

Neurophysiology Danil Hammoudi.MD



Terminology

- Medial toward the midline
- Lateral away from the midline
- Ipsilateral same side
- **Contralateral** opposite side
- **Decussate** crossover ~

Somatosensory Receptors

Several types

- thermoreceptors
- chemoreceptors
- mechanoreceptors
- nociceptors
- proprioceptors
- Transduction of environmental energy ~

Mechanoreceptors

- Unmyelinated axon branches
- Free nerve endings

 glabrous & hair regions
 pain sensation

Basket cells

Hairy regions ~

Mechanoreceptors

Encapsulated end organs

- Glabrous (hairless) skin
- Non-neural tissue
- Merkel's Disks

Meissner's corpuscle
Pacinian corpuscles
Ruffini endings ~

Somatosensory Pathways

- Touch -
 - Dorsal column-medial lemniscal pathway
- Pain and Temperature -
 - Spinothalamic system
- Trigeminal pathway
 - face & neck
 - cranial nerve V, also others \sim

Somatosensory Pathways

- Spinal Cord Columns
 - Ascending tracts of axons
- Dorsal columns
 - touch & proprioception
- Lateral columns
 - pain & temperature \sim

3 Classes of Movement

Voluntary

- complex actions reading, writing, playing piano
- purposeful, goaloriented
- learned
 - improve with practice ~

Reflexes

- involuntary, rapid, stereotyped eye-blink, coughing, knee jerk
- graded control by eliciting stimulus

<u>Rhythmic motor patterns</u>

 combines voluntary & reflexive acts

chewing, walking, running

- initiation & termination voluntary
- once initiated, repetitive & reflexive ~





- synapse,
- a cell junction that mediates the transfer of information from one neuron to the next







• The neuron that conducts impulses away from the synapse is called the postsynaptic neuron





 Most neurons function as presynaptic (information sending) and postsynaptic (information receiving neurons

 In essence they get information from some neurons and dispatch it to others



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- Most synapses <u>occur between the axon terminals</u> of one neuron and the dendrites of another <u>axons</u>
- These are called *axodendritic synapses*



- Less common, and far less understood, are:
- synapses between two axons <u>(axoaxonic</u>),
- between two dendrites (dendrodendritic)
- between a dendrite and a cell body <u>(dendosomatic</u>)



Types of Synapses

§ <u>Axodendritic</u> – synapses between the axon of one neuron and the dendrite of another

§ <u>Axosomatic</u> – synapses between the axon of one neuron and the soma of another

§ Other types of synapses include:

§ Axoaxonic (axon to axon)

§ Dendrodendritic (dendrite to dendrite)

§ Dendrosomatic (dendrites to soma)





2 FUNCTIONAL TYPE OF SYNAPSES

<u>Electrical Synapses</u>

- Are less common than chemical synapses
- Correspond to <u>gap junctions</u> found in other cell types
- Are important in the CNS in:
 - Arousal from sleep
 - Mental attention
 - Emotions and memory
 - Ion and water homeostasis

Chemical Synapses

•Specialized for the release and reception of *neurotransmitters*

- •Typically composed of two parts:
- Axonal terminal of the presynaptic neuron, which contains synaptic vesicles
- Receptor region on the dendrite(s) or soma of the postsynaptic neuron

- Structurally synapses are elaborate cell junctions
- At the typical axodendritic synapse the presynaptic axon terminal contain synaptic vesicles



- Synaptic vesicles are membrane bound sacs filled with molecular neurotransmitters
- These molecules transmit signals across the synapse



Mitochondria are abundant in the axon terminal as the secretion of neurotransmitters requires a great deal o energy



- At the synapse, the plasma membranes of the two neurons are separated by a synaptic cleft
- On the under surfaces of the opposing cell membranes are dense materials; the pre- and post- synaptic densities



- When an impulse travels along the axon of the presynaptic neuron, it signals the synaptic vesicles to fuse with the presynaptic membrane at the presynaptic density
- The released neurotransmitter molecules diffuse across the synaptic cleft and bind to the postsynaptic membrane at the post synaptic density

•The binding of the two membranes changes the membrane charge on the postsynaptic neuron, influencing the generation of a nerve impulse or action potential in that neuron







Receptor Activation

- Ionotropic channel
 - directly controls channel
 - Fast

Metabotropic channel

- second messenger systems
- receptor indirectly controls channel ~





Ionotropic Channels



Ionotropic Channels



Metabotropic Channels

- Receptor separate from channel
- 2d messenger system
 - G proteins
 - cAMP
 - other types
- Effects
 - Control channel
 - Alter properties of receptors
 - regulation of gene expression ~

G protein: direct control

- NT is 1st messenger
- G protein binds to channel
 - opens or closes
 - relatively fast ~




Communication

- Begins with the stimulation of a neuron.
 - One neuron may be stimulated by another, by a *receptor* cell, or even by some physical event such as pressure.
- Once stimulated, a neuron will communicate information about the causative event.
 - Such neurons are sensory neurons and they provide info about both the internal and external environments.
 - Sensory neurons (a.k.a. afferent neurons) will send info to neurons in the brain and spinal cord.
 - There, association neurons (a.k.a. interneurons) will integrate the information and then perhaps send commands to motor neurons (efferent neurons) which synapse with muscles or glands.

Sinus node-(nodus sinuatrialis)

Internodal pathways

Right bundle branch

the conducting system of the heart, showing anterograde conduction of the cardiac impulse.

Terminal branches

Interatrial pathway Atrioventricular node (nodus atrioventricularis) Trunk of bundle (bundle of His) Left bundle branch Anterior fascicle

Posterior fascicle

Types of Nerve Fibers

1. Group A

- <u>Axons of the somatic sensory neurons and motor</u> neurons serving the skin, skeletal muscles, and joints.
- Large diameters and thick myelin sheaths.
 - How does this influence their AP conduction?
- 2. <u>Group B</u>
 - Type B are lightly myelinated and of intermediate diameter.

3. <u>Group C</u>

- Type C are unmyelinated and have the smallest diameter.
- Autonomic nervous system fibers serving the visceral organs, visceral sensory fibers, and small somatic sensory fibers are Type B and Type C fibers.

A group

 Fibers of the A group have a large diameter <u>and high</u> <u>conduction velocity, and are myelinated fibers.</u>

The A group consists of four types of nerve fibers:

- A alpha fibers (afferent or efferent fibers)
- A beta fibers (afferent or efferent fibers)
- A gamma fibers (efferent fibers)
- A delta fibers (afferent fibers)

B Group

- Nerve fibers in these group, are myelinated with a <u>small diameter</u>.
- they are the preganglionic fibers of the autonomic nervous system.
- Preganglionic fibers have a low conduction velocity.

C Group

- The C group fibers are unmyelinated and as the B group fibers have a small diameter and low conduction velocity. These fibers include:
- Postganglionic fibers in the autonomic nervous system (ANS)
- Nerve fibers at the dorsal roots (IV fiber). These fibers carry the following sensory information:
 - Pain
 - Temperature
 - Touch
 - Pressure
 - Itch

Now we know how signals get from one end of an axon to the

other, but how exactly do APs send information?

• Info can't be encoded in AP size, since they're "all or none."

In the diagram on the right, notice the effect that the size of the graded potential has on the frequency of AP's and on the quantity of NT released. The weak stimulus resulted in a small amt of NT release compared to the strong stimulus.



MODE OF ACTION



Chemical Signals

- One neuron will transmit info to another neuron or to a muscle or gland cell by releasing chemicals called neurotransmitters.
- The site of this chemical interplay is known as the synapse.
 - An axon terminal (synaptic knob) will abut another cell, a neuron, muscle fiber, or gland cell.
 - This is the site of transduction the conversion of an electrical signal into a chemical signal.



Synaptic Transmission

I. Within the axons of the neuron are neurotransmitters, which are held in storagelike vesicles until they are released when the neuron is stimulated.

2. The small space between the axon terminal and the dendrite of the next axon is called the synapse. An action potential stimulates the release of neurotransmitters across the synapse.



3. The neurotransmitter binds itself to the receptor sites on dendrites of the next neuron, causing a change in potential.

Synaptic Transmission

- An AP reaches the axon terminal of the presynaptic cell and causes <u>V-gated Ca²⁺</u> channels to open.
- Ca²⁺ rushes in, binds to regulatory proteins & initiates NT exocytosis.
- NTs diffuse across the synaptic cleft and then bind to receptors on the postsynaptic membrane and initiate some sort of response on the postsynaptic cell.



Effects of the Neurotransmitter

- Different neurons can contain different NTs.
- Different postsynaptic cells may contain different receptors.
 - Thus, the effects of an NT can vary.
- Some NTs cause cation channels to open, which results in a graded depolarization.
- Some NTs cause anion channels to open, which results in a graded hyperpolarization.

Phases of the Action Potential

- 1 resting state
- 2 depolarization phase
- 3 repolarization phase
- 4 hyperpolarization





Action Potentials

- If V_M reaches threshold, Na⁺ channels open and Na⁺ influx ensues, depolarizing the cell and causing the V_M to increase. This is the rising phase of an AP.
- Eventually, the Na⁺ channel will have inactivated and the K⁺ channels will be open. Now, K⁺ effluxes and repolarization occurs. This is the falling phase.
 - K^+ channels are slow to open and slow to close. This causes the V_M to take a brief dip below resting V_M . This dip is the undershoot and is an example of hyperpolarization.





The Movements of Ions During the Action Potential



Na⁺ Channels

- They have 2 gates.
 - At rest, one is closed (the activation gate) and the other is open (the inactivation gate).
 - Suprathreshold depolarization affects both of them.

At the resting membrane potential, the activation gate closes the channel.





Absolute Refractory Period

- During the time interval between the opening of the Na⁺ channel activation gate and the opening of the inactivation gate, a Na⁺ channel CANNOT be stimulated.
 - This is the ABSOLUTE REFRACTORY PERIOD.
 - A Na⁺ channel cannot be involved in another AP until the inactivation gate has been reset.
 - This being said, can you determine why an AP is said to be unidirectional.
 - What are the advantages of such a scenario?

Relative Refractory Period

- Could an AP be generated during the undershoot?
 - Yes! But it would take an initial stimulus that is much, much stronger than usual.
 - *WHY*?
 - This situation is known as the relative refractory period.

Imagine, if you will, a toilet.

When you pull the handle, water floods the bowl. This event takes a couple of seconds and you cannot stop it in the middle. Once the bowl empties, the flush is complete. Now the upper tank is empty. If you try pulling the handle at this point, nothing happens (*absolute refractory*). Wait for the upper tank to begin refilling. You can now flush again, but the intensity of the flushes increases as the upper tank refills (*relative refractory*)

Action Potential Conduction

• If an AP is generated at the axon hillock, it will travel all the way down to the synaptic knob.

• The manner in which it travels depends on whether the neuron is myelinated or unmyelinated.

• Unmyelinated neurons undergo the *continuous conduction* of an AP whereas myelinated neurons undergo *saltatory conduction* of an AP.

Continuous Conduction

- Occurs in unmyelinated axons.
- In this situation, the wave of de- and repolarization simply travels from one patch of membrane to the next adjacent patch.



Saltatory Conduction

- Occurs in myelinated axons. propagation of action potentials along myelinated axons from one node of Ranvier to the next node, increasing the conduction velocity of action potentials without needing to increase the diameter of an axon
- *Saltare* is a Latin word meaning "to leap."







Rates of AP Conduction

- Which do you think has a faster rate of AP conduction myelinated or unmyelinated axons?
- 2. Which do you think would conduct an AP faster an axon with a large diameter or an axon with a small diameter?

The answer to #1 is a myelinated axon.

If you can't see why, then answer this question: could you move 100ft faster if you walked heel to toe or if you bounded in a way that there were 3ft in between your feet with each step?

The answer to #2 is an axon with a large diameter. If you can't see why, then answer this question: could you move faster if you walked through a hallway that was 6ft wide or if you walked through a hallway that was 1ft wide?

- Communication btwn neurons is not typically a one-to-one event.
 - Sometimes a single neuron branches and its collaterals synapse on multiple target neurons. This is known as divergence.
 - A single postsynaptic neuron may have synapses with as many as 10,000 postsynaptic neurons. This is convergence.
 - Can you think of an advantage to having convergent and divergent circuits?



Postsynaptic Potentials

 <u>Neurotransmitter receptors mediate changes in membrane potential according</u> to:

The amount of neurotransmitter releasedThe amount of time the neurotransmitter is bound to receptors

• The two types of postsynaptic potentials are:

•EPSP – excitatory postsynaptic potentials •IPSP – inhibitory postsynaptic potentials order

•<u>Spatial summation</u> – postsynaptic neuron is stimulated by a large number of terminals at the same timE

•IPSPs can also summate with EPSPs, canceling each other out

EPSPs & IPSPs

- Typically, a single synaptic interaction will not create a graded depolarization strong enough to migrate to the axon hillock and induce the firing of an AP.
 - However, a graded depolarization will bring the neuronal V_M closer to threshold. Thus, it's often referred to as an excitatory postsynaptic potential or EPSP.
 - Graded hyperpolarizations bring the neuronal V_M farther away from threshold and thus are referred to as inhibitory postsynaptic potentials or IPSPs.



• EPSPs, like IPSPs, are graded (i.e. they have an additive effect)

Excitatory Postsynaptic Potentials(EPSP)

•excitatory postsynaptic potential (EPSP) is a temporary depolarization of postsynaptic membrane potential caused by the flow of positively charged ionsinto the postsynaptic cell as a result of opening of ligand-sensitive channels

•EPSPs are graded potentials that can initiate an action potential in an axon

•Use only chemically gated channels
•Na + and K + flow in opposite directions at the same time

•Postsynaptic membranes do not generate action potentials

A postsynaptic potential is defined as excitatory if it makes the neuron more likely to fire an action potential.

EPSPs can also result from a decrease in outgoing positive charges, while IPSPs are sometimes caused by an increase in positive charge outflow.

The flow of ions that causes an EPSP is an excitatory postsynaptic current (EPSC).

This single EPSP does not sufficiently depolarize the membrane to generate an action potential.



The summation of these three EPSPs generates an action potential.

Inhibitory Synapses and IPSPs

• kind of synaptic potential that makes a postsynaptic neuron less likely to generate an <u>action potential</u>

•Neurotransmitter binding to a receptor at inhibitory synapses:

- Causes the membrane to become more permeable to potassium and chloride ions
- Leaves the charge on the inner surface negative
- Reduces the postsynaptic neuron's ability to produce an action potential

Characteristics of EPSPs

Transient depolarizations

- · Excitatory because Em moves closer to threshold
- Increase in conductance to Na⁺ and K⁺
- Na⁺ influx causes depolarization.
- EPSPs at synapses between neurons are similar to the EPPs at neuromuscular junctions.

Characteristics of IPSPs

Transient hyperpolarizations

- · Inhibitory because Em moves farther away from its threshold
- Increased conductance to Cl⁻
- Cl⁻ influx causes hyperpolarization
- Also can be produced by increased K⁺ conductance and an accelerated K⁺ efflux
Summation

also known as **frequency summation** is the method of signal transduction between neurons, which determines whether or not an action potential will be triggered by the summation of postsynaptic potentials

- A single EPSP cannot induce an action potential
- EPSPs must summate temporally or spatially to induce an action potential
- Temporal summation presynaptic neurons transmit impulses in rapidfire order
- Spatial summation postsynaptic neuron is stimulated by a large number of terminals at the same time
- IPSPs can also summate with EPSPs, canceling each other out

Summation

- One EPSP is usually strong enough cause an AP.
- However, EPSPs may be summed.
- Temporal summation
 - The same presynaptic neuron stimulates the postsynaptic neuron multiple times in a brief period. The depolarization resulting from the combination of all the EPSPs may be able to cause an AP.
- Spatial summation





5. Spatial Summation



6. Temporal Summation





Temporal summation

- another means of transmitting signals with increased frequency of impulse thus increasing the strength of signals in each fiber.
- The effect is generated by a single neuron as a way of achieving action potential.
- Summation occurs when the time constant is sufficiently long, a fraction of a second, and the frequency of rises in potential are high enough that a rise in potential begins before a previous one ends.
- The amplitude of the previous potential at the point where the second begins will algebraically summate, generating a potential that is overall larger than the individual potentials.
- This allows the potential to reach the threshold to generate an action potential

Spatial summation

- is a way of achieving an action <u>potential in</u> <u>a neuron which involves input from multiple</u> <u>presynaptic cells</u>.
 - Multiple neurons all stimulate a postsynaptic neuron resulting in a combination of EPSPs which may yield an AP
- Spatial summation is the algebraic summation of potentials from different areas of input, usually on the dendrites.
- Summation of excitatory postsynaptic potentials allows the potential to reach the threshold to generate an action potential
- inhibitory postsynaptic potentials can prevent the cell from achieving an action potential

The main membrane processes involved in neural activities are:

- 1. resting potential: the transmembrane potential of a resting cell
- 2. graded potential: a temporary localized change in the resting potential, caused by a stimulus
- 3. action potential: an electrical impulse (produced by the graded potential) that propagates along the surface of an axon to a synapse.
- 4. synaptic activity: the release of neurotransmitters at the presynaptic membrane, which produce graded potentials in a postsynaptic membrane.
- 5. information processing: the response (integration of stimuli) of a postsynaptic cell.

The 3 main requirements for a transmembrane potential are:

- 1. A concentration gradient of ions (Na+, K+) across the cell membrane
- 2. The membrane be selectively permeable through membrane channels
- 3. Passive and active transport mechanisms maintain a difference in charge across the membrane (*resting potential* = -70 mV)

Passive forces acting across the membrane are

•chemical •electrical.

ELECTRICAL SYNAPSES

Action potential is transmitted from one cell to another by the direct flow of current.

- Conduction can occur in both directions, and there is essentially no synaptic delay.
- · Cells with electrical synapses are joined by gap junctions.



Electrical synapses are best adapted for regulating rhythmic or synchronized electrical activity for activities like breathing.

1. Chemical gradients:

-concentration gradients of ions (Na+, K+) across the membrane

2. Electrical gradients:

- the charges of positive and negative ions are separated across the membrane, resulting in a *potential difference*.

- positive and negative charges attract one another
- if charges are not separated, they will move to eliminate potential difference, resulting in an electrical current

- how much current a membrane can restrict is called its resistance

Electrochemical gradient:

1. the sum of chemical and electrical forces acting on an ion (Na+, K+) across a cell membrane is the electrochemical gradient for that ion.

2. chemical gradient of potassium tends to move potassium out of the cell, but the electrical gradient of the cell membrane opposes this movement

3. the transmembrane potential at which there is no net movement of a particular ion across the cell membrane is the *equilibrium potential* for that ion (K+ = -90 mV, Na+ = +66 mV).

4. the electrochemical gradient is a form of *potential energy*

Active forces maintain the cell membrane's resting potential (-70 mV).

The cell actively pumps out sodium ions (Na+), and pumps in potassium ions (K+).

The sodium-potassium exchange pump (the carrier protein *sodium-potassium ATPase*), powered by ATP, exchanges 3 Na+ for each 2 K+, balancing the passive forces of diffusion.

 Neurons may also form reverberating circuits.
 A chain of neurons where many give off collaterals that go back and synapse on previous neurons.



Neurotransmitter Removal





Axonal Conduction

- Depolarization
 - Threshold
 - Axon Hillock
 - Na ions rush in resulting in:
 - Action potential;
- All or none phenomenon, high frequency
 Afterpotentials; hyperpolarizing,
- depolarizing; slow frequency
- Changes in membrane permeabilities
 - Propagation

•Refractory period

Synaptic Transmission

Post-synaptic potentials (PSP's);

- Excitatory
- Inhibitory
- Interaction

Summation/Integration

- temporal
- spatial
- decremental conduction on dendrites and soma

axon hillock is critical area at which threshold must be reached

After release of neurotransmitter,

reuptake degradation

Functional Synaptic Units



In a resting (unstimulated) neuron, the membrane is polarized which means that the inner cytoplasmic side is negatively charged with respect to its outer, extracellular side



- When a neuron is stimulated the permeability of the plasma membrane changes at the site of the stimulus, allowing positive ions to rush in.
- As a result, the inner face of the membrane becomes less negative or depolarized



• Any part of the neuron depolarizes if stimulated, but at the axon alone this can result in the triggering of a nerve impulse or action potential

• When a nerve impulse or action potential develops the membrane is not only depolarized , but its polarity is completely reversed so it becomes negative externally and positive internally



(d) Propagation of the action potential

• Once begun, the nerve impulse travels rapidly down the entire length of the axon without decreasing in strength



• After the impulse has passed the membrane repolarizes itself

Graded Potential OR RECEPTOR POTENTIAL

- In humans, natural stimuli are not applied directly to axons, but to dendrites and the cell body which constitute the receptive zone of the neuron
- Stimulation can occur in many ways, including chemical stimulation (neurotransmitters, etc.), mechanical stimulation (certain pain receptors, hair receptor, etc.), light stimulation (photoreceptors)
- When the membrane of this receptive zone is stimulated it does not undergo a polarity reversal
- Instead it undergoes a local depolarization in which the inner surface of the membrane merely becomes less negative

Graded Potential

- <u>This local depolarization is called a graded potential</u> <u>which spreads from the receptive zone to the axon</u> <u>hillock (trigger zone) decreasing in strength as it travels</u>
- If this depolarizing signal is strong enough when it reaches the initial segment of the axon, it acts as the trigger that initiates an action potential in the axon
- Signals from the receptive zone determine if the axon will fire an impulse

Synaptic Potential

- Most neurons in the body do not receive stimuli directly from the environment but are stimulated only by signals received at synapses from other neurons
- Synaptic input influences impulse generation through either excitatory or inhibitory synapses

Synaptic Potential

• In excitatory synapses, neurotransmitters released by presynaptic neurons alter the permeability of the postsysnaptic membrane to certain ions, this depolarizes the postsynapatic membrane and drives the postsynaptic neuron toward impulse generation

Synaptic Potential

- Inhibitory synapses cause the external surface of the postsynaptic membrane to become even more positive, thereby reducing the ability of the postsynaptic neuron to generate an action potential
- Thousands of excitatory and inhibitory synapses act on every neuron, competing to determine whether or not that neuron will generate an impulse

Neural Integration

- The organization of the nervous system is hierarchical
- The parts of the system must be integrated into a smoothly functioning whole
- Neuronal pools represent some of the basic patterns of communication with other parts of the nervous system

Neuronal Pools

 Neuronal pools are functional groups of neurons that process and integrate incoming information from other sources and transmit it forward



One incoming presynaptic fiber synapses with Several different neurons in the pool. WhenIncoming fiber is excited it will excite some Postsynaptic neurons and facilitate others.

Neuronal Pools

- Neurons most likely to generate impulses are those most closely associated with the incoming fiber because they receive the bulk of the synaptic contacts
- These neurons are in the discharge zone



Neuronal Pools

- Neurons farther away from the center are not excited to threshold by the incoming fiber, but are facilitated and can easily brought to threshold by stimuli from another source
- The periphery of the pool is the facilitated zone






