Neural Communication

by Richard H. Hall, 1998

Forces and Membranes

Now that we've considered the structure of the cells of the nervous system it is important to address their principal function, communication. As I have said, at the neuronal level this communication entails the sending of chemical messengers, called neurotransmitters from one neuron to another. As we will find out, the steps that lead to this process are far from simple and one of the most important factors is the movement of molecules across the neuronal membrane. I'm not just referring to the movement of neurotransmitters across the membrane, but the movement of ions that ultimately lead to this basic function of the neuron.

The process of ionic movement across the membrane occurs in two basic ways. The first process is referred to as passive transport. In **passive transport** a substance moves from one area to another (across the neuronal membrane in our discussion below) due to some sort of natural "force". This process requires no energy expenditure on the part of the cell. One of these forces in neuronal communication is **diffusion**. An ion that is in high concentration in one area will tend to move, or diffuse, to an area of lower concentration. So, for example, when an ion is in high concentration on one side of a membrane a force will be propelling it to the other side, and, if the membrane is **permeable** to this ion (i.e., will allow the ion through) the ion will move. A second force that's important in passive transport is **electrostatic pressure**. Ions, by definition, have a negative or positive charge and, as we all know from playing with magnets, positively charged particles will be attracted by negatively charged particles, repelled by other positively charged particles, and vice-versa. So, as with diffusion, an ion that is on a side of a membrane where the charge is the same (e.g., positive with positive) will be propelled by a force to the other side, if the membrane is permeable.

The second basic type of transport is called active transport, and in **active transport** an ion is actively moved ("forced") by some other mechanism *against* the concentration or electrostatic gradient. So, for example, an ion that is on a side of a membrane that has been drawn by either diffusion or electrostatic pressure, can be moved to the other side via active transport. This process requires energy on the part of the cell since the ion does not move in this way naturally. As we will see, all of these processes are fundamental in the process of neurotransmitter release, and, ultimately, neural communication.

Two other terms that are important for the following discussion are presynaptic and postsynaptic. The **presynaptic membrane** is the term used to refer to the membrane from which the neurotransmitter is released, the "sending" neuron. **Postsynaptic membrane** is the term used to refer to the membrane that receives the message carried by the neurotransmitter, the "receiving" neuron.

Resting Potential

When a neuron is not firing it is said to be at rest. Although it is "at rest", it always has the "potential" to fire, and this potential is expressed as the difference in electrical charges across the membrane of the neuron; differences in the electrical charge, that is, between the inside and outside. This creates a sort of tension, and is maintained by the semi-permeable properties of the membrane, the distribution of negatively and positively charged molecules, and active transport mechanisms, all of which we'll learn about below. **Resting potential** is the term used to refer to this difference in charge across the membrane. In a neuron at rest this is approximately —70mV (millivolts), which means the inside is 70mV more negative than the outside. This difference is also called polarization, so as the difference grows the membrane is said to be **hyperpolarized**, and as the number shrinks the neuron is said to be **hypopolarized**.

Figure 1 illustrates this difference in charge, and also the molecules that are important in maintaining this charge, and whose movement will be important in changing the charge, which will result in and will propel the release of neurotransmitters. **K^+** are potassium ions, **Na^+** are sodium ions, **Cl^-** are chloride ions, and **A^-** are organic anions (negatively charge protein molecules). The Cl^- is the only ion that is actually in balance on either side of the membrane in terms of passive transport. That is, the negative charge inside the cell and the concentration of Cl^- outside the cell make it so that, even if the membrane was not there the Cl^- would not move from one side to the other. The other three ions are "forced" to stay on their sides via membrane permeability and/or active transport. The membrane is impermeable to A^- so it cannot cross the membrane. The membrane is also semi-permeable to Na^+ and K^+, and these two ions are also actively transported via a membrane structure, called the **Na^+/ K^+ pump** which constantly moves Na^+ ions to the outside of the membrane and K^+ ions to the inside.

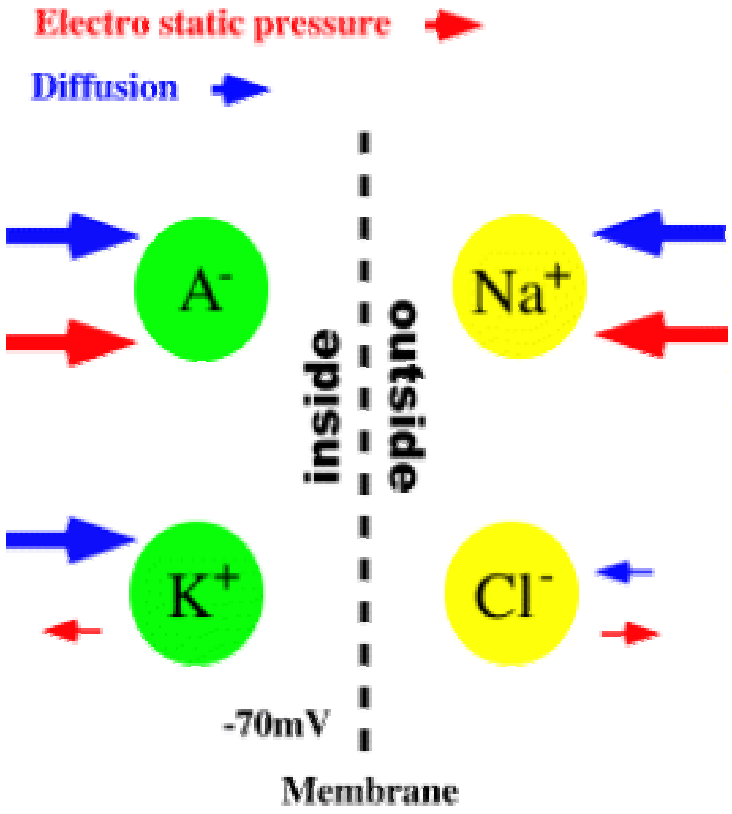

Figure 1. Ion Positions and Forces in a Neuron at Rest

Post Synaptic Potential

The process of neural communication begins, of course, when a neuron receives a signal from a sending neuron via neurotransmitters. These neurotransmitters affect the postsynaptic membrane via a set of processes, and ultimately result in changes in the permeability of the cell membrane to the important ions mentioned previously. Since all of the ions (besides Cl^-) actually are being "forced" to be on one side of the membrane or the other, changes in permeability of the neuron, which happens when **ion channels** open, allows for movement of the ions via diffusion and electrostatic forces, and, consequently causes changes in the charge across the membrane.

The membrane releases its neurotransmitter, as we will discuss below, in response to changes in the electrical charge across the membrane. More specifically, it is due to hypopolarization to the point where the potential reaches approximately —65mV. So, when neurons receive neurotransmitter messages, which result in the eventual movement of ions across the membrane, ions which hyperpolarize the membrane are said to be inhibitory (make the neuron less likely to fire), and those that hypopolarize the membrane are said to be excitatory (make the neuron more likely to fire). An inhibitory signal is called an **inhibitory postsynaptic potential (IPSP)**, and an excitatory signal is called an **excitatory postsynaptic potential (EPSP)**. Figure 2 illustrates how this works in terms of ion flow and channels opening. When an excitatory neurotransmitter contacts the postsynaptic membrane, either directly or indirectly, Na^+ channels are open. The result is

that Na^+ enters the cell and the cell depolarizes, thus becoming more likely to fire. When an inhibitory neurotransmitter affects a cell, the eventual result is that K^+ and/or Cl^- channels open. Of course, if K^+ channels open then K^+ leaves the cell due to the overwhelming force of electrostatic pressure. The effect of Cl^- in IPSPs is more complex and interesting however, in that Cl^- does nothing if the membrane is at rest, since it is in balance as discussed above. However, should a slight excitatory/depolarizing message be received at the same time that Cl^- channels are open, then Cl^- is like a gatekeeper or guard ready to enter to counteract this charge.

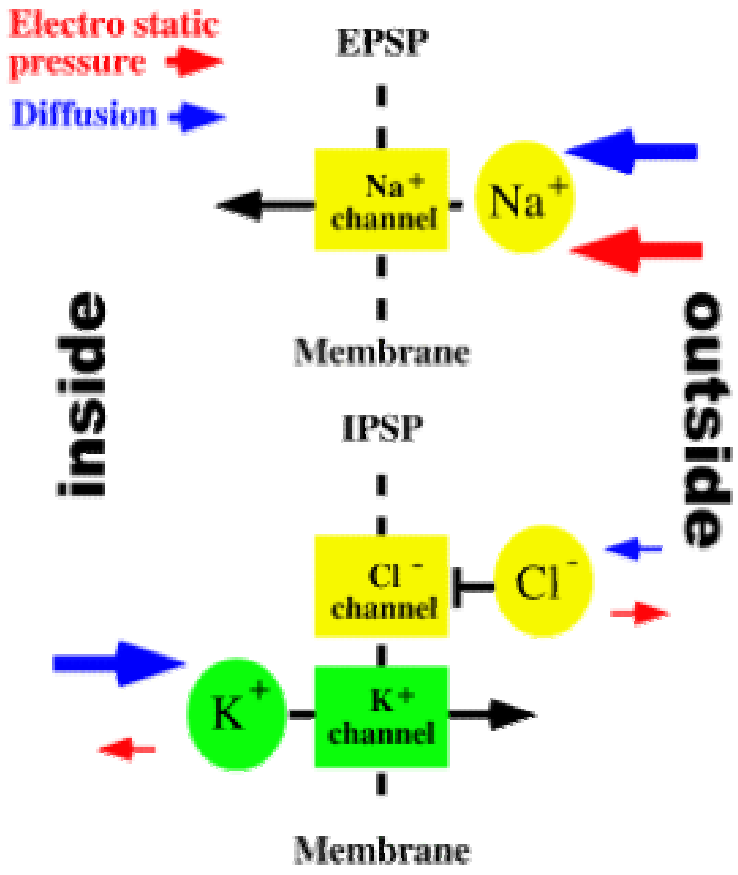

Figure 2. Ion Positions and Forces during EPSPs and IPSPs

So, which of these excitatory or inhibitory responses has the final say in whether or not a neuron fires, or more realistically, in the firing rate of a neuron, you might ask? The answer is that none of the signals on their own result in the final decision, but rather it is the combination of signals that matters, a phenomenon known as **summation**. Neurons synapse on many other neurons simultaneously and are constantly receiving signals, so whether they fire or not is not the result of a single excitatory or inhibitory message, but rather the result of the combination of messages they receive. The exact point where the important "decision" is made to fire or not is made at the junction of the cell body and axon, which is called the **axon hillock**. All of the messages travel to this area via a type of electrical conduction called **decremental conduction**, meaning that the message decreases with distance, and that it moves very quickly (in contrast to non-decremental

conduction, which we'll discuss in the next section). If the potential inside the membrane in this area reaches a "magic" point, an electrical charge of approximately -65mV, then an action potential occurs and the neuron's neurotransmitter is released.

Action Potential

An action potential is a series of events (presented in Figure 3), which involves a drastic change in the membrane's potential due to opening and closing of ion channels, and eventually results in the release of neurotransmitter. Once the membrane potential reaches approximately -65mV, a level which is referred to as the **threshold of excitation**, Na^+ channels in the membrane open and Na^+ enters the cell resulting in a quick depolarization of the cell. Once the potential reaches approximately 0mV, K^+ channels open and K^+ begins to leave the cell, due to pressure from diffusion and from the lessening of electrostatic pressure, since the inside of the cell is becoming positively charged. The potential eventually peaks about +40mV at which time Na^+ channels close and no more Na^+ can get in. The potential quickly returns to resting as K^+ continues to leave the cell, and eventually overshoots the normal resting potential and then quickly returns. This quite dramatic process all occurs in a few thousandths of a second.

This process occurs at a small portion of the membrane along the axon hillock. However, a chain reaction begins in which the action potential is carried down the axon with this dramatic process occurring over and over again as the message moves down the membrane. This type of conduction is called non-decremental in contrast to decremental conduction mentioned above in that the signal does not die down but is constantly regenerated. In fact, once the threshold of excitation is reached, from that point on, neurotransmitter release is inevitable. This phenomenon of firing or not, sort of like an off and on switch on a light, is referred to as the **all or none principle**. The message travels much slower down the axon than is the case in decremental conduction. However, in those nerves that are myelinated the axon potential is only regenerated at the nodes of Ranvier, while it travels via non-decremental conduction through the axon that is covered with the myelin (since the ions cannot cross the membrane in those places). The signal travels much faster under the myelin, and although the signal decreases, it is regenerated to its original strength at each node of Ranvier. In effect, the message bounces from node to node. This is why myelinated neurons carry the nerve signal faster. Conduction down a myelinated neuron is referred to as **saltatory conduction**.

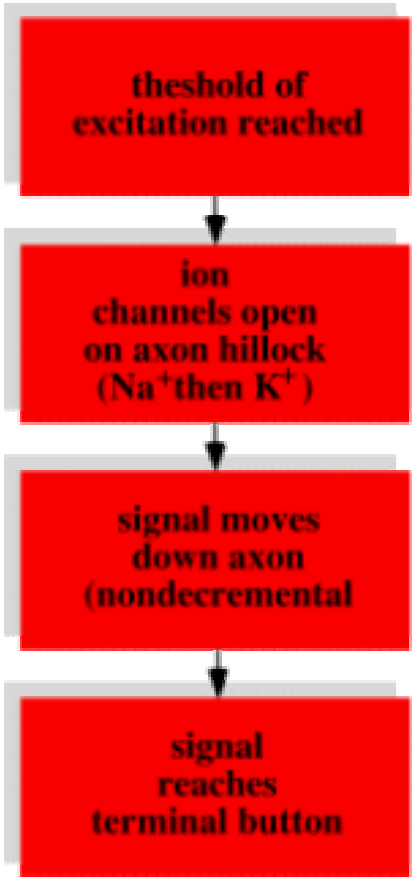

Figure 3. Events in an Action Potential

Neurotransmitter Release

Once the message reaches the terminal button, once again a process involving the opening of ion channels takes place. As with the rest of the neuron, the resting potential for the terminal button membrane is —70mV. Unlike the rest of the process described so far, the important ion is **Ca^{++}** (calcium). When the action potential reaches the terminal button, Ca^{++} channels open. Due to electrostatic pressure and diffusion, Ca^{++} ions enter the cell. Ca^{++} then plays an active role in initiating the release of neurotransmitter in that it affects the vesicles that contain the neurotransmitter molecule by stimulating them to move to fuse with the presynaptic membrane, and the phenomenon of exocytosis mentioned above occurs. Neurotransmitter is released into the synapse, and these neurotransmitters affect the postsynaptic membrane of another neuron and the same process starts all over again. Figure 4 is a schematic illustration of Ca^{++}'s role in neurotransmitter release.

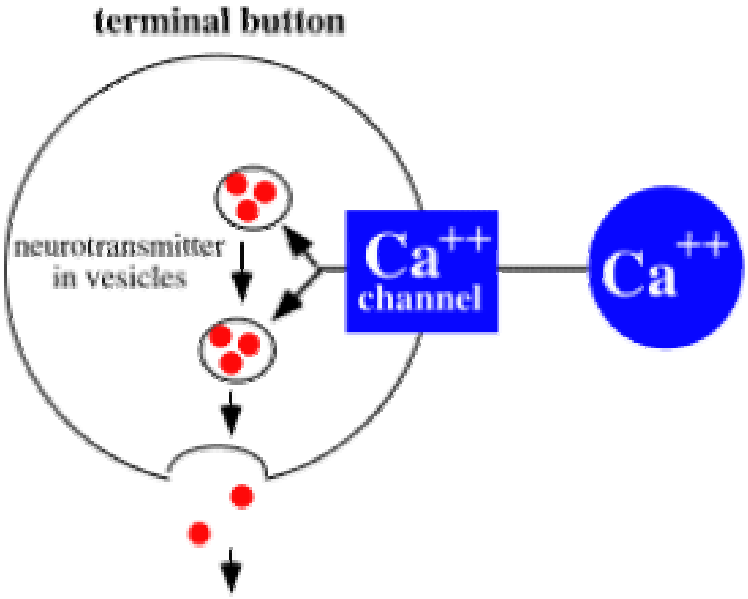

Figure 4. Events within Terminal Button Leading to Neurotransmitter Release

Other Factors

Once the neurotransmitter is released the effect it has on the postsynaptic membrane is very quick, so this brings up an important question. What happens to the neurotransmitter? Well, the nervous system is efficient, and most of the neurotransmitter is recycled in a process called **reuptake**, in which the neurotransmitter is taken back up into the presynaptic membrane and repackaged, to be released again. In the case of one type of neurotransmitter acetylcholine (Ach), the neurotransmitter is broken down into constituent parts by an enzyme called acetylcholinesterase (AchE), in a process called **enzymatic deactivation**.

There are some other factors that do not directly effect neural firing that nevertheless have an impact on the communication among neurons. First, some synapses actually occur directly on the axon. These synapses are called **axoaxonic**, as opposed to the more common synapses on the dendrite (**axodendridic**) or on the cell body (**axosomatic**). These synapses have no effect on whether or not a neuron will fire, since as we covered earlier, once an action potential is initiated at the axon hillock it is destined to move to the terminal button. The axoaxonic synapses actually affect the *amount* of neurotransmitter released. A message at such a synapse that increases the amount of neurotransmitter released results in what is knows as **presynaptic facilitation**, and one that decreases the amount of neurotransmitter released results in **presynaptic inhibition**.

A final factor that we will discuss that indirectly effects communication is the existence of special receptors called **autoreceptors**. These receptors, which are usually located on the presynaptic membrane are sensitive to neurotransmitters, just like receptors on postsynaptic membranes. However, they do not directly affect neural firing. Interestingly, they are usually sensitive to the neurotransmitter that is being release from the neuron

that they are on, and they act as a sort of informational feed back system, conveying information to their host neuron as to how much neurotransmitter is being released.

This completes our discussion of neural communication. I think it would be good at this point to reflect on the fact that this complex process is occurring over and over with 100s of millions of neurons in all of their many connections all over your nervous system at this very moment. It's easy to get caught up in the details and forget this important point, but when it really sinks it, it's certainly hard not to be impressed with such an amazing system.