

Chapter 11 Nervous Tissue and Membrane Potentials

There are two types of nervous tissue cells

- Neuroglia (glia or glial cells) support the functioning of neurons.
- Neurons (nerve cells) transmit electrical signals

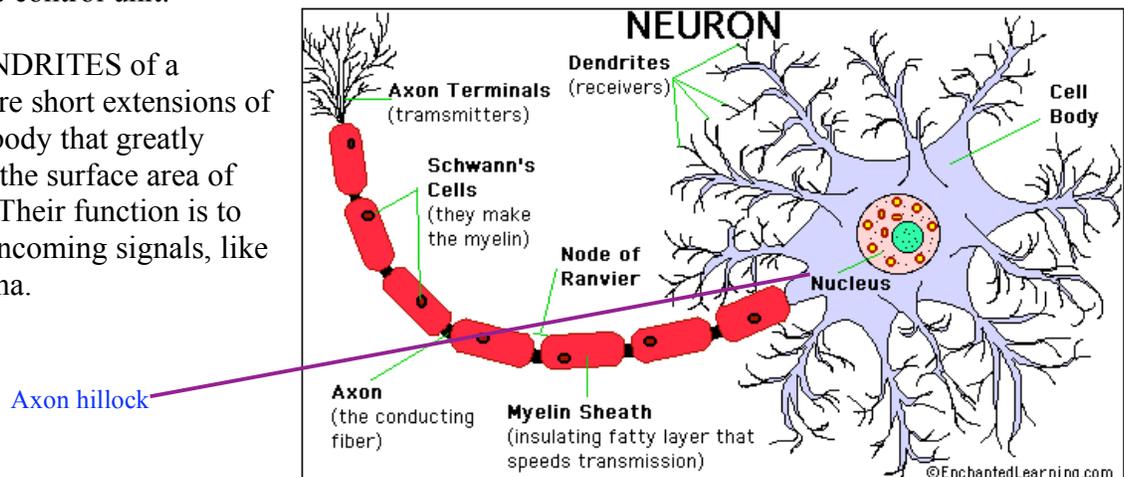
There are six types of NEUROGLIA. Four are in the CNS, two in the PNS

1. ASTROCYTES (CNS)
 - Have many radiating processes
 - They anchor neurons to blood vessels, holding them in place
 - They guide the growth of neurons (pre & post natal)
 - Participate in Blood Brain Barrier
 - Involved in neuronal processing through local impulses and neurotransmitter release
2. MICROGLIA (CNS)
 - Phagocytic cells that destroy pathogens and dead neurons
3. EPENDYMAL CELLS (CNS)
 - Ciliated cells that create and circulate CSF (line choroids plexus and ventricles)
4. OLIGODENDROCYTES (CNS)
 - Create myelin sheath around neuronal axons
5. SATELLITE CELLS (PNS)
 - Surround clusters of neurons
 - Function is unclear, but may support/nourish neurons
6. SCHWANN CELLS (PNS)
 - Create myelin sheath around neuronal axons
 - Assist in regeneration of peripheral nerves (verrrrry sloooooow)

NEURONS

The CELL BODY of the neuron is called the SOMA. It contains the typical organelles, with a few specializations: the nucleus is big, there are no centrioles (*unique feature*) since the neurons don't divide, and an abundance of RER (*nissl bodies*), free ribosomes, mitochondria and Golgi apparatus. The reason for this abundance is that neurons are very metabolically active. The function of neurons is that they process incoming signals and act as the control unit.

The DENDRITES of a neuron are short extensions of the cell body that greatly increase the surface area of the cell. Their function is to receive incoming signals, like an antenna.



The AXON is a single long extension from the cell body. It arises from the AXON HILLOCK. Axons may produce collateral axon branches. The function of the axon is output. It conducts signals away from the neuron (it is the effector of a homeostatic mechanism)

TERMINAL BRANCHES are at the end of each axon. Each branch ends in a slight bulge called the AXON TERMINAL (also called, bouton or synaptic knob). The axon terminal forms a junction with the next cell(s).

The MYELIN SHEATH is created by glial cells (oligodendrocytes and Schwann cells). It is composed of multiple layers of cell membrane that are wrapped around the axon, so essentially is a wrapping of lipid bilayer. The sheath insulates against electrical leakage and speeds the impulse conduction.

NODES OF RANVIER are little gaps between sheath cells. They help the electrical signal speed along the axon, up to 10-30x faster than it would without. This is what makes white matter.

NERVOUS TISSUE

Neurons are classified by their structure and their function. STRUCTURAL CLASSIFICATION has to do with how many extensions protrude from the neuron.

- MULTIPOLAR have many dendrites. This is the most common type
- BIPOLAR have two extensions...one dendrite, one axon. These are fairly rare and are found in some special sense organs
- UNIPOLAR have a single short process that forms a T-shaped extension. Both extensions behave as axons.

When CLASSIFIED BY FUNCTION, it relates to the way stimulus is heading

- SENSORY NEURONS (AFFERENT) are going *toward the CNS*. These carry sensory stimulus from the sense organ to the CNS. Almost all of these are ***unipolar***.
- MOTOR NEURONS (EFFERENT) carry information about what to do in the form of motor impulses *away from the CNS*. The cell body is in CNS
- ASSOCIATION NEURONS (INTERNEURONS) are the **most abundant functional type!** They lie between sensory and motor neurons within the CNS. Almost all of these are ***multipolar***.

MEMBRANE POTENTIALS

POTENTIAL refers to the difference in electrical charges between regions. It is measured in voltage (mV) and is the result of a separation of electrical charges (ions).

RESTING POTENTIAL is the membrane potential when the neuron is NOT sending a stimulus (-70mV) The membrane is negative inside the cell relative to outside the cell.

The principal way neurons send signals over long distances is by generating and propagating ACTION POTENTIALS (APs). Only cells with excitable membranes can

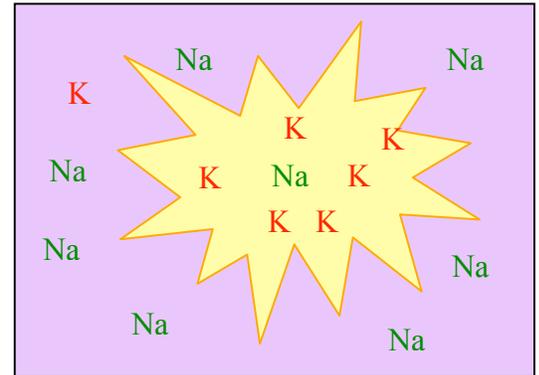
generate APs (muscle fibers and neurons). An AP is a brief reversal of membrane potential with a total change in voltage from -70mV to +30mV, then back to negative.

CONDITIONS FOR RESTING POTENTIAL

Potassium (K⁺) is much more concentrated inside the cell.

Sodium (Na⁺) is more concentrated outside the cell.

- This creates two concentration gradients!
- Both “leak” down the concentration gradient and is a passive process.
 - Sodium (Na⁺) will MOVE IN
 - Potassium (K⁺) will MOVE OUT
- This is not equal! The membrane is more permeable to K⁺, so more K⁺ moves OUT. This



creates a greater loss of cations from the inside as the K⁺ leaves cell at a greater rate than Na⁺ moves in. This creates a more **NEGATIVE ENVIRONMENT INSIDE THE CELL.**

While all this leakiness is going on, Sodium-Potassium pumps are working. The pumps work *against the gradient*. So...

- Sodium (Na⁺) gets pumped OUT
- Potassium (K⁺) gets pumped IN

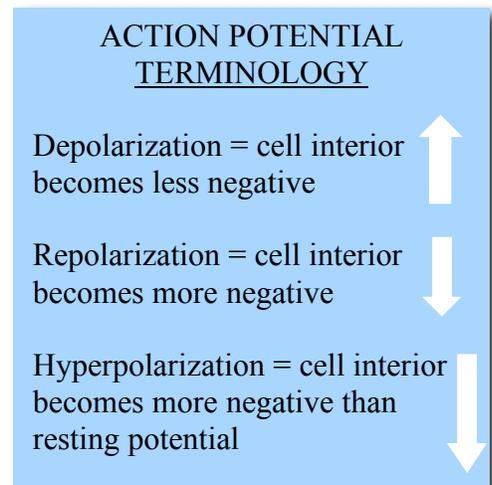
This counteracts leakage! For every three Na⁺ going out, the pump brings two K⁺ in. So, the change here is that more positive charge is going out than coming in...also creating negativity! This restores the gradient and contributes to electrical difference.

ACTION POTENTIAL

First, a few key players in AP. The **AXONAL MEMBRANE PROTEINS** come in a few different types.

- ATP-driven sodium-potassium pump (active)
- Ion leakage channels (passive)
- Voltage-gated channels (passive)

The **VOLTAGE-GATED Na CHANNEL** is only open when membrane potential rises above set value. It is closed during resting potential. The opening is rapid. Once open, Na moves *passively down the gradient*. The channel inactivates after a short period of time, so Na movement stops!



The **VOLTAGE-GATED K Channel** opens when membrane potential rises. The opening is slow. Unlike the sodium channel, the potassium channel does not have an open-but-inactive state. It is either entirely open or all the way closed.

In the RESTING PHASE

1. Na⁺ and K⁺ leakage is going on
2. The Na/K pump is working to keep the gradients
3. Both voltage gates are closed
4. Membrane potential is at about -70mV.

ACTION POTENTIAL INITIATION (at the axon hillock)

1. Local membrane potential is pushed to threshold in area around the gate
2. This initiates the opening of the voltage-gated Na⁺ channel
3. At this point, membrane potential is at about -55mV.

DEPOLARIZATION PHASE (more positive, moving away from resting potential)

1. The voltage-gated Na⁺ channel opens FAST!
2. Na⁺ rushes into the cell (passive process)
3. This raises the number of cations and membrane potential rises, causing...
4. More voltage-gated Na⁺ channels open and more sodium coming into the cell raises membrane potential even higher.
5. This is a positive feedback mechanism
6. Membrane potential rises rapidly to +30mV.

REPOLARIZATION PHASE (more negative, moving toward resting potential)

1. The time-sensitive Na⁺ channels begin inactivating, and this begins the repolarization phase.
2. So, the inward rush of Na⁺ slows to a stop
3. Around the same time, the voltage-gated K⁺ channels open
4. K⁺ moves down its gradient, leaving the cell
5. This is a rapid drop toward resting potential

HYPERPOLARIZATION (more negative, moving away from resting potential)

1. Na⁺ channels reset to their closed state
2. K⁺ channels stay open a little longer. They are closing, but do so slowly
3. So, we go beyond resting potential because we are still losing cations as the potassium is still leaving the cell
4. Membrane potential slowly rises back to resting potential as K⁺ channels close.

CHARACTERISTICS OF ACTION POTENTIAL

- All or none!
 - If you don't reach threshold, then nothing happens. No AP is generated and the cell stays at RP.
- Stereotyped
 - All APs are of a consistent amplitude and duration. You've seen one you've seen 'em all! Depolarization above threshold does not increase size of the stimulus.
- Unidirectional

- Starts at axon hillock and moves down the axon, a propagation toward the terminal branches (like waves in the ocean are a propagation of energy). The AP is generated repeatedly along the axon.

THE REFRACTORY PERIOD is the time during which action potential cannot be generated with normal stimulus.

- ABSOLUTE REFRACTORY PERIOD is the time when voltage-gated Na⁺ channels are already open and no action potential is possible. This ensures that each AP is a separate, *all-or-none* event and enforces one-way transmission of the action potential.
- RELATIVE REFRACTORY PERIOD follows the absolute refractory period. It is when the voltage-gated Na⁺ channels have reset, and some K⁺ are still open so repolarization is occurring. A large stimulus is required, as threshold potential is temporarily elevated. This very large stimulus could reopen the Na⁺ channels and allow another AP to be generated.

Chapter 11 The Synapse

A **SYNAPSE** is where two neurons meet. It is also where a neuron meets its effector cell. There are three types of synapses.

1. Axodendritic synapse = axon to dendrite (the most common)
2. Axosomatic synapse = axon to soma (bypasses dendrite)
3. Axoaxonic synapse = axon to axon (uncommon)

TYPES OF SYNAPSES

ELECTRICAL SYNAPSE is a direct cell-to-cell connection. The cytoplasm of two cells are directly connected via a protein channel (sort of like a gap junction, but not really.) The transmission is very rapid! It is also very uncommon (hippocampus/eye movement).

CHEMICAL SYNAPSE is most common type. There is a space between two synapses. This space is the **SYNAPTIC CLEFT**. On the presynaptic cell, this space is at the axon terminal. It contains synaptic vesicles that are filled with neurotransmitters.

CHEMICAL SYNAPTIC TRANSMISSION PROCESS

1. Action potential reaches axon terminal, causing the voltage-gated calcium channels to open, so...
2. Calcium rushes in!
3. Calcium influx stimulates exocytosis of vesicles containing neurotransmitter. This mechanism is not clear.
4. Neurotransmitter is released into the synaptic cleft and diffuses across cleft
5. Neurotransmitter binds to receptors on postsynaptic cell.

GRADED POTENTIAL is a short-lived change in membrane potential. Graded potentials are not propagated like an action potential, so not a positive feedback loop. It degrades in intensity from the site of stimulation.

- The size varies directly with the size of the stimulus (unlike AP)
- Results from opening chemically-gated ion channels
- The ion channels open in response to the presence of key chemicals
- The effect on the neurotransmitter is that it creates a graded potential in postsynaptic cell
- The potential spreads from the synapse toward the axon hillock (it gets less intense as it spreads away from the synapse)

TERMINATION OF THE CHEMICAL TRANSMISSION

The neurotransmitter binds transiently, and this binding continues as long as neurotransmitter is in the cleft. It is removed from the cleft in three ways:

1. Degradation of the neurotransmitter. There are specific degradation proteins (enzymes) in the cleft or on the postsynaptic cell.

TERMINOLOGY

Presynaptic cell is the cell carrying impulse *toward* synapse

Postsynaptic cell is the cell receiving signal

Most neurons serve in both capacities

All cells pump calcium out of the cell!

2. Reuptake (recycling). Astrocytes or presynaptic endocytose neurotransmitter. The NT may be re-used or destroyed.
3. Diffusion. NTs diffuse out of the cleft and are degraded elsewhere.

POSTSYNAPTIC POTENTIALS are graded potentials. There are two kinds!

- Excitatory Postsynaptic Potential (EPSP)
 - When a NT causes an EPSP, it opens chemically gated Na⁺ channels so sodium moves in!
 - It will also cause chemically-gated K⁺ channels, so potassium will move out!
 - Difference from AP is that in graded potential, both move simultaneously
 - Sodium has larger electrochemical gradient, so more Na⁺ moves IN than K⁺ moves OUT. The membrane potential gets *more positive* and the membrane depolarizes (small amount).
 - The cell is pushed closer to threshold.
- Inhibitory Postsynaptic Potential (IPSP)
 - When a NT causes an IPSP, the NT binds to the membrane and opens chemically-gated K⁺ channel, so potassium moves OUT.
 - This is a loss of + charge, so the cell becomes *more negative*
 - May also open chemically-gated Cl⁻ channel. Since chloride is more concentrated outside the cell, it rushes in so cell becomes *more negative!*
 - With either of these you get hyperpolarization!

INTEGRATION

Individual postsynaptic potentials are not enough to effect axon hillock and push it to threshold. They are either too weak or too far away from the axon hillock. It is also important to note that most neurons synapse with 1,000 to 10,000 other neurons. EPSPs and IPSPs can summate, meaning the effects of many PSPs on the membrane potential are additive. There are two ways to summate:

- TEMPORAL SUMMATION (timing). This uses the same synapse repeatedly...it is repeated stimulation of a single synapse. The interval between impulses is less than the time for the PSP to dissipate. It may be enough to push to threshold.
- SPATIAL SUMMATION. Is stimulation by two or more synapses near simultaneously. The PSPs add together!

Both EPSPs (+) and IPSPs (-) can summate, and you get a net result and a cumulative effect on the axon hillock. If the sum total reaches threshold, then action potential is initiated! Remember, it's all-or-none. If not at threshold, nothing happens!

FACILITATION occurs when the cell doesn't reach threshold. This subthreshold stimulation facilitates the neuron. The membrane potential is closer to threshold until it falls back to resting. During this time, the neuron is easier to stimulate to threshold.

SYNAPTIC POTENTIATION is the repeated use of a synapse, creating larger postsynaptic potentials. This increases the likelihood of postsynaptic cell action potential. The mechanism is that increased calcium levels in the axon terminal increase the release of neurotransmitter. Synaptic potentiation is involved in learning...the efficacy of neural pathway is improved. It has been identified in the hippocampus (which relates to memory consolidation...short term memory to long term memory)

In PRESYNAPTIC INHIBITION one neuron synapses on the axon of another. This interferes with the release of neurotransmitter from the second neuron. The result is smaller EPSPs (not a production of IPSPs).

NEUROTRANSMITTERS

There are over 50 NEUROTRANSMITTERS! Most neurons release two or more, and they are released differentially by stimulation rate. One NT is released at a slow rate, and another is released at a faster rate. This increases the versatility of the neuron.

CLASSIFICATION of NEUROTRANSMITTERS is by chemical structure and by the type of effect/mechanism of action (function).

- **STRUCTURAL CLASSIFICATION OF NTs**
 - Acetylcholine (ACH). The first identified and best understood. It is secreted at neuromuscular jxns at at some autonomic nervous system synapses.
 - Biogenic Amines are derivatives of amino acids. They are common throughout the brain and some autonomic synapses. They play a role in emotion and biological clock as well as imbalances with mental illness. They can be subdivided into two categories:
 - Catecholamines (epinephrine, dopamine, norepinephrine)
 - Indolamines (serotonin, histamine)
 - Amino Acids are difficult to establish because all cells have them
 - Gamma-aminobutyric acid (GABA) – (flucine, aspartate, glutamate)
 - Neuropeptides are small proteins involved with pain processing.
 - “Substance P” is a neuropeptide that mediates pain signals
 - Endorphins reduce pain perception (beta-endorphin, dynorphin, enkaphalins). They are mimicked by morphine and natural opiates...opiates bind to endorphin receptors.
 - Purines. ATP behaves as a neurotransmitter, producing a rapid excitatory response. Adenosine (a nucleotide) has an inhibitory effect. Caffeine blocks adenosine receptors.
 - Dissolved gases are the most recently discovered.
 - Nitric Oxide (NO) is synthesized “on demand” (unique feature). It binds intracellularly, not on the membrane. It may be involved with learning and memory pathways.
 - Carbon Monoxide acts similarly to NO

- FUNCTIONAL CLASSIFICATION of NTs (by type of effect)
 - Excitatory: usually produce EPSP
 - Inhibitory: usually produce IPSP
 - Both: EPSP or IPSP, depends on receptor
- FUNCTIONAL CLASSIFICATION of NTs (by mechanism of action)
 - Direct: neurotransmitter binds to ion channel it opens (Acetylcholine, amino acids, purines)
 - Indirect: stimulates intracellular agent (“second messenger”). It has an activity like many hormones (biogenic amines, neuropeptides, dissolved gases). NTs that act indirectly tend to promote broader, longer-lasting effects.

NEUROMODULATION describes a chemical messenger released by a neuron that does not directly cause EPSPs or IPSPs but does affect the strength of the synaptic transmission. The chemicals effect EPSP/IPSP by making it bigger or smaller. This acts at a site on the cell other than the synapse. When presynaptic it involves an alteration of the neurotransmitter’s synthesis, release (block or stimulate), regradation or reuptake. When postsynaptic, it involves an alteration to the neurotransmitter receptor sensitivity. The distinction between neurotransmitters and neuromodulators is fuzzy, but chemical messengers such as NO and a number of neuropeptides are often referred to as neuromodulators.