forming at the exposed surface of the cell remove and recycle segments of the plasma membrane. This continuous movement and exchange is called **membrane flow.** In an actively secreting cell, an area equal to the entire membrane surface may be replaced each hour.

Membrane flow is an example of the dynamic nature of cells. It provides a mechanism for cells to change the characteristics of their plasma membranes—the lipids, receptors, channels, anchors, and enzymes—as they grow, mature, or respond to a specific environmental stimulus.

Mitochondria

Cells, like other living things, require energy to carry out the functions of life. The organelles responsible for energy production are the **mitochondria** (mī-tō-KON-drē-ūh; singular, *mitochondrion*; *mitos*, thread + *chondrion*, granule). These small structures vary widely in shape, from long and slender to short and fat. The number of mitochondria in a particular cell varies with the cell's energy demands. Red blood cells lack mitochondria altogether, whereas these organelles may account for 30 percent of the volume of a heart muscle cell.

Mitochondria have an unusual double membrane (**Figure 3–9a**). The outer membrane surrounds the organelle. The inner membrane contains numerous folds called **cristae.** Cristae increase the surface area exposed to the fluid contents, or **matrix,** of the mitochondrion. Metabolic enzymes in the matrix catalyze the reactions that provide energy for cellular functions.

Most of the chemical reactions that release energy occur in the mitochondria, but most of the cellular activities that require energy occur in the surrounding cytoplasm. Cells must therefore store energy in a form that can be moved from place to place. Recall from Chapter 2 that cellular energy is stored and transferred in the form of *high-energy bonds*, such as those that attach a phosphate group (PO_4^{3-}) to adenosine diphosphate (ADP), creating the high-energy compound *adenosine triphosphate* (ATP). Cells can break the high-energy bond under controlled conditions, reconverting ATP to ADP and phosphate and thereby releasing energy for the cell's use.

Mitochondrial Energy Production. Most cells generate ATP and other high-energy compounds through the breakdown of carbohydrates, especially glucose. We will examine the entire process in Chapter 25, but a few basic concepts now will help you follow discussions of muscle contraction, neuron function, and endocrine function in Chapters 10–18.

Although most ATP production occurs inside mitochondria, the first steps take place in the cytoplasm (**Figure 3–9b**). In this reaction sequence, called **glycolysis** (*glycos*, sugar + *-lysis*, a loosening), each glucose molecule is broken down into two molecules of *pyruvate*. The pyruvate molecules are then absorbed by mitochondria.

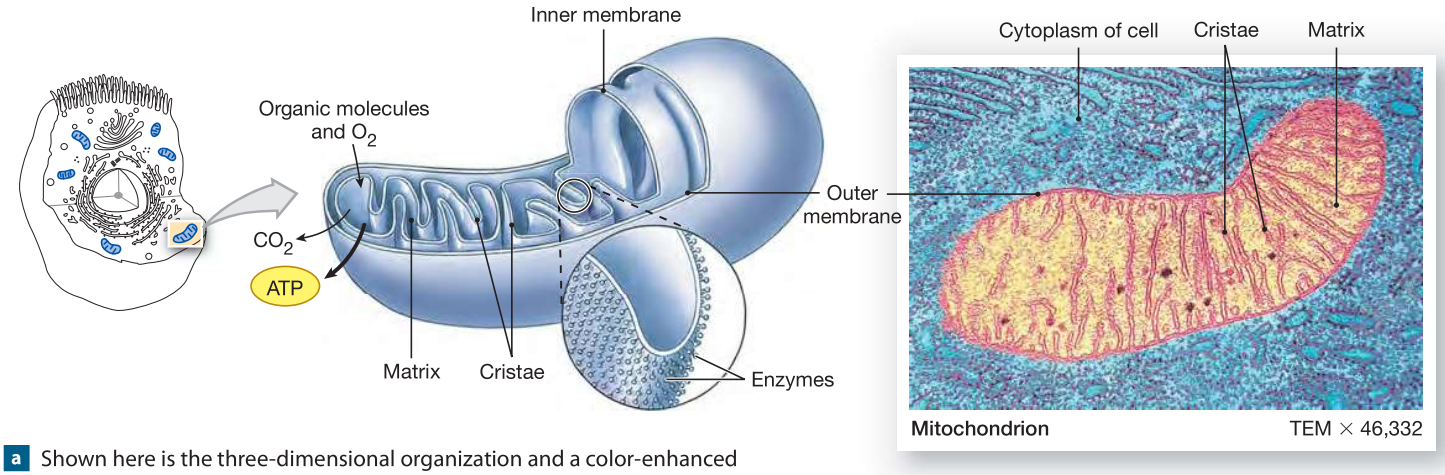
In the mitochondrial matrix, a CO_2 molecule is removed from each absorbed pyruvate molecule; the remainder enters the **citric acid cycle** (also known as the *Krebs cycle* and the *tricarboxylic acid cycle* or *TCA cycle*). The citric acid cycle is an enzymatic pathway that breaks down the absorbed pyruvate. The remnants of pyruvate molecules contain carbon, oxygen, and hydrogen atoms. The carbon and oxygen atoms are released as carbon dioxide, which diffuses out of the cell. The hydrogen atoms are delivered to carrier proteins in the cristae. The electrons from the hydrogen atoms are then removed and passed along a chain of coenzymes until they are ultimately transferred to oxygen atoms. The energy released during these steps indirectly supports the enzymatic conversion of ADP to ATP. p. 57

Because mitochondrial activity requires oxygen, this method of ATP production is known as **aerobic metabolism** (*aer*, air + *bios*, life), or *cellular respiration*. Aerobic metabolism in mitochondria produces about 95 percent of the ATP needed to keep a cell alive. (Enzymatic reactions in the cytoplasm produce the rest.)

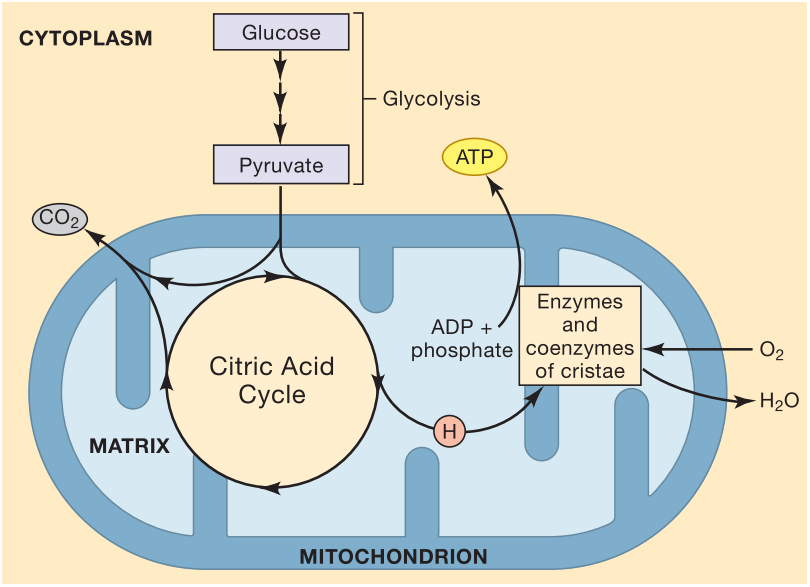
Clinical Note

Inheritable Mitochondrial Disorders Several inheritable disorders result from abnormal mitochondrial activity. While not totally self-sufficient, mitochondria do contain DNA and manufacture many of their own proteins under the direction of the genes on this DNA. The mitochondria involved in congenital diseases contain abnormal DNA, and the enzymes they produce reduce the efficiency of ATP production. Cells throughout the body may be affected, but symptoms involving muscle cells, neurons, and the receptor cells in the eye are most common, because these cells have especially high energy demands.

Figure 3–9 Mitochondria.



a Shown here is the three-dimensional organization and a color-enhanced TEM of a typical mitochondrion in section.



b This is an overview of the role of mitochondria in energy production. Mitochondria absorb short carbon chains (such as pyruvate) and oxygen and generate carbon dioxide and ATP.

Checkpoint

5. Differentiate between the cytoplasm and the cytosol.
6. What are the major differences between cytosol and extracellular fluid?
7. Identify the nonmembranous organelles, and cite a function of each.
8. Identify the membranous organelles, and cite their functions.
9. What does the presence of many mitochondria imply about a cell's energy requirements?
10. Explain why certain cells in the ovaries and testes contain large amounts of smooth endoplasmic reticulum (SER).

See the blue Answers tab at the back of the book.

3-3 The nucleus contains DNA and enzymes essential for controlling cellular activities

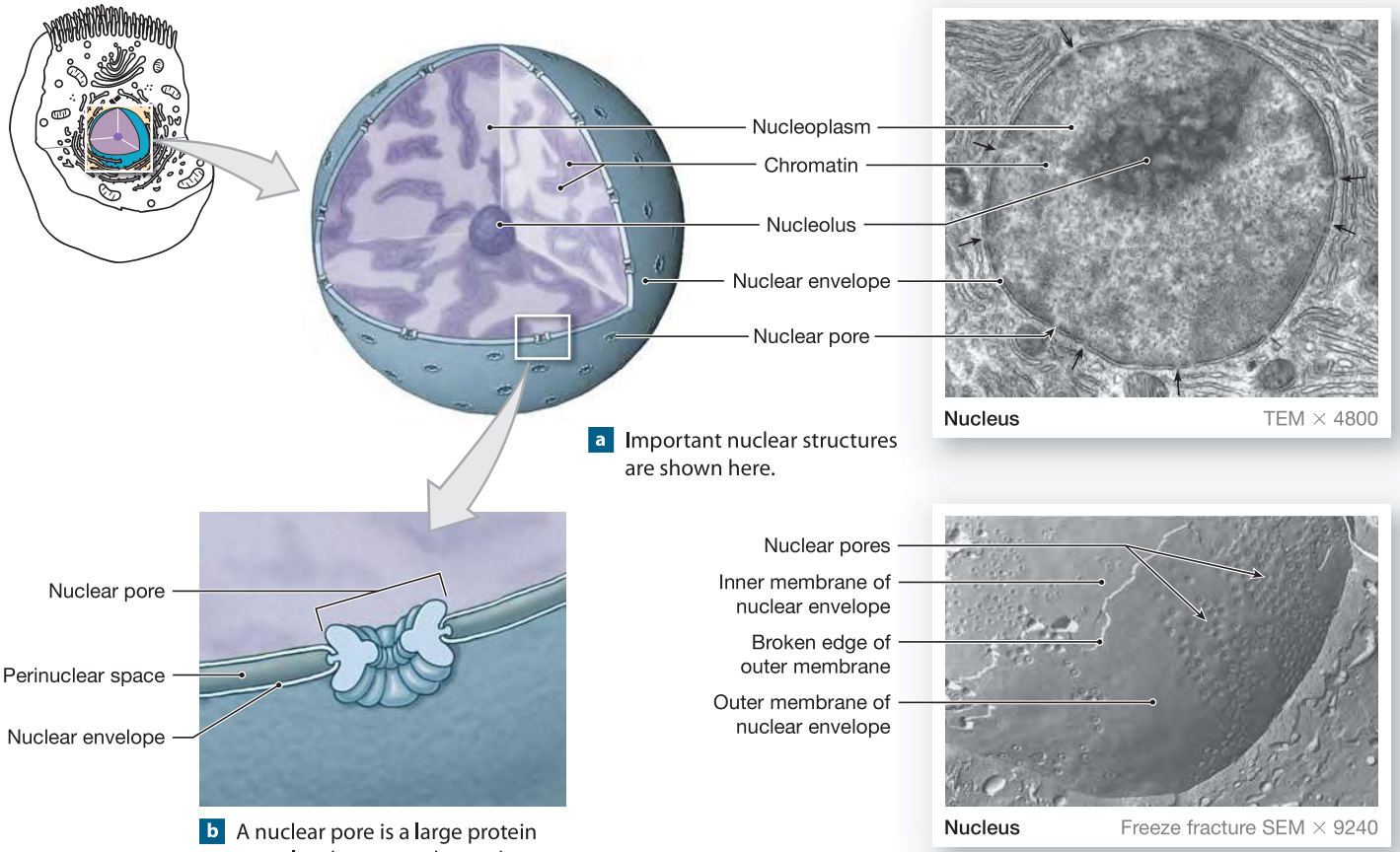
The **nucleus** is usually the largest and most conspicuous structure in a cell; under a light microscope, it is often the only organelle visible. The nucleus serves as the control center for cellular operations. A single nucleus stores all the information needed to direct the synthesis of the more than 100,000 different proteins in the human body. The nucleus determines the structure of the cell and what functions it can perform by controlling which proteins are synthesized, under what circumstances, and in what amounts. A cell without a nucleus cannot repair itself, and it will disintegrate within three or four months.

Most cells contain a single nucleus, but exceptions exist. For example, skeletal muscle cells have many nuclei, whereas mature red blood cells have none. **Figure 3–10** details the structure of a typical nucleus. Surrounding the nucleus and separating it from the cytosol is a **nuclear envelope,** a double membrane with its two layers separated by a narrow **perinuclear space** (*peri-*, around). At several locations, the nuclear envelope is connected to the rough endoplasmic reticulum (**Spotlight Figure 3–1**). To direct processes that take place in the cytoplasm, the nucleus must receive information about conditions and activities in other parts of the cell. Chemical communication between the nucleus and the cytoplasm occurs through **nuclear pores.** These pores, which cover about 10 percent of the surface of the nucleus, are large enough to permit the movement of ions and small molecules, but are too small for the free passage of proteins or DNA. Each nuclear pore contains regulatory proteins that govern the transport of specific proteins and RNA into or out of the nucleus.

Contents of the Nucleus

The fluid contents of the nucleus are called the *nucleoplasm*. The nucleoplasm contains the **nuclear matrix,** a network of fine filaments that provides structural support and may be involved in the regulation of genetic activity. The nucleoplasm also contains ions, enzymes, RNA and DNA nucleotides, small amounts of RNA, and DNA.

Figure 3–10 The Nucleus.



a Important nuclear structures are shown here.

b A nuclear pore is a large protein complex that spans the nuclear envelope.

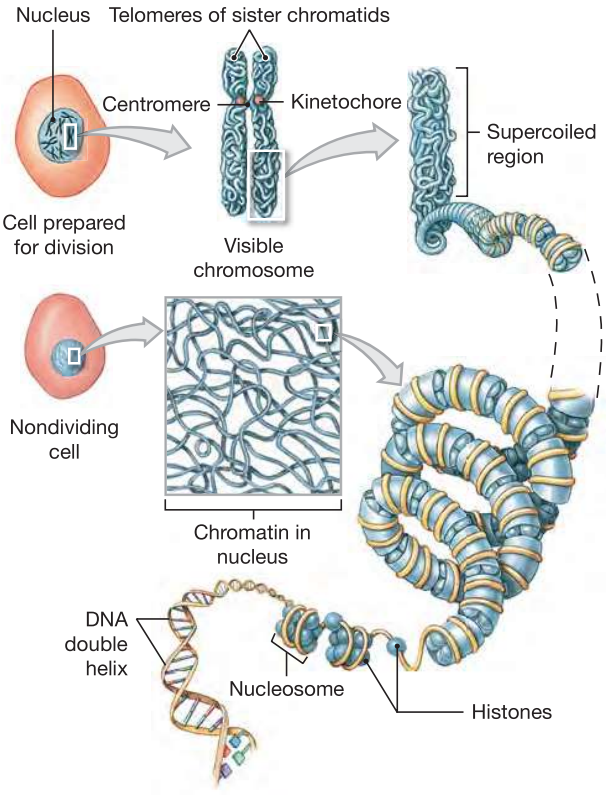
c This cell was frozen and then broken apart to make its internal structures visible. The technique, called *freeze fracture* or *freeze-etching*, provides a unique perspective on the internal organization of cells. The nuclear envelope and nuclear pores are visible. The fracturing process broke away part of the outer membrane of the nuclear envelope, and the cut edge of the nucleus can be seen.

3

Most nuclei contain several dark-staining areas called **nucleoli** (noo-KLĒ-ō-lī; singular, *nucleolus*). Nucleoli are transient nuclear organelles that synthesize ribosomal RNA. They also assemble the ribosomal subunits, which reach the cytoplasm by carrier-mediated transport at the nuclear pores. Nucleoli are composed of RNA, enzymes, and proteins called **histones.** The nucleoli form around portions of DNA that contain the instructions for producing ribosomal proteins and RNA when those instructions are being carried out. Nucleoli are most prominent in cells that manufacture large amounts of proteins, such as liver, nerve, and muscle cells, because those cells need large numbers of ribosomes.

It is the DNA in the nucleus that stores the instructions for protein synthesis. Interactions between the DNA and the histones help determine the information available to the cell at any moment. The organization of DNA within the nucleus is shown in **Figure 3–11**. At intervals, the DNA strands wind around the histones, forming a complex known as a **nucleosome.** Such winding allows a great deal of DNA to be packaged in a small space. The entire chain of nucleosomes may coil around other proteins. The degree of coiling varies depending on whether cell division is under way. In cells that are not dividing, the nucleosomes are loosely coiled within the nucleus, forming a tangle of fine filaments known as **chromatin.** Chromatin gives the nucleus a clumped, grainy appearance. Just before cell division begins, the coiling becomes tighter, forming distinct structures called **chromosomes** (*chroma*, color). In humans, the nuclei of somatic cells contain 23 pairs of chromosomes. One member of each pair is derived from the mother, and one from the father.

Figure 3–11 The Organization of DNA within the Nucleus. DNA strands are coiled around histones to form nucleosomes. Nucleosomes form coils that may be very tight or rather loose. In cells that are not dividing, the DNA is loosely coiled, forming a tangled network known as chromatin. When the coiling becomes tighter, as it does in preparation for cell division, the DNA becomes visible as distinct structures called chromosomes.



Information Storage in the Nucleus

As we saw in Chapter 2, each protein molecule consists of a unique sequence of amino acids. ↩ p. 50 Any "recipe" for a protein, therefore, must specify the order of amino acids in the polypeptide chain. This information is stored in the chemical structure of the DNA strands in the nucleus. The chemical "language" the cell uses is known as the **genetic code.** An understanding of the genetic code has enabled us to determine how cells build proteins and how various structural and functional characteristics are inherited from generation to generation.

To understand how the genetic code works, recall the basic structure of nucleic acids described in Chapter 2. ↩ p. 50 A single DNA molecule consists of a pair of DNA strands held together by hydrogen bonding between complementary

Clinical Note

DNA Fingerprinting Every nucleated somatic cell in the body carries a set of 46 chromosomes that are copies of the set formed at fertilization. Not all the DNA of these chromosomes codes for proteins, however; a significant percentage of DNA segments have no known function. Some of the "useless" segments contain the same nucleotide sequence repeated over and over. The number of segments and the number of repetitions vary among individuals. The chance that any two individuals, other than identical twins, will have the same pattern of repeating DNA segments is less than one in 9 billion. Individuals can therefore be identified on the basis of their DNA pattern, just as they can on the basis of a fingerprint. Skin scrapings, blood, semen, hair, or other tissues can be used as the DNA source. Information from *DNA fingerprinting* has been used to convict or acquit people accused of violent crimes, such as rape or murder. The science of molecular biology has thus become a useful addition to the crime-fighting arsenal.

nitrogenous bases. Information is stored in the sequence of nitrogenous bases along the length of the DNA strands. Those nitrogenous bases are adenine (A), thymine (T), cytosine (C), and guanine (G). The genetic code is called a *triplet code*, because a sequence of three nitrogenous bases specifies the identity of a single amino acid. Thus, the information encoded in the sequence of nitrogenous bases must be read in groups of three. For example, the triplet thymine–guanine–thymine (TGT) on one DNA strand (the *coding strand*) codes for the amino acid cysteine. More than one triplet may represent the same amino acid, however. For example, the DNA triplet thymine–guanine–cytosine (TGC) also codes for cysteine.

A **gene** is the functional unit of heredity; it contains all the DNA triplets needed to produce specific proteins. The number of triplets in a gene depends on the size of the polypeptide represented. A relatively short polypeptide chain might require fewer than 100 triplets, whereas the instructions for building a large protein might involve 1000 or more triplets. Not all of the DNA molecule carries instructions for proteins; some segments contain instructions for the synthesis of transfer RNA or ribosomal RNA, some have a regulatory function, and others have no apparent function.

Checkpoint

11. **Describe the contents and structure of the nucleus.**
12. **What is a gene?**

See the blue Answers tab at the back of the book.

3-4 DNA controls protein synthesis, cell structure, and cell function

We begin this section by examining the major events of protein synthesis: gene activation, transcription, and translation. We then consider how the nucleus controls cell structure and function.

The Role of Gene Activation in Protein Synthesis

Each DNA molecule contains thousands of genes and therefore holds the information needed to synthesize thousands of proteins. Normally, the genes are tightly coiled, and bound histones keep the genes inactive. Before a gene can affect a cell, the portion of the DNA molecule containing that gene must be uncoiled and the histones temporarily removed.

The factors controlling this process, called **gene activation,** are only partially understood. We know, however, that every gene contains segments responsible for regulating its own activity. In effect, these are nitrogenous-based triplets that say "do or do not read this message," "message starts here," or "message ends here." The "read me," "don't read me," and "start" signals form a special region of DNA called the *promoter*, or control segment, at the start of each gene. Each gene ends with a "stop" signal. Gene activation begins with the temporary disruption of the weak hydrogen bonds between the nitrogenous bases of the two DNA strands and the removal of the histone that guards the promoter.

After the complementary strands have separated and the histone has been removed, the enzyme **RNA polymerase** binds to the promoter of the gene. This binding is the first step in the process of **transcription,** the synthesis of RNA from a DNA template. The term *transcription* is appropriate, as it means "to copy" or "rewrite." All three types of RNA are formed through the transcription of DNA, but we will focus here on the transcription of mRNA, which carries the information needed to synthesize proteins. The synthesis of **messenger RNA (mRNA)** is essential, because the DNA cannot leave the nucleus. Instead, its information is copied to messenger RNA, which *can* leave the nucleus and carry the information to the cytoplasm, where protein synthesis occurs.

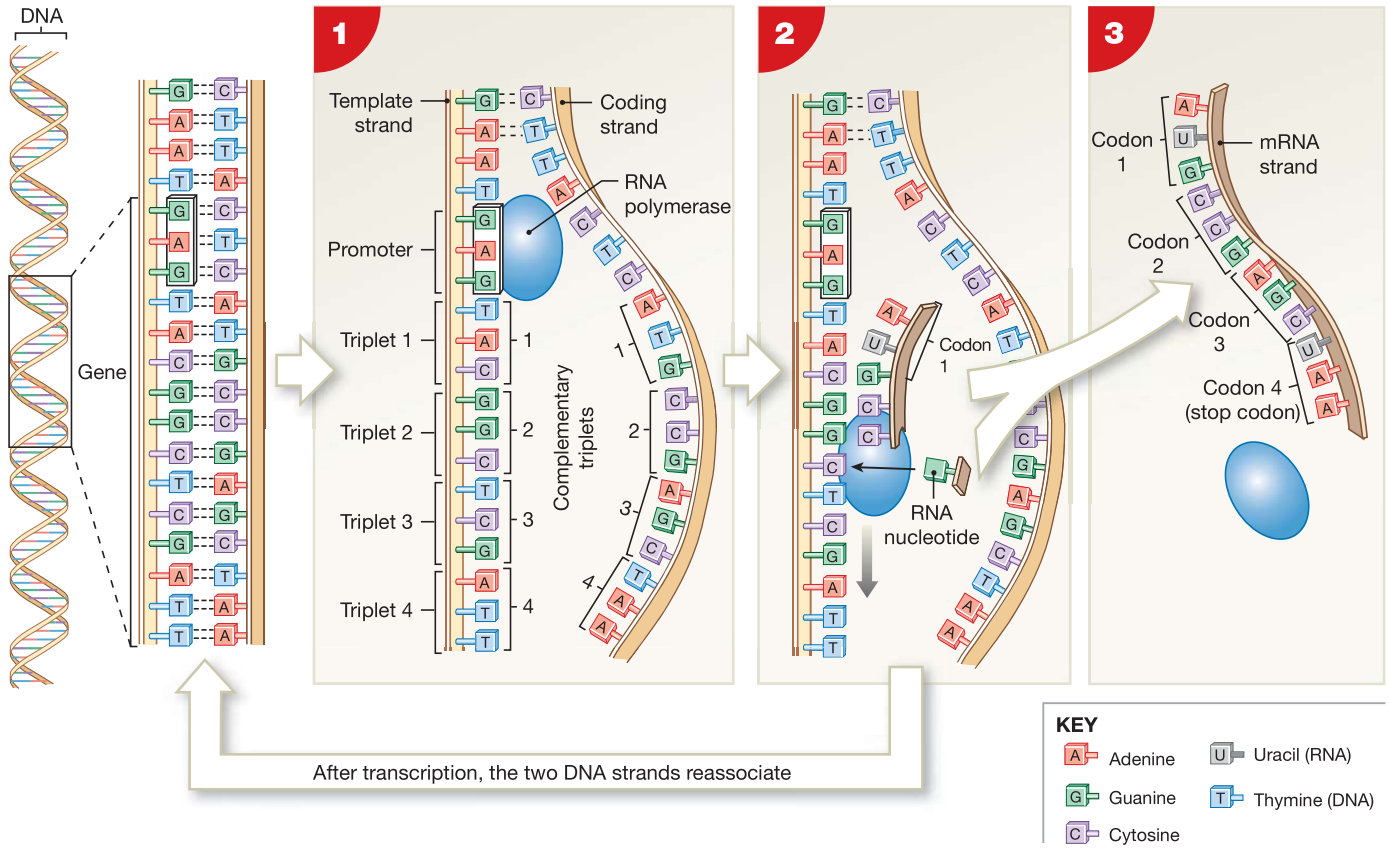
The Transcription of mRNA

The two DNA strands in a gene are complementary. The strand containing the triplets that specify the sequence of amino acids in the polypeptide is the **coding strand.** The other strand, called the **template strand,** contains complementary triplets that will be used as a template for mRNA production. The resulting mRNA will have a nucleotide sequence identical to that of the coding strand, but with uracil substituted for thymine. **Figure 3–12** illustrates the steps in transcription:

1. Once the DNA strands have separated and the promoter has been exposed, transcription can begin. The key event is the attachment of RNA polymerase to the template strand.

2. RNA polymerase promotes hydrogen bonding between the nitrogenous bases of the template strand and complementary nucleotides in the nucleoplasm. This enzyme begins at a "start" signal in the promoter region. It then strings nucleotides together by covalent bonding. The RNA polymerase interacts with only a small portion of the template strand at any one time as it travels along the DNA strand. The complementary strands separate in front of the enzyme as it moves one nucleotide at a time, and they reassociate behind it. The enzyme collects additional nucleotides and attaches them to the growing chain. The nucleotides involved are those characteristic of RNA, not of DNA; RNA polymerase can attach adenine, guanine, cytosine, or uracil, but never thymine. Thus, wherever an A occurs in the DNA strand, the polymerase will attach a U rather than a T to the growing mRNA strand. In this way, RNA polymerase assembles a complete strand of mRNA. The nucleotide sequence of the template strand determines

Figure 3–12 mRNA Transcription. In this figure, a small portion of a single DNA molecule, containing a single gene, is undergoing transcription. 1 The two DNA strands separate, and RNA polymerase binds to the promoter of the gene. 2 The RNA polymerase moves from one nucleotide to another along the length of the template strand. At each site, complementary RNA nucleotides form hydrogen bonds with the DNA nucleotides of the template strand. The RNA polymerase then strings the arriving nucleotides together into a strand of mRNA. 3 On reaching the stop signal at the end of the gene, the RNA polymerase and the mRNA strand detach, and the two DNA strands reassociate.



the nucleotide sequence of the mRNA strand. Thus, each DNA triplet corresponds to a sequence of three nucleotide bases in the mRNA strand. Such a three-base mRNA sequence is called a **codon** (KŌ-don). Codons contain nitrogenous bases that are complementary to those of the triplets in the template strand. For example, if the DNA triplet is TCG, the corresponding mRNA codon will be AGC. This method of copying ensures that the mRNA exactly matches the coding strand of the gene.

3 At the "stop" signal, the enzyme and the mRNA strand detach from the DNA strand, and transcription ends. The complementary DNA strands now complete their reassociation as hydrogen bonding reoccurs between complementary base pairs.

Each gene includes a number of triplets that are not needed to build a functional protein. As a result, the mRNA strand assembled during transcription, sometimes called immature mRNA or *pre-mRNA*, must be "edited" before it leaves the nucleus to direct protein synthesis. In this **RNA processing,** nonsense regions, called **introns,** are snipped out, and the remaining coding segments, or **exons,** are spliced together. The process creates a much shorter, functional strand of mRNA that then enters the cytoplasm through a nuclear pore.

Intron removal is extremely important and tightly regulated. This is understandable because an error in the editing will produce an abnormal protein with potentially disastrous results. Moreover, we now know that by changing the editing instructions and removing different introns, a single gene can produce mRNAs that code for several different proteins. Some introns, however, act as enzymes to catalyze their own removal. How this variable editing is regulated is unknown.

Translation

Protein synthesis is the assembling of functional polypeptides in the cytoplasm. Protein synthesis occurs through

Clinical Note

Mutations are permanent changes in a cell's DNA that affect the nucleotide sequence of one or more genes.

The simplest is a *point mutation*, a change in a single nucleotide that affects one codon. The triplet code has some flexibility, because several different codons can specify the same amino acid. But a point mutation that produces a codon that specifies a different amino acid will usually change the structure of the completed protein. A single change in the amino acid sequence of a structural protein or enzyme can prove fatal. Certain cancers and two potentially lethal blood disorders discussed in Chapter 19, *thalassemia* and *sickle cell anemia*, result from variations in a single nucleotide.

Several hundred inherited disorders have been traced to abnormalities in enzyme or protein structure that reflect single changes in nucleotide sequence. More elaborate mutations, such as additions or deletions of nucleotides, can affect multiple codons in one gene or in several adjacent genes, or they can affect the structure of one or more chromosomes.

Most mutations occur during DNA replication, when cells are duplicating their DNA in preparation for cell division. A single cell, a group of cells, or an entire individual may be affected. This last prospect occurs when the changes are made early in development. For example, a mutation affecting the DNA of an individual's sex cells will be inherited by that individual's children. Our understanding of genetic structure is opening the possibility of diagnosing and correcting some of these problems.

translation, the formation of a linear chain of amino acids, using the information provided by an mRNA strand. Again, the name is appropriate: To *translate* is to present the same information in a different language; in this case, a message written in the "language" of nucleic acids (the sequence of nitrogenous bases) is translated by ribosomes into the "language" of proteins (the sequence of amino acids in a polypeptide chain). Each mRNA codon designates a particular amino acid to be incorporated into the polypeptide chain.

The amino acids are provided by **transfer RNA (tRNA),** a relatively small and mobile type of RNA. Each tRNA molecule binds and delivers a specific type of amino acid. More than 20 kinds of transfer RNA exist—at least one for each of the amino acids used in protein synthesis.

A tRNA molecule has a tail that binds an amino acid. Roughly midway along its length, the nucleotide chain of the tRNA forms a tight loop that can interact with an mRNA strand. The loop contains three nitrogenous bases that form an **anticodon.** During translation, the anticodon bonds complementarily with an appropriate mRNA codon. The base sequence of the anticodon indicates the type of amino acid carried by the tRNA. For example, a tRNA with the anticodon GGC always carries the amino acid *proline*, whereas a tRNA with the anticodon CGG carries *alanine*. **Table 3–1** lists examples of several codons and anticodons that specify individual amino acids and summarizes the relationships among DNA, codons, and anticodons.

The tRNA molecules thus provide the physical link between codons and amino acids. During translation, each codon along the mRNA strand binds a complementary anticodon on a tRNA molecule. Thus, if the mRNA has the codon sequence AUG–CCG–AGC, it will bind to tRNAs with anticodons UAC–GGC–UCG. The amino acid sequence of the polypeptide chain created is dependent upon the arrangement of codons along the mRNA strand. In this case, the amino acid sequence in the resulting polypeptide would be methionine–proline–serine. The translation process is illustrated in **Figure 3–13**:

1. Translation begins as the mRNA strand binds to a small ribosomal subunit. The first codon, or *start codon*, of the mRNA strand always has the base sequence AUG. It binds a tRNA with the complementary anticodon sequence UAC. This tRNA, which carries the amino acid *methionine*, attaches to the first of two tRNA binding sites on the small ribosomal subunit. (The initial methionine will be removed from the finished protein.)
2. When this tRNA binding occurs, a large ribosomal subunit joins the complex to create a complete ribosome. The mRNA strand nestles in the gap between the small and the large ribosomal subunits.
3. A second tRNA now arrives at the second tRNA binding site of the ribosome, and its anticodon binds to the next codon of the mRNA strand.

Table 3–1 Examples of the Triplet Code

DNA Triplets				
Template Strand	**Coding Strand**	**mRNA Codon**	**tRNA Anticodon**	**Amino Acid**
AAA	TTT	UUU	AAA	Phenylalanine
AAT	TTA	UUA	AAU	Leucine
ACA	TGT	UGU	ACA	Cysteine
CAA	GTT	GUU	CAA	Valine
TAC	ATG	AUG	UAC	Methionine
TCG	AGC	AGC	UCG	Serine
GGC	CCG	CCG	GGC	Proline
CGG	GCC	GCC	CGG	Alanine

4 Enzymes of the large ribosomal subunit then break the linkage between the tRNA and its amino acid. At the same time, the enzymes attach the amino acid to its neighbor by means of a peptide bond. The ribosome then moves one codon down the mRNA strand. The cycle is then repeated with the arrival of another molecule of tRNA. The tRNA stripped of its amino acid drifts away. It will soon bind to another amino acid and be available to participate in protein synthesis again.

5 The polypeptide chain continues to grow by the addition of amino acids until the ribosome reaches a "stop" signal, or *stop codon*, at the end of the mRNA strand. The ribosomal subunits now detach, leaving an intact strand of mRNA and a completed polypeptide.

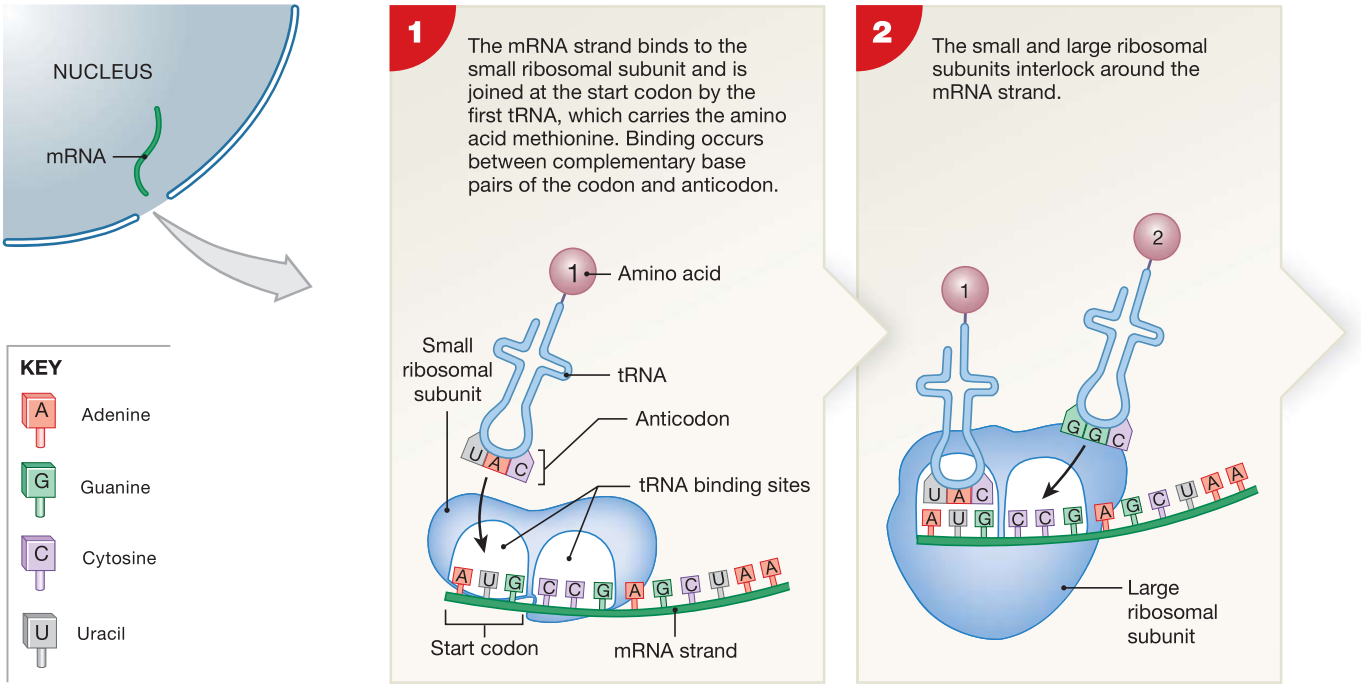
Translation proceeds swiftly, producing a typical protein in about 20 seconds. The mRNA strand remains intact, and it can interact with other ribosomes to create additional copies of the same polypeptide chain. The process does not continue indefinitely, however, because after a few minutes to a few hours, mRNA strands are broken down and the nucleotides are recycled. However, large numbers of protein chains can be produced during that time. Although only two mRNA codons are "read" by a ribosome at any one time, the entire strand may contain thousands of codons. As a result, many ribosomes can bind to a single mRNA strand. At any moment, each ribosome will be reading a different part of the same message, but each will end up constructing a copy of the same protein as the others. The arrangement is similar to a line of people who make identical choices at a buffet lunch; all the people will assemble the same meal, but each person is always a step behind the person ahead. A series of ribosomes attached to the same mRNA strand is called a *polyribosome*, or *polysome*.

How the Nucleus Controls Cell Structure and Function

As noted previously, the DNA of the nucleus controls the cell by directing the synthesis of specific proteins. Through the control of protein synthesis, virtually every aspect of cell structure and function can be regulated. Two levels of control are involved:

1. The DNA of the nucleus has *direct* control over the synthesis of structural proteins, such as cytoskeletal components, membrane proteins (including receptors), and secretory products. By issuing appropriate instructions, in the form of mRNA strands, the nucleus can alter the internal structure of the cell, its sensitivity to substances in its environment, or its secretory functions to meet changing needs.

Figure 3–13 The Process of Translation. For clarity, the components are not drawn to scale and their three-dimensional relationships have been simplified.



2. The DNA of the nucleus has *indirect* control over all other aspects of cellular metabolism, because it regulates the synthesis of enzymes. By ordering or stopping the production of appropriate enzymes, the nucleus can regulate all metabolic activities and functions of the cell. For example, the nucleus can accelerate the rate of glycolysis by increasing the number of needed enzymes in the cytoplasm.

This brings us to a central question: How does the nucleus "know" what genes to activate? Although we don't have all the answers, we know that in many cases gene activation or deactivation is triggered by changes in the surrounding cytoplasm. Such changes in the intracellular environment can, in turn, affect the nucleoplasm enough to turn specific genes on or off. Alternatively, messengers or hormones may enter the nucleus through nuclear pores and bind to specific receptors or promoters along the DNA strands. Thus, continual chemical communication occurs between the cytoplasm and the nucleus. That communication is relatively selective, thanks to the restrictive characteristics of the nuclear pores and the barrier posed by the nuclear envelope.

Of course, continual communication also occurs between the cytoplasm and the extracellular fluid across the plasma membrane, and what crosses the plasma membrane today may alter gene activity tomorrow. In the next section, we will examine how the plasma membrane selectively regulates the passage of materials in and out of the cell.

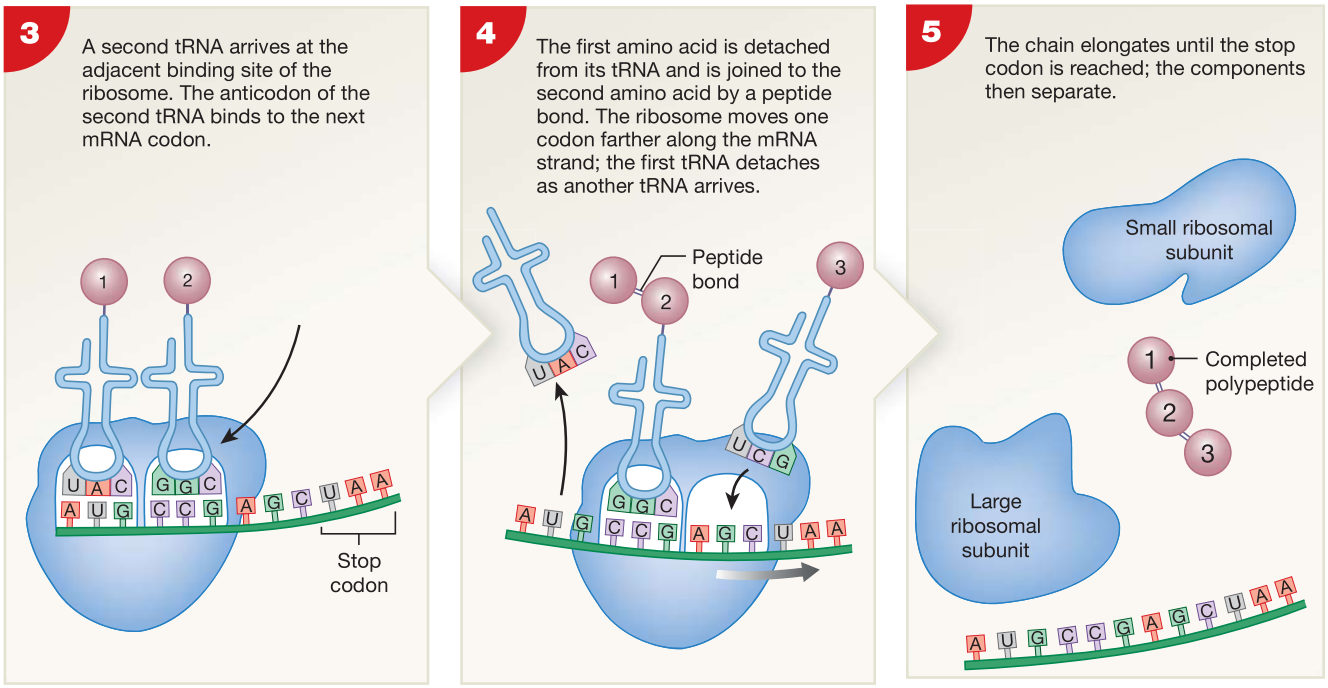
Checkpoint

13. **Define gene activation.**
14. **What is transcription?**
15. **What process would be affected by the lack of the enzyme RNA polymerase?**

See the blue Answers tab at the back of the book.

3-5 Diffusion is a passive transport mechanism that assists membrane passage

The plasma membrane is a barrier that isolates the cytoplasm from the extracellular fluid. Because the plasma membrane is an effective barrier, conditions inside the cell can be much different from conditions outside the cell. However, the barrier cannot be perfect, because cells are not self-sufficient. Each day they require nutrients to provide the energy they need to stay alive and function normally. They also generate waste products that must be eliminated. Whereas your body has passageways and openings



for nutrients, gases, and wastes, a continuous, relatively uniform membrane surrounds the cell. So how do materials—whether nutrients or waste products—get across the plasma membrane without damaging it or reducing its effectiveness as a barrier? To answer this question, we must take a closer look at the structure and function of the plasma membrane.

Permeability is the property of the plasma membrane that determines precisely which substances can enter or leave the cytoplasm. A membrane through which nothing can pass is **impermeable.** A membrane through which any substance can pass without difficulty is **freely permeable.** Because the permeability of plasma membranes lies somewhere between those extremes, plasma membranes are called **selectively permeable.**

A selectively permeable membrane permits the free passage of some materials and restricts the passage of others. The distinction may be based on size, electrical charge, molecular shape, lipid solubility, or other factors. Cells differ in their permeabilities, depending on what lipids and proteins are present in the plasma membrane and how these components are arranged.

Passage across the membrane is either passive or active. *Passive processes* move ions or molecules across the plasma membrane with no expenditure of energy by the cell. *Active processes* require that the cell expend energy, generally in the form of ATP.

The mechanism involved is used to categorize transport processes. The three major categories are diffusion, carrier-mediated transport, and vesicular transport. *Diffusion*, which results from the random motion and collisions of ions and molecules, is a passive process and will be considered first.

Diffusion

Ions and molecules are constantly in motion, colliding and bouncing off one another and off obstacles in their paths. The movement is both passive and random: A molecule can bounce in any direction. One result of this continuous random motion is that, over time, the molecules in any given space will tend to become evenly distributed. This distribution process, the net movement of a substance from an area of higher concentration to an area of lower concentration, is called **diffusion.** The difference between the high and low concentrations is a **concentration gradient** (and thus a potential energy gradient). Diffusion tends to eliminate that gradient.

After the gradient has been eliminated, the molecular motion continues, but net movement no longer occurs in any particular direction. (For convenience, we restrict use of the term *diffusion* to the directional movement that eliminates concentration gradients—a process sometimes called *net diffusion*.) Because diffusion tends to spread materials from a region of higher concentration to one of lower concentration, it is often described as proceeding "down a concentration gradient" or "downhill."

Diffusion in air and water is slow, and it is most important over very short distances. A simple, everyday example can give you a mental image of how diffusion works. Consider a colored sugar cube dropped in water (**Figure 3–14**). Placing the cube in a large volume of clear water sets up a steep concentration gradient for the ingredients as they dissolve: The sugar and dye concentration is high near the cube and negligible elsewhere.

Figure 3–14 **Diffusion.** Placing a colored sugar cube in a glass of water establishes a steep concentration gradient. As the cube dissolves, many sugar and dye molecules are in one location, and none are elsewhere. Over time, the molecules spread through the solution until the concentration gradient is eliminated, the sugar cube has dissolved completely, the molecules are distributed evenly, and there is no net directional movement. The effects of diffusion predominate only over short distances.

Clinical Note

Drugs and the Plasma Membrane Many clinically important drugs affect the plasma membrane. For some anesthetics, such as chloroform, ether, halothane, and nitrous oxide, potency is directly correlated with its lipid solubility. Presumably, high lipid solubility accelerates the drug's entry into cells and enhances its ability to block ion channels or change other properties of plasma membranes and thereby reduce the sensitivity of neurons and muscle cells. However, some common anesthetics have relatively low lipid solubility. For example, the local anesthetics, *procaine* and *lidocaine*, affect nerve cells by blocking sodium channels in their plasma membranes; this blockage reduces or eliminates the responsiveness of these cells to painful (or any other) stimuli. Although procaine and lidocaine are both effective local anesthetics, procaine has very low lipid solubility.

As time passes, the colored sugar molecules spread through the solution until they are distributed evenly. However, compared to a cell, a beaker of water is enormous, and additional factors (which we will ignore) account for dye distribution over distances of centimeters as opposed to micrometers.

Diffusion is important in body fluids, because it tends to eliminate local concentration gradients. For example, every cell in the body generates carbon dioxide, and the intracellular concentration is fairly high. Carbon dioxide concentrations are lower in the surrounding interstitial fluid, and lower still in the circulating blood. Because plasma membranes are freely permeable to carbon dioxide (CO_2), CO_2 can diffuse down its concentration gradient—traveling from the cell's interior into the interstitial fluid and then into the bloodstream, for eventual delivery to the lungs.

To be effective, the diffusion of nutrients, waste products, and dissolved gases must keep pace with the demands of active cells. Important factors that influence diffusion rates include the following:

- *Distance.* The shorter the distance, the more quickly concentration gradients are eliminated. In the human body, few cells are farther than 25 μm from a blood vessel.
- *Molecule Size.* The smaller the molecule size, the faster the diffusion. Ions and small organic molecules, such as glucose, diffuse more rapidly than do large proteins.
- *Temperature.* The higher the temperature, the faster the diffusion rate. Diffusion proceeds somewhat more quickly at human body temperature (about 37°C, or 98.6°F) than at cooler environmental temperatures.
- *Concentration Gradient.* The larger the concentration gradient, the faster diffusion proceeds. When cells become more active, the intracellular concentration of oxygen declines. This change increases the concentration gradient for oxygen between the inside of the cell (somewhat low) and the interstitial fluid outside (somewhat high). The rate of oxygen diffusion into the cell then increases.
- *Electrical Forces.* Opposite electrical charges (+ and –) attract each other; like charges (+ and + *or* – and –) repel each other. The interior of the plasma membrane has a net negative charge relative to the exterior surface, due in part to the high concentration of proteins in the cell. This negative charge tends to pull positive ions from the extracellular fluid into the cell, while opposing the entry of negative ions. For example, interstitial fluid contains higher concentrations of sodium ions (Na^+) and chloride ions (Cl^-) than does cytosol. Diffusion of the positively charged sodium ions into the cell is therefore favored by both the concentration gradient, or *chemical gradient*, and the electrical gradient. In contrast, diffusion of the negatively charged chloride ions into the cell is favored by the chemical gradient, but opposed by the electrical gradient. For any ion, the net result of the chemical and electrical forces acting on it is called the *electrochemical gradient*.

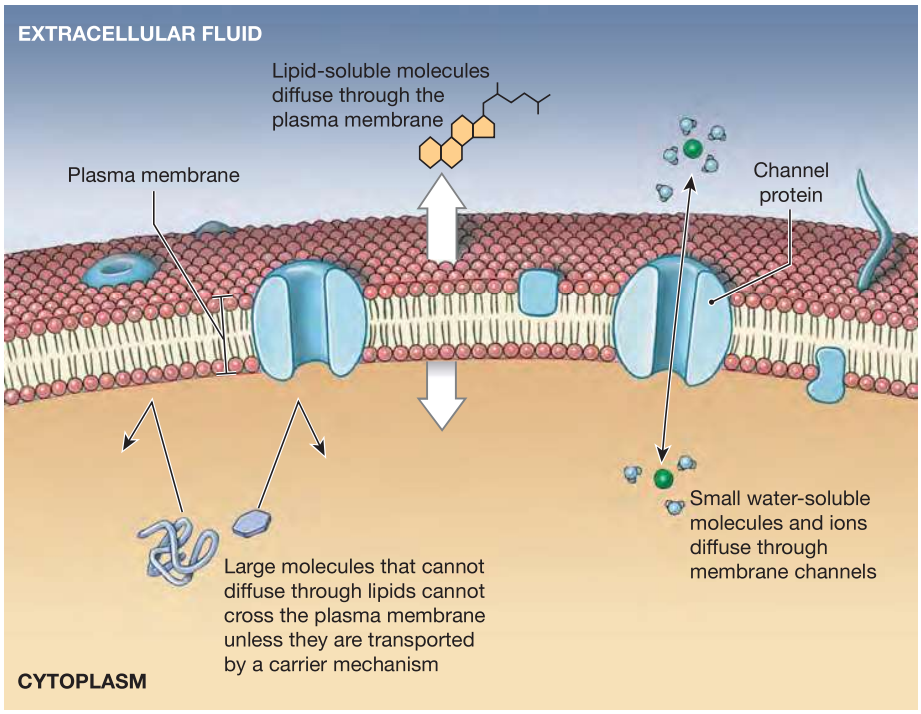
Diffusion across Plasma Membranes

In extracellular fluids, water and dissolved solutes diffuse freely. A plasma membrane, however, acts as a barrier that selectively restricts diffusion: Some substances pass through easily, while others cannot penetrate the membrane. An ion or a molecule can diffuse across a plasma membrane only by (1) crossing the lipid portion of the membrane or (2) passing through a membrane channel (**Figure 3–15**).

Simple Diffusion. Alcohol, fatty acids, and steroids can enter cells easily, because they can diffuse through the lipid portions of the membrane. Lipid-soluble drugs and dissolved gases, such as oxygen and carbon dioxide, also enter and leave our cells by diffusing through the phospholipid bilayer. The situation is more complicated for ions and water-soluble compounds, which are not lipid-soluble. To enter or leave the cytoplasm, these substances must pass through a membrane channel.

Channel-Mediated Diffusion. Membrane channels are very small passageways created by transmembrane proteins. On average, the channel is about 0.8 nm in diameter. Water molecules can enter or exit freely, but even a small organic molecule, such as glucose, is too big to fit through the channels. Whether an ion can cross a particular membrane channel depends on many factors, including the size and charge of the ion, the size of the hydration sphere, and interactions between the ion and the channel walls. **Leak channels,** also called passive channels,

Figure 3–15 Diffusion across the Plasma Membrane. The path a substance takes in crossing a plasma membrane depends on the substance's size and lipid solubility.



remain open and allow the passage of ions across the plasma membrane. The mechanics of diffusion through membrane channels is therefore more complex than simple diffusion. For example, the rate at which a particular ion diffuses across the membrane can be limited by the availability of suitable channels. However, for many ions, including sodium, potassium, and chloride, movement across the plasma membrane occurs at rates comparable to those one would predict if relying on simple diffusion.

Osmosis: A Special Case of Diffusion

The net diffusion of water across a membrane is so important that it is given a special name: **osmosis** (oz-MŌ-sis; *osmos*, a push). For convenience, we will always use the term *osmosis* for the movement of water, and the term *diffusion* for the movement of solutes.

Intracellular and extracellular fluids are solutions that contain a variety of dissolved materials. Each solute diffuses as though it were the only material in solution. The diffusion of sodium ions, for example, occurs only in response to the existence of a concentration gradient for sodium. A concentration gradient for another ion will have no effect on the rate or direction of sodium ion diffusion.

Some solutes diffuse into the cytoplasm, others diffuse out, and a few (such as proteins) are unable to diffuse across the plasma membrane at all. Yet if we ignore the individual identities and simply count ions and molecules, we find that the *total* concentration of dissolved ions and molecules on either side of the plasma membrane stays the same. This state of equilibrium persists because a typical plasma membrane is freely permeable to water.

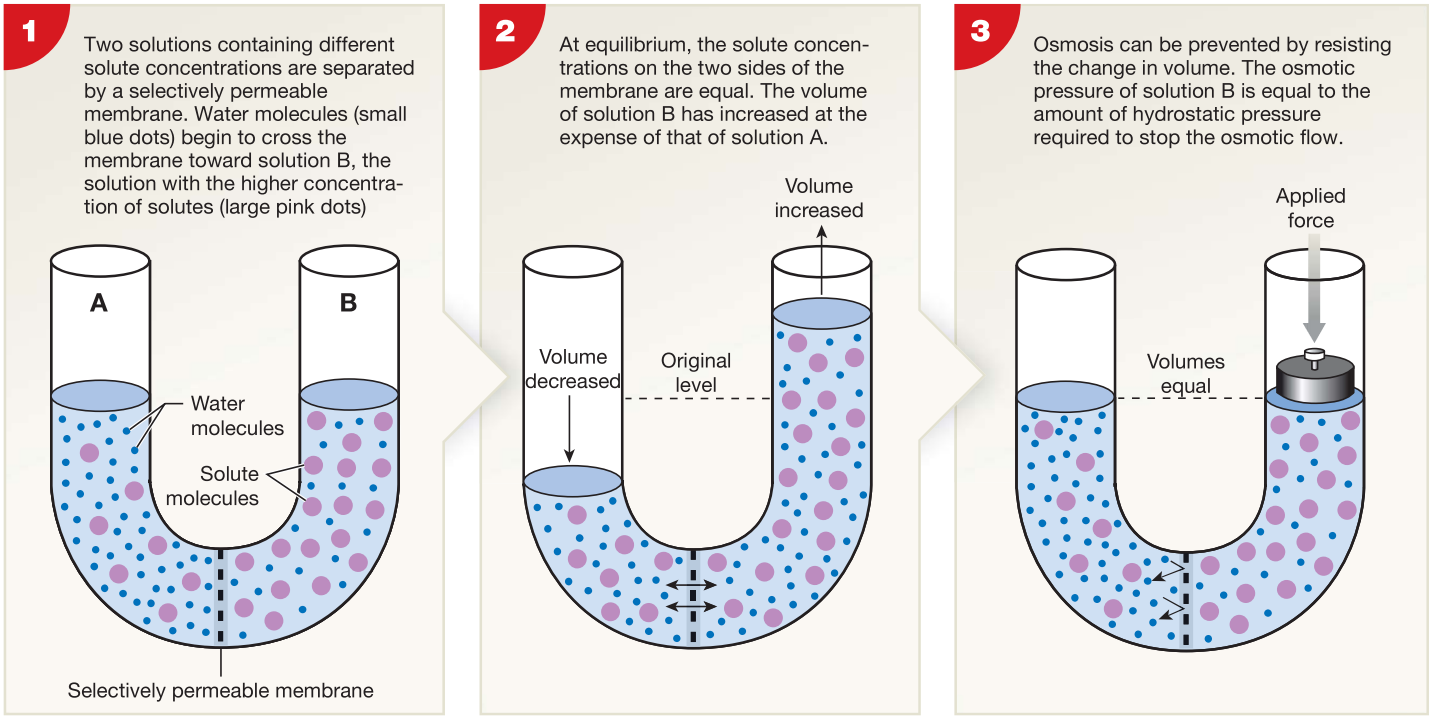
To understand the basis for such equilibrium, consider that whenever a solute concentration gradient exists, a concentration gradient for *water* exists also. Because dissolved solute molecules occupy space that would otherwise be taken up by water molecules, the higher the solute concentration, the lower the water concentration. As a result, *water molecules tend to flow across a membrane toward the solution containing the higher solute concentration*, because this movement is down the concentration gradient for water. Water movement will continue until water concentrations—and thus solute concentrations—are the same on either side of the membrane.

Remember these basic characteristics of osmosis:

- Osmosis is the diffusion of water molecules across a selectively permeable membrane.
- Osmosis occurs across a selectively permeable membrane that is freely permeable to water, but not freely permeable to solutes.
- In osmosis, water flows across a selectively permeable membrane toward the solution that has the higher concentration of solutes, because that is where the concentration of water is lower.

Osmosis and Osmotic Pressure. Figure 3–16 diagrams the process of osmosis. 1 shows two solutions (A and B), with different solute concentrations, separated by a selectively permeable membrane. As osmosis occurs, water molecules cross the membrane until the solute concentrations in the two solutions are identical (2). Thus, the volume of solution B increases while that of solution A decreases. The greater the initial difference in solute concentrations, the stronger is the osmotic flow. The **osmotic pressure** of a solution is an indication of the force with which pure water moves into that solution as a result of its solute concentration. We can measure a solution's osmotic pressure in several ways. For example, an opposing pressure can prevent the osmotic flow of water into the solution. Pushing against a fluid generates **hydrostatic pressure.** In 3, hydro-

Figure 3–16 **Osmosis.** The osmotic pressure of solution B is equal to the amount of hydrostatic pressure required to stop the osmotic flow.



static pressure opposes the osmotic pressure of solution B, so no net osmotic flow occurs.

Osmosis eliminates solute concentration differences more rapidly than solute diffusion. In large part this is because water molecules cross a membrane through abundant water channels called *aquaporins*, which exceed the number of solute channels, through which water can also pass. This difference results in a higher membrane permeability for water compared to solutes.

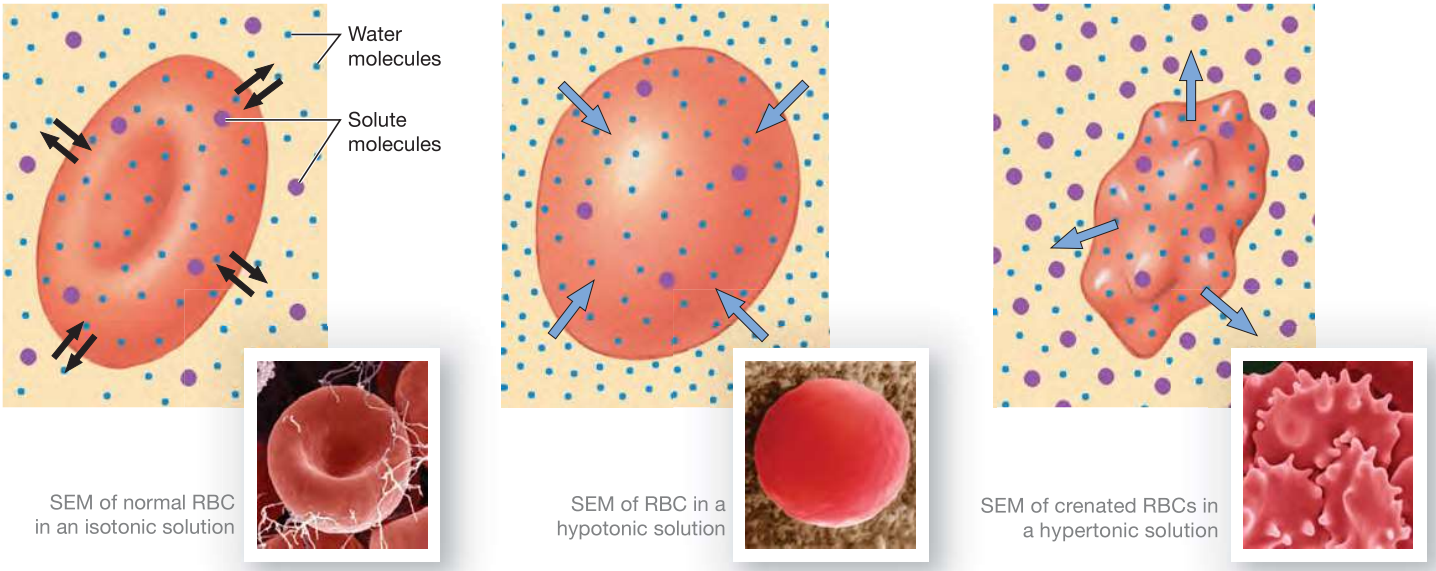
Osmolarity and Tonicity. The total solute concentration in an aqueous solution is the solution's **osmolarity,** or **osmotic concentration.** The nature of the solutes, however, is often as important as the total osmolarity. Therefore, when we describe the effects of various osmotic solutions on cells, we usually use the term **tonicity** instead of osmolarity. A solution that does not cause an osmotic flow of water into or out of a cell is called **isotonic** (*iso-*, same + *tonos*, tension).

Although often used interchangeably, the terms *osmolarity* and *tonicity* do not always mean the same thing. Osmolarity refers to the solute concentration of the solution, while tonicity is a description of how the solution affects a cell. Consider a solution that has the same osmolarity as the intracellular fluid, but a higher concentration of one or more individual ions. If any of those ions can cross the plasma membrane and diffuse into the cell, the osmolarity of the intracellular fluid will increase, and that of the extracellular solution will decrease. Osmosis will then occur, moving water into the cell. If the process continues, the cell will gradually inflate like a water balloon. In this case, the extracellular solution and the intracellular fluid were initially equal in osmolarity, but they were not isotonic.

Figure 3–17a shows a red blood cell in an isotonic solution. If a red blood cell is in a **hypotonic** solution, water will flow into the cell, causing it to swell up like a balloon (**Figure 3–17b**). The cell may eventually burst, releasing its contents. This event is **hemolysis** (*hemo-*, blood + *lysis*, loosening). A cell in a **hypertonic** solution will lose water by osmosis. As it does, the cell shrivels and dehydrates. The shrinking of red blood cells is called **crenation** (**Figure 3–17c**).

It is often necessary to give patients large volumes of fluid to combat severe blood loss or dehydration. One fluid frequently administered is a 0.9 percent (0.9 g/dL) solution of sodium chloride (NaCl). This solution, which approximates the normal osmotic concentration of extracellular fluids, is called *normal saline*. It is used because sodium and chloride are the most abundant ions in the extracellular fluid. Little net movement of either ion across plasma membranes occurs; thus, normal saline is essentially isotonic to body cells. An alternative treatment involves the use of an isotonic saline solution containing *dextran*, a carbohydrate that cannot cross plasma membranes. The dextran molecules elevate the osmolarity of the blood, and as osmosis draws water into the blood vessels from the extracellular fluid, blood volume increases.

Figure 3–17 Osmotic Flow across a Plasma Membrane. Black arrows indicate an equilibrium with no net water movement. Blue arrows indicate the direction of osmotic water movement.



a In an isotonic saline solution, no osmotic flow occurs, and these red blood cells appear normal.

b Immersion in a hypotonic saline solution results in the osmotic flow of water into the cells. The swelling may continue until the plasma membrane ruptures, or lyses.

c Exposure to a hypertonic solution results in the movement of water out of the cell. The red blood cells shrivel and become crenated.

Checkpoint

16. What is meant by "selectively permeable" when referring to a plasma membrane?
17. Define diffusion.
18. List five factors that influence the diffusion of susbstances in the body.
19. How would a decrease in the concentration of oxygen in the lungs affect the diffusion of oxygen into the blood?
20. Define osmosis.
21. Some pediatricians recommend using a 10 percent salt solution as a nasal spray to relieve congestion in infants with stuffy noses. What effect would such a solution have on the cells lining the nasal cavity, and why?

See the blue Answers tab at the back of the book.

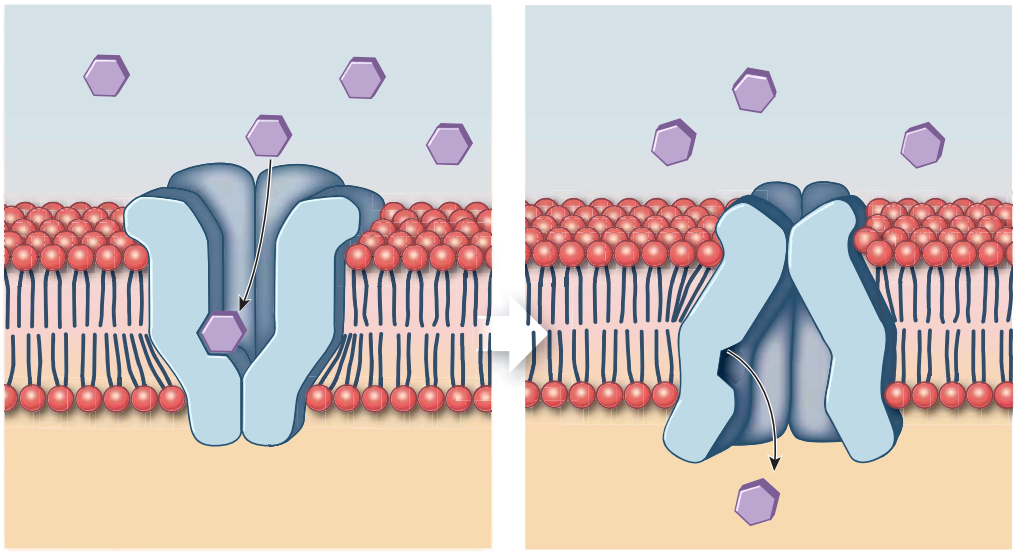
3-6 Carrier-mediated and vesicular transport mechanisms assist membrane passage

In this section we consider two additional ways substances are taken into or removed from cells: carrier-mediated transport and vesicular transport. *Carrier-mediated transport* requires specialized integral membrane proteins. It can be passive or active, depending on the substance transported and the nature of the transport mechanism. *Vesicular transport* involves the movement of materials within small membranous sacs, or *vesicles*. Vesicular transport is always an active process.

Carrier-Mediated Transport

In **carrier-mediated transport,** integral proteins bind specific ions or organic substrates and carry them across the plasma membrane. All forms of carrier-mediated transport have the following characteristics, which they share with enzymes:

- *Specificity.* Each carrier protein in the plasma membrane will bind and transport only certain substances. For example, the carrier protein that transports glucose will not transport other simple sugars.
- *Saturation Limits.* The availability of substrate molecules and carrier proteins limits the rate of transport into or out of the cell, just as enzymatic reaction rates are limited by the availability of substrates and enzymes. When all the available carrier proteins are operating at maximum speed, the carriers are called *saturated*. The rate of transport cannot increase further, regardless of the size of the concentration gradient.
- *Regulation.* Just as enzyme activity often depends on the presence of cofactors, the binding of other molecules, such as hormones, can affect the activity of carrier proteins. Hormones thus provide an important means of coordinating carrier protein activity throughout the body. The interplay between hormones and plasma membranes will be exam-



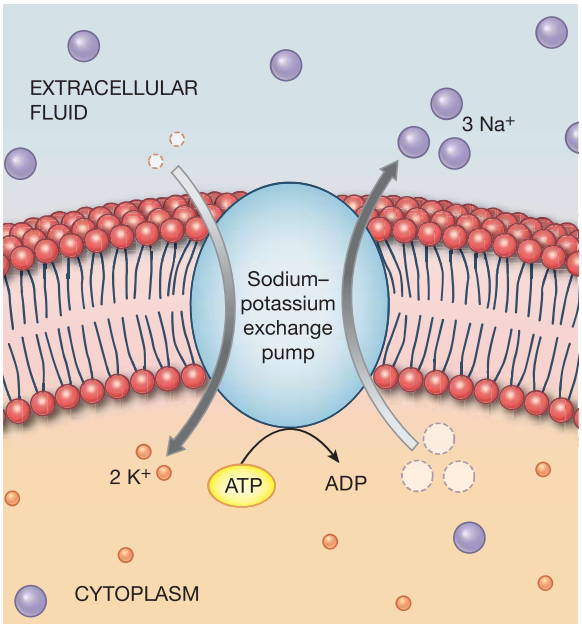
The Sodium–Potassium Exchange Pump. Sodium and potassium ions are the principal cations in body fluids. Sodium ion concentrations are high in the extracellular fluids, but low in the cytoplasm. The distribution of potassium in the body is just the opposite: low in the extracellular fluids and high in the cytoplasm. Because of the presence of leak channels in plasma membranes, sodium ions slowly diffuse into the cell, and potassium ions diffuse out. Homeostasis within the cell depends on the ejection of sodium ions and the recapture of lost potassium ions. This exchange occurs by a **sodium–potassium exchange pump.** The carrier protein involved in the process is called *sodium–potassium ATPase*.

The sodium–potassium exchange pump exchanges intracellular sodium for extracellular potassium (**Figure 3–19**). On average, for each ATP molecule consumed, three sodium ions are ejected and two potassium ions are reclaimed by the cell. If ATP is readily available, the rate of transport depends on the concentration of sodium ions in the cytoplasm. When the concentration rises, the pump becomes more active. The energy demands are impressive: Sodium–potassium ATPase may use up to 40 percent of the ATP produced by a resting cell!

Secondary Active Transport. In **secondary active transport,** the transport mechanism itself does not require energy from ATP, but the cell often needs to expend ATP at a later time to preserve homeostasis. As with facilitated transport, a secondary active transport mechanism moves a specific substrate down its concentration gradient. Unlike the proteins in facilitated transport, however, these carrier proteins can also move another substrate at the same time, without regard to its concentration gradient. In effect, the concentration gradient for one substance provides the driving force needed by the carrier protein, and the second substance gets a "free ride."

The concentration gradient for sodium ions most often provides the driving force for cotransport mechanisms that move materials into the cell. For example, sodium-linked cotransport is important in the absorption of glucose and amino acids along the intestinal tract. Although the initial transport activity proceeds without direct energy expenditure, the cell must expend ATP to pump the arriving sodium ions out of the cell by using the sodium–potassium exchange pump (**Figure 3–20**). Sodium ions are also involved with many countertransport mechanisms. Sodium–calcium countertransport is responsible for keeping intracellular calcium ion concentrations very low.

Figure 3–19 The Sodium–Potassium Exchange Pump. The operation of the sodium–potassium exchange pump is an example of active transport. For each ATP converted to ADP, this carrier protein pump, also called sodium–potassium ATPase, carries three Na^+ out of the cell and two K^+ into the cell.



Vesicular Transport

In **vesicular transport,** materials move into or out of the cell in **vesicles,** small membranous sacs that form at, or fuse with, the plasma membrane. Because tiny droplets of fluid and solutes are transported rather than single molecules, this process is also known as *bulk transport*. The two major categories of vesicular transport are *endocytosis* and *exocytosis*.

Endocytosis

As we saw earlier in this chapter, extracellular materials can be packaged in vesicles at the cell surface and imported into the cell. This process, called **endocytosis,** involves relatively large volumes of extracellular material and requires energy in the form of ATP. The three major types of endocytosis are (1) *receptor-mediated endocytosis*, (2) *pinocytosis*, and (3) *phagocytosis*. All three are active processes that require energy in the form of ATP.

Endocytic vesicles are generally known as *endosomes*. Endosomes formed by pinocytosis are also called *pinosomes*, and those formed by phagocytosis are called *phagosomes*. Their contents remain isolated from the cytoplasm, trapped within the vesicle. The movement of materials into the surrounding cytoplasm may involve active transport, simple or facilitated diffusion, or the destruction of the vesicle membrane.

Receptor-Mediated Endocytosis. A highly selective process, **receptor-mediated endocytosis** produces vesicles that contain a specific target molecule in high concentrations. Receptor-mediated endocytosis begins when materials in the extracellular fluid bind to receptors on the membrane surface (**Figure 3–21**). Most receptor molecules are glycoproteins, and each binds a specific ligand, or target, such as a transport protein or a hormone. Some receptors are distributed widely over the surface of the plasma membrane; others are restricted to specific regions or in depressions on the cell surface.

Figure 3–20 Secondary Active Transport. In secondary active transport, glucose transport by a carrier protein will occur only after the carrier has bound two sodium ions. In three cycles, three glucose molecules and six sodium ions are transported into the cytoplasm. The cell then pumps the sodium ions across the plasma membrane via the sodium–potassium exchange pump, at a cost of two ATP molecules.

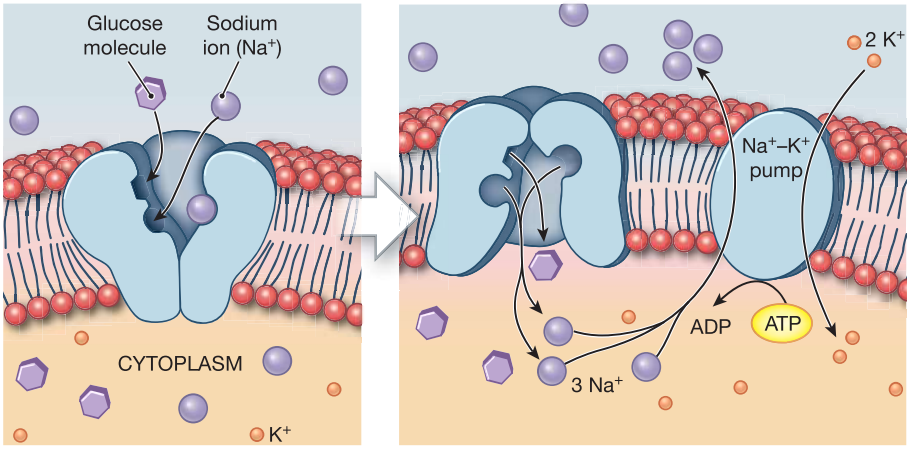
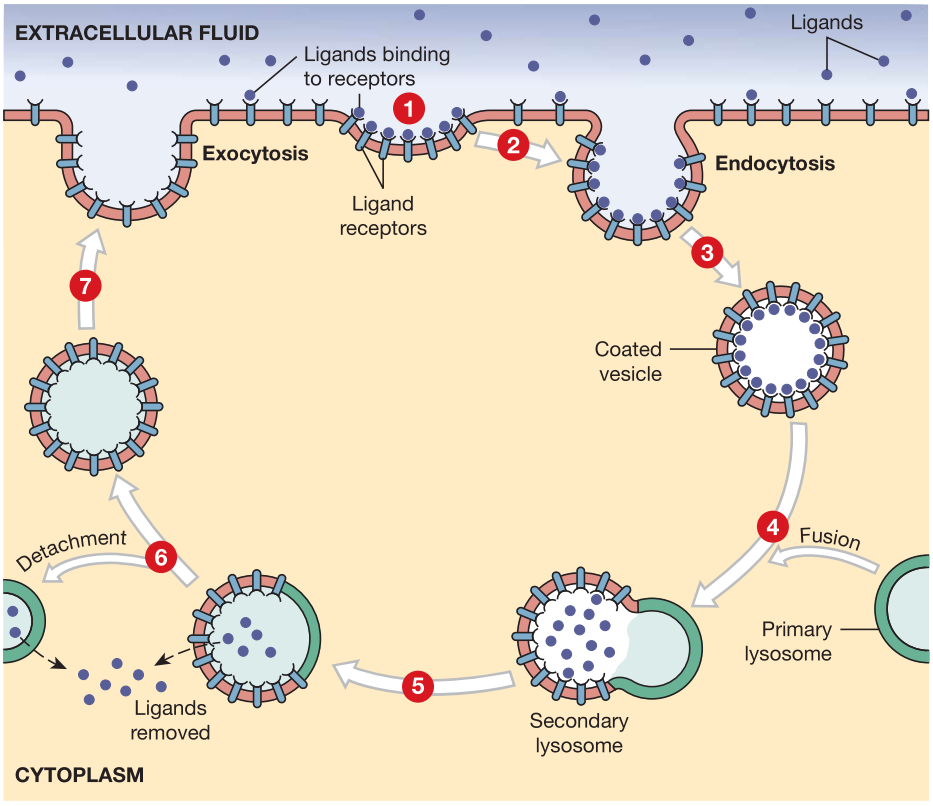


Figure 3–21 Receptor-Mediated Endocytosis.



Receptor-Mediated Endocytosis

1. Target molecules (ligands) bind to receptors in plasma membrane.
2. Areas coated with ligands form deep pockets in plasma membrane surface.
3. Pockets pinch off, forming endosomes known as coated vesicles.
4. Coated vesicles fuse with primary lysosomes to form secondary lysosomes.
5. Ligands are removed and absorbed into the cytoplasm.
6. The lysosomal and endosomal membranes separate.
7. The endosome fuses with the plasma membrane, and the receptors are again available for ligand binding.

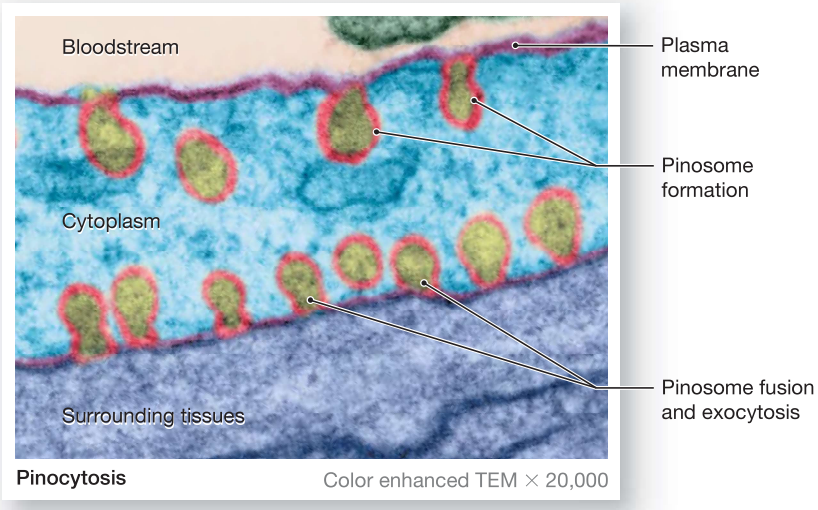
Receptors bound to ligands cluster together. Once an area of the plasma membrane has become covered with ligands, it forms grooves or pockets that move to one area of the cell and then pinch off to form an endosome, a processing and sorting vesicle. The endosomes produced in this way are called **coated vesicles,** because a protein–fiber network that originally carpeted the inner membrane surface beneath the receptor–ligand clusters now surrounds them. This coating is essential to endosome formation and movement. Inside the cell, the coated vesicles fuse with primary lysosomes filled with digestive enzymes, creating secondary lysosomes. The lysosomal enzymes then free the ligands from their receptors, and the ligands enter the cytoplasm by diffusion or active transport. The vesicle membrane detaches from the secondary lysosome and returns to the cell surface, where its receptors are available to bind more ligands.

Many important substances, including cholesterol and iron ions (Fe^{2+}), are distributed through the body attached to special transport proteins. These proteins are too large to pass through membrane pores, but they can and do enter cells by receptor-mediated endocytosis.

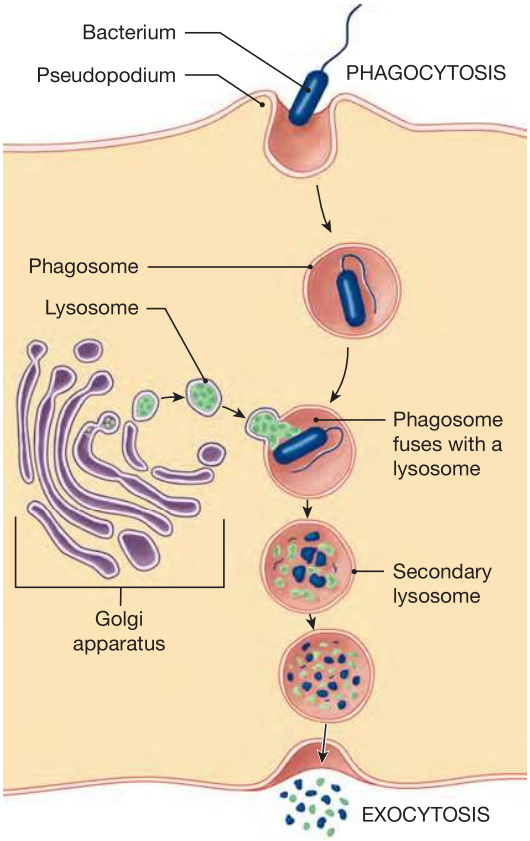
Pinocytosis. "Cell drinking," or **pinocytosis** (pi-nō-sī-TŌ-sis), is the formation of endosomes filled with extracellular fluid. This process is not as selective as receptor-mediated endocytosis, because no receptor proteins are involved. The target appears to be the fluid contents in general, rather than specific bound ligands. In pinocytosis, a deep groove or pocket forms in the plasma membrane and then pinches off (**Figure 3–22a**). The steps involved in the formation and fate of a pinosome created by pinocytosis are similar to the steps in receptor-mediated endocytosis, except that ligand binding is not involved.

Phagocytosis. "Cell eating," or **phagocytosis** (fag-ō-sī-TŌ-sis), produces phagosomes containing solid objects that may be as large as the cell itself. In this process, cytoplasmic extensions called **pseudopodia** (soo-dō-PŌ-dē-ah; *pseudo-*, false + *podon*, foot; singular *pseudopodium*) surround the object, and their

Figure 3–22 **Pinocytosis and Phagocytosis.**



a This is an electron micrograph showing pinocytosis at the surface of a cell in contact with the bloodstream.



b In phagocytosis, material is brought into the cell enclosed in a phagosome that is subsequently exposed to lysosomal enzymes. After nutrients are absorbed from the vesicle, the residue is discharged by exocytosis.

membranes fuse to form a phagosome (**Figure 3–22b**). This vesicle then fuses with many lysosomes, whereupon lysosomal enzymes digest its contents. Although most cells display pinocytosis, phagocytosis is performed only by specialized cells, such as the *macrophages* that protect tissues by engulfing bacteria, cell debris, and other abnormal materials.

Exocytosis

Exocytosis (ek-sō-sī-TŌ-sis), introduced in our discussion of the Golgi apparatus, is the functional reverse of endocytosis. In exocytosis, a vesicle created inside the cell fuses with, and becomes part of, the plasma membrane. When this occurs, the vesicle contents are released into the extracellular environment (**Figure 3–22b**). The ejected material may be secretory products, such as mucins or hormones, or waste products, such as those accumulating in endocytic vesicles. In a few specialized cells, endocytosis produces vesicles on one side of the cell that are discharged through exocytosis on the opposite side. This method of bulk transport is common in cells lining capillaries, which use a combination of pinocytosis and exocytosis to transfer fluid and solutes from the bloodstream into the surrounding tissues (**Figure 3–22a**). This process is called *vesicular transport*.

Many different mechanisms are moving materials into and out of the cell at any moment. Before proceeding further, review and compare the mechanisms summarized in **Table 3–2**.

Checkpoint

22. **Describe the process of carrier-mediated transport.**
23. **During digestion in the stomach, the concentration of hydrogen ions (H^+) rises to higher levels than in the cells lining the stomach. Which transport process must be operating?**
24. **Describe endocytosis.**
25. **Describe exocytosis.**
26. **What is the process called whereby certain types of white blood cells engulf bacteria?**

See the blue Answers tab at the back of the book.

Table 3–2 Mechanisms Involved in Movement across Plasma Membranes

Mechanism	Process	Factors Affecting Rate	Substances Involved (Sites)
Diffusion (includes simple diffusion and channel-mediated diffusion)	Molecular movement of solutes; direction determined by relative concentrations	Size of concentration gradient; size of molecules; electrical charge; lipid solubility, temperature; additional factors apply to channel-mediated diffusion	Small inorganic ions; most gases and lipid-soluble materials (all cells)
Osmosis	Movement of water molecules toward solution containing relatively higher solute concentration; requires selectively permeable membrane	Concentration gradient; opposing osmotic or hydrostatic pressure; number of aquaporins (water channels)	Water only (all cells)
Carrier-Mediated Transport			
Facilitated diffusion	Carrier proteins passively transport solutes across a membrane down a concentration gradient	Size of gradient, temperature, and availability of carrier protein	Glucose and amino acids (all cells, but several different regulatory mechanisms exist)
Active transport	Carrier proteins actively transport solutes across a membrane, often against a concentration gradient	Availability of carrier, substrates, and ATP	Na^+, K^+, Ca^{2+}, Mg^{2+} (all cells); other solutes by specialized cells
Secondary active transport	Carrier proteins passively transport two solutes, with one (normally Na^+) moving down its concentration gradient; the cell must later expend ATP to eject the Na^+	Availability of carrier, substrates, and ATP	Glucose and amino acids (specialized cells); iodide
Vesicular Transport			
Endocytosis	Creation of membranous vesicles containing fluid or solid material	Stimulus and mechanics incompletely understood; requires ATP	Fluids, nutrients (all cells); debris, pathogens (specialized cells)
Exocytosis	Fusion of vesicles containing fluids or solids (or both) with the plasma membrane	Stimulus and mechanics incompletely understood; requires ATP	Fluids, debris (all cells)

3-7 The transmembrane potential results from the unequal distribution of ions across the plasma membrane

As noted, the inside of the plasma membrane has a slight negative charge with respect to the outside. The cause is a slight excess of positive charges (due to cations) outside the plasma membrane, and a slight excess of negative charges (due primarily to negatively charged proteins) inside the plasma membrane. This unequal charge distribution is created by differences in the permeability of the membrane to various ions, as well as by active transport mechanisms.

Although the positive and negative charges are attracted to each other and would normally rush together, they are kept apart by the phospholipid membrane. When positive and negative charges are held apart, a **potential difference** exists between them. We refer to the potential difference across a plasma membrane as the **transmembrane potential.**

The unit of measurement of potential difference is the *volt* (V). Most cars, for example, have 12-V batteries. The transmembrane potentials of cells are much smaller, typically in the vicinity of 0.07 V. Such a value is usually expressed as 70 mV, or 70 *millivolts* (thousandths of a volt). The transmembrane potential in an undisturbed cell is called the **resting potential.** Each type of cell has a characteristic resting potential between −10 mV (−0.01 V) and −100 mV (−0.1 V), with the minus sign signifying that the inside of the plasma membrane contains an excess of negative charges compared with the outside. Examples include fat cells (−40 mV), thyroid cells (−50 mV), neurons (−70 mV), skeletal muscle cells (−85 mV), and cardiac muscle cells (−90 mV).

If the lipid barrier were removed, the positive and negative charges would rush together and the potential difference would be eliminated. The plasma membrane thus acts like a dam across a stream. Just as a dam resists the water pressure that builds up on the upstream side, a plasma membrane resists electrochemical forces that would otherwise drive ions into or out of the cell. The water retained behind a dam and the ions held on either side of the plasma membrane have *potential energy*—stored energy that can be released to do work. People have designed many ways to use the potential energy stored behind a dam—for example, turning a mill wheel or a turbine. Similarly, cells have ways of utilizing the potential energy stored in the transmembrane potential. For example, it is the transmembrane potential that makes possible the transmission of information in the nervous system, and thus our perceptions and thoughts. As we will see in later chapters, changes in the transmembrane potential also trigger the contractions of muscles and the secretions of glands.

Checkpoint

27. What is the transmembrane potential, and in what units is it expressed?
28. If the plasma membrane were freely permeable to sodium ions (Na^+), how would the transmembrane potential be affected?

See the blue Answers tab at the back of the book.

3-8 Stages of a cell's life cycle include interphase, mitosis, and cytokinesis

The period between fertilization and physical maturity involves tremendous changes in organization and complexity. At fertilization, a single cell is all there is; at maturity, your body has roughly 75 trillion cells. This amazing transformation involves a form of cellular reproduction called **cell division.** The division of a single cell produces a pair of **daughter cells,** each half the size of the original. Before dividing, each of the daughter cells will grow to the size of the original cell.

Even when development is complete, cell division continues to be essential to survival. Cells are highly adaptable, but physical wear and tear, toxic chemicals, temperature changes, and other environmental stresses can damage them. And, like individuals, cells age. The life span of a cell varies from hours to decades, depending on the type of cell and the stresses involved. Many cells apparently self-destruct after a certain period of time as a result of the activation of specific "suicide genes" in the nucleus. The genetically controlled death of cells is called **apoptosis** (ap-op-TŌ-sis; *apo-*, separated from + *ptosis*, a falling). Several genes involved in the regulation of this process have been identified. For example, a gene called *bcl-2* appears to prevent apoptosis and to keep a cell alive and functional. If something interferes with the function of this gene, the cell self-destructs.

Because a typical cell does not live nearly as long as a typical person, cell populations must be maintained over time by cell division. For cell division to be successful, the genetic material in the nucleus must be duplicated accurately, and one copy must be distributed to each daughter cell. The duplication of the cell's genetic material is called **DNA replication,** and nuclear division is called **mitosis** (mī-TŌ-sis). Mitosis occurs during the division of somatic cells. The production of sex cells involves a different process, **meiosis** (mī-Ō-sis), described in Chapter 28.

DNA Replication

Each DNA molecule consists of a pair of DNA strands joined by hydrogen bonds between complementary nitrogenous bases.

p. 55 **Figure 3–23** diagrams DNA replication. The process begins when enzymes called *helicases* unwind the strands and disrupt the weak bonds between the bases. As the strands unwind, molecules of **DNA polymerase** bind to the exposed nitrogenous bases. This enzyme (1) promotes bonding between the nitrogenous bases of the DNA strand and complementary DNA nucleotides dissolved in the nucleoplasm and (2) links the nucleotides by covalent bonds.

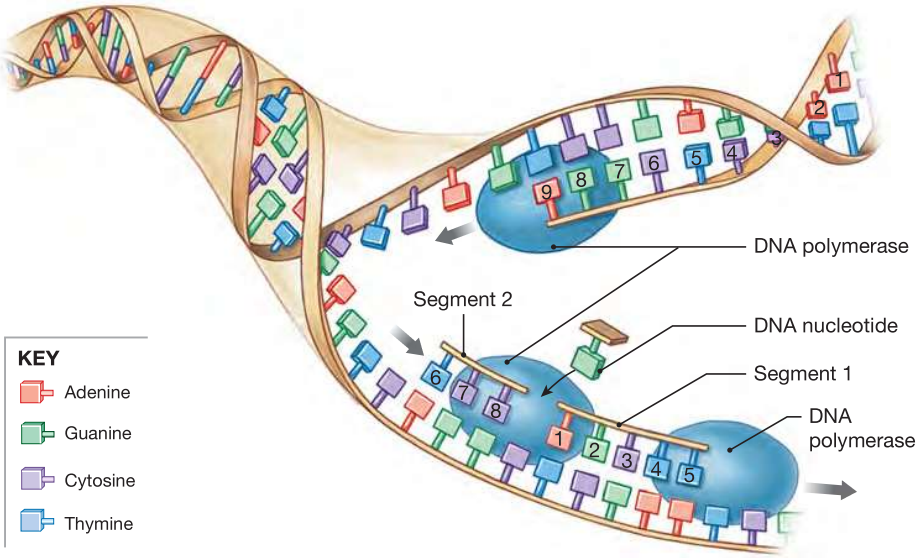
Many molecules of DNA polymerase work simultaneously along the DNA strands (**Figure 3–23**). DNA polymerase can work in only one direction along a strand of DNA, but the two strands in a DNA molecule are oriented in opposite directions. As a result, the DNA polymerase on one strand works toward the site where the strands are unzipping, but those on the other strand work away from it. As the two original strands gradually separate, the DNA polymerase bound to one strand (the upper strand in the figure) adds nucleotides to make a single, continuous complementary copy of that strand. This copy grows toward the "zipper" from right to left, adding nucleotides 1 through 9 in sequence; the 1 is added first, then 2 to the left of 1, and so on.

DNA polymerase on the other original strand, however, can work only away from the unzipping site. In the lower strand in **Figure 3–23**, the first DNA polymerase to bind to it must work from left to right, adding nucleotides in the sequence 1 ⟶ 2 ⟶ 3 ⟶ 4 ⟶ 5. But as the original strands continue to unzip, additional nucleotides are continuously exposed. This molecule of DNA polymerase cannot go into reverse; it can only continue working from left to right. Thus, a second molecule of DNA polymerase must bind closer to the point of unzipping and assemble a complementary copy that grows in the sequence until it bumps into the segment created by the first DNA polymerase. The two segments are then spliced together by enzymes called **ligases** (LĪ-gās-ez; *liga*, to tie). Eventually, the unzipping completely separates the original strands. The copying ends, the last splicing is done, and two identical DNA molecules have formed.

Interphase, Mitosis, and Cytokinesis

Spotlight Figure 3–24 depicts the life cycle of a typical cell. That life cycle includes a fairly brief period of mitosis alternating with an *interphase* of variable duration. In a cell preparing to divide, interphase can be divided into the G_1, S, and G_2 phases. DNA replication occurs during the S phase. Mitosis is the duplication of the chromosomes in the nucleus and their separation into two identical sets in the process of somatic cell division. Although we describe mitosis in stages, *prophase*, *metaphase*, *anaphase*, and *telophase*, it is really one continuous process. Cytokinesis is the division into two daughter cells. This process usually begins in late anaphase and continues throughout telophase. The completion of cytokinesis marks the end of cell division, creating two separate and complete cells, each surrounded by its own plasma membrane.

Figure 3–23 **DNA Replication.** In DNA replication, the DNA strands unwind, and DNA polymerase begins attaching complementary DNA nucleotides along each strand. On one original strand, the complementary copy is produced as a continuous strand. Along the other original strand, the copy begins as a series of short segments spliced together by ligases. This process ultimately produces two identical copies of the original DNA molecule.



Spotlight

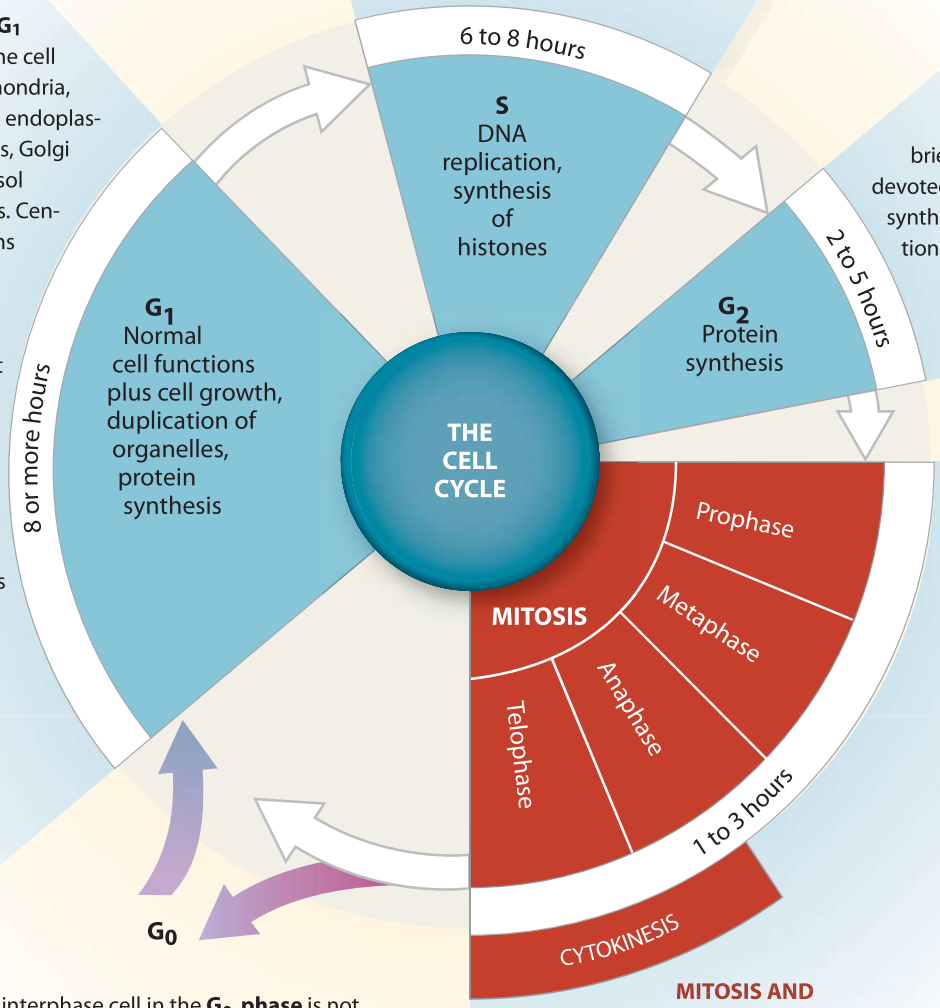
Figure 3–24
Stages of a Cell's Life Cycle

INTERPHASE

Most cells spend only a small part of their time actively engaged in cell division. Somatic cells spend the majority of their functional lives in a state known as **interphase.** During interphase, a cell performs all its normal functions and, if necessary, prepares for cell division.

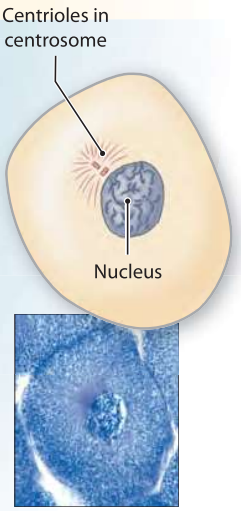
A cell that is ready to divide first enters the **G_1** phase. In this phase, the cell makes enough mitochondria, cytoskeletal elements, endoplasmic reticula, ribosomes, Golgi membranes, and cytosol for two functional cells. Centriole replication begins in G_1 and commonly continues until G_2. In cells dividing at top speed, G_1 may last just 8–12 hours. Such cells pour all their energy into mitosis, and all other activities cease. If G_1 lasts for days, weeks, or months, preparation for mitosis occurs as the cells perform their normal functions.

When the activities of **G_1** have been completed, the cell enters the **S phase**. Over the next 6–8 hours, the cell duplicates its chromosomes. This involves DNA replication and the synthesis of histones and other proteins in the nucleus.



MITOSIS AND CYTOKINESIS

Once DNA replication has ended, there is a brief (2–5-hour) **G_2 phase** devoted to last-minute protein synthesis and to the completion of centriole replication.



Interphase

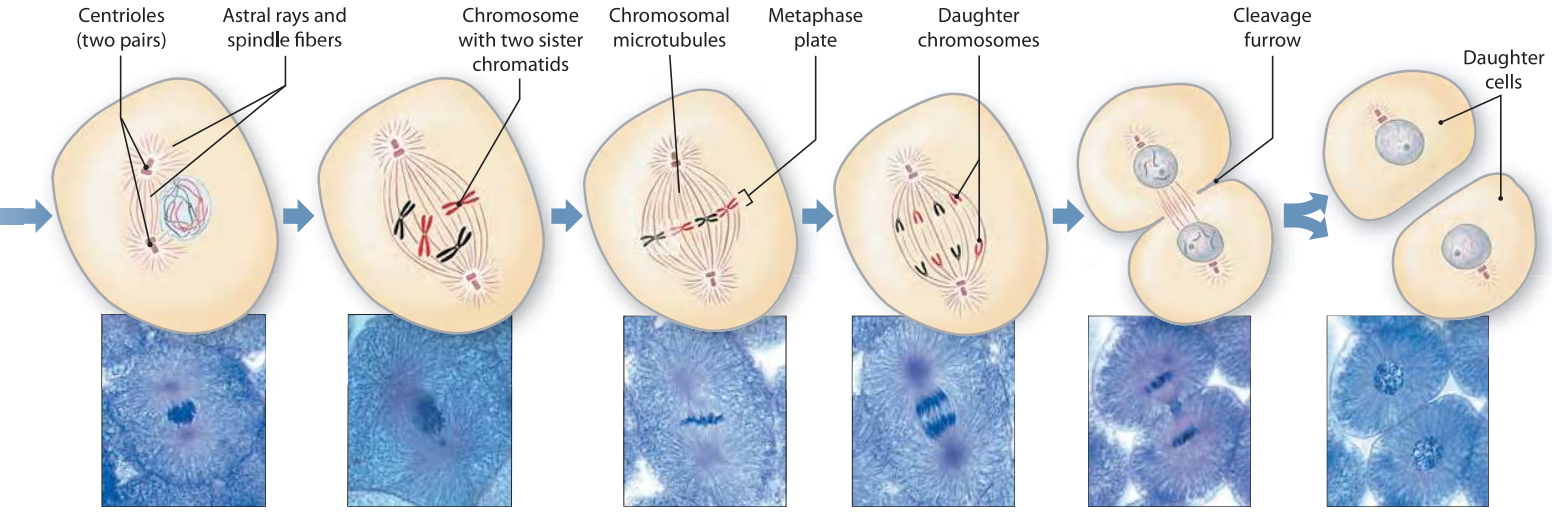
During interphase, the DNA strands are loosely coiled and chromosomes cannot be seen.

An interphase cell in the **G_0 phase** is not preparing for division, but is performing all of the other functions appropriate for that particular cell type. Some mature cells, such as skeletal muscle cells and most neurons, remain in G_0 indefinitely and never divide. In contrast, stem cells, which divide repeatedly with very brief interphase periods, never enter G_0.

A dividing cell shown held in place by a sucker pipe to the left and being injected with a needle from the right.

MITOSIS AND CYTOKINESIS

Mitosis separates the duplicated chromosomes of a cell into two identical nuclei. The term mitosis specifically refers to the division and duplication of the cell's nucleus; division of the cytoplasm to form two distinct new cells involves a separate but related process known as **cytokinesis.**



Early prophase

Prophase (PRŌ-fāz; *pro*, before) begins when the chromosomes coil so tightly they become visible as single structures under a light microscope. An array of microtubules called **spindle fibers** extends between the centriole pairs. Smaller microtubules called **astral rays** radiate into the cytoplasm.

Late prophase

As a result of DNA replication during the S phase, two copies of each chromosome now exist. Each copy, called a **chromatid** (KRŌ-ma-tid), is connected to its duplicate copy at a single point, the **centomere** (SEN-trō-mēr). **Kinetochores** (ki-NĒ-tō-korz) are the protein-bound area of the centromere; they attach to spindle fibers forming **chromosomal microtubules.**

Metaphase

Metaphase (MET-a-fāz; *meta*, after) begins as the chromatids move to a narrow central zone called the metaphase plate. Metaphase ends when all the chromatids are aligned in the plane of the metaphase plate.

Anaphase

Anaphase (AN-a-fāz; *ana-*, apart) begins when the centromere of each chromatid pair splits and the chromatids separate. The two **daughter chromosomes** are now pulled toward opposite ends of the cell along the chromosomal microtubules.

Telophase

During telophase (TĒL-ō-fāz; *telo-*, end), each new cell prepares to return to the interphase state. The nuclear membranes re-form, the nuclei enlarge, and the chromosomes gradually uncoil. This stage marks the end of mitosis.

Cytokinesis

Cytokinesis is the division of the cytoplasm into two daughter cells. Cytokinesis usually begins with the formation of a cleavage furrow and continues throughout telophase. The completion of cytokinesis marks the end of cell division.

3

Tips & Tricks

In order to remember the correct sequence of events during mitosis, imagine the contour rug in front of your toilet as the P-MAT, for ***p***rophase, ***m***etaphase, ***a***naphase, and ***t***elophase.

The Mitotic Rate and Energy Use

The preparations for cell division that occur between G_1 and the M phase are difficult to recognize in a light micrograph. However, the start of mitosis is easy to recognize, because the chromosomes become condensed and highly visible. The frequency of cell division can be estimated by the number of cells in mitosis at any time. As a result, we often use the term **mitotic rate** when we discuss rates of cell division. In general, the longer the life expectancy of a cell type, the slower the mitotic rate. Long-lived cells, such as muscle cells and neurons, either never divide or do so only under special circumstances. Other cells, such as those covering the surface of the skin or the lining of the digestive tract, are subject to attack by chemicals, pathogens, and abrasion. They survive for only days or even hours. Special cells called **stem cells** maintain these cell populations through repeated cycles of cell division.

Stem cells are relatively unspecialized; their only function is the production of daughter cells. Each time a stem cell divides, one of its daughter cells develops functional specializations while the other prepares for further stem cell divisions. The rate of stem cell division can vary with the type of tissue and the demand for new cells. In heavily abraded skin, stem cells may divide more than once a day, but stem cells in adult connective tissues may remain inactive for years.

Dividing cells use an unusually large amount of energy. For example, they must synthesize new organic materials and move organelles and chromosomes within the cell. All these processes require ATP in substantial amounts. Cells that do not have adequate energy sources cannot divide. In a person who is starving, normal cell growth and maintenance grind to a halt. For this reason, prolonged starvation stunts childhood growth, slows wound healing, lowers resistance to disease, thins the skin, and changes the lining of the digestive tract.

Checkpoint

29. Give the biological terms for (a) cellular reproduction and (b) cellular death.
30. Describe interphase, and identify its stages.
31. A cell is actively manufacturing enough organelles to serve two functional cells. This cell is probably in what phase of its life cycle?
32. Define mitosis, and list its four stages.
33. What would happen if spindle fibers failed to form in a cell during mitosis?

See the blue Answers tab at the back of the book.

Tips & Tricks

When considering the relative length of time that a cell spends in interphase compared to mitosis, think about taking a test. You prepare a long time (interphase) for something that happens quickly (mitosis).

3-9 Several growth factors affect the cell life cycle

In normal tissues, the rate of cell division balances the rate of cell loss or destruction. Mitotic rates are genetically controlled, and many different stimuli may be responsible for activating genes that promote cell division. Some of the stimuli are internal, and many cells set their own pace of mitosis and cell division. An important internal trigger is the level of **M-phase promoting factor (MPF),** also known as *maturation-promoting factor*. MPF is assembled from two parts: a cell division cycle protein called *Cdc2* and a second protein called *cyclin*. Cyclin levels climb as the cell life cycle proceeds. When levels are high enough, MPF appears in the cytoplasm and mitosis gets under way.

Various extracellular compounds—generally, peptides—can stimulate the division of specific types of cells. These compounds include several hormones and a variety of **growth factors.** Table 3–3 lists some of these chemical factors and their target tissues; we will discuss these in later chapters.

Genes that inhibit cell division have been identified. Such genes are known as *repressor genes*. One gene, called *p53*, controls a protein that resides in the nucleus and activates genes that direct the production of growth-inhibiting factors inside the cell. Roughly half of all cancers are associated with abnormal forms of the *p53* gene.

There are indications that in humans, the *number* of cell divisions performed by a cell and its descendants is regulated at the chromosome level by structures called **telomeres.** Telomeres are terminal segments of DNA with associated proteins. These DNA-protein complexes bend and fold repeatedly to form caps at the ends of chromosomes, much like the plastic sheaths on the tips of shoestrings. Telomeres have several functions, notably to attach chromosomes to the nuclear matrix and to protect the ends of the chromosomes from damage during mitosis. The telomeres themselves, however, are subject to wear and tear over the years. Each time a cell divides during adult life, some of the repeating segments break off, and the telomeres get shorter. When they get too short, repressor gene activity signals the cell to stop dividing.

Checkpoint

34. Define growth factor, and identify several growth factors that affect cell division.

See the blue Answers tab at the back of the book.

Table 3–3 Chemical Factors Affecting Cell Division

Factor	Sources	Effects	Targets
M-phase promoting factor (maturation-promoting factor)	Forms within cytoplasm from Cdc2 and cyclin	Initiates mitosis	Regulatory mechanism active in all dividing cells
Growth hormone	Anterior lobe of the pituitary gland	Stimulation of growth, cell division, differentiation	All cells, especially in epithelial and connective tissues
Prolactin	Anterior lobe of the pituitary gland	Stimulation of cell growth, division, development	Gland and duct cells of mammary glands
Nerve growth factor (NGF)	Salivary glands; other sources suspected	Stimulation of nerve cell repair and development	Neurons and neuroglia
Epidermal growth factor (EGF)	Duodenal glands; other sources suspected	Stimulation of stem cell divisions and epithelial repairs	Epidermis
Fibroblast growth factor (FGF)	Unknown	Division and differentiation of fibroblasts and related cells	Connective tissues
Erythropoietin	Kidneys (primary source)	Stimulation of stem cell divisions and maturation of red blood cells	Bone marrow
Thymosins and related compounds	Thymus	Stimulation of division and differentiation of lymphocytes (especially T cells)	Thymus and other lymphoid tissues and organs
Chalones	Many tissues	Inhibition of cell division	Cells in the immediate area

3-10 Tumors and cancers are characterized by abnormal cell growth and division

When the rates of cell division and growth exceed the rate of cell death, a tissue begins to enlarge. A **tumor,** or *neoplasm,* is a mass or swelling produced by abnormal cell growth and division. In a *benign tumor,* the cells usually remain within the epithelium (one of the four primary tissue types) or a connective tissue capsule. Such a tumor seldom threatens an individual's life and can usually be surgically removed if its size or position disturbs tissue function.

Cells in a *malignant tumor* no longer respond to normal control mechanisms. These cells do not remain confined within the epithelium or a connective tissue capsule, but spread into surrounding tissues. The tumor of origin is called the *primary tumor* (or *primary neoplasm*), and the spreading process is called **invasion.** Malignant cells may also travel to distant tissues and organs and establish *secondary tumors*. This dispersion, called **metastasis** (me-TAS-ta-sis; *meta-*, after + *stasis*, standing still), is very difficult to control.

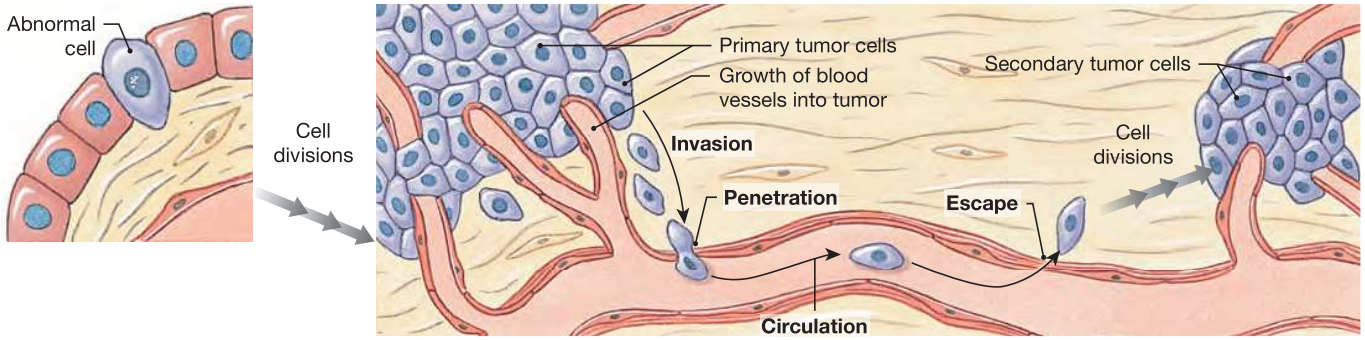
Cancer is an illness characterized by mutations that disrupt normal control mechanisms and produce potentially malignant cells. Cancer develops in the series of steps diagrammed in **Figure 3–25**. Initially, the cancer cells are restricted to the primary tumor. In most cases, all the cells in the tumor are the daughter cells of a single malignant cell. Normal cells often become malignant when a mutation occurs in a gene involved with cell growth, differentiation, or division. The modified genes are called **oncogenes** (ON-kō-gēnz; *oncōs*, tumor).

Cancer cells gradually lose their resemblance to normal cells. They change shape and typically become abnormally large or small. At first, the growth of the primary tumor distorts the tissue, but the basic tissue organization remains intact. Metastasis begins with invasion as tumor cells "break out" of the primary tumor and invade the surrounding tissue. They may then enter the lymphatic system and accumulate in nearby lymph nodes. When metastasis involves the penetration of blood vessels, the cancer cells circulate throughout the body.

Responding to cues that are as yet unknown, cancer cells in the bloodstream ultimately escape out of blood vessels to establish secondary tumors at other sites. These tumors are extremely active metabolically, and their presence stimulates the growth of blood vessels into the area. The increased circulatory supply provides additional nutrients to the cancer cells and further accelerates tumor growth and metastasis.

As malignant tumors grow, organ function begins to deteriorate. The malignant cells may no longer perform their original functions, or they may perform normal functions in an abnormal way. For example, endocrine cancer cells may produce normal hormones, but in excessively large amounts. Cancer cells do not use energy very efficiently. They grow and multiply at the expense of healthy tissues, competing for space and nutrients with normal cells. This competition contributes to the starved appearance of many patients in the late stages of

Figure 3–25 The Development of Cancer.



Clinical Note

Telomerase, Aging, and Cancer

Each telomere contains a sequence of about 8000 nitrogenous bases, but they are multiple copies of the same base sequence, TTAGGG, repeated over and over again. Telomeres are not formed by DNA polymerase; instead, they are created by an enzyme called *telomerase*. Telomerase is functional early in life, but by adulthood it has become inactive. As a result, the telomere segments lost during each mitotic division are not replaced. Eventually, shortening of the telomere reaches a point at which the cell no longer divides.

This mechanism is a factor in the aging process, since many of the signs of age result from the gradual loss of functional stem cell populations. Experiments are in progress to determine whether activating telomerase (or a suspected alternative repair enzyme) can forestall or reverse the effects of aging. This would seem to be a very promising area of research. Activate telomerase, and halt aging—sounds good, doesn't it? Unfortunately, there's a catch: In adults, telomerase activation is a key step in the development of cancer.

If for some reason a cell with short telomeres does *not* respond normally to repressor genes, it will continue to divide. The result is mechanical damage to the DNA strands, chromosomal abnormalities, and mutations. Interestingly, one of the first consequences of such damage is the abnormal activation of telomerase. Once this occurs, the abnormal cells can continue dividing indefinitely. Telomerase is active in at least 90 percent of all cancer cells. Research is therefore under way to find out how to turn off telomerase that has been improperly activated.

cancer. Death may occur as a result of the compression of vital organs when nonfunctional cancer cells have killed or replaced the healthy cells in those organs, or when the cancer cells have starved normal tissues of essential nutrients. We will return to the subject of cancer in later chapters that deal with specific systems.

Checkpoint

35. **An illness characterized by mutations that disrupt normal control mechanisms and produce potentially malignant cells is termed _____.**
36. **Define metastasis.**

See the blue Answers tab at the back of the book.

3-11 Differentiation is cellular specialization as a result of gene activation or repression

An individual's liver cells, fat cells, and neurons all contain the same set of chromosomes and genes, but in each case a different set of genes has been turned *off*. In other words, liver cells and fat cells differ because liver cells have one set of genes accessible for transcription, and fat cells another.

When a gene is functionally eliminated, the cell loses the ability to produce a particular protein—and thus to perform any functions involving that protein. Each time another gene switches off, the cell's functional abilities become more restricted. This development of specific cellular features is called **differentiation.**

Fertilization produces a single cell with all its genetic potential intact. Repeated cell divisions follow, and differentiation begins as the number of cells increases. Differentiation produces specialized cells with limited capabilities. These cells form organized collections known as *tissues*, each with discrete functional roles. In Chapter 4, we will examine the structure and function of tissues and will consider the role of tissue interactions in maintaining homeostasis.

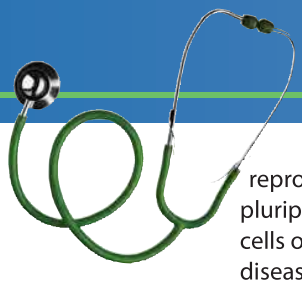
Checkpoint

37. **Define differentiation.**

See the blue Answers tab at the back of the book.

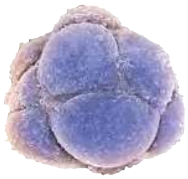
Clinical Note

Parkinson's Disease



Could **stem cells** treat **Parkinson's disease**?

In most cases, differentiation is irreversible: Once genes are turned off, they won't be turned back on. However, some cells, such as stem cells, are relatively undifferentiated. These cells can differentiate into any of several different types of cell, depending on local conditions. For example, if nutrients are abundant, stem cells in many parts of the body can differentiate into fat cells. Researchers are gradually discovering what chemical cues and genes are responsible for controlling the differentiation of specific cell types. A recent turn in this research has resulted in the ability to "turn back the clock" in some types of adult somatic cells and



reprogram them into a form of stem cells called induced pluripotent stem (iPS) cells. The ability to take a person's stem cells or somatic cells and create new cells or neurons to treat diseased cells may one day revolutionize the practice of medicine.

Parkinson's disease, a neurodegenerative disease characterized by progressive degeneration and loss of dopamine (DA)-producing neurons, may be the first disorder suited to stem cell implantation treatment. (Dopamine is one kind of neurotransmitter, a substance that one neuron releases to communicate with other neurons.) Several laboratories have demonstrated success in inducing either iPS cells or embryonic stem cells to differentiate into cells that function as dopamine-producing neurons. Studies on animal models show that both iPS and embryonic stem cell–derived DA neurons reinnervated the brains of rats with Parkinson's disease, released dopamine, and improved motor function.

Related Clinical Terms

anaplasia: An irreversible change in the size and shape of tissue cells.
carcinogen: A cancer-causing agent.
dysplasia: A reversible change in the normal shape, size, and organization of tissue cells.
genetic engineering: A general term that encompasses attempts to change the genetic makeup of cells or organisms, including humans.
hyperplasia: An increase in the number of normal cells (not tumor formation) in a tissue or organ, thus enlarging that tissue or organ.
hypertrophy: The enlargement of an organ or tissue due to an increase in the size of its cells.
liposome: A minute spherical sac of lipid molecules enclosing a water droplet. Often formed artificially to carry drugs into the tissues.
necrosis: Death of one or more cells in an organ or tissue due to disease, injury, or inadequate blood supply.
oncologist: Physician who specializes in the identification and treatment of cancers.
prion: A protein particle that is not visible microscopically, contains no nucleic acid, is resistant to destruction, and is thought to be the cause of some brain diseases such as bovine spongiform encephalopathy (BSE), scrapie, and Creutzfeldt-Jakob disease.
scanning electron micrograph (SEM): An image produced by an electron microscope in which a beam of focused electrons moves across an object with that object producing secondary electrons that are scattered and formatted into a three-dimensional image on a cathode-ray tube—also called *scanning microscope*.
transmission electron micrograph (TEM): A cross-sectional image produced by an electron microscope that passes a beam of electrons through an extremely small specimen. After passing through the sample the electrons are focused to form a magnified sectional view.

Chapter Review

Study Outline

An Introduction to Cells p. 63

1. Contemporary *cell theory* incorporates several basic concepts: (1) Cells are the building blocks of all plants and animals; (2) cells are produced by the division of preexisting cells; (3) cells are the smallest units that perform all vital physiological functions; and (4) each cell maintains homeostasis at the cellular level *(Spotlight Figure 3–1)*
2. **Cytology,** the study of cellular structure and function, is part of **cell biology.**
3. The human body contains two types of cells: **sex cells** *(sperm* and *oocytes)* and **somatic cells** (all other cells). *(Spotlight Figure 3–1)*

3-1 The plasma membrane separates the cell from its surrounding environment and performs various functions p. 63

4. A typical cell is surrounded by **extracellular fluid**—specifically, the **interstitial fluid** of the tissue. The cell's outer boundary is the **plasma membrane (cell membrane).**

5. The plasma membrane's functions include physical isolation, regulation of exchange with the environment, sensitivity to the environment, and structural support. *(Figure 3–2)*
6. The plasma membrane, which is a **phospholipid bilayer,** contains other lipids, proteins, and carbohydrates.
7. **Integral proteins** are part of the membrane itself; **peripheral proteins** are attached to, but can separate from, the membrane.
8. Membrane proteins can act as anchors **(anchoring proteins),** identifiers **(recognition proteins),** enzymes, receptors **(receptor proteins),** carriers **(carrier proteins),** or **channels.**
9. The **glycocalyx** on the outer cell surface is formed by the carbohydrate portions of *proteoglycans*, *glycoproteins*, and *glycolipids*. Functions include lubrication and protection, anchoring and locomotion, specificity in binding, and recognition.

3-2 Organelles within the cytoplasm perform particular functions p. 68

10. The **cytoplasm** contains the fluid **cytosol** and the **organelles** suspended in the cytosol.
11. Cytosol differs from extracellular fluid in composition and in the presence of **inclusions.**
12. **Nonmembranous organelles** are not completely enclosed by membranes, and all of their components are in direct contact with the cytosol. They include the *cytoskeleton*, *microvilli*, *centrioles*, *cilia*, *ribosomes*, and *proteasomes*. *(Spotlight Figure 3–1)*
13. **Membranous organelles** are surrounded by phospholipid membranes that isolate them from the cytosol. They include the *endoplasmic reticulum*, the *Golgi apparatus*, *lysosomes*, *peroxisomes*, *mitochondria*, and *nucleus*. *(Spotlight Figure 3–1)*
14. The **cytoskeleton** gives the cytoplasm strength and flexibility. It has four components: **microfilaments** (typically made of **actin**), **intermediate filaments, microtubules** (made of **tubulin**), and **thick filaments** (made of **myosin**). *(Figure 3–3)*
15. **Microvilli** are small projections of the plasma membrane that increase the surface area exposed to the extracellular environment. *(Figure 3–3)*
16. **Centrioles** direct the movement of chromosomes during cell division and organize the cytoskeleton. The **centrosome** is the cytoplasm surrounding the centrioles. *(Figure 3–4)*
17. **Cilia,** anchored by a **basal body,** beat rhythmically to move fluids or secretions across the cell surface. *(Figure 3–4)*
18. **Ribosomes,** responsible for manufacturing proteins, are composed of a **small** and a **large ribosomal subunit,** both of which contain **ribosomal RNA (rRNA). Free ribosomes** are in the cytoplasm, and **fixed ribosomes** are attached to the endoplasmic reticulum. *(Spotlight Figure 3–1)*
19. **Proteasomes** remove and break down damaged or abnormal proteins that have been tagged with *ubiquitin*.
20. The **endoplasmic reticulum (ER)** is a network of intracellular membranes that function in synthesis, storage, transport, and detoxification. The ER forms hollow tubes, flattened sheets, and chambers called **cisternae. Smooth endoplasmic reticulum (SER)** is involved in lipid synthesis; **rough endoplasmic reticulum (RER)** contains ribosomes on its outer surface and forms **transport vesicles.** *(Figure 3–5)*
21. The **Golgi apparatus** forms **secretory vesicles** and new membrane components, and packages *lysosomes*. Secretions are discharged from the cell by exocytosis. *(Figures 3–6; Spotlight Figure 3–7)*
22. **Lysosomes,** vesicles filled with digestive enzymes, are responsible for the **autolysis** of injured cells. *(Figures 3–6, 3–8)*
23. **Peroxisomes** carry enzymes that neutralize potentially dangerous free radicals.
24. **Membrane flow** refers to the continuous movement and recycling of the membrane among the ER, vesicles, the Golgi apparatus, and the plasma membrane.
25. **Mitochondria** are responsible for ATP production through aerobic metabolism. The **matrix,** or fluid contents of a mitochondrion, lies inside the **cristae,** or folds of an inner membrane. *(Figure 3–9)*

3-3 The nucleus contains DNA and enzymes essential for controlling cellular activities p. 78

26. The **nucleus** is the control center of cellular operations. It is surrounded by a **nuclear envelope** (a double membrane with a **perinuclear space**), through which it communicates with the cytosol by way of **nuclear pores.** *(Spotlight Figure 3–1; Figure 3–10)*
27. The nucleus contains a supportive **nuclear matrix;** one or more **nucleoli** typically are present.
28. The nucleus controls the cell by directing the synthesis of specific proteins, using information stored in **chromosomes,** which consist of DNA bound to **histones.** In nondividing cells, DNA and associated proteins form a tangle of filaments called **chromatin.** *(Figure 3–11)*
29. The cell's information storage system, the **genetic code,** is called a *triplet code* because a sequence of three nitrogenous bases specifies the identity of a single amino acid. Each **gene** contains all the DNA triplets needed to produce a specific polypeptide chain.

3-4 DNA controls protein synthesis, cell structure, and cell function p. 81

30. As **gene activation** begins, **RNA polymerase** must bind to the gene.
31. **Transcription** is the production of RNA from a DNA template. After transcription, a strand of **messenger RNA (mRNA)** carries instructions from the nucleus to the cytoplasm. *(Figure 3–12)*
32. During **translation,** a functional polypeptide is constructed using the information contained in the sequence of **codons** along an mRNA strand. The sequence of codons determines the sequence of amino acids in the polypeptide.
33. By complementary base pairing of **anticodons** to mRNA codons, **transfer RNA (tRNA)** molecules bring amino acids to the ribosomal complex. *(Figure 3–13; Table 3–1)*
34. The DNA of the nucleus has both direct and indirect control over protein synthesis.

3-5 Diffusion is a passive transport mechanism that assists membrane passage p. 86

35. The **permeability** of a barrier such as the plasma membrane is an indication of the barrier's effectiveness. Nothing can pass through an **impermeable** barrier; anything can pass through a **freely permeable** barrier. Plasma membranes are **selectively permeable.**
36. **Diffusion** is the net movement of material from an area of higher concentration to an area of lower concentration. Diffusion occurs until the **concentration gradient** is eliminated. *(Figures 3–14, 3–15)*
37. Most lipid-soluble materials and gases freely diffuse across the phospholipid bilayer of the plasma membrane. Water and small ions rely on channel-mediated diffusion through a passageway within a transmembrane protein. **Leak channels**

are passive channels that allow ions across the plasma membrane.

38. **Osmosis** is the net flow of water across a membrane in response to differences in osmotic pressure. **Osmotic pressure** is the force of water movement into a solution resulting from solute concentration. **Hydrostatic pressure** can oppose osmotic pressure. *(Figure 3–16)*
39. **Tonicity** describes the effects of osmotic solutions on cells. A solution that does not cause an osmotic flow is **isotonic.** A solution that causes water to flow into a cell is **hypotonic** and can lead to **hemolysis** of red blood cells. A solution that causes water to flow out of a cell is **hypertonic** and can lead to **crenation.** *(Figure 3–17)*

3-6 Carrier-mediated and vesicular transport mechanisms assist membrane passage p. 90

40. Carrier-mediated transport involves the binding and transporting of specific ions by integral proteins. **Cotransport** moves two substances in the same direction; **countertransport** moves them in opposite directions.
41. In **facilitated diffusion,** compounds are transported across a membrane after binding to a **receptor site** within the channel of a carrier protein. *(Figure 3–18)*
42. **Active transport** mechanisms consume ATP and are not dependent on concentration gradients. Some **ion pumps** are **exchange pumps. Secondary active transport** may involve cotransport or countertransport. *(Figures 3–19, 3–20)*
43. In **vesicular transport,** materials move into or out of the cell in membranous **vesicles.** Movement into the cell is accomplished through **endocytosis,** an active process that can take three forms: **receptor-mediated endocytosis** (by means of **coated vesicles**), **pinocytosis,** or **phagocytosis** (using **pseudopodia).** The ejection of materials from the cytoplasm is accomplished by **exocytosis.** *(Figures 3–21, 3–22; Table 3–2)*

3-7 The transmembrane potential results from the unequal distribution of ions across the plasma membrane p. 96

44. The **potential difference,** measured in volts, between the two sides of a plasma membrane is a **transmembrane potential.** The transmembrane potential in an undisturbed cell is the cell's **resting potential.**

3-8 Stages of a cell's life cycle include interphase, mitosis, and cytokinesis p. 96

45. **Cell division** is the reproduction of cells. **Apoptosis** is the genetically controlled death of cells. **Mitosis** is the nuclear division of somatic cells. Sex cells are produced by **meiosis.** *(Spotlight Figure 3–24)*
46. Most somatic cells spend the majority of their time in **interphase,** which includes the **G_1, S (DNA replication),** and **G_2 phases.** *(Figure 3–23; Spotlight Figure 3–24)*
47. Mitosis proceeds in four stages: **prophase, metaphase, anaphase,** and **telophase.** *(Spotlight Figure 3–24)*
48. During **cytokinesis,** the cytoplasm is divided and cell division ends. *(Spotlight Figure 3–24)*
49. In general, the longer the life expectancy of a cell type, the slower is the **mitotic rate. Stem cells** undergo frequent mitosis to replace other, more specialized cells.

3-9 Several growth factors affect the cell life cycle p. 100

50. A variety of **growth factors** can stimulate cell division and growth. *(Table 3–3)*

3-10 Tumors and cancers are characterized by abnormal cell growth and division p. 101

51. Produced by abnormal cell growth and division, a **tumor,** or **neoplasm,** can be **benign** or **malignant.** Malignant cells may spread locally (by **invasion**) or to distant tissues and organs (through **metastasis**). The resultant illness is called **cancer.** Modified genes called **oncogenes** often cause malignancy. *(Figure 3–25)*

3-11 Differentiation is cellular specialization as a result of gene activation or repression p. 102

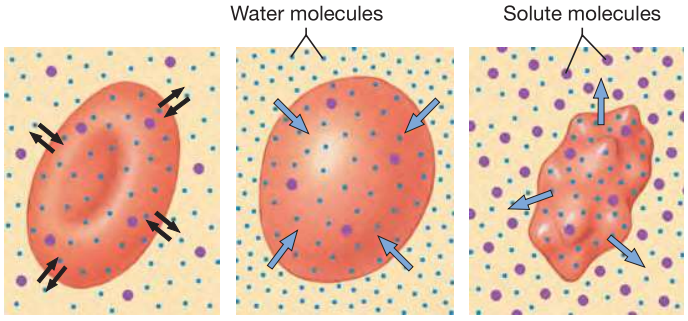
52. **Differentiation,** a process of specialization, results from the inactivation of particular genes in different cells, producing populations of cells with limited capabilities. Specialized cells form organized collections called *tissues*, each of which has certain functional roles.

Review Questions

See the blue Answers tab at the back of the book.

LEVEL 1 Reviewing Facts and Terms

1. In the following diagram, identify the type of solution (hypertonic, hypotonic, or isotonic) in which the red blood cells are immersed.



2. The process that transports solid objects such as bacteria into the cell is called
   (a) pinocytosis.
   (b) phagocytosis.
   (c) exocytosis.
   (d) receptor-mediated endocytosis.
   (e) channel-mediated transport.
3. Plasma membranes are said to be
   (a) impermeable.
   (b) freely permeable.
   (c) selectively permeable.
   (d) actively permeable.
   (e) slightly permeable.

3

4. _____ ion concentrations are high in extracellular fluids, and _____ ion concentrations are high in the cytoplasm.
   (a) Calcium, magnesium
   (b) Chloride, sodium
   (c) Potassium, sodium
   (d) Sodium, potassium
5. In a resting transmembrane potential, the inside of the cell is _____, and the cell exterior is _____.
   (a) slightly negative, slightly positive
   (b) slightly positive, slightly negative
   (c) slightly positive, neutral
   (d) slightly negative, neutral
6. The organelle responsible for a variety of functions centering around the synthesis of lipids and carbohydrates is
   (a) the Golgi apparatus.
   (b) the rough endoplasmic reticulum.
   (c) the smooth endoplasmic reticulum.
   (d) mitochondria.
7. The construction of a functional polypeptide by using the information in an mRNA strand is
   (a) translation.
   (b) transcription.
   (c) replication.
   (d) gene activation.
8. Our somatic cell nuclei contain _____ pairs of chromosomes.
   (a) 8
   (b) 16
   (c) 23
   (d) 46
9. The movement of water across a membrane from an area of low solute concentration to an area of higher solute concentration is known as
   (a) osmosis.
   (b) active transport.
   (c) diffusion.
   (d) facilitated transport.
   (e) filtration.
10. The interphase of the cell life cycle is divided into
    (a) prophase, metaphase, anaphase, and telophase.
    (b) G_0, G_1, S, and G_2.
    (c) mitosis and cytokinesis.
    (d) all of these.
11. List the four basic concepts that make up modern-day cell theory.
12. What are four general functions of the plasma membrane?
13. What are the primary functions of membrane proteins?
14. By what three major transport mechanisms do substances get into and out of cells?
15. List five important factors that influence diffusion rates.
16. What are the four major functions of the endoplasmic reticulum?

LEVEL 2 Reviewing Concepts

17. Diffusion is important in body fluids, because it tends to
    (a) increase local concentration gradients.
    (b) eliminate local concentration gradients.
    (c) move substances against concentration gradients.
    (d) create concentration gradients.
18. Microvilli are found
    (a) mostly in muscle cells.
    (b) on the inside of plasma membranes.
    (c) in large numbers on cells that secrete hormones.
    (d) in cells that are actively engaged in absorption.
    (e) only on cells lining the reproductive tract.
19. When a cell is placed in a(n) _____ solution, the cell will lose water through osmosis. This process results in the _____ of red blood cells.
    (a) hypotonic, crenation
    (b) hypertonic, crenation
    (c) isotonic, hemolysis
    (d) hypotonic, hemolysis
20. Suppose that a DNA segment has the following nucleotide sequence: CTC–ATA–CGA–TTC–AAG–TTA. Which nucleotide sequences would a complementary mRNA strand have?
    (a) GAG–UAU–GAU–AAC–UUG–AAU
    (b) GAG–TAT–GCT–AAG–TTC–AAT
    (c) GAG–UAU–GCU–AAG–UUC–AAU
    (d) GUG–UAU–GGA–UUG–AAC–GGU
21. How many amino acids are coded in the DNA segment in Review Question 20?
    (a) 18
    (b) 9
    (c) 6
    (d) 3
22. The sodium–potassium exchange pump
    (a) is an example of facilitated diffusion.
    (b) does not require the input of cellular energy in the form of ATP.
    (c) moves the sodium and potassium ions along their concentration gradients.
    (d) is composed of a carrier protein located in the plasma membrane.
    (e) is not necessary for the maintenance of homeostasis.
23. If a cell lacked ribosomes, it would not be able to
    (a) move.
    (b) synthesize proteins.
    (c) produce DNA.
    (d) metabolize sugar.
    (e) divide.
24. List, in sequence, the phases of the interphase stage of the cell life cycle, and briefly describe what happens in each.
25. List the stages of mitosis, and briefly describe the events that occur in each.
26. (a) What is cytokinesis?
    (b) What is the role of cytokinesis in the cell cycle?

LEVEL 3 Critical Thinking and Clinical Applications

27. The transport of a certain molecule exhibits the following characteristics: (1) The molecule moves down its concentration gradient; (2) at concentrations above a given level, the rate of transport does not increase; and (3) cellular energy is not required for transport to occur. Which transport process is at work?
28. Solutions A and B are separated by a selectively permeable barrier. Over time, the level of fluid on side A increases. Which solution initially had the higher concentration of solute?
29. A molecule that blocks the ion channels in integral proteins in the plasma membrane would interfere with
    (a) cell recognition.
    (b) the movement of lipid-soluble molecules.
    (c) producing changes in the electrical charges across a plasma membrane.
    (d) the ability of protein hormones to stimulate the cell.
    (e) the cell's ability to divide.
30. What is the benefit of having some of the cellular organelles enclosed by a membrane similar to the plasma membrane?