3

Cells: The Living Units

Just as bricks and timbers are the structural units of a house, cells are the structural units of all living things, from one-celled "generalists" like amoebas to complex multicellular organisms such as humans, dogs, and trees. The human body has 50 to 100 trillion of these tiny building blocks.

This chapter focuses on structures and functions shared by all cells. We address specialized cells and their unique functions in later chapters.

The Cellular Basis of Life

✓ Define cell.

✓ List the three major regions of a generalized cell and their functions.

The English scientist Robert Hooke first observed plant cells with a crude microscope in the late 1600s. Then, in the 1830s two German scientists, Matthias Schleiden and Theodor Schwann, proposed that all living things are composed of cells. German pathologist Rudolf Virchow extended this idea by contending that cells arise only from other cells.

Since the late 1800s, cell research has been exceptionally fruitful and provided us with four concepts collectively known as the **cell theory**:

- A *cell* is the basic structural and functional unit of living organisms. When you define cell properties, you define the properties of life.
- The activity of an organism depends on both the individual and the collective activities of its cells.
- According to the *principle of complementarity of structure and function*, the biochemical activities of cells are dictated by their shapes or forms, and by the relative number of their specific subcellular structures.
- Continuity of life from one generation to another has a cellular basis.

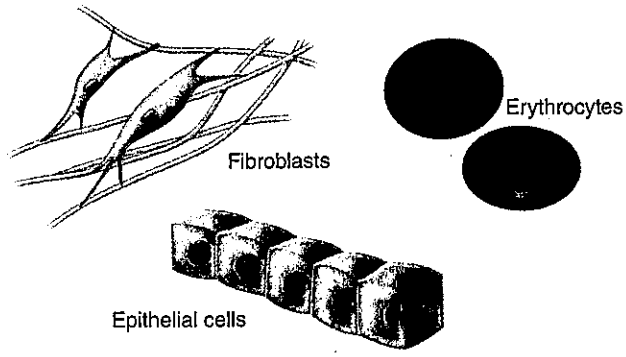
We will expand on all of these concepts as we progress. Let us begin with the idea that the cell is the smallest living unit. Whatever its form, however it behaves, the cell is the microscopic package that contains all the parts necessary to survive in an ever-changing world. It follows then that loss of cellular homeostasis underlies virtually every disease.

The trillions of cells in the human body include over 200 different cell types that vary greatly in shape, size, and function **(Figure 3.1)**. The disc-shaped red blood cells, branching nerve cells, and cubelike cells of kidney tubules are just a few examples of the shapes cells take. Cells also vary in length—ranging from 2 micrometers (1/12,000 of an inch) in the smallest cells to over a meter in the nerve cells that cause you to wiggle your toes. A cell's shape reflects its function. For example, the flat, tilelike epithelial cells that line the inside of your cheek fit closely together, forming a living barrier that protects underlying tissues from bacterial invasion.

Regardless of type, all cells are composed chiefly of carbon, hydrogen, nitrogen, oxygen, and trace amounts of several other elements. In addition, all cells have the same basic parts and some common functions. For this reason, it is possible to speak of a **generalized**, or **composite, cell (Figure 3.2)**.

A human cell has three main parts:

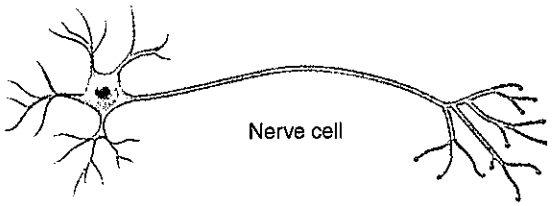
- The *plasma membrane*: the outer boundary of the cell.
- The *cytoplasm* (si'to-plazm): the intracellular fluid packed with *organelles*, small structures that perform specific cell functions.
- The *nucleus* (nu'kle-us): an organelle that controls cellular activities. Typically the nucleus lies near the cell's center.



(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 3.1 Cell diversity. (Note that cells are not drawn to the same scale.)

☑ Check Your Understanding

1. Summarize the four key points of the cell theory.
2. How would you explain the meaning of a "generalized cell" to a classmate?

For answers, see Appendix H.

Next, let's examine the three main parts of the cell in greater detail.

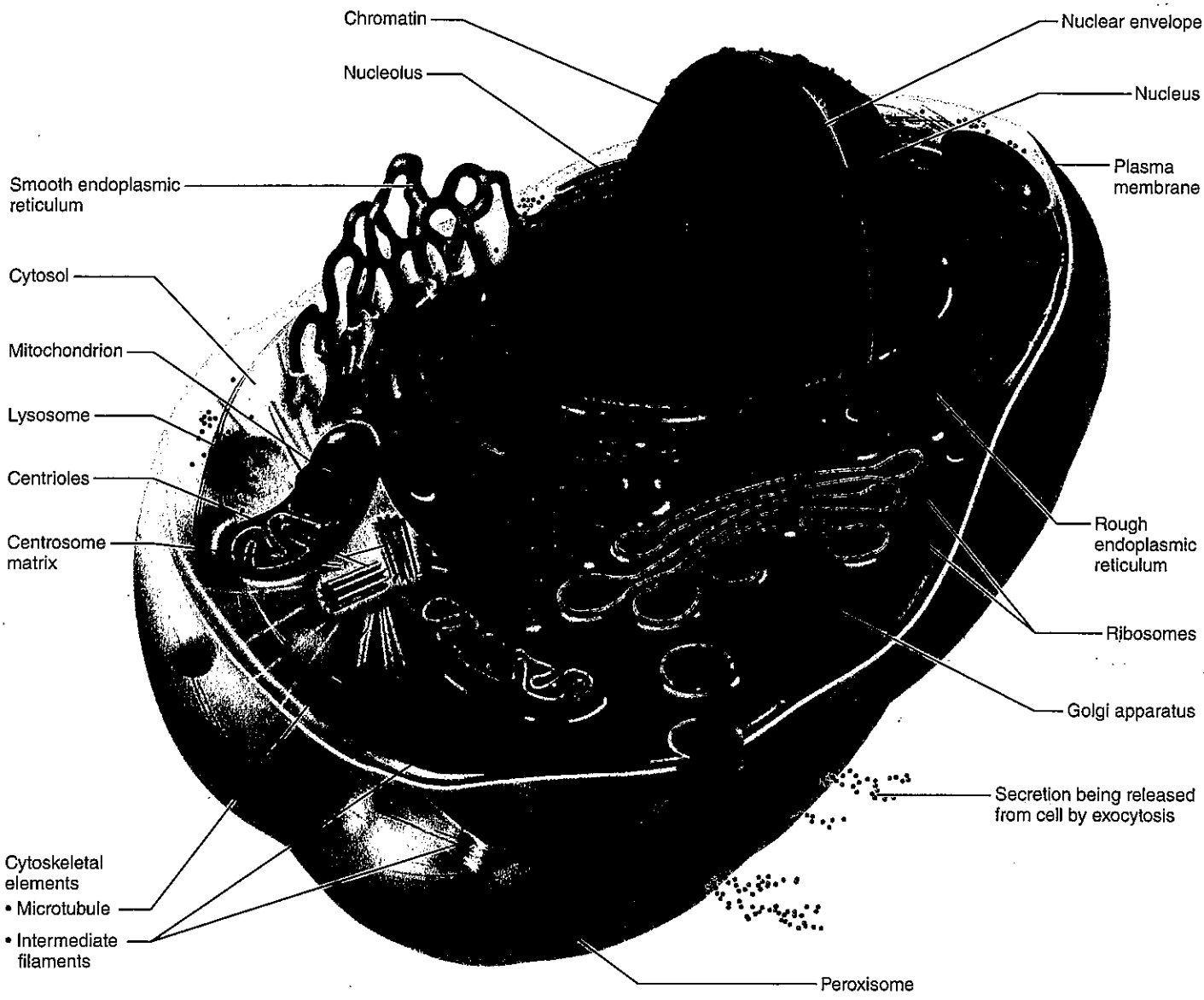


Figure 3.2 Structure of the generalized cell. No cell is exactly like this one, but this composite illustrates features common to many human cells. Note that not all of the organelles are drawn to the same scale in this illustration.

The Plasma Membrane: Structure

✓ Describe the chemical composition of the plasma membrane and relate it to membrane functions.

✓ Compare the structure and function of tight junctions, desmosomes, and gap junctions.

The flexible **plasma membrane** defines the extent of a cell, thereby separating two of the body's major fluid compartments—the *intracellular* fluid within cells and the *extracellular* fluid (ECF) outside cells. The term *cell membrane* is commonly used as a synonym for plasma membrane, but because nearly all cellular organelles are enclosed in a membrane, in this book we will always refer to the cell's surface, or outer limiting membrane, as the plasma membrane. The plasma membrane is much more than a passive envelope. As you will see, its unique structure allows it to play a dynamic role in cellular activities.

The Fluid Mosaic Model

The **fluid mosaic model** of membrane structure depicts the plasma membrane as an exceedingly thin (7–10 nm) structure composed of a double layer, or bilayer, of lipid molecules with protein molecules "plugged into" or dispersed in it **(Figure 3.3)**. The proteins, many of which float in the fluid *lipid bilayer*, form a constantly changing mosaic pattern. The model is named for this characteristic.

Membrane Lipids

The lipid bilayer forms the basic "fabric" of the membrane. It is constructed largely of *phospholipids*, with smaller amounts of *glycolipids*, *cholesterol*, and areas called *lipid rafts*.

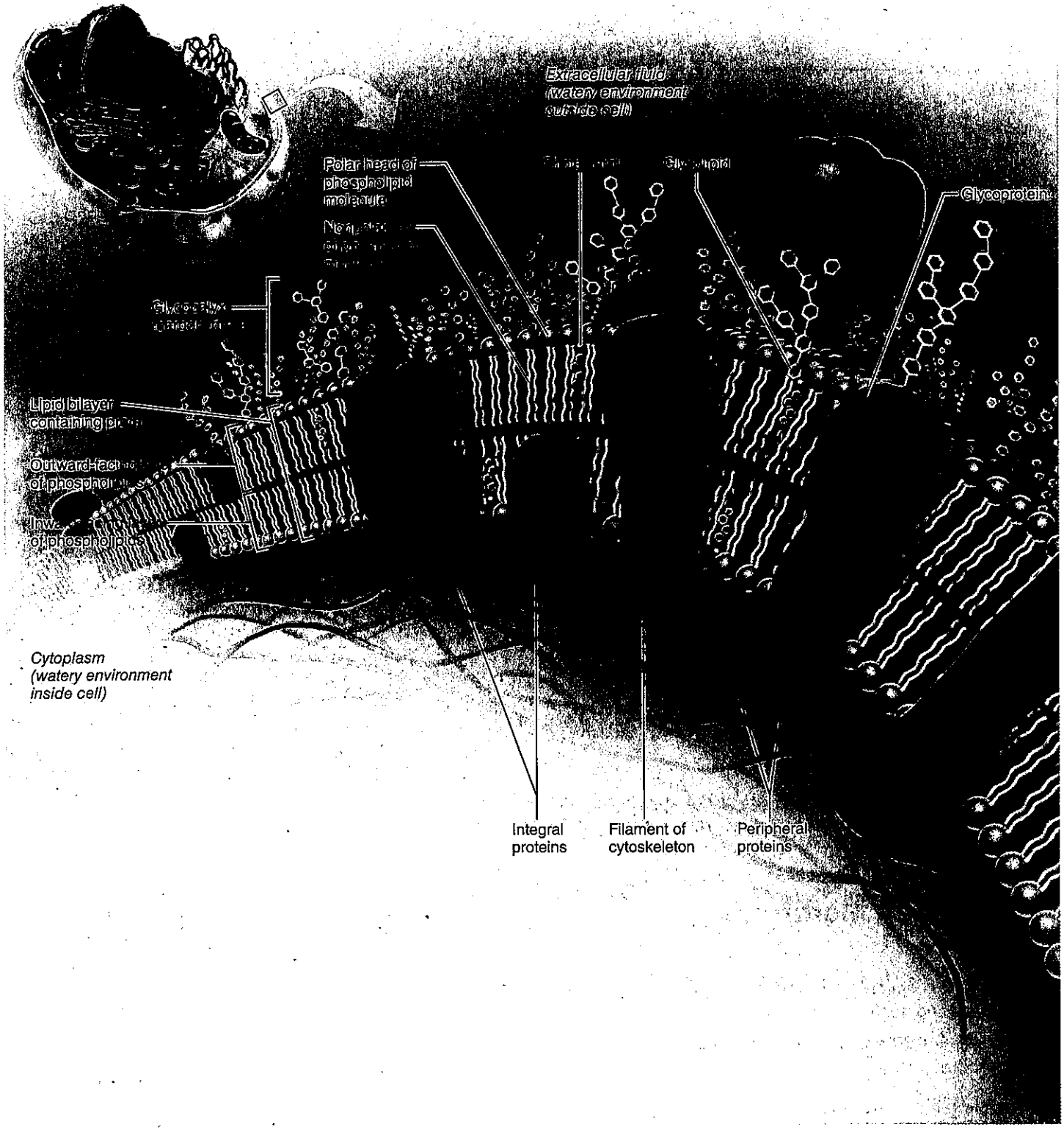


Figure 3.3 The plasma membrane. The lipid bilayer forms the basic structure of the membrane. The associated proteins are involved in membrane functions such as membrane transport, catalysis, and cell-to-cell recognition.

Phospholipids Each lollipop-shaped phospholipid molecule has a polar "head" that is charged and is **hydrophilic** (*hydro* = water, *philic* = loving), and an uncharged, nonpolar "tail" that is made of two fatty acid chains and is **hydrophobic** (*phobia* = fear). The polar heads are attracted to water—the main constituent of both the intracellular and extracellular fluids—and so they lie on both the inner and outer surfaces of the membrane. The nonpolar tails, being hydrophobic, avoid water and line up in the center of the membrane.

The result is that all plasma membranes, indeed all biological membranes, share a sandwich-like structure: They are composed of two parallel sheets of phospholipid molecules lying tail to tail, with their polar heads exposed to water on either side of the membrane or organelle. This self-orienting property of phospholipids encourages biological membranes to self-assemble into closed, generally spherical, structures and to reseal themselves when torn.

With a consistency similar to olive oil, the plasma membrane is a dynamic fluid structure in constant flux. Its lipid molecules move freely from side to side, parallel to the membrane surface, but their polar-nonpolar interactions prevent them from flip-flopping or moving from one half of the bilayer to the other half. The inward-facing and outward-facing surfaces of the plasma membrane differ in the kinds and amounts of lipids they contain, and these variations are important in determining local membrane structure and function. Most membrane phospholipids are unsaturated, a condition which kinks their tails (increasing the space between them) and increases membrane fluidity. (See the illustration of phosphatidylcholine in Figure 2.16b, p. 45.)

Glycolipids **Glycolipids** (gli"ko-lip'idz) are lipids with attached sugar groups. Found only on the outer plasma membrane surface, glycolipids account for about 5% of total membrane lipids. Their sugar groups, like the phosphate-containing groups of phospholipids, make that end of the glycolipid molecule polar, whereas the fatty acid tails are nonpolar.

Cholesterol Some 20% of membrane lipid is cholesterol. Like phospholipids, cholesterol has a polar region (its hydroxyl group) and a nonpolar region (its fused ring system). It wedges its platelike hydrocarbon rings between the phospholipid tails, stabilizing the membrane, while decreasing the mobility of the phospholipids and the fluidity of the membrane.

Membrane Proteins

A cell's plasma membrane bristles with proteins that allow it to communicate with its environment. Proteins make up about half of the plasma membrane by mass and are responsible for most of the specialized membrane functions. Some membrane proteins float freely. Others are "tethered" to intracellular structures that make up the *cytoskeleton* and are restricted in their movement.

There are two distinct populations of membrane proteins, integral and peripheral (Figure 3.3).

Integral Proteins **Integral proteins** are firmly inserted into the lipid bilayer. Some protrude from one membrane face only, but most are *transmembrane proteins* that span the entire membrane and protrude on both sides. Whether transmembrane or not, all integral proteins have both hydrophobic and hydrophilic regions. This structural feature allows them to interact with both the nonpolar lipid tails buried in the membrane and the water inside and outside the cell.

Some transmembrane proteins are involved in transport, and cluster together to form *channels*, or pores, through which small, water-soluble molecules or ions can move, thus bypassing the lipid part of the membrane. Others act as *carriers* that bind to a substance and then move it through the membrane **(Figure 3.4a)**. Some transmembrane proteins are enzymes (Figure 3.4d). Still others are receptors for hormones or other chemical messengers and relay messages to the cell interior—a process called *signal transduction* (Figure 3.4b).

Peripheral Proteins Unlike integral proteins, **peripheral proteins** (Figure 3.3) are not embedded in the lipid bilayer. Instead, they attach loosely to integral proteins and are easily removed without disrupting the membrane. Peripheral proteins include a network of filaments that helps support the membrane from its cytoplasmic side (Figure 3.4c). Some peripheral proteins are enzymes. Others are motor proteins involved in mechanical functions, such as changing cell shape during cell division and muscle cell contraction. Still others link cells together.

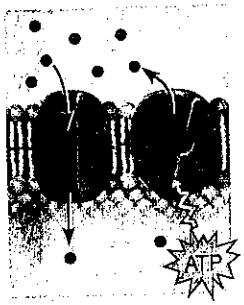
Lipid Rafts

About 20% of the outer membrane surface contains **lipid rafts**, dynamic assemblies of saturated phospholipids (which pack together tightly) associated with unique lipids called sphingolipids and lots of cholesterol. The quiltlike lipid rafts are more stable and less fluid than the rest of the membrane, and they can include or exclude specific proteins to various extents. Because of these qualities, lipid rafts are assumed to be concentrating platforms for certain receptor molecules or for protein molecules needed for cell signaling (discussed on p. 81), membrane invagination (see endocytosis, p. 77), or other functions.

The Glycocalyx

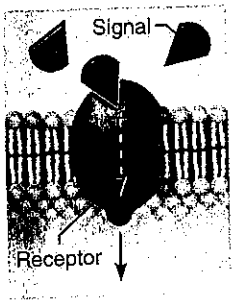
Many of the proteins that abut the extracellular fluid are glycoproteins with branching sugar groups. The term **glycocalyx** (gli"ko-kal'iks; "sugar covering") describes the fuzzy, sticky, carbohydrate-rich area at the cell surface. Quite honestly, you can think of your cells as sugar-coated. The glycocalyx on each cell's surface is enriched both by glycolipids and by glycoproteins secreted by the cell.

Because every cell type has a different pattern of sugars in its glycocalyx, the glycocalyx provides highly specific biological markers by which approaching cells recognize each other (Figure 3.4f). For example, a sperm recognizes an ovum (egg cell) by the ovum's unique glycocalyx. Cells of the immune system identify a bacterium by binding to certain membrane glycoproteins in the bacterial glycocalyx.



(a) Transport

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

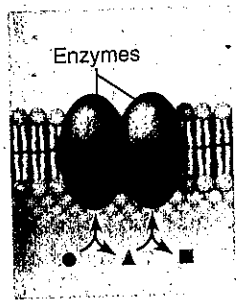


(b) Receptors for signal transduction

- A membrane protein exposed to the outside of the cell may have a binding site that fits the shape of a specific chemical messenger, such as a hormone.
- When bound, the chemical messenger may cause a change in shape in the protein that initiates a chain of chemical reactions in the cell.

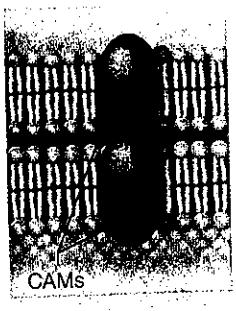
(c) Attachment to the cytoskeleton and extracellular matrix

- Elements of the cytoskeleton (cell's internal supports) and the extracellular matrix (fibers and other substances outside the cell) may anchor to membrane proteins, which helps maintain cell shape and fix the location of certain membrane proteins.
- Others play a role in cell movement or bind adjacent cells together.



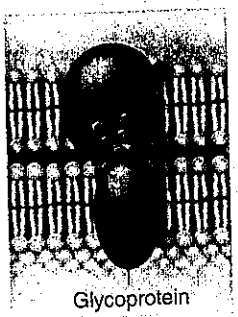
(d) Enzymatic activity

- A membrane protein may be an enzyme with its active site exposed to substances in the adjacent solution.
- A team of several enzymes in a membrane may catalyze sequential steps of a metabolic pathway as indicated (left to right) here.



(e) Intercellular joining

- Membrane proteins of adjacent cells may be hooked together in various kinds of intercellular junctions.
- Some membrane proteins (cell adhesion molecules or CAMs) of this group provide temporary binding sites that guide cell migration and other cell-to-cell interactions.



(f) Cell-cell recognition

- Some glycoproteins (proteins bonded to short chains of sugars) serve as identification tags that are specifically recognized by other cells.

Figure 3.4 Membrane proteins perform many tasks. A single protein may perform a combination of these functions.

Homeostatic Imbalance 3.1

Definite changes occur in the glycocalyx of a cell that is becoming cancerous. In fact, a cancer cell's glycocalyx may change almost continuously, allowing it to keep ahead of immune system recognition mechanisms and avoid destruction. (Cancer is discussed on pp. 145–146.) ✚

☑ Check Your Understanding

3. What basic structure do all cellular membranes share?
4. Why do phospholipids, which form the greater part of membranes, organize into a bilayer—tail-to-tail—in a watery environment?
5. What is the importance of the glycocalyx in cell interactions?

For answers, see Appendix H.

Cell Junctions

Although certain cell types—blood cells, sperm cells, and some immune system cells—are "footloose" in the body, many other types are knit into tight communities. Typically, three factors act to bind cells together:

- Glycoproteins in the glycocalyx act as an adhesive.
- Wavy contours of the membranes of adjacent cells fit together in a tongue-and-groove fashion.
- Special cell junctions form **(Figure 3.5)**.

Because junctions are the most important factor securing cells together, let's look more closely at the various types.

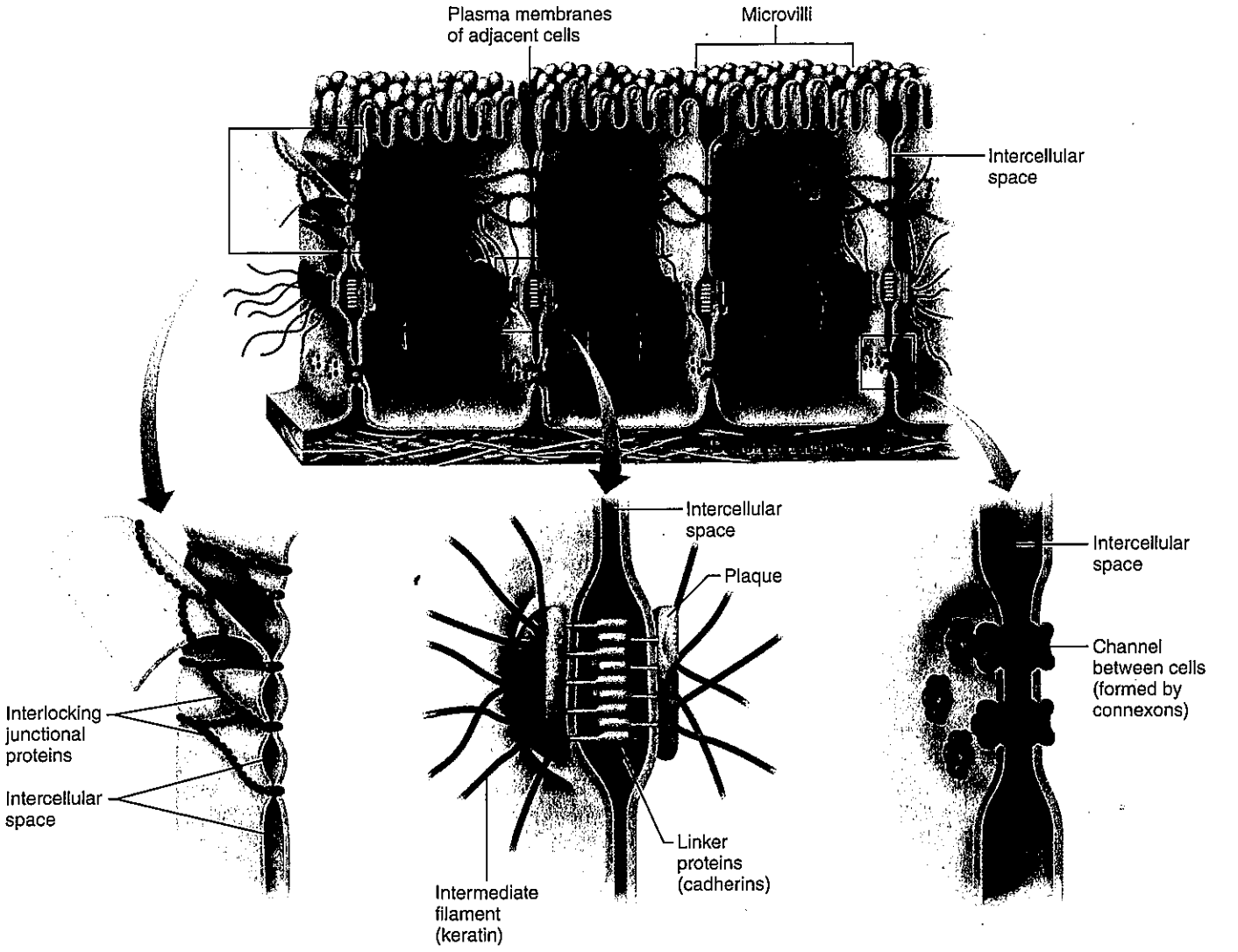
Tight Junctions

In a **tight junction**, a series of integral protein molecules in the plasma membranes of adjacent cells fuse together, forming an *impermeable junction* that encircles the cell (Figure 3.5a). Tight junctions help prevent molecules from passing through the extracellular space between adjacent cells. For example, tight junctions between epithelial cells lining the digestive tract keep digestive enzymes and microorganisms in the intestine from seeping into the bloodstream. (Although called "impermeable" junctions, some tight junctions are leaky and may allow certain ions to pass.)

Desmosomes

Desmosomes (des'muh-sōmz; "binding bodies") are *anchoring junctions*—mechanical couplings scattered like rivets along the sides of abutting cells to prevent their separation (Figure 3.5b). On the cytoplasmic face of each plasma membrane is a buttonlike thickening called a *plaque*. Adjacent cells are held together by thin linker protein filaments (cadherins) that extend from the plaques and fit together like the teeth of a zipper in the intercellular space. Thicker keratin filaments (intermediate filaments, which form part of the cytoskeleton) extend from the cytoplasmic side of the plaque across the width of the cell to anchor to the plaque on the cell's opposite side. In this way, desmosomes bind neighboring cells together and also contribute to a continuous internal network of strong "guy-wires."

This arrangement distributes tension throughout a cellular sheet and reduces the chance of tearing when it is subjected to



(a) Tight junctions: Impermeable junctions prevent molecules from passing through the intercellular space.

(b) Desmosomes: Anchoring junctions bind adjacent cells together like a molecular "Velcro" and help form an internal tension-reducing network of fibers.

(c) Gap junctions: Communicating junctions allow ions and small molecules to pass for intercellular communication.

Figure 3.5 Cell junctions. An epithelial cell is shown joined to adjacent cells by three common types of cell junctions. (Note: Except for epithelia, it is unlikely that a single cell will have all three junction types.)

pulling forces. Desmosomes are abundant in tissues subjected to great mechanical stress, such as skin and heart muscle.

Gap Junctions

A **gap junction**, or *nexus* (nek'sus; "bond"), is a communicating junction between adjacent cells. At gap junctions the adjacent plasma membranes are very close, and the cells are connected by hollow cylinders called *connexons* (kŏ-nek'sonz), composed of transmembrane proteins. The many different types of connexon proteins vary the selectivity of the gap junction channels. Ions, simple sugars, and other small molecules pass through these water-filled channels from one cell to the next (Figure 3.5c).

Gap junctions are present in electrically excitable tissues, such as the heart and smooth muscle, where ion passage from cell to cell helps synchronize their electrical activity and contraction.

☑ Check Your Understanding

6. Which two types of cell junctions would you expect to find between muscle cells of the heart?

For answer, see Appendix H.

The Plasma Membrane: Membrane Transport

✓ Relate plasma membrane structure to active and passive transport processes.

✓ Compare and contrast simple diffusion, facilitated diffusion, and osmosis relative to substances transported, direction, and mechanism.

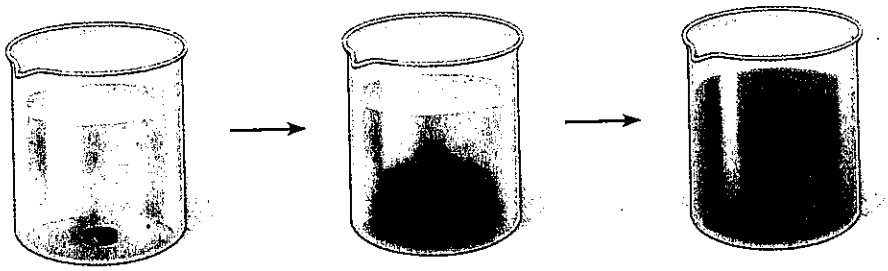


Figure 3.6 Diffusion. Molecules in solution move continuously and collide constantly with other molecules, causing them to move away from areas of their highest concentration and become evenly distributed. From left to right, molecules from a dye pellet diffuse into the surrounding water down their concentration gradient.

Our cells are bathed in an extracellular fluid called **interstitial fluid** (in″ter-stish′al) that is derived from the blood. Like a rich, nutritious "soup," interstitial fluid contains thousands of ingredients, including amino acids, sugars, fatty acids, vitamins, regulatory substances such as hormones and neurotransmitters, salts, and waste products. To remain healthy, each cell must extract from this mix the exact amounts of the substances it needs at specific times.

Although there is continuous traffic across the plasma membrane, it is a **selectively, or differentially, permeable** barrier: It allows some substances to pass while excluding others. It allows nutrients to enter the cell, but keeps many undesirable substances out. At the same time, it keeps valuable cell proteins and other necessary substances in the cell, but allows wastes to exit.

Substances move through the plasma membrane in essentially two ways—passively or actively. In **passive processes**, substances cross the membrane without any energy input from the cell. In **active processes**, the cell provides the metabolic energy (usually ATP) needed to move substances across the membrane. Table 3.1 on p. 72 summarizes passive transport processes, and Table 3.2 on p. 78 summarizes active transport.

Homeostatic Imbalance 3.2

Selective permeability is a characteristic of healthy, intact cells. When a cell (or its plasma membrane) is severely damaged, the membrane becomes permeable to virtually everything, and substances flow into and out of the cell freely. This phenomenon is evident when someone has been severely burned. Precious fluids, proteins, and ions "weep" from the damaged cells. ✚

Passive Processes

The two main types of passive transport are *diffusion* (dĭ-fu′zhun) and *filtration*. Diffusion is an important means of passive membrane transport for every cell of the body. Because filtration generally occurs only across capillary walls, we will discuss it later in conjunction with capillary transport.

Diffusion

Diffusion is the tendency of molecules or ions to move from an area where they are in higher concentration to an area where they are in lower concentration, that is, down or along their **concentration gradient**. The constant random and high-speed motion of molecules and ions (a result of their intrinsic kinetic energy) results in collisions. With each collision, the particles ricochet off one another and change direction. The overall effect of this erratic movement is to scatter or disperse the particles throughout the environment **(Figure 3.6)**. The greater the difference in concentration of the diffusing molecules and ions between the two areas, the more collisions occur and the faster the net diffusion of the particles.

Because the driving force for diffusion is the kinetic energy of the molecules themselves, the speed of diffusion is influenced by molecular *size* (the smaller, the faster) and by *temperature* (the warmer, the faster). In a closed container, diffusion eventually produces a uniform mixture of molecules. In other words, the system reaches equilibrium, with molecules moving equally in all directions (no *net* movement).

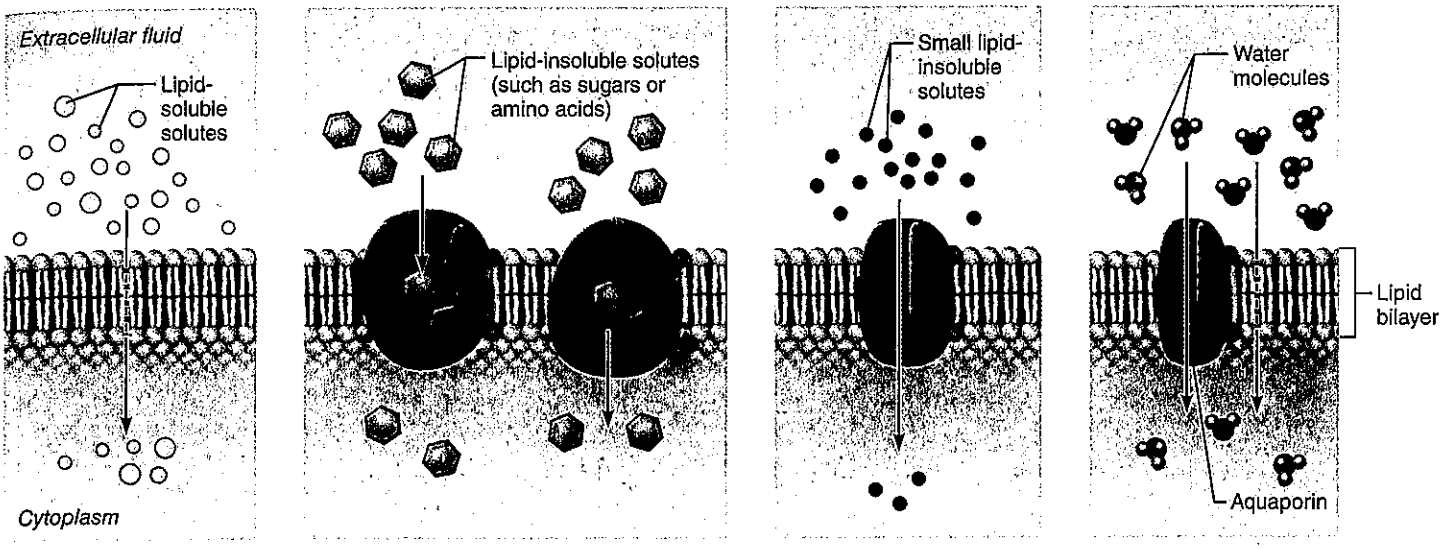
Diffusion is immensely important in physiological systems and it occurs rapidly because the distances molecules are moving are very short, perhaps 1/1000 (or less) the thickness of this page! Examples include the movement of ions across cell membranes and the movement of neurotransmitters between two nerve cells.

The plasma membrane is a physical barrier to free diffusion because of its hydrophobic core. However, a molecule or ion *will* diffuse through the membrane if the molecule is (1) lipid soluble, (2) small enough to pass through membrane channels, or (3) assisted by a carrier molecule.

The unassisted diffusion of lipid-soluble or very small particles is called *simple diffusion*. Assisted diffusion is known as *facilitated diffusion*. A special name, *osmosis*, is given to the diffusion of a solvent (usually water) through a membrane.

Simple Diffusion In **simple diffusion**, nonpolar and lipid-soluble substances diffuse directly through the lipid bilayer **(Figure 3.7a)**. Such substances include oxygen, carbon dioxide, and fat-soluble vitamins. Because oxygen concentration is always higher in the blood than in tissue cells, oxygen continuously diffuses from the blood into the cells. Carbon dioxide, on the other hand, is in higher concentration within the cells, so it diffuses from tissue cells into the blood.

Facilitated Diffusion Certain molecules, notably glucose and other sugars, some amino acids, and ions are transported



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

(b) **Carrier-mediated facilitated diffusion** via protein carrier specific for one chemical; binding of substrate causes transport protein to change shape

(c) **Channel-mediated facilitated diffusion** through a channel protein; mostly ions selected on basis of size and charge

(d) **Osmosis**, diffusion of a solvent such as water through a specific channel protein (aquaporin) or through the lipid bilayer

Figure 3.7 Diffusion through the plasma membrane.

passively even though they are unable to pass through the lipid bilayer. Instead they move through the membrane by a passive transport process called **facilitated diffusion** in which the transported substance either (1) binds to protein carriers in the membrane and is ferried across or (2) moves through water-filled protein channels.

- **Carrier-mediated facilitated diffusion. Carriers** are transmembrane integral proteins that are specific for transporting certain polar molecules or classes of molecules, such as sugars and amino acids, that are too large to pass through membrane channels. Alterations in the shape of the carrier allow it to first envelop and then release the transported substance, shielding it en route from the nonpolar regions of the membrane. Essentially, changes in the conformation of the carrier protein move the binding site from one face of the membrane to the other (Figure 3.7b and Table 3.1).

  Note that a substance transported by carrier-mediated facilitated diffusion, such as glucose, moves down its concentration gradient, just as in simple diffusion. Glucose is normally in higher concentrations in the blood than in the cells, where it is rapidly used for ATP synthesis. So, glucose transport within the body is *typically* unidirectional—into the cells. However, carrier-mediated transport is limited by the number of protein carriers present. For example, when all the glucose carriers are "engaged," they are said to be *saturated*, and glucose transport is occurring at its maximum rate.
- **Channel-mediated facilitated diffusion. Channels** are transmembrane proteins that transport substances, usually ions or water, through aqueous channels from one side of the membrane to the other (Figure 3.7c and d). Channels are selective due to pore size and the charges of the amino acids lining the channel. *Leakage channels* are always open and simply allow ions or water to move according to concentration gradients. *Gated channels* are controlled (opened or closed) by chemical or electrical signals.

  Like carriers, many channels can be inhibited by certain molecules, show saturation, and tend to be specific. Substances moving through them also follow the concentration gradient (always moving down the gradient). When a substance crosses the membrane by simple diffusion, the rate of diffusion is not controllable because the lipid solubility of the membrane is not immediately changeable. By contrast, the rate of facilitated diffusion *is* controllable because the permeability of the membrane can be altered by regulating the activity or number of individual carriers or channels.

Oxygen, water, glucose, and various ions are vitally important to cellular homeostasis. Their passive transport by diffusion (either simple or facilitated) represents a tremendous saving of cellular energy. Indeed, if these substances had to be transported actively, cell expenditures of ATP would increase exponentially!

Osmosis The diffusion of a solvent, such as water, through a selectively permeable membrane is **osmosis** (oz-mo'sis; *osmos* = pushing). Even though water is highly polar, it passes via osmosis through the lipid bilayer (Figure 3.7d). This is surprising because you'd expect water to be repelled by the hydrophobic lipid tails. One hypothesis is that random movements of the membrane lipids open small gaps between their wiggling tails, allowing water to slip and slide its way through the membrane by moving from gap to gap.

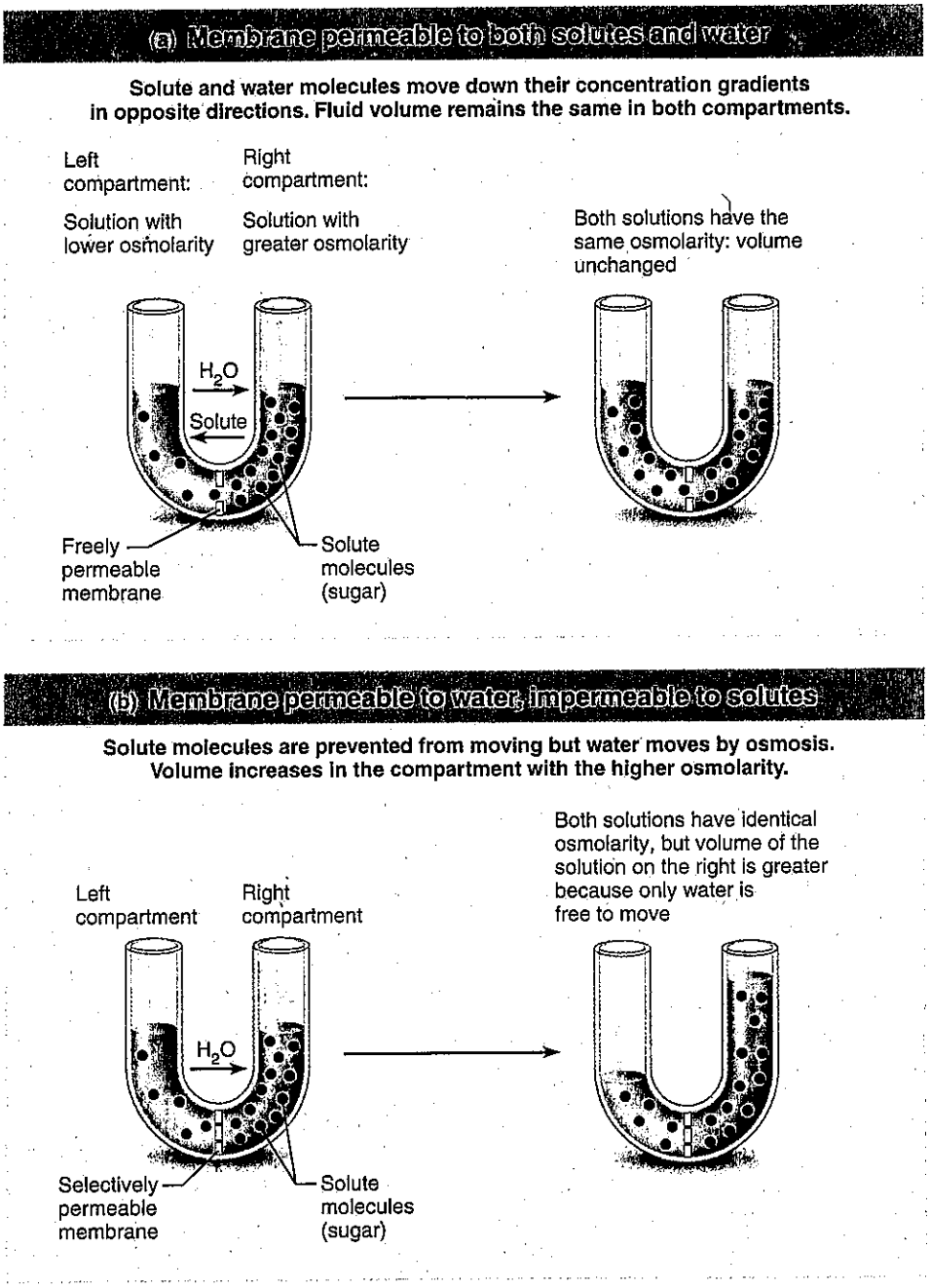


Figure 3.8 Influence of membrane permeability on diffusion and osmosis.

Water also moves freely and reversibly through water-specific channels constructed by transmembrane proteins called **aquaporins (AQPs)**, which allow single-file diffusion of water molecules. Although water-filled aquaporin channels are believed to be present in all cell types, they are particularly abundant in red blood cells and in cells involved in water balance such as kidney tubule cells.

Osmosis occurs whenever the water concentration differs on the two sides of a membrane. If distilled water is present on both sides of a selectively permeable membrane, no *net* osmosis occurs, even though water molecules move in both directions through the membrane. If the solute concentration on the two sides of the membrane differs, water concentration differs as well (as solute concentration increases, water concentration decreases).

The extent to which solutes decrease water's concentration depends on the *number*—not the *type*—of solute particles, because one molecule or one ion of solute (theoretically) displaces one water molecule. The total concentration of all solute particles in a solution is referred to as the solution's **osmolarity** (oz″mo-lar′ĭ-te). When equal volumes of aqueous solutions of different osmolarity are separated by a membrane that is *permeable to all molecules* in the system, net diffusion of both solute

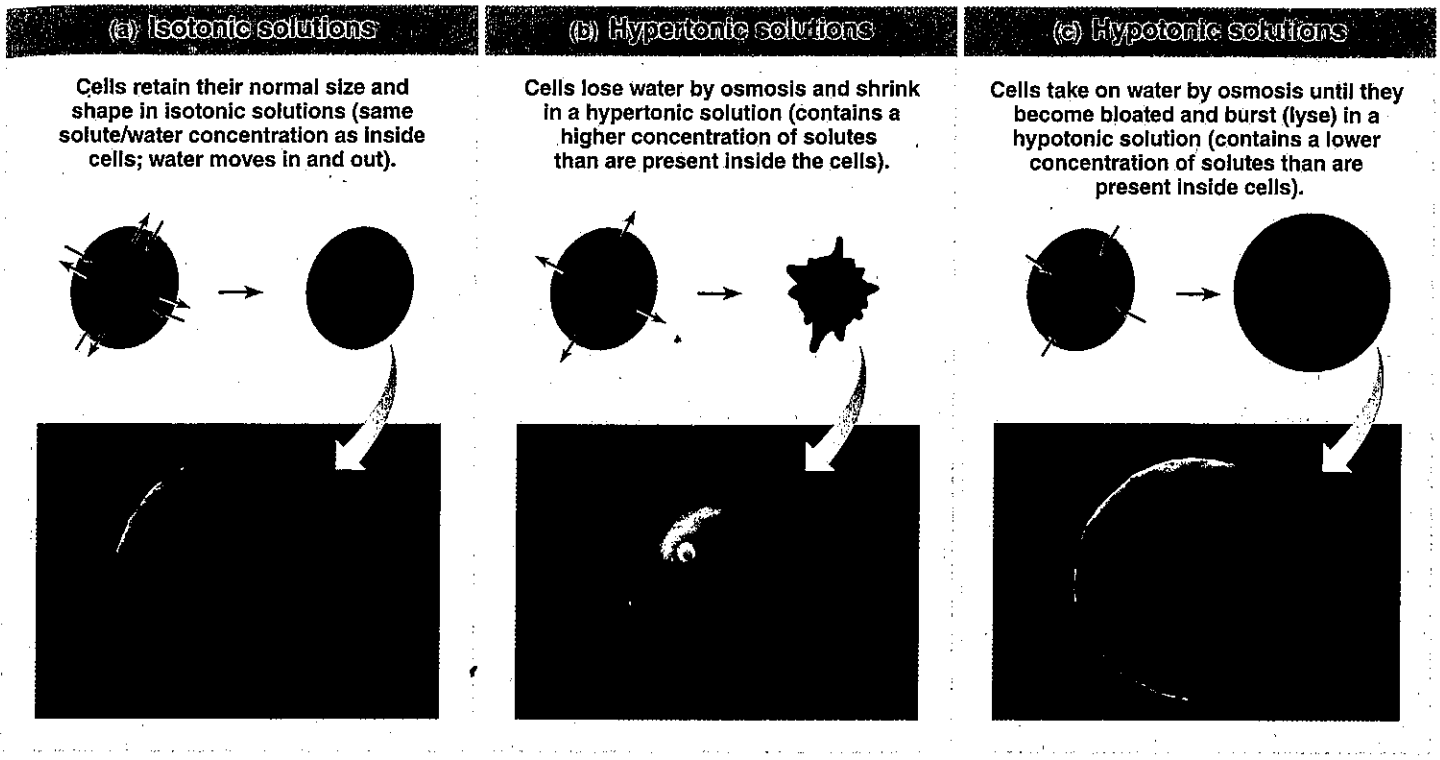


Figure 3.9 The effect of solutions of varying tonicities on living red blood cells.

and water occurs, each moving down its own concentration gradient. Equilibrium is reached when the water (and solute) concentration on both sides of the membrane is the same **(Figure 3.8a)**.

If we consider the same system, but make the membrane *impermeable to solute particles*, we see quite a different result (Figure 3.8b). Water quickly diffuses from the left to the right compartment and continues to do so until its concentration is the same on the two sides of the membrane. Notice that in this case equilibrium results from the movement of water alone (the solutes are prevented from moving). Notice also that the movement of water leads to dramatic changes in the volumes of the two compartments.

The last situation mimics osmosis across plasma membranes of living cells, with one major difference. In our examples, the volumes of the compartments are infinitely expandable and the effect of pressure exerted by the added weight of the higher fluid column is not considered. In living plant cells, which have rigid cell walls external to their plasma membranes, this is not the case. As water diffuses into the cell, the point is finally reached where the **hydrostatic pressure** (the back pressure exerted by water against the membrane) within the cell is equal to its **osmotic pressure** (the tendency of water to move into the cell by osmosis). At this point, there is no further (net) water entry. As a rule, the higher the amount of nondiffusible, or *nonpenetrating*, solutes in a cell, the higher the osmotic pressure and the greater the hydrostatic pressure must be to resist further net water entry. In our plant cell, hydrostatic pressure is pushing water out, and osmotic pressure is pulling water in; therefore, you could think of the osmotic pressure as an osmotic "suck."

However, such major changes in hydrostatic (and osmotic) pressures do not occur in living animal cells, which lack rigid cell walls. Osmotic imbalances cause animal cells to swell or shrink (due to net water gain or loss) until either (1) the solute concentration is the same on both sides of the plasma membrane, or (2) the membrane stretches to its breaking point.

Tonicity Such changes in animal cells lead us to the important concept of *tonicity* (to-nis'ĭ-te). As noted, many solutes, particularly intracellular proteins and selected ions, cannot diffuse through the plasma membrane. Consequently, any change in their concentration alters the water concentration on the two sides of the membrane and results in a net loss or gain of water by the cell.

Tonicity refers to the ability of a solution to change the shape or tone of cells by altering the cells' internal water volume (*tono* = tension).

- **Isotonic** ("the same tonicity") **solutions** have the same concentrations of nonpenetrating solutes as those found in cells (0.9% saline or 5% glucose). Cells exposed to isotonic solutions retain their normal shape, and exhibit no net loss or gain of water **(Figure 3.9a)**. As you might expect, the body's extracellular fluids and most intravenous solutions (solutions infused into the body via a vein) are isotonic.
- **Hypertonic solutions** have a higher concentration of nonpenetrating solutes than seen in the cell (for example, a strong saline solution). Cells immersed in hypertonic solutions lose water and shrink, or *crenate* (kre'nat) (Figure 3.9b).

Table 3.1 Passive Membrane Transport Processes

PROCESS	ENERGY SOURCE	DESCRIPTION	EXAMPLES
Diffusion			
Simple diffusion	Kinetic energy	Net movement of molecules from an area of their higher concentration to an area of their lower concentration, that is, along their concentration gradient	Fats, oxygen, carbon dioxide move through the lipid bilayer of the membrane
Facilitated diffusion	Kinetic energy	Same as simple diffusion, but the diffusing substance is attached to a lipid-soluble membrane carrier protein (carrier-mediated facilitated diffusion) or moves through a membrane channel (channel-mediated facilitated diffusion)	Glucose and some ions move into cells
Osmosis	Kinetic energy	Diffusion of water through a selectively permeable membrane	Movement of water into and out of cells directly through the lipid bilayer of the membrane or via membrane channels (aquaporins)

- **Hypotonic solutions** are more dilute (contain a lower concentration of nonpenetrating solutes) than cells. Cells placed in a hypotonic solution plump up rapidly as water rushes into them (Figure 3.9c). Distilled water represents the most extreme example of hypotonicity. Because it contains *no* solutes, water continues to enter cells until they finally burst, or *lyse*.

Notice that osmolarity and tonicity are not the same. A solution's osmolarity is based solely on its total solute concentration. In contrast, its tonicity is based on how the solution affects cell volume, which depends on (1) solute concentration and (2) solute permeability of the plasma membrane. Osmolarity is expressed as osmoles per liter (osmol/L) where 1 osmol is equal to 1 mole of nonionizing molecules.* A 0.3 osmol/L solution of NaCl is isotonic because sodium ions are usually prevented from diffusing through the plasma membrane. But if the cell is immersed in a 0.3 osmol/L solution of a penetrating solute, the solute will enter the cell and water will follow. The cell will swell and burst, just as if it had been placed in pure water.

Osmosis is extremely important in determining distribution of water in the various fluid-containing compartments of the body (cells, blood, and so on). In general, osmosis continues until osmotic and hydrostatic pressures acting at the membrane are equal. For example, the hydrostatic pressure of blood against the capillary wall forces water out of capillary blood, but the solutes in blood that are too large to cross the capillary membrane draw water back into the bloodstream. As a result, very little net loss of plasma fluid occurs.

Simple diffusion and osmosis occurring directly through the plasma membrane are not selective processes. In those processes, whether a molecule can pass through the membrane depends chiefly on its size or its solubility in lipid, not on its structure. Facilitated diffusion, on the other hand, is often highly selective. The carrier for glucose, for example, combines specifically with glucose, in much the same way an enzyme binds to its specific substrate and ion channels allow only selected ions to pass.

Homeostatic Imbalance 3.3

Hypertonic solutions are sometimes infused intravenously into the bloodstream of patients who are edematous (swollen because their tissues retain water). This is done to draw excess water out of the extracellular space and move it into the bloodstream so the kidneys can eliminate it. Hypotonic solutions may be used (with care) to rehydrate the tissues of extremely dehydrated patients. In mild cases of dehydration, drinking hypotonic fluids (such as apple juice and sports drinks) usually does the trick. ✚

Table 3.1 summarizes passive membrane transport processes.

Check Your Understanding

7. What is the energy source for all types of diffusion?
8. What determines the direction of any diffusion process?
9. What are the two types of facilitated diffusion and how do they differ?

For answers, see Appendix H.

Active Processes

- ✓ Differentiate between primary and secondary active transport.
- ✓ Compare and contrast endocytosis and exocytosis in terms of function and direction.
- ✓ Compare and contrast pinocytosis, phagocytosis, and receptor-mediated endocytosis.

*Osmolarity (Osm) is determined by multiplying molarity (moles per liter, or *M*) by the number of particles resulting from ionization. For example, since NaCl ionizes to $Na^+ + Cl^-$, a 1 *M* solution of NaCl is a 2 Osm solution. For substances that do not ionize (e.g., glucose), molarity and osmolarity are the same. More precisely, the term *osmolality* is used, which is equal to the number of particles mixed into a kilogram of water.

Whenever a cell uses energy to move solutes across the membrane, the process is referred to as *active*. Substances moved actively across the plasma membrane are usually unable to pass in the necessary direction by passive transport processes. The substance may be too large to pass through the channels, incapable of dissolving in the lipid bilayer, or unable to move down its concentration gradient.

There are two major means of active membrane transport: active transport and vesicular transport.

Active Transport

Like carrier-mediated facilitated diffusion, **active transport** requires carrier proteins that combine *specifically* and *reversibly* with the transported substances. However, facilitated diffusion always follows concentration gradients because its driving force is kinetic energy. In contrast, active transporters or **solute pumps** move solutes, most importantly ions, "uphill" *against* a concentration gradient. To do this work, cells must expend energy.

Active transport processes are distinguished according to their source of energy:

- In *primary active transport*, the energy to do work comes *directly from hydrolysis of ATP*.
- In *secondary active transport*, transport is driven indirectly *by energy stored in ionic gradients* created by primary active transport pumps. Secondary active transport systems are all *coupled systems*; that is, they move more than one substance at a time.

  In a **symport system,** the two transported substances move in the same direction (*sym* = same). In an **antiport system** (*anti* = opposite, against), the transported substances "wave to each other" as they cross the membrane in opposite directions.

Primary Active Transport In **primary active transport**, hydrolysis of ATP results in the phosphorylation of the transport protein. This step causes the protein to change its shape in such a manner that it "pumps" the bound solute across the membrane.

Primary active transport systems include calcium and hydrogen pumps, but the most investigated example of a primary active transport system is the **sodium-potassium pump**, for which the carrier, or "pump," is an enzyme called **Na^+-K^+ ATPase**. In the body, the concentration of K^+ inside the cell is some 10 times higher than that outside, and the reverse is true of Na^+. These ionic concentration differences are essential for excitable cells like muscle and nerve cells to function normally and for all body cells to maintain their normal fluid volume. Because Na^+ and K^+ leak slowly but continuously through leakage channels in the plasma membrane along their concentration gradient (and cross more rapidly in stimulated muscle and nerve cells), the Na^+-K^+ pump operates almost continuously as an antiporter. It simultaneously drives Na^+ out of the cell against a steep concentration gradient and pumps K^+ back in.

Earlier we said that solutes diffuse down their concentration gradients. This is true for uncharged solutes, but only partially true for ions. The negatively and positively charged faces of the plasma membrane can help or hinder diffusion of ions driven by a concentration gradient. It is more correct to say that ions diffuse according to **electrochemical gradients**, thereby recognizing the effect of both electrical and concentration (chemical) forces. Hence, the electrochemical gradients maintained by the Na^+-K^+ pump underlie most secondary active transport of nutrients and ions, and are crucial for cardiac, skeletal muscle, and neuron function.

Figure 3.10 on p. 74, *Focus on Primary Active Transport: The Na^+-K^+ Pump*, describes the operation of the Na^+-K^+ pump. Make sure you understand this process thoroughly before moving on to the topic of secondary active transport.

Secondary Active Transport A single ATP-powered pump, such as the Na^+-K^+ pump, can indirectly drive the **secondary active transport** of several other solutes. By moving sodium across the plasma membrane against its concentration gradient, the pump stores energy (in the ion gradient). Then, just as water pumped uphill can do work as it flows back down (to turn a water wheel, for instance), a substance pumped across a membrane can do work as it leaks back, propelled "downhill" along its concentration gradient. In this way, as sodium moves back into the cell with the help of a carrier protein, other substances are "dragged along," or cotransported, by the same carrier protein **(Figure 3.11)**. This is a symport system.

For example, some sugars, amino acids, and many ions are cotransported via secondary active transport into cells lining the small intestine. Because the energy for this type of transport is the concentration gradient of the ion (in this case Na^+), Na^+ has to be pumped back out of the cell to maintain its diffusion gradient. Ion gradients can also drive antiport systems such as those that help regulate intracellular pH by using the sodium gradient to expel hydrogen ions.

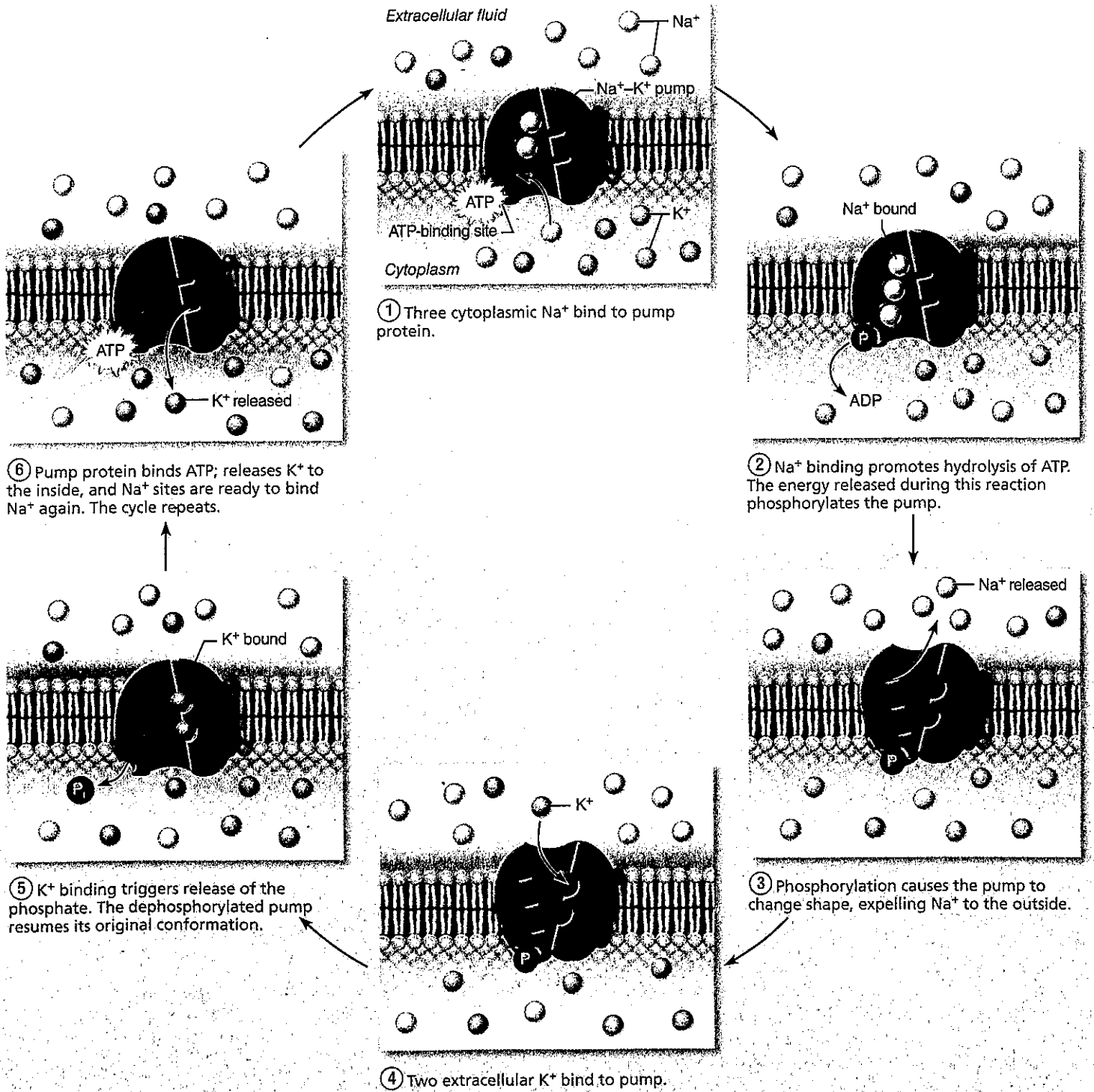
Regardless of whether the energy is provided directly (primary active transport) or indirectly (secondary active transport), each membrane pump or cotransporter transports only specific substances. Active transport systems provide a way for the cell to be very selective in cases where substances cannot pass by diffusion. No pump—no transport.

Vesicular Transport

In **vesicular transport**, fluids containing large particles and macromolecules are transported across cellular membranes inside membranous sacs called *vesicles*. Like active transport, vesicular transport moves substances into the cell (endocytosis) and out of the cell (exocytosis). It is also used for combination processes such as *transcytosis*, moving substances into, across, and then out of the cell, and *vesicular trafficking*, moving substances from one area (or membranous organelle) in the cell to another. Vesicular transport processes are energized by ATP (or in some cases another energy-rich compound, *GTP*—guanosine triphosphate).

Endocytosis, Transcytosis, and Vesicular Trafficking Virtually all forms of vesicular transport involve an assortment of protein-coated vesicles of three types and, with some exceptions, all are mediated by membrane receptors. Before we get specific about each type of coated vesicular transport, let's look at the general scheme of endocytosis.

Figure 3.10 Primary active transport is the process in which solutes are moved across cell membranes against electrochemical gradients using energy supplied directly by ATP. The action of the Na^+–K^+ pump is an important example of primary active transport. A&PFlix *Available at www.masteringaandp.com*



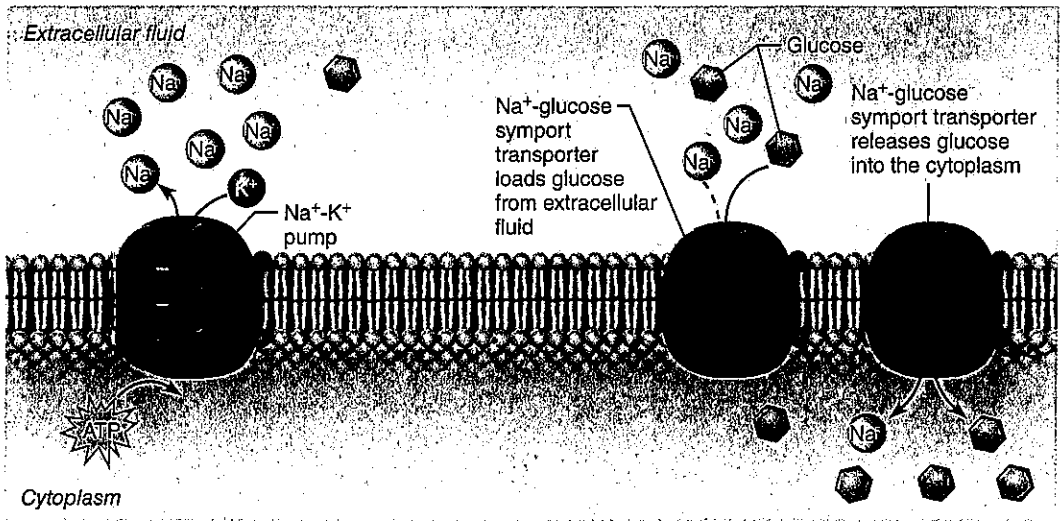


Figure 3.11 Secondary active transport is driven by the concentration gradient created by primary active transport.

Protein-coated vesicles provide the main route for endocytosis and transcytosis of bulk solids, most macromolecules, and fluids. On occasion, these vesicles are also hijacked by pathogens seeking entry into a cell.

Figure 3.12 shows the basic steps in endocytosis and transcytosis. ① An infolding portion of the plasma membrane, called a *coated pit*, progressively encloses the substance to be taken into the cell. The coating found on the cytoplasmic face of the pit is most often the bristlelike protein **clathrin** (klă'thrin; "lattice clad"). The clathrin coat (clathrin and some accessory proteins) acts in both selecting the cargo and deforming the membrane to produce the vesicle. ② The vesicle detaches, and ③ the coat proteins are recycled back to the plasma membrane. ④ The uncoated vesicle then typically fuses with a sorting vesicle called an *endosome*. ⑤ Some membrane components and receptors of the fused vesicle may be recycled back to the plasma membrane in a transport vesicle. ⑥ The remaining contents of the vesicle may (a) combine with a *lysosome* (li'so-sōm), a specialized cell structure containing digestive enzymes, where the ingested substance is degraded or released (if iron or cholesterol), or (b) be transported completely across the cell and released by exocytosis on the opposite side (*transcytosis*). Transcytosis is common in the endothelial cells lining blood vessels because it provides a quick means to get substances from the blood to the interstitial fluid.

Based on the nature and quantity of material taken up and the means of uptake, three types of endocytosis that use clathrin-coated vesicles are recognized: phagocytosis, pinocytosis, and receptor-mediated endocytosis.

- **Phagocytosis.** In **phagocytosis** (fag"o-si-to'sis; "cell eating"), the cell engulfs some relatively large or solid material, such as a clump of bacteria, cell debris, or inanimate particles (asbestos fibers or glass, for example) **(Figure 3.13a)**. When a particle binds to receptors on the cell's surface, cytoplasmic extensions called pseudopods (soo'do-pahdz; *pseudo* = false, *pod* = foot) form and flow around the particle. This forms an endocytotic vesicle called a **phagosome** (fag'o-sōm; "eaten body"). In most cases, the phagosome then fuses with a lysosome and its contents are digested. Any indigestible contents are ejected from the cell by exocytosis.

  In the human body, only macrophages and certain white blood cells are "experts" at phagocytosis. Commonly referred to as *phagocytes*, these cells help protect the body by ingesting and disposing of bacteria, other foreign substances, and dead tissue cells. The disposal of dying cells is crucial, because dead cell remnants trigger inflammation in the surrounding area or may stimulate an undesirable immune response. Most phagocytes move about by **amoeboid motion** (ah-me'boyd; "changing shape"); that is, the flowing of their cytoplasm into temporary extensions allows them to creep along.

- **Pinocytosis.** In **pinocytosis** ("cell drinking"), also called **fluid-phase endocytosis**, a bit of infolding plasma membrane (which begins as a protein-coated pit) surrounds a very small volume of extracellular fluid containing dissolved molecules (Figure 3.13b). This droplet enters the cell and fuses with an endosome. Unlike phagocytosis, pinocytosis is a routine activity of most cells, affording them a nonselective way of sampling the extracellular fluid. It is particularly important in cells that absorb nutrients, such as cells that line the intestines.

  As mentioned, bits of the plasma membrane are removed when the membranous sacs are internalized. However, these membranes are recycled back to the plasma membrane by exocytosis as described shortly, so the surface area of the plasma membrane remains remarkably constant.

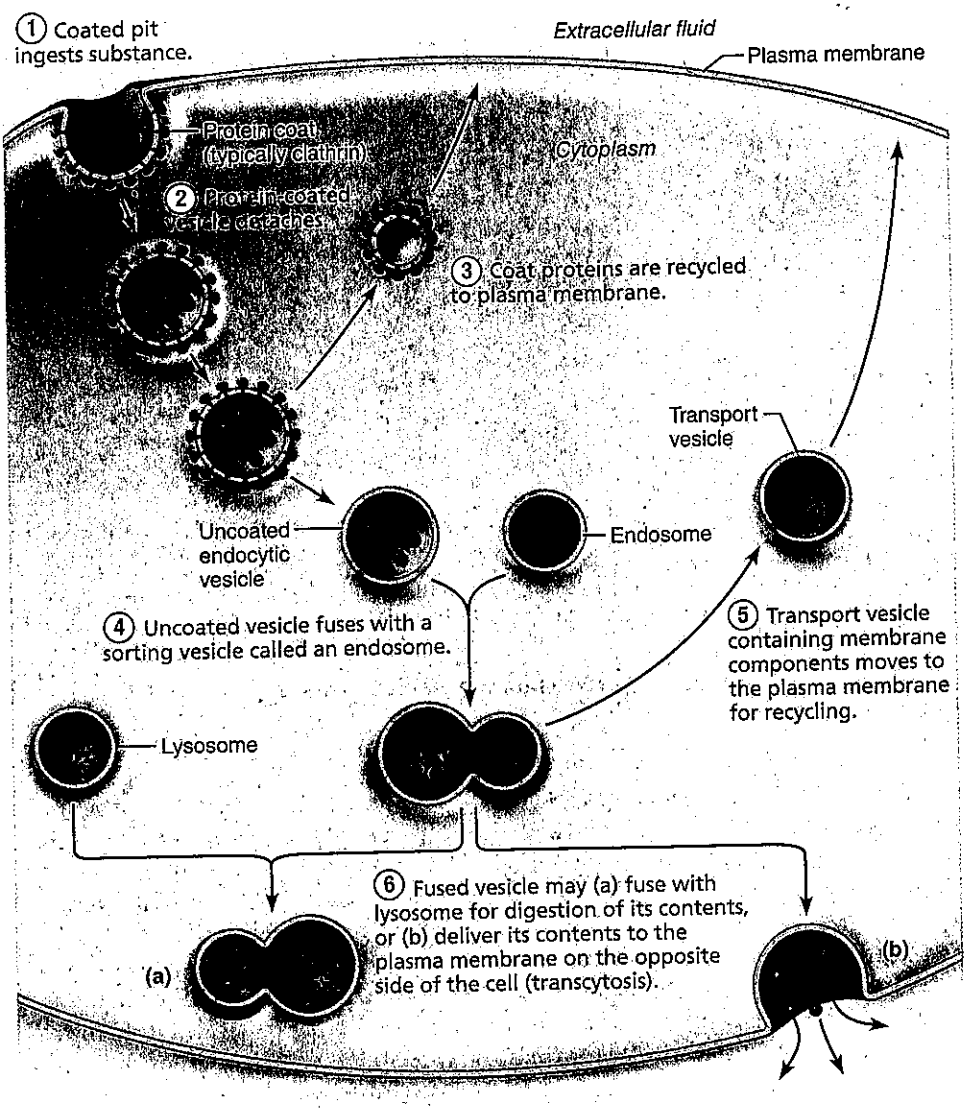


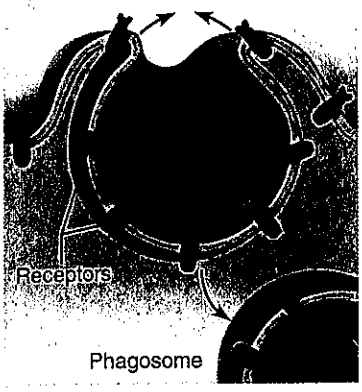
Figure 3.12 Events of endocytosis mediated by protein-coated pits. Note the three possible fates for a vesicle and its contents, shown in ⑤ and ⑥.

- **Receptor-mediated endocytosis.** The main mechanism for the *specific* endocytosis and transcytosis of most macromolecules by body cells is **receptor-mediated endocytosis** (Figure 3.13c). This exquisitely selective mechanism allows cells to concentrate material that is present only in small amounts in the extracellular fluid. The receptors for this process are plasma membrane proteins that bind only certain substances. Both the receptors and attached molecules are internalized in a clathrin-coated pit and then dealt with in one of the ways discussed above. Substances taken up by receptor-mediated endocytosis include enzymes, insulin (and some other hormones), low-density lipoproteins (such as cholesterol attached to a transport protein), and iron. Unfortunately, flu viruses, diphtheria, and cholera toxins also use this route to enter our cells.

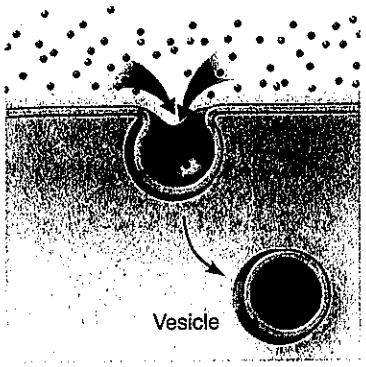
Different coat proteins are used for certain other types of vesicular transport. For example, **caveolae** (ka″ve-o′le; "little caves"), tubular or flask-shaped inpocketings of the plasma membrane seen in many cell types, are involved in a unique kind of receptor-mediated endocytosis. Like clathrin-coated pits, caveolae capture specific molecules (folic acid, tetanus toxin) from the extracellular fluid in coated vesicles and participate in some forms of transcytosis. However, caveolae are smaller than clathrin-coated vesicles. Additionally, their cage-like protein coat is thinner.

Caveolae are closely associated with lipid rafts that are platforms for G proteins, receptors for hormones (for example, insulin), and enzymes involved in cell regulation. These vesicles appear to provide sites for cell signaling and cross talk between signaling pathways. Their precise role in the cell is still being worked out.

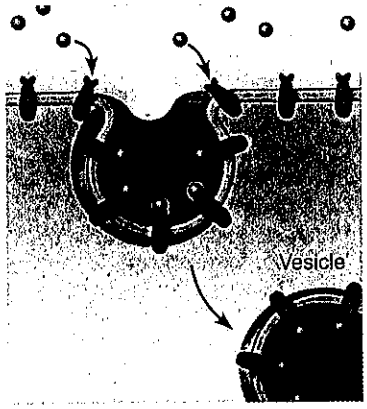
Vesicles coated with still another coat protein (coatomer) function in most types of intracellular vesicular trafficking. Perhaps the most important thing to remember about the coat



(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 is combined with a lysosome. Undigested contents remain in the vesicle (now called a residual body) or are ejected by exocytosis. Vesicle may or may not be protein-coated but has receptors capable of binding to microorganisms or solid particles.



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

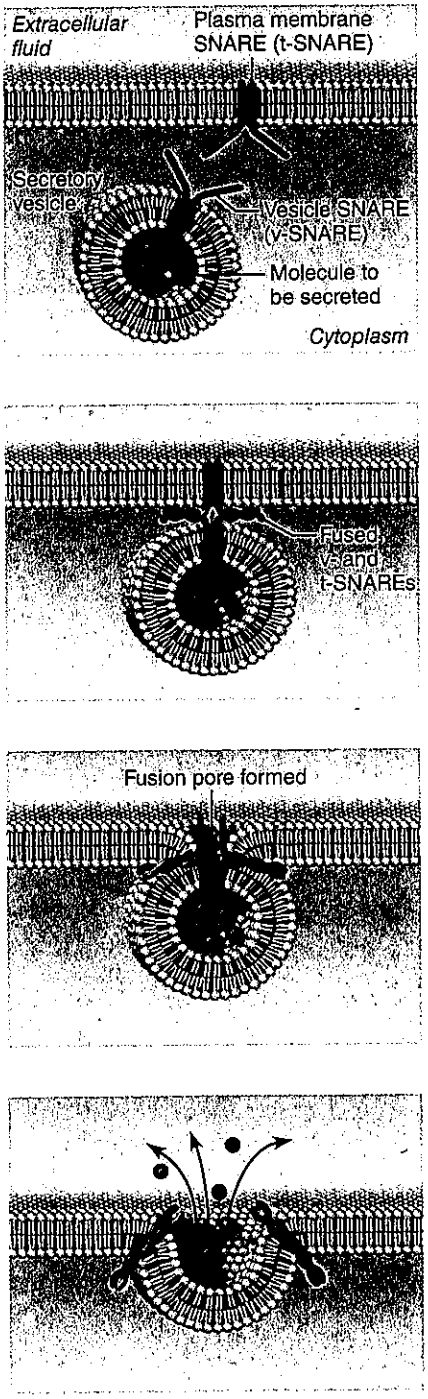


(c) Receptor-mediated endocytosis
Extracellular substances bind to specific receptor proteins, enabling the cell to ingest and concentrate specific substances (ligands) in protein-coated vesicles. Ligands may simply be released inside the cell, or combined with a lysosome to digest contents. Receptors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

Figure 3.13 Comparison of three types of endocytosis.

proteins in general is that they play a significant role in all forms of endocytosis.

Exocytosis Vesicular transport processes that eject substances from the cell interior into the extracellular fluid are called **exocytosis** (ek″so-si-to′sis; "out of the cell"). Typically stimulated by a cell-surface signal such as binding of a hormone to a membrane receptor or a change in membrane voltage, exocytosis accounts for hormone secretion, neurotransmitter release, mucus secretion, and in some cases, ejection of wastes. The substance to be removed from the cell is first enclosed in a protein-coated membranous sac called a *secretory vesicle*. In most cases, the vesicle migrates to the plasma membrane, fuses with it, and then ruptures, spilling the sac contents out of the cell **(Figure 3.14)**.



(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 (100,000×)

Figure 3.14 Exocytosis.

Table 3.2 Active Membrane Transport Processes

PROCESS	ENERGY SOURCE	DESCRIPTION	EXAMPLES
Active Transport			
Primary active transport	ATP	Transport of substances against a concentration (or electrochemical) gradient. Performed across the plasma membrane by a solute pump, directly using energy of ATP hydrolysis.	Ions (Na^+, K^+, H^+, Ca^{2+}, and others)
Secondary active transport	Ion concentration gradient maintained with ATP	Cotransport (coupled transport) of two solutes across the membrane. Energy is supplied indirectly by the ion gradient created by primary active transport. Symporters move the transported substances in the same direction; antiporters move transported substances in opposite directions across the membrane.	Movement of polar or charged solutes, e.g., amino acids (into cell by symporters); Ca^{2+}, H^+ (out of cells via antiporters)
Vesicular Transport			
Endocytosis			
▪ Via clathrin-coated vesicles			
Phagocytosis	ATP	"Cell eating": A large external particle (proteins, bacteria, dead cell debris) is surrounded by a "seizing foot" and becomes enclosed in a vesicle (phagosome).	In the human body, occurs primarily in protective phagocytes (some white blood cells and macrophages)
Pinocytosis (fluid-phase endocytosis)	ATP	Plasma membrane sinks beneath an external fluid droplet containing small solutes. Membrane edges fuse, forming a fluid-filled vesicle.	Occurs in most cells; important for taking in dissolved solutes by absorptive cells of the kidney and intestine
Receptor-mediated endocytosis	ATP	Selective endocytosis and transcytosis. External substance binds to membrane receptors.	Means of intake of some hormones, cholesterol, iron, and most macromolecules
▪ Via caveolin-coated vesicles (caveolae)	ATP	Selective endocytosis (and transcytosis). External substance binds to membrane receptors (often associated with lipid rafts).	Roles not fully known; proposed roles include cholesterol regulation and trafficking, and platforms for signal transduction
Vesicular trafficking			
▪ Via coatomer-coated vesicles	ATP	Vesicles pinch off from organelles and travel to other organelles to deliver their cargo.	Accounts for nearly all intracellular trafficking between certain organelles (endoplasmic reticulum and Golgi apparatus). Exceptions include vesicles budding from the trans face of the Golgi apparatus, which are clathrin-coated.
Exocytosis	ATP	Secretion or ejection of substances from a cell. The substance is enclosed in a membranous vesicle, which fuses with the plasma membrane and ruptures, releasing the substance to the exterior.	Secretion of neurotransmitters, hormones, mucus, etc.; ejection of cell wastes

Exocytosis, like other mechanisms in which vesicles are targeted to their destinations, involves a "docking" process in which transmembrane proteins on the vesicles, fancifully called v-SNAREs (*v* for vesicle), recognize certain plasma membrane proteins, called t-SNAREs (*t* for target), and bind with them. This binding causes the membranes to "corkscrew" together and fuse, rearranging the lipid monolayers without mixing them (Figure 3.14a). As described, membrane material added by exocytosis is removed by endocytosis—the reverse process.

Table 3.2 summarizes active membrane transport processes.

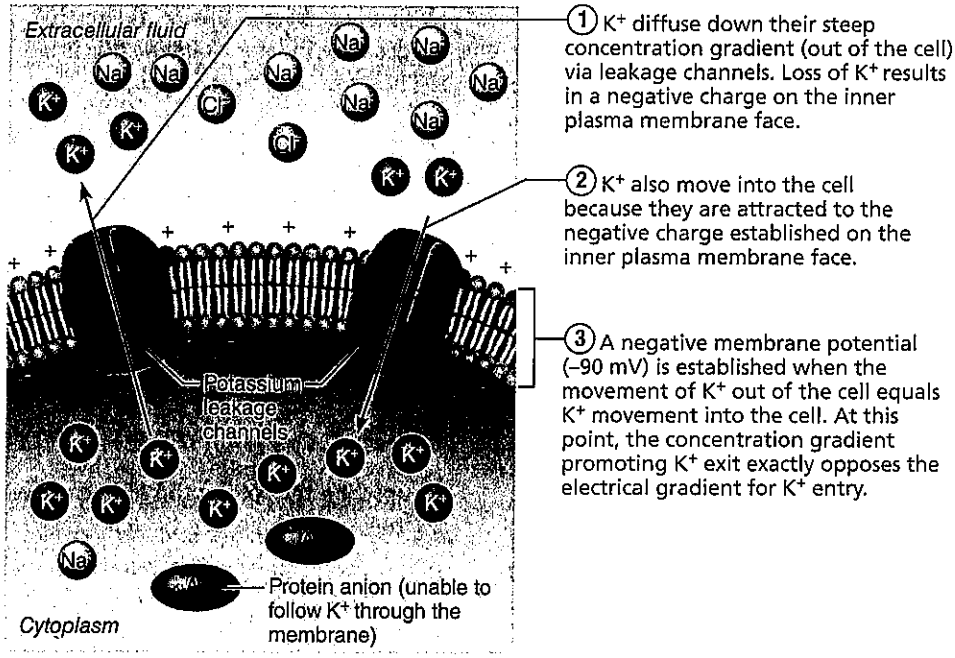


Figure 3.15 The key role of K^+ in generating the resting membrane potential. The resting membrane potential is largely determined by K^+ because at rest, the membrane is much more permeable to K^+ than Na^+. The active transport of sodium and potassium ions (in a ratio of 3:2) by the Na^+-K^+ pump maintains these conditions.

☑ Check Your Understanding

10. What happens when the Na^+-K^+ pump is phosphorylated? When K^+ binds to the pump protein?
11. As a cell grows, its plasma membrane expands. Does this membrane expansion involve endocytosis or exocytosis?
12. Phagocytic cells gather in the lungs, particularly in the lungs of smokers. What is the connection?
13. Which vesicular transport process allows a cell to take in cholesterol from the extracellular fluid?

For answers, see Appendix H.

The Plasma Membrane: Generation of a Resting Membrane Potential

✓ Define membrane potential and explain how the resting membrane potential is established and maintained.

As you're now aware, the selective permeability of the plasma membrane can lead to dramatic osmotic flows, but that is not its only consequence. An equally important result is the generation of a **membrane potential**, or voltage, across the membrane. A *voltage* is electrical potential energy resulting from the separation of oppositely charged particles. In cells, the oppositely charged particles are ions, and the barrier that keeps them apart is the plasma membrane.

In their resting state, all body plasma membranes exhibit a **resting membrane potential** that typically ranges from −50 to −100 millivolts (mV), depending on cell type. For this reason, all cells are said to be **polarized**. The minus sign before the voltage indicates that the *inside* of the cell is negative compared to its outside. This voltage (or charge separation) exists *only at the membrane*. If we added up all the negative and positive charges in the cytoplasm, we would find that the cell interior is electrically neutral. Likewise, the positive and negative charges in the extracellular fluid balance each other exactly.

So how does the resting membrane potential come about, and how is it maintained? The short answer is that diffusion causes ionic imbalances that polarize the membrane, and active transport processes *maintain* that membrane potential. First, let's look at how diffusion polarizes the membrane.

Selective Diffusion Establishes Membrane Potential

Many kinds of ions are found both inside cells and in the extracellular fluid, but the resting membrane potential is determined mainly by the concentration gradient of potassium (K^+) and by the differential permeability of the plasma membrane to K^+ and other ions **(Figure 3.15)**. Recall that K^+ and protein anions predominate inside body cells, and the extracellular fluid contains relatively more Na^+, which is largely balanced by Cl^-. The unstimulated plasma membrane is somewhat permeable to K^+ because of leakage channels, but impermeable to the protein anions. Consequently, K^+ diffuses out of the cell along its concentration gradient but the protein anions are unable to follow, and this loss of positive charges makes the membrane interior more negative (Figure 3.15 ①).

As more and more K^+ leaves the cell, the negativity of the inner membrane face becomes great enough to attract K^+ back toward and even into the cell (Figure 3.15 ②). At a membrane voltage of −90 mV, potassium's concentration gradient is exactly balanced by the electrical gradient (membrane potential), and one K^+ enters the cell as one leaves (Figure 3.15 ③).

In many cells, sodium (Na^+) also contributes to the resting membrane potential. Sodium is strongly attracted to the cell interior by its concentration gradient, bringing the resting membrane potential to −70 mV. However, potassium still largely determines the resting membrane potential because the membrane is much more permeable to K^+ than to Na^+. Even though the membrane is permeable to Cl^-, in most cells Cl^- does not contribute to the resting membrane potential, because its concentration and electrical gradients exactly balance each other.

We may be tempted to believe that massive flows of K^+ ions are needed to generate the resting potential, but this is not the case. Surprisingly, the number of ions producing the membrane potential is so small that it does not change ion concentrations in any significant way.

In a cell at rest, very few ions cross its plasma membrane. However, Na^+ and K^+ are not at equilibrium and there is some net movement of K^+ out of the cell and of Na^+ into the cell. Na^+ is strongly pulled into the cell by both its concentration gradient and the interior negative charge. If only passive forces were at work, these ion concentrations would eventually become equal inside and outside the cell.

Active Transport Maintains Electrochemical Gradients

Now let's look at how active transport processes maintain the membrane potential that diffusion has established, with the result that the cell exhibits a *steady state*. The rate of active transport is equal to, and depends on, the rate of Na^+ diffusion into the cell. If more Na^+ enters, more is pumped out. (This is like being in a leaky boat. The more water that comes in, the faster you bail!) The Na^+-K^+ pump couples sodium and potassium transport and, on average, each "turn" of the pump ejects $3Na^+$ out of the cell and carries $2K^+$ back in (see Figure 3.10). Because the membrane is always 50 to 100 times more permeable to K^+, the ATP-dependent Na^+-K^+ pump maintains both the membrane potential (the charge separation) and the osmotic balance. Indeed, if Na^+ was not continuously removed from cells, so much would accumulate intracellularly that the osmotic gradient would draw water into the cells, causing them to burst.

As we described on p. 73, diffusion of charged particles across the membrane is affected not only by concentration gradients, but by the electrical charge on the inner and outer faces of the membrane. Together these gradients make up the *electrochemical gradient*. The diffusion of K^+ across the plasma membrane is aided by the membrane's greater permeability to it and by the ion's concentration gradient, but the negative charges on the cell interior resist K^+ diffusion. In contrast, a steep electrochemical gradient draws Na^+ into the cell, but the membrane's relative impermeability to it limits Na^+ diffusion.

The transient opening of gated Na^+ and K^+ channels in the plasma membrane "upsets" the resting membrane potential. As we describe in later chapters, this is a normal means of activating neurons and muscle cells.

☑ Check Your Understanding

14. What process establishes the resting membrane potential?
15. Is the inside of the plasma membrane negative or positive relative to its outside in a polarized membrane?

For answers, see Appendix H.

The Plasma Membrane: Cell-Environment Interactions

✓ Describe the role of the glycocalyx when cells interact with their environment.

✓ List several roles of membrane receptors and that of voltage-gated membrane channel proteins.

Cells are biological minifactories and, like other factories, they receive and send orders from and to the outside community. But *how* does a cell interact with its environment, and *what* activates it to carry out its homeostatic functions?

Sometimes cells interact directly with other cells. However, in many cases cells respond to extracellular chemicals, such as hormones and neurotransmitters distributed in body fluids. Cells also interact with extracellular molecules that act as signposts to guide cell migration during development and repair.

Whether cells interact directly or indirectly, however, the glycocalyx is always involved. The best-understood glycocalyx molecules fall into two large families—cell adhesion molecules and plasma membrane receptors (see Figure 3.4, p. 66). Another group of membrane proteins, voltage-gated channel proteins, are important in cells that respond to electrical signals.

Roles of Cell Adhesion Molecules (CAMs)

Thousands of **cell adhesion molecules** (CAMs) are found on almost every cell in the body. CAMs play key roles in embryonic development and wound repair (situations where cell mobility is important) and in immunity. These sticky glycoproteins (*cadherins* and *integrins*) act as

- The molecular "Velcro" that cells use to anchor themselves to molecules in the extracellular space and to each other (see desmosome discussion on pp. 66–67)
- The "arms" that migrating cells use to haul themselves past one another
- SOS signals sticking out from the blood vessel lining that rally protective white blood cells to a nearby infected or injured area
- Mechanical sensors that respond to changes in local tension or fluid movement at the cell surface by stimulating synthesis or degradation of adhesive membrane (tight) junctions
- Transmitters of intracellular signals that direct cell migration, proliferation, and specialization

Roles of Plasma Membrane Receptors

A huge and diverse group of integral proteins and glycoproteins that serve as binding sites are collectively known as **membrane receptors**. Some function in contact signaling, and others in chemical signaling. Let's take a look.

Contact Signaling

Contact signaling, in which cells come together and touch, is the means by which cells recognize one another. It is particularly important for normal development and immunity. Some bacteria and other infectious agents use contact signaling to identify their "preferred" target tissues.

Chemical Signaling

Most plasma membrane receptors are involved in *chemical signaling*. **Ligands** are chemicals that bind specifically to plasma membrane receptors. Ligands include most *neurotransmitters* (nervous system signals), *hormones* (endocrine system signals), and *paracrines* (chemicals that act locally and are rapidly destroyed).

Different cells respond in different ways to the same ligand. Acetylcholine, for instance, stimulates skeletal muscle cells to contract, but inhibits heart muscle. Why do different cells respond so differently? The reason is that a target cell's response depends on the internal machinery that the receptor is linked to, not the specific ligand that binds to it.

Though cell responses to receptor binding vary widely, there is a fundamental similarity: When a ligand binds to a membrane receptor, the receptor's structure changes, and cell proteins are altered in some way. For example:

- *Catalytic receptor proteins* are membrane proteins that respond to ligands by becoming activated enzymes.
- *Chemically gated channel-linked receptors*, common in muscle and nerve cells, respond by transiently opening or closing ion gates, which in turn changes the excitability of the cell.
- **G protein–linked receptors** exert their effect indirectly through a **G protein**, a regulatory molecule that acts as a middleman or relay to activate (or inactivate) a membrane-bound enzyme or ion channel. This in turn generates one or more intracellular chemical signals, commonly called **second messengers**, which connect plasma membrane events to the internal metabolic machinery of the cell. Two important second messengers are **cyclic AMP** and ionic calcium, both of which typically activate *protein kinase enzymes*, which transfer phosphate groups from ATP to other proteins. In this way, the protein kinases can activate a whole series of enzymes that bring about the desired cellular activity. Because a single enzyme can catalyze hundreds of reactions, the amplification effect of such a chain of events is tremendous, much like that stirred up by a chain letter. *Focus on G Proteins* **(Figure 3.16)** on p. 82 describes a G protein signaling system. Take a moment to study this carefully because this key signaling pathway is involved in neurotransmission, smell, vision, and hormone action (Chapters 11, 15, and 16).

Nitric oxide (*NO*) is an important signaling molecule even though it doesn't act in any of the ways we have already described. One of nature's simplest molecules, NO is made of a single atom of nitrogen and one of oxygen. It is also an environmental pollutant and the first gas known to act as a biological messenger. Because of its tiny size, it slips into and out of cells easily. Its unpaired electron makes it highly reactive and it reacts with head-spinning speed with other key molecules to spur cells into a broad array of activities. You will hear more about NO in the neural, cardiovascular, and immune system chapters.

Role of Voltage-Gated Membrane Channel Proteins: Electrical Signaling

In *electrical signaling*, certain plasma membrane proteins are channel proteins that respond to changes in membrane potential by opening or closing the channel. Such voltage-gated channels are common in excitable tissues like neural and muscle tissues, and are crucial to their normal function.

☑ Check Your Understanding

16. What term is used to indicate signaling chemicals that bind to membrane receptors? Which type of membrane receptor is most important in directing intracellular events by promoting formation of second messengers?

For answer, see Appendix H.

The Cytoplasm

- ✓ Describe the composition of the cytosol.
- ✓ Discuss the structure and function of mitochondria.
- ✓ Discuss the structure and function of ribosomes, the endoplasmic reticulum, and the Golgi apparatus, including functional interrelationships among these organelles.
- ✓ Compare the functions of lysosomes and peroxisomes.

Cytoplasm ("cell-forming material"), the cellular material between the plasma membrane and the nucleus, is the site of most cellular activities. Although early microscopists thought that the cytoplasm was a structureless gel, the electron microscope reveals that it consists of three major elements: the cytosol, organelles, and inclusions.

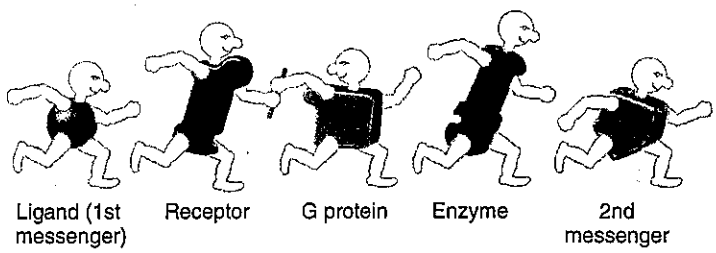
The **cytosol** (si'to-sol) is the viscous, semitransparent fluid in which the other cytoplasmic elements are suspended. It is a complex mixture with properties of both a colloid and a true solution. Dissolved in the cytosol, which is largely water, are proteins, salts, sugars, and a variety of other solutes.

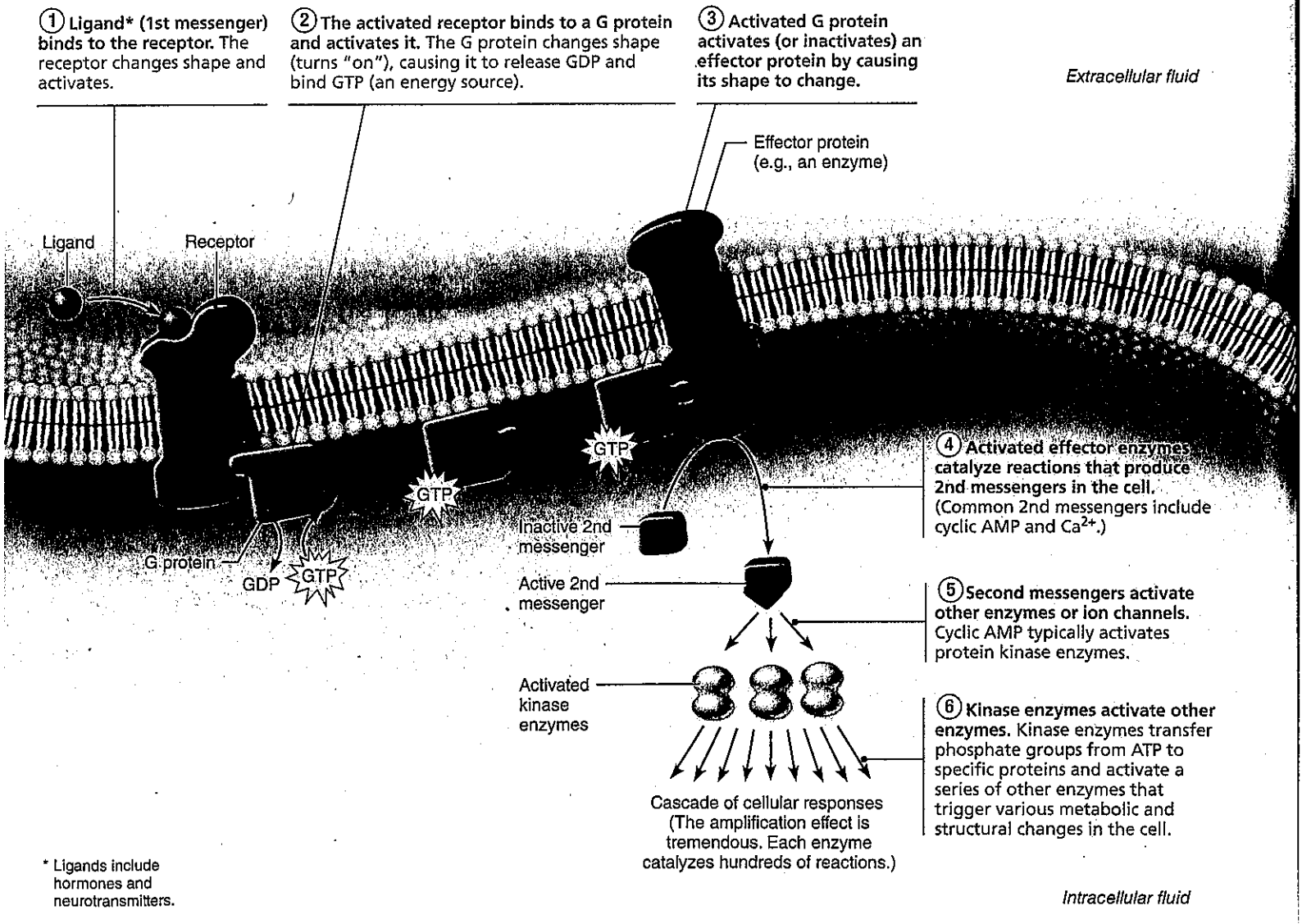
The **organelles** are the metabolic machinery of the cell. Each type of organelle carries out a specific function for the cell—some synthesize proteins, others package those proteins, and so on.

Inclusions are chemical substances that may or may not be present, depending on cell type. Examples include stored nutrients, such as the glycogen granules in liver and muscle cells; lipid droplets in fat cells; pigment (melanin) granules in certain skin and hair cells; and crystals of various types.

Figure 3.16 G proteins act as middlemen or relays between extracellular first messengers and intracellular second messengers that cause responses within the cell.

The sequence described here is like a molecular relay race. Instead of a baton passed from runner to runner, the message (a shape change) is passed from molecule to molecule as it makes its way across the cell membrane from outside to inside the cell.





* Ligands include hormones and neurotransmitters.

Cytoplasmic Organelles

The organelles ("little organs") are specialized cellular compartments or structures, each performing its own job to maintain the life of the cell. Some organelles, the *nonmembranous organelles*, lack membranes. Examples are the cytoskeleton, centrioles, and ribosomes.

Most organelles, however, are bounded by a membrane similar in composition to the plasma membrane. This membrane enables the *membranous organelles* (such as peroxisomes, lysosomes, endoplasmic reticulum, and Golgi apparatus) to maintain an internal environment different from that of the surrounding cytosol. This compartmentalization is crucial to cell functioning. Without it, thousands of enzymes would be randomly mixed and biochemical activity would be chaotic. Besides providing splendid isolation for an organelle, its membrane often unites it with the rest of an interactive intracellular system called the *endomembrane system* (see p. 87), and the lipid and protein makeup of the membrane allows it to recognize and interact with other organelles. Now let's consider what goes on in each of the workshops of our cellular factory.

Mitochondria

Mitochondria (mi″to-kon′dre-ah) are threadlike (*mitos* = thread) or lozenge-shaped membranous organelles. In living cells they squirm, elongate, and change shape almost continuously. They are the power plants of a cell, providing most of its ATP supply. The density of mitochondria in a particular cell reflects that cell's energy requirements, and mitochondria generally cluster where the action is. Busy cells like kidney and liver cells have hundreds of mitochondria, whereas relatively inactive cells (such as unchallenged lymphocytes) have just a few.

A mitochondrion is enclosed by *two* membranes, each with the general structure of the plasma membrane **(Figure 3.17)**. The *outer membrane* is smooth and featureless, but the *inner membrane* folds inward, forming shelflike **cristae** (krĭ′ste; "crests") that protrude into the *matrix*, the gel-like substance within the mitochondrion. Intermediate products of food fuels (glucose and others) are broken down to water and carbon dioxide by teams of enzymes, some dissolved in the mitochondrial matrix and others forming part of the crista membrane.

As the metabolites are broken down and oxidized, some of the energy released is captured and used to attach phosphate groups to ADP molecules to form ATP. This multistep mitochondrial process (described in Chapter 24) is called *aerobic cellular respiration* (a-er-o′bik) because it requires oxygen.

Mitochondria are complex organelles: They contain their own DNA, RNA, and ribosomes and are able to reproduce themselves. Mitochondrial genes (some 37 of them) direct the synthesis of 1% of the proteins required for mitochondrial function, and the DNA of the cell's nucleus encodes the remaining proteins needed to carry out cellular respiration. When cellular requirements for ATP increase, the mitochondria synthesize more cristae or simply pinch in half (a process called *fission*) to increase their number, then grow to their former size.

Intriguingly, mitochondria are similar to bacteria in the purple bacteria phylum, and mitochondrial DNA is bacteria-like.

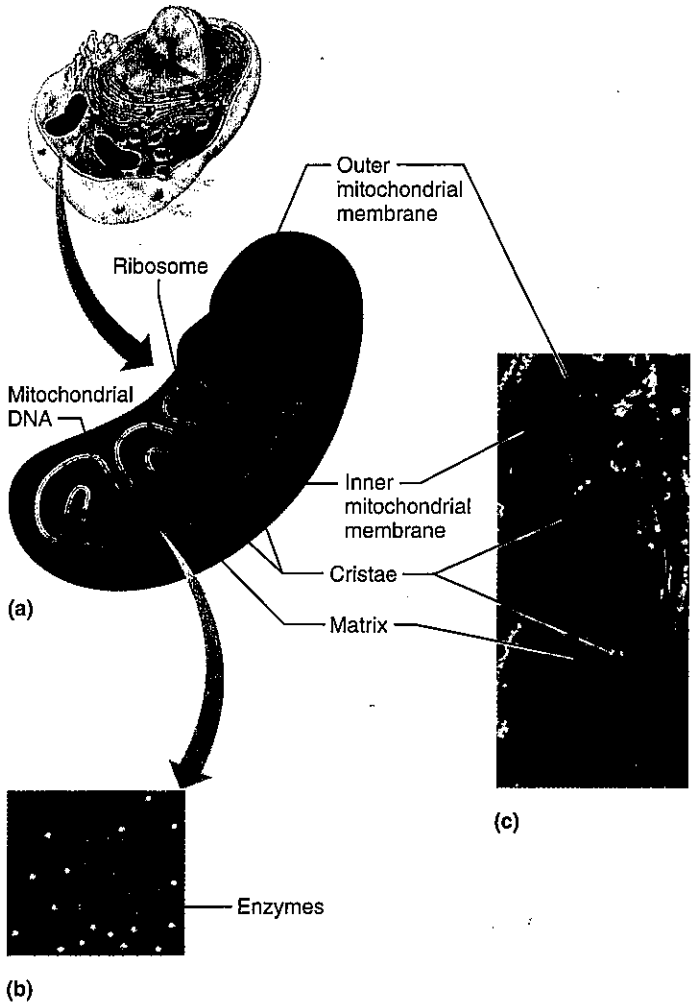


Figure 3.17 Mitochondrion. (a) Diagram of a longitudinally sectioned mitochondrion. **(b)** Close-up of a crista showing enzymes (stalked particles). **(c)** Electron micrograph of a mitochondrion (50,000×).

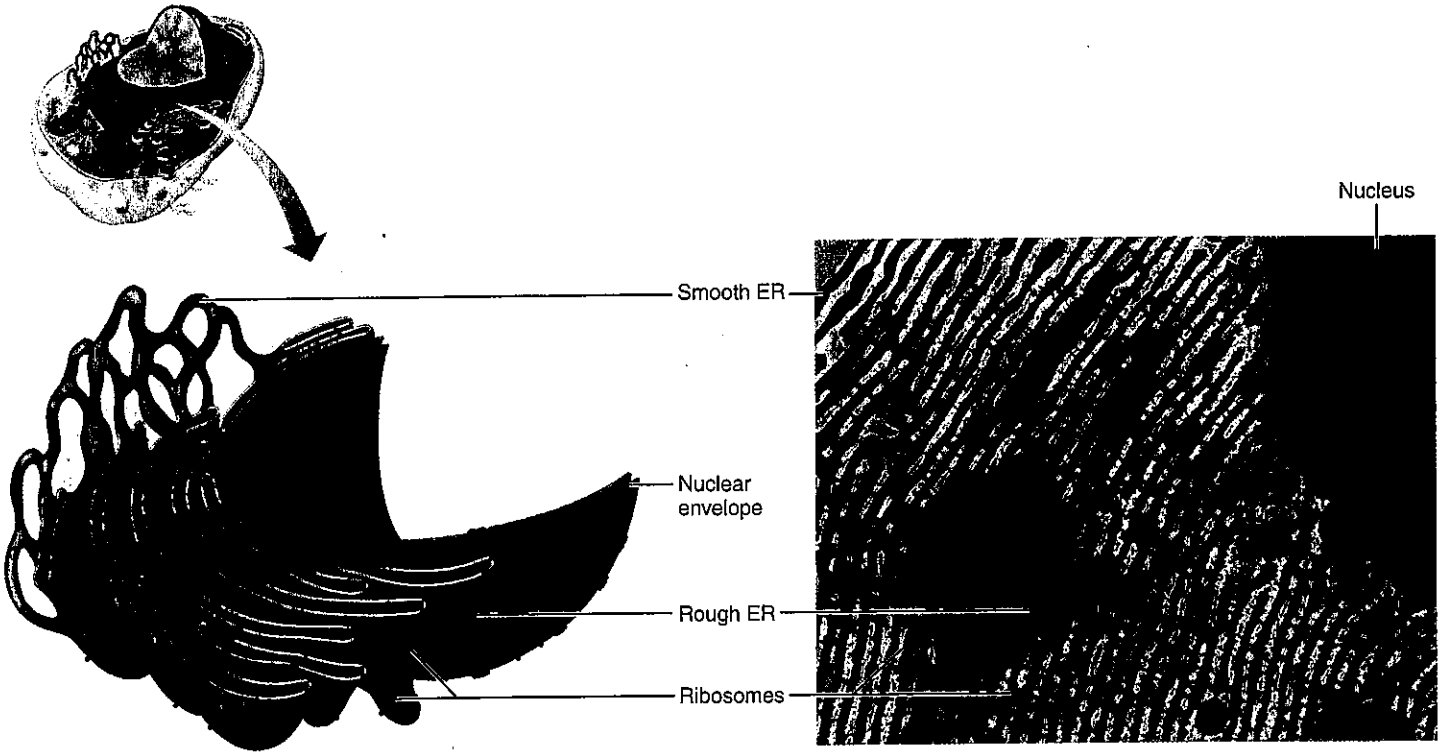
It is widely believed that mitochondria arose from bacteria that invaded the ancient ancestors of plant and animal cells, and that this unique merger gave rise to all complex cells.

Ribosomes

Ribosomes (ri′bo-sōmz) are small, dark-staining granules composed of proteins and a variety of RNAs called *ribosomal RNAs*. Each ribosome has two globular subunits that fit together like the body and cap of an acorn. Ribosomes are sites of protein synthesis, a function we discuss in detail later in this chapter.

Some ribosomes float freely in the cytoplasm. Others are attached to membranes, forming a complex called the *rough endoplasmic reticulum* (see p. 84). These two ribosomal populations appear to divide the chore of protein synthesis.

- *Free ribosomes* float freely in the cytoplasm. They make soluble proteins that function in the cytosol, as well as those imported into mitochondria and some other organelles.



(a) Diagrammatic view of smooth and rough ER

(b) Electron micrograph of smooth and rough ER (25,000×)

Figure 3.18 The endoplasmic reticulum.

- *Membrane-bound ribosomes* are attached to membranes, forming a complex called the *rough endoplasmic reticulum* **(Figure 3.18)**. They synthesize proteins destined either for incorporation into cell membranes or lysosomes, or for export from the cell.

Ribosome subunits can switch back and forth between these two functions, attaching to and detaching from the membranes of the endoplasmic reticulum, according to the type of protein they are making at a given time.

Endoplasmic Reticulum (ER)

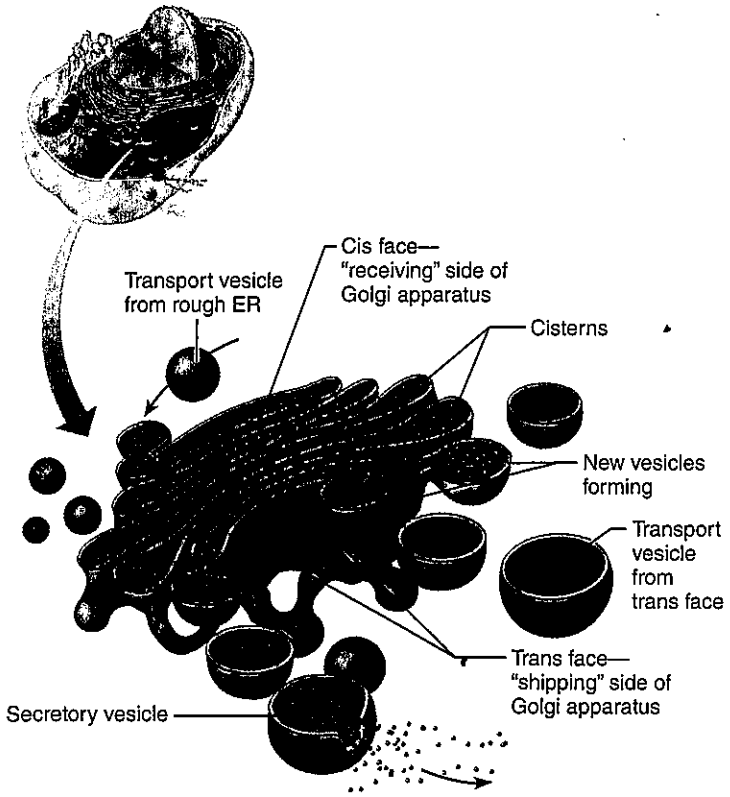
The **endoplasmic reticulum** (ER) (en″do-plaz′mik rĕ-tik′u-lum; "network within the cytoplasm") is an extensive system of interconnected tubes and parallel membranes enclosing fluid-filled cavities, or **cisterns** (sis-ternz) as shown in Figure 3.18. Coiling and twisting through the cytosol, the ER is continuous with the outer nuclear membrane and accounts for about half of the cell's membranes. There are two distinct varieties: rough ER and smooth ER.

Rough Endoplasmic Reticulum The external surface of the **rough ER** is studded with ribosomes, hence the name "rough" (see Figures 3.2 and 3.18a, b). Proteins assembled on these ribosomes thread their way into the fluid-filled interior of the ER cisterns (as described on pp. 105 and 108). When complete, the newly made proteins are enclosed in vesicles for their journey to the Golgi apparatus where they undergo further processing.

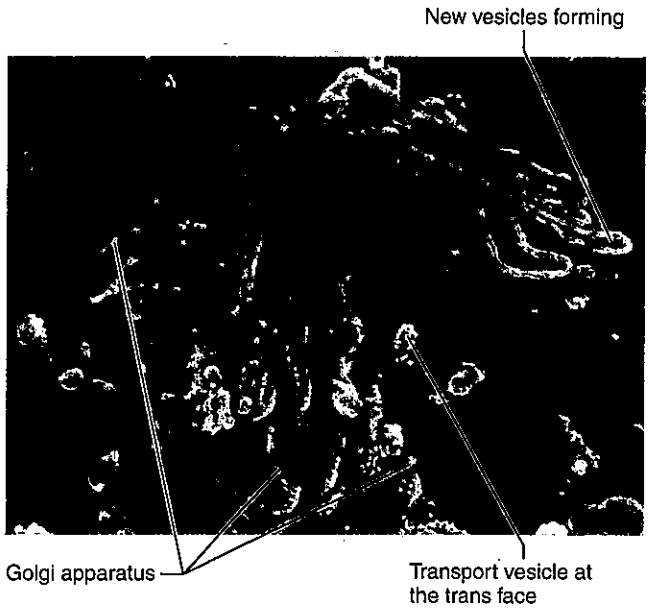
The rough ER has several functions. Its ribosomes manufacture all proteins secreted from cells. For this reason, the rough ER is particularly abundant and well developed in most secretory cells, antibody-producing plasma cells, and liver cells, which produce most blood proteins. It is also the cell's "membrane factory" where integral proteins and phospholipids that form part of all cellular membranes are manufactured. The enzymes needed to catalyze lipid synthesis have their active sites on the external (cytosolic) face of the ER membrane, where the needed substrates are readily available.

Smooth Endoplasmic Reticulum The **smooth ER** (see Figures 3.2 and 3.18) is continuous with the rough ER and consists of tubules arranged in a looping network. Its enzymes (all integral proteins forming part of its membranes) play no role in protein synthesis. Instead, the enzymes catalyze reactions involved with the following tasks:

- Metabolize lipids, synthesize cholesterol, and synthesize the lipid components of lipoproteins (in liver cells)
- Synthesize steroid-based hormones such as sex hormones (testosterone-synthesizing cells of the testes are full of smooth ER)
- Absorb, synthesize, and transport fats (in intestinal cells)
- Detoxify drugs, certain pesticides, and cancer-causing chemicals (in liver and kidneys)
- Break down stored glycogen to form free glucose (in liver cells especially)



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



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

Figure 3.19 Golgi apparatus. Note: In (a), the vesicles shown in the process of pinching off from the membranous Golgi apparatus would have a protein coating on their external surfaces. The diagram omits these proteins for simplicity.

Additionally, skeletal and cardiac muscle cells have an elaborate smooth ER (called the sarcoplasmic reticulum) that plays an important role in storing and releasing calcium ions during muscle contraction. Except for the examples given above, most body cells contain relatively little, if any, smooth ER.

Golgi Apparatus

The **Golgi apparatus** (gol'je) consists of stacked and flattened membranous sacs, shaped like hollow dinner plates, associated with swarms of tiny membranous vesicles **(Figure 3.19)**. The Golgi apparatus is the principal "traffic director" for cellular proteins. Its major function is to modify, concentrate, and package the proteins and lipids made at the rough ER and destined for export from the cell.

The Golgi's odd shape is a side effect of its job. A protein complex pulls membranous sacs containing newly synthesized proteins off the Golgi and in the process, the membranes are flattened like rubber bands. Transport vesicles that bud off from the rough ER move to and fuse with the membranes at the convex *cis face*, the "receiving" side, of the Golgi apparatus. Inside the apparatus, the proteins are modified: Some sugar groups are trimmed while others are added, and in some cases, phosphate groups are added.

The various proteins are "tagged" for delivery to a specific address, sorted, and packaged in at least three types of vesicles that bud from the concave *trans face* (the "shipping" side) of the Golgi stack:

- Vesicles containing proteins destined for export pinch off from the trans face as **secretory vesicles, or granules**, which migrate to the plasma membrane and discharge their contents from the cell by exocytosis (**Figure 3.20**, pathway A). Specialized secretory cells, such as the enzyme-producing cells of the pancreas, have a prominent Golgi apparatus.
- The Golgi apparatus pinches off other vesicles containing lipids and transmembrane proteins destined for the plasma membrane (Figure 3.20, pathway B) or for other membranous organelles.
- The Golgi apparatus also packages digestive enzymes into membranous lysosomes that remain in the cell (Figure 3.20, pathway C), as discussed shortly.

Peroxisomes

Peroxisomes (pĕ-roks'ĭ-sōmz; "peroxide bodies") are spherical membranous sacs containing a variety of powerful enzymes, the most important of which are oxidases and catalases.

Oxidases use molecular oxygen (O_2) to detoxify harmful substances, including alcohol and formaldehyde. Their most important function is to neutralize **free radicals**, highly reactive

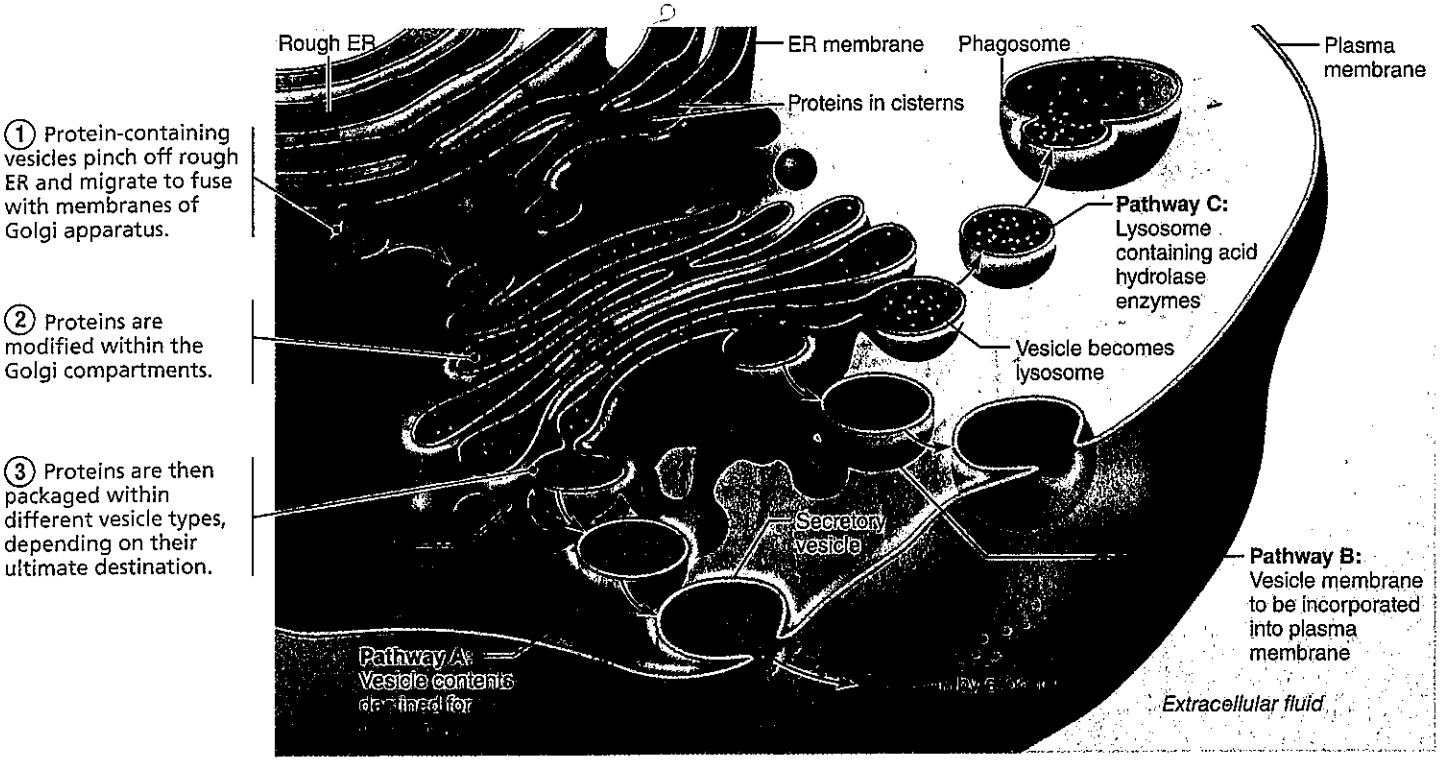


Figure 3.20 The sequence of events from protein synthesis on the rough ER to the final distribution of those proteins. The protein coats on the transport vesicles are not illustrated.

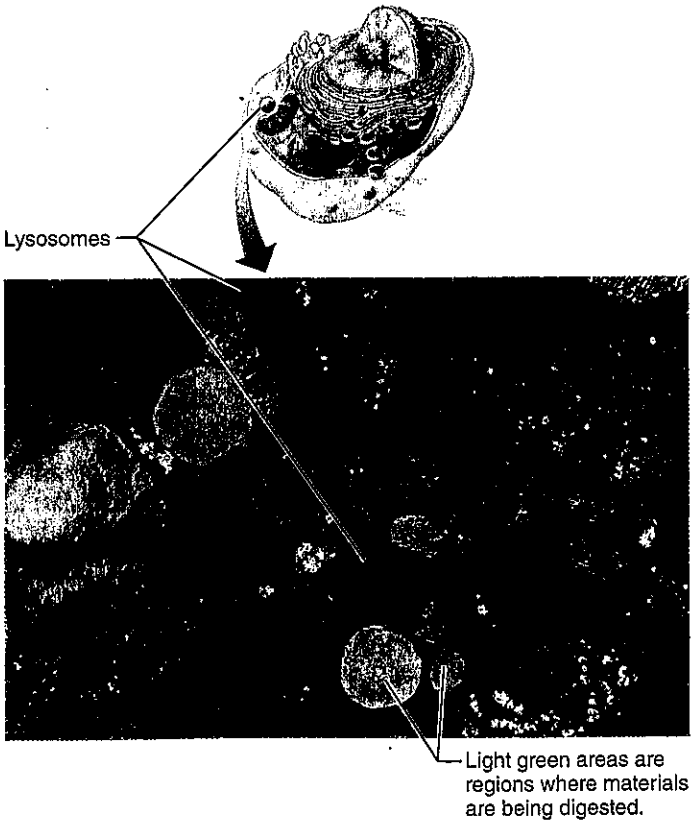


Figure 3.21 Electron micrograph of lysosomes (20,000×).

chemicals with unpaired electrons that can scramble the structure of biological molecules. Oxidases convert free radicals to hydrogen peroxide, which is also reactive and dangerous but which the catalases quickly convert to water. Free radicals and hydrogen peroxide are normal by-products of cellular metabolism, but they have devastating effects on cells if allowed to accumulate.

Peroxisomes are especially numerous in liver and kidney cells, which are very active in detoxification. They also play a role in energy metabolism by breaking down and synthesizing fatty acids. Peroxisomes look like small lysosomes (see Figure 3.2), and for many years it was thought that they were self-replicating organelles formed when existing peroxisomes simply pinch in half. Recent evidence, however, suggests that most new peroxisomes form by budding off of the endoplasmic reticulum via a special ER machinery that differs from that used for vesicles destined for modification in the Golgi apparatus.

Lysosomes

Born as endosomes which contain inactive enzymes, **lysosomes** ("disintegrator bodies") are spherical membranous organelles containing activated digestive enzymes **(Figure 3.21)**. As you might guess, lysosomes are large and abundant in phagocytes, the cells that dispose of invading bacteria and cell debris. Lysosomal enzymes can digest almost all kinds of biological molecules. They work best in acidic conditions and so are called *acid hydrolases.*

The lysosomal membrane is adapted to serve lysosomal functions in two important ways. First, it contains H^+ (proton)

"pumps," which are ATPases that gather hydrogen ions from the surrounding cytosol to maintain the organelle's acidic pH. Second, it retains the dangerous acid hydrolases while permitting the final products of digestion to escape so that they can be used by the cell or excreted. In this way, lysosomes provide sites where digestion can proceed *safely* within a cell.

Lysosomes function as a cell's "demolition crew" by

- Digesting particles taken in by endocytosis, particularly ingested bacteria, viruses, and toxins
- Degrading worn-out or nonfunctional organelles
- Performing metabolic functions, such as glycogen breakdown and release
- Breaking down nonuseful tissues, such as the webs between the fingers and toes of a developing fetus and the uterine lining during menstruation
- Breaking down bone to release calcium ions into the blood

The lysosomal membrane is ordinarily quite stable, but it becomes fragile when the cell is injured or deprived of oxygen and when excessive amounts of vitamin A are present. When lysosomes rupture, the cell digests itself, a process called **autolysis** (aw"tol'ĭ-sis). Autolysis is the basis for desirable destruction of cells, as in the fourth list item above.

Homeostatic Imbalance 3.4

Lysosomes degrade glycogen and certain lipids in the brain at a relatively constant rate. In *Tay-Sachs disease*, an inherited condition seen mostly in Jews from Central Europe, the lysosomes lack an enzyme needed to break down a glycolipid abundant in nerve cell membranes. As a result, the nerve cell lysosomes swell with undigested lipids, which interfere with nervous system functioning. Affected infants typically have doll-like features and pink translucent skin. At 3 to 6 months of age, the first signs of disease appear (listlessness, motor weakness). These symptoms progress to mental retardation, seizures, blindness, and ultimately death within 18 months. ✚

The Endomembrane System

The **endomembrane system** is a system of organelles (most described above) that work together mainly to (1) produce, degrade, store, and export biological molecules, and (2) degrade potentially harmful substances. It includes the ER, Golgi apparatus, secretory vesicles, and lysosomes, as well as the nuclear membrane—that is, all of the membranous organelles or elements that are either structurally continuous or arise via forming or fusing transport vesicles **(Figure 3.22)**. There are continuities between the nuclear envelope (itself an extension of the rough ER) and the rough and smooth ER (Figure 3.18). The plasma membrane, though not actually an *endo*membrane, is also functionally part of this system.

Besides these direct structural relationships, a wide variety of indirect interactions (indicated by arrows in Figure 3.22) occur among the members of the system. Some of the vesicles "born" in the ER migrate to and fuse with the Golgi apparatus or the plasma membrane, and vesicles arising from the Golgi apparatus can become part of the plasma membrane, secretory vesicles, or lysosomes.

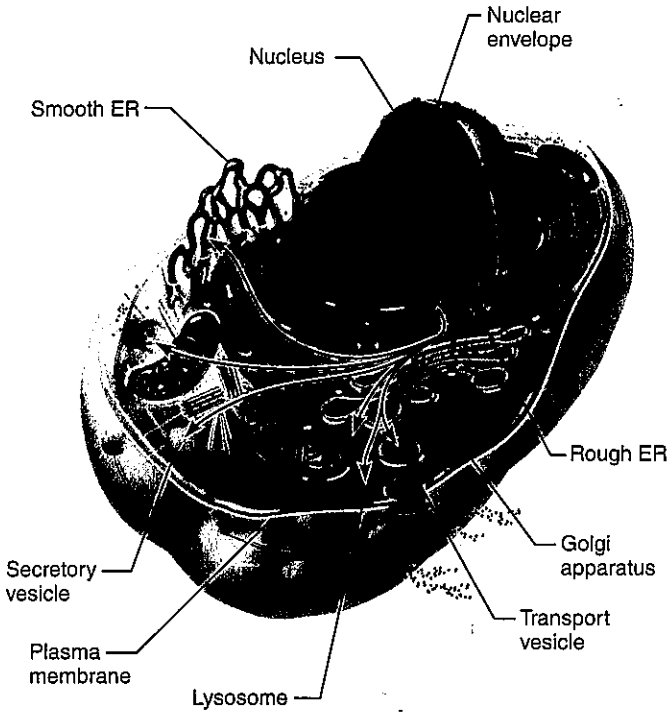


Figure 3.22 The endomembrane system.

Check Your Understanding

17. Which organelle is the major site of ATP synthesis?
18. What are three organelles involved in protein synthesis and how do these organelles interact in that process?
19. Compare the functions of lysosomes and peroxisomes.

For answers, see Appendix H.

Cytoskeleton

✓ Name and describe the structure and function of cytoskeletal elements.

The **cytoskeleton**, literally, "cell skeleton," is an elaborate network of rods running through the cytosol and hundreds of accessory proteins that link these rods to other cell structures. It acts as a cell's "bones," "muscles," and "ligaments" by supporting cellular structures and providing the machinery to generate various cell movements. The three types of rods in the cytoskeleton are *microfilaments*, *intermediate filaments*, and *microtubules*. None of these is membrane covered.

Microfilaments The thinnest elements of the cytoskeleton, **microfilaments** (mi"kro-fil'ah-ments), are semiflexible strands of the protein *actin* ("ray") **(Figure 3.23a)**. Each cell has its own unique arrangement of microfilaments, so no two cells are alike. However, nearly all cells have a fairly dense cross-linked network of microfilaments, called the *terminal web*, attached to

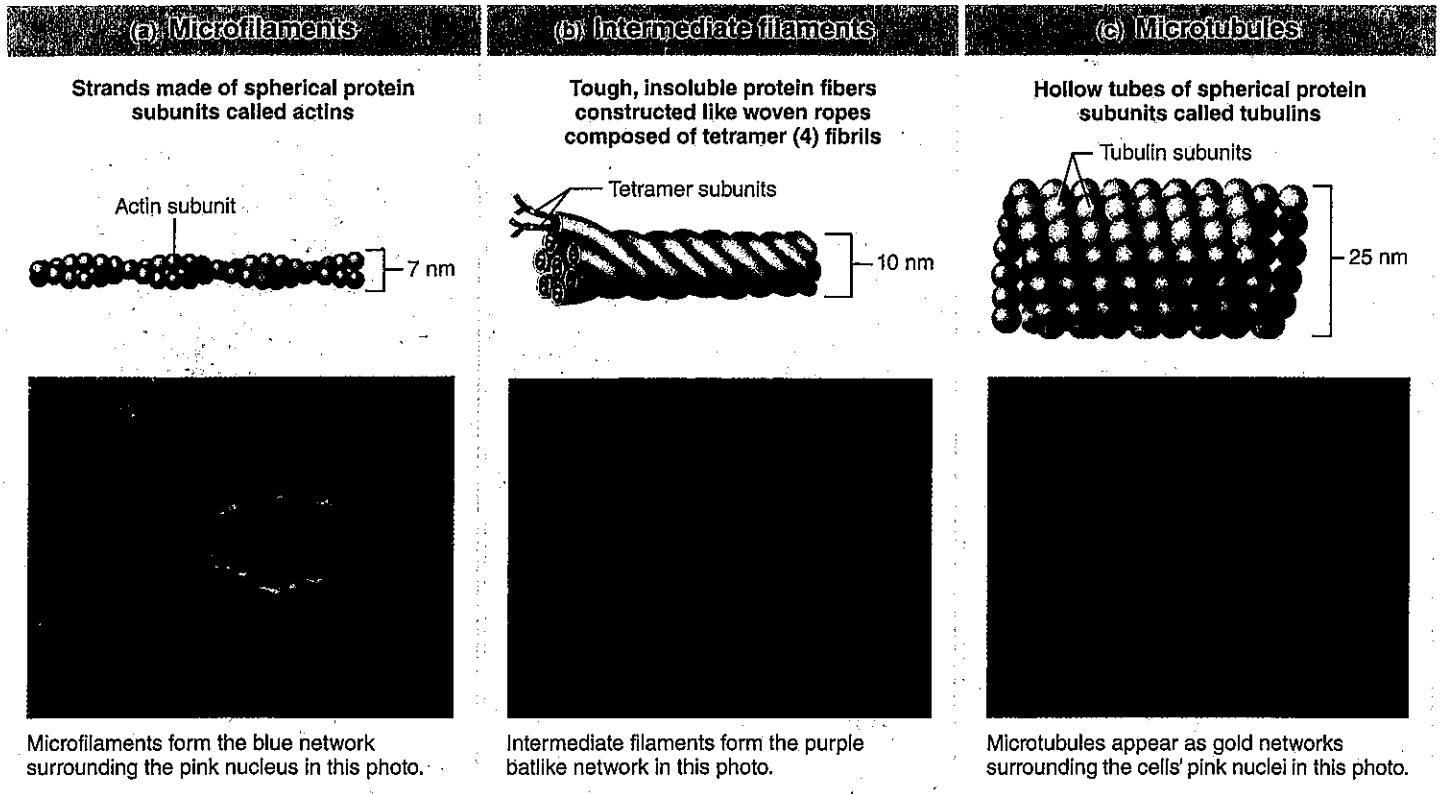


Figure 3.23 Cytoskeletal elements support the cell and help to generate movement.
Diagrams (above) and photos (below). The photos are of fibroblasts treated to fluorescently tag the structure of interest.

the cytoplasmic side of their plasma membrane (see Figure 3.28 on p. 91). The web strengthens the cell surface, resists compression, and transmits force during cellular movements and shape changes.

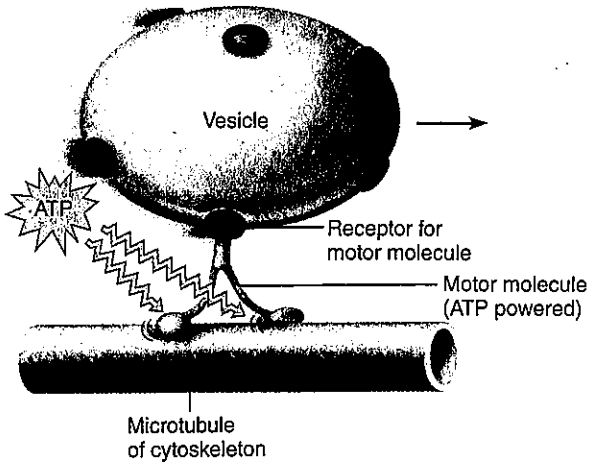
Most microfilaments are involved in cell motility (movement) or changes in cell shape. You could say that cells move "when they get their act(in) together." For example, actin filaments interact with another protein, *unconventional myosin* (mi'o-sin), to generate contractile forces in a cell **(Figure 3.24b)**. This interaction also forms the cleavage furrow that pinches one cell into two during cell division. Microfilaments attached to cell adhesion molecules (see Figure 3.4e) are responsible for the crawling movements of amoeboid motion, and for the membrane changes that accompany endocytosis and exocytosis. Except in muscle cells, where they are highly developed, stable, and long-lived, actin filaments are constantly breaking down and re-forming from smaller subunits whenever and wherever their services are needed.

Intermediate Filaments **Intermediate filaments** are tough, insoluble protein fibers that resemble woven ropes. Made of twisted units of *tetramer* (4) *fibrils*, they have a diameter between those of microfilaments and microtubules (Figure 3.23b). Intermediate filaments are the most stable and permanent of the cytoskeletal elements and have high tensile strength. They attach to desmosomes, and their main job is to act as internal guy-wires to resist pulling forces exerted on the cell. Because the protein composition of intermediate filaments varies in different cell types, there are numerous names for these cytoskeletal elements—for example, they are called neurofilaments in nerve cells and keratin filaments in epithelial cells.

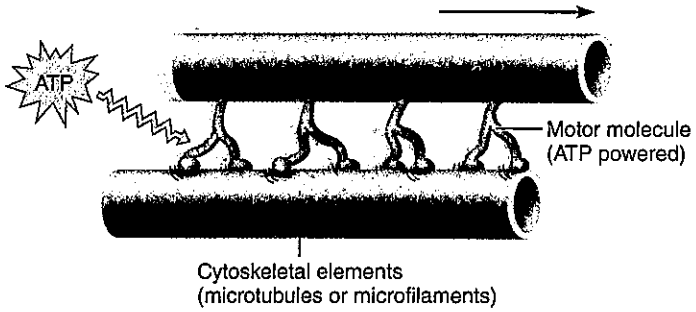
Microtubules The elements with the largest diameter, **microtubules** (mi"kro-tu'būlz), are hollow tubes made of spherical protein subunits called *tubulins* (Figure 3.23c). Most microtubules radiate from a small region of cytoplasm near the nucleus called the *centrosome* or *cell center* (see Figures 3.2, 3.25). Microtubules are remarkably dynamic organelles, constantly growing out from the centrosome, disassembling, and then reassembling at the same or different sites. The stiff but bendable microtubules determine the overall shape of the cell, as well as the distribution of cellular organelles.

Mitochondria, lysosomes, and secretory vesicles attach to the microtubules like ornaments hanging from tree branches. Tiny protein machines called **motor proteins** (*kinesins*, *dyneins*, and others) continually move and reposition the organelles along the microtubules.

Motor proteins work by changing their shapes. Powered by ATP, some motor proteins appear to act like train engines moving substances along on the microtubular "railroad tracks."



(a) Motor molecules can attach to receptors on vesicles or organelles, and carry the organelles along the microtubule "tracks" of the cytoskeleton.



(b) In some types of cell motility, motor molecules attached to one element of the cytoskeleton can cause it to slide over another element, which the motor molecules grip, release, and grip at a new site. Muscle contraction and cilia movement work this way.

Figure 3.24 Microtubules and microfilaments function in cell motility by interacting with motor molecules powered by ATP.

Others move "hand over hand" somewhat like an orangutan—gripping, releasing, and then gripping again at a new site further along the microtubule (Figure 3.24).

Centrosome and Centrioles

✓ Describe the roles of centrioles in cell division and in formation of cilia and flagella.

As mentioned, microtubules are anchored at one end in an inconspicuous region near the nucleus called the **centrosome** or *cell center*. The centrosome acts as a *microtubule organizing center*. It has few distinguishing marks other than a granular-looking *matrix* that contains paired **centrioles**, small, barrel-shaped organelles oriented at right angles to each other **(Figure 3.25)**. The centrosome matrix is best known for generating microtubules and organizing the mitotic spindle in cell division (see Figure 3.33). Each centriole consists of

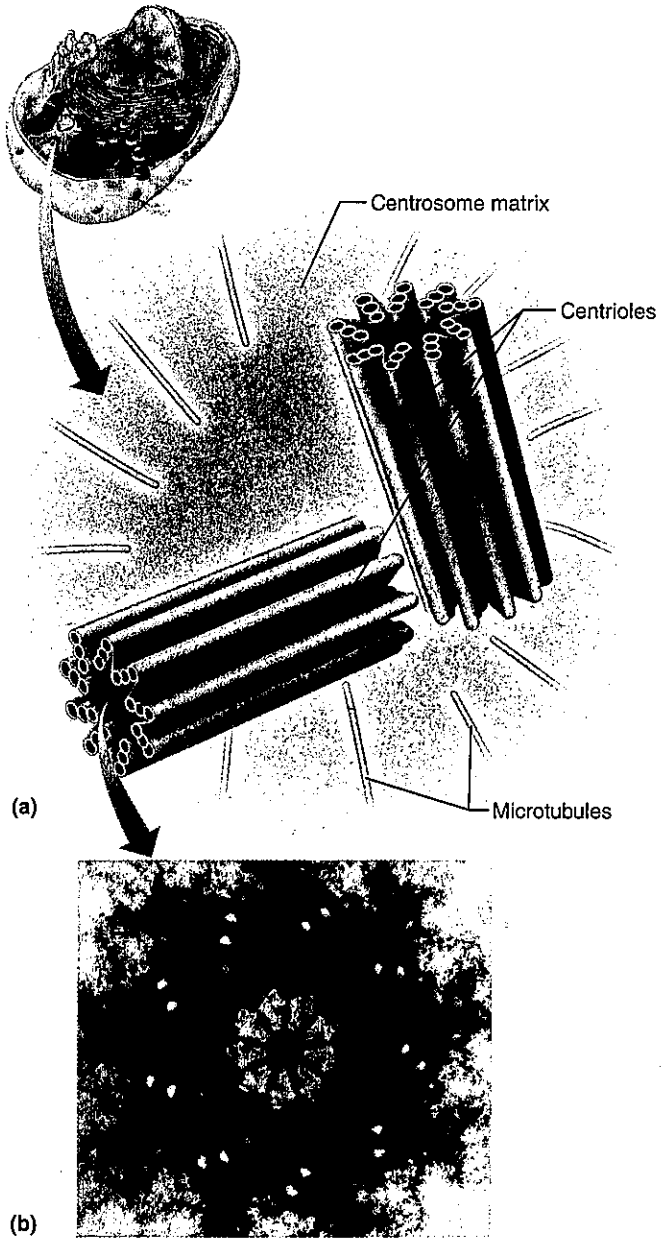


Figure 3.25 Centrioles. (a) Three-dimensional view of a centriole pair oriented at right angles, as they are usually seen in the cell. The centrioles are located in an inconspicuous region to one side of the nucleus called the centrosome, or cell center. **(b)** An electron micrograph showing a cross section of a centriole (190,000×). Notice that it is composed of nine microtubule triplets.

a pinwheel array of nine *triplets* of microtubules, each connected to the next by nontubulin proteins and arranged to form a hollow tube. Centrioles also form the bases of cilia and flagella, our next topics.

Cellular Extensions

✓ Describe how the two main types of cell extensions, cilia and microvilli, differ in structure and function.

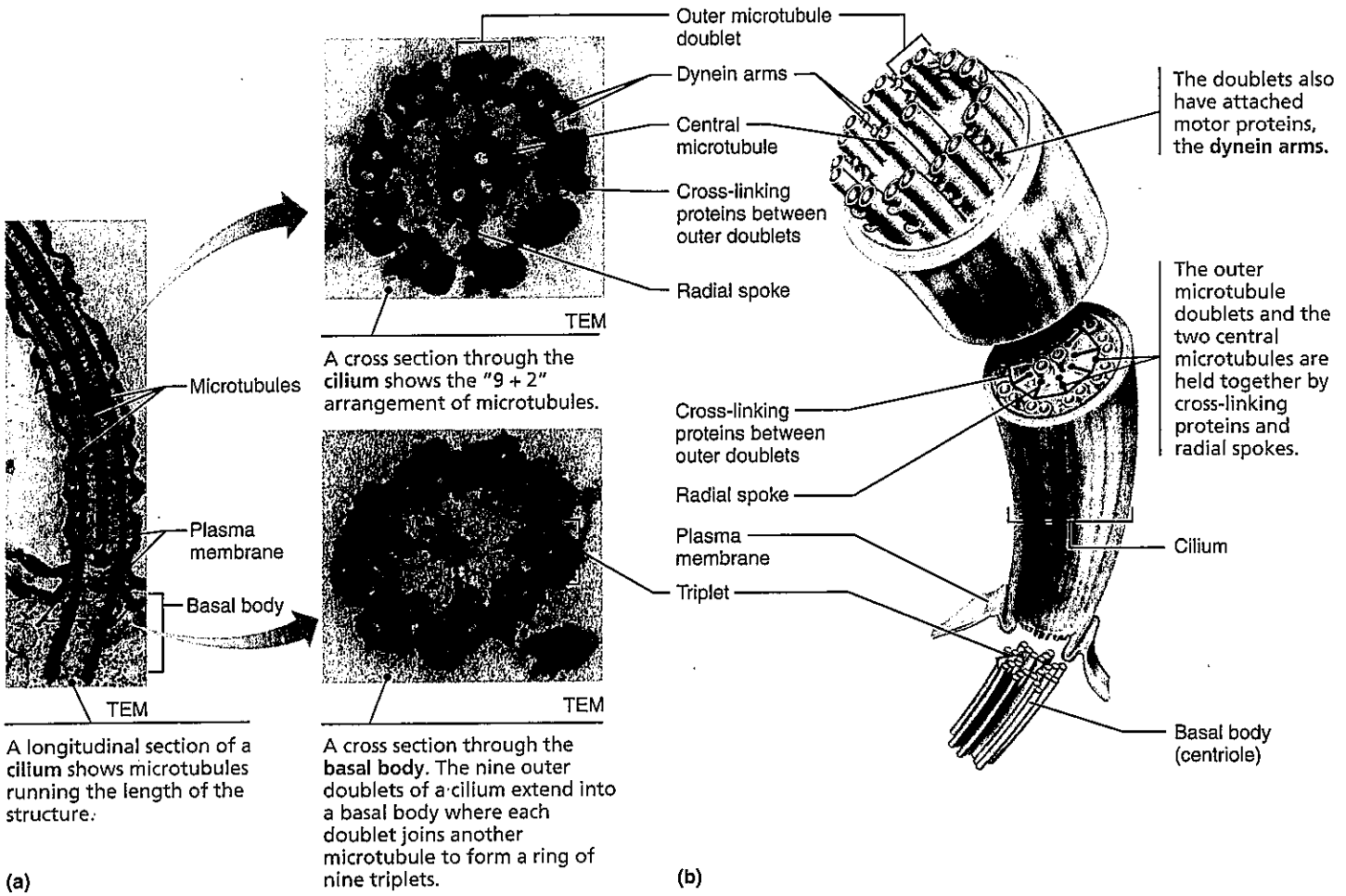


Figure 3.26 Structure of a cilium. (TEM = transmission electron micrograph.)

Cilia and Flagella

Cilia (sil'e-ah; "eyelashes") are whiplike, motile cellular extensions **(Figure 3.26)** that occur, typically in large numbers, on the exposed surfaces of certain cells. Ciliary action moves substances in one direction across cell surfaces. For example, ciliated cells that line the respiratory tract propel mucus laden with dust particles and bacteria upward away from the lungs.

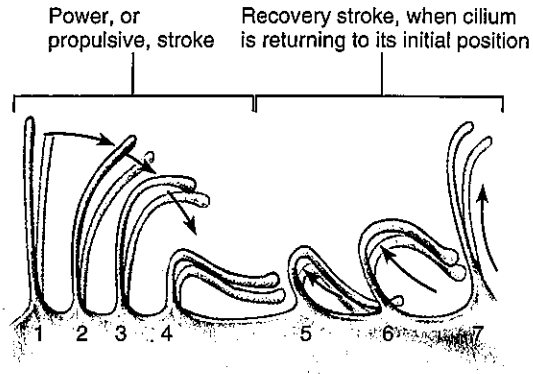
When a cell is about to form cilia, the centrioles multiply and line up beneath the plasma membrane at the cell's free (exposed) surface. Microtubules then "sprout" from each centriole, forming the ciliary projections by exerting pressure on the plasma membrane.

Flagella (flah-jel'ah) are also projections formed by centrioles, but are substantially longer than cilia. The only flagellated cell in the human body is a sperm, which has one propulsive flagellum, commonly called a tail. Notice that cilia *propel other substances* across a cell's surface, whereas a flagellum *propels the cell itself.*

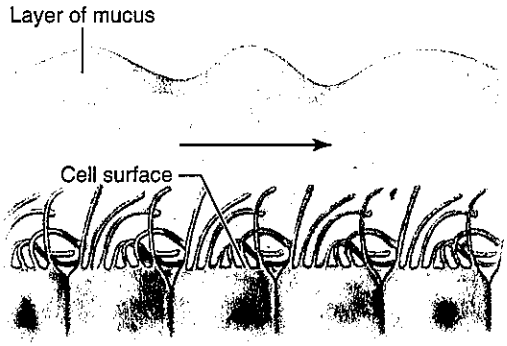
Centrioles forming the bases of cilia and flagella are commonly referred to as **basal bodies** (ba'sal) (Figure 3.26a). The "9 + 2" pattern of microtubules in the cilium or flagellum itself (nine *doublets*, or pairs, of microtubules encircling one central pair) differs slightly from that of a centriole (nine microtubule *triplets*). Additionally, the cilium has flexible "wagon wheels" of cross-linking proteins (purple in Figure 3.26b), and motor proteins (green dynein arms in Figure 3.26b) that promote movement of the cilium or flagellum.

Just how ciliary activity is coordinated is not fully understood, but microtubules are definitely involved. Extending from the microtubule doublets are arms composed of the motor protein dynein (Figure 3.26). The dynein side arms of one doublet grip the adjacent doublet, and powered by ATP, push it up, release, and then grip again. Because the doublets are physically restricted by other proteins, they cannot slide far and instead are forced to bend. The collective bending action of all the doublets causes the cilium to bend.

As a cilium moves, it alternates rhythmically between a propulsive *power stroke*, when it is nearly straight and moves in an arc, and a *recovery stroke*, when it bends and returns to its initial position **(Figure 3.27a)**. With these two strokes, the cilium produces a pushing motion in a single direction that repeats some 10 to 20 times per second. The bending of one cilium is quickly followed by the bending of the next and then the next, creating a current at the cell surface that brings to mind the traveling waves that pass across a field of grass on a windy day (Figure 3.27b).



(a) Phases of ciliary motion.



(b) Traveling wave created by the activity of many cilia acting together propels mucus across cell surfaces.

Figure 3.27 Ciliary function.

The motile cilia just discussed are familiar to most biology students, but many have not heard of *primary cilia*, their nonmotile cousins. Present as a single cilium on the surface of most body cells, primary cilia function as antennae that probe the external environment for molecules their receptors can recognize. Because of this ability, primary cilia can coordinate several intracellular pathways that regulate embryonic development and maintain healthy tissues later in life.

Microvilli

Microvilli (mi″kro-vil′i; "little shaggy hairs") are minute, fingerlike extensions of the plasma membrane that project from an exposed cell surface (Figure 3.5 top and **Figure 3.28**). They increase the plasma membrane surface area tremendously and are most often found on the surface of absorptive cells such as intestinal and kidney tubule cells. Microvilli have a core of bundled actin filaments that extend into the so-called *terminal web* of the cytoskeleton of the cell. Actin is sometimes a contractile protein, but in microvilli it appears to function as a mechanical "stiffener."

☑ Check Your Understanding

20. How are microtubules and microfilaments related functionally?

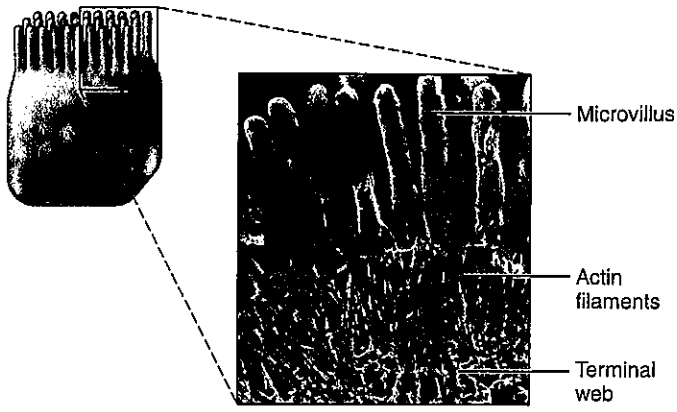


Figure 3.28 Microvilli.

21. Of microfilaments, microtubules, or intermediate filaments, which is most important in maintaining cell shape?
22. The major function of cilia is to move substances across the free cell surface. What is the major role of microvilli?

For answers, see Appendix H.

The Nucleus

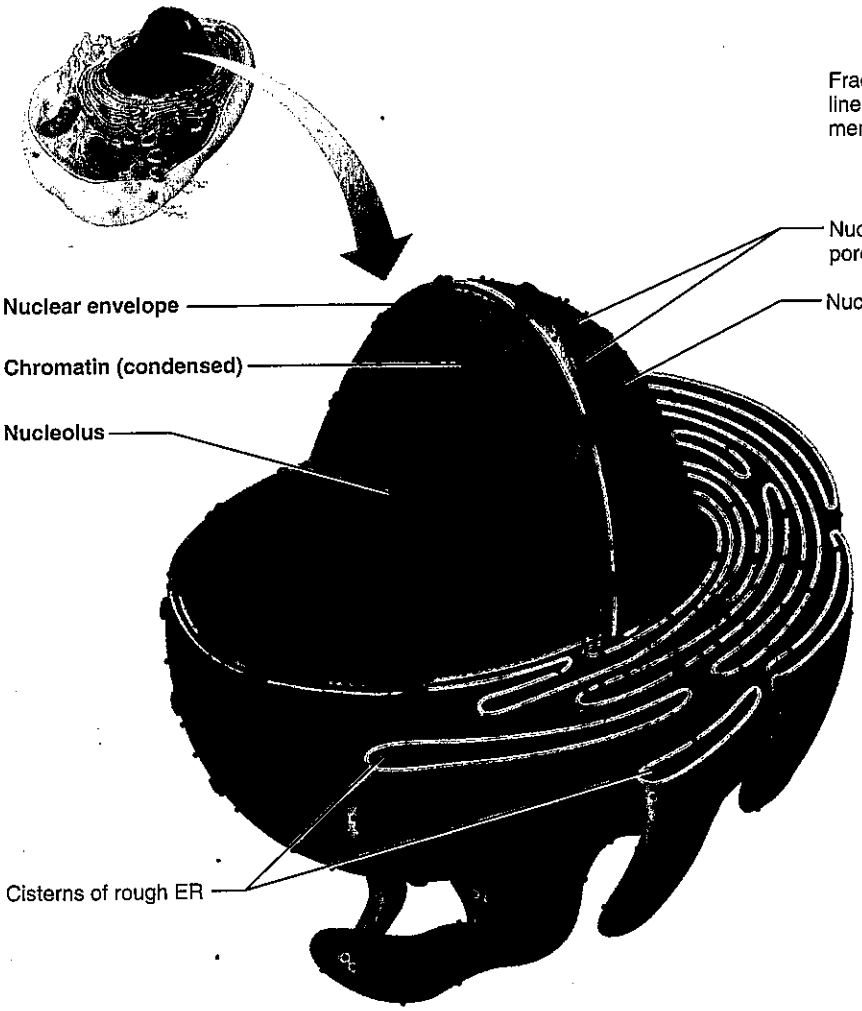
✓ Outline the structure and function of the nuclear envelope, nucleolus, and chromatin.

Anything that works, works best when it is controlled. For cells, the control center is the gene-containing **nucleus** (*nucle* = pit, kernel). The nucleus can be compared to a computer, design department, construction boss, and board of directors—all rolled into one. As the genetic library, it contains the instructions needed to build nearly all the body's proteins. Additionally, it dictates the kinds and amounts of proteins to be synthesized at any one time in response to signals acting on the cell.

Most cells have only one nucleus, but some, including skeletal muscle cells, bone destruction cells, and some liver cells, are **multinucleate** (mul″tĭ-nu′kle-āt), that is, they have many nuclei. The presence of more than one nucleus usually signifies that a larger-than-usual cytoplasmic mass must be regulated.

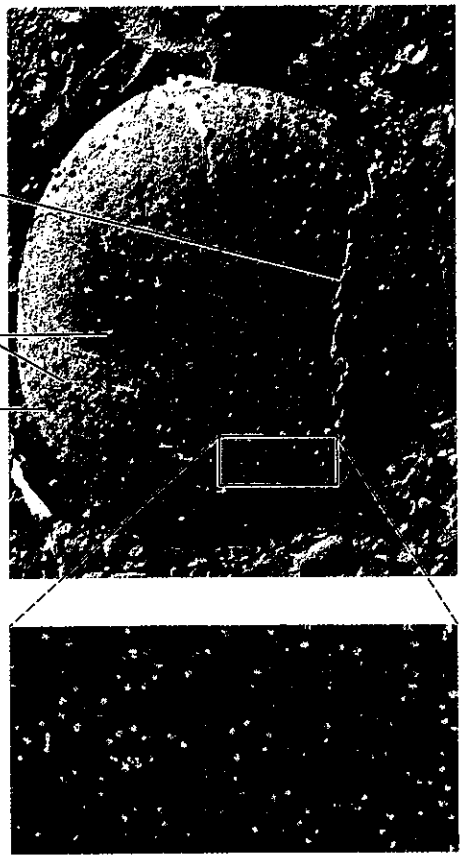
Except for mature red blood cells, whose nuclei are ejected before the cells enter the bloodstream, all of our body cells are nucleated. **Anucleate** (a-nu′kle-āt; *a* = without) cells cannot reproduce and therefore live in the bloodstream for only three to four months before they deteriorate. Without a nucleus, a cell cannot produce mRNA to make proteins, and when its enzymes and cell structures start to break down (as all eventually do), they cannot be replaced.

The nucleus, averaging 5 μm in diameter, is larger than any of the cytoplasmic organelles. Although most often spherical or oval, its shape usually conforms to the shape of the cell. The nucleus has three recognizable regions or structures: the *nuclear envelope* (*membrane*), *nucleoli*, and *chromatin* **(Figure 3.29a)**.

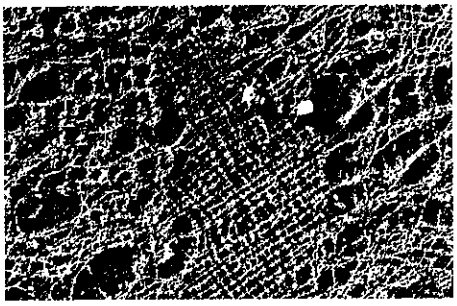


(a)

Surface of nuclear envelope.



Nuclear pore complexes. Each pore is ringed by protein particles.



Nuclear lamina. The netlike lamina composed of intermediate filaments formed by lamins lines the inner surface of the nuclear envelope.

(b)

Figure 3.29 The nucleus. (a) Three-dimensional diagram of the nucleus, showing the continuity of its double membrane with the ER. **(b)** Freeze-fracture transmission electron micrographs (TEMs).

The Nuclear Envelope

The nucleus is bounded by the **nuclear envelope**, a *double* membrane barrier separated by a fluid-filled space (similar to the mitochondrial membrane). The outer nuclear membrane is continuous with the rough ER of the cytoplasm and is studded with ribosomes on its external face. The inner nuclear membrane is lined by the *nuclear lamina*, a network of *lamins* (rod-shaped proteins that assemble to form intermediate filaments) that maintains the shape of the nucleus and acts as a scaffold to organize DNA in the nucleus (Figure 3.29b, bottom).

At various points, the nuclear envelope is punctuated by **nuclear pores**. An intricate complex of proteins, called a *nuclear pore complex*, lines each pore, forming an aqueous transport channel and regulating entry and exit of molecules (e.g., mRNAs) and large particles into and out of the nucleus (Figure 3.29b, middle).

Like other cell membranes, the nuclear envelope is selectively permeable, but here substances pass much more freely than elsewhere. Small molecules pass through the relatively large nuclear pore complexes unhindered. Protein molecules imported from the cytoplasm and RNA molecules exported from the nucleus are transported through the central channel of the pores in an energy-dependent process by soluble transport proteins (importins and others). Such large molecules must display specific signals to enter or exit the nucleus.

The nuclear envelope encloses a jellylike fluid called *nucleoplasm* (nu'kle-o-plazm) in which other nuclear elements are suspended. Like the cytosol, the nucleoplasm contains dissolved salts, nutrients, and other essential solutes.

Nucleoli

Nucleoli (nu-kle'o-li; "little nuclei") are the dark-staining spherical bodies found within the nucleus where ribosomal subunits are assembled. They are not membrane bounded. Typically, there are one or two nucleoli per nucleus, but there may be more. Nucleoli are usually large in growing cells that are making large amounts of tissue proteins.

Nucleoli are associated with *nucleolar organizer regions*, which contain the DNA that issues genetic instructions for synthesizing ribosomal RNA (rRNA). As molecules of rRNA are synthesized, they are combined with proteins to form the two kinds of ribosomal subunits. (The proteins are manufactured on ribosomes in the cytoplasm and "imported" into the nucleus.) Most of these subunits leave the nucleus through the nuclear pores and enter the cytoplasm, where they join to form functional ribosomes.

Chromatin

Seen through a light microscope, **chromatin** (kro'mah-tin) appears as a fine, unevenly stained network, but special techniques reveal it as a system of bumpy threads weaving through the nucleoplasm. Chromatin is composed of approximately

- 30% **DNA**, our genetic material
- 60% globular **histone proteins** (his'tōn), which package and regulate the DNA
- 10% RNA chains, newly formed or forming

The fundamental units of chromatin are **nucleosomes** (nu'kle-o-sōmz; "nuclear bodies"), which consist of flattened disc-shaped cores or clusters of eight histone proteins connected like beads on a string by a DNA molecule. The DNA winds (like a ribbon of Velcro) twice around each nucleosome and continues on to the next cluster via *linker* DNA segments (**Figure 3.30** ① and ②).

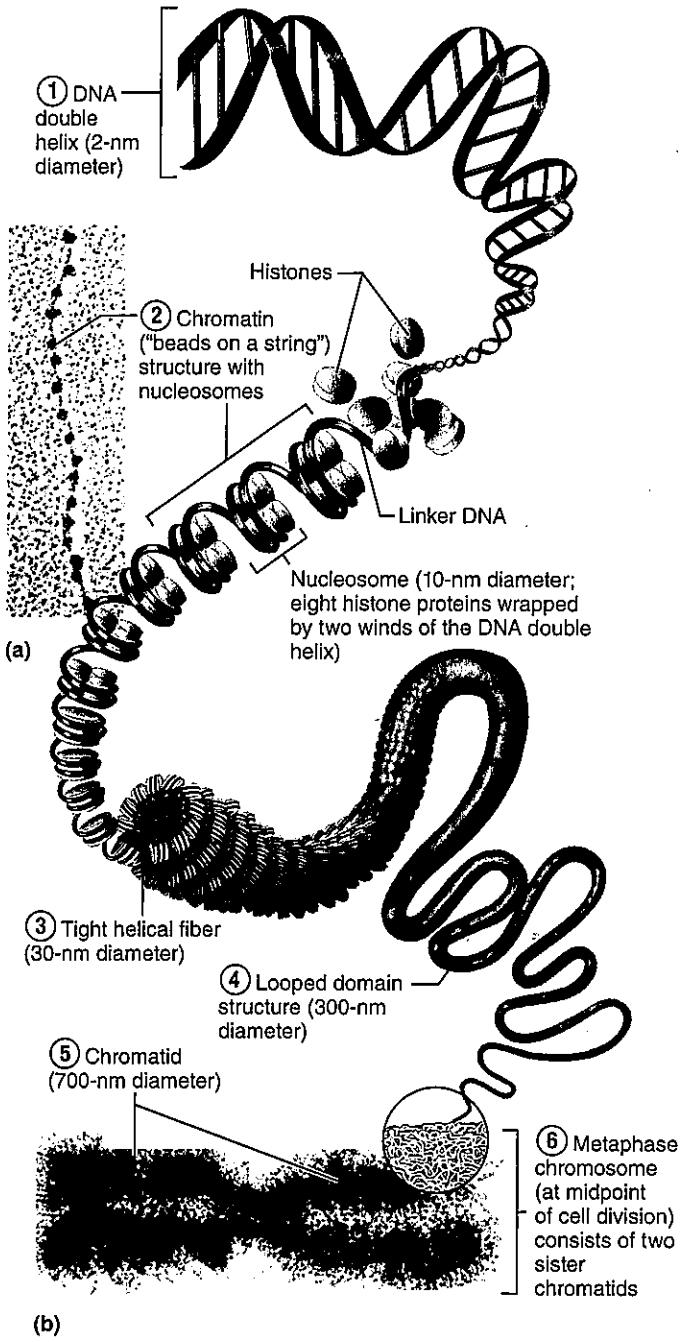
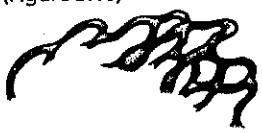
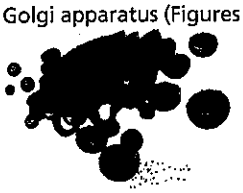
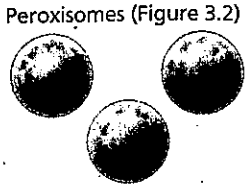


Figure 3.30 Chromatin and chromosome structure.
(a) Electron micrograph of chromatin fiber (125,000×).
(b) DNA packed in a chromosome. The levels of increasing structural complexity (coiling) from the DNA helix to the metaphase chromosome are indicated in order from the smallest (① DNA double helix) to the largest and most complex (⑥ chromosome).

Histones provide a physical means for packing the very long DNA molecules (some 2 meters' worth per cell) in a compact, orderly way, but they also play an important role in gene regulation. In a nondividing cell, for example, the presence of methyl groups on histone proteins shuts down the nearby DNA, and attachment of a phosphate group to a particular histone protein

(Text continues on p. 96)

Table 3.3 Parts of the Cell: Structure and Function

CELL PART*	STRUCTURE	FUNCTIONS
Plasma Membrane (Figure 3.3)		
	Membrane made of a double layer of lipids (phospholipids, cholesterol, and so on) within which proteins are embedded. Proteins may extend entirely through the lipid bilayer or protrude on only one face. Most externally facing proteins and some lipids have attached sugar groups.	Serves as an external cell barrier, and acts in transport of substances into or out of the cell. Maintains a resting potential that is essential for functioning of excitable cells. Externally facing proteins act as receptors (for hormones, neurotransmitters, and so on), transport proteins, and in cell-to-cell recognition.
Cytoplasm		
	Cellular region between the nuclear and plasma membranes. Consists of fluid **cytosol** containing dissolved solutes, **organelles** (the metabolic machinery of the cytoplasm), and **inclusions** (stored nutrients, secretory products, pigment granules).	
Organelles		
• Mitochondria (Figure 3.17) 	Rodlike, double-membrane structures; inner membrane folded into projections called cristae.	Site of ATP synthesis; powerhouse of the cell.
• Ribosomes (Figures 3.18, 3.37–3.39) 	Dense particles consisting of two subunits, each composed of ribosomal RNA and protein. Free or attached to rough endoplasmic reticulum.	The sites of protein synthesis.
• Rough endoplasmic reticulum (Figures 3.18, 3.39) 	Membranous system enclosing a cavity, the cistern, and coiling through the cytoplasm. Externally studded with ribosomes.	Sugar groups are attached to proteins within the cisterns. Proteins are bound in vesicles for transport to the Golgi apparatus and other sites. External face synthesizes phospholipids.
• Smooth endoplasmic reticulum (Figure 3.18) 	Membranous system of sacs and tubules; free of ribosomes.	Site of lipid and steroid (cholesterol) synthesis, lipid metabolism, and drug detoxification.
• Golgi apparatus (Figures 3.19, 3.20) 	A stack of flattened membranes and associated vesicles close to the nucleus.	Packages, modifies, and segregates proteins for secretion from the cell, inclusion in lysosomes, and incorporation into the plasma membrane.
• Peroxisomes (Figure 3.2) 	Membranous sacs of catalase and oxidase enzymes.	The enzymes detoxify a number of toxic substances. The most important enzyme, catalase, breaks down hydrogen peroxide.

* Individual cellular structures are not drawn to scale.

Table 3.3

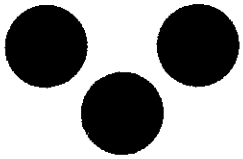
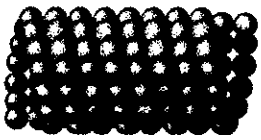
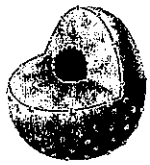
CELL PART*	STRUCTURE	FUNCTIONS
Cytoplasm		
▪ Lysosomes (Figure 3.21) 	Membranous sacs containing acid hydrolases.	Sites of intracellular digestion.
▪ Microtubules (Figures 3.23–3.25) 	Cylindrical structures made of tubulin proteins.	Support the cell and give it shape. Involved in intracellular and cellular movements. Form centrioles and cilia and flagella, if present.
▪ Microfilaments (Figures 3.23, 3.24) 	Fine filaments composed of the protein actin.	Involved in muscle contraction and other types of intracellular movement, help form the cell's cytoskeleton.
▪ Intermediate filaments (Figure 3.23) 	Protein fibers; composition varies.	The stable cytoskeletal elements; resist mechanical forces acting on the cell.
▪ Centrioles (Figure 3.25) 	Paired cylindrical bodies, each composed of nine triplets of microtubules.	Organize a microtubule network during mitosis (cell division) to form the spindle and asters. Form the bases of cilia and flagella.
Inclusions	Varied; includes stored nutrients such as lipid droplets and glycogen granules, protein crystals, pigment granules.	Storage for nutrients, wastes, and cell products.
Cellular Extensions		
▪ Cilia (Figures 3.26, 3.27) 	Short cell-surface projections; each cilium composed of nine pairs of microtubules surrounding a central pair.	Coordinated movement creates a unidirectional current that propels substances across cell surfaces.
▪ Flagellum 	Like a cilium, but longer; only example in humans is the sperm tail.	Propels the cell.
▪ Microvilli (Figure 3.28) 	Tubular extensions of the plasma membrane; contain a bundle of actin filaments.	Increase surface area for absorption.
Nucleus (Figures 3.2, 3.29)		
	Largest organelle. 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.

Table 3.3 Parts of the Cell: Structure and Function

CELL PART	STRUCTURE	FUNCTIONS
Nucleus (Figures 3.2, 3.29)		
▪ Nuclear envelope (Figure 3.29) 	Double-membrane structure pierced by pores. Outer membrane continuous with the endoplasmic reticulum.	Separates the nucleoplasm from the cytoplasm and regulates passage of substances to and from the nucleus.
▪ Nucleolus (Figure 3.29) 	Dense spherical (non-membrane-bounded) bodies, composed of ribosomal RNA and proteins.	Site of ribosome subunit manufacture.
▪ Chromatin (Figure 3.30) 	Granular, threadlike material composed of DNA and histone proteins.	DNA constitutes the genes.

may indicate that the cell is about to commit suicide. On the other hand, addition of acetyl groups to histone exposes different DNA segments, or genes, so that they can dictate the specifications for synthesizing proteins or various RNA species. Such active chromatin segments, referred to as *extended chromatin*, are not usually visible under the light microscope. The generally inactive *condensed chromatin* segments are darker staining and more easily detected. Understandably, the most active body cells have much larger amounts of extended chromatin.

Interestingly, particular chromatin strands occupy discrete regions in the nucleus called *chromosome territories*. Depending on the specific genes contained, and the cell and tissue type, the chromosome territory patterns change during development. At the simplest level, active and inactive genetic regions can be separated from each other, which in turn would enhance or repress genetic expression.

When a cell is preparing to divide, the chromatin threads coil and condense enormously to form short, barlike bodies called **chromosomes** ("colored bodies") (Figure 3.30 ⑤ and ⑥). Chromosome compactness prevents the delicate chromatin strands from tangling and breaking during the movements that occur during cell division. Next, we describe the functions of DNA and the events of cell division.

Table 3.3 summarizes the parts of the cell beginning on p. 94.

Check Your Understanding

23. If a cell ejects or loses its nucleus, what is its fate and why?
24. What is the role of nucleoli?
25. What is the importance of the histone proteins present in the nucleus?

For answers, see Appendix H.

Cell Growth and Reproduction

The Cell Cycle

✓ List the phases of the cell cycle and describe the key events of each phase.

✓ Describe the process of DNA replication.

The **cell cycle** is the series of changes a cell goes through from the time it is formed until it reproduces. The outer ring of **Figure 3.31** shows the two major periods of the cell cycle:

- *Interphase* (in green), in which the cell grows and carries on its usual activities
- *Cell division* or the *mitotic phase* (in yellow), during which it divides into two cells

Interphase

Interphase is the period from cell formation to cell division. Early cytologists, unaware of the constant molecular activity in cells and impressed by the obvious movements of cell division, called interphase the resting phase of the cell cycle. (The term *interphase* reflects this idea of a stage *between* cell divisions.) However, this image is misleading because during interphase a cell is carrying out all its routine activities and is "resting" only from dividing. Perhaps a more accurate name for this phase would be *metabolic phase* or *growth phase*.

Subphases In addition to carrying on its life-sustaining reactions, an interphase cell prepares for the next cell division. Interphase is divided into G_1, S, and G_2 subphases (the Gs stand for *gaps* before and after the S phase, and S is for *synthetic*). In all three subphases, the cell grows by producing proteins and organelles, but chromatin is reproduced only during the S subphase.

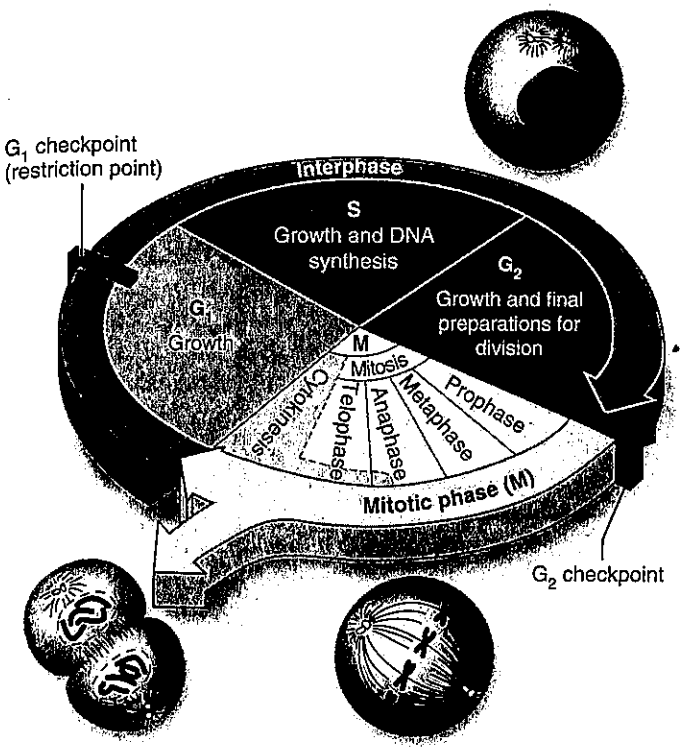


Figure 3.31 The cell cycle. During G_1, cells grow rapidly and carry out their routine functions. The S phase is the period of DNA synthesis. In G_2, materials needed for cell division are synthesized and growth continues. During the M phase (cell division), mitosis and cytokinesis occur, producing two daughter cells. Important checkpoints at which mitosis may be prevented from occurring are found throughout interphase; the diagram shows two.

- **G_1 (gap 1 subphase):** The cell is metabolically active, synthesizing proteins rapidly and growing vigorously (Figure 3.31, light green area). This is the most variable phase in terms of length. In cells that divide rapidly, G_1 typically lasts several minutes to hours, but in those that divide slowly, G_1 may last for days or even years. Cells that permanently cease dividing are said to be in the **G_0 phase.** For most of G_1, virtually no activities directly related to cell division occur. However, as G_1 ends, the centrioles start to replicate in preparation for cell division.
- **S phase:** DNA is replicated, ensuring that the two future cells being created will receive identical copies of the genetic material (Figure 3.31, blue area). New histones are made and assembled into chromatin. One thing is sure, without a proper S phase, there can be no correct mitotic phase. (We will describe DNA replication next.)
- **G_2 (gap 2 subphase):** The final phase of interphase is brief (Figure 3.31, dark green area). Enzymes and other proteins needed for division are synthesized and moved to their proper sites. By the end of G_2, centriole replication (begun in G_1) is complete. The cell is now ready to divide. Throughout S and G_2, the cell continues to grow and carries on with business as usual.

DNA Replication Before a cell can divide, its DNA must be replicated exactly, so that identical copies of the cell's genes can be passed to each of its offspring. During the S phase, replication begins simultaneously on several chromatin threads and continues until all the DNA has been replicated.

Human DNA molecules are very long. Replication of a DNA molecule begins at several *origins of replication* along its length that have a specific nucleotide sequence, a strategy that greatly increases the speed of replication.

Replication is still being studied but appears to involve several events:

1. Enzymes attach to origins of replication and separate the DNA strands so that *replication bubbles* form. At each end of a replication bubble is a Y-shaped area, a *replication fork*, where the helical parental DNA strands are being unwound **(Figure 3.32)**.
2. Once the bubbles are formed, the parental DNA strands are ready to serve as templates for making complementary DNA strands from free DNA precursors dissolved in the nucleoplasm (Figure 3.32). However, there is a problem here because the *polymerase enzymes* that synthesize DNA cannot start a new DNA strand from scratch. They can only add new nucleotides to a strand that already exists. This problem is solved by formation of a short, complementary **RNA primer**, about 10 bases long, by a *primase enzyme.*
3. Continuing from the primer, the enzyme **DNA polymerase** positions complementary nucleotides along the template strand and then covalently links them together. DNA polymerase works only in one direction. Consequently, one strand, the **leading strand**, is synthesized continuously once primed, following the movement of the replication fork. The other strand, called the **lagging strand**, is constructed in segments in the opposite direction and requires that a primer initiate replication of each segment.
4. Ligase enzymes splice the short segments of DNA together. Eventually DNA polymerases replace the primers with DNA nucleotides.

The end result is that two DNA molecules are formed from the original DNA helix (the template strands) and are identical to it. Because each new molecule consists of one old and one new nucleotide strand, this mechanism of DNA replication is called **semiconservative replication** (Figure 3.32).

As soon as replication ends, histones (synthesized in the cytoplasm and imported into the nucleus) associate with the DNA, completing the formation of two new chromatin strands. The chromatin strands, united by a buttonlike centromere (a stretch of repetitive DNA), remain held together by the centromere and a protein complex called *cohesin*, until the cell enters the anaphase stage of mitotic cell division (see p. 101). They are then distributed to the daughter cells as described next, ensuring that each cell has identical genetic information.

The progression from DNA replication into cell division presumes that the newly synthesized DNA is not damaged in any way. If damage occurs, the cell cycle stops until the DNA repair mechanism has fixed the problem.

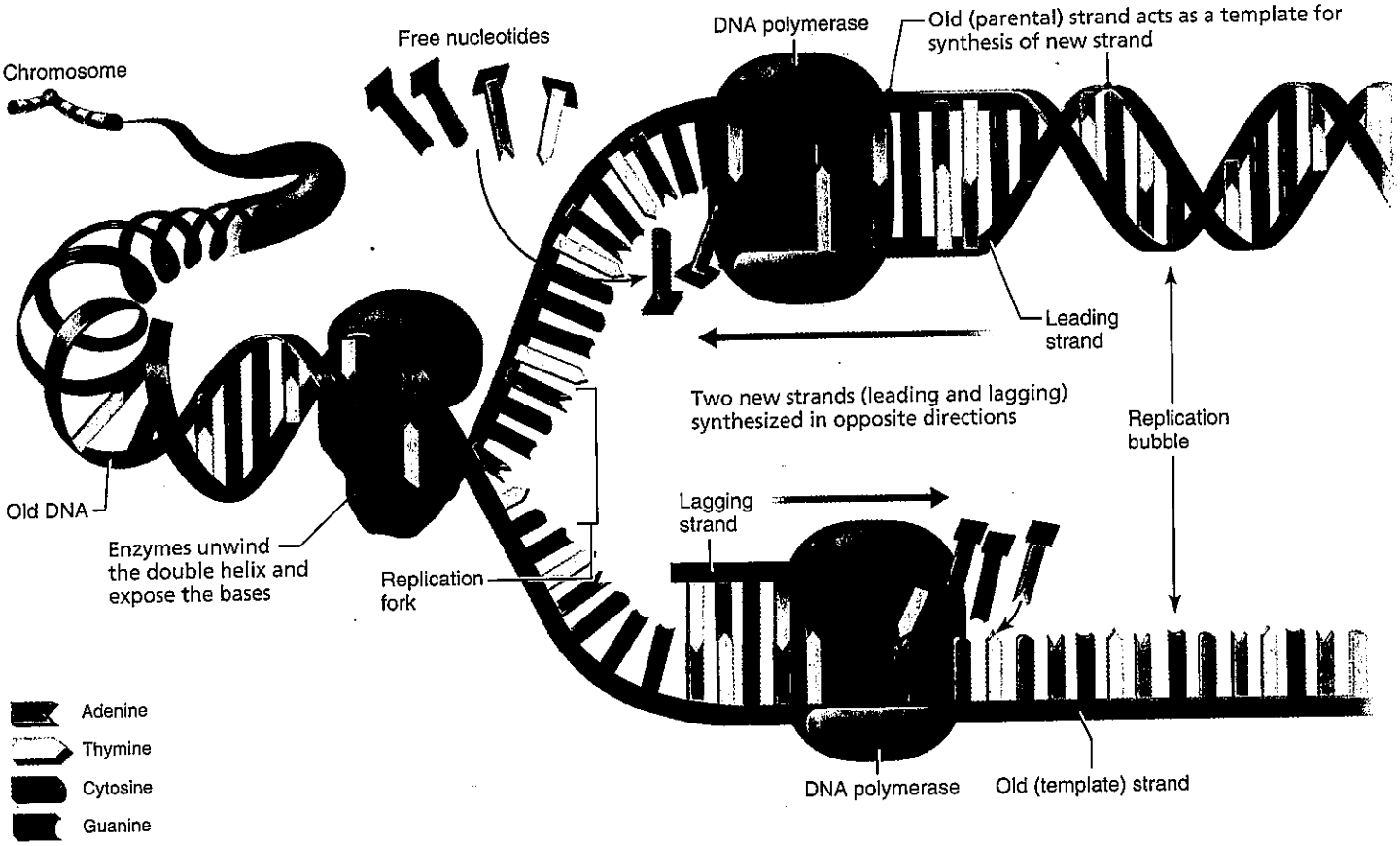


Figure 3.32 Replication of DNA: summary. Once the DNA helix is uncoiled, and the hydrogen bonds between its base pairs are broken, each nucleotide strand of the DNA acts as a template for constructing a complementary strand, as illustrated on the right-hand side of the diagram. (The step in which RNA primers are formed to start the process at replication bubbles is not shown.) DNA polymerases work in one direction only, so the two new strands (leading and lagging) are synthesized in opposite directions. (The DNA ligase enzymes that join the DNA fragments on the lagging strand are not illustrated.) Each DNA molecule formed consists of one old (template) strand and one newly assembled strand and constitutes a chromatid of a chromosome.

Cell Division

Cell division is essential for body growth and tissue repair. Cells that continually wear away, such as cells of the skin and intestinal lining, reproduce themselves almost continuously. Others, such as liver cells, divide more slowly (to maintain the size of the organ they compose) but retain the ability to reproduce quickly if the organ is damaged. Most cells of nervous tissue, skeletal muscle, and heart muscle lose their ability to divide when they are fully mature, and repairs are made with scar tissue (a fibrous type of connective tissue).

Events of Cell Division In most body cells, cell division, which is called the **M (mitotic) phase** of the cell cycle, involves two distinct events (Figure 3.31, yellow area):

- **Mitosis** (mi-to'sis; *mit* = thread; *osis* = process), the division of the nucleus
- **Cytokinesis** (si-to-ki-ne'sis; *kines* = movement), the division of the cytoplasm

A different process of nuclear division called *meiosis* (mi-o'sis) produces sex cells (ova and sperm) with only half the number of genes found in other body cells. We discuss the details of meiosis in Chapter 27. Here we concentrate on mitotic cell division.

Mitosis Mitosis is the series of events that parcels out the replicated DNA of the mother cell to two daughter cells. Described as four phases—**prophase**, **metaphase**, **anaphase**, and **telophase**—mitosis is actually a continuous process, with one phase merging smoothly into the next. Its duration varies according to cell type, but in human cells it typically lasts about an hour or less. *Focus on Mitosis* **(Figure 3.33)**, pp. 100–101, describes the phases of mitosis in detail.

Cytokinesis Cytokinesis, or the division of the cytoplasm, begins during late anaphase and is completed after mitosis ends. A *contractile ring* made of actin filaments (Figure 3.33) draws the plasma membrane inward to form a **cleavage furrow** over the center of the cell. The furrow deepens until it pinches the cytoplasmic mass into two parts, yielding two daughter cells. Each is smaller and has less cytoplasm than the mother cell, but is genetically identical to it. The daughter cells then enter the interphase portion of the life cycle until it is their turn to divide.

Control of Cell Division The signals that prod cells to divide are incompletely understood, but we know that the ratio of cell surface area to cell volume is important. The amount of nutrients a growing cell requires is directly related to its volume. Volume increases with the cube of cell radius, whereas surface area increases more slowly with the square of the radius.

For example, a 64-fold (4^3) increase in cell volume is accompanied by only a 16-fold (4^2) increase in surface area. Consequently, the surface area of the plasma membrane becomes inadequate for nutrient and waste exchange when a cell reaches a certain critical size. Cell division solves this problem because the smaller daughter cells have a favorable ratio of surface area to volume. These surface-volume relationships help explain why most cells are microscopic in size.

Two other factors that influence when cells divide are chemical signals (growth factors, hormones, and others) released by other cells and the availability of space. Normal cells stop proliferating when they begin touching, a phenomenon called *contact inhibition.* The system that controls the cell cycle has been compared to the timer on a washing machine. Like that timer, the control system for the cell cycle is driven by a built-in clock. However, just as the washer's cycle is subject to adjustments (by regulating the flow from the faucet, say, or by an internal water-level sensor), the cell cycle is regulated by both internal and external factors.

Two groups of proteins are crucial to the ability of a cell to accomplish the S phase and enter mitosis:

- **Cyclins**, regulatory proteins whose levels rise and fall during each cell cycle
- **Cdks (cyclin-dependent kinases)**, which are present in a constant concentration in the cell and are activated by binding to particular cyclins

A new batch of cyclins accumulates during each interphase. Subsequent joining of specific Cdk and cyclin proteins initiates enzymatic cascades that phosphorylate histones and other proteins needed for cell division. At the end of mitosis, enzymes destroy the cyclins.

A number of "switches" and crucial checkpoints for cell division occur throughout interphase. These built-in stop signals halt the cell cycle until overridden by internal or external go-ahead signals. In many cells, a G_1 checkpoint, called the *restriction point*, seems to be most important (see Figure 3.31). If the cell is prevented from progressing past this checkpoint, it enters the nondividing state (G_0). Another important checkpoint, and the first to be understood, occurs late in G_2, when a threshold amount of a protein complex called **MPF (M-phase promoting factor)** is required to give the okay signal to pass the G_2 checkpoint and enter M phase. Later in M phase, MPF is inactivated.

Besides these "go" signals, there are a number of so-called repressor genes that inhibit cell division. One example is the *p53* gene that initiates a series of enzymatic events that produce growth-inhibiting factors. Roughly half of all cancers have abnormal *p53* genes. Contact with other cells does not inhibit these cancerous cells and they divide wildly, making them dangerous to their host.

☑ Check Your Understanding

26. If one of the DNA strands being replicated "reads" CGAATG, what will be the base sequence of the corresponding DNA strand?
27. During what phase of the cell cycle is DNA synthesized?
28. What are three events occurring in prophase that are undone in telophase?

For answers, see Appendix H.

3

Protein Synthesis

✓ Define gene and genetic code and explain the function of genes.

✓ Name the two phases of protein synthesis and describe the roles of DNA, mRNA, tRNA, and rRNA in each phase.

✓ Contrast triplets, codons, and anticodons.

In addition to directing its own replication, DNA serves as the master blueprint for protein synthesis. Although cells also make lipids and carbohydrates, DNA does not dictate their structure. Historically, DNA is said to specify *only* the structure of protein molecules, including the enzymes that catalyze the synthesis of all classes of biological molecules.

Much of the metabolic machinery of the cell is concerned in some way with protein synthesis. This is not surprising, seeing as structural proteins constitute most of the dry cell material, and functional proteins direct almost all cellular activities. Essentially, cells are miniature protein factories that synthesize the huge variety of proteins that determine the chemical and physical nature of cells—and therefore of the whole body.

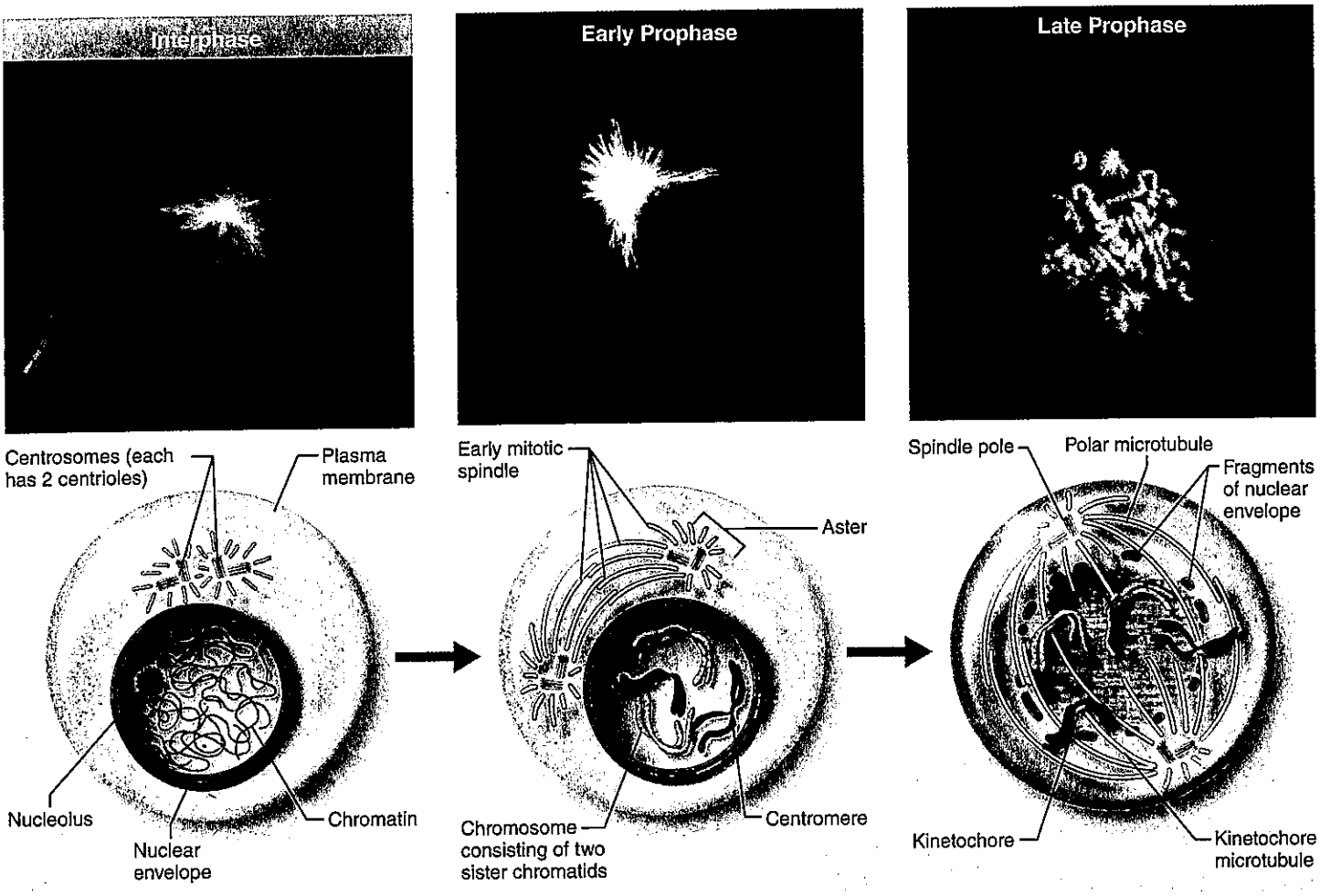
Recall from Chapter 2 that proteins are composed of polypeptide chains, which in turn are made up of amino acids. For purposes of this discussion, we define a **gene** as a segment of a DNA molecule that carries instructions for creating one polypeptide chain. Supposedly we humans have an estimated 25,000 protein coding genes. (Note, however, that some genes specify the structure of certain varieties of RNA as their final product.)

The four nucleotide bases (A, G, T, and C) are the "letters" used in the genetic alphabet, and the information of DNA is found in the sequence of these bases. Each sequence of three bases, called a **triplet**, can be thought of as a "word" that specifies a particular amino acid. For example, the triplet AAA calls for the amino acid phenylalanine, and CCT calls for glycine. The sequence of triplets in each gene forms a "sentence" that tells exactly how a particular polypeptide is to be made: It specifies the number, kinds, and order of amino acids needed to build a particular polypeptide.

Variations in the arrangement of A, T, C, and G allow our cells to make all the different kinds of proteins needed. Even a "small" gene has an estimated 210 base pairs in sequence. The ratio between DNA bases in the gene and amino acids in the polypeptide is 3:1 (because each triplet stands for one amino acid), so we would expect the polypeptide specified by such a gene to contain 70 amino acids.

(Text continues on p. 102.)

Figure 3.33 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. A&P Flix Available at www.masteringaandp.com



Interphase

Interphase
Interphase is the period of a cell's life when it carries out its normal metabolic activities and grows. Interphase is not part of mitosis.

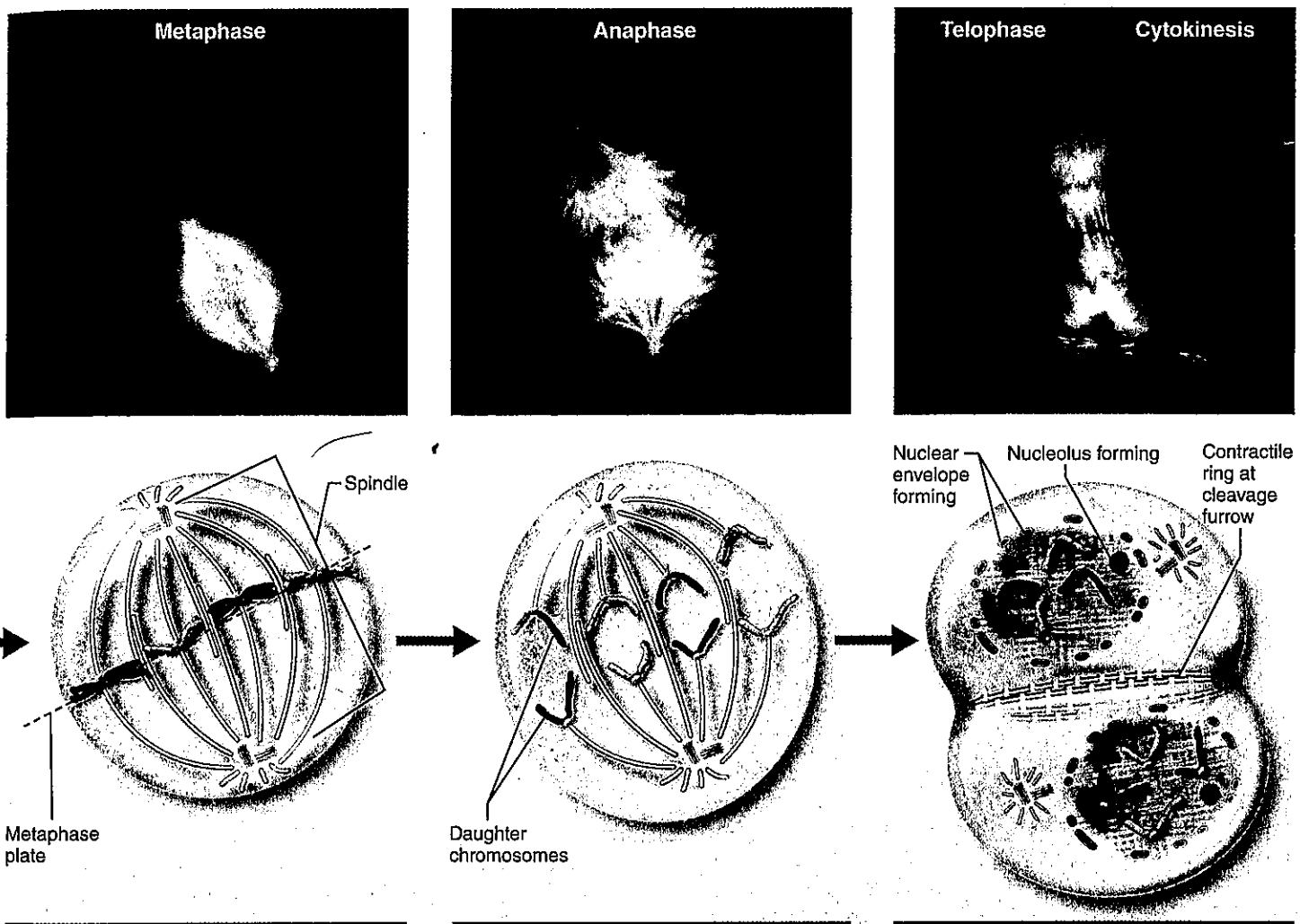
- During interphase, the DNA-containing material is in the form of chromatin. The nuclear envelope and one or more nucleoli are intact and visible.
- There are three distinct periods of interphase:
  G_1: The centrioles begin replicating.
  S: DNA is replicated.
  G_2: Final preparations for mitosis are completed and centrioles finish replicating.

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.

Prophase—first phase of mitosis

Early Prophase
- The chromatin condenses, forming barlike *chromosomes*.
- Each duplicated chromosome consists of two identical threads, called *sister chromatids*, held together at the *centromere*. (Later when the chromatids separate, each will be a new chromosome.)
- As the chromosomes appear, the nucleoli disappear, and the two centrosomes separate from one another.
- The centrosomes act as focal points for growth of a microtubule assembly called the *mitotic spindle*. As the microtubules lengthen, they propel the centrosomes toward opposite ends (poles) of the cell.
- Microtubule arrays called *asters* ("stars") extend from the centrosome matrix.

Late Prophase
- The nuclear envelope breaks up, allowing the spindle to interact with the chromosomes.
- Some of the growing spindle microtubules attach to *kinetochores* (ki-ne´ to-korz), special protein structures at each chromosome's centromere. Such microtubules are called *kinetochore microtubules*.
- The remaining spindle microtubules (not attached to any chromosomes) are called *polar microtubules*. The microtubules slide past each other, forcing the poles apart.
- The kinetochore microtubules pull on each chromosome from both poles in a tug-of-war that ultimately draws the chromosomes to the center, or equator, of the cell.



Metaphase—second phase of mitosis

- The two centrosomes are at opposite poles of the cell.
- The chromosomes cluster at the midline of the cell, with their centromeres precisely aligned at the *equator* of the spindle. This imaginary plane midway between the poles is called the *metaphase plate*.
- Enzymes act to separate the chromatids from each other.

Anaphase—third phase of mitosis

The shortest phase of mitosis, anaphase begins abruptly as the centromeres of the chromosomes split simultaneously. Each chromatid now becomes a chromosome in its own right.

- The kinetochore microtubules, moved along by motor proteins in the kinetochores, gradually pull each chromosome toward the pole it faces.
- At the same time, the polar microtubules slide past each other, lengthen, and push the two poles of the cell apart.
- The moving chromosomes look V shaped. The centromeres lead the way, and the chromosomal "arms" dangle behind them.
- Moving and separating the chromosomes is helped by the fact that the chromosomes are short, compact bodies. Diffuse threads of chromatin would trail, tangle, and break, resulting in imprecise "parceling out" to the daughter cells.

Telophase—final phase of mitosis

Telophase

Telophase begins as soon as chromosomal movement stops. This final phase is like prophase in reverse.

- The identical sets of chromosomes at the opposite poles of the cell uncoil and resume their threadlike chromatin form.
- A new nuclear envelope forms around each chromatin mass, nucleoli reappear within the nuclei, and the spindle breaks down and disappears.
- Mitosis is now ended. The cell, for just a brief period, is binucleate (has two nuclei) and each new nucleus is identical to the original mother nucleus.

Cytokinesis—division of cytoplasm

Cytokinesis begins during late anaphase and continues through and beyond telophase. A contractile ring of actin microfilaments forms the *cleavage furrow* and pinches the cell apart.

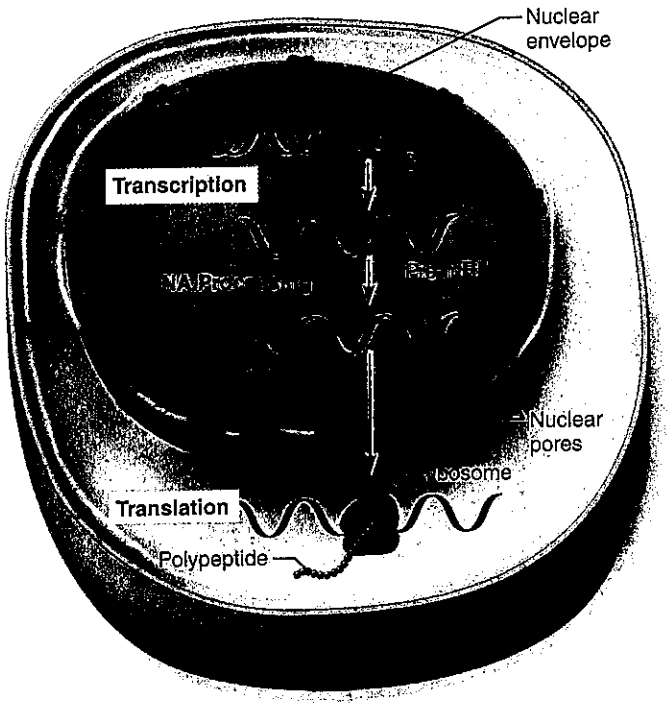


Figure 3.34 Simplified scheme of information flow from the DNA gene to mRNA to protein structure during transcription and translation. (Note that mRNA is first synthesized as pre-mRNA, which is processed by enzymes before leaving the nucleus.)

Most genes of higher organisms contain **exons**, which are amino acid–specifying informational sequences. Exons are often separated by **introns**, which are noncoding, often repetitive, segments that range from 60 to 100,000 nucleotides. Once considered a type of "junk DNA," intron DNA is believed to serve as a reservoir or scrapyard of ready-to-use DNA segments for genome evolution, as well as a rich source of small RNA molecules. The rest of the DNA (indeed, most of it) is essentially "dark matter" whose function is still a mystery. It is in these regions that *pseudogenes* (false genes) are found. Pseudogenes are genetic fossils that are the remains of damaged genes. They "look like" real genes but have deficits that render them functionless.

The Role of RNA

By itself, DNA is like a CD recording: The information it contains cannot be used without a decoding mechanism (a CD player). Furthermore, most polypeptides are manufactured at ribosomes in the cytoplasm, but in interphase cells, DNA never leaves the nucleus. So, DNA requires not only a decoder, but a messenger as well. The decoding and messenger functions are carried out by RNA, the second type of nucleic acid.

As you learned in Chapter 2, RNA differs from DNA: RNA is single stranded, and it has the sugar ribose instead of deoxyribose, and the base uracil (U) instead of thymine (T). Three forms of RNA typically act together to carry out DNA's instructions for polypeptide synthesis:

- **Messenger RNA (mRNA)**, relatively long nucleotide strands resembling "half-DNA" molecules (one of the two strands of a DNA molecule coding for protein structure). mRNA carries a transcript of the code to the cytoplasm, where protein synthesis occurs.
- **Ribosomal RNA (rRNA)**, along with proteins, forms the ribosomes, which consist of two subunits—one large and one small. The two subunit types combine to form functional ribosomes, which are the sites of protein synthesis.
- **Transfer RNA (tRNA)**, small, roughly L-shaped molecules that ferry amino acids to the ribosomes. There they decode mRNA's message for amino acid sequence in the polypeptide to be built.

All types of RNA are formed on the DNA in the nucleus in much the same way as DNA replicates itself: The DNA helix separates and one of its strands serves as a template for synthesizing a complementary RNA strand. Once formed, the RNA molecule is released from the DNA template and migrates into the cytoplasm. Its job done, the DNA recoils into its helical, inactive form.

Approximately 2% of the nuclear DNA codes for the synthesis of short-lived mRNA. DNA in the nucleolar organizer regions (mentioned previously) codes for the synthesis of rRNA, which is long-lived and stable, as is tRNA coded by other DNA sequences. Because rRNA and tRNA do not transport codes for synthesizing other molecules, they are the final products of the genes that code for them. Ribosomal RNA and tRNA act together to "translate" the message carried by mRNA.

Essentially, polypeptide synthesis involves two major steps:

1. *Transcription*, in which DNA's information is encoded in mRNA
2. *Translation*, in which the information carried by mRNA is decoded and used to assemble polypeptides

Figure 3.34 summarizes the information flow in these two major steps. The figure also indicates the "RNA processing" that removes introns from mRNA before this molecule leaves the nucleus and moves into the cytoplasm.

Transcription

A transcriptionist converts a message from a recording or shorthand notes into a written copy. In other words, information is transferred from one form or format to another.

In cells, **transcription** transfers information from a DNA base sequence to the complementary base sequence of an mRNA molecule. The form is different, but the same information is being conveyed. Once the mRNA molecule is made, it detaches and leaves the nucleus via a nuclear pore, and heads for the protein synthesis machinery, the ribosome.

Transcription cannot begin until gene-activating chemicals called *transcription factors* stimulate histones at the site-to-be of gene transcription to loosen. The transcription factors then bind to the promoter. The **promoter** is a special DNA sequence that contains the *start point* (beginning of the gene to be transcribed). It specifies where mRNA synthesis starts and which DNA strand is going to serve as the *template strand* (Figure 3.35,

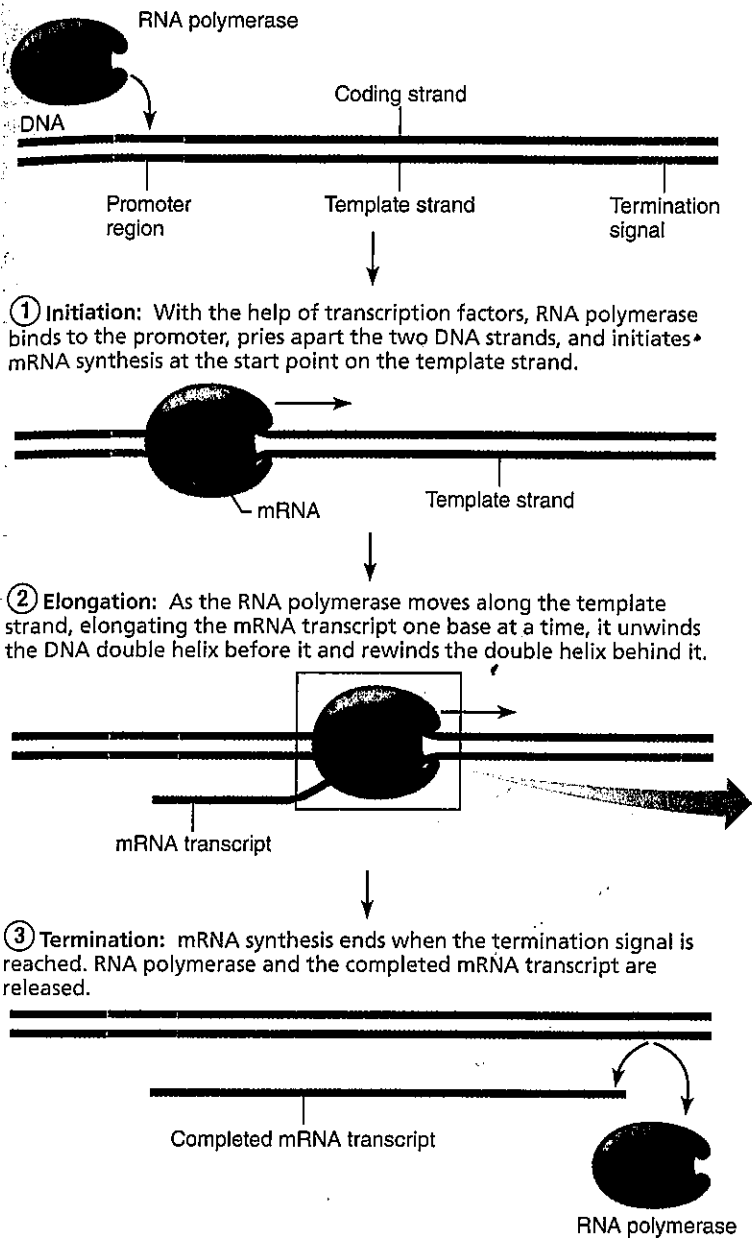
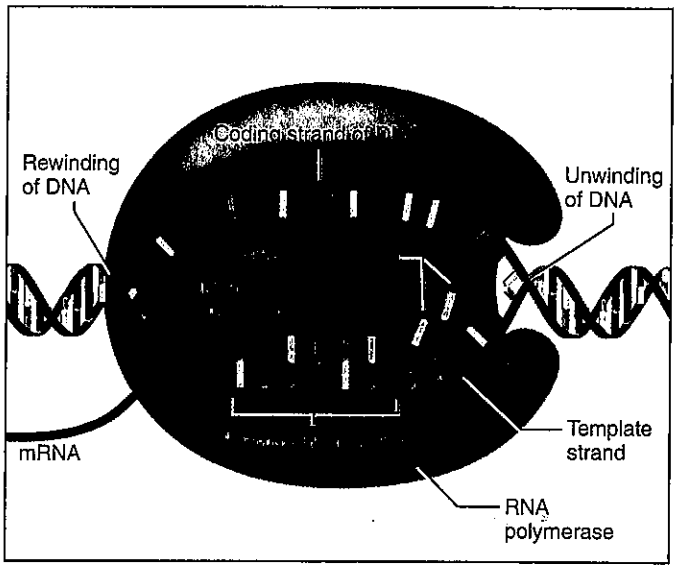


Figure 3.35 Overview of stages of transcription.



The DNA-RNA hybrid: At any given moment, 16–18 base pairs of DNA are unwound and the most recently made RNA is still bound to DNA. This small region is called the DNA-RNA hybrid.

top). The uncoiled DNA strand not used as a template is called the *coding strand* because it has the same (coded) sequence as the mRNA to be built (except for the U in mRNA in place of T in DNA). The transcription factors also help position **RNA polymerase**, the enzyme that oversees the synthesis of mRNA, correctly at the promoter. Once these preparations are made, RNA polymerase can initiate transcription.

Transcription involves three basic phases: initiation, elongation, and termination **(Figure 3.35)**.

① **Initiation.** Once properly positioned, RNA polymerase pulls apart the strands of the DNA double helix so transcription can begin at the start point in the promoter.

② **Elongation.** Using incoming RNA nucleotides as substrates, the RNA polymerase aligns them with complementary DNA bases on the template strand and then links them together. As RNA polymerase elongates the mRNA strand one base at a time, it unwinds the DNA helix in front of it, and rewinds the helix behind it. At any given moment, 16 to 18 base pairs of DNA are unwound and the most recently made mRNA is still hydrogen-bonded (H-bonded) to the template DNA. This small region—called the **DNA-RNA hybrid**—is up to 12 base pairs long.

③ **Termination.** When the polymerase reaches a special base sequence called a **termination signal**, transcription ends and the newly formed mRNA separates from the DNA template.

Processing of mRNA Before translation can begin, editing and further processing are needed to clean up the mRNA transcript. Recall that mammalian DNA like ours has coding regions (exons) separated by non-protein-coding regions (introns). Because the DNA is transcribed sequentially, the mRNA initially made, called *pre-mRNA* or *primary transcript*, is still

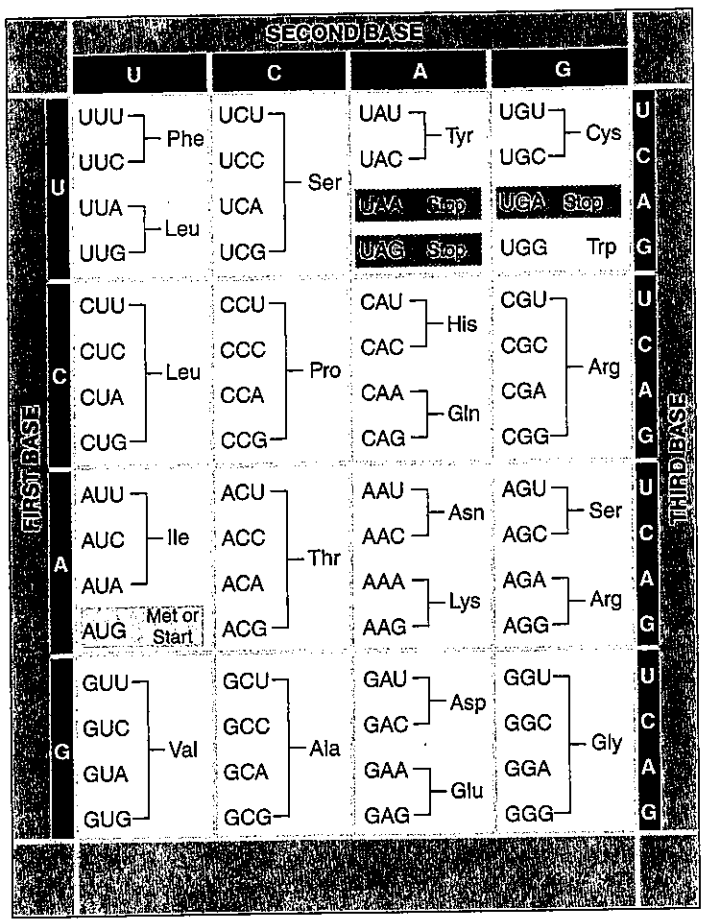


Figure 3.36 The genetic code. The three bases in an mRNA codon are designated as the first, second, and third. Each set of three specifies a particular amino acid, represented here by an abbreviation (see list below). The codon AUG (which specifies the amino acid methionine) is the usual start signal for protein synthesis. The word *stop* indicates the codons that serve as signals to terminate protein synthesis.

Abb.*	Amino acid	Abb.*	Amino acid
Ala	alanine	Leu	leucine
Arg	arginine	Lys	lysine
Asn	asparagine	Met	methionine
Asp	aspartic acid	Phe	phenylalanine
Cys	cysteine	Pro	proline
Glu	glutamic acid	Ser	serine
Gln	glutamine	Thr	threonine
Gly	glycine	Trp	tryptophan
His	histidine	Tyr	tyrosine
Ile	isoleucine	Val	valine

*Abbreviation for the amino acid

littered with introns. Before the newly formed RNA can be used as a messenger, it must be processed, or edited—that is, sections corresponding to introns must be removed. Large RNA-protein complexes called *spliceosomes* snip out the introns and splice together the remaining exon-coded sections in the order in which they occurred in the DNA, producing functional mRNA.

Although many introns degrade naturally, some contain active segments (such as microRNAs) that can function to control, interfere with, or silence other genes. Additionally, a number of specific RNA-binding proteins, called *mRNA complex proteins*, must become associated with the edited mRNA. These mRNA complex proteins guide the export of mRNA from the nucleus, determine its localization, translation, and stability, and check it for premature termination codons.

Translation

A translator takes a message in one language and restates it in another. In the **translation** step of protein synthesis, the language of nucleic acids (base sequence) is translated into the language of proteins (amino acid sequence).

Genetic Code The rules by which the base sequence of a gene is translated into an amino acid sequence are called the **genetic code.** For each triplet, or three-base sequence on DNA, the corresponding three-base sequence on mRNA is called a **codon.** Since there are four kinds of RNA (or DNA) nucleotides, there are 4^3, or 64, possible codons. Three of these 64 codons are "stop signs" that call for termination of polypeptide synthesis. All the rest code for amino acids.

Because there are only about 20 amino acids, some are specified by more than one codon. This redundancy in the genetic code helps protect against problems due to transcription (and translation) errors. **Figure 3.36** shows the genetic code and a complete codon list.

Role of tRNA Translation involves the mRNAs, tRNAs, and rRNAs mentioned above. Before we get into the actual details of the translation process, let's look at how the tRNAs are so well suited for their roles in translation.

Shaped like a handheld drill, tRNA is well suited to its dual function of binding to both an amino acid and an mRNA codon. The amino acid (picked up from the cytoplasmic pool) is bound to one end of tRNA, at a region called the stem. At the other end, the head, is its **anticodon** (an"ti-ko'don), a three-base sequence complementary to the mRNA codon calling for the amino acid carried by that particular tRNA. Because anticodons form hydrogen bonds with complementary codons, tRNA is the link between the language of nucleic acids and the language of proteins. For example, if the mRNA codon is AUA, which specifies isoleucine, the tRNAs carrying isoleucine will have the anticodon UAU, which can bind to the AUA codons.

There are approximately 45 types of tRNA, each capable of binding with a specific amino acid. The attachment process is controlled by an aminoacyl-tRNA synthetase enzyme and is activated by ATP. Once its amino acid is loaded, the tRNA (now called an *aminoacyl-tRNA* because of its amino acid cargo) migrates to the ribosome, where its amino acid is maneuvered into the proper position, as specified by the mRNA codons and described below. The ribosome is more than just a passive attachment site for mRNA and tRNA. Like a vise, the ribosome holds the tRNA and mRNA close together to coordinate the coupling of codons and anticodons, and positions the next (incoming) amino acid for addition to the growing polypeptide chain. To do its job, the ribosome has a binding site for mRNA and three binding sites for tRNA: an A (aminoacyl) site for an incoming aminoacyl-tRNA, a P (peptidyl) site for the tRNA holding the growing polypeptide chain, and an E (exit) site for

an outgoing tRNA, as illustrated in *Focus on Translation* (**Figure 3.37**, on pp. 106–107). Now we are ready to put the parts together—so let's go!

Sequence of Events in Translation Translation entails a now familiar sequence of named events—*initiation*, *elongation*, and *termination*—which occur in the cytoplasm. Each of these phases requires energy in the form of ATP and a specific set of protein factors and enzymes. Figure 3.37 summarizes these events.

① **Initiation.** A small ribosomal subunit binds to a special methionine-carrying **initiator tRNA**, and then to the "new" mRNA to be decoded. With the initiator tRNA still in tow, the small ribosomal subunit scans along the mRNA until it encounters the *start codon*—the first AUG triplet it meets. When the initiator tRNA's UAC anticodon "recognizes" and binds to the start codon, a large ribosomal subunit unites with the small one, forming a functional ribosome.

At the end of this phase the mRNA is firmly positioned in the groove between the ribosomal subunits, the initiator tRNA is sitting in the P site, and the A site is vacant, ready for the next aminoacyl tRNA to deliver its cargo. The next phase, elongation of the polypeptide, now begins.

② **Elongation.** During the three-step cycle of elongation, the mRNA is moved through the ribosome in one direction and one amino acid at a time is added to the growing polypeptide (Figure 3.37).

ⓐ **Codon recognition.** The incoming aminoacyl-tRNA binds to a complementary codon in the A site of a ribosome.

ⓑ **Peptide bond formation.** Once the accuracy of the codon-anticodon binding is checked, an enzymatic component in the large ribosomal subunit catalyzes peptide bond formation between the amino acid of the tRNA in the P site to that of the tRNA in the A site.

ⓐ **Translocation.** This step translocates, or moves, the tRNA in the A site to the P site. The unloaded (vacant) tRNA is transferred to the E site, from which it is released and ready to be recharged with an amino acid from the cytoplasmic pool.

This orderly "musical chairs" process continues: the peptidyl-tRNAs transfer their polypeptide cargo to the aminoacyl-tRNAs, and then the P-site-to-E-site and A-site-to-P-site movements of the tRNAs occur (Figure 3.37). As the ribosome "chugs" along the mRNA track and the mRNA is progressively read, its initial portion passes through the ribosome and may become attached successively to several other ribosomes, all reading the same message simultaneously and sequentially. This multiple ribosome–mRNA complex, a *polyribosome*, efficiently produces multiple copies of the same protein (**Figure 3.38**, on p. 108).

③ **Termination.** The mRNA strand continues to be read sequentially until its last codon, the *stop codon* (one UGA, UAA, or UAG) enters the A site. The stop codon is the "period" at the end of the mRNA sentence—it tells the ribosome that translation of that mRNA is finished. As a result, a *protein release factor* binds to the stop codon at the A site and directs the addition of water (instead of an amino acid) to the polypeptide chain. This hydrolyzes (breaks) the bond between the polypeptide and the tRNA in the P site. The completed polypeptide chain is then released from the ribosome, and the ribosome separates into its two subunits (Figure 3.38a). The released protein may undergo processing before it folds into its complex 3-D structure and floats off, ready to work. When the message of the mRNA that directed its formation is no longer needed, it is degraded.

Processing in the Rough ER As noted earlier in the chapter, ribosomes attach to and detach from the rough ER. When a short "leader" peptide called an ER **signal sequence** is present in a protein being synthesized, the associated ribosome attaches to the membrane of the rough ER. This signal sequence, with its attached cargo of a ribosome and mRNA, is guided to appropriate receptor sites on the ER membrane by a signal recognition particle (SRP), a protein chaperone that cycles between the ER and the cytosol. **Figure 3.39** on p.108 details the subsequent events occurring at the ER.

Summary: From DNA to Proteins The genetic information of a cell is translated into the production of proteins via a sequence of information transfer that is completely directed by complementary base pairing. The transfer of information goes from DNA base sequence (triplets) to the complementary base sequence of mRNA (codons) and then to the tRNA base sequence (anticodons), which is identical to the template DNA sequence except for the substitution of uracil (U) for thymine (T) (**Figure 3.40**, on p. 109).

Other Roles of DNA

The story of DNA doesn't end with the production of proteins encoded by exons. Scientists are finding that intron DNA actually codes for a surprising variety of active RNA species, including the following:

- **Antisense RNAs**, made on the DNA strand complementary to the template strand for mRNA, can intercept and bind to the protein-coding mRNA strand and prevent it from being translated into protein.
- **MicroRNAs** are small RNAs that can use RNA interference machinery to interfere with and suppress mRNAs made by certain exons, thus effectively silencing them.
- **Riboswitches** are folded RNAs that code, like mRNA, for a particular protein. What sets them apart from other mRNAs is a region that acts as a switch to turn protein synthesis on or off in response to metabolic changes in their immediate environment, such as shifting concentrations of amino acids or other small molecules in the cell. When it senses these changes, the riboswitch changes shape, thereby stopping or starting production of the protein it specifies.

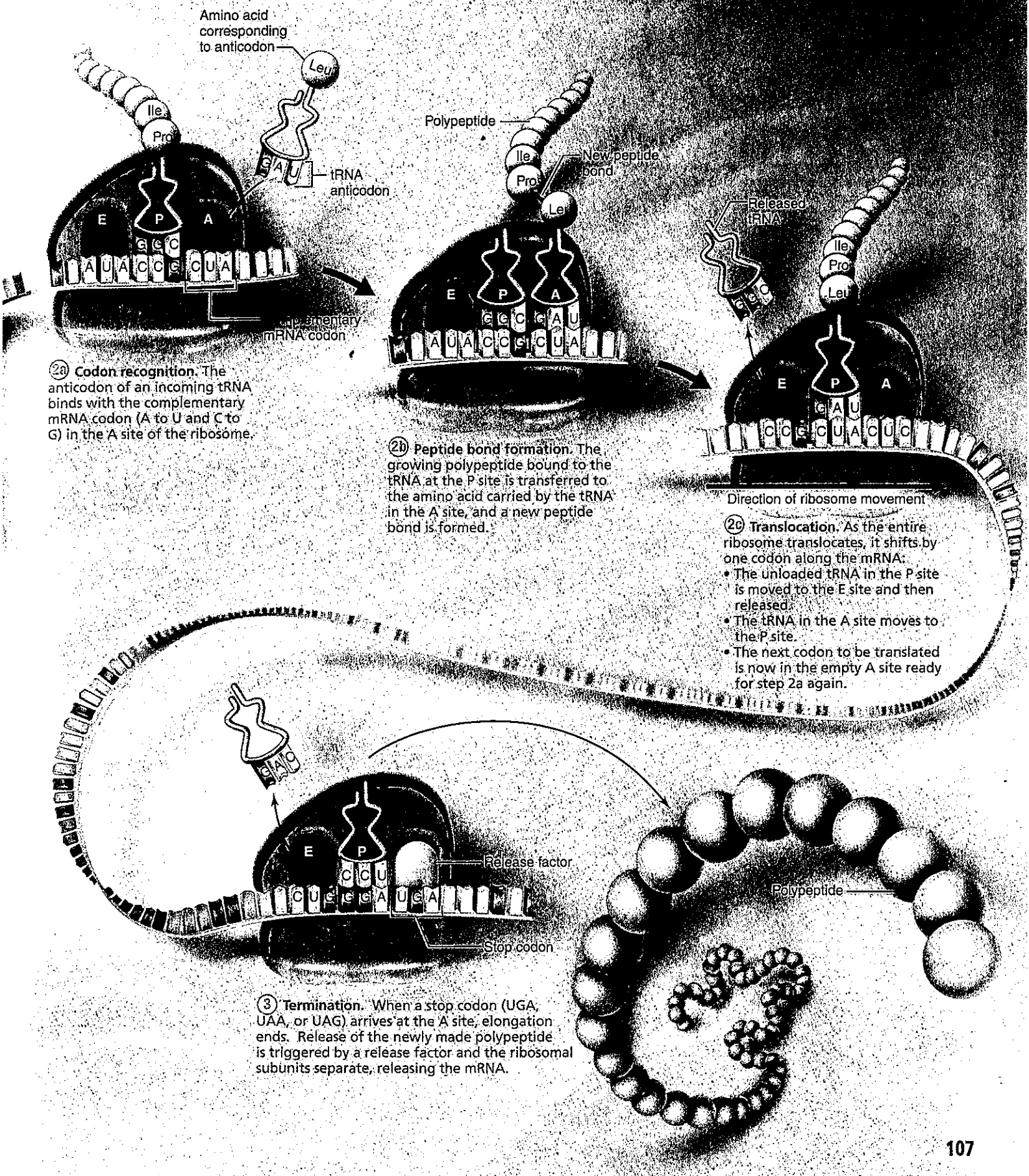
Beyond the discussion here and in Chapter 29, we still have much to learn about these versatile RNA species that arise from intron DNA and appear to play a role in heredity. Another area of research focuses on the multitasking of DNA segments.

(Text continues on p. 109)

Translation

Translation is the process in which genetic information carried by an mRNA is decoded in the ribosome to form a particular polypeptide. The "translators" are tRNA molecules that can recognize and bind specifically both to a codon and an amino acid. A&PFlix Available at www.masteringaandp.com

(2) **Elongation.** Amino acids are added one at a time to the growing peptide chain via a process that has three repeating steps.



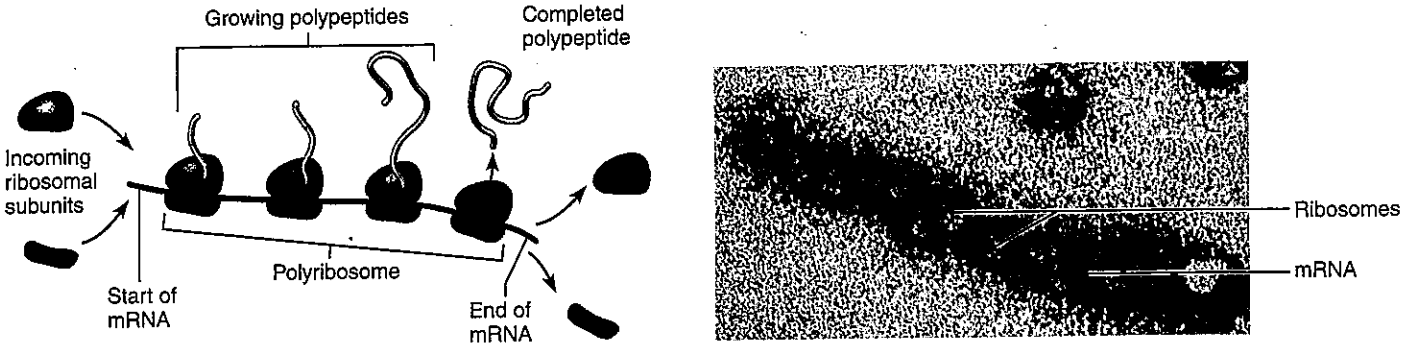
(2a) **Codon recognition.** The anticodon of an incoming tRNA binds with the complementary mRNA codon (A to U and C to G) in the A site of the ribosome.

(2b) **Peptide bond formation.** The growing polypeptide bound to the tRNA at the P site is transferred to the amino acid carried by the tRNA in the A site, and a new peptide bond is formed.

(2c) **Translocation.** As the entire ribosome translocates, it shifts by one codon along the mRNA:

- The unloaded tRNA in the P site is moved to the E site and then released.
- The tRNA in the A site moves to the P site.
- The next codon to be translated is now in the empty A site ready for step 2a again.

(3) **Termination.** When a stop codon (UGA, UAA, or UAG) arrives at the A site, elongation ends. Release of the newly made polypeptide is triggered by a release factor and the ribosomal subunits separate, releasing the mRNA.



(a) Each polyribosome consists of one strand of mRNA being read by several ribosomes simultaneously. In this diagram, the mRNA is moving to the left and the "oldest" functional ribosome is farthest to the right.

(b) This transmission electron micrograph shows a large polyribosome (400,000×).

Figure 3.38 Polyribosome arrays. Polyribosome arrays allow a single strand of mRNA to be translated into hundreds of the same polypeptide molecules in a short time.

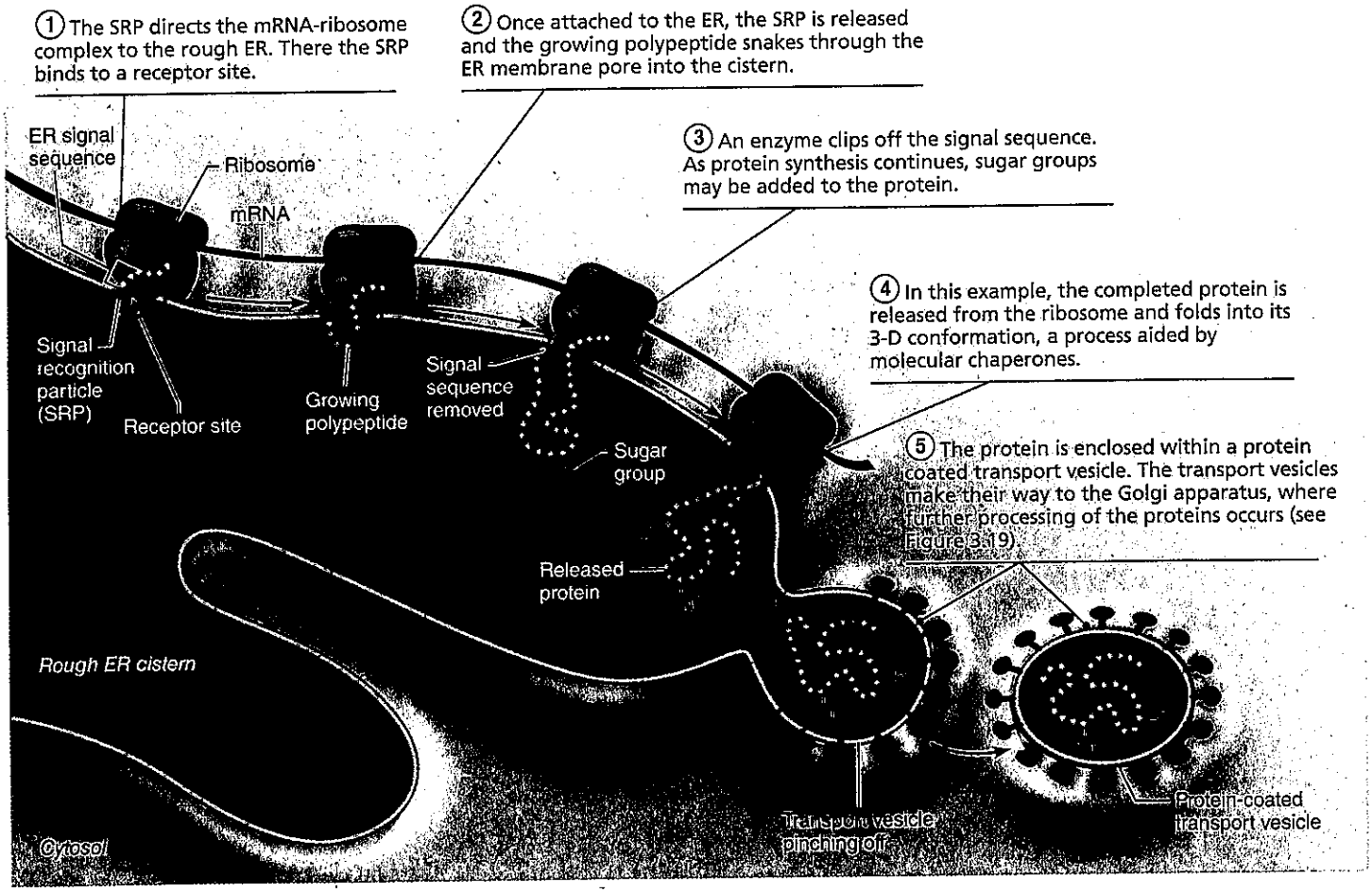


Figure 3.39 Rough ER processing of proteins. An endoplasmic reticulum (ER) signal sequence in a newly forming protein causes the signal recognition particle (SRP) to direct the mRNA-ribosome complex to the rough ER.

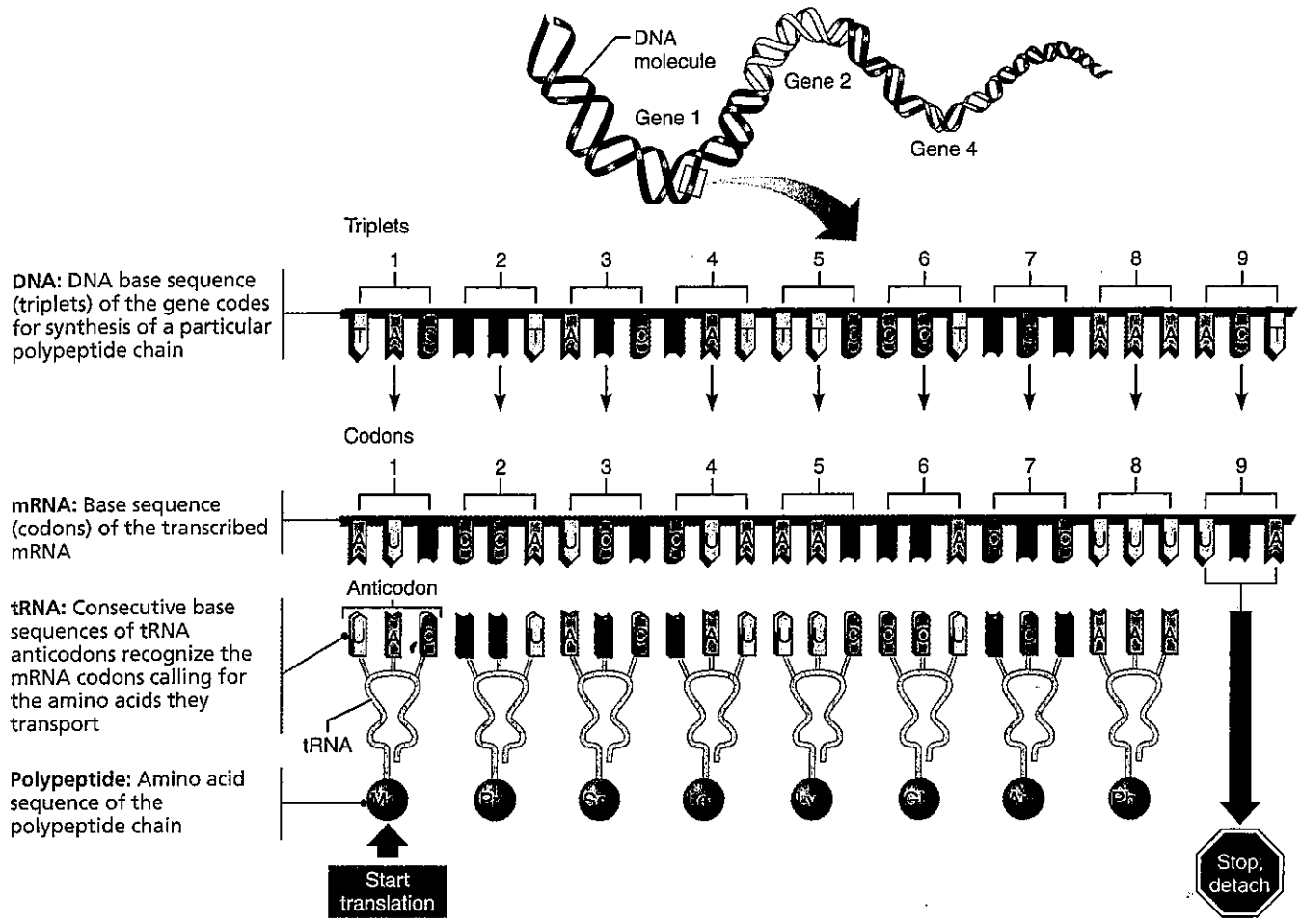


Figure 3.40 Information transfer from DNA to RNA to polypeptide. Information is transferred from the DNA of the gene to the complementary messenger RNA molecule, whose codons are then "read" (translated) by transfer RNA anticodons. Notice that the "reading" of the mRNA by tRNA anticodons reestablishes the base (triplet) sequence of the DNA genetic code (except that T is replaced by U).

☑ Check Your Understanding

29. Codons and anticodons are both three-base sequences. How do they differ?
30. How do the A, P, and E ribosomal sites differ functionally during protein synthesis?
31. What is the role of DNA in transcription?

For answers, see Appendix H.

Degradation of Organelles and Cytosolic Proteins

✓ Define autophagy and indicate its major cellular function.

✓ Describe the importance of ubiquitin-dependent degradation of soluble proteins.

The workings of the cytoplasm are complex and seemingly unending. Without some system to get rid of malfunctioning or obsolete organelles, cells would soon become gummed up with debris.

Not to worry. The process called *autophagy* ("self-eating") sweeps up bits of cytoplasm and excess organelles into double-membrane vesicles called *autophagosomes*. They are then delivered to lysosomes for digestion of the contents to amino acids, fatty acids, and the like, which the cell reuses.

Autophagy may have evolved as a response to cell starvation and it speeds up in response to several kinds of stress, such as low oxygen, high temperature, or lack of growth factors. However, autophagosomes are busy continuously. Although autophagy can lead to programmed cell death (see apoptosis, p. 110), it makes a greater contribution to cell survival and provides a fail-safe system against complete self-destruction when such a dire response is not necessary.

Autophagy is exactly what the doctor ordered for disposal of large cytoplasmic structures and protein aggregates. But lysosomal enzymes do not have access to soluble proteins that are misfolded, damaged, or unneeded and need to be disposed of. Examples of unneeded proteins include some that are used only in cell division and must be degraded at precise points in the cell cycle, and short-lived transcription factors.

So how does the cell prevent such proteins from accumulating while stopping the cytosolic enzymes from destroying virtually all soluble proteins? It seems that the cell has a different strategy for destroying such proteins.

Proteins called **ubiquitins** (u-bĭ′kwĭ-tinz) mark doomed proteins for attack (proteolysis) by attaching to them in an ATP-dependent reaction. The tagged proteins are then hydrolyzed to small peptides by soluble enzymes or by **proteasomes**, giant "waste disposal" complexes composed of protein-digesting enzymes, and the ubiquitin is recycled. Proteasome activity is critical during starvation when these complexes degrade preexisting proteins to provide amino acids for synthesis of new and needed proteins.

Extracellular Materials

✓ Name and describe the composition of extracellular materials.

Extracellular materials are any substances contributing to body mass that are found outside the cells. Classes of extracellular materials include

- *Body fluids*, mainly interstitial fluid, blood plasma, and cerebrospinal fluid. These fluids are important transport and dissolving media.
- *Cellular secretions*, such as substances that aid in digestion (intestinal and gastric fluids) and some that act as lubricants (saliva, mucus, and serous fluids).
- The *extracellular matrix*, the most abundant extracellular material. Most body cells are in contact with a jellylike substance composed of proteins and polysaccharides. Secreted by the cells, these molecules self-assemble into an organized mesh in the extracellular space, where they serve as a universal "cell glue" that helps to hold body cells together. As described in Chapter 4, the extracellular matrix is particularly abundant in connective tissues—in some cases so abundant that it (rather than living cells) accounts for the bulk of that tissue type. Depending on the structure to be formed, the extracellular matrix in connective tissue ranges from soft to rock-hard.

☑ Check Your Understanding

32. What is the importance of ubiquitin in the life of a cell?
33. What are two body fluids that inhabit the extracellular space and what role does each play in the body?

For answers, see Appendix H.

Developmental Aspects of Cells

✓ Discuss some theories of cell differentiation and aging.

✓ Indicate the value of apoptosis to the body.

We all begin life as a single cell, the fertilized egg, and all the cells of our body arise from it. Very early in development, cells begin to specialize, some becoming liver cells, some nerve cells, and so on. All our cells carry the same genes, so how can one cell become so different from another? This is a fascinating question.

Apparently, cells in various regions of the embryo are exposed to different chemical signals that channel them into specific pathways of development. When the embryo consists of just a few cells, the major signals may be nothing more than slight differences in oxygen and carbon dioxide concentrations between the more superficial and the deeper cells. But as development continues, cells release chemicals that influence development of neighboring cells by triggering processes that switch some genes "off" and others "on." Some genes are active in all cells. For example, genes for rRNA and ATP synthesis are "on" in all cells, but genes for synthesizing the enzymes needed to produce thyroxine are "on" only in cells that are going to be part of the thyroid gland. Hence, the story of cell specialization lies in the kinds of proteins made and reflects the activation of different genes in different cell types.

Cell specialization leads to *structural* variation—different organelles come to predominate in different cells. For example, muscle cells make large amounts of actin and myosin, and their cytoplasm fills with microfilaments. Liver and phagocytic cells produce more lysosomes. The development of specific and distinctive features in cells is called **cell differentiation.**

Apoptosis and Modified Rates of Cell Division

During early development, cell death and destruction are normal events. Nature takes few chances. More cells than needed are produced, and excesses are eliminated later in a type of programmed cell death called **apoptosis** (ap″o-to′sis; "falling away"). Apoptosis is particularly common in the developing nervous system. It is also responsible for "carving out" fingers and toes from their embryonic webbed precursors. This process of controlled cellular suicide also eliminates cells that are stressed, no longer needed, injured, or aged.

How does apoptosis work? In response to internal cellular damage or to some extracellular signal, mitochondrial membranes become permeable, allowing cytochrome c and other factors to leak into the cytosol. These chemicals trigger apoptosis by activating intracellular enzymes called *caspases*. The activated caspases unleash a torrent of digestive activity within the cell, destroying the cell's DNA, cytoskeleton, and so on, producing a quick, neat death. The apoptotic cell shrinks without leaking its contents into the surrounding tissue, detaches from other cells, and rounds up. Because the dying cell releases a chemical that attracts macrophages, and sprouts "eat me" signals, it is immediately phagocytized.

Most organs are well formed and functional long before birth, but the body continues to grow and enlarge by forming new cells throughout childhood and adolescence. Once we reach adult size, cell division is important mainly to replace short-lived cells and repair wounds.

During young adulthood, cell numbers remain fairly constant. However, local changes in the rate of cell division are common. For example, when a person is anemic, his or her bone marrow undergoes **hyperplasia** (hi″per-pla′ze-ah), or accelerated growth (*hyper* = over; *plas* = grow), to produce red blood cells at a faster rate. If the anemia is remedied, the excessive marrow activity ceases. **Atrophy** (at′ro-fe), a decrease in size of an organ or body tissue, can result from loss of normal stimulation or from diseases like muscular dystrophy. Muscles that lose their nerve supply atrophy and waste away, and lack of exercise leads to thinned, brittle bones.

Cell Aging

Cell aging is a complicated process with many causes, but to be perfectly frank, the precise reason an otherwise healthy person grows old and dies is still a mystery.

The *wear-and-tear theory* attributes aging to little chemical insults and formation of free radicals, both of which have cumulative effects. For example, environmental toxins such as pesticides, alcohol, and bacterial toxins may damage cell membranes, poison enzyme systems, or cause "mistakes" in DNA replication. Temporary lack of oxygen, which occurs increasingly with age as our blood vessels clog with fatty materials, accelerates rates of cell death throughout the body.

According to the *mitochondrial theory of aging*, free radicals deserve most of the blame. Most free radicals are produced in the mitochondria, because these organelles have the highest metabolic rate. This finding implies that diminished energy production by radical-damaged mitochondria, due perhaps to an increasing burden of mutations in mitochondrial DNA, weakens (and ages) cells. X rays and other types of radiation, and some chemicals, also generate huge numbers of free radicals, which can overwhelm the peroxisomal enzymes. Vitamins C and E act as antioxidants in the body and may help to absorb or defuse free radicals. With age, glucose (blood sugar) becomes party to cross-linking proteins together, a condition that severely disrupts protein function and accelerates the course of atherosclerosis.

Another theory attributes cell aging to progressive disorders in the immune system. According to this theory, cell damage results from (1) autoimmune responses, which means the immune system turns against one's own tissues, and (2) a progressive weakening of the immune response, so that the body is less able to get rid of cell-damaging pathogens.

The idea that cell aging and chronic illnesses result from inflammation (and an overactive immune system) has been kicking around since the 1800s. In the 1990s evidence did in fact emerge to link inflammation to aging. C-reactive protein, a protein that indicates acute inflammation, is elevated in heart disease and is an amazingly accurate predictor of future heart attacks. It seems that as we age, acute episodes of inflammation tend to become chronic.

Perhaps the most widely accepted theory of cell aging is the *genetic theory*, which suggests that cessation of mitosis and cell aging are "programmed into our genes." One interesting notion here is that a *telomere clock* determines the number of times a cell can divide. **Telomeres** (*telo* = end; *mer* = piece) are nonsensical strings of nucleotides that cap the ends of chromosomes and provide protection from fraying, fusing with other chromosomes, inappropriate repair, and losing important genetic information, much like plastic caps preserve the ends of shoelaces. In human telomeres, the base sequence TTAGGG is repeated a thousand times or more (like a DNA stutter). Though telomeres carry no genes, they appear to be vital for chromosomal survival, because each time DNA is replicated, 100 to 200 of the end nucleotides are lost and the telomeres get a bit shorter. When telomeres reach a certain minimum length, it is thought that the stop-division signal is given.

The idea that cell longevity depends on telomere integrity was supported by the discovery of *telomerase*, an enzyme that lengthens the previously shortened telomeres. Pegged as the "immortality enzyme," telomerase is found in germ line cells (cells that give rise to sperm and ova), but it is absent or barely detectable in other adult cell types.

☑ Check Your Understanding

34. What is apoptosis and what is its importance in the body?
35. What is the wear-and-tear theory of aging?

For answers, see Appendix H.

In this chapter we have described the structure and function of the generalized cell. One of the wonders of the cell is the disparity between its minute size and its extraordinary activity, which reflects the diversity of its organelles. The evidence for division of labor and functional specialization among organelles is inescapable. Only ribosomes synthesize proteins, while protein packaging is the bailiwick of the Golgi apparatus. Membranes compartmentalize most organelles, allowing them to work without hindering or being hindered by other cell activities, and the plasma membrane regulates molecular traffic across the cell's boundary. Now that you know what cells have in common, you are ready to explore how they differ in the various body tissues, the topic of Chapter 4.

Chapter Summary

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The Cellular Basis of Life (p. 62)

1. All living organisms are composed of cells—the basic structural and functional units of life. Cells vary widely in both shape and size.
2. The principle of complementarity states that the biochemical activity of cells reflects the operation of their organelles.
3. The generalized cell is a concept that typifies all cells. The generalized cell has three major regions—the nucleus, cytoplasm, and plasma membrane.

The Plasma Membrane: Structure (pp. 63–67)

1. The plasma membrane encloses cell contents, mediates exchanges with the extracellular environment, and plays a role in cellular communication.

The Fluid Mosaic Model (pp. 63–65)

2. The plasma membrane is a fluid bilayer of lipids (phospholipids, cholesterol, and glycolipids) within which proteins are inserted.
3. The lipids have both hydrophilic and hydrophobic regions that organize their aggregation and self-repair. The lipids form the structural part of the plasma membrane.
4. Most proteins are integral transmembrane proteins that extend entirely through the membrane. Some, appended to the integral proteins, are peripheral proteins.
5. Proteins are responsible for most specialized membrane functions: Some are enzymes, some are receptors, and others mediate membrane transport functions.

The Glycocalyx (pp. 65–66)

6. Externally facing glycoproteins contribute to the glycocalyx.

Cell Junctions (pp. 66–67)

7. Cell junctions join cells together and may aid or inhibit movement of molecules between or past cells.
8. Tight junctions are impermeable junctions. Desmosomes mechanically couple cells into a functional community. Gap junctions allow joined cells to communicate.

The Plasma Membrane: Membrane Transport (pp. 67–69)

1. The plasma membrane acts as a selectively permeable barrier. Substances move across the plasma membrane by passive processes, which depend on the kinetic energy of molecules, and by active processes, which depend on the use of cellular energy (ATP).

Passive Processes (pp. 68–72)

2. Diffusion is the movement of molecules (driven by kinetic energy) down a concentration gradient. Fat-soluble solutes can diffuse directly through the membrane by dissolving in the lipid.
3. Facilitated diffusion is the passive movement of certain solutes across the membrane either by their binding with a membrane carrier protein or by their moving through a membrane channel. As with other diffusion processes, it is driven by kinetic energy, but the carriers and channels are selective.
4. Osmosis is the diffusion of a solvent, such as water, through a selectively permeable membrane. Water diffuses through membrane channels (aquaporins) or directly through the lipid portion of the membrane from a solution of lesser osmolarity (total concentration of all solute particles) to a solution of greater osmolarity.
5. The presence of solutes unable to permeate the plasma membrane leads to changes in cell tone that may cause the cell to swell or shrink. Net osmosis ceases when the solute concentration on both sides of the plasma membrane reaches equilibrium.
6. Solutions that cause a net loss of water from cells are hypertonic. Those causing net water gain are hypotonic. Those causing neither gain nor loss of water are isotonic.

Active Processes (pp. 72–79)

7. Active transport (solute pumping) depends on a carrier protein and energy. Substances transported move against concentration or electrical gradients. In primary active transport, such as that provided by the Na^+-K^+ pump, ATP directly provides the energy.
8. In secondary active transport, the energy of an ion gradient (produced by a primary active transport process) is used to transport a substance passively. Many active transport systems are coupled, and cotransported substances move in either the same (symport) or opposite (antiport) directions across the membrane.
9. Vesicular transport also requires that energy be provided. Endocytosis brings substances into the cell, typically in protein-coated vesicles. If the substance is relatively large particles, the process is called phagocytosis. If the substance is dissolved molecules, the process is pinocytosis. Receptor-mediated endocytosis is selective: Engulfed molecules attach to receptors on the membrane before endocytosis occurs. Exocytosis, which uses SNAREs to anchor the vesicles to the plasma membrane, ejects substances (hormones, wastes, secretions) from the cell.
10. Most endocytosis (and transcytosis) is mediated by clathrin-coated vesicles. Other types of protein coating are found in caveolae and vesicles involved in vesicular trafficking. Caveolae appear to be important as sites that accumulate receptors involved in cell signaling.

The Plasma Membrane: Generation of a Resting Membrane Potential (pp. 79–80)

1. All cells in the resting stage exhibit a voltage across their membrane, called the resting membrane potential. Because of the membrane potential, both concentration and electrical gradients determine the ease of an ion's diffusion.

Selective Diffusion Establishes Membrane Potential (pp. 79–80)

2. The resting membrane potential is generated by concentration gradients of ions and the differential permeability of the plasma membrane to ions, particularly potassium ions. Sodium is in high extracellular concentration and low intracellular concentration, and the membrane is poorly permeable to it. Potassium is in high concentration in the cell and low concentration in the extracellular fluid. The membrane is more permeable to potassium than to sodium. Protein anions in the cell are too large to cross the membrane and Cl^-, the main anion in extracellular fluid, is repelled by the negative charge on the inner membrane face.

Active Transport Maintains Electrochemical Gradients (p. 80)

3. Essentially, a negative membrane potential is established when the movement of K^+ out of the cell equals K^+ movement into the cell. Na^+ movements across the membrane contribute minimally to establishing the membrane potential. The greater outward diffusion of potassium (than inward diffusion of sodium) leads to a charge separation at the membrane (inside negative). This charge separation is maintained by the operation of the sodium-potassium pump.

iP Nervous System I; Topics: Ion Channels, pp. 3, 8, 9; The Membrane Potential, pp. 1–17.

The Plasma Membrane: Cell-Environment Interactions (pp. 80–81)

1. Cells interact directly and indirectly with other cells. Indirect interactions involve extracellular chemicals carried in body fluids or forming part of the extracellular matrix.
2. Molecules of the glycocalyx are intimately involved in cell-environment interactions. Most are cell adhesion molecules or membrane receptors.
3. Activated membrane receptors act as catalysts, regulate channels, or, like G protein–linked receptors, act through second messengers such as cyclic AMP and Ca^{2+}. Ligand

binding results in changes in protein structure or function within the targeted cell.

The Cytoplasm (pp. 81–91)

1. The cytoplasm, the cellular region between the nuclear and plasma membranes, consists of the cytosol (fluid cytoplasmic environment), inclusions (nonliving nutrient stores, pigment granules, crystals, etc.), and cytoplasmic organelles.

Cytoplasmic Organelles (pp. 83–89)

2. The cytoplasm is the major functional area of the cell. These functions are mediated by organelles.
3. Mitochondria, organelles limited by a double membrane, are sites of ATP formation. Their internal enzymes carry out the oxidative reactions of cellular respiration.
4. Ribosomes, composed of two subunits containing ribosomal RNA and proteins, are the sites of protein synthesis. They may be free or attached to membranes.
5. The rough endoplasmic reticulum is a ribosome-studded membrane system. Its cisterns act as sites for protein modification. Its external face acts in phospholipid synthesis. Vesicles pinched off from the ER transport the proteins to other cell sites.
6. The smooth endoplasmic reticulum synthesizes lipid and steroid molecules. It also acts in fat metabolism and in drug detoxification. In muscle cells, it is a calcium ion depot.
7. The Golgi apparatus is a membranous system close to the nucleus that packages protein secretions for export, packages enzymes into lysosomes for cellular use, and modifies proteins destined to become part of cellular membranes.
8. Lysosomes are membranous sacs of acid hydrolases packaged by the Golgi apparatus. Sites of intracellular digestion, they degrade worn-out organelles and tissues that are no longer useful, and they release ionic calcium from bone.
9. Peroxisomes are membranous sacs containing oxidase enzymes that protect the cell from the destructive effects of free radicals and other toxic substances by converting them first to hydrogen peroxide and then water.
10. The cytoskeleton includes microtubules, intermediate filaments, and microfilaments. Microtubules organize the cytoskeleton and are important in intracellular transport. Microfilaments are important in cell motility or movement of cell parts. Motility functions involve motor proteins. Intermediate filaments help cells resist mechanical stress and connect other elements.

Cellular Extensions (pp. 89–91)

11. Centrioles organize the mitotic spindle and are the bases of cilia and flagella.
12. Microvilli are extensions of the plasma membrane that increase its surface area for absorption.

The Nucleus (pp. 91–96)

1. The nucleus is the control center of the cell. Most cells have a single nucleus. Without a nucleus, a cell cannot divide or synthesize more proteins, and is destined to die.
2. The nucleus is surrounded by the nuclear envelope, a double membrane penetrated by fairly large pores.
3. Nucleoli are nuclear sites of ribosome subunit synthesis.
4. Chromatin is a complex network of slender threads containing histone proteins and DNA. The chromatin units are called nucleosomes. When a cell begins to divide, the chromatin coils and condenses, forming chromosomes.

Cell Growth and Reproduction (pp. 96–110)

The Cell Cycle (pp. 96–99)

1. The cell cycle is the series of changes that a cell goes through from the time it is formed until it divides.
2. Interphase is the nondividing phase of the cell cycle. Interphase consists of G_1, S, and G_2 subphases. During G_1, the cell grows and centriole replication begins. During the S phase, DNA replicates. During G_2, the final preparations for division are made. Many checkpoints occur during interphase at which the cell gets the go-ahead signal to go through mitosis or is prevented from continuing to mitosis.
3. DNA replication occurs before cell division, ensuring that both daughter cells have identical genes. The DNA helix uncoils, and each DNA nucleotide strand acts as a template for the formation of a complementary strand. Base pairing provides the guide for the proper positioning of nucleotides.
4. The semiconservative replication of a DNA molecule produces two DNA molecules identical to the parent molecule, each formed of one "old" and one "new" strand.
5. Cell division, essential for body growth and repair, occurs during the M phase. Cell division consists of two distinct phases: mitosis (nuclear division) and cytokinesis (division of the cytoplasm).
6. Mitosis, consisting of prophase, metaphase, anaphase, and telophase, parcels out the replicated chromosomes to two daughter nuclei, each genetically identical to the mother nucleus. Cytokinesis, which begins late in mitosis, divides the cytoplasmic mass into two parts.
7. Cell division is stimulated by certain chemicals (including growth factors and some hormones) and increasing cell size. Lack of space and inhibitory chemicals deter cell division. Cyclin-Cdk complexes regulate cell division.

Protein Synthesis (pp. 99–105)

8. A gene is defined as a DNA segment that provides the instructions to synthesize one polypeptide chain. Since the major structural materials of the body are proteins, and all enzymes are proteins, this amply covers the synthesis of all biological molecules.
9. The base sequence of exon DNA provides the information for protein structure. Each three-base sequence (triplet) calls for a particular amino acid to be built into a polypeptide chain.
10. The RNA molecules acting in protein synthesis are synthesized on single strands of the DNA template. RNA nucleotides are joined according to base-pairing rules.
11. Instructions for making a polypeptide chain are carried from the DNA to the ribosomes via messenger RNA. Ribosomal RNA forms part of the protein synthesis sites. A transfer RNA ferries each amino acid to the ribosome and binds to a codon on the mRNA strand specifying its amino acid.
12. Protein synthesis involves (a) transcription, synthesis of a complementary mRNA, and (b) translation, "reading" of the mRNA by tRNA and peptide bonding of the amino acids into the polypeptide chain. Ribosomes coordinate translation.

Other Roles of DNA (pp. 105–109)

13. Introns and other DNA sequences encode many RNA species that may interfere with or promote the function of specific genes.

Degradation of Organelles and Cytosolic Proteins (pp. 109–110)

14. Organelles and large protein aggregates are picked up by autosomes and delivered to lysosomes for digestion. This process, autophagy, is very important for keeping the cytoplasm free of deteriorating organelles and other debris.

15. Soluble proteins that are damaged or no longer needed are targeted for destruction by attachment of ubiquitin. Cytosolic enzymes or proteasomes then degrade these proteins.

Extracellular Materials (p. 110)

1. Extracellular materials are substances found outside the cells. They include body fluids, cellular secretions, and extracellular matrix. Extracellular matrix is particularly abundant in connective tissues.

Developmental Aspects of Cells (pp. 110–111)

1. The first cell of an organism is the fertilized egg. Early in development, cell specialization begins and reflects differential gene activation.

Apoptosis and Modified Rates of Cell Division (p. 110)

2. Apoptosis is programmed cell death. Its function is to dispose of damaged or unnecessary cells.
3. During adulthood, cell numbers remain fairly constant. Cell division occurs primarily to replace lost cells.

Cell Aging (p. 111)

4. Cellular aging may reflect chemical insults, progressive disorders of immunity, or a genetically programmed decline in the rate of cell division with age.

Review Questions

Multiple Choice/Matching

(Some questions have more than one correct answer. Select the best answer or answers from the choices given.)

1. The smallest unit capable of life by itself is (a) the organ, (b) the organelle, (c) the tissue, (d) the cell, (e) the nucleus.
2. The major types of lipid found in the plasma membranes are (choose two) (a) cholesterol, (b) triglycerides, (c) phospholipids, (d) fat-soluble vitamins.
3. Membrane junctions that allow nutrients or ions to flow from cell to cell are (a) desmosomes, (b) gap junctions, (c) tight junctions, (d) all of these.
4. The term used to describe the type of solution in which cells will lose water to their environment is (a) isotonic, (b) hypertonic, (c) hypotonic, (d) catatonic.
5. Osmosis always involves (a) a selectively permeable membrane, (b) a difference in solvent concentration, (c) diffusion, (d) active transport, (e) a, b, and c.
6. A physiologist observes that the concentration of sodium inside a cell is decidedly lower than that outside the cell. Sodium diffuses easily across the plasma membrane of such cells when they are dead, but *not* when they are alive. What cellular function that is lacking in dead cells explains the difference? (a) osmosis, (b) diffusion, (c) active transport (solute pumping), (d) dialysis.
7. The solute-pumping type of active transport is accomplished by (a) exocytosis, (b) phagocytosis, (c) electrical forces in the cell membrane, (d) changes in shape and position of carrier molecules in the plasma membrane.
8. The endocytotic process in which a sampling of particulate matter is engulfed and brought into the cell is called (a) phagocytosis, (b) pinocytosis, (c) exocytosis.
9. Which is *not* true of 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.
10. The nuclear substance composed of histone proteins and DNA is (a) chromatin, (b) the nucleolus, (c) nuclear sap, or nucleoplasm, (d) nuclear pores.
11. The information sequence that determines the nature of a protein is the (a) nucleotide, (b) gene, (c) triplet, (d) codon.
12. Mutations may be caused by (a) X rays, (b) certain chemicals, (c) radiation from ionizing radioisotopes, (d) all of these.
13. The phase of mitosis during which centrioles reach the poles and chromosomes attach to the spindle is (a) anaphase, (b) metaphase, (c) prophase, (d) telophase.
14. Final preparations for cell division are made during the life cycle subphase called (a) G_1, (b) G_2, (c) M, (d) S.
15. The RNA synthesized on one of the DNA strands is (a) mRNA, (b) tRNA, (c) rRNA, (d) all of these.
16. The RNA species that travels from the nucleus to the cytoplasm carrying the coded message specifying the sequence of amino acids in the protein to be made is (a) mRNA, (b) tRNA, (c) rRNA, (d) all of these.
17. If DNA has a sequence of AAA, then a segment of mRNA synthesized on it will have a sequence of (a) TTT, (b) UUU, (c) GGG, (d) CCC.
18. A nerve cell and a lymphocyte are presumed to differ in their (a) specialized structure, (b) suppressed genes and embryonic history, (c) genetic information, (d) a and b, (e) a and c.
19. A pancreas cell makes proteins (enzymes) that it releases to the small intestine. Which of the following best describes the path of these proteins from synthesis to exocytosis at the pancreatic cell's plasma membrane (PM)? (a) Golgi → rough ER → PM, (b) smooth ER → Golgi → lysosome → PM, (c) rough ER → Golgi → PM, (d) nucleus → Golgi → PM.

Short Answer Essay Questions

20. Which organelle is responsible for a newborn having distinctive toes and fingers instead of webbed digits?
21. Explain why mitosis can be thought of as cellular immortality.
22. Contrast the roles of ER-bound ribosomes with those free in the cytosol.
23. Cells lining the trachea have whiplike motile extensions on their free surfaces. What are these extensions, what is their source, and what is their function?
24. Name the three phases of interphase and describe an activity unique to each phase.
25. Comment on the role of the sodium-potassium pump in maintaining a cell's resting membrane potential.
26. Differentiate between primary and secondary active transport processes.
27. Cell division typically yields two daughter cells, each with one nucleus. How is the occasional binucleate condition of liver cells explained?

Critical Thinking and Clinical Application Questions

1. Explain why limp celery becomes crisp and the skin of your fingertips wrinkles when placed in tap water. (The principle is exactly the same.)
2. A "red-hot" bacterial infection of the intestinal tract irritates the intestinal cells and interferes with digestion. Such a condition is often accompanied by diarrhea, which causes loss of body water. On the basis of what you have learned about osmotic water flows, explain why diarrhea may occur.
3. Two examples of chemotherapeutic drugs (drugs used to treat cancer) and their cellular actions are listed below. Explain why each drug could be fatal to a cell.
   - Vincristine (brand name Oncovin): damages the mitotic spindle
   - Doxorubicin (Adriamycin): binds to DNA and blocks mRNA synthesis
4. The normal function of one tumor suppressor gene is to prevent cells with damaged chromosomes and DNA from "progressing from G_1 to S," whereas another tumor suppressor gene 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.
5. In their anatomy lab, 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?
6. Dynein is missing from the cilia and flagella of individuals with a specific inherited disorder. These individuals have severe respiratory problems and, if males, are sterile. What is the structural connection between these two symptoms?
7. Explain why alcoholics are likely to have much more smooth ER than teetotalers.
8. Fresh water is a precious natural resource in Florida and it is said that supplies are dwindling. Desalinizing (removing salt from) ocean water has been recommended as a solution to the problem. Why shouldn't we drink salt water?

AT THE CLINIC

Related Clinical Terms

Anaplasia (an′ah-pla′ze-ah; *an* = without, not; *plas* = to grow) Abnormalities in cell structure and loss of differentiation; for example, cancer cells typically lose the appearance of the parent cells and come to resemble undifferentiated or embryonic cells.

Dysplasia (dis-pla′ze-ah; *dys* = abnormal) A change in cell size, shape, or arrangement due to chronic irritation or inflammation (infections, etc.).

Hypertrophy (hi-per′tro-fe) 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 when they are challenged to lift excessive weight; differs from hyperplasia, which is an increase in size due to an increase in cell number.

Liposomes (lip′o-sōmz) Hollow microscopic sacs formed of phospholipids that can be filled with a variety of drugs. Serve as multipurpose vehicles for drugs, genetic material, and cosmetics.

Mutation A change in DNA base sequence that may lead to incorporation of incorrect amino acids in particular positions in the resulting protein; the affected protein may remain unimpaired or may function abnormally or not at all, leading to disease.

Necrosis (nĕ-kro′sis; *necros* = death; *osis* = process) Death of a cell or group of cells due to injury or disease. Acute injury causes the cells to swell and burst, and induces the inflammatory response. (This is uncontrolled cell death, in contrast to apoptosis described in the text.)