Molecules enter the cell through either energy-independent or energy-dependent mechanisms. The two primary examples of energy-independent uptake are *passive diffusion* and *facilitated diffusion*. Energy-dependent uptake mechanisms include *active transport* and *group translocation*.

In passive diffusion, molecules move down a concentration gradient (from high to low concentration) that is thermodynamically favorable. Consequently,

$$J_A = K_p(C_{AE} - C_{AI}) \tag{4.1}$$

where J_A is the flux of species A across the membrane (mol/cm^2 – s), K_p is the permeability (cm/s), C_{AE} is the extracellular concentration of species A (mol/cm^3), and C_{AI} is the intracellular concentration. The cytoplasmic membrane consists of a lipid core with perhaps very small pores. For charged or large molecules, the value K_p is very low and the flow of material across the membrane is negligible. The cellular uptake of water and oxygen appears to be due to passive diffusion. Furthermore, lipids or other highly hydrophobic compounds have relatively high diffusivities (10^{-8} cm^2/s) in cellular membranes, and passive diffusion can be a mechanism of quantitative importance in their transport.

With facilitated transport, a carrier molecule (protein) can combine specifically and reversibly with the molecule of interest. The carrier protein is considered embedded in the membrane. By mechanisms that are not yet understood, the carrier protein, after binding the target molecule, undergoes conformational changes, which result in release of the molecule on the intracellular side of the membrane. The carrier can bind to the target molecule on the intracellular side of the membrane, resulting in the efflux or exit of the molecule from the cell. Thus, the net flux of a molecule depends on its concentration gradient.

The carrier protein effectively increases the solubility of the target molecule in the membrane. Because the binding of the molecule to the carrier protein is saturable (just as the active sites in the enzyme solution can be saturated), the flux rate of the target molecule into the cell depends on concentration differently than indicated in eq. 4.1. A simple equation to represent uptake by facilitated transport is

$$J_A = J_{A\ \mathrm{MAX}}\left[\frac{C_{AE}}{K_{MT} + C_{AE}} - \frac{C_{AI}}{K_{MT} + C_{AI}}\right] \tag{4.2}$$

where K_{MT} is related to the binding affinity of the substrate (mol/cm^3) and $J_{A\ \mathrm{MAX}}$ is the maximum flux rate of A (mol/cm^2–s). When $C_{AE} > C_{AI}$, the net flux will be into the cell. If $C_{AI} > C_{AE}$, there will be a net efflux of A from the cell. The transport is down a concentration gradient and is thermodynamically favorable. Facilitated transport of sugars and other low-molecular-weight organic compounds is common in eucaryotic cells, but infrequent in procaryotes. However, the uptake of glycerol in enteric bacteria (such as *E. coli*) is a good example of facilitated transport.

Active transport is similar to facilitated transport in that proteins embedded in the cellular membrane are necessary components. The primary difference is that active transport occurs *against a concentration gradient*. The intracellular concentration of a molecule may be a hundredfold or more greater than the extracellular concentration. The movement of a molecule up a concentration gradient is thermodynamically unfavorable and will not occur spontaneously; energy must be supplied. In active transport, several energy sources are possible: (1) the electrostatic or pH gradients of the proton-motive force,