15.3: Membrane Transport with Selective Permeability

Transport across the membrane

Design challenge problem and subproblems

*General Problem:* The cell membrane must simultaneously act as a barrier between "IN" and "OUT" and control specifically which substances enter and leave the cell and how quickly and efficiently they do so.

*Subproblems:* The chemical properties of molecules that must enter and leave the cell are highly variable. Some subproblems associated with this are: (a) Large and small molecules or collections of molecules must be able to pass across the membrane. (b) Both hydrophobic and hydrophilic substances must have access to transport. (c) Substances must be able to cross the membrane with and against concentration gradients. (d) Some molecules look very similar (e.g. Na\(^+\) and K\(^+\)) but transport mechanisms must still be able to distinguish between them.

Energy story perspective

Transport across a membrane can be considered from an energy story perspective; it is a process after all. For instance, at the beginning of the process a generic substance X may be either on the inside or outside of the cell. At the end of the process, the substance will be on the opposite side from which it started.

\[ \text{e.g. } X_{(\text{in})} \rightarrow X_{(\text{out})}, \]

where in and out refer to inside the cell and outside the cell, respectively.
At the beginning the matter in the system might be a very complicated collection of molecules inside and outside of the cell but with one molecule of X more inside the cell than out. At the end, there is one more molecule of X on the outside of the cell and one less on the inside. The energy in the system at the beginning is stored largely in the molecular structures and their motions and in electrical and chemical concentration imbalances across the cell membrane. The transport of X out of the cell will not change the energies of the molecular structures significantly but it will change the energy associated with the imbalance of concentration and or charge across the membrane. That is the transport will, like all other reactions, be either exergonic or endergonic. Finally, some mechanism or sets of mechanisms of transport will need to be described.

Selective permeability

One of the great wonders of the cell membrane is its ability to regulate the concentration of substances inside the cell. These substances include: ions such as Ca$^{2+}$, Na$^{+}$, K$^{+}$, and Cl$^{-}$; nutrients including sugars, fatty acids, and amino acids; and waste products, particularly carbon dioxide (CO$_2$), which must leave the cell.

The membrane’s lipid bilayer structure provides the first level of control. The phospholipids are tightly packed, and the membrane has a hydrophobic interior. This structure alone creates what is known as a selectively permeable barrier, one that only allows substances meeting certain physical criteria to pass through it. In the case of the cell membrane, only relatively small, nonpolar materials can move through the lipid bilayer at biologically relevant rates (remember, the lipid tails of the membrane are nonpolar).

Selective permeability of the cell membrane refers to its ability to differentiate between different types of molecules, only allowing some molecules through while blocking others. Some of this selective property stems from the intrinsic diffusion rates for different molecules across a membrane. A second factor affecting the relative rates of movement of various substances across a biological membrane is activity of various protein-based membrane transporters, both passive and active, that will be discussed in more detail in subsequent sections. First, we take on the notion of intrinsic rates of diffusion across the membrane.

Relative permeability

The fact that different substances might cross a biological membrane at different rates should be relatively intuitive. There are differences in the mosaic composition of membranes in biology and differences in the sizes, flexibility, and chemical properties of molecules so it stands to reason that the permeability rates vary. It is a complicated landscape. The permeability of a substance across a biological membrane can be measured experimentally and the rate of movement across a membrane can be reported in what are known as membrane permeability coefficients.

Membrane permeability coefficients

Below, a variety of compounds are plotted with respect to their membrane permeability coefficients (MPC) as measured against a simple biochemical approximation of a real biological membrane. The reported permeability coefficient for this system is the rate at which simple diffusion through a membrane occurs and is reported in units of centimeters per second (cm/s). The permeability coefficient is proportional to the partition coefficient and is inversely proportional to the...
membrane thickness.

It is important that you are able to read and interpret the diagram below. The larger the coefficient, the more permeable the membrane is to the solute. For example, hexanoic acid is very permeable, a MPC of 0.9; acetic acid, water, and ethanol have MPCs between 0.01 and 0.001, and they are less permeable than hexanoic acid. Where as ions, such as sodium (Na$^+$), have an MPC of $10^{-12}$, and cross the membrane at a comparatively slow rate.

![Figure 1. Membrane permeability coefficient diagram. The diagram was taken from BioWiki and can be found at http://biowiki.ucdavis.edu/Biochemistry...e_Permeability.](image)

While there are certain trends or chemical properties that can be roughly associated with different compound permeability (small thing go through "fast", big things "slowly", charged things not at all etc.), we caution against over-
generalizing. The molecular determinants of membrane permeability are complicated and involve numerous factors including: the specific composition of the membrane, temperature, ionic composition, hydration; the chemical properties of the solute; the potential chemical interactions between the solute in solution and in the membrane; the dielectric properties of materials; and the energy trade-offs associated with moving substances into and out of various environments. So, in this class, rather than try to apply "rules" and try to develop too many arbitrary "cut-offs", we will strive to develop a general sense of some properties that can influence permeability and leave the assignment of absolute permeability to experimentally reported rates. In addition, we will also try to minimize the use of vocabulary that depends on a frame of reference. For instance, saying that compound A diffuses "quickly" or "slowly" across a bilayer only means something if the terms "quickly" or "slowly" are numerically defined or the biological context is understood.

**Energetics of transport**

All substances that move through the membrane do so by one of two general methods, which are categorized based on whether or not the transport process is exergonic or endergonic. **Passive transport** is the exergonic movement of substances across the membrane. In contrast, **active transport** is the endergonic movement of substances across the membrane that is coupled to an exergonic reaction.

**Passive transport**

**Passive transport** does not require the cell to expend energy. In passive transport, substances move from an area of higher concentration to an area of lower concentration, down their **concentration gradient**. Depending on the chemical nature of the substance, different processes may be associated with passive transport.

**Diffusion**

**Diffusion** is a passive process of transport. A single substance tends to move from an area of high concentration to an area of low concentration until the concentration is equal across a space. You are familiar with diffusion of substances through the air. For example, think about someone opening a bottle of ammonia in a room filled with people. The ammonia gas is at its highest concentration in the bottle; its lowest concentration is at the edges of the room. The ammonia vapor will diffuse, or spread away, from the bottle; gradually, more and more people will smell the ammonia as it spreads. Materials move within the cell’s cytosol by diffusion, and certain materials move through the plasma membrane by diffusion.
Figure 2.
Diffusion through a permeable membrane moves a substance from an area of high concentration (extracellular fluid, in this case) down its concentration gradient (into the cytoplasm). Each separate substance in a medium, such as the extracellular fluid, has its own concentration gradient, independent of the concentration gradients of other materials. In addition,
Factors that affect diffusion

If unconstrained, molecules will move through and explore space randomly at a rate that depends on their size, their shape, their environment, and their thermal energy. This type of movement underlies the diffusive movement of molecules through whatever medium they are in. The absence of a concentration gradient does not mean that this movement will stop, just that there may be no net movement of the number of molecules from one area to another, a condition known as dynamic equilibrium.

Factors influencing diffusion include:

- Extent of the concentration gradient: The greater the difference in concentration, the more rapid the diffusion. The closer the distribution of the material gets to equilibrium, the slower the rate of diffusion becomes.
- Shape, size and mass of the molecules diffusing: Large and heavier molecules move more slowly; therefore, they diffuse more slowly. The reverse is typically true for smaller, lighter molecules.
- Temperature: Higher temperatures increase the energy and therefore the movement of the molecules, increasing the rate of diffusion. Lower temperatures decrease the energy of the molecules, thus decreasing the rate of diffusion.
• **Solvent density:** As the density of a solvent increases, the rate of diffusion decreases. The molecules slow down because they have a more difficult time getting through the denser medium. If the medium is less dense, rates of diffusion increase. Since cells primarily use diffusion to move materials within the cytoplasm, any increase in the cytoplasm's density will decrease the rate at which materials move in the cytoplasm.

• **Solubility:** As discussed earlier, nonpolar or lipid-soluble materials pass through plasma membranes more easily than polar materials, allowing a faster rate of diffusion.

• **Surface area and thickness of the plasma membrane:** Increased surface area increases the rate of diffusion, whereas a thicker membrane reduces it.

• **Distance traveled:** The greater the distance that a substance must travel, the slower the rate of diffusion. This places an upper limitation on cell size. A large, spherical cell will die because nutrients or waste cannot reach or leave the center of the cell, respectively. Therefore, cells must either be small in size, as in the case of many prokaryotes, or be flattened, as with many single-celled eukaryotes.

### Facilitated transport

In **facilitated transport**, also called facilitated diffusion, materials diffuse across the plasma membrane with the help of membrane proteins. A concentration gradient exists that allows these materials to diffuse into or out of the cell without expending cellular energy. In the case that the materials are ions or polar molecules (compounds that are repelled by the hydrophobic parts of the cell membrane), facilitated transport proteins help shield these materials from the repulsive force of the membrane, allowing them to diffuse into the cell.

Note: possible discussion

Compare and contrast passive diffusion and facilitated diffusion.

### Channels

The integral proteins involved in facilitated transport are collectively referred to as **transport proteins**, and they function as either channels for the material or carriers. In both cases, they are transmembrane proteins. Different channel proteins have different transport properties. Some have evolved to have very high specificity for the substance that is being transported while others transport a variety of molecules sharing some common characteristic(s). The interior "passageway" of **channel proteins** have evolved to provide a low energetic barrier for transport of substances across the membrane through the complementary arrangement of amino acid functional groups (of both backbone and side-chains). Passage through the channel allows polar compounds to avoid the nonpolar central layer of the plasma membrane that would otherwise slow or prevent their entry into the cell. While at any one time significant amounts of water crosses the membrane both in and out, the rate of individual water molecule transport may not be fast enough to adapt to changing environmental conditions. For such cases Nature has evolved a special class of membrane proteins called **aquaporins** that allow water to pass through the membrane at a very high rate.
Facilitated transport moves substances down their concentration gradients. They may cross the plasma membrane with the aid of channel proteins. (credit: modification of work by Mariana Ruiz Villareal)

Channel proteins are either open at all times or they are “gated.” The latter controls the opening of the channel. Various mechanisms may be involved in the gating mechanism. For instance, the attachment of a specific ion or small molecule...
to the channel protein may trigger opening. Changes in local membrane "stress" or changes in voltage across the membrane may also be triggers to open or close a channel.

Different organisms and tissues in multicellular species express different sets of channel proteins in their membranes depending on the environments they live in or specialized function they play in an organisms. This provides each type of cell with a unique membrane permeability profile that is evolved to complement its "needs" (note the anthropomorphism). For example, in some tissues, sodium and chloride ions pass freely through open channels, whereas in other tissues a gate must be opened to allow passage. This occurs in the kidney, where both forms of channels are found in different parts of the renal tubules. Cells involved in the transmission of electrical impulses, such as nerve and muscle cells, have gated channels for sodium, potassium, and calcium in their membranes. Opening and closing of these channels changes the relative concentrations on opposing sides of the membrane of these ions, resulting a change in electrical potential across the membrane that lead to message propagation in the case of nerve cells or in muscle contraction in the case of muscle cells.

Carrier proteins

Another type of protein embedded in the plasma membrane is a carrier protein. This aptly named protein binds a substance and, in doing so, triggers a change of its own shape, moving the bound molecule from the outside of the cell to its interior; depending on the gradient, the material may move in the opposite direction. Carrier proteins are typically specific for a single substance. This selectivity adds to the overall selectivity of the plasma membrane. The molecular-scale mechanism of function for these proteins remains poorly understood.
Figure 4.

Some substances are able to move down their concentration gradient across the plasma membrane with the aid of carrier proteins. Carrier proteins change shape as they move molecules across the membrane. (credit: modification of work by Mariana Ruiz Villareal)
Carrier protein play an important role in the function of kidneys. Glucose, water, salts, ions, and amino acids needed by the body are filtered in one part of the kidney. This filtrate, which includes glucose, is then reabsorbed in another part of the kidney with the help of carrier proteins. Because there are only a finite number of carrier proteins for glucose, if more glucose is present in the filtrate than the proteins can handle, the excess is not reabsorbed and it is excreted from the body in the urine. In a diabetic individual, this is described as “spilling glucose into the urine.” A different group of carrier proteins called glucose transport proteins, or GLUTs, are involved in transporting glucose and other hexose sugars through plasma membranes within the body.

Channel and carrier proteins transport material at different rates. Channel proteins transport much more quickly than do carrier proteins. Channel proteins facilitate diffusion at a rate of tens of millions of molecules per second, whereas carrier proteins work at a rate of a thousand to a million molecules per second.

## Active transport

**Active transport** mechanisms require the use of the cell’s energy, usually in the form of adenosine triphosphate (ATP). If a substance must move into the cell against its concentration gradient—that is, if the concentration of the substance inside the cell is greater than its concentration in the extracellular fluid (and vice versa)—the cell must use energy to move the substance. Some active transport mechanisms move small-molecular weight materials, such as ions, through the membrane. Other mechanisms transport much larger molecules.

### Moving against a gradient

To move substances against a concentration or electrochemical gradient, the cell must use energy. This energy is harvested from ATP generated through the cell’s metabolism. Active transport mechanisms, collectively called pumps, work against electrochemical gradients. Small substances constantly pass through plasma membranes. Active transport maintains concentrations of ions and other substances needed by living cells in the face of these passive movements. Much of a cell’s supply of metabolic energy may be spent maintaining these processes. (Most of a red blood cell’s metabolic energy is used to maintain the imbalance between exterior and interior sodium and potassium levels required by the cell.) Because active transport mechanisms depend on a cell’s metabolism for energy, they are sensitive to many metabolic poisons that interfere with the supply of ATP.

Two mechanisms exist for the transport of small-molecular weight material and small molecules. **Primary active transport** moves ions across a membrane and creates a difference in charge across that membrane, which is directly dependent on ATP. **Secondary active transport** describes the movement of material that is due to the electrochemical gradient established by primary active transport that does not directly require ATP.

### Carrier proteins for active transport

An important membrane adaption for active transport is the presence of specific carrier proteins or pumps to facilitate movement: there are three types of these proteins or transporters. A uniporter carries one specific ion or molecule. A symporter carries two different ions or molecules, both in the same direction. An antiporter also carries two different ions or molecules, but in different directions. All of these transporters can also transport small, uncharged organic molecules like glucose. These three types of carrier proteins are also found in facilitated diffusion, but they do not require ATP to work in that process. Some examples of pumps for active transport are Na⁺-K⁺ ATPase, which carries...
sodium and potassium ions, and $\text{H}^+\text{-K}^+$ ATPase, which carries hydrogen and potassium ions. Both of these are antiporter carrier proteins. Two other carrier proteins are $\text{Ca}^{2+}$ ATPase and $\text{H}^+$ ATPase, which carry only calcium and only hydrogen ions, respectively. Both are pumps.
Primary active transport

In primary active transport, the energy is often - though not exclusively - derived directly from the hydrolysis of ATP. Often, primary active transport, such as that shown below, which functions to transport sodium and potassium ions allows secondary active transport to occur (discussed in the section below). The second transport method is still considered active because it depends on the use of energy from the primary transport.
One of the most important pumps in animal cells is the sodium-potassium pump (Na\(^+\)-K\(^+\) ATPase), which maintains the electrochemical gradient (and the correct concentrations of Na\(^+\) and K\(^+\)) in living cells. The sodium-potassium pump moves K\(^+\) into the cell while moving Na\(^+\) out at the same time, at a ratio of three Na\(^+\) for every two K\(^+\) ions moved in. The Na\(^+\)-K\(^+\)ATPase exists in two forms depending on its orientation to the interior or exterior of the cell and its affinity for either sodium or potassium ions. The process consists of the following six steps.

1. With the enzyme oriented towards the interior of the cell, the carrier has a high affinity for sodium ions. Three ions bind to the protein.
2. ATP is hydrolyzed by the protein carrier and a low-energy phosphate group attaches to it.
3. As a result, the carrier changes shape and re-orients itself towards the exterior of the membrane. The protein’s affinity for sodium decreases and the three sodium ions leave the carrier.
4. The shape change increases the carrier’s affinity for potassium ions, and two such ions attach to the protein. Subsequently, the low-energy phosphate group detaches from the carrier.
5. With the phosphate group removed and potassium ions attached, the carrier protein repositions itself towards the interior of the cell.
6. The carrier protein, in its new configuration, has a decreased affinity for potassium, and the two ions are released into the cytoplasm. The protein now has a higher affinity for sodium ions, and the process starts again.

Several things have happened as a result of this process. At this point, there are more sodium ions outside of the cell than inside and more potassium ions inside than out. For every three ions of sodium that move out, two ions of potassium move in. This results in the interior being slightly more negative relative to the exterior. This difference in charge is important in creating the conditions necessary for the secondary process. The sodium-potassium pump is, therefore, an **electrogenic pump** (a pump that creates a charge imbalance), creating an electrical imbalance across the membrane and contributing to the membrane potential.

**Link to learning**

Visit the [site](https://bio.libretexts.org/Courses/University_of_California_Davis/BIS_2A%3A_Introductory_Biology_(Easlon)/Readings/15.3…) to see a simulation of active transport in a sodium-potassium ATPase.

**Secondary active transport (co-transport)**

Secondary active transport brings sodium ions, and possibly other compounds, into the cell. As sodium ion concentrations build outside of the plasma membrane because of the action of the primary active transport process, an electrochemical gradient is created. If a channel protein exists and is open, the sodium ions will be pulled through the membrane. This movement is used to transport other substances that can attach themselves to the transport protein through the membrane. Many amino acids, as well as glucose, enter a cell this way. This secondary process is also used to store high energy hydrogen ions in the mitochondria of plant and animal cells for the production of ATP. The potential energy that accumulates in the stored hydrogen ions is translated into kinetic energy as the ions surge through the channel protein ATP synthase, and that energy is used to convert ADP into ATP.
An electrochemical gradient, created by primary active transport, can move other substances against their concentration gradients, a process called co-transport or secondary active transport. (credit: modification of work by Mariana Ruiz Villarreal)

### Osmosis

Osmosis is the movement of water through a semipermeable membrane according to the concentration gradient of water across the membrane, which is inversely proportional to the concentration of solutes. While diffusion transports material across membranes and within cells, osmosis transports only water across a membrane and the membrane limits the diffusion of solutes in the water. Not surprisingly, the aquaporins that facilitate water movement play a large role in osmosis, most prominently in red blood cells and the membranes of kidney tubules.

### Mechanism

Osmosis is a special case of diffusion. Water, like other substances, moves from an area of high concentration to one of low concentration. An obvious question is what makes water move at all? Imagine a beaker with a semipermeable membrane...
membrane separating the two sides or halves. On both sides of the membrane the water level is the same, but there are different concentrations of a dissolved substance, or **solute**, that cannot cross the membrane (otherwise the concentrations on each side would be balanced by the solute crossing the membrane). If the volume of the solution on both sides of the membrane is the same, but the concentrations of solute are different, then there are different amounts of water, the solvent, on either side of the membrane.
Figure 8.
In osmosis, water always moves from an area of higher water concentration to one of lower concentration. In the diagram shown, the solute cannot pass through the selectively permeable membrane, but the water can.

To illustrate this, imagine two full glasses of water. One has a single teaspoon of sugar in it, whereas the second one contains one-quarter cup of sugar. If the total volume of the solutions in both cups is the same, which cup contains more water? Because the large amount of sugar in the second cup takes up much more space than the teaspoon of sugar in the first cup, the first cup has more water in it.

Returning to the beaker example, recall that it has a mixture of solutes on either side of the membrane. A principle of diffusion is that the molecules move around and will spread evenly throughout the medium if they can. However, only the material capable of getting through the membrane will diffuse through it. In this example, the solute cannot diffuse through the membrane, but the water can. Water has a concentration gradient in this system. Thus, water will diffuse down its concentration gradient, crossing the membrane to the side where it is less concentrated. This diffusion of water through the membrane—osmosis—will continue until the concentration gradient of water goes to zero or until the hydrostatic pressure of the water balances the osmotic pressure. Osmosis proceeds constantly in living systems.
**Tonicity**

*Tonicity* describes how an extracellular solution can change the volume of a cell by affecting osmosis. A solution's tonicity often directly correlates with the osmolarity of the solution. *Osmolarity* describes the total solute concentration of the solution. A solution with low osmolarity has a greater number of water molecules relative to the number of solute particles; a solution with high osmolarity has fewer water molecules with respect to solute particles. In a situation in which solutions of two different osmolarities are separated by a membrane permeable to water, though not to the solute, water will move from the side of the membrane with lower osmolarity (and more water) to the side with higher osmolarity (and less water). This effect makes sense if you remember that the solute cannot move across the membrane, and thus the only component in the system that can move—the water—moves along its own concentration gradient. An important distinction that concerns living systems is that osmolarity measures the number of particles (which may be molecules) in a solution. Therefore, a solution that is cloudy with cells may have a lower osmolarity than a solution that is clear if the second solution contains more dissolved molecules than there are cells.

**Hypotonic solutions**

Three terms—hypotonic, isotonic, and hypertonic—are used to relate the osmolarity of a cell to the osmolarity of the extracellular fluid that contains the cells. In a hypotonic situation, the extracellular fluid has lower osmolarity than the fluid inside the cell, and water enters the cell (in living systems, the point of reference is always the cytoplasm, so the prefix hypo- means that the extracellular fluid has a lower concentration of solutes, or a lower osmolarity, than the cell cytoplasm). It also means that the extracellular fluid has a higher concentration of water in the solution than does the cell. In this situation, water will follow its concentration gradient and enter the cell.

**Hypertonic solutions**

As for a hypertonic solution, the prefix hyper- refers to the extracellular fluid having a higher osmolarity than the cell’s cytoplasm; therefore, the fluid contains less water than the cell does. Because the cell has a relatively higher concentration of water, water will leave the cell.

**Isotonic solutions**

In an isotonic solution, the extracellular fluid has the same osmolarity as the cell. If the osmolarity of the cell matches that of the extracellular fluid, there will be no net movement of water into or out of the cell, although water will still move in and out. Blood cells and plant cells in hypertonic, isotonic, and hypotonic solutions take on characteristic appearances.
A doctor injects a patient with what the doctor thinks is an isotonic saline solution. The patient dies, and an autopsy reveals that many red blood cells have been destroyed. Do you think the solution the doctor injected was really isotonic?

**Tonicity in living systems**

In a hypotonic environment, water enters a cell, and the cell swells. In an isotonic condition, the relative concentrations of solute and solvent are equal on both sides of the membrane. There is no net water movement; therefore, there is no...
change in the size of the cell. In a hypertonic solution, water leaves a cell and the cell shrinks. If either the hypo- or hyper- condition goes to excess, the cell’s functions become compromised, and the cell may be destroyed.

A red blood cell will burst, or lyse, when it swells beyond the plasma membrane’s capability to expand. Remember, the membrane resembles a mosaic, with discrete spaces between the molecules composing it. If the cell swells, and the spaces between the lipids and proteins become too large, the cell will break apart.

In contrast, when excessive amounts of water leave a red blood cell, the cell shrinks, or crenates. This has the effect of concentrating the solutes left in the cell, making the cytosol denser and interfering with diffusion within the cell. The cell’s ability to function will be compromised and may also result in the death of the cell.

Various living things have ways of controlling the effects of osmosis—a mechanism called osmoregulation. Some organisms, such as plants, fungi, bacteria, and some protists, have cell walls that surround the plasma membrane and prevent cell lysis in a hypotonic solution. The plasma membrane can only expand to the limit of the cell wall, so the cell will not lyse. In fact, the cytoplasm in plants is always slightly hypertonic to the cellular environment, and water will always enter a cell if water is available. This inflow of water produces turgor pressure, which stiffens the cell walls of the plant. In nonwoody plants, turgor pressure supports the plant. Conversely, if the plant is not watered, the extracellular fluid will become hypertonic, causing water to leave the cell. In this condition, the cell does not shrink because the cell wall is not flexible. However, the cell membrane detaches from the wall and constricts the cytoplasm. This is called plasmolysis. Plants lose turgor pressure in this condition and wilt.
Figure 10.
The turgor pressure within a plant cell depends on the tonicity of the solution that it is bathed in.
(credit: modification of work by Mariana Ruiz Villareal)
Figure 11.

Without adequate water, the plant on the left has lost turgor pressure, visible in its wilting; the turgor pressure is restored by watering it (right). (credit: Victor M. Vicente Selvas)

Tonicity is a concern for all living things. For example, paramecia and amoebas, which are protists that lack cell walls, have contractile vacuoles. This vesicle collects excess water from the cell and pumps it out, keeping the cell from bursting as it takes on water from its environment.
Figure 12. A paramecium’s contractile vacuole, here visualized using bright field light microscopy at 480x magnification, continuously pumps water out of the organism’s body to keep it from bursting in a hypotonic medium. (credit: modification of work by NIH; scale-bar data from Matt Russell)

Many marine invertebrates have internal salt levels matched to their environments, making them isotonic with the water in which they live. Fish, however, must spend approximately five percent of their metabolic energy maintaining osmotic homeostasis. Freshwater fish live in an environment that is hypotonic to their cells. These fish actively take in salt through their gills and excrete diluted urine to rid themselves of excess water. Saltwater fish live in the reverse environment, which is hypertonic to their cells, and they secrete salt through their gills and excrete highly concentrated urine.

In vertebrates, the kidneys regulate the amount of water in the body. Osmoreceptors are specialized cells in the brain that monitor the concentration of solutes in the blood. If the levels of solutes increase beyond a certain range, a hormone is released that retards water loss through the kidney and dilutes the blood to safer levels. Animals also have high concentrations of albumin, which is produced by the liver, in their blood. This protein is too large to pass easily through plasma membranes and is a major factor in controlling the osmotic pressures applied to tissues.