energy because the molecules are moving down their concentration gradient in the same direction they tend to move anyway.

Active Transport

During **active transport,** ions or molecules move through the plasma membrane, accumulating either inside or outside the cell. For example, iodine collects in the cells of the thyroid gland; nutrients are completely absorbed from the gut by the cells lining the digestive tract; and sodium ions (Na^+) can be almost completely withdrawn from urine by cells lining the kidney tubules. In these instances, substances have moved to the region of higher concentration, exactly opposite to the process of diffusion. It has been estimated that up to 40% of a cell's energy supply may be used for active transport of solute across its membrane.

Both carrier proteins and an expenditure of energy are needed to transport molecules against their concentration gradient (Fig. 4.9). In this case, energy (ATP molecules) is required for the carrier to combine with the substance to be transported. Therefore, it is not surprising that cells involved primarily in active transport, such as kidney cells, have a large number of mitochondria near the membrane through which active transport is occurring.

Proteins involved in active transport are often called *pumps,* because just as a water pump uses energy to move water against the force of gravity, proteins use energy to move a substance against its concentration gradient. One type of pump that is active in all animal cells, but is especially associated with nerve and muscle cells, moves sodium ions (Na^+) to the outside of the cell and potassium ions (K^+) to the inside of the cell. These two events are linked, and the carrier protein is called a **sodium-potassium pump.** A change in carrier shape after the attachment, and again after the detachment, of a phosphate group allows the carrier to combine alternately with sodium ions and potassium ions (Fig. 4.10). The phosphate group is donated by ATP, which is broken down enzymatically by the carrier.

The passage of salt (NaCl) across a plasma membrane is of primary importance in cells. The chloride ion (Cl^-) usually crosses the plasma membrane because it is attracted by positively charged sodium ions (Na^+). First, sodium ions are pumped across a membrane, and then chloride ions simply diffuse through channels that allow their passage. As noted in Figure 4.2, the chloride ion channels malfunction in persons with cystic fibrosis, and this leads to the symptoms of this inherited (genetic) disorder.

During facilitated transport, substances follow their concentration gradient. During active transport, substances are moved against their concentration gradient.

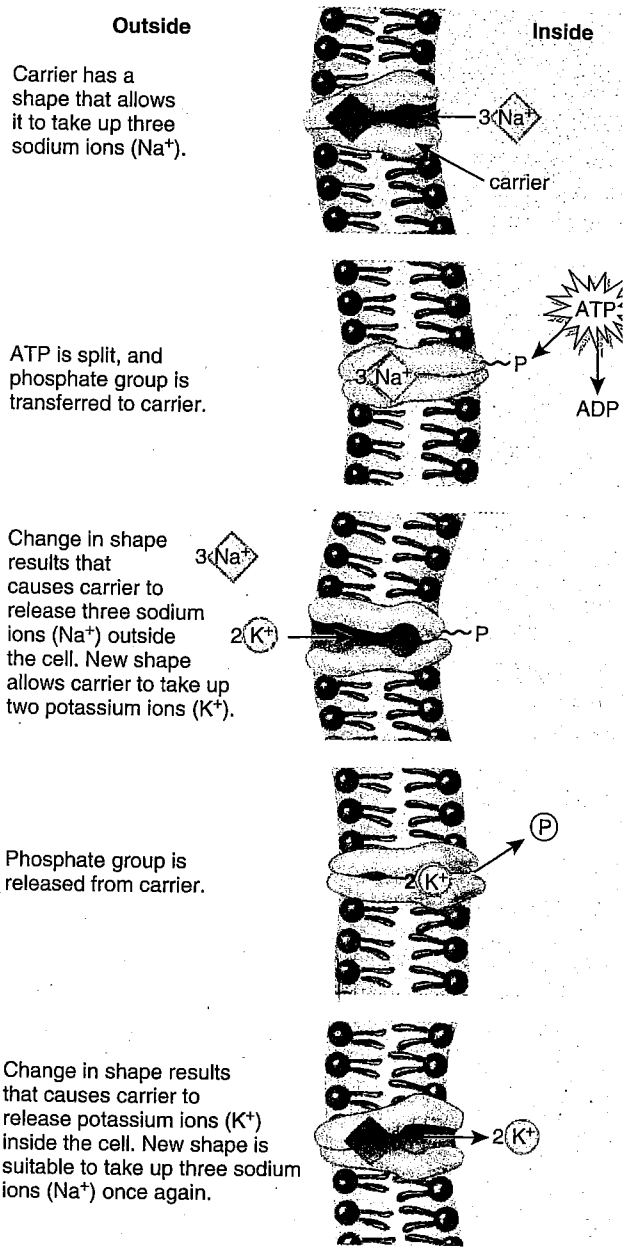


Figure 4.10 The sodium-potassium pump.
A carrier protein actively moves three sodium ions (Na^+) to the outside of the cell for every two potassium ions (K^+) pumped to tl inside of the cell. Note that chemical energy of ATP is required.

4.5 Exocytosis and Endocytosis

What about macromolecules such as polypeptides, polysaccharides, or polynucleotides, which are too large to be transported by carrier proteins? They are transported into or out of the cell by vesicle formation, thereby keeping the macromolecules contained so that they do not mix with those in the cytoplasm. Vesicle formation is an energy requiring process and therefore exocytosis and endocytosis are listed as forms of active transport in Table 4.1.

Exocytosis

During **exocytosis,** vesicles fuse with the plasma membrane as secretion occurs (Fig. 4.11). Often these vesicles have been produced by the Golgi apparatus and contain proteins. Notice that during exocytosis, the membrane of the vesicle becomes a part of the plasma membrane, which is thereby enlarged. For this reason, exocytosis occurs automatically during cell growth. The proteins released from the vesicle adhere to the cell surface or become incorporated in an extracellular matrix. Some diffuse into tissue fluid where they nourish or signal other cells.

Some cells are specialized to produce and release particular molecules. In humans, molecules transported out of the cell by exocytosis include digestive enzymes, such as those produced by the pancreatic cells, and hormones, such as growth hormone produced by anterior pituitary cells. In these cells, secretory vesicles accumulate near the plasma membrane. These vesicles release their contents only when the cell is stimulated by a signal received at the plasma membrane. A rise in blood sugar, for example, signals pancreatic cells to release the hormone insulin. This is called regulated secretion, because vesicles fuse with the plasma membrane only when it is appropriate to the needs of the body.

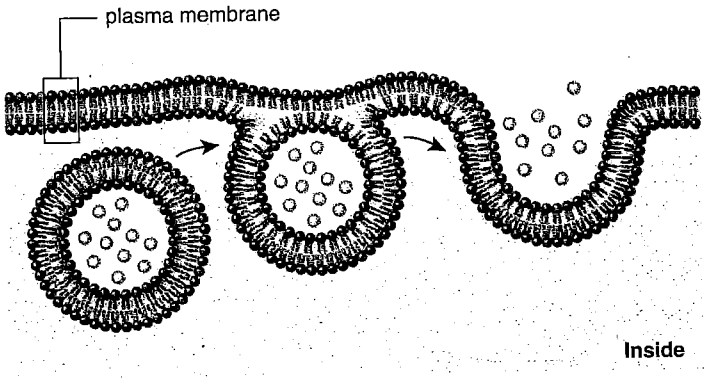


Figure 4.11 Exocytosis.
Exocytosis deposits substances on the outside of the cell and allows secretion to occur.

Endocytosis

During **endocytosis,** cells take in substances by vesicle formation. A portion of the plasma membrane invaginates to envelop the substance, and then the membrane pinches off to form an intracellular vesicle. Endocytosis occurs in one of three ways, as illustrated in Figure 4.12.

Phagocytosis

When the material taken in by endocytosis is large, such as a food particle or another cell, the process is called **phagocytosis.** Phagocytosis is common in unicellular organisms such as amoebas (Fig. 4.12*a*). It also occurs in humans. Certain types of human white blood cells are amoeboid—they are mobile like an amoeba, and are able to engulf debris such as worn-out red blood cells or bacteria. When an endocytic vesicle fuses with a lysosome, digestion occurs. We will see that this process is a necessary and preliminary step toward the development of immunity for bacterial diseases.

Pinocytosis

Pinocytosis occurs when vesicles form around a liquid or around very small particles. Blood cells, cells that line the kidney tubules or the intestinal wall, and plant root cells all use pinocytosis to ingest substances.

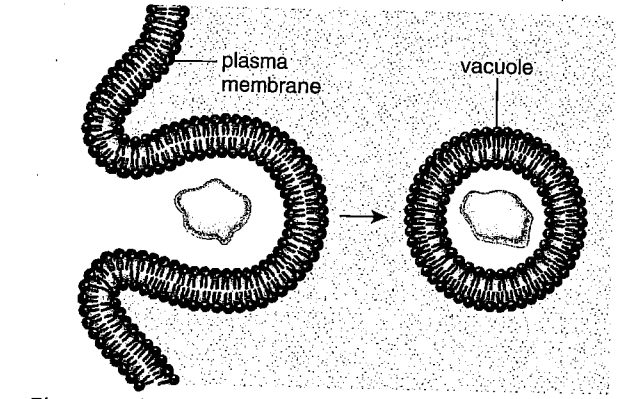
Whereas phagocytosis can be seen with the light microscope, the electron microscope must be used to observe pinocytic vesicles, which are no larger than 0.1–0.2 μm. Still, pinocytosis involves a significant amount of the plasma membrane because it occurs continuously. The loss of plasma membrane due to pinocytosis is balanced by the occurrence of exocytosis, however.

Receptor-Mediated Endocytosis

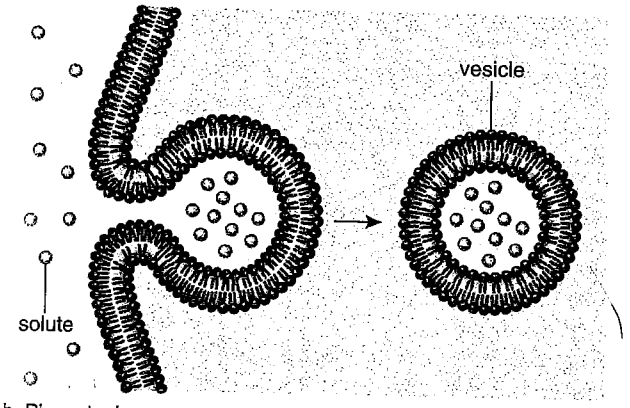
Receptor-mediated endocytosis is a form of pinocytosis that is quite specific because it uses a receptor protein shaped in such a way that a specific molecule such as a vitamin, peptide hormone, or lipoprotein can bind to it. The receptors for these substances are found at one location in the plasma membrane. This location is called a coated pit because there is a layer of protein on the cytoplasmic side of the pit. Once formed, the vesicle is uncoated and may fuse with a lysosome. If a vesicle fuses with the plasma membrane, the receptors return to their former location.

Receptor-mediated endocytosis is selective and much more efficient than ordinary pinocytosis. It is involved in uptake and also in the transfer and exchange of substances between cells. Such exchanges take place when substances move from maternal blood into fetal blood at the placenta, for example.

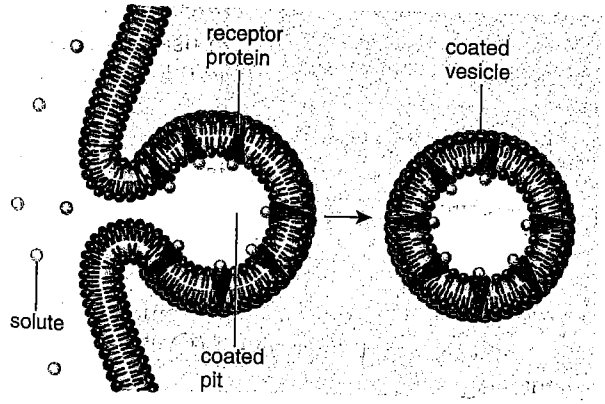
The importance of receptor-mediated endocytosis is demonstrated by a genetic disorder called familial hypercholesterolemia. Cholesterol is transported in blood by a complex of lipids and proteins called low-density lipopro-



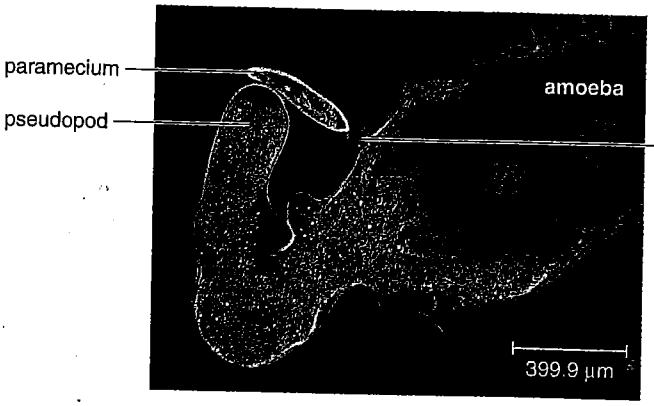
a. Phagocytosis

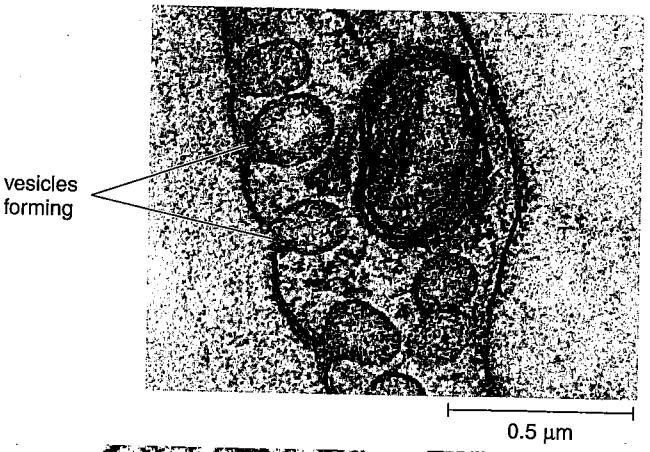


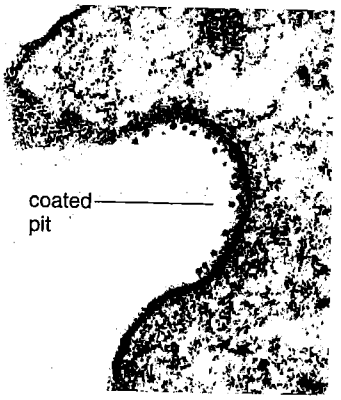
b. Pinocytosis



c. Receptor-mediated endocytosis







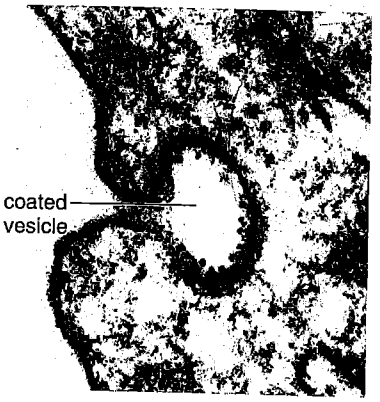


Figure 4.12 Three methods of endocytosis.
a. Phagocytosis occurs when the substance to be transported into the cell is large; amoebas ingest by phagocytosis. Digestion occurs when the resulting vacuole fuses with a lysosome. **b.** Pinocytosis occurs when a macromolecule such as a polypeptide is to be transported into the cell. The result is a vesicle (small vacuole). **c.** Receptor-mediated endocytosis is a form of pinocytosis. Molecules of substance to be taken in first bind to specific receptor proteins, which migrate to or are already in a coated pit. The vesicle that forms contains the molecules and their receptors.

tein (LDL). Ordinarily, body cells take up LDL when LDL receptors gather in a coated pit. In these individuals, the LDL receptor is unable to properly bind to the coated pit, and their cells are unable to take up cholesterol. Instead, cholesterol accumulates in the walls of arterial blood vessels, leading to high blood pressure, occluded (blocked) arteries, and heart attacks.

Substances are secreted from a cell by exocytosis. Substances enter a cell by endocytosis. Receptor-mediated endocytosis allows cells to take up specific kinds of molecules and then process them within the cell.