Neuroscience Notes

Contents

The Resting Membrane Potential

Write an overview of the topic here.

1 Basics of Neuronal Communication

1. Individual neurons are activated by **electrical signals**.
2. Neurons communicate with other neurons via **chemical signals**.

There are both electrical and chemical properties of cell membranes that must be understood for the conceptualization of neuronal transmission.

2 The Cell Membrane

- The wall of the cell that separates the intracellular space (inside of the cell) from the extracellular space (outside of the cell, i.e., extracellular fluid).
- Phospholipid bilayer with embedded proteins/sugars.

3 Selective Permeability

- Most chemicals cannot pass through the cell membrane freely.

  Flow and allowance of molecules controlled by specific protein channels embedded within the membrane.

  The opening and closing of these channels is dependent on electrical dynamics of the cell itself vs. the extracellular fluid.

4 Membrane Potential

Think of neurons like batteries...

- There is a difference in **voltage, or electrical charge,** between the intracellular and extracellular space.
- This difference is called the membrane potential.

4.1 How was the membrane potential discovered?

Scientists used the axon of a giant squid to examine the membrane potential:

- Used **microelectrodes**: extremely fine electrodes used for cellular recordings.
- How this was done:
  1. Isolated an axon and placed it in salt water.
  2. Placed one electrode in the axon, and one in the salt water.
  3. Measured the **difference in charge** between the inside and outside of the axon.

5 The resting potential

The **resting potential**: the membrane potential of a neuron at rest (i.e., not sending a signal)

- The resting membrane potential of a neuron is typically at **-70 millivolts (-70mV)**

5.1 Neuron polarization

- When a neuron is at rest, the inside of the neuron is negatively charged in relation to the extracellular fluid.
- In this case, we say that the membrane is **polarized**.

6 Why is there a "resting potential"?

- There is variation in the distribution of different **ions** inside and outside of the membrane.

6.1 What are ions?

- Ions are **charged particles** that make up the salts in neural tissue and extracellular fluid.
- There are two basic types.
  1. Cations: all positively charged ions.
  2. Anions: all negatively charged ions.
- Important ions for basic neuronal transmission are:

  Sodium (Na^+)

  Potassium (K^+)

  Chloride (Cl^-)

  Calcium (Ca^{2+})

  Organic anions (-)

6.2 Ion Distribution

There is variation in the distribution of different ions inside and outside of the cell when the neuron is at rest...

- There is more Na^+, Cl^-, and Ca^{2+} ions outside of the cell in the extracellular fluid.
- There are more K^+ ions inside of the cell.
- There are also organic anions (-) "stuck" inside of the cell (too large to move out).

6.3 Ion Channels

Ions can only move in and out of the cell via **ion channels** embedded in the cell membrane.

- Each ion channel is selective to only one ion channel (i.e., sodium only moves through sodium ion channels)
- These channels are **voltage-gated**

  Opening and closing is dependent on the value of the membrane potential.
- Most of these **ion channels** are **closed at rest**.

6.4 Sodium-Potassium Pumps

Sodium-potassium pumps also contribute to the uneven distribution of ions at rest...

- These are protein complexes that are also embedded within the cell membrane, but are different from typical ion channels.
- Utilize **active transport mechanisms** that rely on **ATP** (adenosine triphosphate, provides energy to support cellular processes) for energy.
- Transports **three Na^+ ions out** of the cell for every **two K^+ ions** it draws **in** ¿ brings neuron back to resting state following activation.

The Action Potential

Write an overview of the topic here.

7 Action Potentials

Action potentials are electrical impulses that are triggered when neurons are stimulated:

- Action potentials, or APs, occur due to ions moving through voltage-gated channels in the cell membrane.

7.1 Steps of an Action Potential

1. Resting state
2. Depolarizing phase
3. Repolarizing phase
4. Hyperpolarizing phase

7.1.1 Resting Phase

The state of a neuron at rest, or not signaling.

7.1.2 Depolarizing Phase

- A threshold of excitation is reached at the cell membrane.
- Voltage-gated Na^+ ion channels open, Na^+ ions rush into the cell (remember, at rest, Na^+ is highly concentrated on the outside of the cell).

  The "Peak" of the AP

  The action potential quickly reaches its peak; Na^+ ion channels become inactivated and close, this means no more Na^+ is able to enter the cell from the outside.

7.1.3 Repolarizing Phase

- K^+ ion channels open; K^+ ions flow out of the neuron (remember, at rest, K^+ is highly concentrated on the inside of the cell).

  Cell membrane begins to repolarize (return to the resting potential value).

7.1.4 Hyperpolarizing Phase

- **Hyperpolarization**: Increase in negative charge relative to the resting potential.
- K^+ channels stay open, K^+ ions continue to leave the cell.

  Causes cell membrane to "understood" the normal resting potential value.

7.1.5 Return to Resting State

- K^+ ion channels close

  Causes the membrane potential to return to the resting value.

  Sodium-potassium pumps help to restore the resting potential.

7.2 Refractory Periods

Absolute refractory period

- 1-2 ms after an AP has been fired, during an absolute refractory period, it is impossible for the cell to fire another AP.

Relative refractory period

- For a few more ms, an AP can only be fired with a higher-than-normal level of stimulation.

7.3 The All-or-None Law

- Once an action potential is triggered, the impulse travels the length of the axon without decreasing the strength.
- This will be the maximal response for the maintenance of the same amplitude.

7.3.1 How is the all-or-none law possible?

- Na^+ ion channels are heavily concentrated at the **Nodes of Ranvier**.
- Action potentials "jumps" from node to node.

  I.e., **Saltatory conduction**
- The **myelin sheath** thus speeds up the conduction of action potentials.
- **Multiple sclerosis**: autoimmune disease that results in destruction of the myelin sheaths of neurons.

  Results in slower transmission of action potentials.

8 Postsynaptic Potentials

8.1 Pre vs. Postsynatpic Neurons

- When a neuron fires an AP, a chemical signal is released from its terminal buttons.
- The signal then diffuses across the synapse.

  Synapse: the gap and point of communication between two neurons.
- The presynaptic neuron releases the signal, the postsynaptic neuron receives it.

8.2 Postsynaptic potentials

- The chemical signal binds to receptors in the postsynaptic neuron's cell membrane.
- The signal can have one of two effects on the postsynaptic membrane.

  Depolarization (increases the membrane potential)

  Hyperpolarization (decreases the membrane potential)

8.3 EPSPs and IPSPs

- Depolarizations are called excitatory postsynaptic potentials (EPSPs).

  These increase the likelihood that the postsynaptic neuron will fire an action potential.
- Hyperpolarizations are inhibitory postsynaptic potentials (IPSPs).

  These decrease the likelihood that the postsynaptic neuron will fire an action potential.

8.4 Summation of postsynaptic potentials

- Both EPSPs and IPSPs are graded responses

  Weak signals elicit weak PSPs.

  Strong signals elicit strong PSPs.
- Multiple PSPs are integrated and summed together to produce an overall effect to a postsynaptic neuron.

8.5 Integration of PSPs

- Spatial summation: PSPs produced simultaneously on different parts of the postsynaptic neuron.
- Temporal summation PSPs produced in rapid sequence at the same part of the postsynaptic neuron.

9 The Synapse and Neurotransmitters

9.1 The Synapse

Definition: The Synapse

The gap between neurons where chemical communication happens.

9.2 Types of synapses

- Axodendritic

  Terminal buttons of the presynaptic neuron synapse onto dendrites of the postsynaptic neuron.
- Axosomatic

  Terminal buttons of the presynaptic neuron synapse onto the soma of the postsynaptic neuron.
- Axoaxonic

  Terminal buttons of the presynaptic neuron synapse onto the axon of the postsynaptic neuron.

9.3 Anatomy of a Synapse

- Presynaptic membrane: cell membrane at the ends of the terminal buttons of the presynaptic cell.

  Site from which chemical signals called neurotransmitter are released into the synapse.
- Neurotransmitters are stored in synaptic vesicles until release.
- Postsynaptic membrane: cell membrane of the cell receiving the signal, or the postsynaptic neuron.

  Contain receptors, which are binding sites for chemicals released from the presynaptic cell.

10 Neurotransmitters

Neurotransmitters are the chemical signals released across the synapse

There are several classes:

1. Amino acids
2. Monoamines
3. Acetylcholine
4. Neuropeptides
5. "Unconventional" neurotransmitters

10.1 Amino Acid Neurotransmitters

- Amino acids: The building blocks of proteins.
- We have excitatory and inhibitory neurotransmitters...

  Excitatory: **glutamate**, aspartate.

  Inhibitory: GABA, glycine.

10.2 Monoamine Neurotransmitters

- These are called "monoamines" because they are synthesized from a single amino acid.

  Aromatic amino acids such as phenylalanine, tryptophan (indolamines), and tyrosine (catecholamines)

- Within this group, we have catecholamines and indolamines.

  Catecholamines: dopamine, norepinephrine, epinephrine.

  Indolamines: Serotonin.

10.3 Acetylcholine

- Choline molecule with an added acetyl group.
- Widespread in the CNS and at neuromuscular junctions.

10.4 Neuropeptides

- Long chain of amino acids

  Pituitary peptides: Oxytocin.

  Hypothalamic peptides: Corticotropin-releasing hormone (CRH)

  Brain-gut peptides: cholecystokinin.

  Opioid peptides: substance P.

Synaptic Transmission

Write an overview of the topic here.

11 Synaptic Transmission

- APs arrive at the terminal buttons of a neuron and trigger the release of neurotransmitter molecules into the synapse.
- 4 major events:
  1. Neurotransmitter synthesis and storage
  2. Neurotransmitter release.
  3. Activation of postsynaptic receptors.
  4. Neurotransmitter inactivation and reuptake.

11.1 Neurotransmitter synthesis and storage

- Neurotransmitters are synthesized in the cytoplasm of the cell body or terminal buttons.
- These synthesized NTs are then packaged into vesicles.
- Vesicles are stored in clusters next to the presynaptic membrane.
- A neuron can synthesize and release more than one kind of neurotransmitter (i.e., **co-existence**)

  Example: GABA and a neuropeptide

11.2 Neurotransmitter Release

- Exocytosis: the process of neurotransmitter molecule release from synaptic vesciles and into the synaptic cleft.
  1. An AP is transmitted down the axon of the presynaptic neuron and reaches the terminal buttons.
  2. Depolarization causes voltage-gated calcium ion channels to open on the presynaptic membrane.
  3. Calcium ions enter the presynaptic membrane.
  4. Synaptic vesicles fuse with the presynaptic membrane and empty their contents into the synaptic cleft.

11.3 Activation of Postsynaptic Receptors

- Released NTs attach to **receptors** on the postsynaptic membrane (usually on the dendrites).
- **Ligand**: any molecule that binds to a receptor (NTs are ligands).
- Each receptor contains binding sites for particular types on NTs.

  A NT can only influence cells that have receptors for that specific NT.

11.3.1 Receptor Subtypes

- Most neurotransmitters can bind to more than one receptor subtype.

  Example: $GABA_A$ and $GABA_B$, dopamine $D_{1\text{-}5}$, $GluN2_{A\text{-}D}$.

- Receptor subtypes typically trigger different types of responses in the postsynaptic neuron...

  Dopamine binds to D1 ¿ excitatory effect.

  Dopamine binds to D2 ¿ inhibitory effect.

11.4 Neurotransmitter Inactivation and Uptake

- Neurotransmitter signals must be terminated after release and binding to postsynaptic receptors.
- Via two mechanisms...

  1. Reuptake
  2. Enzymatic degradation

11.4.1 Neurotransmitter Reuptake

- **Transporters**: proteins in the cell membrane that bring neurotransmitter molecules back into the presynaptic neuron for repackaging and re-use.

  Example: Serotonin (5-HT) is taken back up by serotonin transporters (SERTs)

11.4.2 Enzymatic Degradation of NTs

- Enzymes break neurotransmitter molecules down into inactive chemicals that eventually wash away.

  Example: Acetylcholinesterase (AChE) breaks down acetylcholine (ACh)

12 Effects of Drugs on Synaptic Transmission

12.1 Effects of Drugs on Neurotransmission

- **Ligand:** any molecule that binds to a receptor (NTs are ligands).
- Thus, drugs are also considered ligands.

12.2 Agonists vs. Antagonists

- Agonist: a drug that mimics or facilitates the actions of a neurotransmitter.

  Example: nicotine is an agonist of acetylcholine.

- Antagonist: a drug that inhibits the actions of a neurotransmitter.

  Example: Many antipsychotic drugs are antagonists of dopamine.

13 Figures and Diagrams

14 References

Include all references used here in standard citation format.