and (2) secondary gradients (for example, of Na^+ or other ions) derived from the proton-motive force by other active transport systems and by the hydrolysis of ATP.

The *proton-motive force* results from the extrusion of hydrogen as protons. The respiratory system of cells (see Section 5.4) is configured to ensure the formation of such gradients. Hydrogen atoms, removed from hydrogen carriers (most commonly NADH) on the inside of the membrane, are carried to the outside of the membrane, while the electrons removed from these hydrogen atoms return to the cytoplasmic side of the membrane. These electrons are passed to a final electron acceptor, such as O_2. When O_2 is reduced, it combines with H^+ from the cytoplasm, causing the net formation of OH^- on the inside. Because the flow of H^+ and OH^- across the cellular membrane by passive diffusion is negligible, the concentration of chemical species cannot equilibrate. This process generates a pH gradient and an electrical potential across the cell. The inside of the cell is alkaline compared to the extracellular compartment. The cytoplasmic side of the membrane is electrically negative, and the outside is electrically positive. The proton-motive force is essential to the transport of many species across the membrane, and any defect in the cellular membrane that allows free movement of H^+ and OH^- across the cell boundary can collapse the proton-motive force and lead to cell death.

Some molecules are actively transported into the cell without coupling to the ion gradients generated by the proton-motive force. By a mechanism that is not fully understood, the hydrolysis of ATP to release phosphate bond energy is utilized directly in transport (e.g., the transport of maltose in *E. coli*).
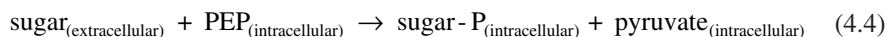
For these mechanisms of active transport, irrespective of energy source, we can write an equation analogous to Michaelis–Menten kinetics to describe uptake:

$$J_A = J_{A\ MAX}\ \frac{C_{AE}}{K_{MT} + C_{AE}} \qquad (4.3)$$

The use of eq. 4.3 is meaningful only when the cell is in an energy-sufficient state.

Another energy-dependent approach to the uptake of nutrients is group translocation. The key factor here is the chemical modification of the substrate during the process of transport. The best-studied system of this type is the *phosphotransferase system*. This system is important in the uptake of many sugars in bacteria. The biological system itself is complex, consisting of four separate phosphate-carrying proteins. The source of energy is phosphoenolpyruvate (PEP).

Effectively, the process can be represented by:

$$\text{sugar}_{(extracellular)} + \text{PEP}_{(intracellular)} \rightarrow \text{sugar-P}_{(intracellular)} + \text{pyruvate}_{(intracellular)} \qquad (4.4)$$

By converting the sugar to the phosphorylated form, the sugar is trapped inside the cell. The asymmetric nature of the cellular membrane and this process make the process essentially irreversible. Because the phosphorylation of sugars is a key step in their metabolism, nutrient uptake of these compounds by group translocation is energetically preferable to active transport. In active transport, energy would be expended to move the unmodified substrate into the cell, and then further energy would be expended to phosphorylate it.

Certainly, the control of nutrient uptake is a critical cellular interface with its extracellular environment. In some cases, however, cells can sense their external environment without the direct uptake of nutrients.