Active transport

Electrochemical gradients and the membrane potential. Primary and secondary active transport. Na^+/K^+ pump.

Introduction

Passive transport is a great strategy for moving molecules into or out of a cell. It's cheap, it's easy, and all the cell has to do is sit there and let the molecules diffuse in. But...it also doesn't work in every situation. For instance, suppose the sugar glucose is more concentrated inside of a cell than outside. If the cell needs more sugar in to meet its metabolic needs, how can it get that sugar in?

Here, the cell can't import glucose for free using diffusion, because the natural tendency of the glucose will be to diffuse *out* rather than flowing *in*. Instead, the cell must bring in more glucose molecules via **active transport**. In active transport, unlike passive transport, the cell expends energy (for example, in the form of ATP) to move a substance against its concentration gradient.

Here, we'll look in more detail at gradients of molecules that exist across cell membranes, how they can help or hinder transport, and how active transport mechanisms allow molecules to move against their gradients.

Electrochemical gradients

We have already discussed simple concentration gradients, in which a substance is found in different concentrations over a region of space or on opposite sides of a membrane. However, because atoms and molecules can form ions and carry positive or negative electrical charges, there may also be an electrical gradient, or difference in charge, across a plasma membrane. In fact, living cells typically have what's called a **membrane potential**, an electrical potential difference (voltage) across their cell membrane.

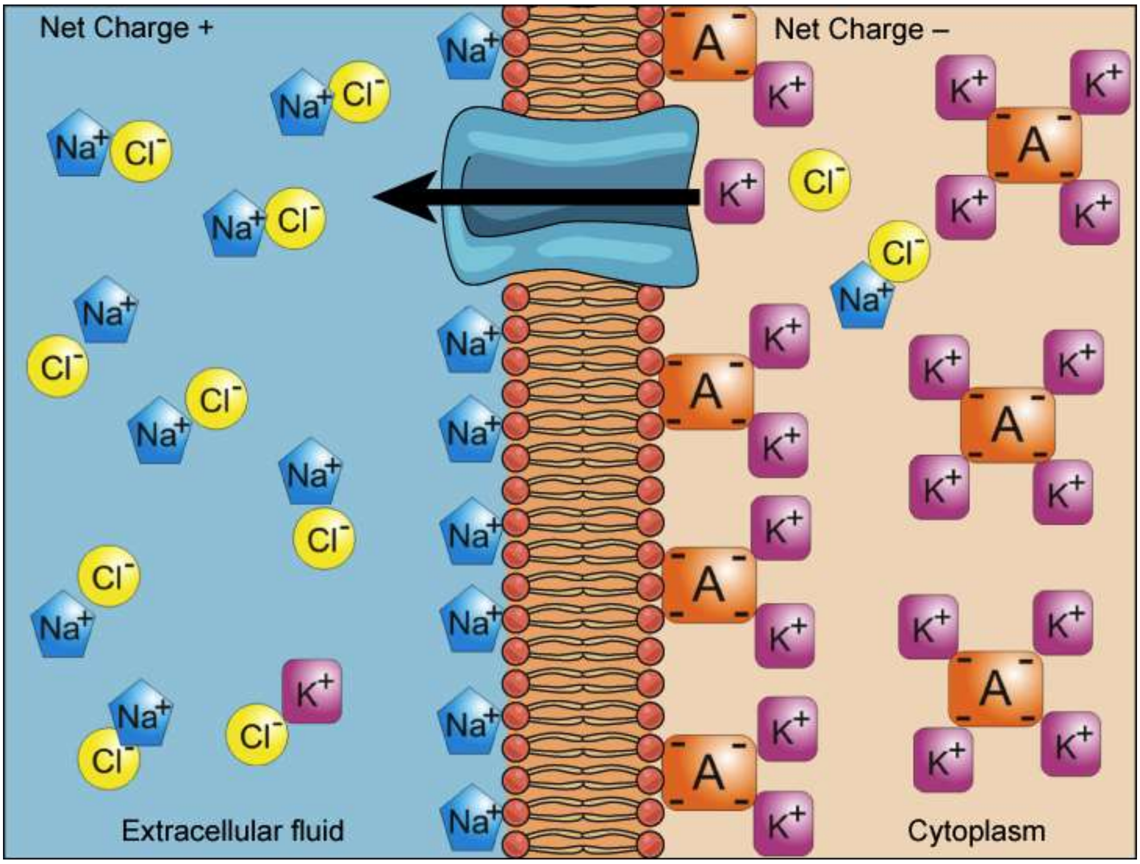


Image depicting the charge and ion distribution across the membrane of a typical cell. Overall, there are more positive charges on the outside of the membrane than on the inside. The concentration of sodium ions is lower inside the cell than in the extracellular fluid, while the reverse is true for potassium ions.

Image credit: image from OpenStax Biology, originally by Synaptitude/Wikimedia Commons.

An electrical potential difference exists whenever there is a net separation of charges in space. In the case of a cell, positive and negative charges are separated by the barrier of the cell membrane, with the inside of the cell having extra negative charges relative to the outside. The membrane potential of a typical cell is -40 to -80 millivolts, with the minus sign meaning that inside of the cell is more negative than the outside. The cell actively maintains this membrane potential, and we'll see how it forms in the section on the sodium-potassium pump (below).

As an example of how the membrane potential can affect ion movement, let's look at sodium and potassium ions. In general, the inside of a cell has a higher concentration of potassium (K^+) and a lower concentration of sodium (Na^+) than the extracellular fluid around it.

- If sodium ions are outside of a cell, they will tend to move into the cell based on both their concentration gradient (the lower concentration of Na^+ in the cell) and the voltage across the membrane (the more negative charge on the inside of the membrane).
- Because K^+ is positive, the voltage across the membrane will encourage its movement into the cell, but its concentration gradient will tend to drive it out of the cell (towards the region of lower concentration). The final concentrations of potassium on the two sides of the membrane will be a balance between these opposing forces.

The combination of concentration gradient and voltage that affects an ion's movement is called the **electrochemical gradient**.

Active transport: moving against a gradient

To move substances against a concentration or electrochemical gradient, a cell must use energy. Active transport mechanisms do just this, expending energy (often in the form of ATP) to maintain the right concentrations of ions and molecules in living cells. In fact, cells spend much of the energy they harvest in metabolism to keep their active transport processes running. For instance, most of a red blood cell's energy is used to maintain internal sodium and potassium levels that differ from those of the surrounding environment.

Active transport mechanisms can be divided into two categories. **Primary active transport** directly uses a source of chemical energy (e.g., ATP) to move molecules across a membrane against their gradient. **Secondary active transport** (**co-transport)**, on the other hand, uses an electrochemical gradient – generated by active transport – as an energy source to move molecules against their gradient, and thus does not directly require a chemical source of energy such as ATP. We'll look at each type of active transport in greater detail below.

Primary active transport

One of the most important pumps in animal cells is the **sodium-potassium pump**, which moves Na^+ out of cells, and K^+ into them. Because the transport process uses ATP as an energy source, it is considered an example of primary active transport.

Not only does the sodium-potassium pump maintain correct concentrations of Na^+ and K^+ in living cells, but it also plays a major role in generating the voltage across the cell membrane in animal cells. Pumps like this, which are involved in the establishment and maintenance of membrane voltages, are known as **electro-genic pumps**. The primary electro-genic pump in plants is one that pumps hydrogen ions (H^+) rather than sodium and potassium[2,3].

The sodium-potassium pump cycle

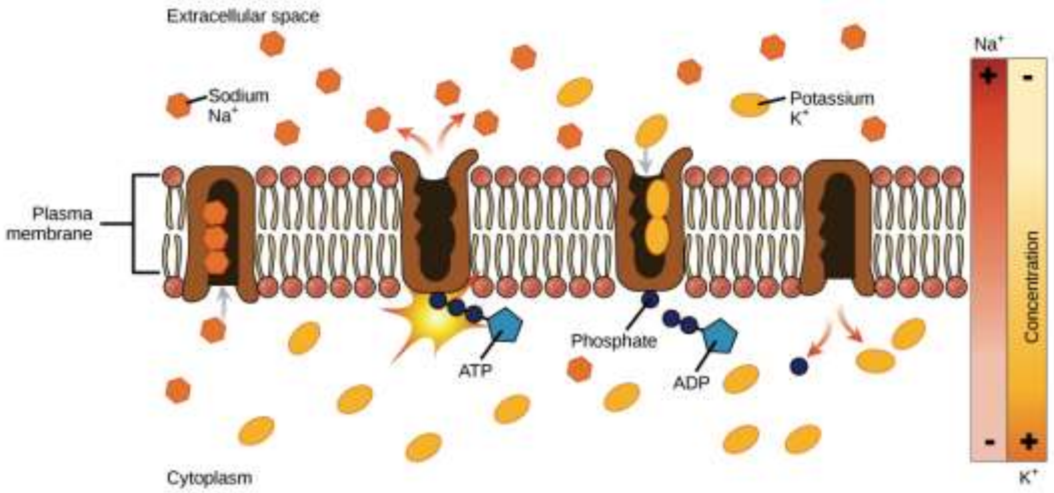


Figure showing the transport cycle of the sodium-potassium pump.

Image credit: OpenStax Biology. Image modified from original work by Mariana Ruiz Villareal.

The sodium-potassium pump transports sodium out of and potassium into the cell in a repeating cycle of conformational (shape) changes. In each cycle, three sodium ions exit the cell, while two potassium ions enter. This process takes place in the following steps:

1. To begin, the pump is open to the inside of the cell. In this form, the pump really likes to bind (has a high affinity for) sodium ions, and will take up three of them.
2. When the sodium ions bind, they trigger the pump to hydrolyse (break down) ATP. One phosphate group from ATP is attached to the pump, which is then said to be phosphorylated. ADP is released as a by-product.
3. Phosphorylation makes the pump change shape, re-orienting itself so it opens towards the extracellular space. In this conformation, the pump no longer likes to bind to sodium ions (has a low affinity for them), so the three sodium ions are released outside the cell.
4. In its outward-facing form, the pump switches allegiances and now really likes to bind to (has a high affinity for) potassium ions. It will bind two of them, and this triggers removal of the phosphate group attached to the pump in step 2.
5. With the phosphate group gone, the pump will change back to its original form, opening towards the interior of the cell.
6. In its inward-facing shape, the pump loses its interest in (has a low affinity for) potassium ions, so the two potassium ions will be released into the cytoplasm. The pump is now back to where it was in step 1, and the cycle can begin again.

This may seem like a complicated cycle, but it just involves the protein going back and forth between two forms: an inward-facing form with high affinity for sodium (and low affinity for potassium) and an outward-facing form with high affinity for potassium (and low affinity for sodium). The protein can be toggled back and forth between these forms by the addition or removal of a phosphate group, which is in turn controlled by the binding of the ions to be transported.

How the sodium-potassium pump generates a membrane potential

How, exactly, does the sodium-potassium pump establish a voltage across the membrane? It's tempting to simply make an argument based on stoichiometry: for every three ions of sodium that move out, only two ions of potassium move in, resulting in a more negative cell interior. While this charge ratio does make the cell's interior slightly more negative, it actually accounts for only a tiny fraction of the sodium-potassium pump's effect on membrane potential.

Instead, the sodium-potassium pump acts primarily by building up a high concentration of potassium ions inside the cell, which makes potassium's concentration gradient very steep. The gradient is steep enough that potassium ions will move out of the cell (via channels), despite a growing negative charge on the interior. This process continues until the voltage across the membrane is large enough to counterbalance potassium's concentration gradient. At this balance point, the inside of the membrane is negative relative to the outside. This voltage will be maintained as long as K^+ concentration in the cell stays high, but will disappear if K^+ stops being imported[4,5].

For more explanation of how the voltage across the membrane is established, take a look at the membrane potential article in the neurobiology section.

Secondary active transport

The electrochemical gradients set up by primary active transport store energy, which can be released as the ions move back down their gradients. Secondary active transport uses the energy stored in these gradients to move other substances against their own gradients.

As an example, let's suppose we have a high concentration of sodium ions in the extracellular space (thanks to the hard work of the sodium-potassium pump). If a route such as a channel or carrier protein is open, sodium ions will move down their concentration gradient and return to the interior of the cell.

In secondary active transport, the movement of the sodium ions down their gradient is coupled to the uphill transport of other substances by a shared carrier protein (a **co-transporter**). For instance, in the figure below, a carrier protein lets sodium ions move down their gradient, but simultaneously brings a glucose molecule up its gradient and into the cell. The carrier protein uses the energy of the sodium gradient to drive the transport of glucose molecules.

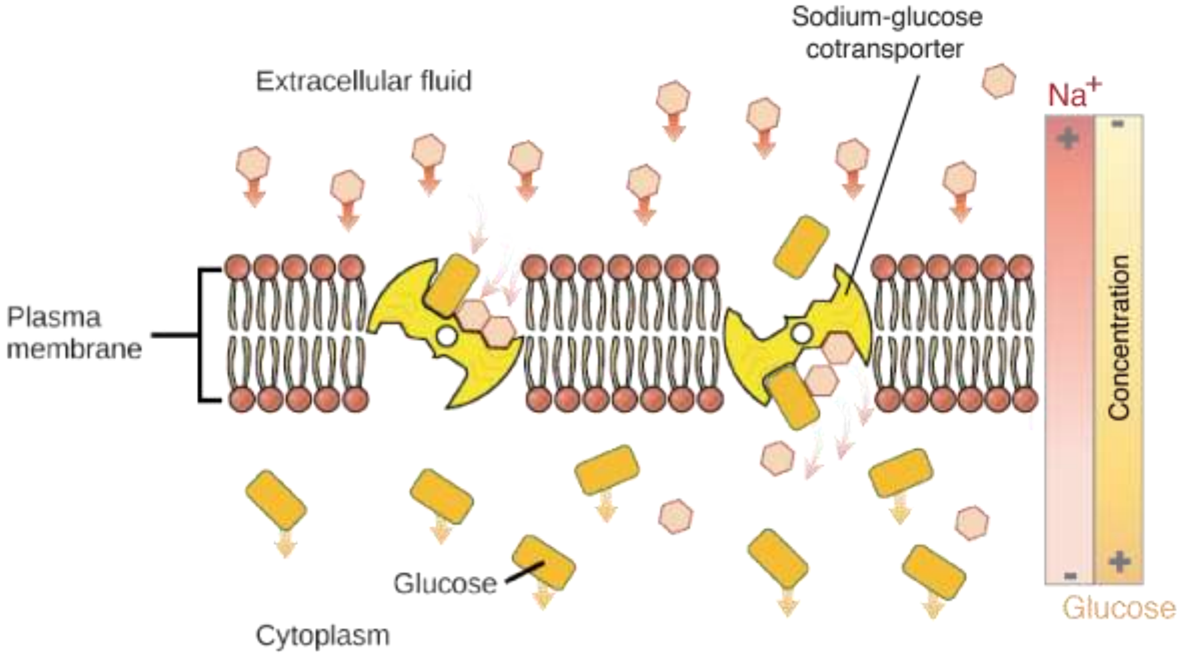
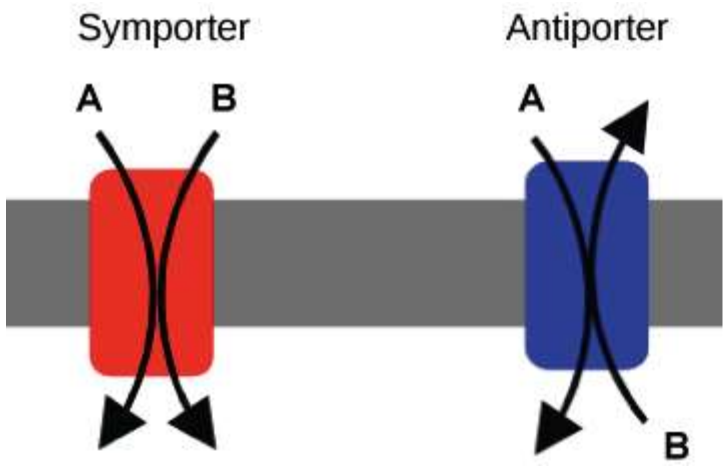


Diagram of a sodium-glucose co-transporter, which uses the energy stored in a sodium ion gradient to transport glucose "uphill" against its gradient. The co-transporter accomplishes this by physically coupling the transport of glucose to the movement of sodium ions down their concentration gradient.

Image modified from "Active transport: Figure 4," by OpenStax College, Biology (CC BY 3.0) and "Scheme secondary transport," by Mariana Ruiz Villareal (public domain).

In secondary active transport, the two molecules being transported may move either in the same direction (i.e., both into the cell), or in opposite directions (i.e., one into and one out of the cell). When they move in the same direction, the protein that transports them is called a **symporter**, while if they move in opposite directions, the protein is called an **antiporter**.



Simple diagram of a symporter (carrying two molecules in the same direction) and an antiporter (carrying two molecules in opposite directions).

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