“Neuro 101” Refresher for Perception Students

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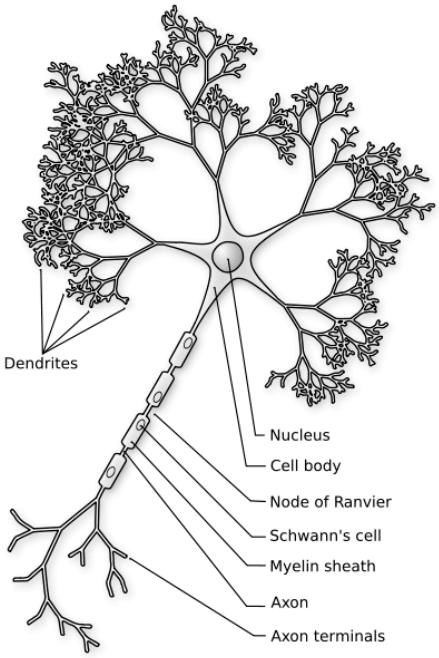
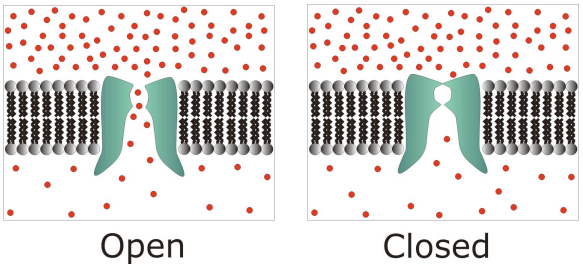


A prototypical neuron, with lots of branching processes. Image from Wikipedia.

Starting with the basics: **Neurons** are cells in the nervous system that are specialized to process information. They have all the odds and ends that most cells have (a nucleus with DNA, mitochondria that turn sugar into ATP, ribosomes that make proteins, etc). They also have some unique features, most notable of which is that they have long **processes** (branches) that reach out towards (but don’t quite touch) other cells. The general flow of information is that the cell takes in signals from other cells adjacent to its dendrites, and sends signals down its axon to other cells (whose dendrites in turn are adjacent to that axon).

Like all animal cells, neurons are bounded by a **cell membrane**, whose most important property in this context is that **ions** (charged particles such as potassium (K+), sodium (Na+), calcium (Ca2+), or chlorine (Cl-)) cannot pass through the membrane. The only way an ion can get from outside a cell to inside a cell (or from inside to outside) is by passing through an **ion channel**. Ion channels are proteins that span the cell membrane and have a pore in the middle that allow ions to pass through. They can open and close, and they are specific to certain ions. A sodium channel won’t let potassium through; a calcium channel won’t let chlorine through.

One effect of cell membranes is that a cell can maintain a mix of ions that is different than the mix in the surrounding fluid. When cells do this, it can result in a **membrane potential**. If the interior of the cell has more negative ions than the exterior fluid, we say the cell is maintaining a negative membrane potential. When there are more positive ions inside the cell, it has a positive membrane potential. (Actually, it’s the ratio of positive to negative charge that matters here. If a cell has 2 negative ions and 2 positive ions, and the extracellular fluid has 6 positive ions and 6 negative ions, the membrane potential will be zero. But if the extracellular fluid has 6 positive ions and no negative ions, the membrane potential will be negative. Potential (volts) is a measure of difference in charge.)



Ion channels are proteins that span the cell membrane and have a pore in the middle that allows ions to pass through. Image from www.sophion.dk

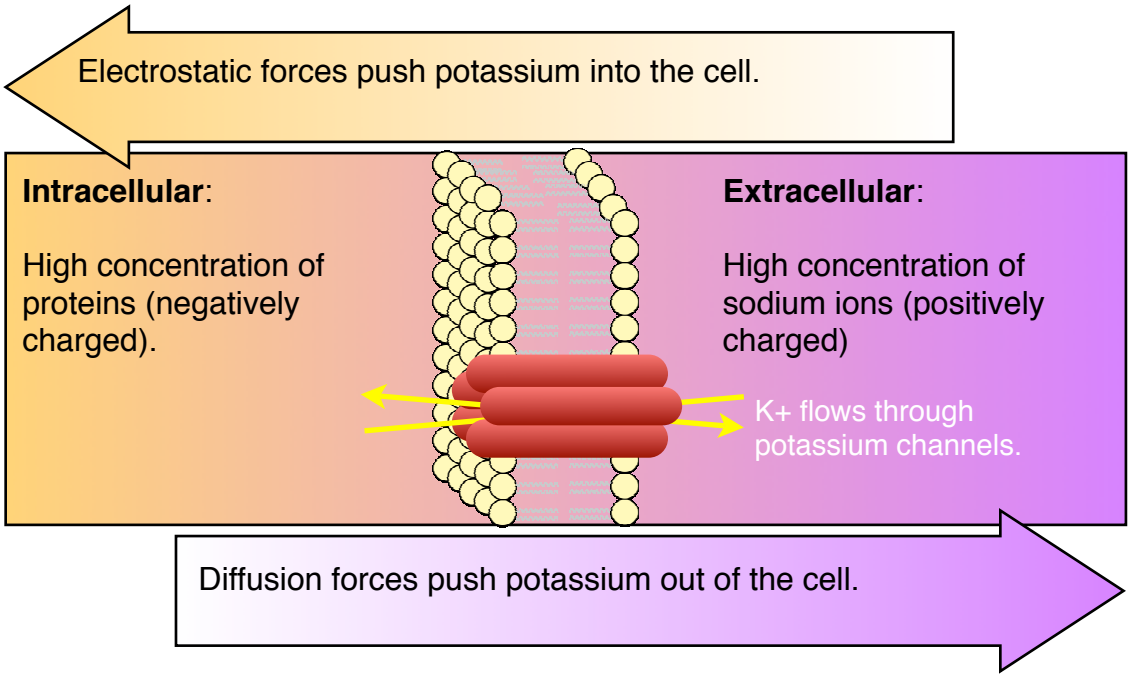
There are two main forces that push ions around. One is electrostatic force: positively charged ions are attracted to negatively charged areas, and vice versa. The other is diffusion force. Highly concentrated ions are attracted to less-concentrated areas - they want to travel “down the concentration gradient,” from high to low.

When a neuron is neither receiving nor sending signals, the concentration of various ions is as in the table. Don’t worry too much about the exact numbers; note that potassium is high inside the cell and low outside; sodium and calcium are the other way around. As well, the interior of the cell contains many negatively charged proteins.

	Intracellular	Extracellular
Potassium (K+)	140 mMolar	5 mM
Sodium (Na+)	~10 mM	145 mM
Calcium (Ca2+)	0.0001 mM	1 mM

Concentrations of ions in a typical mammalian neuron at rest. mMolar is a unit of concentration - a 1 Molar solution has 1 mole of ions per liter of water. A 1 mMolar solution has 1/1000 mole of ions per liter of water.

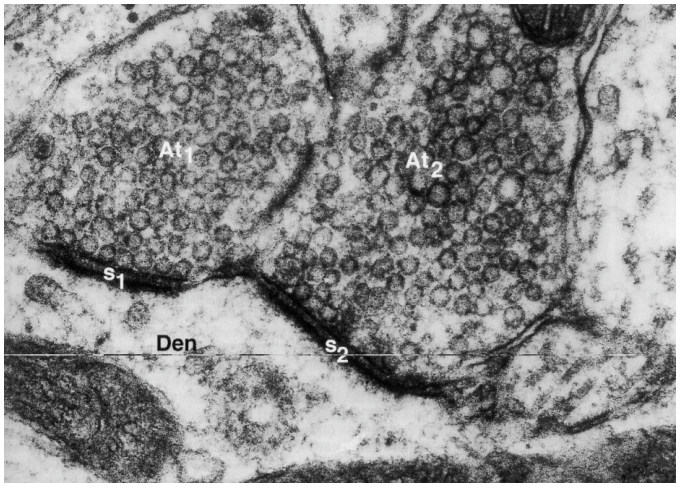
While the neuron is in this resting state, only some potassium channels are open. This means that potassium is the only ion that can flow across the membrane. Since the interior of the cell is negatively charged (all those proteins), electrostatic forces push potassium in. But, as more potassium fills the interior of the cell, diffusion forces come into play, forcing the potassium back out. The point at which these two forces are in balance is when the intracellular concentration of potassium is as above, and the potential across the membrane is approximately -70 mV: the **resting potential**. (This is about 1/22 of the potential across the two terminals of a AA battery.)



At rest, some potassium channels are open. Two conflicting forces on potassium ions (electrostatic and diffusion) are in balance when the membrane potential is approximately -70 mV.

If the configuration of ion channels changes, the membrane potential of the cell also changes. For example, if sodium channels are opened (by a neurotransmitter binding, for example), sodium ions will move in a direction guided by the concentration gradient and the electrostatic forces -- into the cell. This influx of positive ions will make the membrane potential more positive - closer to zero - and thus the effect is referred to as **depolarization**. If chlorine channels are opened, chlorine will flow into the cell (the diffusion force is stronger than the electrostatic force), and the cell becomes **hyperpolarized**.

But how might a neuron become depolarized or hyperpolarized? Generally, because it receives a signal from another neuron that joins with it at a **synapse**. (If you really want to know ~~all~~ some of the details about synaptic transmission, go here: http://scienceblogs.com/neurotopia/2009/06/things_i_like_to_blog_about_ne.php and read Scicurious's very good overview. I'll wait.)



Two axon terminals (A1 and A2) synapsing onto a dendrite (Den). Note all the vesicles of neurotransmitter waiting to be released. The synapses (S1 and S2) are dark due to the density of receptors along the cell membrane. Image from starklab.slu.edu.

Basically, at a synapse, when the presynaptic neuron releases a **neurotransmitter** (such as glutamate, or GABA, or serotonin, etc) from its axon terminals, those molecules bind with receptors on the dendrites of the post-synaptic neuron. This causes the receptors to change shape and thus change how they interact with other molecules.

One major class of receptors is indirect, slow-acting (aka metabotropic) receptors, whose effects are to trigger a long chain of chemical events that results in longer-term changes to the cell's behavior (such as increasing the production of certain proteins). The other major class is direct, fast-acting (aka ionotropic) receptors, which are ion channels that require the presence of the neurotransmitter to open or close. For example, the most common type of glutamate receptor is a sodium channel. When glutamate is released from the presynaptic cell, it binds to this receptor, which opens, allowing sodium to enter the cell and depolarize it. The most common type of GABA receptor is a chlorine channel. When GABA binds to this molecule, it opens the channel, chlorine flows in, and the cell becomes hyperpolarized. Remember that channels are specific to a certain type (or types - some are more selective than others) of ions.

A neuron often receives input from multiple other cells, and these inputs can work together (all depolarizing or all hyperpolarizing) or against each other (some depolarizing, some hyperpolarizing). When these inputs work against each other, they

can cancel out, while when they work together, they have a larger effect on the neuron in question.

The reason why all of this matters is that the level of depolarization is what determines whether a neuron releases neurotransmitter. In typical neurons, depolarization past a threshold triggers an **action potential** (the electrical signal sent down the axon - more about it here: http://faculty.washington.edu/chudler/ap.html) which in turn triggers the release of neurotransmitter from the axon terminals. This is why depolarizing inputs are also called **excitatory** inputs (and hyperpolarizing are **inhibitory** inputs).

In most of the neurons in the retina that we've been studying (except retinal ganglion cells: RGCs do produce action potentials), there are no action potentials, but local **graded potentials**. Graded means that they can be bigger or smaller - the opposite of the all-or-none nature of the action potential. The cell membrane of the axon terminal are calcium channels that are sensitive to the membrane potential. When the cell depolarizes, these channels open. The calcium signals the vesicles - little "pouches" - of neurotransmitter to move to the cell membrane and release the neurotransmitter into the synapse.

In sum:

- Neurons have a membrane potential.
- This potential is changed when ions move across the membrane.
- Changing these ion flows is one way neurons communicate.
- The membrane potential effectively controls how the neuron releases neurotransmitter.