1.2.3

Diffusion of Solutes

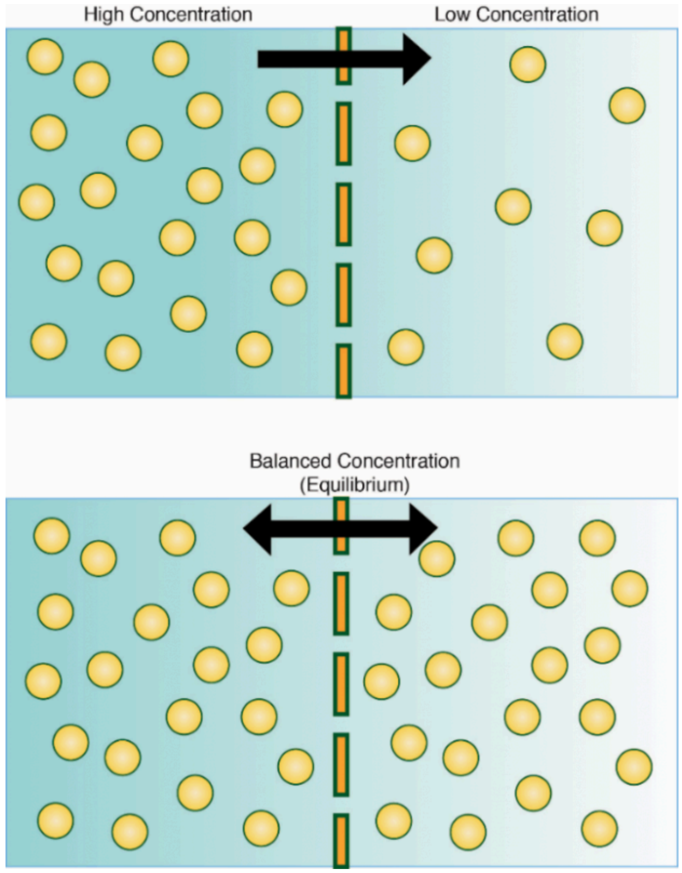
The video on Transport across a membrane can help with the following readings.

Because the hydrophobic core of cell membranes creates a barrier; (preventing hydrophilic substances, such as ions, water and large polar molecules, from moving across the membrane), the membrane makes use of proteins to facilitate movement of most solutes and water. Processes that move substances (solutes) across membranes can be grouped into two general categories based on whether the process requires an input of cellular energy or not. If no energy input is required for the transport, then we say particles move via a **passive transport process**. On the other hand, if the process requires cellular energy, usually in the form of ATP, then it is an **active transport process**.

Simple Diffusion

Diffusion is a process that results from the fact that all molecules, including solids, liquids, and gasses, are constantly in a state of random movement. This motion causes collisions between neighboring molecules, thus altering directions and creating a state of "random" motion. This random motion can be further altered by temperature, with increases in temperature stimulating a more rapid random movement. If there is an initial, unequal distribution of the molecules (i.e. more concentrated in one area than another), the constant random movement and collisions cause them to eventually become equally distributed. This process of gradual movement from more concentrated to less concentrated is called *diffusion*. We refer to the concentration difference as the **concentration gradient**.

Substances diffuse down their concentration gradients (from high to low concentration). Once the molecules are evenly distributed, we say that we have reached a state of **diffusion equilibrium,** and even though the molecules are still moving, there is no longer any net change in concentration. You can observe this phenomenon by carefully placing a drop of food coloring into a glass of water. The dye gradually moves through the liquid until it is evenly dispersed in the water. In the body, if the material in question can pass through the cell membrane without the aid of a membrane protein, we refer to the process as **simple diffusion**. Solutes that cross the membrane by simple diffusion tend to be hydrophobic. Examples of substances that cross the membrane by simple diffusion are the gasses CO_2 and O_2.



Simple Diffusion: Process of Moving from High to Low Concentration to Reach Equilibrium
Image created by BYU-Idaho student, Hannah Crowder 2013.

The top panel shows the diffusion of solute from left (high concentration) to the right (low concentration) until an equilibrium is established. Once a diffusion equilibrium exists, there will no longer be any net movement of solute (lower panel).

Factors That Affect the Rate of Diffusion

The speed at which a molecule moves across a membrane depends in part on the mass, or molecular weight, of the molecule. The higher the mass, the slower the molecule will diffuse (rate is proportional to $1/MW^{1/2}$). Another factor that affects the rate of diffusion across the membrane is the solubility of the substance. Nonpolar substances, such as oxygen, carbon dioxide, steroids and fatty acids, will diffuse rapidly while polar substances, having a much lower solubility in the membrane phospholipids move through more slowly, or not at all. Ions, such as Na+ and Cl-, tend to diffuse across a membrane rather rapidly. The diffusion rate across a membrane is proportional to the area of the membrane and to the difference in concentration of the diffusing substance on the two sides of the membrane. This relationship can be demonstrated by Fick's first law of diffusion, which states that:

$$J = -DA(\Delta C/\Delta X)$$

J = net rate of diffusion in moles or grams per unit time

D = diffusion coefficient of the diffusing solute in the membrane (this coefficient takes into account the size of the substance as well as its solubility in the membrane)

A = surface area of the membrane

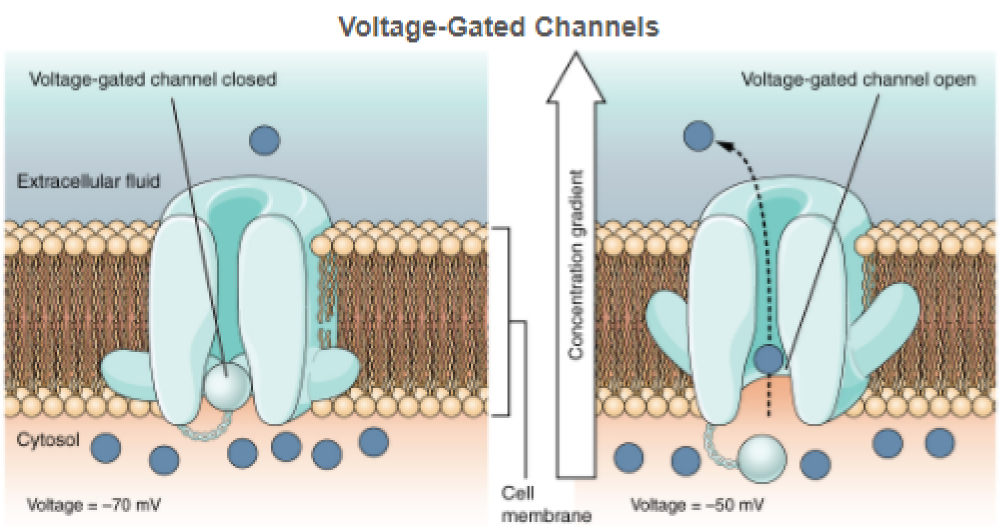
ΔC = concentration difference across the membrane

ΔX = thickness of the membrane. Diffusion is quite rapid over short distances but gets slower the further it goes. The time it takes for something to diffuse is proportional to the square of the distance. Therefore, if it takes one second to diffuse one centimeter, it would take 100 seconds to diffuse 10 cm and 10,000 seconds to diffuse 100 cm. So, to go 100 times further takes 10,000 times longer. In the body, diffusion is quite sufficient to cross the thin cell membrane, but traveling long distances by diffusion would be very slow. This is why we have other mechanisms, like blood circulation, for moving substances long distances.

Facilitated Diffusion

Facilitated diffusion represents the movement of substances across the membrane that are too big and/or too polar to pass through the membrane. This type of movement is mediated by integral membrane proteins called transport proteins. Unlike simple diffusion, this process of diffusion exhibits saturation, and its rate is directly related to the concentration of specific transport proteins within the membrane. In addition, this type of transport, like simple diffusion, does not require an input of energy. Facilitated diffusion can occur in two different ways, through channel proteins and carrier proteins.

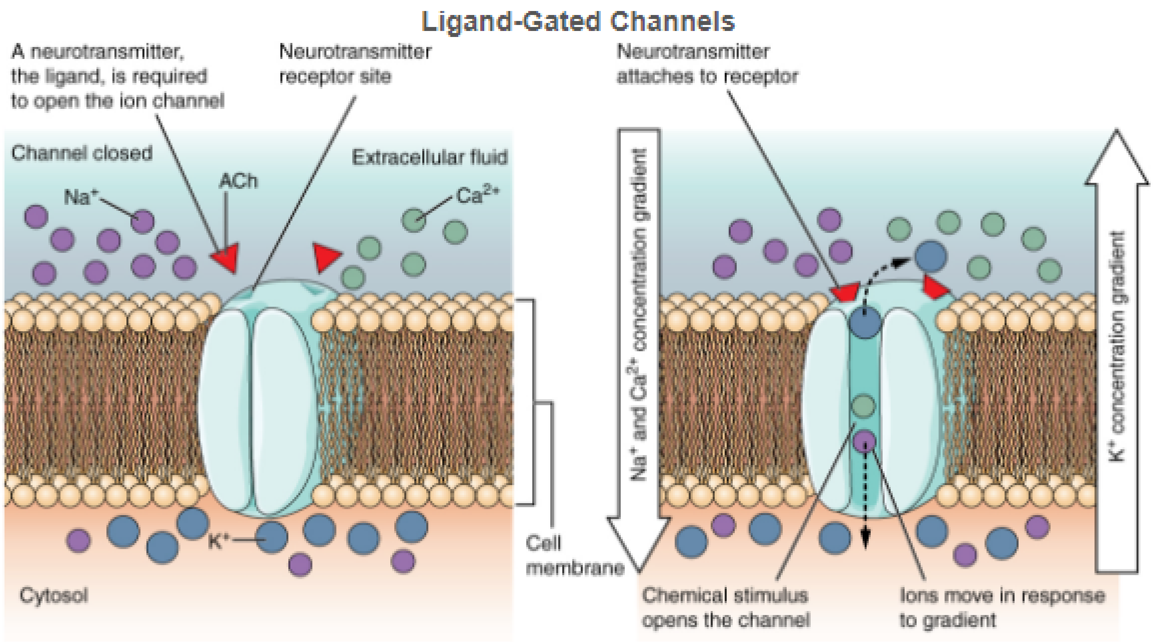
Channel proteins resemble fluid filled tubes through which the solutes can move down their concentration gradients across the membrane. These channels are often responsible for helping ions, such as Na^+, K^+, Ca^{2+}, and Cl^-, cross the membranes. Even though they are open tubes, they often only allow very specific ions to pass through them. For instance, a K^+ channel may allow K^+ to pass through but not Na^+ or Cl^-. This is due to the presence of a **selectivity filter** that selects for hydrated or dehydrated states of the specific ion. Also, as we will learn later, the regulation of the movement of the various ions across the membranes is crucial for many important cellular functions. These channels, therefore, are often gated (they have doors or gates that can be opened or closed). Depending on the channel, these gates may respond to voltage differences across the membrane (**voltage-gated channels**), specific signal molecules (**ligand-gated channels**), or even stretching or compressing of the membrane (**mechanically-gated channels**).



Voltage Gated Channel

Voltage-gated channels (shown above) open when membrane voltage changes. The concentration of ions in the intracellular fluid create the voltage. Amino acids in the protein transporter are sensitive to charge and cause the channel to open for a specific ion.

In ligand-gated channels the pore opens to ions when the ligand binds to a specific location on the extracellular surface of the channel protein. Acetylcholine is the ligand shown in the example below.



Ligand-Gated Channels

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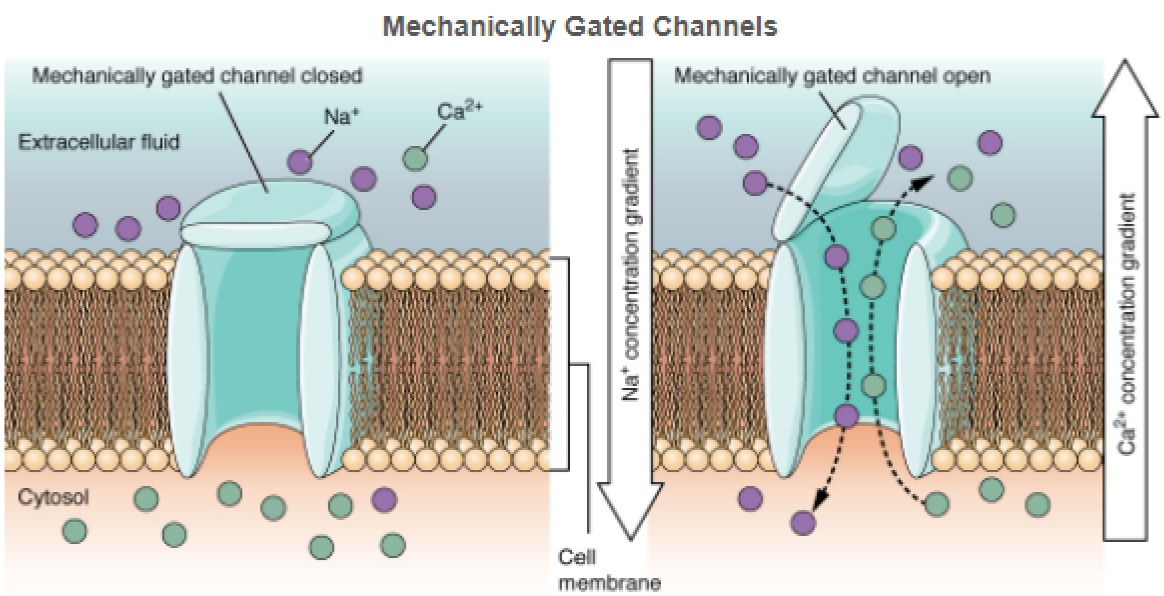
When a mechanical change such as pressure, touch, or a change in temperature happens, mechanically-gated channels open.



Mechanical-Gated Channels

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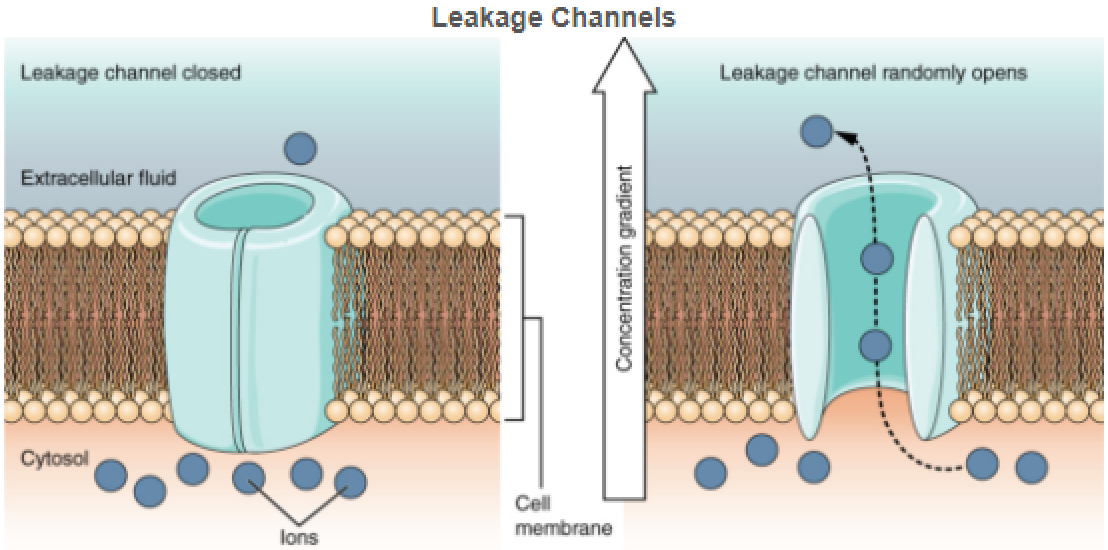
Another example of a gated channel protein is the K+ **leak channel** which opens and closes intrinsically and contributes to the cells electrical potential (discussed in more detail later).



Leak Channel

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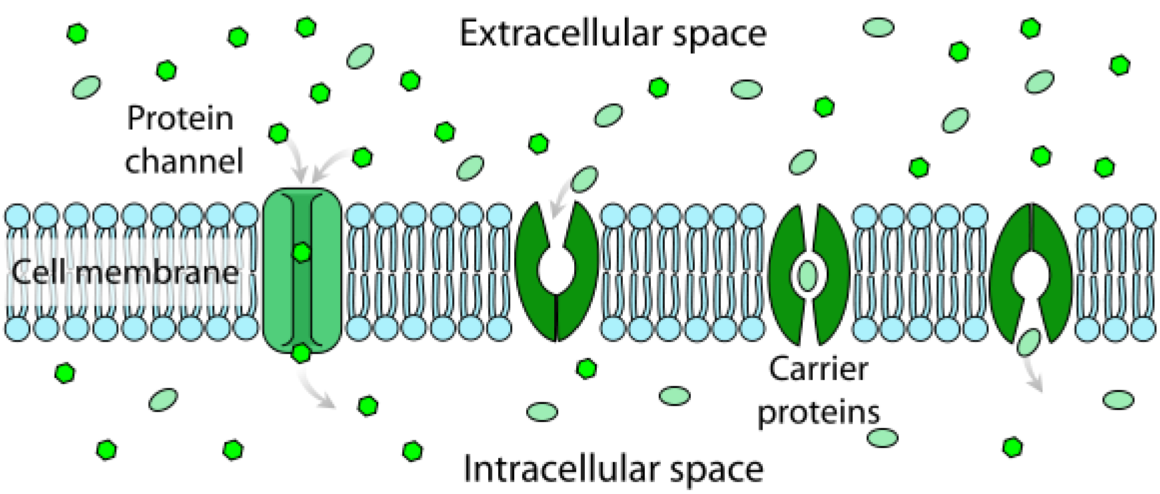
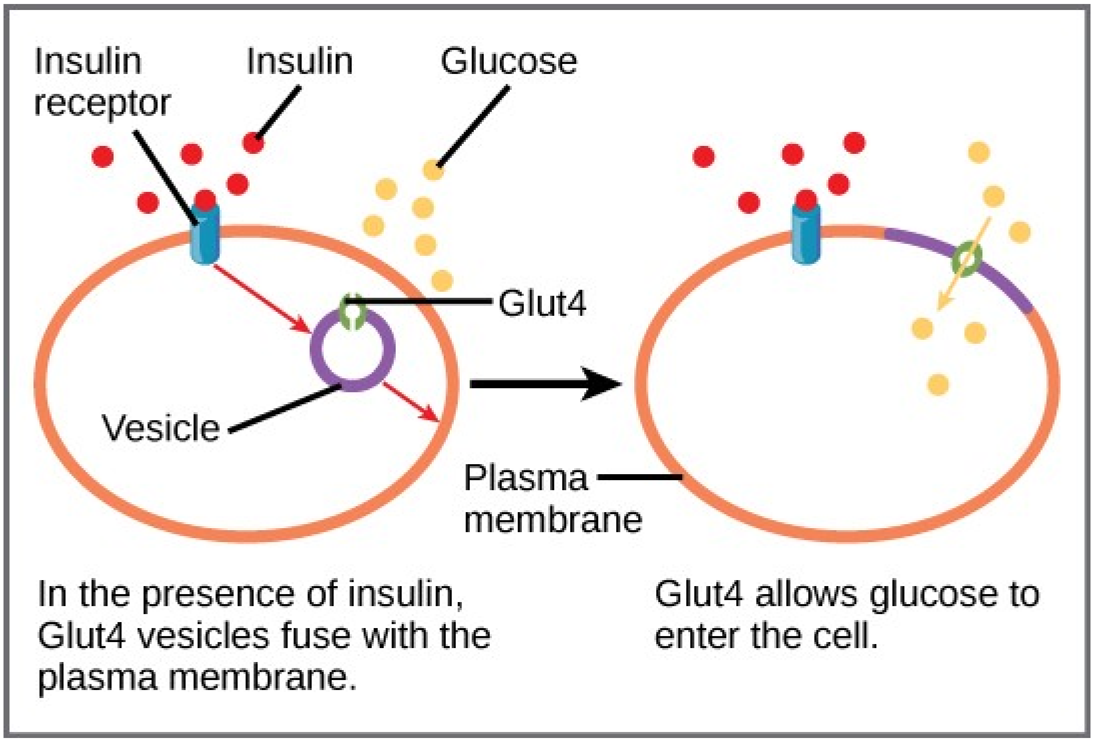
The second type of facilitated diffusion utilizes **carrier proteins** in the membrane and is known as carrier-mediated transport. Unlike the channel proteins, these carriers do not open to both sides of the membrane simultaneously. Instead, they bind to a specific solute on one side of the membrane. This binding causes the carrier to change shape, which moves the solute to the other side of the membrane (think of a revolving door).



Carrier Proteins

By LadyofHats Mariana Ruiz Villarreal [Public domain], via Wikimedia Commons

Like the channel proteins, these carriers can be very specific in the solute they transport since the solute must bind to a receptor site that is designed to fit a specific solute. Another interesting characteristic of these carriers is; similar to all channel proteins, that they have a maximum rate of transport and can thus become **saturated** if the solute concentration is high enough. An important family of carrier proteins transports glucose across cell membranes. To date, 12 carriers in this family have been identified. They are simply identified as GLUT1 through GLUT12, and their distribution and specificity vary. For example, **GLUT2** is found in the liver and pancreatic islets, while **GLUT4** is found in skeletal muscle and fat tissue. Interestingly, GLUT4 is the only one of these carriers that requires insulin for maximal activity.



GLUT 4 Carrier Protein

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As mentioned above, one of the characteristics of carrier proteins is that they can become saturated. One of the symptoms of uncontrolled diabetes is the presence of glucose in the urine. This is due to the fact that so much glucose is entering the kidney tubules, so the transporters that normally move the glucose back into the blood become saturated, and the excess glucose ends up in the urine.