The membrane potential

How the resting membrane potential is established in a neuron.

Key points:

A resting (non-signalling) neuron has a voltage across its membrane called the resting membrane potential, or simply the resting potential.
The resting potential is determined by concentration gradients of ions across the membrane and by membrane permeability to each type of ion.

In a resting neuron, there are concentration gradients across the membrane for Na^+ and K^+. Ions move down their gradients via channels, leading to a separation of charge that creates the resting potential.

The membrane is much more permeable to K^+ than to Na^+, so the resting potential is close to the equilibrium potential of K^+ (the potential that would be generated by K^+ if it were the only ion in the system).

Introduction

Suppose you have a dead frog. (Yes, that's kind of gross, but let's just imagine it for a second.) What would happen if you applied an electrical stimulus to the nerve that feeds the frog's leg? Creepily enough, the dead leg would kick!

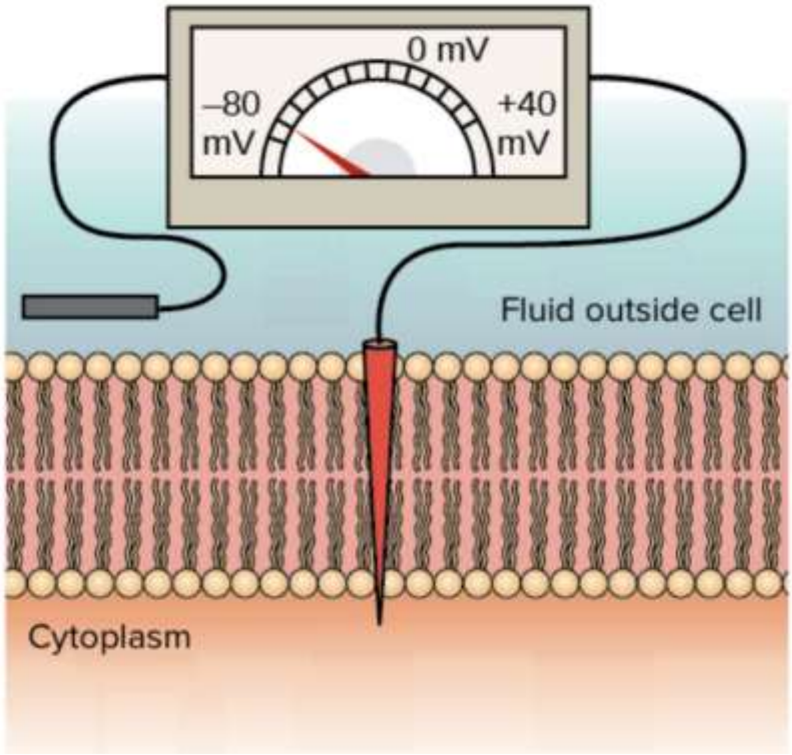
The Italian scientist Luigi Galvani discovered this fun fact back in the 1700s, somewhat by accident during a frog dissection. Today, we know that the frog's leg kicks because neurons (nerve cells) carry information via electrical signals.

How do neurons in a living organism produce electrical signals? At a basic level, neurons generate electrical signals through brief, controlled changes in the permeability of their cell membrane to particular ions (such as Na^+ and K^+). Before we look in detail at how these signals are generated, we first need to understand how membrane permeability works in a resting neuron (one that is not sending or receiving electrical signals).

In this article, we'll see how a neuron establishes and maintains a stable voltage across its membrane – that is, a resting membrane potential.

The resting membrane potential

Imagine taking two electrodes and placing one on the outside and the other on the inside of the plasma membrane of a living cell. If you did this, you would measure an electrical potential difference, or voltage, between the electrodes. This electrical potential difference is called the membrane potential.



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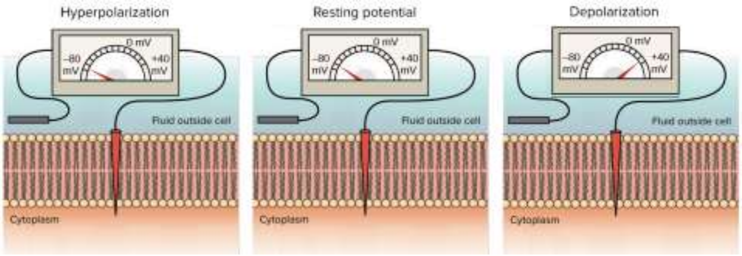
Like distance, potential difference is measured relative to a reference point. In the case of distance, the reference point might be a city. For instance, we can say that Boston is 190 miles northeast, but only if we know that our reference point is New York City. For a cell's membrane potential, the reference point is the outside of the cell. In most resting neurons, the potential difference across the membrane is about 30 to 90 mV (an mV is 1/1000 of a volt), with the inside of the cell more negative than the outside. That is, neurons have a resting membrane potential (or simply, resting potential) of about −30 mV to −90 mV.

Because there is a potential difference across the cell membrane, the membrane is said to be polarized. If the membrane potential becomes more positive than it is at the resting potential, the membrane is said to be depolarized.

If the membrane potential becomes more negative than it is at the resting potential, the membrane is said to be hyperpolarized.



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All of the electrical signals that neurons use to communicate are either depolarization’s or hyperpolarization’s from the resting membrane potential.

Where does the resting membrane potential come from?

The resting membrane potential is determined by the uneven distribution of ions (charged particles) between the inside and the outside the cell, and by the different permeability of the membrane to different types of ions.

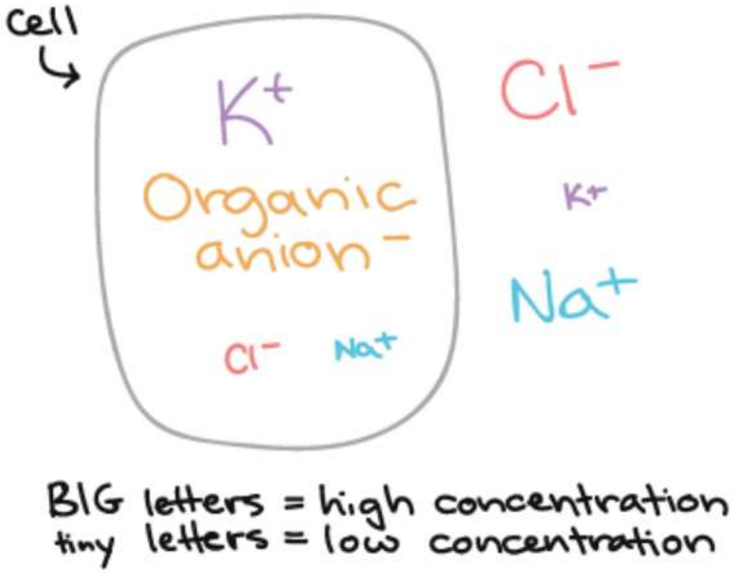
Types of ions found in neurons

In neurons and their surrounding fluid, the most abundant ions are:

Positively charged (cations): Sodium (Na^+) and potassium (K^+)

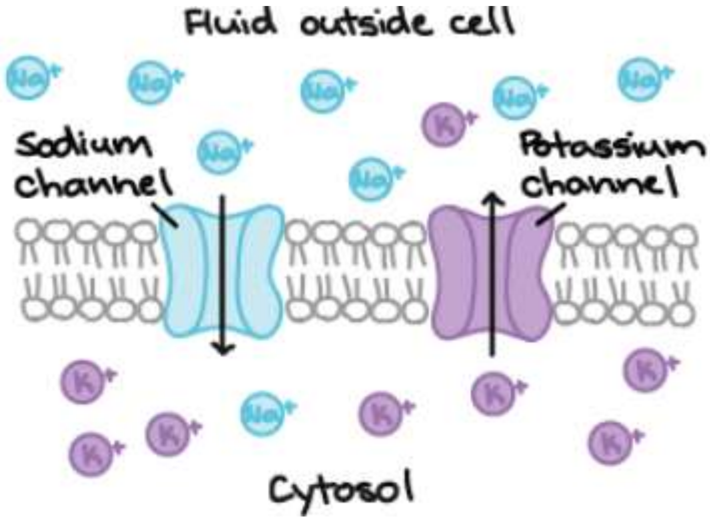
Negatively charged (anions): Chloride (Cl^-) and organic anions

In most neurons, K^+ and organic anions (such as those found in proteins and amino acids) are present at higher concentrations inside the cell than outside. In contrast, Na^+ and Cl^- are usually present at higher concentrations outside the cell. This means there are stable concentration gradients across the membrane for all of the most abundant ion types.



How ions cross the membrane

Because they are charged, ions can't pass directly through the hydrophobic ("water-fearing") lipid regions of the membrane. Instead, they have to use specialized channel proteins that provide a hydrophilic ("water-loving") tunnel across the membrane. Some channels, known as leak channels, are open in resting neurons. Others are closed in resting neurons and only open in response to a signal.



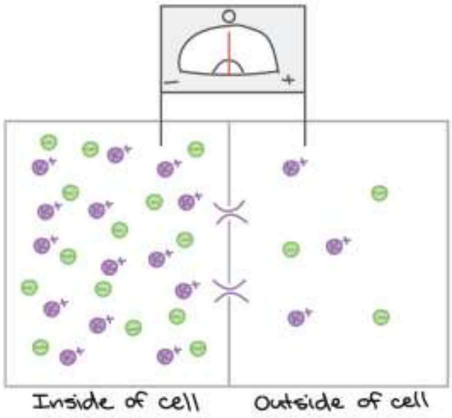
Some ion channels are highly selective for one type of ion, but others let various kinds of ions pass through. Ion channels that mainly allow K^+ to pass are called potassium channels, and ion channels that mainly allow Na^+ to pass are called sodium channels.

In neurons, the resting membrane potential depends mainly on movement of K^+ through potassium leak channels. Let's see how this works.

What happens if only K^+ can cross the membrane?

The membrane potential of a resting neuron is primarily determined by the movement of K^+ ions across the membrane. So, let's get a feeling for how the membrane potential works by seeing what would happen in a case where only K^+ can cross the membrane.

We'll start out with K^+ at a higher concentration inside the cell than in the surrounding fluid, just as for a regular neuron. (Other ions are also present, including anions that counterbalance the positive charge on K^+, but they will not be able to cross the membrane in our example.)

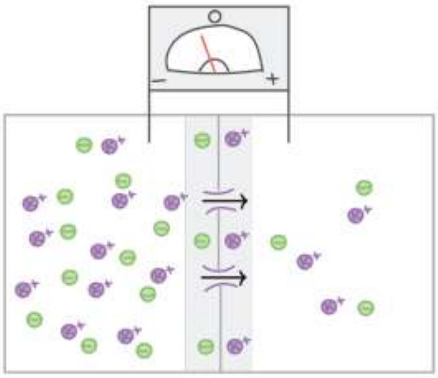


STARTING STATE:

There are potassium (K^+) ions and other ions (including anions) inside and outside the cell.

K^+ is more concentrated on the inside and less concentrated outside of the cell.

If potassium channels in the membrane open, K^+ will begin to move down its concentration gradient and out of the cell. Every time a K^+ ion leaves the cell, the cell's interior loses a positive charge. Because of this, a slight excess of positive charge builds up on the outside of the cell membrane, and a slight excess of negative charge builds up on the inside. That is, the inside of the cell becomes negative relative to the outside, setting up a difference in electrical potential across the membrane.



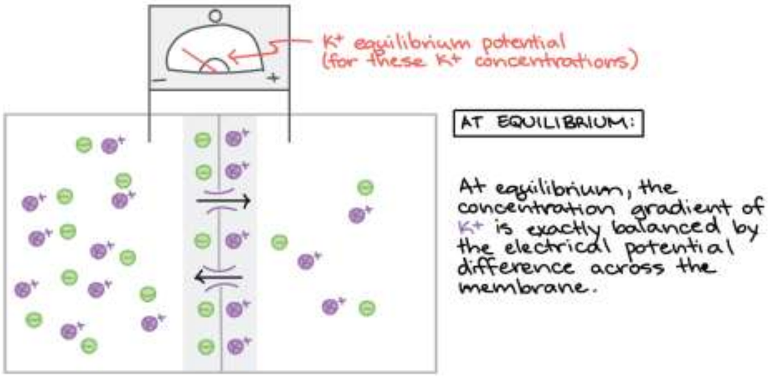
If K^+ can cross via channels, it will begin to move down its concentration gradient and out of the cell.

The movement of K^+ ions down their concentration gradient creates a charge imbalance across the membrane.

The charge imbalance opposes the flow of K^+ down the concentration gradient.

For ions (as for magnets), like charges repel each other and unlike charges attract. So, the establishment of the electrical potential difference across the membrane makes it harder for the remaining K^+ ions to leave the cell. Positively charged K^+ ions will be attracted to the free negative charges on the inside of the cell membrane and repelled by the positive charges on the outside, opposing their movement down the concentration gradient. The electrical and diffusional forces that influence movement of K^+ across the membrane jointly form its electrochemical gradient (the gradient of potential energy that determines in which direction K^+ will flow spontaneously).

Eventually, the electrical potential difference across the cell membrane builds up to a high enough level that the electrical force driving K^+ back into the cell is equal to the chemical force driving K^+ out of the cell. When the potential difference across the cell membrane reaches this point, there is no net movement of K^+ in either direction, and the system is considered to be in equilibrium. Every time one K^+ leaves the cell, another K^+ will enter it.

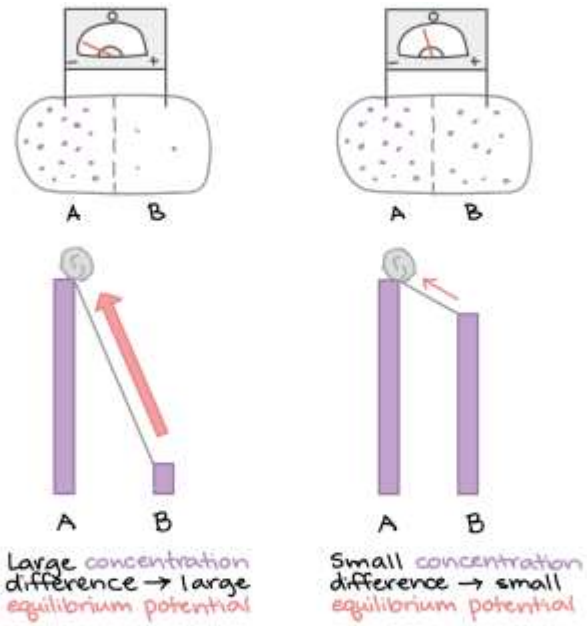


At equilibrium, the concentration gradient of K+ is exactly balanced by the electrical potential difference across the membrane.

The equilibrium potential

The electrical potential difference across the cell membrane that exactly balances the concentration gradient for an ion is known as the equilibrium potential. Because the system is in equilibrium, the membrane potential will tend to stay at the equilibrium potential. For a cell where there is only one permeant ionic species (only one type of ion that can cross the membrane), the resting membrane potential will equal the equilibrium potential for that ion.

The steeper the concentration gradient is, the larger the electrical potential that balances it has to be. You can get an intuitive feeling for this by imagining the ion concentrations on either side of the membrane as hills of different sizes and thinking of the equilibrium potential as the force you'd need to exert to keep a boulder from rolling down the slopes between them.



If you know the K^+ concentration on both sides of the cell membrane, then you can predict the size of the potassium equilibrium potential.

Does membrane potential equal K^+ equilibrium potential?

In glial cells, which are the support cells of the nervous system, the resting membrane potential is equal to the K^+ equilibrium potential.

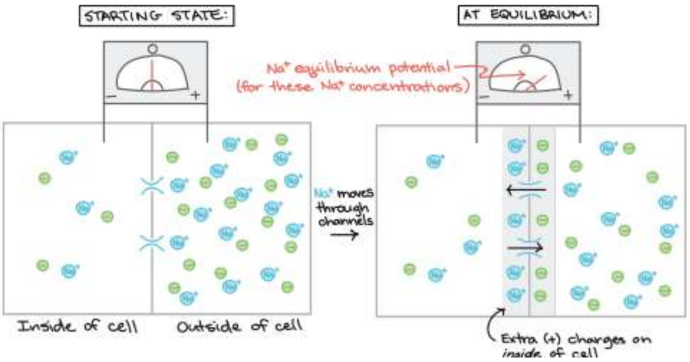
In neurons, however, the resting membrane potential is close but not identical to the K^+ equilibrium potential. Instead, under physiological conditions (conditions like those in the body), neuron resting membrane potentials are slightly less negative than the K^+ equilibrium potential.

What does that mean? In a neuron, other types of ions besides K^+ must contribute significantly to the resting membrane potential.

Both K and Na contribute to resting potential in neurons

as it turns out, most resting neurons are permeable to Na^+ and Cl^- as well as K^+. Permeability to Na^+, in particular, is the main reason why the resting membrane potential is different from the potassium equilibrium potential.

Let’s go back to our model of a cell permeable to just one type of ion and imagine that Na^+ (rather than K^+) is the only ion that can cross the membrane. Na^+ is usually present at a much higher concentration outside of a cell than inside, so it will move down its concentration gradient into the cell, making the interior of the cell positive relative to the outside. Because of this, the sodium equilibrium potential—the electrical potential difference across the cell membrane that exactly balances the Na^+ concentration gradient—will be positive. So, in a system where Na^+ is the only permeant ion, the membrane potential will be positive.



In a resting neuron, both Na^+ and K^+ are permeant, or able to cross the membrane.

Na will try to drag the membrane potential

toward its (positive) equilibrium potential.
K^+ will try to drag the membrane potential toward its (negative) equilibrium potential.

You can think of this as being like a tug-of-war. The real membrane potential will be in between the Na^+ equilibrium potential and the K^+ equilibrium potential. However, it will be closer to the equilibrium potential of the ion type with higher permeability (the one that can more readily cross the membrane).

Opening and closing ion channels alters the membrane potential

In a neuron, the resting membrane potential is closer to the potassium equilibrium potential than it is to the sodium equilibrium potential. That's because the resting membrane is much more permeable to K^+ than to Na^+.

If more potassium channels were to open up—making it even easier for K^+ to cross the cell membrane—the membrane would hyperpolarize, getting even closer to the potassium equilibrium potential.

If, on the other hand, additional sodium channels were to open up—making it easier for Na^+ to cross the membrane—the cell membrane would depolarize toward the sodium equilibrium potential.

Changing the number of open ion channels provides a way to control the cell’s membrane potential and a great way to produce electrical signals. (We will see the opening and closing of channels again when we discuss action potentials.)

The Na$^+$ -K$^+$ pump maintains Na$^+$ and K$^+$ gradients

The Na$^+$ and K$^+$ concentration gradients across the membrane of the cell (and thus, the resting membrane potential) are maintained by the activity of a protein called the Na$^+$ -K$^+$ ATPase, often referred to as the sodium-potassium pump. If the Na$^+$ -K$^+$ pump is shut down, the Na$^+$ and K$^+$ concentration gradients will dissipate, and so will the membrane potential.

Like the ion channels that allow Na$^+$ and K$^+$ to cross the cell membrane, the Na$^+$ -K$^+$ pump is a membrane-spanning protein. Unlike potassium channels and sodium channels, however, the Na$^+$ –K$^+$ pump doesn’t just give Na$^+$ and K$^+$ a way to move down their electrochemical gradients.

Instead, it actively transports Na$^+$ and K$^+$ against their electrochemical gradients.

The energy for this "uphill" movement comes from ATP hydrolysis (the splitting of ATP into ADP and inorganic phosphate). For every molecule of ATP that's broke down, 3 Na$^+$ ions are moved from the inside to the outside of the cell, and 2 K$^+$ ions are moved from the outside to the inside.

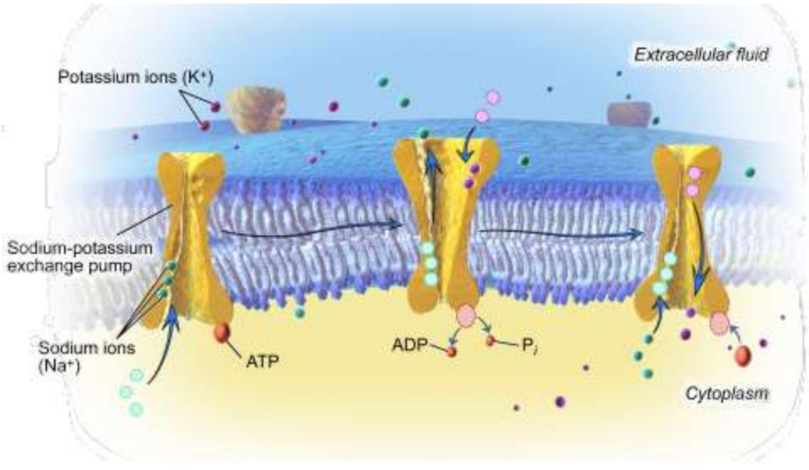


Image modified from "The sodium-potassium exchange pump," by Blausen staff (CC BY 3.0).

Because 3 Na^+ are exported for every 2 K^+ brought into the cell, the pump makes a small direct contribution to the resting membrane potential (making it slightly more negative than it would otherwise be). The pump's big contribution to the membrane potential, however, is indirect: It maintains steady Na^+ and K^+ gradients, which give rise to the membrane potential as Na^+ and K^+ move down their respective concentration gradients through leak channels.