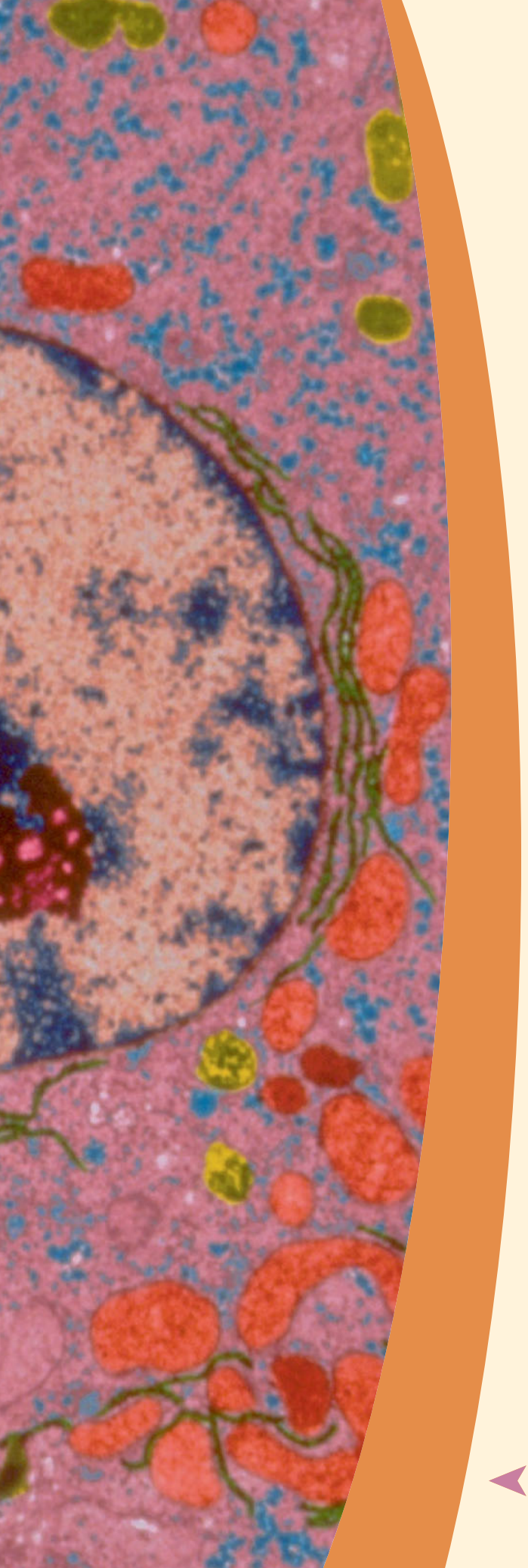


Cells: The Living Units

2

Liver cell (colored TEM).

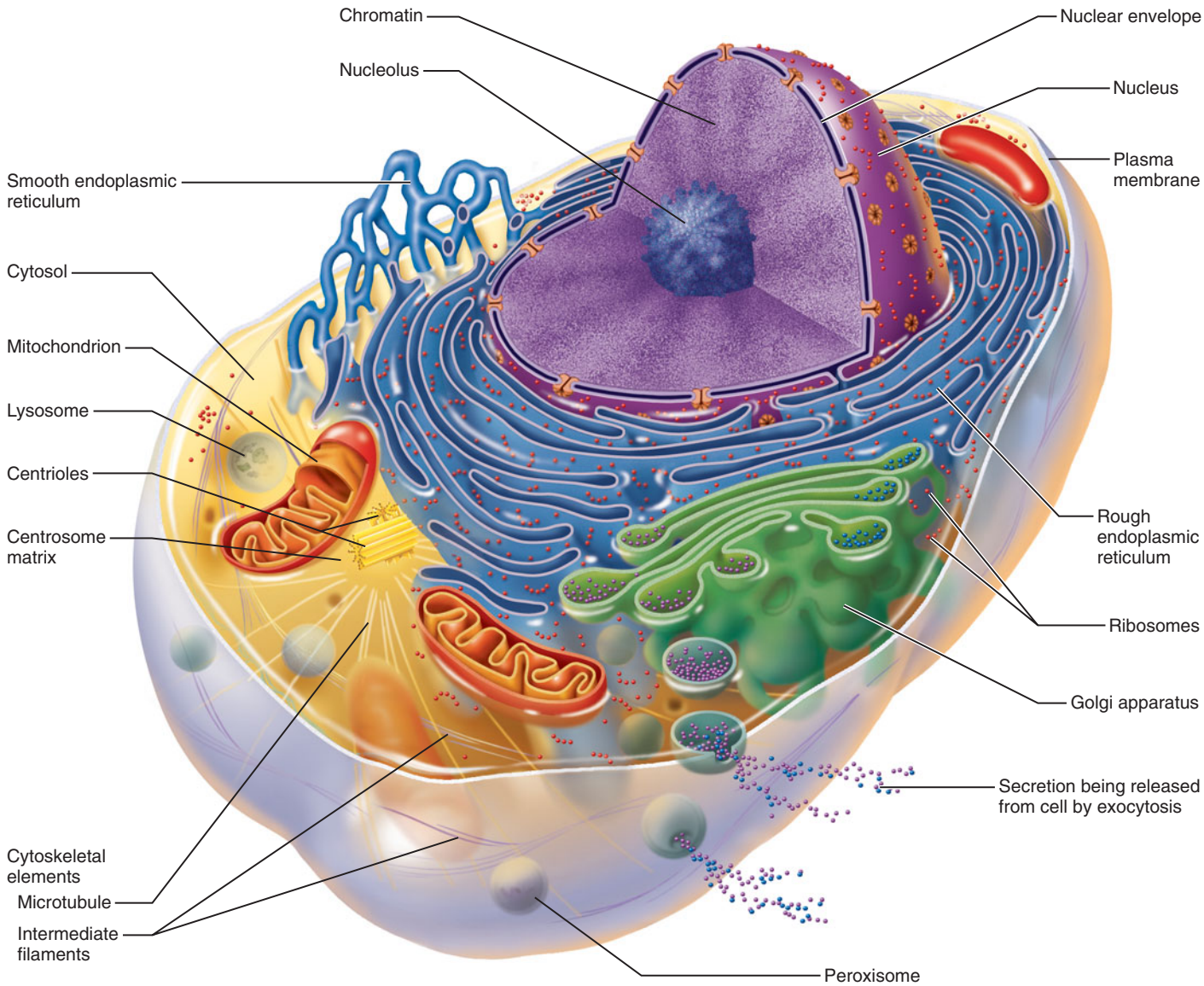


FIGURE 2.1 Structure of a generalized cell. No cell type is exactly like this one, but this composite illustrates features common to animal cells. Not all of the organelles are drawn to the same scale in this illustration.

All living organisms are cellular in nature, from one-celled "generalists" such as amoebas to complex multicellular organisms such as trees, dogs, and humans. Just as bricks and timbers are the structural units of a house, cells are structural units of all living things. The human body has about *50 to 100 trillion cells.* This chapter examines the structures and functions that are common to the different cells of the body. Specialized cells and their unique functions are addressed in detail in later chapters.

OVERVIEW OF CELLS

➤ Define a cell, its basic activities, and its three major regions.

The scientist Robert Hooke first observed plant cells with a crude microscope in the late 1600s. However, it was not until the 1830s that two scientists, Matthias Schleiden and Theodor Schwann, boldly asserted that all living things are composed of cells. Shortly thereafter, the pathologist Rudolf Virchow extended this idea by contending that cells arise only from other cells. Virchow's thesis was revolutionary because it challenged the prevailing theory of spontaneous generation, which held that organisms can arise from nonliving matter. Since the late 1800s, cell research has been exceptionally fruitful. Currently, scientific knowledge about the cell is increasing exponentially.

Cells are the smallest living units in the body. Each cell performs all the functions necessary to sustain life. It can obtain nutrients and other essential substances from the surrounding body fluids and use these nutrients to make the molecules it needs to survive. Each cell also disposes of its wastes and maintains its shape and integrity. Finally, cells can replicate themselves. These functions are carried out by the cell's many subunits, most of which are called **organelles**

("little organs"). Although different cell types perform different functions, virtually all human cells contain the same basic parts and can be described in terms of a generalized cell **(Figure 2.1)**. Human cells have three main parts: the plasma membrane, the cytoplasm, and the nucleus. The *plasma membrane* is the outer boundary. Internal to this membrane is the *cytoplasm* (si′to-plazm), which makes up the bulk of the cell, contains most of the cellular organelles, and surrounds the nucleus. The *nucleus* (nu′kle-us) controls cellular activities and lies near the cell's center. To understand the functions of a cell and its diverse cellular organelles, you can think of the cell as a manufacturing plant. The cell, like the manufacturing plant, has many divisions with specific functions. This analogy will be extended throughout this chapter. These cell structures are discussed next and summarized in **Table 2.1** on p. 29.

check your understanding

1. What are the three general regions of a cell?

For the answer, see Appendix B.

THE PLASMA MEMBRANE

- Describe the composition and basic functions of the plasma membrane.
- Explain the different processes used to move molecules across the plasma membrane.

The outer cell membrane **(Figure 2.2)** is called the **plasma membrane** or **plasmalemma** (plaz′mah-lem′ah;

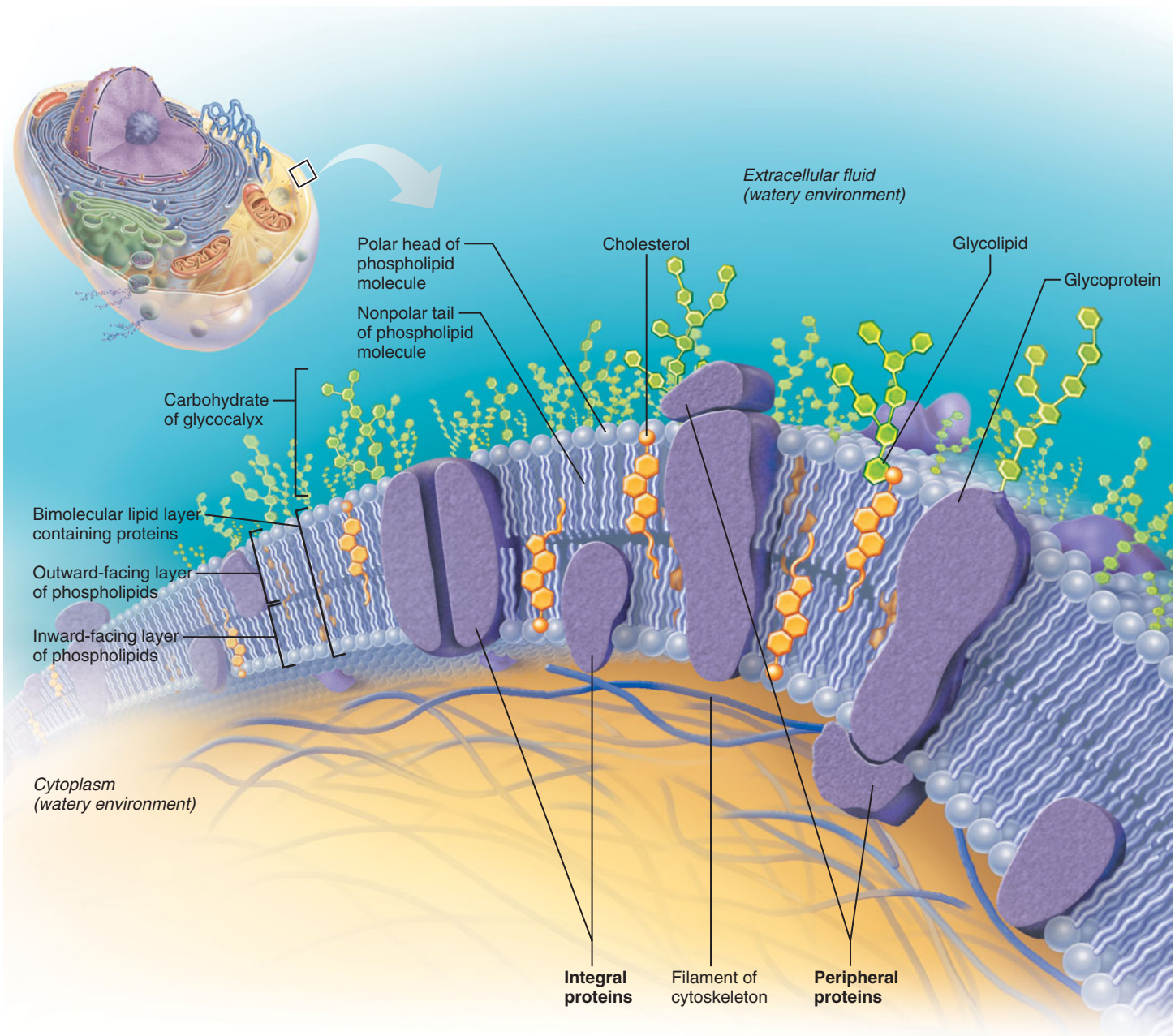
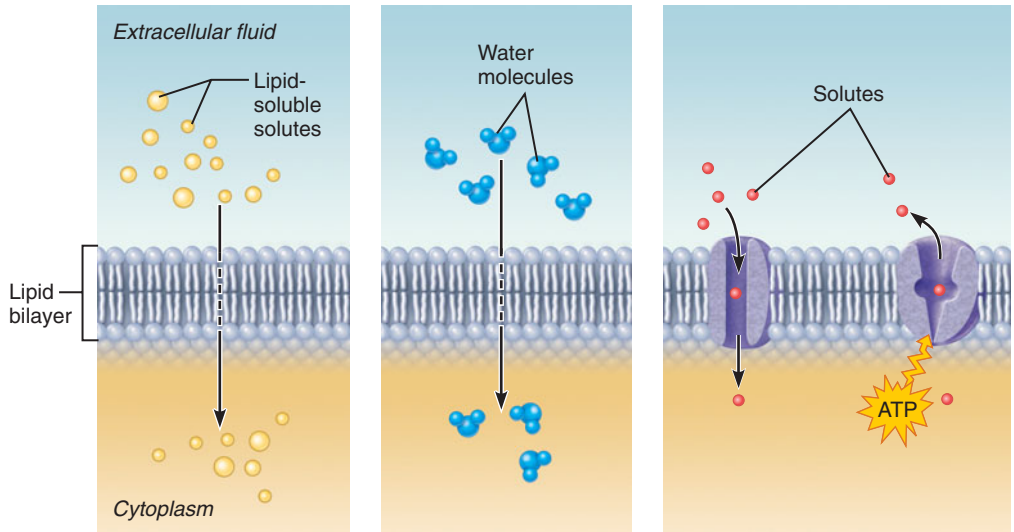


FIGURE 2.2 The plasma membrane according to the fluid mosaic model.



(a) Simple diffusion of fat-soluble molecules directly through the phospholipid bilayer.

(b) Osmosis, diffusion of water through the lipid bilayer.

(c) Transport via integral proteins A protein (left) that spans the membrane may provide a channel across the membrane that is selective for a particular solute. Some transport proteins (right) use ATP as an energy source to actively pump substances across the membrane.

FIGURE 2.3 Membrane transport mechanisms.

lemma = sheath, husk). This thin, flexible layer defines the extent of the cell, thereby separating two of the body's major fluid compartments: the *intracellular fluid* within the cells and the *extracellular fluid* that lies outside and between cells. You can think of the plasma membrane as a security fence surrounding the manufacturing plant (cell). This boundary contains specific checkpoints (receptors) that influence cellular activity in various ways.

Structure

The *fluid mosaic model* of membrane structure depicts the plasma membrane as a double layer, or bilayer, of lipid molecules with protein molecules dispersed within it (Figure 2.2). The most abundant lipids in the plasma membrane are phospholipids. Like a lollipop on two sticks, each phospholipid molecule has a polar "head" that is charged, and an uncharged, nonpolar "tail" made of two chains of fatty acids. The polar heads are attracted to water—the main constituent of both the cytoplasm and the fluid external to the cell—so they lie along the inner as well as the outer face of the membrane. The nonpolar tails avoid water and line up in the center of the membrane. The result is two parallel sheets of phospholipid molecules lying tail to tail, forming the membrane's basic bilayered structure.

The inner and outer layers of the membrane differ some what in the kinds of lipids they contain. Sugar groups are attached to about 10% of the outer lipid molecules, making them "sugar-fats," or glycolipids (gli″ko-lip′ids). The plasma membrane also contains substantial amounts of cholesterol, another lipid. Cholesterol makes the membrane more rigid and increases its impermeability to water and water-soluble molecules.

Proteins make up about half of the plasma membrane by weight. The membrane proteins are of two distinct types: integral and peripheral (Figure 2.2). **Integral proteins** are firmly embedded in or strongly attached to the lipid bilayer. Some integral proteins protrude from one side of the membrane only, but most are *transmembrane proteins* that span the whole width of the membrane and protrude from both sides (*trans* = across). **Peripheral proteins,** by contrast, are not embedded in the lipid bilayer at all. Instead, they attach rather loosely to the membrane surface. The peripheral proteins include a network of filaments that helps support the membrane from its cytoplasmic side. Without this strong, supportive base, the plasma membrane would tear apart easily.

Short chains of carbohydrate molecules attach to the integral proteins to form glycoproteins. These sugars project from the external cell surface, forming the *glycocalyx* (gli″ko-kal′iks; "sugar covering"), or *cell coat*. Also contributing to the glycocalyx are the sugars of the membrane's glycolipids. You can therefore think of your cells as "sugar-coated." The glycocalyx is sticky and may help cells to bind when they come together. Because every cell type has a different pattern of sugars that make up its glycocalyx, the glycocalyx is also a distinctive biological marker by which approaching cells recognize each other. For example, a sperm recognizes the ovum (egg cell) by the distinctive composition of the ovum's glycocalyx.

Functions

The functions of the plasma membrane relate to its location at the interface between the cell's exterior and interior:

1. The plasma membrane provides a protective barrier against substances and forces outside the cell.

2. Some of the membrane proteins act as **receptors;** that is, they have the ability to bind to specific molecules arriving from outside the cell. After binding to the receptor, the molecule can induce a change in the cellular activity. Membrane receptors act as part of the body's cellular communication system.
3. The plasma membrane controls which substances can enter and leave the cell. The membrane is a selectively permeable barrier that allows some substances to pass between the intracellular and extracellular fluids while preventing others from doing so. The processes involved in moving substances across the plasma membrane are described next.

Membrane Transport

Small, uncharged molecules, such as oxygen, carbon dioxide, and fat-soluble molecules, can pass freely through the lipid bilayer of the plasma membrane through a process called **simple diffusion.** Diffusion is the tendency of molecules in a solution to move down their concentration gradient; that is, the molecules move from a region where they are more concentrated to a region where they are less concentrated **(Figure 2.3a)**. Water, like other molecules, diffuses down its concentration gradient. The diffusion of water molecules across a membrane is called **osmosis** (oz-mo′sis, Figure 2.3b).

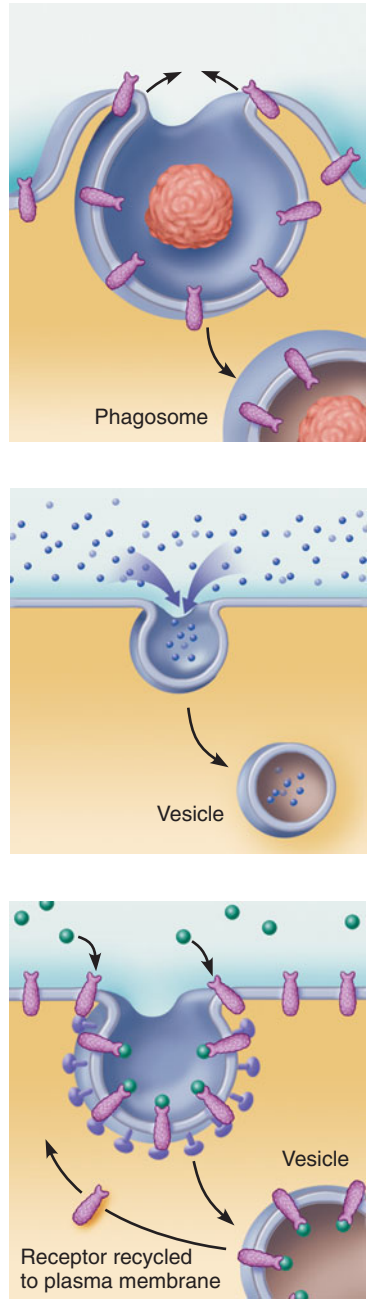
However, most water-soluble or charged molecules, such as glucose, amino acids, and ions, cannot pass through the lipid bilayer by simple diffusion. Such substances can cross the plasma membrane only by means of specific transport mechanisms that use the integral proteins to carry or pump molecules across the membrane or to form channels through which specific molecules pass. Some of these molecules move down their concentration gradient, diffusing through the plasma membrane by moving through a specific integral protein. This transport process is called **facilitated diffusion** (Figure 2.3c, left side). Other integral proteins move molecules across the plasma membrane against their concentration gradient, a process called **active transport,** which requires the use of energy (Figure 2.3c, right side).

The largest molecules (macromolecules) and large solid particles are transported through the plasma membrane by another set of processes, called *vesicular* or *bulk transport.* Knowledge of the two general types of bulk transport, *exocytosis* and *endocytosis,* is essential to the understanding of basic functional anatomy.

Endocytosis (en″do-si-to′sis; "into the cell") is the mechanism by which large particles and macromolecules *enter* cells **(Figure 2.4)**. The substance to be taken into the cell is enclosed by an infolding part of the plasma membrane. In the region of invagination, specific proteins may cover the inner surface of the plasma membrane (the purple, tack-shaped structures shown in Figure 2.4c). This protein coat aids in the selection of the substance to be transported and deforms the membrane to form a membrane-walled sac called a **vesicle.** The membranous vesicle is pinched off from the plasma membrane and moves into the cytoplasm, where its contents are digested. Three types of endocytosis are recognized: phagocytosis, pinocytosis, and receptor-mediated endocytosis.

Phagocytosis (fag″o-si-to′sis) is literally "cell eating." In this process, pseudopods (parts of the plasma membrane and cytoplasm) protrude and flow around some relatively large material, such as a clump of bacteria or cellular debris, and engulf it (Figure 2.4a). The membranous vesicle thus formed is called a **phagosome** (fag′o-sōm; "eaten body"). In most cases, the phagosome then fuses with *lysosomes* (li′so-sōmz), organelles containing digestive enzymes that break down the contents of the phagosome. (For more on lysosomes, see p. 32.) Some cells—most white blood cells, for example—are experts at phagocytosis. Such cells help to police and protect the body by ingesting bacteria, viruses, and other foreign substances. They also "eat" the body's dead and diseased cells.

Just as cells eat in a manner of speaking, they also drink. **Pinocytosis** (pin″o-si-to′sis) is "cell drinking." In pinocytosis, a bit of infolding plasma membrane surrounds a tiny

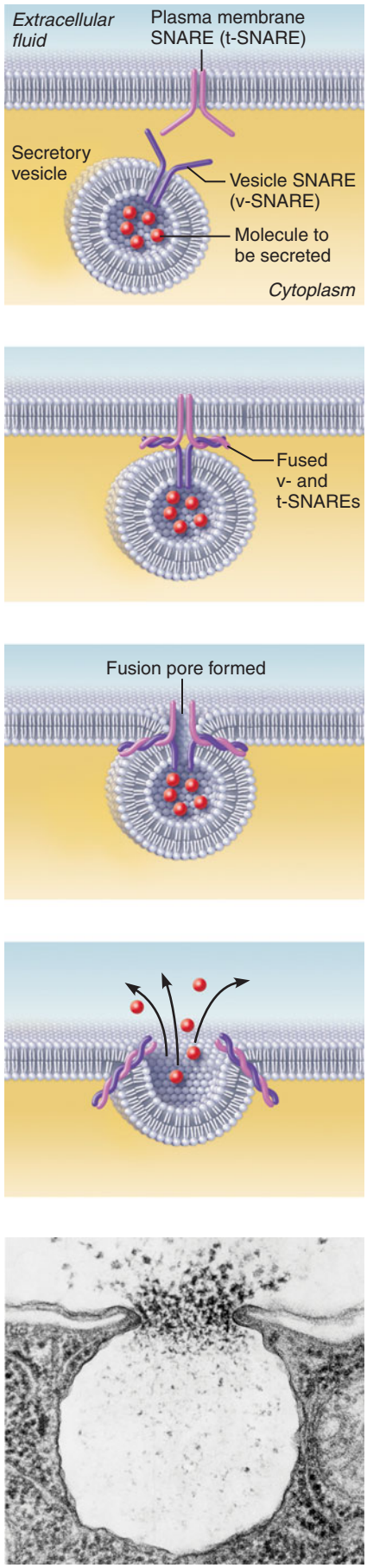


(a) Phagocytosis
The cell engulfs a large particle by forming projecting pseudopods ("false feet") around it and enclosing it within a membrane sac called a phagosome. The phagosome then combines with a lysosome, and its contents are digested. Vesicle may or may not be protein-coated but has receptors capable of binding to microorganisms or solid particles.

(b) Pinocytosis
The cell "gulps" drops of extracellular fluid containing solutes into tiny vesicles. No receptors are used, so the process is nonspecific. Most vesicles are protein-coated.

(c) Receptor-mediated endocytosis
Extracellular substances bind to specific receptor proteins in regions of protein-coated pits, enabling the cell to ingest and concentrate specific substances in protein-coated vesicles. The ingested substance may simply be released inside the cell, or combined with a lysosome to digest contents. Receptors are recycled to the plasma membrane in vesicles.

FIGURE 2.4 The three types of endocytosis.



(a) The process of exocytosis

(1) The membrane-bound vesicle migrates to the plasma membrane.

(2) There, proteins at the vesicle surface (v-SNAREs) bind with t-SNAREs (plasma membrane proteins).

(3) The vesicle and plasma membrane fuse and a pore opens up.

(4) Vesicle contents are released to the cell exterior.

(b) Photomicrograph of a secretory vesicle releasing its contents by exocytosis (110,000×)

FIGURE 2.5 Exocytosis.

quantity of extracellular fluid containing dissolved molecules (Figure 2.4b). This fluid enters the cell in a tiny membranous vesicle. Pinocytosis, a routine activity of most cells, is an unselective way of sampling the extracellular fluid. This process is particularly important in cells that function in nutrient absorption, such as cells that line the intestines.

Some molecules, such as insulin and other hormones, enzymes, and *low-density lipoproteins* (*LDLs*, the molecules that carry cholesterol through the bloodstream to the body's cells) are brought into cells through **receptor-mediated endocytosis,** an exquisitely selective transport process (Figure 2.4c). These substances bind to specific receptors on the cell membrane. Upon binding, the portion of the plasma membrane bearing the molecules and attached receptors invaginates and is pinched off, bringing into the cell the membrane-bound vesicle containing the molecules. The vesicle binds with a lysosome, and the contents of the vesicle are released to be used by the cell. The receptors are recycled back to the plasma membrane. Unfortunately, harmful substances such as some toxins and viruses also use receptor-mediated endocytosis to enter and attack cells.

HYPERCHOLESTEROLEMIA In an inherited disease called *familial hypercholesterolemia,* the body's cells lack the protein receptors that bind to cholesterol-delivering LDLs. As a result, cholesterol cannot enter the cells and accumulates in the blood. If untreated, hypercholesterolemia causes atherosclerosis, also known as "hardening of the arteries," a condition that places the individual at high risk of stroke (blockage of a blood vessel in the brain) or of coronary artery disease and heart attack

Exocytosis (ek″so-si-to′sis; "out of the cell") is a mechanism by which substances move from the cytoplasm to the outside of the cell **(Figure 2.5)**. Exocytosis accounts for most secretion processes, such as the release of mucus or protein hormones from the gland cells of the body. In exocytosis the substance or cell product to be released from the cell is first enclosed in a membrane-bound vesicle in the cytoplasm. The vesicle migrates to the plasma membrane. Proteins extending from the vesicle membrane, v-SNAREs (*v* for vesicle), bind with distinct plasma membrane proteins, t-SNAREs (*t* for target). These proteins cause the lipid layers from both membranes to join together, thus inserting the vesicle membrane into the plasma membrane and releasing the contents of the sac into the space outside the cell.

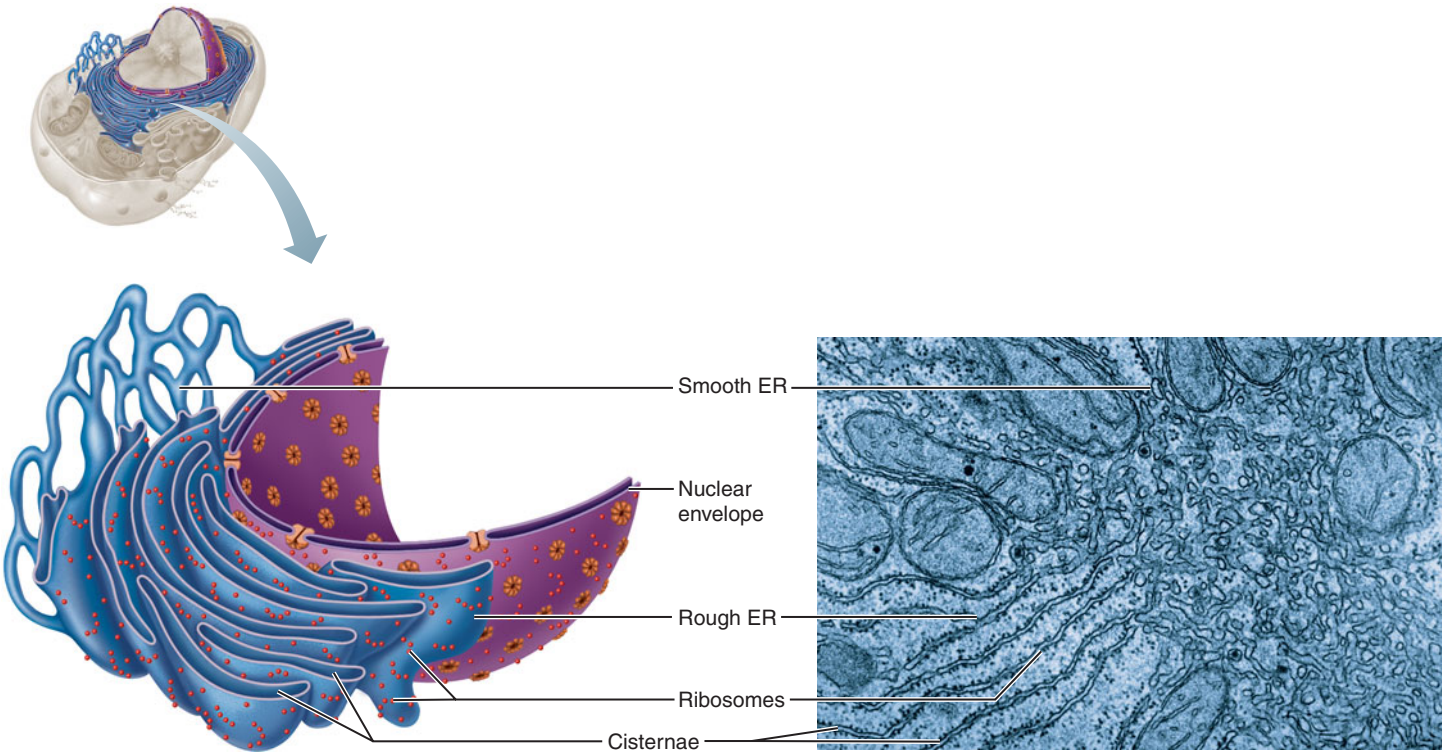
check your understanding

2. What types of macromolecules compose the plasma membrane?
3. By what process does water enter and leave the cell?
4. Which transport process carries large macromolecules out of the cell?

For answers, see Appendix B.

TABLE 2.1 Parts of the Cell: Structure and Function

Cell Part	Structure	Functions
PLASMA MEMBRANE (Figure 2.2)	Membrane made of a double layer of lipids (phospholipids, cholesterol, etc.) within which proteins are embedded; proteins may extend entirely through the lipid bilayer or protrude on only one face; externally facing proteins and some lipids have attached sugar groups	Serves as an external cell barrier; acts in transport of substances into or out of the cell; externally facing proteins act as receptors (for hormones, neurotransmitters, etc.) and in cell-to-cell recognition
CYTOPLASM	Cellular region between the nuclear and plasma membranes; consists of fluid **cytosol** containing dissolved solutes, **inclusions** (stored nutrients, pigment granules), and **organelles**, the metabolic machinery of the cytoplasm	
Cytoplasmic organelles		
• Ribosomes (Figure 2.6)	Dense particles consisting of two subunits, each composed of ribosomal RNA and protein; free or attached to rough ER	The sites of protein synthesis
• Rough endoplasmic reticulum (Figure 2.6)	Membrane system enclosing a cavity, the cisterna, and coiling through the cytoplasm; externally studded with ribosomes	Makes proteins that are secreted from the cell; makes the cell's membranes
• Smooth endoplasmic reticulum (Figure 2.6)	Membranous system of sacs and tubules; free of ribosomes	Site of lipid and steroid synthesis, lipid metabolism, and drug detoxification
• Golgi apparatus (Figures 2.7, 2.8)	A stack of smooth membrane sacs close to the nucleus	Packages, modifies, and segregates proteins for secretion from the cell, inclusion in lysosomes, and incorporation into the plasma membrane
• Lysosomes (Figure 2.9)	Membranous sacs containing acid hydrolases	Sites of intracellular digestion
• Mitochondria (Figure 2.10)	Rodlike, double-membrane structures; inner membrane folded into projections called cristae	Site of ATP synthesis; powerhouse of the cell
• Peroxisomes (Figure 2.1)	Membranous sacs of oxidase enzymes	The enzymes detoxify a number of toxic substances; the most important enzyme, catalase, breaks down hydrogen peroxide
• Microfilaments (Figure 2.11a)	Fine filaments of the contractile protein actin	Involved in muscle contraction and other types of intracellular movement; help form the cell's cytoskeleton
• Intermediate filaments (Figure 2.11b)	Protein fibers; composition varies	The stable cytoskeletal elements; resist tension forces acting on the cell
• Microtubules (Figure 2.11c)	Cylindrical structures made of tubulin proteins	Support the cell and give it shape; involved in intracellular and cellular movements; form centrioles
• Centrioles (Figure 2.12)	Paired cylindrical bodies, each composed of nine triplets of microtubules	Organize a microtubule network during mitosis to form the spindle and asters; form the bases of cilia and flagella
NUCLEUS (Figure 2.13)	Surrounded by the nuclear envelope; contains fluid nucleoplasm, nucleoli, and chromatin	Control center of the cell; responsible for transmitting genetic information and providing the instructions for protein synthesis
• Nuclear envelope (Figure 2.13)	Double-membrane structure; pierced by the pores; continuous with the cytoplasmic ER	Separates the nucleoplasm from the cytoplasm and regulates passage of substances to and from the nucleus
• Nucleoli (Figure 2.13)	Dense spherical (non-membrane-bounded) bodies	Site of ribosome subunit manufacture
• Chromatin (Figures 2.13, 2.15)	Granular, threadlike material composed of DNA and histone proteins	DNA constitutes the genes



(a) Diagrammatic view of smooth and rough ER

(b) Electron micrograph of smooth and rough ER (85,000×)

FIGURE 2.6 The endoplasmic reticulum (ER) and ribosomes.

THE CYTOPLASM

- Describe the structure and cellular activity of each organelle: ribosomes, endoplasmic reticulum, Golgi apparatus, lysosomes, peroxisomes, mitochondria, cytoskeleton, centrosome, and centrioles.
- Explain the structure of glycosomes and lipid droplets.

Cytoplasm, literally "cell-forming material," is the part of the cell that lies internal to the plasma membrane and external to the nucleus. Most cellular activities are carried out in the cytoplasm, which consists of three major elements: *cytosol, organelles,* and *inclusions*.

Cytosol

The **cytosol** (si′to-sol), is the jellylike, fluid-containing substance within which the other cytoplasmic elements are suspended (see Figure 2.1). It consists of water, ions, and many enzymes. Some of these enzymes start the breakdown of nutrients (sugars, amino acids, and lipids) that are the raw materials and energy source for cell activities. In many cell types, the cytosol makes up about half the volume of the cytoplasm.

Cytoplasmic Organelles

Typically, the cytoplasm contains about nine types of organelles, each with a different function that is essential to the survival of the cell. As separate units, the organelles compartmentalize the cell's biochemical reactions, thus preventing reactions from interfering with one another and promoting functional efficiency. The organelles include mitochondria, ribosomes, rough and smooth endoplasmic reticulum, Golgi apparatus, lysosomes, peroxisomes, the cytoskeleton, and centrioles (see Figure 2.1). As you will learn, most organelles are bounded by a membrane that is similar in composition to the plasma membrane but lacks a glycocalyx.

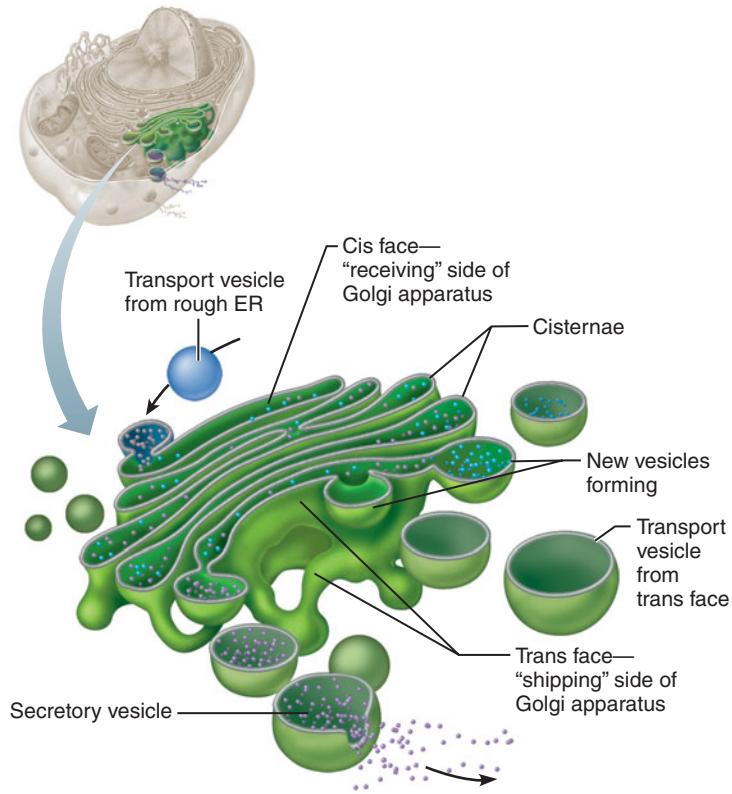
With very few exceptions, all cells of the human body share the same kinds of organelles. However, when a cell type performs a special body function, the organelles that contribute to that function are especially abundant in that cell. Thus, certain organelles are better developed in some cells than in others. You will see examples of this principle as you explore the organelles and their roles.

Ribosomes

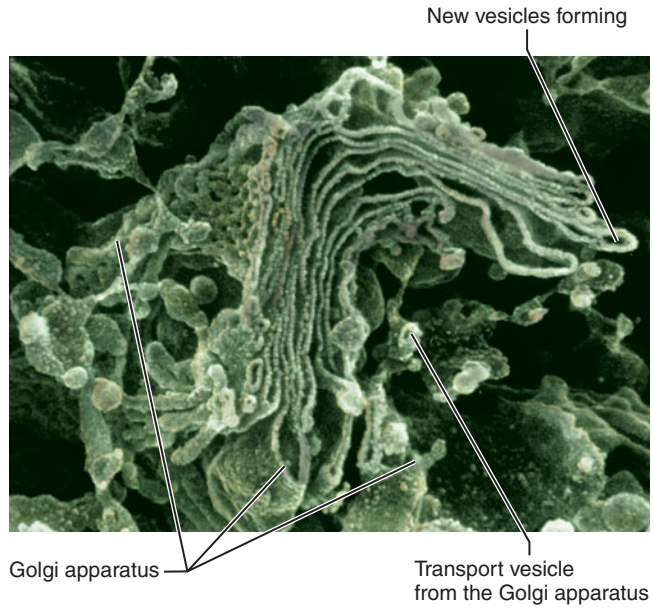
Ribosomes (ri′bo-sōmz) are the assembly line of the manufacturing plant, producing proteins for cellular or extracellular function. They are small, dark-staining granules **(Figure 2.6)**. Unlike most organelles, they are not surrounded by a membrane, but are constructed of proteins plus **ribosomal RNA** (*RNA* = ribonucleic acid). Each ribosome consists of two subunits that fit together like the body and cap of an acorn.

Almost all cells make large amounts of protein, and ribosomes are the site of protein synthesis. On the ribosomes, building blocks called amino acids are linked together to form protein molecules. This assembly process is called *translation*. It is dictated by the genetic material in the cell nucleus (DNA), whose instructions are carried to the ribosomes by messenger molecules called **messenger RNA (mRNA).**

Many ribosomes float freely within the cytosol. Such **free ribosomes** make the soluble proteins that function



(a) Many vesicles in the process of pinching off from the membranous Golgi apparatus



(b) Electron micrograph of the Golgi apparatus (90,000×)

FIGURE 2.7 Golgi apparatus.

within the cytosol itself. Ribosomes attached to the membranes of the rough endoplasmic reticulum, as shown in Figure 2.6, make proteins that become part of the cell membrane or that are exported out of the cell.

Endoplasmic Reticulum

The **endoplasmic reticulum** (en″do-plaz′mik ret-tik′u-lum), or **ER,** is literally the "network within the cytoplasm." As shown in Figure 2.6, the ER is an extensive system of membrane-walled envelopes and tubes that twists through the cytoplasm. It accounts for more than half of the membranous surfaces inside an average human cell. There are two distinct types of ER: *rough ER* and *smooth ER*. Either type may predominate in a given cell type, depending on the specific functions of the cell.

Rough Endoplasmic Reticulum The **rough endoplasmic reticulum (rough ER)** consists mainly of stacked envelopes called **cisternae** (sis-ter′ne; "fluid-filled cavities"). Ribosomes stud the external faces of the membranes of the rough ER, assembling proteins. The ribosomes attach to the membrane when the protein is being made, then detach when the protein is completed.

The rough ER has several functions. Its ribosomes make all proteins that are secreted from cells; thus, rough ER is especially well developed in gland cells that secrete a large amount of protein (mucous cells, for example). It makes the digestive enzymes that will be contained in lysosomes. The rough ER also makes both the integral proteins and the phospholipid molecules of the cell's membranes. In other words, all cell membranes start out as rough ER membrane. The rough ER can therefore be considered the cell's "membrane factory."

Smooth Endoplasmic Reticulum The **smooth endoplasmic reticulum (smooth ER)** is continuous with the rough ER (Figure 2.6). It consists of tubules arranged in a branching network. Because no ribosomes are attached to its membranes, the smooth ER is not a site of protein synthesis. It performs different functions in different cell types, but most of these relate to lipid metabolism, the making or breaking down of fats. Smooth ER is abundant in cells that make lipid steroid hormones from cholesterol and in liver cells that detoxify lipid-soluble drugs. Most cell types, however, have little smooth ER.

Another important function of smooth ER is storing calcium ions. Ionic calcium is a signal for the beginning of many cellular events, including muscle contraction and glandular secretion. The calcium concentration in the cytosol is kept low when such events are not occurring, because most calcium ions are pumped into the ER and held there until the cell needs them. The ER in muscle cells is very extensive, reflecting this essential function.

Golgi Apparatus

The **Golgi** (gōl′je) **apparatus** is a stack of three to ten disc-shaped envelopes (cisternae), each bound by a membrane (Figure 2.7). It resembles a stack of hollow saucers, one cupped inside the next. The products of the rough ER move through the Golgi stack from the convex *(cis)* to the concave

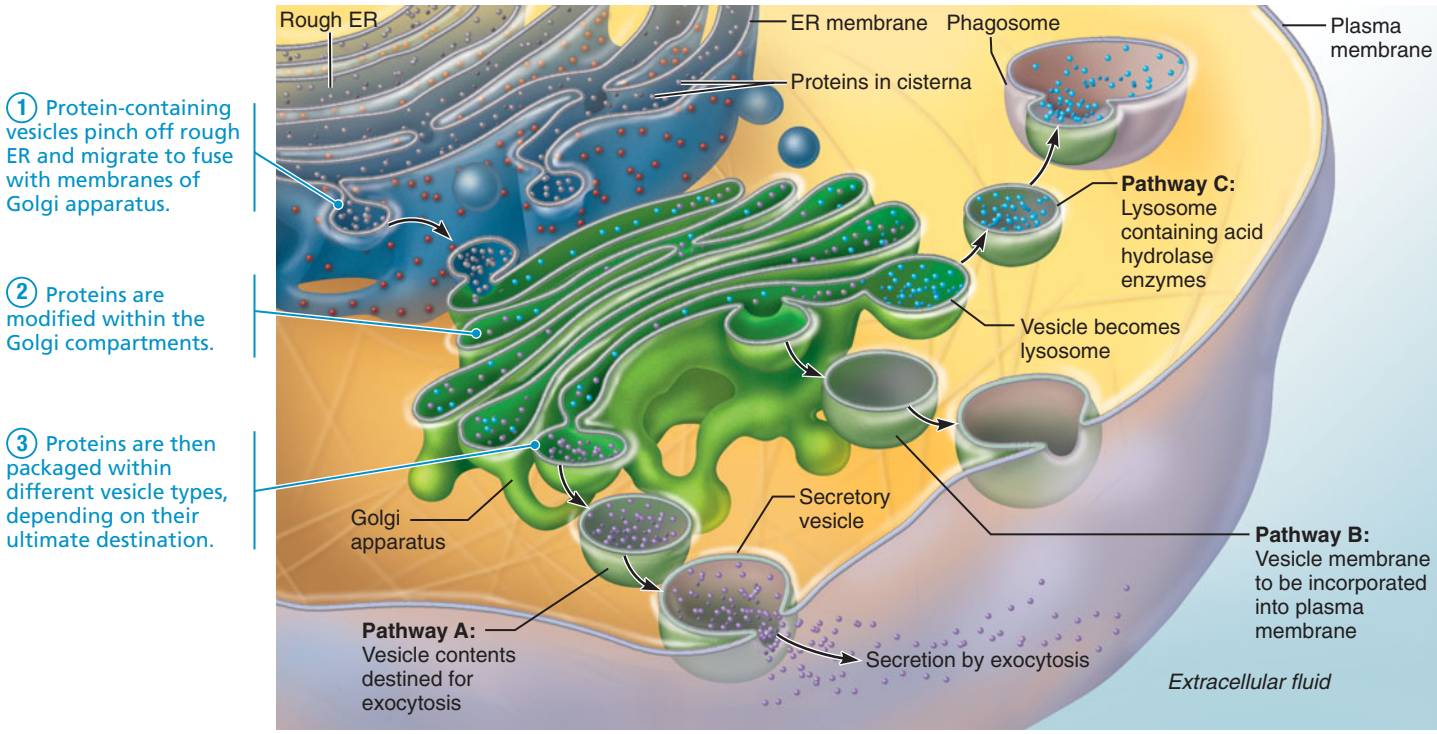


FIGURE 2.8 The sequence of events from protein synthesis on the rough ER to the final distribution of these proteins.

(trans) side. More specifically, the **cis face** receives spherical, membranous **transport vesicles** from the rough ER; new vesicles bud off a **trans face** to leave the apparatus.

The Golgi apparatus sorts, processes, and packages the proteins and membranes made by the rough ER. For example, the Golgi apparatus distinguishes which newly made membranes will become part of the lysosomes (discussed shortly), and which ones are destined for the plasma membrane. It then sends these membranes to their correct destinations in the vesicles that leave the trans face. Thus, the Golgi apparatus is the packaging and shipping division of the manufacturing plant. It receives product produced by the rough ER, packages it, and ships it to its appropriate destination.

Figure 2.8 illustrates the activities of the Golgi apparatus and shows the pathways traveled by products leaving the Golgi apparatus. In pathway A, which occurs in gland cells, the protein product is contained in **secretory vesicles;** these vesicles ultimately release their contents to the cell's exterior by exocytosis. In pathway B, common in all cells, the membrane of the vesicle fuses to and contributes to the plasma membrane, whose components are constantly being renewed and recycled. In pathway C, also common in all cells, the vesicle leaving the Golgi apparatus is a lysosome, a sac filled with digestive enzymes, that remains inside the cell.

Lysosomes

Lysosomes are spherical, membrane-walled sacs containing many kinds of digestive enzymes (Figure 2.9). These enzymes, called acid hydrolases, can digest almost all types of large biological molecules. Lysosomes can be considered the cell's "demolition crew," because they break apart and digest unwanted substances. For example, they fuse with phagosomes, emptying their enzymes into these vesicles and breaking down their contents (Figure 2.8, pathway C).

When a cell's own internal membranes, proteins, or organelles are damaged or wear out, they are encircled by a new membrane from the rough ER, forming a vesicle. Then, nearby lysosomes fuse with this vesicle to digest its contents. Within such vesicles, digestion can proceed safely, because the enclosing membrane keeps the destructive enzymes away from other cell components. Phagocytic cells, such as some white blood cells, have an exceptional number of lysosomes to degrade ingested bacteria and viruses.

TAY-SACHS DISEASE In an inherited condition called Tay-Sachs disease, an infant's lysosomes lack a specific enzyme that breaks down certain glycolipids in the normal recycling of worn-out cellular membranes. Such glycolipids are especially abundant in the membranes of nerve cells. Accumulation of undigested glycolipids in the lysosomes interferes with nerve cell function, resulting in mental retardation, blindness, spastic movements, and death of the child within a year and a half of birth.

Mitochondria

Mitochondria (mi′to-kon″dre-ah) are analogous to the power plant of the manufacturing company. These organelles produce the energy for cellular function. They

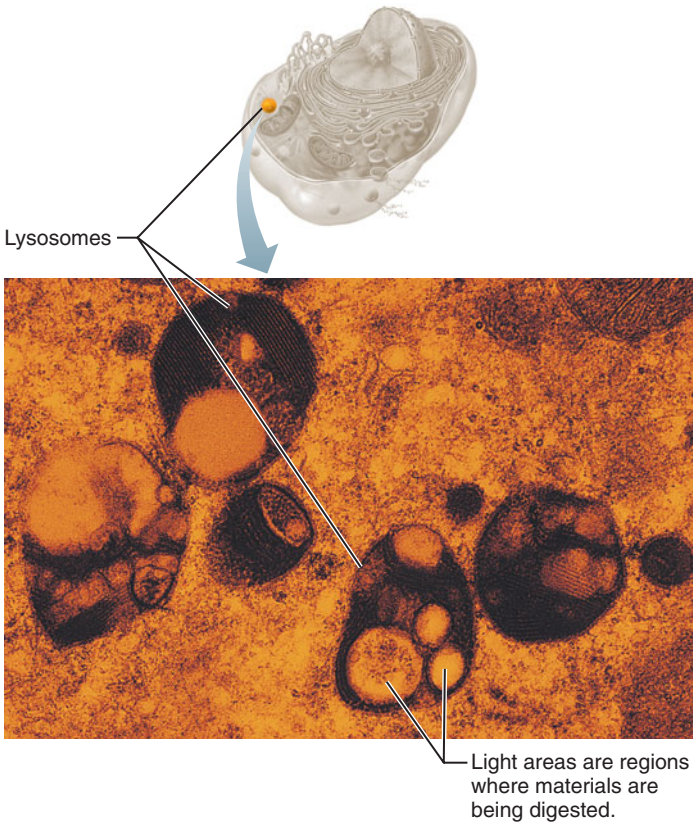


FIGURE 2.9 Electron micrograph of a cell containing lysosomes (93,000×), artificially colored.

usually are depicted as bean-shaped structures because of their appearance in sections under the microscope (Figure 2.10). In reality, mitochondria are long and threadlike (*mitos* = thread). In living cells, they squirm about and change shape as they move through the cytoplasm. Most organelles are surrounded by a membrane, but mitochondria are enclosed by two membranes: The outer membrane is smooth and featureless, and the inner membrane folds inward to produce shelflike **cristae** (krĭ′ste; "crests"). These protrude into the **matrix,** the jellylike substance within the mitochondrion.

Mitochondria generate most of the energy the cell uses to carry out work. They do this by systematically releasing the energy stored in the chemical bonds of nutrient molecules and then transferring this energy to produce **adenosine triphosphate (ATP),** the high-energy molecules that cells use to power chemical reactions. Within the mitochondrion, the ATP-generating process starts in the matrix (by a process called the citric acid cycle) and is completed on the inner membrane of the cristae (by the processes called oxidative phosphorylation and electron transport). Cell types with high energy requirements, muscle cells for example, have large numbers of mitochondria in their cytoplasm. These types of cells also have large numbers of cristae within their mitochondria.

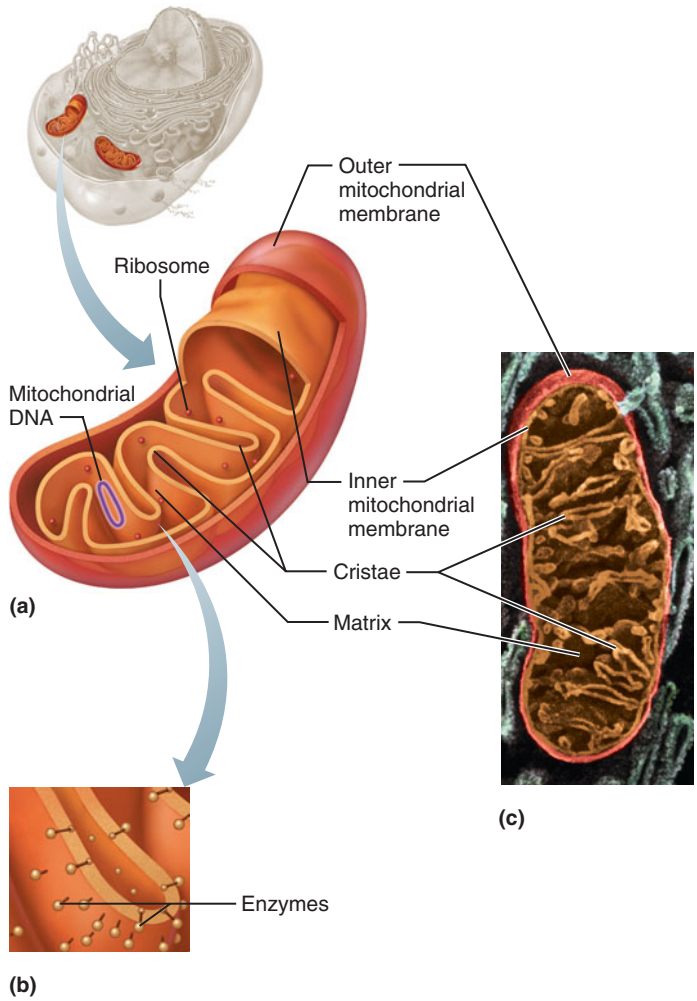


FIGURE 2.10 Mitochondria. (a) Diagram of a longitudinally sectioned mitochondrion. **(b)** Enlargement of crista showing enzymes involved in ATP production. **(c)** Electron micrograph of a mitochondrion (6000×).

Mitochondria are far more complex than any other organelle. They even contain some maternally inherited genetic material (DNA) and divide to form new mitochondria, as if they were miniature cells themselves. Intriguingly, mitochondria are very similar to a group of bacteria, the purple bacteria phylum. It is now widely believed that mitochondria arose from bacteria that invaded the ancient ancestors of animal and plant cells.

Peroxisomes

Peroxisomes (pĕ-roks′ĭ-sōmz; "peroxide bodies") are like the toxic waste removal system of the manufacturing plant. They are membrane-walled sacs that resemble small lysosomes (see Figure 2.1). They contain a variety of enzymes, most importantly oxidases and catalases. Oxidases use oxygen to neutralize aggressively reactive molecules called **free radicals,** converting these to hydrogen peroxide. Free radicals are normal by-products of cellular metabolism, but if allowed to accumulate they can destroy the cell's proteins,

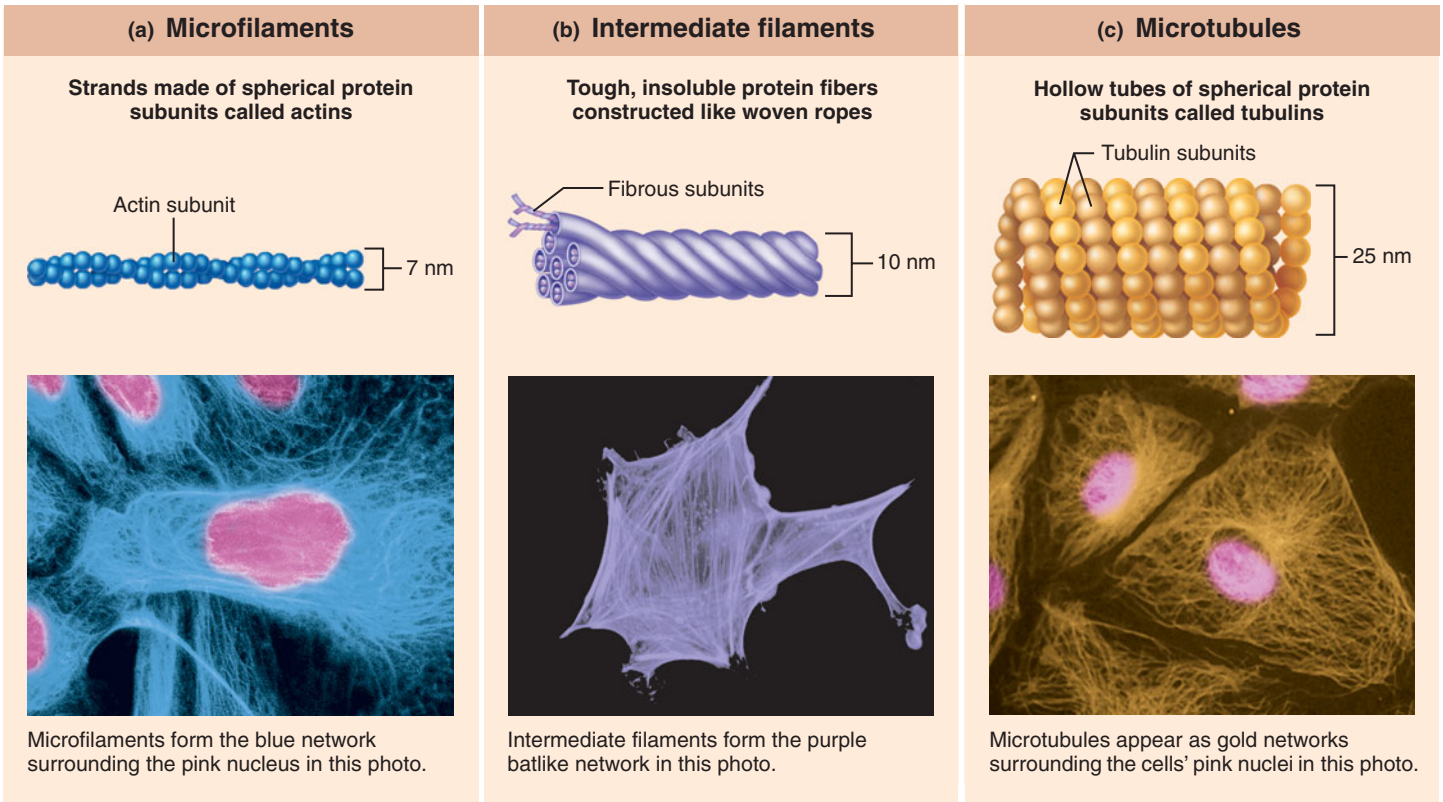


FIGURE 2.11 Cytoskeletal elements. Diagrams (above) and photos (below) of cells treated to fluorescently tag the structure of interest.

membranes, and DNA. Hydrogen peroxide is also reactive and dangerous, but it is converted by catalase into water and oxygen. This catalase-driven reaction breaks down poisons that have entered the cell, such as alcohol, formaldehyde, and phenol. Peroxisomes are numerous in liver and kidney cells, which play a major role in removing toxic substances from the body. Peroxisomes also perform other metabolic reactions, such as breaking down long chains of fatty acids in lipid metabolism.

Cytoskeleton

The **cytoskeleton,** literally "cell skeleton," is an elaborate network of rods running throughout the cytosol (the framework of the manufacturing building, Figure 2.11). This network acts as a cell's "bones," "muscles," and "ligaments" by supporting cellular structures and generating various cell movements. The three types of rods in the cytoskeleton are *microfilaments, intermediate filaments,* and *microtubules,* none of which is covered by a membrane.

Microfilaments, the thinnest elements of the cytoskeleton, are strands of the protein **actin** (ak′tin) (Figure 2.11a). Also called **actin filaments,** they concentrate most heavily in a layer just deep to the plasma membrane. Actin filaments interact with another protein called **myosin** (mi′o-sin) to generate contractile forces within the cell. The interaction of actin and myosin squeezes one cell into two during cell division (cytokinesis, p. 39), causes the membrane changes that accompany endocytosis and exocytosis, and enables some cells to send out and then retract extensions called *pseudopods* (soo′do-pods; "false feet"), in a crawling action called amoeboid motion (ah-me′boid; "changing shape"). Additionally, myosin acts as a motor protein to move some organelles within the cell. Except in muscle cells, where they are stable and permanent, the actin microfilaments are unstable, constantly breaking down and re-forming from smaller subunits.

Intermediate filaments (Figure 2.11b) are tough, insoluble protein fibers, with a diameter between those of microfilaments and microtubules. Intermediate filaments are the most stable and permanent of the cytoskeletal elements. Their most important property is high tensile strength; that is, they act like strong guy-wires to resist *pulling* forces that are placed on the cell. They also function to link adjacent cells together by attaching to specific cell junctions called desmosomes (p. 75).

Microtubules, the elements with the largest diameter, are hollow tubes made of spherical protein subunits called tubulins (Figure 2.11c). They are stiff but bendable. All microtubules radiate from a small region of cytoplasm near the nucleus called the *centrosome* ("center body"; see Figure 2.1). This radiating pattern of stiff microtubules determines the overall shape of the cell, as well as the distribution of cellular organelles. Mitochondria, lysosomes, and secretory granules attach to the microtubules like ornaments hanging from the limbs of a Christmas tree. Organelles move within the cytoplasm,

pulled along the microtubules by small *motor proteins, kinesins* (ki-ne′sinz) and *dyneins* (di′ne-inz), that act like train engines on the microtubular railroad tracks. Microtubules are remarkably dynamic organelles, constantly growing out from the cell center, disassembling, then reassembling.

Centrosome and Centrioles

The **centrosome** (sen′tro-sōm) is a spherical structure in the cytoplasm near the nucleus **(Figure 2.12)**. It contains no membranes. Instead, it consists of an outer cloud of protein called the **centrosome matrix** and an inner pair of **centrioles** (sen′tre-ōlz). The matrix protein seeds the growth and elongation of microtubules, which explains why the long microtubules of the cytoskeleton radiate from the centrosome in nondividing cells (see Figure 2.11c), and why a mitotic spindle of microtubules radiates from it in dividing cells (see Figure 2.17, p. 40).

In the core of the centrosome, the two barrel-shaped centrioles lie perpendicular to one another. The wall of each centriole consists of 27 short microtubules, arranged in nine groups of three. Unlike most other microtubules, those in centrioles are stable and do not disassemble. Functionally, centrioles act in forming cilia and flagella (p. 76 in Chapter 4) and the mitotic spindle (Figure 2.17).

Cytoplasmic Inclusions

Inclusions are temporary structures in the cytoplasm that may or may not be present in a given cell type. Inclusions include pigments, crystals of protein, and food stores. The food stores, by far the most important kind, are lipid droplets and glycosomes. **Lipid droplets** are spherical drops of stored fat. They can have the same size and appearance as lysosomes but can be distinguished by their lack of a surrounding membrane. Only a few cell types contain lipid droplets: Small lipid droplets are found in liver cells, large ones in fat cells. **Glycosomes** (“sugar-containing bodies”) store sugar in the form of glycogen (gli′ko-jen), which is a long branching chain of glucose molecules, the cell’s main energy source. Glycosomes also contain enzymes that make and degrade the glycogen into its glucose subunits. Structurally, glycosomes are dense, spherical granules. They resemble ribosomes, but their diameter is twice as large.

check your understanding

5. What cellular organelles are involved with protein synthesis and packaging?
6. What organelle produces the energy needed for cellular activity?
7. What organelle would be prevalent in a cell that specialized in phagocytosis?
8. Which cytoskeletal element functions to resist tension and thus helps to keep the cell intact?

For answers, see Appendix B.

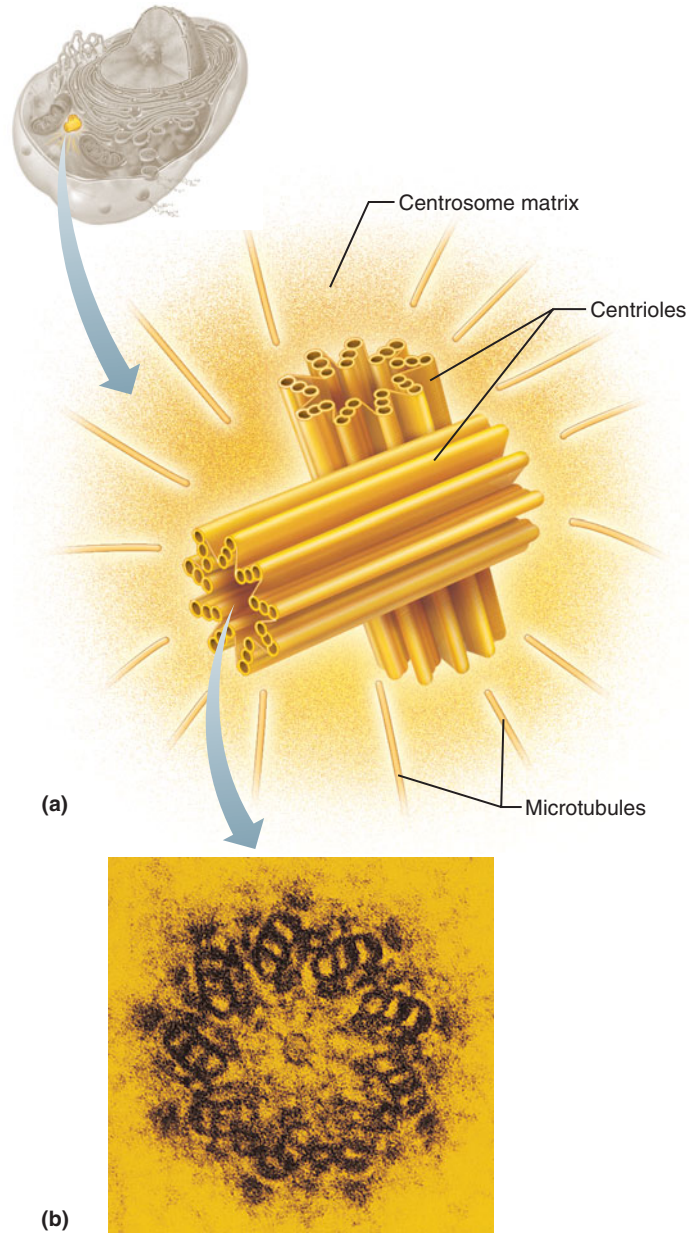


FIGURE 2.12 Centrosome and centrioles. (a) A centrosome. **(b)** Electron micrograph of a centriole in cross section. Its wall consists of nine groups of three microtubules (124,000×).

THE NUCLEUS

➤ Describe the role of each of the three parts of the nucleus in the control of cellular activities: the nuclear envelope, the nucleolus, and chromatin.

The **nucleus,** literally a “little nut,” is the control center of the cell. Its genetic material, **deoxyribonucleic acid (DNA),** directs the cell’s activities by providing the instructions for protein synthesis. In our manufacturing analogy, the nucleus can be compared to a central library, design department, construction superintendent, and board of directors all rolled into one. Whereas most cells have only one nucleus, some, including skeletal muscle cells, have many; that is, they are *multinucleate*

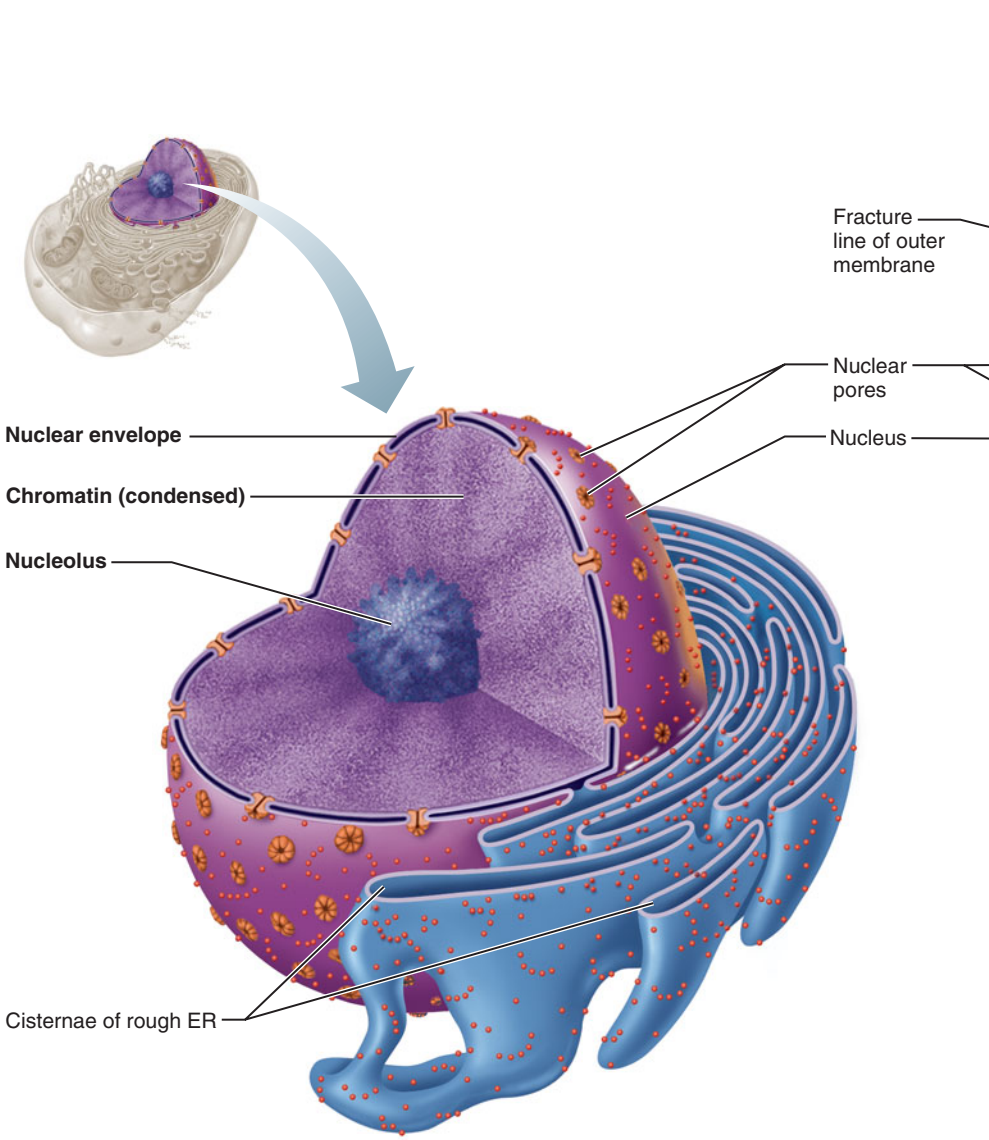


FIGURE 2.13 The nucleus. (a) Three-dimensional illustration of the nucleus, showing the continuity of the nuclear envelope with the rough ER. **(b)** Freeze-fracture micrograph transmission electron micrographs (TEMs).

(mul″tĭ-nu′kle-āt; *multi* = many). The presence of more than one nucleus usually signifies that a cell has a larger-than-usual amount of cytoplasm to regulate. One cell type in the body, the mature red blood cell, is *anucleate;* that is, it has no nucleus at all. Its nucleus normally is ejected before this cell first enters the bloodstream.

The nucleus, which averages 5 μm in diameter, is larger than any of the cytoplasmic organelles (see Figure 2.1). Although it is usually spherical or oval, it generally conforms to the overall shape of the cell. If a cell is elongated, for example, the nucleus may also be elongated. The main parts of the nucleus are the *nuclear envelope, nucleolus,* and *chromatin and chromosomes* (Figure 2.13).

Nuclear Envelope

The nucleus is surrounded by a **nuclear envelope** that consists of two parallel membranes separated by a fluid-filled space (Figure 2.13a). The outer membrane is continuous with the rough ER and has ribosomes on its external face. It forms anew from rough ER after every cell division, so it is evidently a specialized part of the rough ER. The inner membrane is

lined by protein filaments, the **nuclear lamina,** which maintain the shape of the nucleus (Figure 2.13b).

At various points, the two layers of the nuclear envelope fuse, and **nuclear pores** penetrate the fused regions (Figure 2.13a and b). Each pore is formed by a bracelet-shaped complex of more than 22 proteins, and there are several thousand pores per nucleus. Like other cellular membranes, the membranes of the nuclear envelope are selectively permeable, but the pores allow large molecules to pass in and out of the nucleus as necessary. For example, protein molecules imported from the cytoplasm and RNA molecules exported from the nucleus routinely travel through the pores.

The nuclear envelope encloses a jellylike fluid called *nucleoplasm* (nu′kle-o-plazm″), in which the chromatin and nucleolus are suspended. Like the cytosol, the nucleoplasm contains salts, nutrients, and other essential chemicals.

Nucleolus

The **nucleolus** (nu-cle′o-lus, "little nucleus") is a dark-staining body in the cell nucleus (Figure 2.13). There may be one or several within a cell nucleus. A nucleolus contains parts of several different chromosomes and serves as the cell's "ribosome-producing machine." Specifically, it has hundreds of copies of the genes that code for ribosomal RNA and serves as the site where the large and small subunits of ribosomes are assembled. These subunits leave the nucleus through the nuclear pores and join within the cytoplasm to form complete ribosomes.

Chromatin and Chromosomes

DNA is a long double helix that resembles a spiral staircase **(Figure 2.14)**. This double helix is in turn composed of four kinds of subunits called nucleotides, each of which contains a distinct base. These bases—thymine (T), adenine (A), cytosine (C), and guanine (G)—bind to form the "stairs" of the "staircase" and to hold the DNA helix together.

The double helix of DNA (**Figure 2.15** ①) is packed with protein molecules and coiled in strands of increasing structural complexity and thickness. The DNA molecule plus the proteins form **chromatin.** Each two turns of the DNA helix is packed with eight disc-shaped protein molecules called **histones** (his′tōnz, Figure 2.15 ②). Each cluster of DNA and histones is called a nucleosome. In an electron micrograph of chromatin, the nucleosomes have the appearance of beads on a string. Chromatin in this form is called **extended chromatin.** Further coiling of the nucleosomes forms a tight helical fiber, as shown in Figure 2.15 ③. These thick fibers of chromatin are called **condensed chromatin.**

During a cell's nondividing phase, when it is performing its normal activities, the chromatin is in either its extended or condensed form. The tightly coiled DNA of condensed chromatin is inactive. The extended chromatin is the active region of the DNA, directing the synthetic activities of the cell. Specifically, extended chromatin is the site where DNA's genetic code is copied onto messenger RNA molecules in a process called **transcription.** The most active cells in the body have a large amount of extended chromatin and little condensed chromatin.

During cell division, the chromatin is further packed: The helical fibers of nucleosomes are looped (Figure 2.15 ④) and

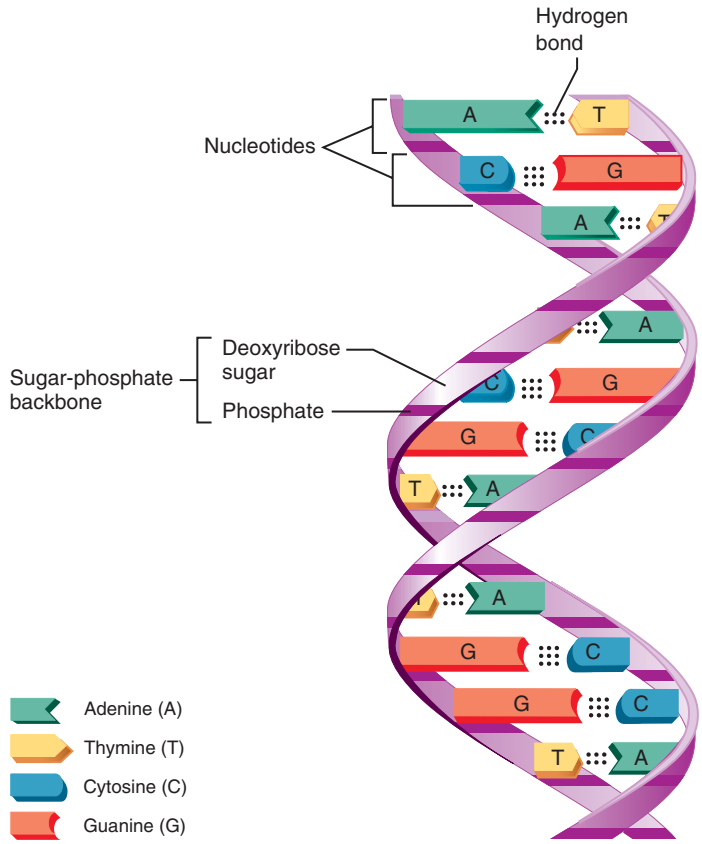


FIGURE 2.14 Molecular structure of DNA. DNA is a double helix constructed of chains of nucleotide molecules. Each nucleotide consists of a sugar, phosphate, and one of four bases: thymine (T), adenine (A), cytosine (C), or guanine (G).

then packed further into the most complex structure, the chromatid (Figure 2.15 ⑤) of a **chromosome** (kro′mo-sōm; "colored body"). Each chromosome contains a single, very long molecule of DNA, and there are 46 chromosomes in a typical human cell. When a cell is dividing, its chromosomes are maximally coiled, so they appear as thick rods (see state ⑤ in Figure 2.15). Chromosomes move extensively during cell division (pp. 40–41), and their compact nature helps to keep the delicate chromatin strands from tangling and breaking as the chromosomes move. When cell division stops, many parts of the chromosome uncoil to form the extended chromatin, thereby allowing transcription to occur.

check your understanding

9. What does the nucleolus produce?
10. What cytoplasmic organelle is continuous with the nuclear envelope?
11. How does the appearance of extended chromatin differ from that of condensed chromatin? What is the difference in function between these forms of chromatin?

For answers, see Appendix B.

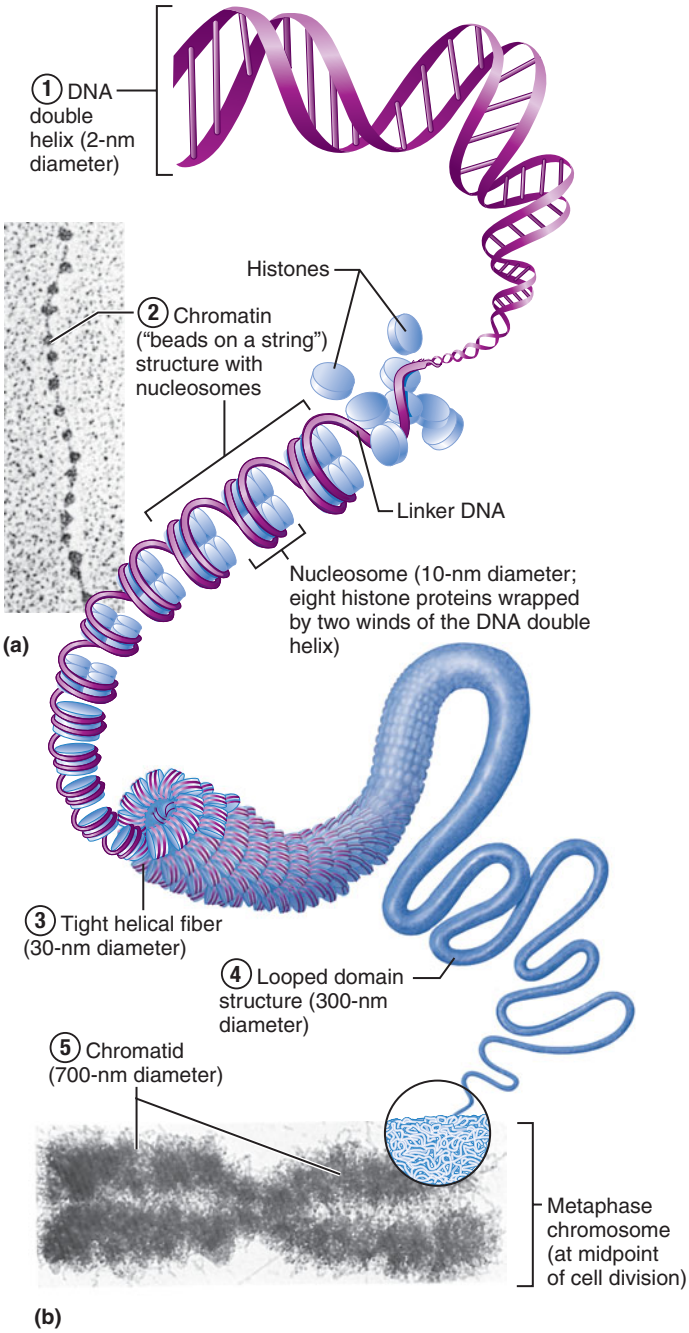


FIGURE 2.15 Chromatin and chromosome structure. **(a)** Electron micrograph of extended chromatin (36,500×). **(b)** The arrangement of DNA and histones in chromatin, from its most extended state ① to its most condensed state ⑤, in a chromosome.

THE CELL LIFE CYCLE

➤ List the phases of the cell life cycle, and describe a key event of each phase.

The **cell life cycle** is the series of changes a cell undergoes from the time it forms until it reproduces itself. This cycle can be divided into two major periods **(Figure 2.16)**: *interphase,* in which the cell grows and carries on its usual activities; and *cell division,* or the *mitotic phase,* during which it divides into two cells.

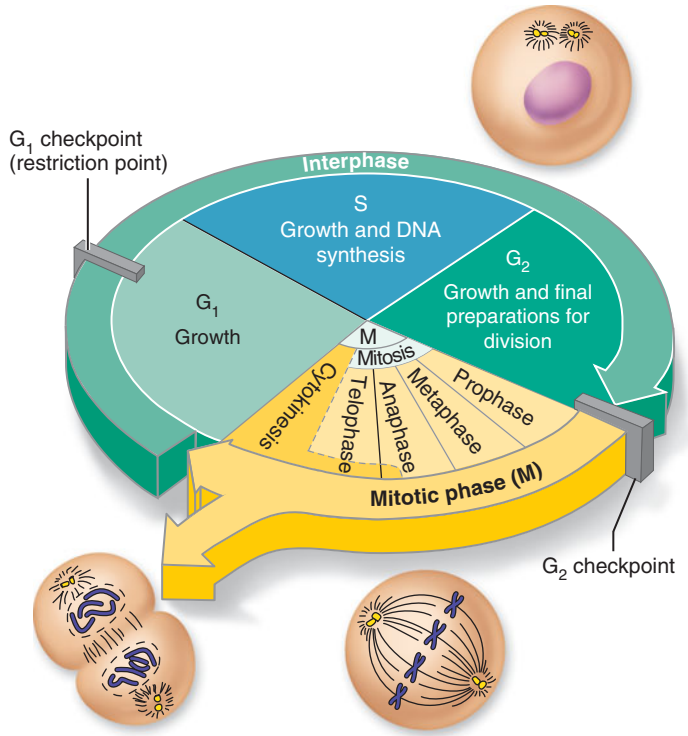


FIGURE 2.16 The cell cycle. The two basic phases in the life and reproduction of each cell are interphase and the mitotic (M) phase. The length of the cell cycle varies in different cell types, but the G_1 stage of interphase tends to be the longest and the most variable in duration. See the text for details.

Interphase

In addition to carrying on its life-sustaining activities, a cell in **interphase** prepares for the next cell division. Interphase is divided into G_1, S, and G_2 subphases. During **G_1 (gap 1),** the first part of interphase, cells are metabolically active, make proteins rapidly, and grow vigorously. This is the most variable phase in terms of duration. In cells with fast division rates, G_1 lasts several hours; in cells that divide slowly, it can last days or even years. Near the end of G_1, the centrioles start to replicate in preparation for cell division. During the next stage, the **S (synthetic) phase,** DNA replicates itself, ensuring that the two daughter cells will receive identical copies of the genetic material. The final part of interphase, called **G_2 (gap 2),** is brief. In this period, the enzymes needed for cell division are synthesized. Centrioles finish copying themselves at the end of G_2. The cell is now ready to divide. Throughout all three subphases, the cell continues to grow, producing proteins and cytoplasmic organelles, and to carry out its normal metabolic activities.

Checkpoints that evaluate cellular activities such as cell growth, DNA replication, and mitotic spindle formation occur throughout the cell cycle. Two of these checkpoints are shown in Figure 2.16: The G_1 checkpoint assesses cell size before DNA synthesis, and the G_2 checkpoint checks for DNA damage

and accuracy of replication. Mitosis can be halted at these checkpoints, thus preventing damaged cells from dividing.

Cell Division

Cell division is essential for body growth and tissue repair. Short-lived cells that continuously wear away, such as cells of the skin and the intestinal lining, reproduce themselves almost continuously. Others, such as liver cells, reproduce slowly (replacing those cells that gradually wear out), but can divide quickly if the organ is damaged. Cells of nervous tissue and for the most part skeletal muscle are unable to divide after they are fully mature; repair is carried out by scar tissue (a fibrous connective tissue).

Cells divide in the **M (mitotic) phase** of their life cycle, which follows interphase (see Figure 2.16). In most cell types, division involves two distinct events: *mitosis* (mi-to′-sis), or division of the nucleus, and *cytokinesis* (si″to-ki-ne′-sis), or division of the entire cell into two cells.

Mitosis

Mitosis is the series of events during which the replicated DNA of the original cell is parceled out into two new cells, culminating in the division of the nucleus. Throughout these events, the chromosomes are evident as thick rods or threads. Indeed, *mitosis* literally means "the stage of threads." Mitosis is described in terms of four consecutive phases: prophase, metaphase, anaphase, and telophase. However, it is actually a continuous process, with each phase merging smoothly into the next. Its duration varies according to cell type, but it typically lasts about 2 hours. Mitosis is described in detail in *Focus on Mitosis* **(Figure 2.17)**.

Cytokinesis

The separation of one cell into two at the end of the cell cycle is called **cytokinesis,** literally "cells moving (apart)." It begins during anaphase and is completed after mitosis ends (Figure 2.17). Essentially, a ring of contractile actin and myosin filaments in the center of the original cell constricts to pinch that cell in two. The two new cells, called daughter cells, then enter the interphase part of their life cycle.

check your understanding

12. In what basic phase of the cell life cycle does the cell spend most of its life?
13. What is the meaning of the root words that form the terms anaphase, metaphase, and telophase? What is happening during each of these phases of mitosis?

For answers, see Appendix B.

DEVELOPMENTAL ASPECTS OF CELLS

- Name some specific cell types, and relate their overall shape to their special functions.
- Compare theories of cell differentiation and aging.

Cell Differentiation

All humans begin life as a single cell, the fertilized egg, from which all the cells in the body arise. Early in embryonic development, the cells begin to specialize: Some become liver cells; some become nerve cells; others become the transparent lens of the eye. Every cell in the body carries the same genes. (A *gene,* simply speaking, is a segment of DNA that dictates a specific cell function, usually by coding for a specific protein.) If all our cells have identical genes, how do cells differentiate and take on specialized structures and functions?

Cells in various regions of the developing embryo are exposed to different chemical signals that channel the cells into specific pathways of development. The cytoplasm of a fertilized egg contains gradients of maternally produced messenger RNA (mRNA) molecules and proteins. In the early days of development as the fertilized egg divides, the cytoplasm of each daughter cell receives a different composition of these molecules. These maternally derived molecules in the cytoplasm influence the activity of the embryonic genome. In this way, different genes are activated in each cell, leading to cellular differentiation. Once the cell-specific gene expression begins, a cell may produce signaling molecules that influence the development of neighboring cells by switching some of their genes "on" or "off." Some genes are active in all cells; for example, all cells must carry out protein synthesis and make ATP. However, the genes for the synthesis of specialized proteins, such as hormones or mucus, are activated only in certain cell populations. The key to cell specialization lies in the kinds of proteins made and reflects differential gene activation in the different cell types.

Cell specialization, also called *cell differentiation,* leads to *structural* variation among the cell types in the body. Different organelles come to predominate in different cells. For example, muscle cells make tremendous quantities of actin and myosin proteins, and lipid accumulates in fat cells. Phagocytic cells produce more lysosomal enzymes and contain many lysosomes. There are about 200 different cell types in the body, which vary greatly in size, shape, and function. They include sphere-shaped fat cells, disc-shaped red blood cells, branching nerve cells, and cube-shaped cells of kidney tubules. **Figure 2.18** illustrates how the shapes of cells and their arrangement of organelles relate to the specialized function of these cells. Cells fall into these functional groups:

(a) Cells that connect body parts or cover and line organs

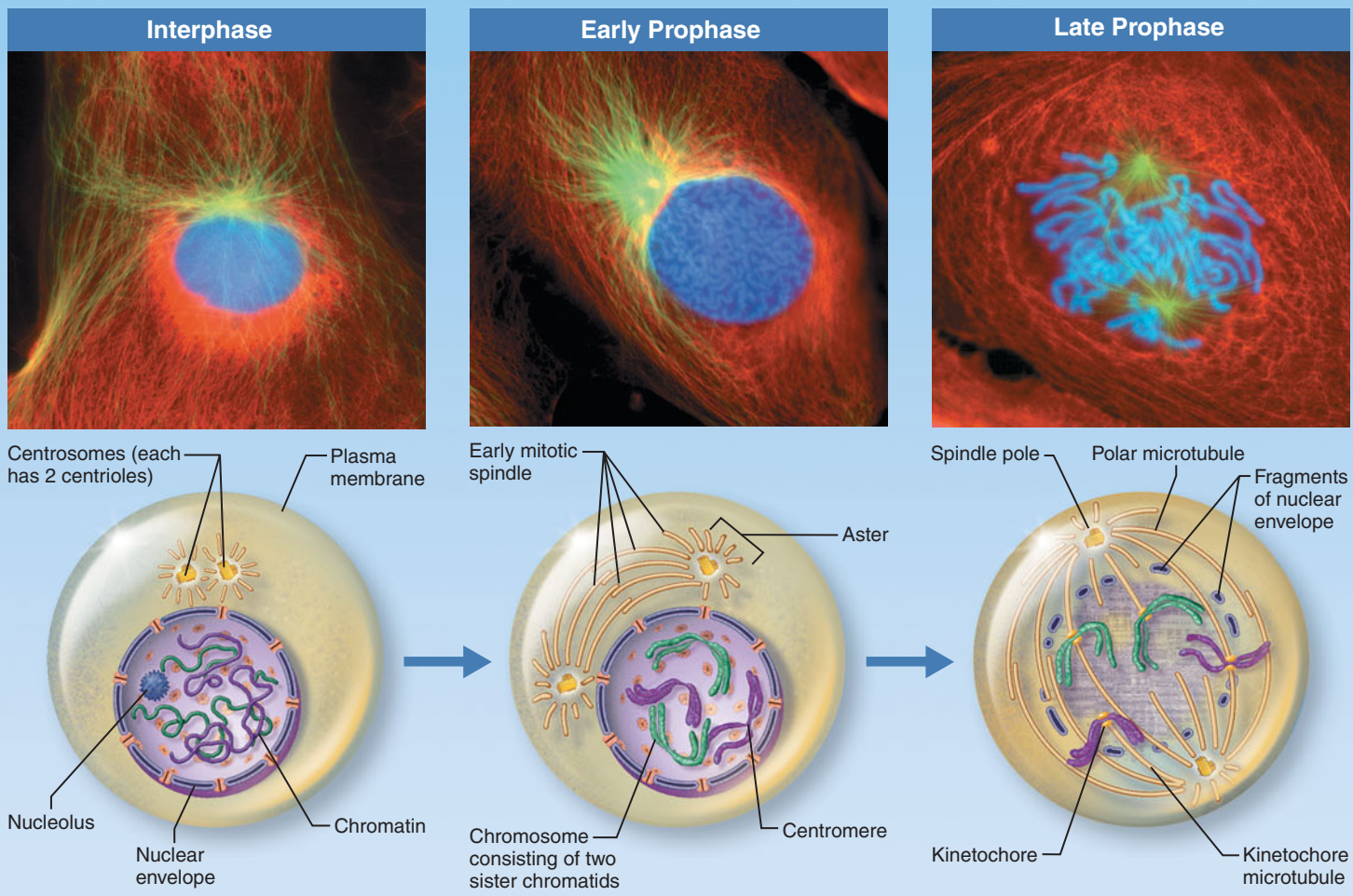
Fibroblast. The elongated shape of this cell extends along the cablelike fibers that it secretes. It also has an abundant rough ER and a large Golgi apparatus to make and secrete the protein components of these fibers.

Erythrocyte (red blood cell). This cell carries the respiratory gases, oxygen and carbon dioxide. Its concave disc shape provides extra surface area for the uptake of respiratory gases. This streamlined shape also allows the cell to flow easily through the bloodstream. So much oxygen-carrying pigment is packed in erythrocytes that all other organelles have been shed to make room.

Epithelial cell. The shape of these cells allows the maximum number of epithelial cells to be packed together in a

FIGURE 2.17

Mitosis is the process of nuclear division in which the chromosomes are distributed to two daughter nuclei. Together with cytokinesis, it produces two identical daughter cells.



Interphase

- Cell is carrying out its normal metabolic activities.
- Chromatin in extended and condensed forms.
- Three phases (as shown in Figure 2.16).
  G_1 phase — centrioles begin replication.
  S phase — DNA is replicated.
  G_2 phase — the final preparations for mitosis; centriole replication complete.

Early prophase — first phase of mitosis

- Chromatin condenses to form chromosomes. Each chromosome consists of two identical chromatids, called sister chromatids, held together at the centromere.
- Nucleoli and cytoskeletal microtubules disassemble.
- Mitotic spindles form from microtubules surrounding the centrosomes and push the centrosomes toward opposite ends of the cell.
- Microtubule arrays called asters extend from the centrosome matrix.

Late prophase

- Nuclear envelope disassembles, and its components are stored in ER.
- Mitotic spindle microtubules extend from each centrosome and attach to the centromere of each chromosome. Each chromosome is pulled by the spindle microtubules toward opposing poles of the cell, resulting in the chromosomes clustering in the center of the cell.

The light micrographs show dividing lung cells from a newt. The chromosomes appear blue and the microtubules green. (The red fibers are intermediate filaments.) The schematic drawings show details not visible in the micrographs. For simplicity, only four chromosomes are drawn.

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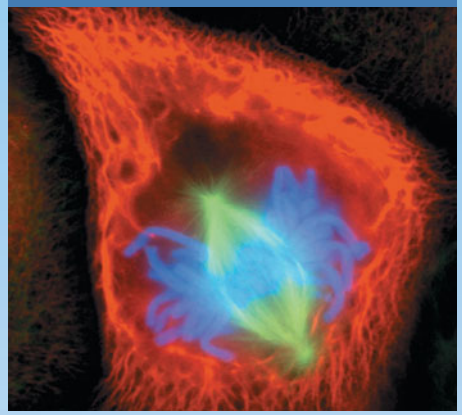
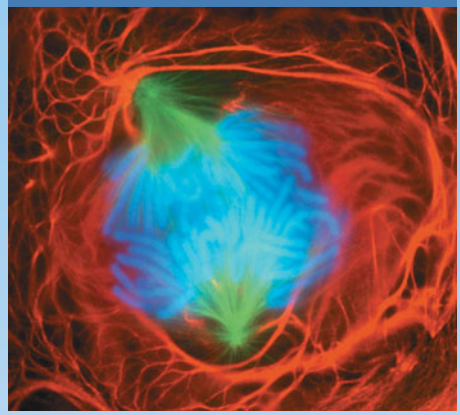
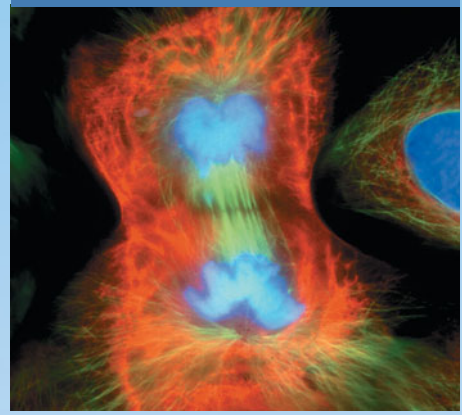
Metaphase

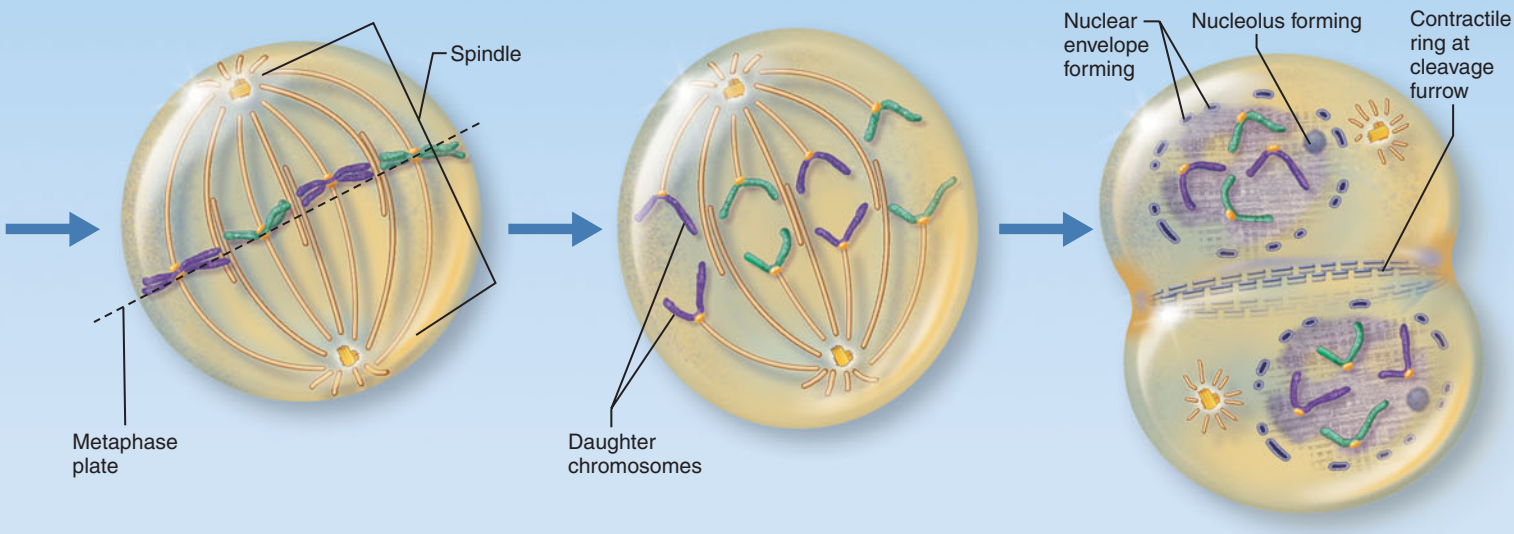


Anaphase



Telophase and Cytokinesis





Metaphase — second phase of mitosis

- Chromosomes align at the middle of the cell along the metaphase plate.
- Chromatids are separated from each other by enzyme action.

Anaphase — third phase of mitosis

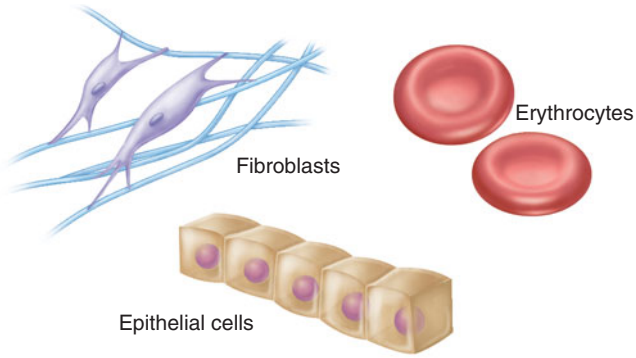
- Centromeres split apart; each chromatid is now considered a chromosome.
- Spindle fibers, moved by motor proteins, pull the chromosomes toward opposite poles.
- Other spindle fibers that are not attached to chromosomes lengthen and push the poles of the cells apart, thus elongating the cell.
- In anaphase, the chromosomes look V-shaped as they are pulled away from the metaphase plate.

Telophase — final phase of mitosis

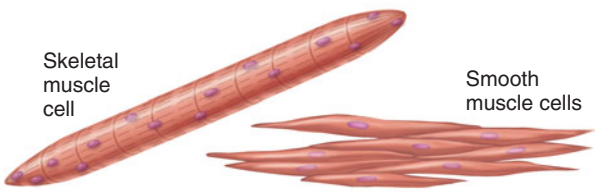
- Identical sets of chromosomes at opposite poles uncoil and resume their threadlike form as extended chromatin.
- Nuclear envelope reassembles around each chromatin group.
- Nucleoli reappear within the nuclei.
- Mitotic spindle breaks down.

Cytokinesis

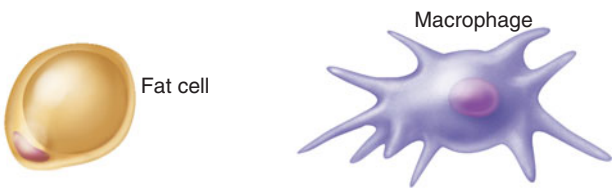
- A ring of contractile microfilaments forms at the cleavage furrow and then squeezes the cells apart. Division of the cytoplasm actually begins during late anaphase and continues through and beyond telophase.



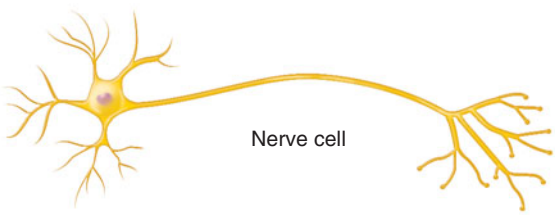
(a) Cells that connect body parts, form linings, or transport gases



(b) Cells that move organs and body parts



(c) Cell that stores nutrients **(d) Cell that fights disease**



(e) Cell that gathers information and controls body functions

(f) Cell of reproduction

FIGURE 2.18 Cellular diversity. (Note that cells are not drawn to the same scale.)

sheet called *epithelium*. An epithelial cell has abundant intermediate filaments that resist tearing when the epithelium is rubbed or pulled. Some epithelial cells are gland cells, with an abundant rough ER, Golgi apparatus, and secretory granules.

(b) Cells that produce movement and move body parts

Skeletal muscle and *smooth muscle cells.* These cells are elongated and filled with abundant actin and myosin filaments, so they can shorten forcefully.

(c) Cell that stores nutrients

Fat cell. The huge spherical shape of a fat cell is produced by a large lipid droplet in its cytoplasm.

(d) Cell that fights disease

Macrophage (a phagocytic cell). This cell extends long pseudopods to crawl through tissue to reach infection sites. The many lysosomes within the cell digest the infectious microorganisms it takes up.

(e) Cell that gathers information and controls body functions

Nerve cell (neuron). This cell has long processes for receiving messages and transmitting them to other structures in the body. The processes are covered with an extensive plasma membrane, whose components are continually recycled; a large rough ER is present to synthesize membrane components.

(f) Cell of reproduction

Sperm (male). This cell is long and streamlined for swimming to the egg for fertilization. The swimming tail is a motile whip called a *flagellum* (p. 76 in Chapter 4).

Most organs are well formed and functional long before birth, but the body continues to grow by forming more cells throughout childhood and adolescence. Once adult size is reached, cell division slows considerably and occurs primarily to replace short-lived cell types and to repair wounds.

Aging

There is no doubt that cellular aging occurs and that it accounts for most problems associated with old age. Although aging is complex and certainly the result of many mechanisms, the best-documented theory proposes that free radicals play the major role. These highly reactive and thus destructive molecules are primarily by-products of normal cellular metabolism, although they also form in response to external insults, such as radiation and chemical pollutants. The theory proposes that free radicals build up and progressively damage the essential cell molecules. Most evidence for this comes from experiments on less complex animals such as worms and fruit flies, where neutralizing the free radicals and repairing their damage have been shown to increase life span. Vitamins E and C appear to act as antioxidants in the human body and may help to prevent excessive free-radical formation.

Most free radicals are produced in the mitochondria, the organelle with the highest rate of metabolism. Scientists propose that a decrease in energy production by free-radical-damaged mitochondria weakens and ages the cells. This is called the *mitochondrial theory of aging.* It has long been known that when laboratory rats and mice are slightly undernourished, their life span increases by up to 30%. The same finding has also been demonstrated in primates. Because caloric restriction lowers the metabolic rate and makes metabolism more efficient, fewer of the destructive free radicals are produced, and aging slows.

Genetic theories of aging propose that aging is programmed into our genes. These theories originated from the observation that the body ages in a predictable pattern, as if aging were a normal part of human development (and development is known to be controlled by genes). Rats and fruit flies can be bred to live longer than usual, and genes that increase and decrease longevity have been identified in animals. Although some of these genes work by influencing free radicals, others act in less understood ways.

The best evidence for planned senescence (programmed aging) involves **telomeres,** structures that limit the maximum number of times cells can divide. Telomeres are repeating, seemingly nonsensical stretches of DNA that cap the ends of chromosomes (*telo* = end; *mere* = piece). Although they carry no genes, they appear to be vital for chromosomal survival: Each time DNA is replicated, 50 to 100 of the end nucleotides are lost, and the telomeres get a bit shorter. When the telomeres reach a certain minimum length, the "stop-division" signal is given. The idea that cell longevity depends on telomere length was supported by the 1994 discovery of *telomerase,* an enzyme that prevents telomeres from degrading by adding more repeating DNA to the ends. Pegged as the "immortality enzyme," telomerase occurs in our endlessly replicating germ-line cells and in cancer cells, but not in other cell types. Great excitement was generated in 1998 when it was reported that adding telomerase to laboratory-grown human cells greatly increased the number of times these cells could divide, without showing any signs of senescence.

check your understanding

14. What cellular structures would be abundant in cells that specialize in producing movement, such as muscle cells?
15. What organelles would be abundant in cells that produce and secrete hormones?
16. According to which aging theory presented here can the aging process be altered by individual behavior?

For answers, see Appendix B.

RELATED CLINICAL TERMS

APOPTOSIS (ap″op-to′sis; "falling away") Programmed cell death. This process of controlled cellular suicide eliminates cells that are stressed, unneeded, excessive, or aged. In response to damaged macromolecules within the cell or to some extracellular signal, a series of intracellular enzymes is activated that destroy the cell's DNA, cytoskeleton, and other structures, producing a quick, neat death. The apoptotic cell shrinks without leaking its contents into the surrounding tissue. It detaches from other cells and is immediately consumed by nearby cells. This tidy sequence avoids inflammation (p. 93), and therefore minimizes tissue injury. Cancer cells fail to undergo apoptosis, but oxygen-starved cells do so excessively (heart-muscle and brain cells during heart attacks and strokes, for example).

DYSPLASIA (dis-pla′ze-ah) (*dys* = abnormal) A change in cell size, shape, or arrangement due to long-term irritation or inflammation (from infections, for example).

HYPERPLASIA (hi″per-pla′ze-ah; "excess shape") Excessive cell proliferation. Unlike cancer cells, hyperplastic cells retain their normal form and arrangement within tissues.

HYPERTROPHY (hi-per′tro-fe; "excess growth") Growth of an organ or tissue due to an increase in the size of its cells. Hypertrophy is a normal response of skeletal muscle cells to exercise. Hypertrophy differs from hyperplasia, the condition in which cells increase in number but not in size.

NECROSIS (ne-kro′sis) (*necros* = death; *osis* = process; condition) Death of a cell or group of cells due to injury or disease. Acute injury causes the cells to swell and burst, and they induce an inflammatory response. This is accidental, *uncontrolled* cell death, in contrast to apoptosis.

CHAPTER SUMMARY

Overview of Cells (pp. 24–25)

1. Cells are the basic structural and functional units of life.
2. There are 50 to 100 trillion cells in the human body. This chapter emphasizes the features common to all cells.
3. Each cell has three main regions: plasma membrane, cytoplasm, and nucleus.

The Plasma Membrane (pp. 25–28)

Structure (p. 27)

4. The plasma membrane defines the cell's outer boundary. The fluid mosaic model interprets this membrane as a flexible bilayer of lipid molecules (phospholipids, cholesterol, and glycolipids) with embedded proteins. When viewed by electron microscopy, the membrane has two dark layers (phospholipid heads) that sandwich an inner, light layer (phospholipid tails).
5. Most proteins in the membrane are integral proteins and extend entirely through the membrane. Peripheral proteins, by contrast, are attached to the membrane surface, helping to support the membrane along with other functions.
6. Sugar groups of membrane glycoproteins and glycolipids project from the cell surface and contribute to the cell coat (glycocalyx), which functions in cell-to-cell binding and recognition.

Functions (p. 27)

7. The plasma membrane functions as a fragile barrier to protect the cell contents. It determines what enters and leaves the cell, and some proteins in the plasma membrane function as receptors for extracellular signal molecules.

Membrane Transport (pp. 27–29)

8. Small uncharged molecules pass through the membrane by simple diffusion; water enters and leaves by osmosis; larger or charged molecules pass through by transport mechanisms that involve the integral proteins. The movement of molecules down their concentration gradient by way of an integral protein is called facilitated diffusion. Movement against the concentration gradient is active transport, a process that requires the use of energy.

9. Large particles and macromolecules pass through the membrane by endocytosis and exocytosis. Endocytosis brings large substances into the cell as packets of plasma membrane fold in to form cytoplasmic vesicles. If the substance is a particle, the process is called phagocytosis; if the substance is dissolved molecules in the extracellular fluid, the process is known as pinocytosis. Receptor-mediated endocytosis is selective: Specific molecules attach to receptors on the membrane before being taken into the cell in protein-coated vesicles.

10. In exocytosis, membrane-lined cytoplasmic vesicles fuse with the plasma membrane and release their contents to the outside of the cell.

The Cytoplasm (pp. 30–35)

Cytosol (p. 30)

11. The cytosol, or cytoplasmic matrix, is the viscous, fluid-containing substance in which cytoplasmic organelles and inclusions are embedded.

Cytoplasmic Organelles (pp. 30–35)

12. Each organelle performs specific functions. The various cell types in the body have different numbers of each organelle type.

13. Ribosomes are dark-staining granules that consist of two subunits, each made of protein and ribosomal RNA. Ribosomes are the sites of protein synthesis (translation). Free ribosomes make proteins used in the cytosol.

14. The rough endoplasmic reticulum is a ribosome-studded system of membrane-walled envelopes (cisternae). Its ribosomes make proteins, which enter the cisternae and which may ultimately be secreted by the cell. The rough ER also makes all the cell's membranes.

15. The smooth endoplasmic reticulum, a network of membrane-walled tubes containing no ribosomes, is involved in the metabolism of lipids. All ER stores calcium ions.

16. The Golgi apparatus is a stack of disc-shaped envelopes that has a cis (convex) and a trans (concave) face. It sorts the products of the rough endoplasmic reticulum and then sends these products, in membrane-bound vesicles, to their proper destination. Lysosomes and secretory granules arise from the Golgi apparatus.

17. Lysosomes are spherical, membrane-walled sacs of digestive enzymes. They digest deteriorated organelles and substances brought into the cell in membrane-bound vesicles.

18. Mitochondria are threadlike organelles covered by two membranes, the inner of which forms shelflike cristae. Mitochondria are the main sites of ATP synthesis, the cell's main energy generators.

19. Peroxisomes are membrane-walled, enzyme-containing sacs that perform several metabolic processes. They protect the cell from free radicals and hydrogen peroxide. They also use hydrogen peroxide to break down some organic poisons and carcinogens.

20. The cytoskeleton includes protein rods of three distinct types—actin microfilaments, intermediate filaments, and microtubules—all in the cytosol. Actin microfilaments interact with myosin to produce contractile forces. Intermediate filaments, which act to resist tension placed on the cell, are stable. Microtubules, which radiate out from the centrosome region, give the cell its shape; they also organize the distribution and the transport of various organelles within the cytoplasm. Both microtubules and microfilaments tend to be unstable, breaking down and re-forming.

21. The centrosome is a spherical region of cytoplasm near the nucleus. It consists of a cloudlike matrix surrounding a pair of centrioles. Proteins in the matrix anchor long microtubules of the cytoskeleton and mitotic spindle. The centrioles are barrel-shaped structures with walls of short microtubules.

Cytoplasmic Inclusions (p. 35)

22. Inclusions are impermanent structures in the cytoplasm. Examples include food stores, such as lipid droplets and glycogen-containing glycosomes.

The Nucleus (pp. 35–38)

23. The nucleus contains genetic material (DNA) and is the control center of the cell. Most cells have one centrally located nucleus shaped like a sphere or an egg.

Nuclear Envelope (pp. 36–37)

24. The nucleus is surrounded by a selectively permeable nuclear envelope, which is penetrated by nuclear pores. These pores allow the passage of large molecules such as RNA and proteins into and out of the nucleus. The nuclear envelope is continuous with the rough endoplasmic reticulum.

Nucleolus (p. 37)

25. A nucleolus is a dark-staining body within the nucleus, associated with parts of several chromosomes. Nucleoli make the subunits of ribosomes.

Chromatin and Chromosomes (pp. 37–38)

26. The DNA molecule is a double helix consisting of four types of nucleotides, with bases of thymine, adenine, cytosine, and guanine.

27. Chromatin is strandlike material (DNA and histones) in the nucleus that forms chromosomes. During cell division, all chromatin is highly coiled, making the chromosomes appear as thick rods. In nondividing cells, the chromatin is a mixture of inactive, coiled regions (condensed chromatin) and active, uncoiled regions (extended chromatin).

The Cell Life Cycle (pp. 38–39, 40–41)

28. The cell life cycle is the series of changes a cell experiences from the time it forms until it divides.

Interphase (pp. 38–39)

29. Interphase is the nondividing phase of the cell life cycle. It consists of the subphases G_1, S, and G_2. During G_1, the cell grows; during S, DNA replicates; and during G_2, the final preparations for division are made.

Cell Division (pp. 39, 40–41)

30. Cell division, essential for growth and repair of the body, occurs during the M (mitotic) phase. Cell division has two distinct aspects: mitosis and cytokinesis.

31. Mitosis, the division of the nucleus, has four stages: (1) *prophase,* when chromatids appear, the nuclear membrane is lost, and the mitotic spindle forms; (2) *metaphase,* when the chromatids line up at the cell's equator; (3) *anaphase,* when the V-shaped chromatids are pulled apart; and (4) *telophase,* when the chromatin extends and the nucleus reassembles. Mitosis parcels out the replicated chromosomes to two daughter nuclei. Cytokinesis, completed after mitosis, is the division of the cell into two cells.

Developmental Aspects of Cells (pp. 39, 42–43)

Cell Differentiation (pp. 39, 42)

32. The first cell of a human is the fertilized egg. Cell differentiation begins early in development and is thought to reflect differential gene activation.

33. There are about 200 different cell types in the human body. These cells have a variety of shapes, which reflect their functions; different organelles dominate in different cell types (see Figure 2.18).

34. During adulthood, cell numbers remain fairly constant, and cell division occurs primarily to replace lost cells.

Aging (pp. 42–43)

35. Aging of cells (and of the whole body) may reflect accumulated damage from free radicals, or it may be a genetically influenced process, or both. It may also reflect a loss of the capacity for cell division over time.

REVIEW QUESTIONS

Multiple Choice/Matching Questions

For answers, see Appendix B.

1. The endocytotic process in which particulate matter is brought into the cell is called (a) phagocytosis, (b) pinocytosis, (c) exocytosis.

2. The nuclear substance composed of histone proteins and DNA is (a) chromatin, (b) the nuclear envelope, (c) nucleoplasm, (d) nuclear pores.

3. Final preparations for cell division are made during this stage of the cell life cycle: (a) G_1, (b) G_2, (c) M, (d) S.

4. The fundamental bilayered structure of the plasma membrane is determined almost exclusively by (a) phospholipid molecules, (b) peripheral proteins, (c) cholesterol molecules, (d) integral proteins.

5. Identify the cell structure or organelle described by each of the following statements.

(a) A stack of 3–10 membranous discs, with vesicles.
(b) A continuation of the nuclear envelope forms this ribosome-covered cytoplasmic organelle.
(c) In nondividing cells, the highly coiled parts of chromosomes form this type of chromatin.
(d) This type of endoplasmic reticulum is a network of hollow tubes involved in lipid metabolism.
(e) This is a cluster of eight histone molecules and the DNA strand that wraps them.
(f) These are the cytoskeletal rods with the thickest diameter (choose from microtubules, microfilaments, intermediate filaments).
(g) The only organelle with DNA and cristae.
(h) This energy-producing organelle is probably descended from bacteria.
(i) Protein synthesis occurs at this organelle.

6. Circle the false statement about centrioles. (a) They start to duplicate in G_1. (b) They lie in the centrosome. (c) They are made of microtubules. (d) They are membrane-walled barrels lying parallel to each other.

7. The trans face of the Golgi apparatus (a) is its convex face, (b) is where products leave the Golgi apparatus in vesicles, (c) receives transport vesicles from the rough ER, (d) is in the very center of the Golgi stack, (e) is the same as the cis face.

8. Circle the false statement about lysosomes. (a) They have the same structure and function as peroxisomes. (b) They form by budding off the Golgi apparatus. (c) Lysosomal enzymes do not occur freely in the cytosol in healthy cells. (d) They are abundant in phagocytic cells.

9. Name the appropriate stage of mitosis (prophase, metaphase, anaphase, telophase) for each of the following.

(a) The chromosomes are lined up in the middle of the cell.
(b) The nuclear membrane fragments.
(c) The nuclear membrane re-forms.
(d) The mitotic spindles form.
(e) The chromosomes (chromatids) are V-shaped.

10. Name the cytoskeletal element (actin microfilaments, intermediate filaments, or microtubules) for each of the following.

(a) give the cell its shape
(b) resist tension placed on a cell
(c) radiate from the centrosome
(d) interact with myosin to produce contraction force
(e) are the most stable
(f) associated with kinesins and dyneins
(g) associated with the motor protein myosin

11. Different organelles are abundant in different cell types. Match the cell types with their abundant organelles by placing the correct letter from column B into each blank in column A. Follow the hints provided in parentheses.

Column A	**Column B**
____ **(1)** cell lining the small intestine (assembles fats)	**(a)** mitochondria
____ **(2)** white blood cell (phagocytic)	**(b)** smooth ER
____ **(3)** liver cell (detoxifies carcinogens)	**(c)** peroxisomes
____ **(4)** muscle cell (highly contractile)	**(d)** microfilaments
____ **(5)** mucous cell (secretes protein product)	**(e)** rough ER
____ **(6)** epithelial cell in the outer layer of skin (withstands tension)	**(f)** intermediate filaments
____ **(7)** kidney tubule cell (makes and uses large amounts of ATP)	**(g)** lysosomes

12. Which of these processes involves specific membrane receptors? (a) phagocytosis, (b) receptor-mediated endocytosis, (c) exocytosis, (d) pinocytosis.

Short Answer Essay Questions

13. List all the cytoplasmic organelles that are composed (at least in part) of lipid-bilayer membranes. Then list all the cytoplasmic organelles that are not membranous.

14. Martin missed a point on his anatomy test because he thought *nucleus* and *nucleolus* were the same word and the same structure. Distinguish the nucleus from the nucleolus.

15. In this chapter, we claimed that mitochondria are the most complex organelles in the cytoplasm. What evidence supports this claim?

16. Define chromosome. Then compare the arrangement of the chromatin in a dividing versus a nondividing cell.

CRITICAL REASONING & CLINICAL APPLICATION QUESTIONS

1. Chrissy, who is 30 years old, stays 5 kg (11 pounds) underweight because she thinks being thin will slow her aging process. After warning her not to lose any more weight or to become anorectic, her doctor admitted that there is at least some scientific evidence to support her view. What is that evidence?
2. Kareem had a nervous habit of chewing on the inner lining of his lip with his front teeth. The lip grew thicker and thicker from years of continual irritation. Kareem's dentist noticed his greatly thickened lip, then told him to have it checked to see if the thickening was a tumor. A biopsy revealed hyperplasia and scattered areas of dysplasia, but no evidence of tumor. What do these terms mean? Did Kareem have cancer of the mouth?
3. The normal function of one tumor-suppressor gene acting at the G_1 checkpoint is to prevent cells with damaged chromosomes and DNA from "progressing from G_1 to S." Another tumor-suppressor gene, acting at the G_2 checkpoint, prevents "passage from G_2 to M." When these tumor-suppressor genes fail to work, cancer can result. Explain what the phrases in quotations mean.
4. In their anatomy labs, many students are exposed to the chemical preservatives phenol, formaldehyde, and alcohol. Our cells break down these toxins very effectively. What cellular organelle is responsible for this?
5. The sedative phenobarbital is a lipid-soluble drug. What may happen to the smooth ER in liver cells of people who use this drug for a period of time?
6. The drug vinblastine is used in cancer therapy to stop the runaway division of cancer cells. Vinblastine inhibits the assembly and growth of microtubules. Referring to Figure 2.17, explain how the action of this drug prevents mitosis.
7. Use the analogy of the cell as a manufacturing factory to describe the function of the following cellular structures: plasma membrane, mitochondria, nucleus, Golgi apparatus, ribosomes, lysosomes, peroxisomes.