

Neural Control and Exercise*

I. Introduction: Up to this point our discussions of excitable cells have entirely dealt with the ways by which a signal, the depolarization known as an action potential (AP), is spread along a neuron to muscle cells. That was the essence of our discussion of EC coupling -- we were interested in communication. However, groups of neurons "plan". We will see that "cellular network decision-making" is the fundamental basis for all neural decisions and for memory. These are highly complicated topics and we will not delve into deeply at all. But we will examine how it is that neurons can make simple decisions and we will overview the way that the body plans movement. These handouts should go nicely with your book chapter and amplify certain important points.

Today, we will deal with the mechanism by which one cell communicates with another. We will see that this inter-cellular communication allows for decision-making by groups of cells. As in the last class, the decision will be between whether or not to register a specific event or not.

II. Gross Anatomy and Physiology of the Nervous System The complexity of the nervous system prevents a complete understanding of organismic physiology and behavior at the present time, but basic principles of neuronal control can give us an idea of how the nervous system integrates responses as contrasted with hormonal integration (our next topic of discussion) which involves chemical messengers carried by the circulatory system. The nervous system consists of two main subdivisions:

- the **central nervous system (CNS)** which consists of the brain and spinal cord, and
- the **peripheral nervous system (PNS)** which is organized into **sensory** and **motor** units innervating **somatic** and **visceral** organs.

The complex functions of the brain are beyond the scope of our discussion of basic principles. We will concentrate on the PNS and only include the CNS in our discussion of the role of the spinal cord in integration. **The PNS** itself can be divided into two components:

- The **somatic system** is concerned with the control of skeletal muscles and with receiving certain types of peripheral sensory input. We often say that the effector side of the somatic system is **voluntary** because it is controlled in humans at least by processes that can be conscious.

The **visceral system** is concerned with sensory information from the major organs and the blood vessels and the control of these same organs and tissues. The effector side of the visceral system has its own name -- the **autonomic nervous system**. Its effectors are the smooth muscles of organs and the blood

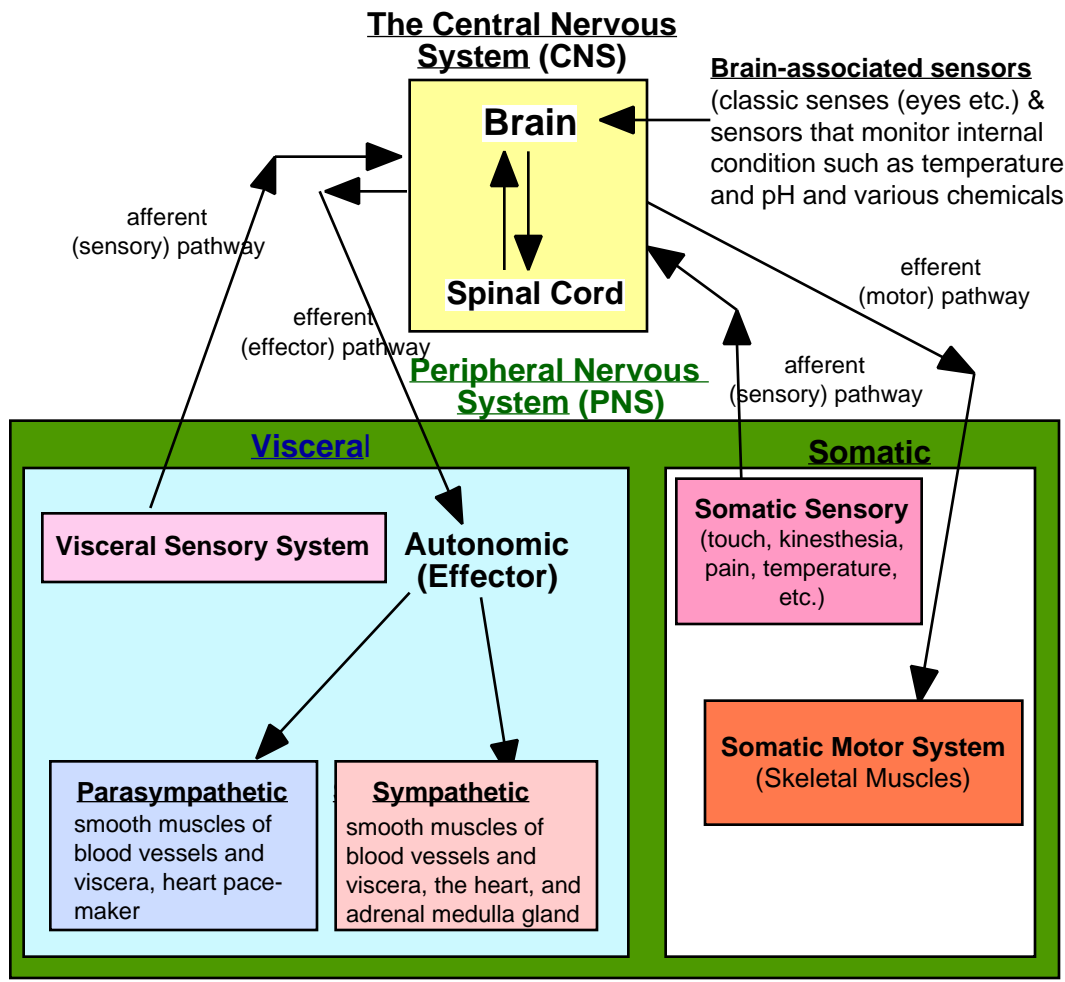
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vessels, the heart itself, and it also controls one endocrine organ -- the adrenal gland. The autonomic effectors are characterized as **involuntary** since most of the systems cannot (easily at least) be controlled by conscious processes.

Sensory Components of the PNS:

There are two sensory components of the PNS both of which possess specialized nerve endings and complex sense organs which respond to changes in their immediate environment.

- The **somatic subdivision** detects changes in the external environment and provides information as to motion and position (kinesthetic sense). More about this later.
- the **visceral subdivision** responds to changes in the internal environment. Please note that it is not the only monitoring area for the internal environment, there are also internal sensors in parts of the brain.



Visceral sensory systems tend to monitor specific areas of the body; in many ways, central sensors tend to monitor general body functions (such as "core" temperature or blood pH, or hormone levels). More about some of these specific sensors later.

III. The cells of the nervous system and their function

A. Support cells -- so called glial cells --

1. they are actually the most numerous cells in the brain and spinal cord.
2. There are a number of types and they perform many vital functions.

Examples of function include:

a. general chemical protection and support (for instance, the so-called "**blood brain barrier**" exists because many of the materials in blood must pass through glial cells before they can arrive at neurons; thus, some chemicals are prevented from potentially harming neural function.

b. Likewise, glial cells often serve as depots for the storage of energy rich compounds.

c. Glial cells may also have a role in fighting infections of the nervous system and

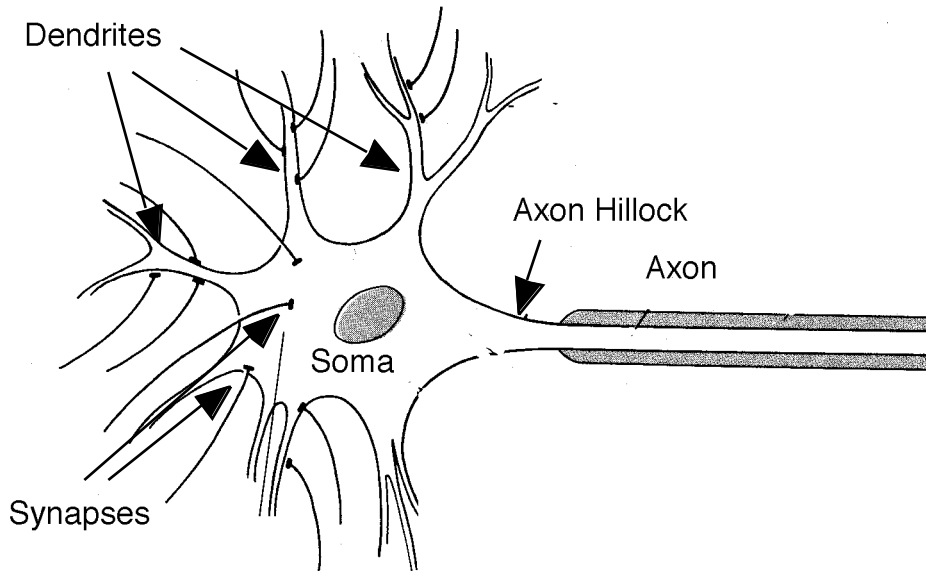
d. one type is responsible for producing a fatty "wrapping" around the axons of some neurons that speeds the rate at which action potentials move (this is called myelin).

Although they are very interesting, we will do nothing more with glial cells in this course.

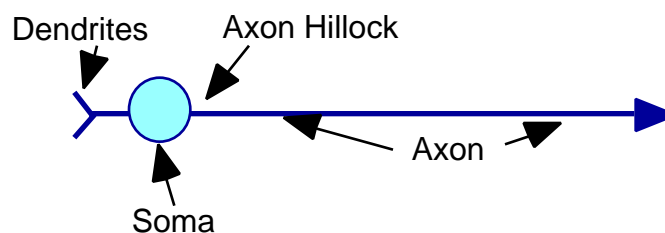
B. Computation, Information Transmission and Storage -- the Neurons

1. We have already been introduced to neurons when we considered motor units and EC Coupling. In this section, we are going to learn a bit about how neurons do something unique -- they can gather and represent information, transmit and store it, and make decisions based on a number of informational inputs. We will look at this in terms of the control of some very stereotyped reflexes and also in terms of the general ways that complicated movement, such as would be found in normal activity and sport, is controlled. Unfortunately, the latter is far too complex for us to look at closely in this course. But we should be able to understand how reflexes work.

2. About neurons -- a review. Neurons all have the same basic structure. Here is the central part of a typical neuron (next page):



The **soma** (body) is the "main" and the part of the neuron that most resembles other cells. It contains the nucleus, is the site of protein synthesis etc. Attached to the soma are a number of projections. Typically there are numerous short (typically shorter than the diameter of the soma) projections called **dendrites** and one or more long projections called **axons**. The axons typically have a constant diameter and may extend for a considerable distance (in some cases several meters but more commonly less than a cm¹). The point where axons leave the soma is very important (it is a major decision making center) and is called the **axon hillock**. One final point. In most cases, axons divide at their distal ends (the ends away from the soma) into many, many small "processes" (fine cylinders -- not shown in the previous diagram). We can schematize an axon as below:



IV. Resting, Graded and Action potentials

A. **Resting Potentials**: we learned earlier in the course that every kind of cell is electrically polarized. What this means is that if an electrode is placed inside and outside of the cell (*i.e.*, "across" the cell's membrane) a voltage is read. It is like the cell is a small battery. For all cells, the voltage is normally negative on the inside, typically somewhere between -50 and -100 millivolts (*i.e.*, between 0.05 and 0.1 V). We call this the **resting membrane potential**,

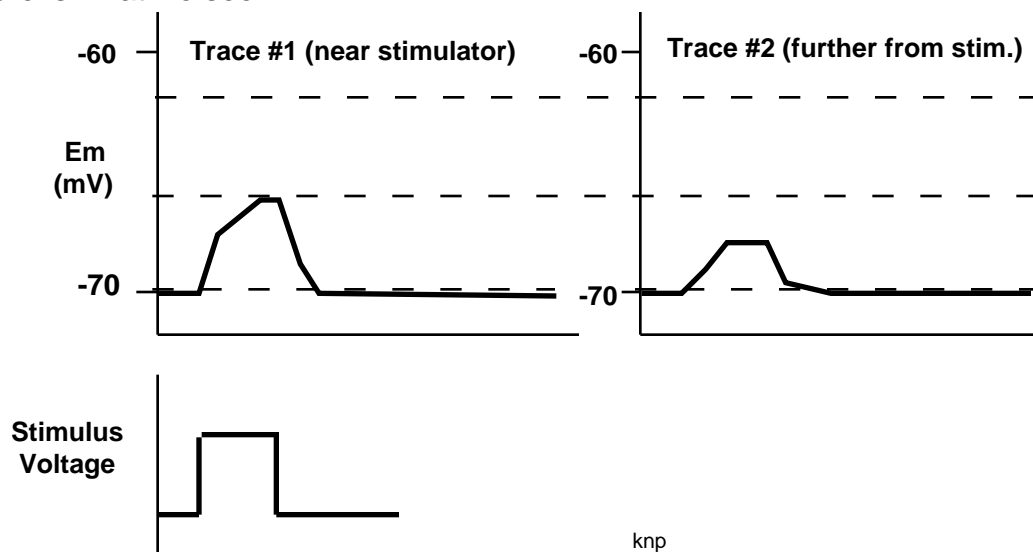
¹ But this is still very long compared to the length of a cell.

resting potential or **RMP** and for our purposes it represents the state of a cell that is not presently passing information from one place to another.

B. **Stimulation -- graded potentials.** Let's assume that we do something to the cell that somehow can cause the membrane potential to change from its resting value. We call this something that results in an electrical change a **stimulus**. Examples of stimuli are electrical currents, pressure, chemicals or perhaps even light. It generally depends on the cell in terms of what will act as a stimulus. However, electricity always works and so it is commonly used by physiologists to explore some of the properties of cells.

We will soon see that electricity is not the normal external stimulus. Instead, physiologists use it as a standin for the normal stimulus (examples -- pressure or motion).

1. Let's suppose that we give a small stimulus that causes the voltage across the membrane to become less negative (*i.e.*, more positive). We call such a stimulus a **depolarizing stimulus**. Now suppose that we place a couple of electrodes in the cell at varying distances from where we depolarize it. Here is what we see:

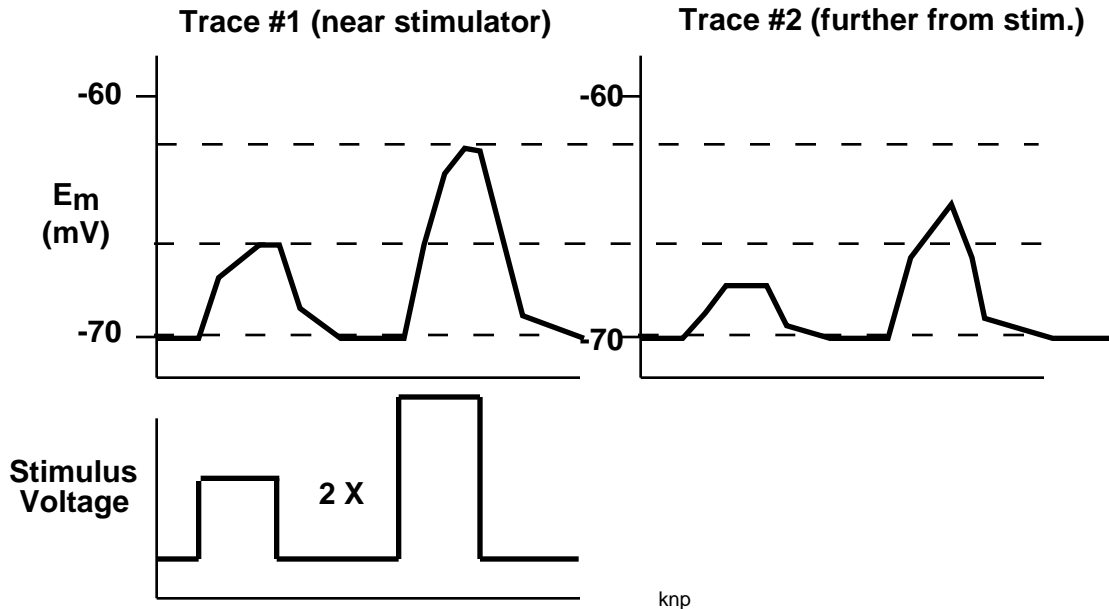


Notice that:

- The response travels away from the place where it was created (recall that both monitoring points were some distance away).
- The response decreases with distance and tends to return to the resting potential (-70 mV in the above example)

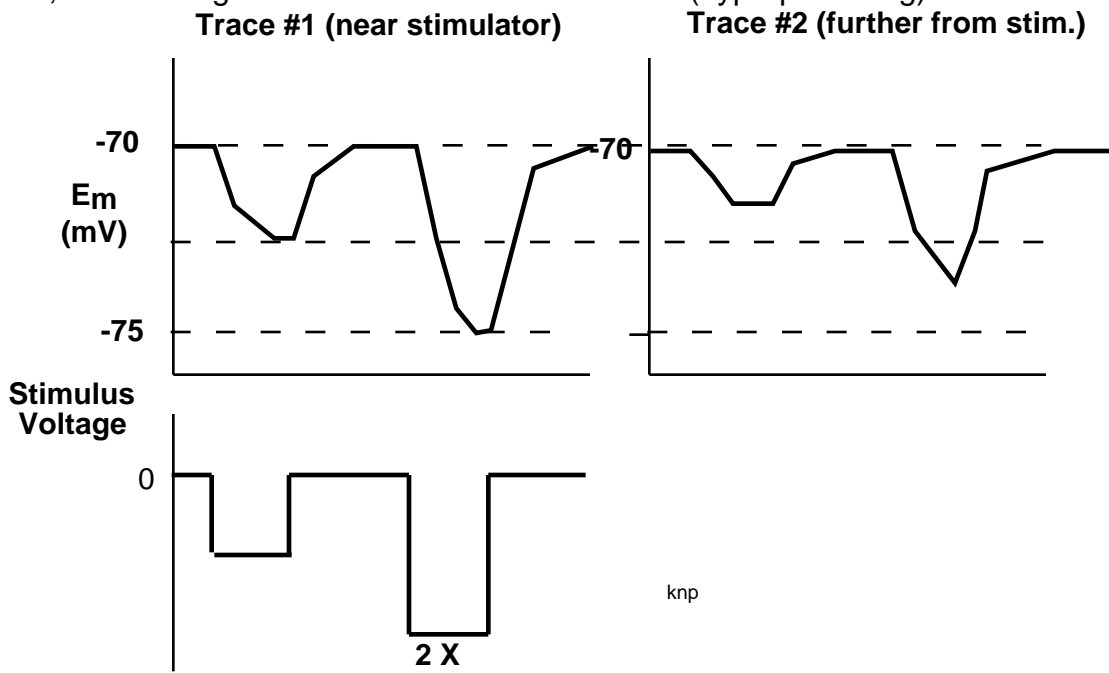
Here is the experiment repeated again this time with two different levels of stimulation where the second one is twice as great as the first (marked "2X"). Notice that everything we observed before is still true but also that we can see that

- the size of the response on the membrane is proportional to the size of the stimulus:



We say that this response is a **GRADED RESPONSE** because it decreases with distance and because its size is proportional to the size of the stimulus. These

2. It is also possible to provide a stimulus that makes the cell more negative than normal. We call this **hyperpolarizing** the cell (making the membrane more negative than the resting potential). The next graph shows the result; we once again use two levels of stimulation (hyperpolarizing):



Once again we get two graded responses each of which is **proportional in size and direction (hyperpolarizing in this case) to the stimulus** and each **decreases in magnitude as distance from the stimulus increases.**

Notice that with both the hyperpolarizing and depolarizing graded potentials, the membrane potential moves back towards the resting potential after the stimulus was over and as it travels. We call the return to the resting potential repolarization or restoration of the RMP.

It is a fundamental property of excitable cells that when they disturbed (hyperpolarized or depolarized) they tend to return to their resting potentials as soon as the disturbance is over. We will not investigate the mechanism in this course.

3. Three final comments about graded responses.

(a) they are always very small disturbances, especially when compared to an action potential (see below).

(b) they never travel great distances -- they quickly die out kind of like a weak wave on a pond.

(c) **They can be found on any part of an excitable cell.**

We will see shortly that **they are the only types of changes in membrane potential that occur on the soma and dendrites.**

C. **Action Potentials**

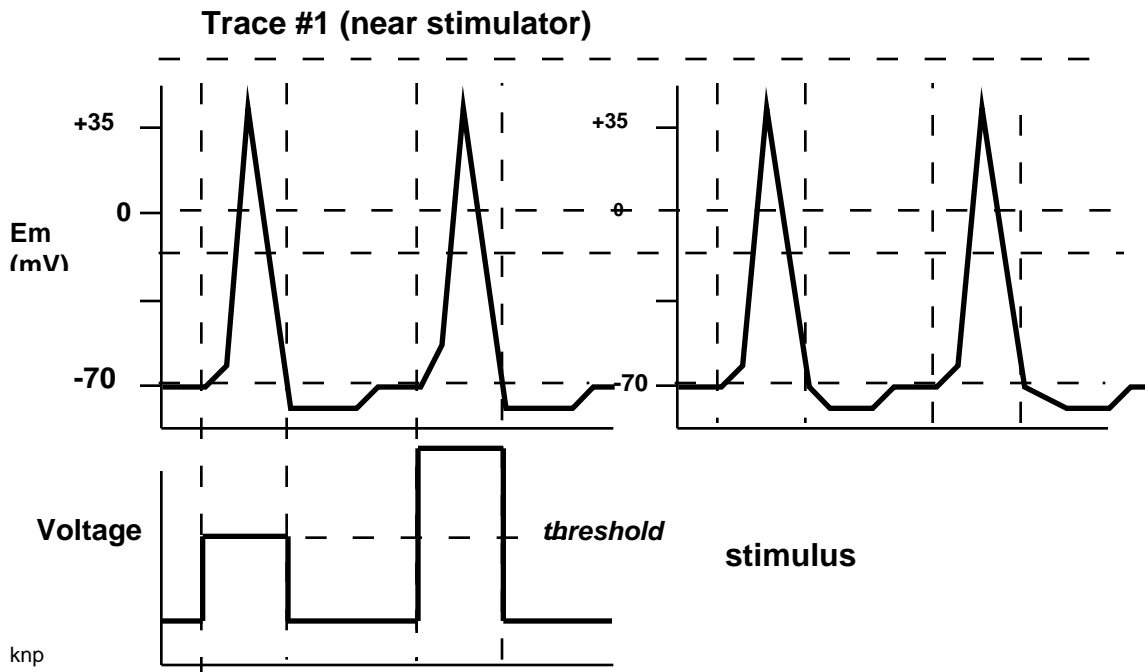
1. Action potentials are what the early neurophysiologists termed "nerve impulses". However, they are found on more than neurons -- muscles produce these interesting potentials also.

2. **On neurons, action potentials only occur on the axon -- they cannot be produced or transmitted over the soma or dendrites.**

3. How does one elicit an action potential? Using the same set-up as the two previous experiments, imagine that we continue to "turn up" a depolarizing stimulus.

a. For a while, if we increase the stimulus size in small amounts, we will continue to get larger and larger graded responses.

b. However, at some point termed the **THRESHOLD**, the cell suddenly responds with a very large change in electrical potential. Here are the results of two stimulations -- one where the stimulus exactly equals the threshold and the other where it exceeds the threshold:



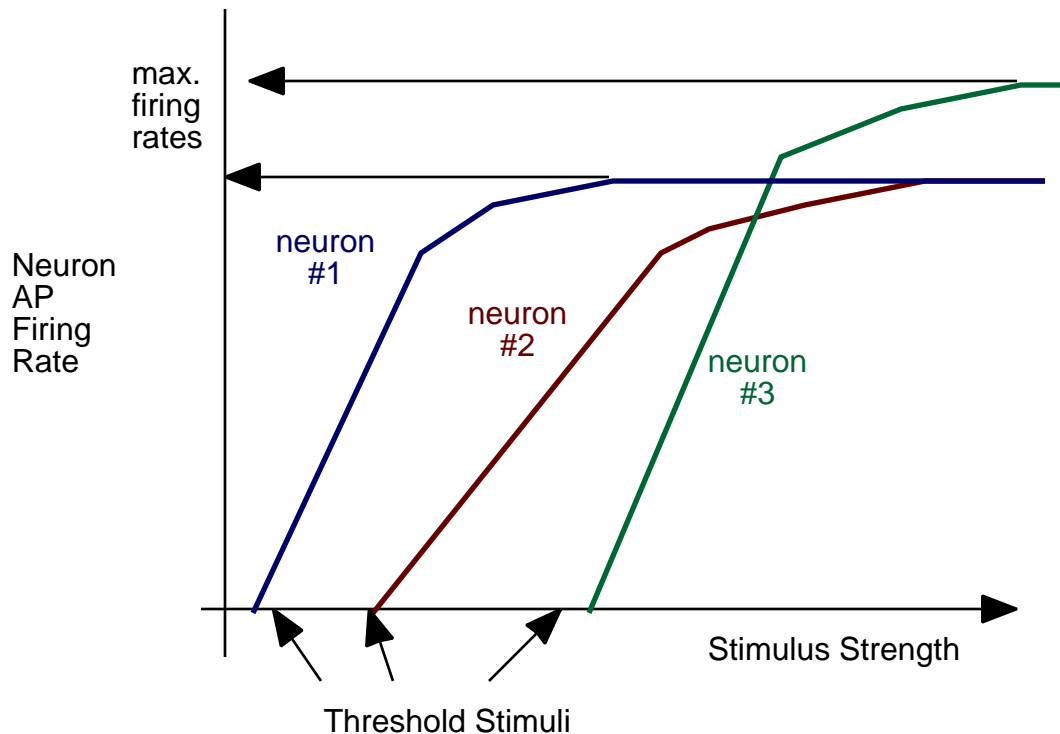
What can we summarize about these action potentials?

- APs appear only after some minimum stimulus has been reached. Again, this minimum level of stimulus is termed the **THRESHOLD**.
- As long as the threshold is exceeded, the action potential for a particular excitable cell has a set amplitude and duration -- it is always the same.
- The two previous observations are associated with a property of action potentials called "**ALL OR NONE**". In other words, either the conditions for an action potential are reached or they are not -- either you get an action potential or not and if you do, they are always the same (the "all" part).
- The membrane rapidly depolarizes and even becomes polarized in the positive direction (however, *we still call this "depolarized" -- in neurophysiology all discussion of polarity is relative to the resting potential, not to zero volts*). Then, it rapidly repolarizes and even becomes, for a brief period of time, more negative than normal resting values. Finally, it returns to normal resting values.
- **The action potential does not decrease in strength over distance.** Unlike the graded potential, notice how the action potential looks exactly the same at each point along the axon. A graded potential would, of course, become weaker and converge on the resting potential as the distance traveled increases. In contrast, we say that action potentials are **CONDUCTED WITHOUT DECREMENT**.

4. **Coding Information in the Nervous System:** We just stated that all APs are pretty much the same. Stronger stimuli do not result in stronger action potentials. So, how is information such as stimulus strength coded by neurons.

a. We have already seen that with graded responses, the response is proportional to the stimulus strength.

b. With action potentials, different strength stimuli are usually represented by differences in **firing frequency** -- the number of APs produced per unit time. The overall picture looks like this:



Notice in the picture above that each neuron has its own characteristic threshold, rate of response to the stimulus (note the different slopes which tell how much the firing rate changes with a given stimulus change) and maximum firing rate. So, they all "code" stimulus information in a somewhat different manner which is very useful. For instance, neuron #1 is very sensitive to both low levels of stimulus and to change in strength while neuron #2 is less sensitive to low levels but can deal with a wider range of strengths, etc. We will shortly learn a bit more about firing rates and information. However, first we need to consider the normal direction of information flow in neurons.

5. **Normal Flow of Information Within a Neuron:**

a. Normally, the dendrite soma part of a neuron is what is stimulated. We will see that stimulation can be through **either the action of other neurons** (next section) or, in the case of what are termed **sensors**, some event in the environment (chemical, pressure, temperature, movement, etc).

- b. The result of stimulation is to produce a graded potential.
- (i) the graded potential propagates away from the place where it was created (probably on the soma or dendrite) decreasing as it travels (see above).
 - (ii) eventually it reaches the axon hillock. If it exceeds threshold, it causes an action potential to be propagated down the axon from the hillock to its end. If the graded potential is less than threshold, it simply dies out. More about all of this shortly.
 - (iii) When the AP reaches the end of the axon in a region called the **synapse**, it normally causes the release of a chemical substance, called a **neurotransmitter** which is used to communicate with the next cell. We have already seen an example of this with acetylcholine. The next section will look closely at how one cell communicates with the next,

V. Intercellular Communication

A. Generally, neuronal communication between cells is very specifically directed at or received from certain other cells. An area of close contact between a neuron and another neuron or effector cell (example -- muscle cell) is called a **synapse**. There are two general types of synapse:

1. **Electrical synapses**: These occur in regions called gap junctions where two cells are essentially tied to each other. Thus, the cells are continuous with each other at the gap junction. Electrical synapses are found between smooth muscle cells, between cardiac muscle cells and are also common within the central nervous system and related structures such as the retina of the eye. Although quite common and vital for many examples of cell to cell communication, electrical synapses lack the ability to be involved in decision making. We will say little more about this type of synapse.

2. **Chemical synapses** are the more common and interesting synapse; these are of course, what we considered previously when we discussed the neuromuscular junction. So, chemical synapses are found between neurons and neurons and target tissues such as glands and muscles. With chemical synapses, there is **no direct contact between the cells**. Nevertheless, these are areas where cells can communicate with each other via chemicals called **neurotransmitters**. We will learn in some detail how these work and how they are involved in neural decision making.

3. As mentioned above, information generally moves through the nervous system from dendrite and soma to axon and then to another cell first via the dendrite or soma and then eventually to the axon. We will see that one of the features of chemical synapses is that they are what force information to move in one direction. So, a bit of terminology that centers around the synapse². With respect to the flow of information:

² which could be called the informational connection between two cells.

- a. the cell that first possesses information is termed the **presynaptic neuron**
- b. the receiver of this information is the **postsynaptic neuron**.
- c. Typically the post-synaptic portion of the synapse is on neural dendrites or the soma. In the case of a connection with a muscle, the post synaptic part is a specialized region of the muscle called the neuromuscular endplate (don't learn this)

B. A Review of How Chemical Synapses Work;

1. Recall that axons divide near their ends (for example, think of a motor unit).
2. When there are chemical synapses, they do not touch the next cell; instead there is a fluid-filled **synaptic gap** between them.
3. Communication is the result of the release of a chemical. Most signalling involves chemicals being released from storage areas (called **synaptic vesicles**) located at the end of the axon.
4. The released chemical, called a **neurotransmitter (NT)** is typically released for the period of time when the action potential is present (it dies out at this point).
5. It travels the short distance to the post-synaptic cell.
6. There communication will only occur if the NT binds to a protein that is specific for it -- called **neurotransmitter receptor**. Furthermore, we will see that a large number of receptors must actually bind the NT for there to be any chance of getting the next neuron to fire an AP. More about this shortly.
7. Finally, **it is very important the NT be broken down or removed**. We have previously seen an example of this with ACHase which breaks down ACH.

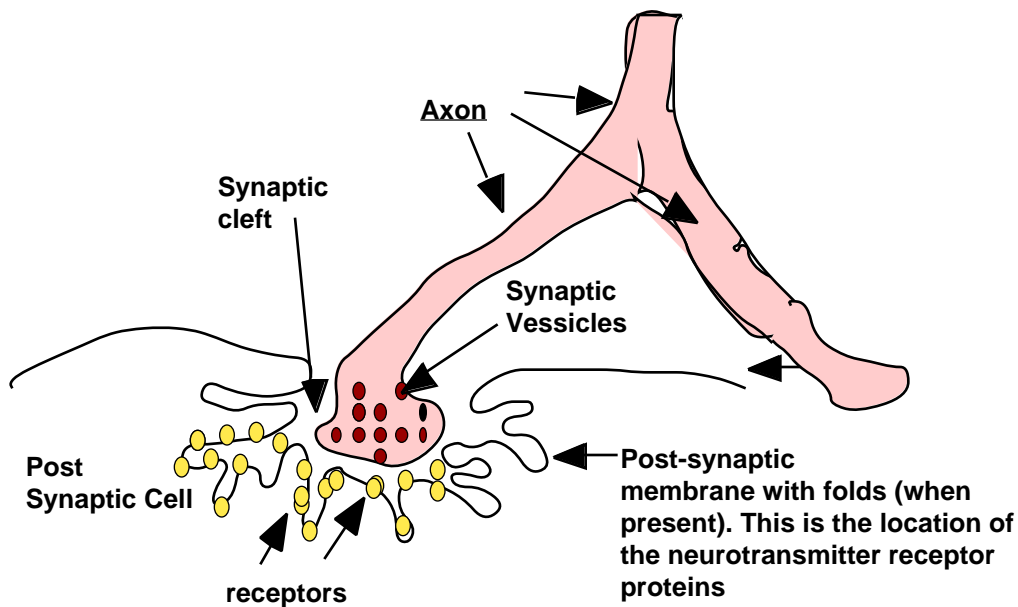
Why must the NT be removed?

What do you suppose would happen if NT is not removed?

Could information continue to pass from cell to cell?

Would changes in the rate of NT removal affect how the entire nervous system operated?

On the top of the next page is a diagram of a chemical synapse; this one would be found between a motor neuron and a skeletal muscle cell:



8. Receptors, Post-Synaptic Potentials, and Neural

Computation: *The effect of NT binding to its specific receptor is to create a **small graded response**.* The more NT receptors that are activated at a given moment, the larger the response. Thus, this will have something to do with:

- the number of NT molecules released
- the number of NT receptors available
- the NT receptor types (not all proteins are the same) and the resulting potential.

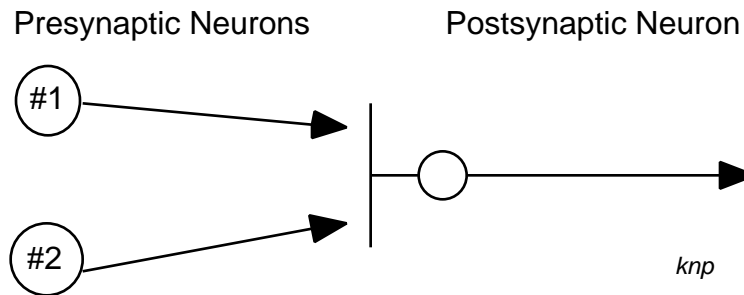
9. **Post-synaptic electrotonic potentials come in two types:**

- a. those that represent depolarizations and which move the cell towards threshold are called **EXCITATORY POST SYNAPTIC POTENTIALS (EPSPs)** and
- b. those which hyperpolarize the cell and therefore move the potential further from threshold and make it less likely to fire an AP -- they are called **INHIBITORY POST-SYNAPTIC POTENTIALS (IPSPs)**

10. **Neural Decision Making and Post-Synaptic Potentials.**

Neurons decide whether or not fire in response to stimuli based on a number of factors but the crucial factor is always whether or not they are depolarized to threshold. We can call this decision making process **neural computation**. Let's consider a simple model of it:

Neural Computation -- the Basic Model



Notice that the post-synaptic cell can receive input from either cell 1, cell 2 or both. Let's review what happens and then add a few new wrinkles:

a. The original potential on the post synaptic cell are all graded responses.

b. The binding of a neurotransmitter causes the membrane to depolarize (or hyperpolarize) locally, this disturbance will spread as a graded potential. **Think of the moving graded potential as being like a wave on a pond that spreads outward from where a rock hit. Keep one problem with this analogy in mind -- these "waves" will only be above the mean water level (i.e., let's say depolarized from normal E_m) or below the normal level (like an IPSP) in the other -- no continuous up and down movement as in "real" waves.**

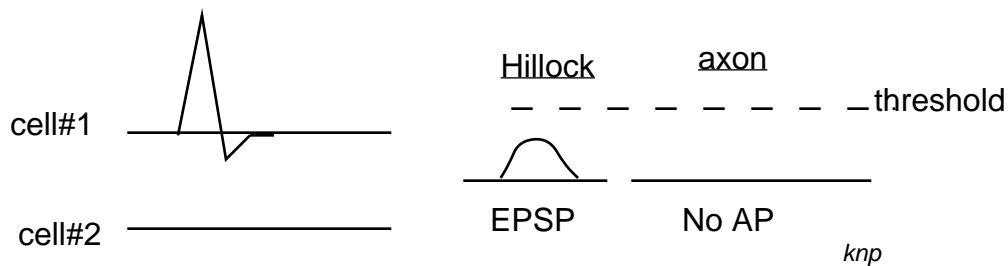
c. The only way to go *that matters* is towards the soma and axon. However, as these waves spread from the source, they gradually decay to a value that is closer and closer to the mean water level (resting potential) -- just like graded responses always do.

d. If the wave is an EPSP depolarization, it, by itself, is unlikely to ever be large enough to reach the first point where an AP can be produced³ at a sufficiently large depolarization to cause an AP. Usually a process called **summation** is necessary.

e. Before looking at summation let's familiarize ourselves with a simple system we will use to illustrate summation. First let's consider again what happens if there is no summation. In the example on the next page, the EPSP that results from cell #1's release of NT is sub-threshold -- there is no AP:

³ Recall that on a neuron this is called the **axon hillock** the place where the axon emerges from the soma

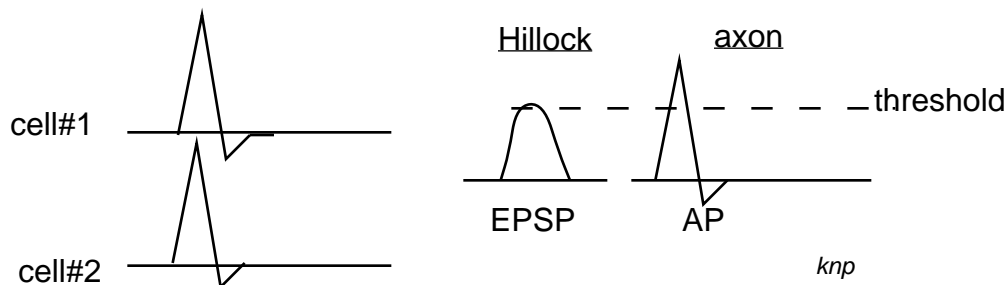
I. No Summation



f. How can we get a graded response that exceeds the threshold at the axon hillock. The answer is **SUMMATION** -- processes whereby one or more graded responses are added together. There are two general types of summation:

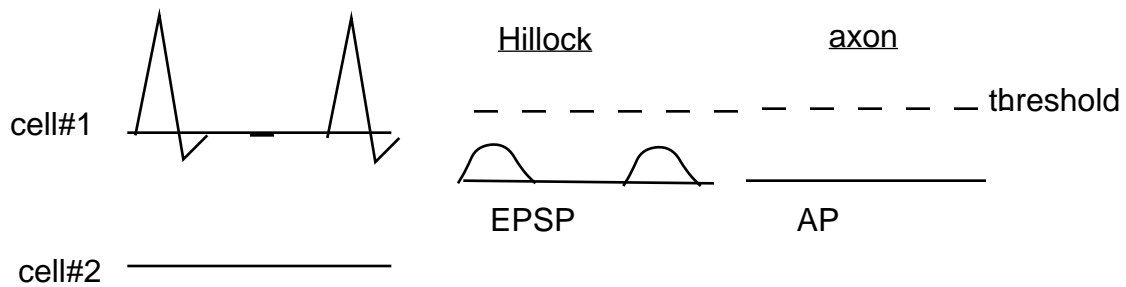
(i) **SPATIAL SUMMATION**: where potentials that originated in different parts of the post synaptic potential come together at the same time on the hillock. If the voltages add enough to exceed threshold, an AP is triggered (see figure):

II. Spatial Summation

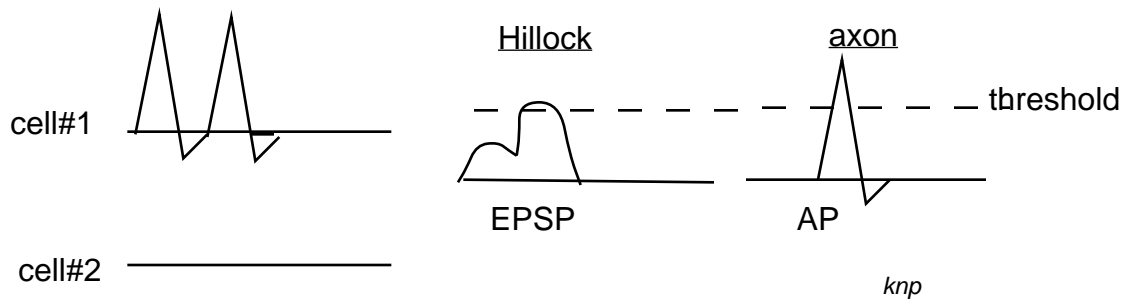


(ii) . **TEMPORAL SUMMATION**: occurs where two or more potentials that originated at slightly different times come together and sum at the hillock. The figure on the next page shows such a process where cell #1 fires. In the top diagram, the APs are far enough apart that the graded potentials do not add and neither can reach threshold and fire the neuron. In the second example, the APs come so close together that the EPSPs merge into a stronger potential that triggers an AP. This is temporal summation. We will be less concerned with this one.

IIIa. Temporal Summation Fails

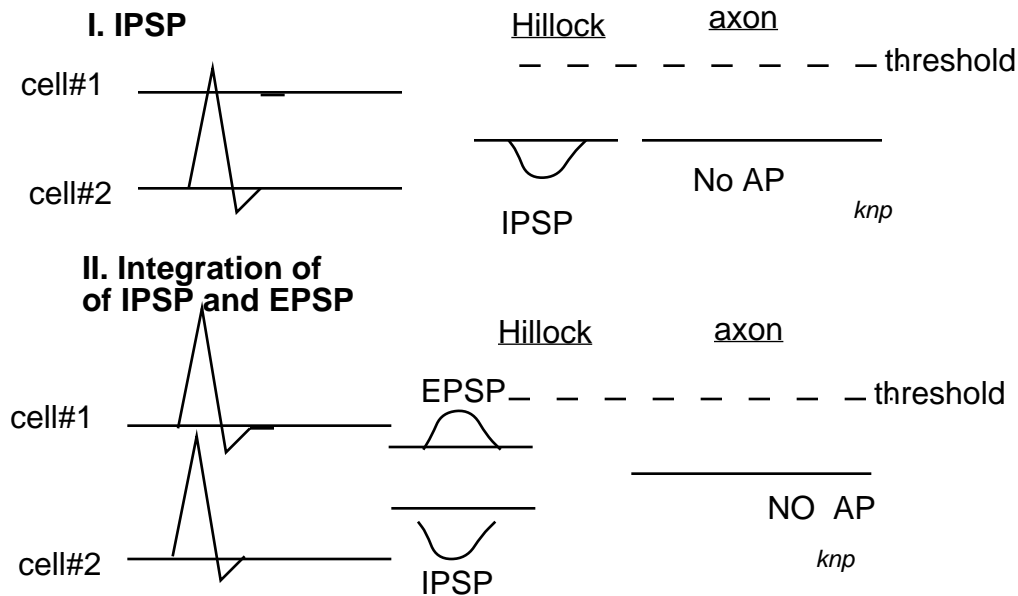
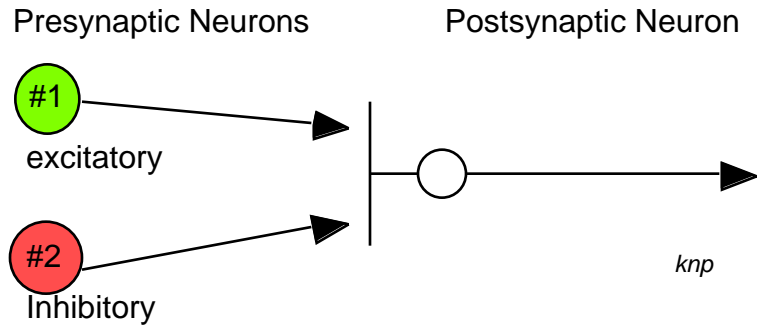


IIIb. Temporal Summation



g. In many cells it is possible that both IPSPs and EPSPs will come together and sum. Obviously, they will tend to cancel each other out -- the IPSPs make it more difficult for the cell to fire, even when it is also generating EPSPs. A diagram is shown on the next page:

Neural Computation #2



C. Splitting Information into Excitatory and Inhibitory Signals.

1. Imagine the following scenario. Suppose that a particular neuron is caused to fire. For example, assume that it is hooked up to a pressure sensor and that pressure has been applied. The neuron eventually generates an action potential.

2. Now, suppose that the presence of pressure on this particular neural pathway requires some muscles to be excited and others to be inhibited. How can a single excitatory event produce both excitation and inhibition? After all, the neuron only releases one type of neurotransmitter.

3. The answer is that there are different receptors connected to the neuron. The receptors on one cell, the one to be excited, generate an EPSP in response to the neurotransmitter they receive. By contrast, the cell that is supposed to be inhibited has a different type of receptor that in turn generates an IPSP in response to the same signal and it becomes harder to fire. Check out the diagram below, it is an important concept!

