MEMBRANE POTENTIALS and SYNAPSES
In Physiology Today
April 1, 2020

- Membrane potentials
- Synapses
- In Lab Next Time
  - That’s cute
  - We can’t have real labs
  - I’ll go over lab stuff later

Teenager Post # 6650
The human brain is amazing. It functions 24/7 from the time we were born and only stops when we take tests.

//teenagerposts.tumblr.com
Reinvented by about9800 for iFunny :)}
Information Flow

Afferent Pathway

BRAIN

Efferent Pathway

SPINAL CORD

stimulus detected

neurons

Effector
Cells that can receive signals via chemical messengers

Muscle cells

Glands

Neurons

Effector cell types
Neuron Communication

• Neurons are stimulated by receptors on dendrites and cell bodies (soma)
  – Ligand gated ion channels
  – GPCR’s

• Neurons stimulate cells by releasing NT from synaptic bulbs
  – Binds to receptors on the effector cell
  – Ligand gated ion channels
  – GPCR’s
Neuron Communication

• Neurons stimulate cells by releasing NT
  – The stimulus will trigger a cellular response in the effector cell
• NT is released from the synaptic bulb
• NT release is the result of an *electrical current* traveling down the axon reaching the synaptic bulb
• A *current* is the flow/movement of an electrical charge
• An electrical *current* can only be generated in cells with *excitable membranes*
Current

Ohm’s Law $I = \frac{V}{R}$

• The **current** ($I$) through a conductor is directly proportional to the **voltage** ($V$) across the two points and inversely proportional to the **resistance** ($R$) between them.

• The plasma membrane is the conductor
  • Voltage ($V$) = Electrical potential measured in mV
  • Current ($I$) = Movement of electrical charge
  • Resistance ($R$) = Factors that prevent movement
    – Plasma membranes (lipids) have high electrical resistance
    – Water has low electrical resistance (cytoplasm, ECF)
Excitable Membranes

Membranes capable of generating a voltage

Neurons, Muscle cells

A few others
(endocrine, immune, reproductive)

• **Voltage** = difference in the charge across a membrane
• Ions are charged
• Cell membranes separate ions across the membrane
  – Membranes are semipermeable
  – Membranes are permeable to ions through ion channels
  – Cells maintain concentration gradients of ions
Receptors Involved in Detecting a Stimulus

1. Ligand-gated ion channels
2. GPCR that opens an ion channel

When a positive ion moves in, it will make the voltage inside the cell less negative.

The types of receptors that you find on cells with excitable membranes (neurons and muscle cells) are going to need to result in an ion moving across the membrane to change the voltage.

IF voltage = 0 mV

Thin shell of (-) charges inside cell

Chemical messenger

Plasma membrane of neuron (dendrites + soma)
Membrane Potential

- **Membrane potential (mV)** is the difference in charge across the membrane
- Extracellular fluid (IF) voltage is set at 0
- Membrane potential is reported compared to the voltage of the IF
  - Inside < Outside (-) value
  - Inside > Outside (+) value
Membrane Potential

- Ions that can move across the membrane collect in a thin shell very close to each side of the membrane.

- The bulk of the intracellular and extracellular ions in the fluids remain the same.
Equilibrium Potential

• *Theoretical* voltage produced across a cell membrane with the movement of only *ONE* ion

• Individual ions have different membrane permeabilities
  – Ion channels present
  – Characteristics of ion channels (gated, leaky)

• *Each ion contributes its own voltage to the overall membrane potential of a membrane*
Equilibrium Potential

• The Nernst Equation calculates the equilibrium potential of a single ion

\[ E_{\text{ion}} = \frac{-61 \log (C_o/C_i)}{Z} \]

\[ E_{\text{ion}} = \text{equilibrium potential of a particular ion in mV} \]
\[ C_i = \text{concentration of ion inside the cell} \]
\[ C_o = \text{concentration of ion outside the cell} \]
\[ Z = \text{valence of ion} \]
Electrochemical gradients favor
Inward movement of Na⁺
Outward movement of K⁺
Equilibrium potential of each ion contributes to the overall membrane potential of a cell.

\[ E_{Na^+} = +61\text{mV} \]
\[ E_{K^+} = -90\text{mV} \]
Resting Membrane Potential (RMP)

- Resting Membrane Potential (RMP) is the difference in charge across the membrane in a resting cell
  - The overall difference charge from **ALL** of the ions that move across the membrane

A resting cell is not receiving a stimulus
Resting Membrane Potential (RMP)

*RMP is established and maintained by:*

\[ \text{Na}^+/\text{K}^+/\text{ATPase pump} \]

The permeability of the membrane to ions
Resting Membrane Potential (RMP)
Na\(^+\)/K\(^+\)/ATPase Pump

- Always pumping 3 (+) charges out and 2 (+) charges in

- Generates a (-) potential
Resting Membrane Potential (RMP)

The Permeability of the Membrane to Ions

• Permeability is movement across the membrane
  • Ions move through ion channels
    – Ions that move across all excitable membranes are Na\(^+\) and K\(^+\)
    – K\(^+\) has a greater permeability than Na\(^+\)

• RMP of neurons range from -20mV to -90 mV
  – Membrane is polarized

• Average RMP is -70mV

A resting cell is not receiving a stimulus
Voltage-Gated Ion Channels

Found on the Axon and Synaptic Bulb

**\( \text{Na}_{vg}^+ \) channels**
- All are gated
- Closed at RMP
- Fast to open
- Fast to inactivate
  - Have inactivation gates
    - Intracellular structure
    - Stops ion flux by blocking ion channels

**\( \text{K}_{vg}^+ \) channels**
- Most are gated
  - Closed at RMP
  - Slow to open
  - Slow to close
- Some are Leaky
  - “leak” at threshold
  - Allow a slow, steady flux of \( \text{K}^+ \) at threshold
  - Generates a (-) potential
Voltage-Gated Na\textsuperscript{+} and K\textsuperscript{+} Channels

Channel states

- **Sodium**
  - Closed
  - Open
  - Inactivated
  - Inactivation gate

- **Potassium**
  - Closed
  - Open

Rate

- Open and inactivate very rapidly
- Open and close slowly
Changes in Membrane Potential

Membranes are polarized at rest: $-70\text{mV}$

- **Depolarizing a membrane**
  - A stimulus causes the voltage to change and move towards $0\text{mv}$
  - Caused by the inward movement of a (+) ion: $\text{Na}^+, \text{Ca}^{2+}$

- **Repolarizing a membrane**
  - The voltage changes and moves towards the resting, polarized voltage
  - Caused by the outward movement of a (+) ion: $\text{K}^+$

- **Hyperpolarizing a membrane**
  - The voltage changes and becomes more polarized ($\text{voltage} < -70\text{mV}$)
  - Caused by the inward movement of a (-) ion: $\text{Cl}^-$
  - Caused by the outward movement of a (+) ion: $\text{K}^+$
Changes in Membrane Potential

- **Depolarization**
  - Caused by the inward movement of a (+) ion: \( \text{Na}^+, \text{Ca}^+ \)

- **Repolarization**
  - Caused by the outward movement of a (+) ion: \( \text{K}^+ \)

- **Hyperpolarization**
  - Caused by the inward movement of a (-) ion: \( \text{Cl}^- \)
  - Caused by the outward movement of a (+) ion: \( \text{K}^+ \)

Membrane potential may change 100mV
Changes in Membrane Potential

• Graded potentials
  – Transmit info over a short distance
  – Dendrites, soma, NMJ
  – Moves the membrane towards threshold or away from threshold

• Action potentials
  – Transmit info over a long distance
  – Axons and muscle cell membranes
  – Results in the release of NT
Difference Between Graded Potentials and Action Potentials

**Graded Potentials**

- May or may not cause an AP
- Receptors:
  - Ligand gated ion channels
  - GPCR that opens an ion channel
- Location:
  - Dendrites
  - Soma
- All input is additive which will either result in an AP or not

**Action Potentials**

- All or nothing
- Receptors:
  - Voltage gated Na⁺, K⁺ ion channels
  - Leaky K⁺ channels
- Location:
  - Axon synaptic bulb
- Once an AP is initiated it will travel all the way down the axon to the synaptic bulb
- NT is released
Graded Potentials

- Transient changes in membrane potential
  - Due to the movement of Na⁺, K⁺, Ca²⁺, Cl⁻
- Occur where a stimulus is received
- Variable magnitude
  - Changes the membrane potential towards threshold
  - Changes the membrane potential away from threshold
- “Fizzle Out”
  - Conducted decrementally
Graded Potentials

• 4 Types of Graded Potentials

• *Sensory potential*
  – Occurs on sensory receptors

• *Synaptic potential*
  – Occurs at a nerve to nerve synapse

• *Pacemaker potential*
  – Occurs on pacemaker cells of the heart (SA Node)

• *EPP*
  – Occurs on the motor end plate of skeletal muscle
Action Potentials

• Rapid reversal of membrane potential
  – Due to the movement of Na\(^+\) and K\(^+\)
• Triggered by the membrane reaching threshold
  – Graded potentials move a membrane towards threshold
• Results in the release of a neurotransmitter
• One Way conduction
  – Travels in one direction down the axon to the synaptic bulb
• Propagated across axons, muscle cell membranes
• All or nothing response
• Action potentials are rapid (0.5-100 m/s)
Steps of AP

1. RMP
2. Threshold
3. Membrane depolarizes
4. Membrane stops depolarizing
5. Membrane repolarizes
6. Membrane hyperpolarizes
7. RMP
Steps of AP

1. RMP
2. Threshold
3. Membrane depolarizes
4. Membrane stops depolarizing
5. Membrane repolarizes
6. Membrane hyperpolarizes
7. RMP
Action Potential Mechanism

1. RMP maintained due to Na\(^+\)/K\(^+\)/ATPase pumps and *leaky* K\(^+\) channels

2. A stimulus causes the membrane voltage to reach threshold

3. *voltage-gated* Na\(^+\) channels open causing the membrane to quickly depolarize

4. *voltage-gated* Na\(^+\) channels are quickly inactivated. Membrane depolarization stops.

5. *voltage-gated* K\(^+\) channels open and the membrane begins to repolarize

6. *voltage-gated* K\(^+\) channels close

7. Na\(^+\)/K\(^+\)/ATPase pumps reestablish RMP
One Way Conduction

- AP only travels down the axon to the synaptic bulb
- Presynaptic membrane to postsynaptic membrane
One Way Conduction

- *Refractory periods* ensure the AP moves in one direction down the axon
  - A period immediately following stimulation during which a nerve or muscle is unresponsive or less responsive to further stimulation
- Prevents a subsequent AP from beginning before the first AP is complete
- Limits number of AP a nerve can produce in a given time period
Absolute Refractory Period

- Follows the AP
- Can not produce an AP on the membrane
- \( \text{Na}^+ \) channels inactivated
- \( \text{Na}^+ \) channels can not open
- No way to depolarize the membrane
Relative Refractory Period

- Follows the absolute refractory period
- Can produce an AP on the membrane
- **Na⁺ channels are now closed**
- Axon membrane is hyperpolarized
- Stronger than normal stimulus required
Refractory Periods

- **Absolute refractory period**
  - $\text{Na}^+$ channels inactivated

- **Relative refractory period**
  - $\text{Na}^+$ channels are now closed
Action Potential Propagation

• An AP can only travel the length of an axon if each point along the membrane is depolarized to threshold.

• The current during an AP is sufficient to easily depolarize the adjacent membrane to threshold potential:
  – Ions leak to next segment, initiating AP
  – Sequential opening/closing of Na⁺ and K⁺ channels along the membrane

• AP does not move, it sets off a new AP in the region just ahead of it.
Action Potential Propagation
(AP travels down axon)
Action Potential Velocity

- Velocity of AP is determined by:
  - Diameter of fiber
    - Small – slower
    - Large - faster
  - Myelination
    - Insulation
    - Increases speed of conduction
    - Nodes of Ranvier
    - Saltatory conduction

Conduction Velocities
Small, unmyelinated – 0.5 m/s
Large, myelinated – 100 m/s
Actions Potential Velocity

- **Unmyelinated** axons
  - Depolarization of each segment
  - Slower

- **Myelinated** axons
  - Saltatory conduction
  - Nodes of Ranvier
  - Na\(^+\) channel concentration
  - Faster
Action Potentials are All-or-None

- Membrane approaching threshold
  - Subthreshold stimuli do not generate an AP

- Membrane reaches threshold
  - If threshold is reached, depolarization proceeds with the same amplitude
Release of Neurotransmitter

• NT is released from the synaptic bulb
  – Functional connection between cells
• NT is a chemical
• *Chemical synapse*
  – Synaptic bulb
  – Synaptic cleft
  – Synaptic vesicles
  – Neurotransmitter
Chemical Synapse

(a) A vesicular synapse

(b) Synapses on the surface of a neuron
Chemical Synapse

- Synaptic bulb
- Axon
- Vesicle
- Presynaptic membrane
- Synaptic cleft
- Post-synaptic membrane (effector cell)
- Neurotransmitter (NT)
- SNAP/SNARE proteins
- Calcium ions ($Ca^{2+}$)
- Voltage-gated channels ($V_G$)
- Effector Cells: Neurons, Muscle Cells, Gland Cells
- Receptor
Chemical Synapse

- Presynaptic membrane is separated from the postsynaptic membrane by synaptic cleft
- NT released from synaptic vesicles
- Vesicles fuse with axon membrane and NT released by exocytosis
- Amount of NT released depends upon frequency of AP

* N-type Ca\(^{2+}\) Channels present in the synaptic bulb
Videos to Watch

• Don’t forget to watch the videos I posted links to in canvas to help understand NT release.

• You are only responsible for the detail in this lecture. One of the videos goes into a lot more detail of vesicle docking.

1. 2-Minute Neuroscience: Neurotransmitter Release
2. Neurotransmitter Release
3. Release of Neurotransmitter