Biopsychology

Function of a Neuron part 1:
Resting membrane potential, Graded potentials and Action potentials

Lecture 5
Outline/Schema

• So far:
  – Cells of the nervous system, structures of the nervous system
  – Now we will learn how neurons in these structures communicate

• Resting membrane potential
  – Importance of semi-permeable membrane
  – Ion channels, Na/K pump
  – Ions and forces involved

• Post-synaptic potentials

• Action Potentials
Neuron Anatomy

3 compartments of neuron Why?

- **Cell body**
  - Houses the nucleus and organelles
- **Dendrites**
  - Project from cell body and increase surface area available for receiving signals from other nerve cells
  - Incoming signals (graded potentials) are conducted toward the cell body

Dendrites and cell body serve as the neuron’s **input zone**.

- **Conducting Zone**
  - Axon (may be from 1mm to more than 1m long)

- **Output Zone**
  - Axon terminals

Arrows indicate the direction in which nerve signals are conveyed.
**Neuron Anatomy**

3 compartments of neuron: Why?

- **Axon**
  - Nerve ‘fiber’
  - Single, elongated tubular extension that conducts action potentials away from the cell body
  - Collaterals – axon side branches
  
  **Conducting zone** of the neuron
  - Axon hillock
    - First portion of the axon plus the region of the cell body from which the axon leaves
  - Neuron’s AP **trigger zone**
    - Membrane is dense in voltage-gated Na⁺ channels
  - Axon terminals
    - Release chemical messengers that simultaneously influence other cells with which they come into close association

- **Output zone** of the neuron

Arrows indicate the direction in which nerve signals are conveyed.

Sunday, February 12, 2012
Neurons are linked through the complex converging and diverging pathways.

Convergence of input (one cell is influenced by many others)

Divergence of output (one cell influences many others)

Need Molecular players!

Arrows indicate direction in which information is being conveyed.
Resting Potential

(A) The flow of electricity through the stimulating electrode provides sufficient current to produce a physiological response.

(B) If there is a difference in voltage between the tip of the recording electrode and a reference electrode, current flows, deflecting a needle that indicates the voltage.
Semi-permeable membrane: ____________________________

Ions: -Cations = ________________________________

Examples 1. __________  2. _______________

-Anions = ________________________________

Examples 1. __________  2. _______________

Channels: _______________________________________________________________________

Forces that “drive” ions across cell membrane

1. ____________________________

2. ____________________________
Changes in Membrane Potential

• Since ions **cannot** pass through the lipid bilayer, they must pass through *ion channels* to cross membrane
  – *Leak* channels

  – *Gated* channels
    • Voltage gated channel
    • Chemically (ligand) gated
    • Others
Ion Channel (Protein)
Unique for each Ion

Gated Channel
-Voltage Gated
-Ligand Gated
-Mechanical Gated

Gating: channels can be opened and closed by changes in the microenvironment

Ion Pump (protein)

These membrane proteins keep forces unequal why is this important?

1. Differential permeability: ions move through channels in the membrane. Some ionic channels leak.

2. Sodium-Potassium Pump: pumps out 3Na and pumps in 2K

   These two forces maintain the resting potential at -70mV

Membrane spanning proteins--joined together (4-6 subunits) to make a channel. Nature of the proteins creates ion selectivity
Distribution of ions

**Random motion:** concentration gradients-high to low

**Electrostatic pressure:** repulsion among like charges

**Membrane:** separates ions, if not ions would equally distribute = no membrane potential no energy!

**Ions involved:** sodium (Na$^+$), potassium (K$^+$), chloride (Cl$^-$)

Na$^+$ and Cl$^-$ concentration greater outside at rest
K$^+$ concentration greater inside at rest
Electrochemical gradients

Extracellular

Forces
Concentration & Electric

Wants to enter cell

Wants to leave cell

Forces are balanced
**Intracellular**

- $\text{Na}^+$ channel
- $\text{Cl}^-$ channel

**Forces**

**Concentration & Electric**

- $\downarrow \text{Na}^+$: Wants to enter cell
- $\uparrow \text{K}^+$: Wants to leave cell
- $\downarrow \text{Cl}^-$: Forces are balanced

**Extracellular**

- $\downarrow \text{Na}^+$: Wants to enter cell
- $\uparrow \text{K}^+$: Wants to leave cell
- $\downarrow \text{Cl}^-$: Forces are balanced

**Ion channels are usually closed**
Voltage-Gated Sodium Channel

Extracellular fluid (ECF)

Plasma membrane

Intracellular fluid (ICF)

Inactivation gate

Activation gate

Rapid opening triggered at threshold

Slow closing triggered at threshold

Closed but capable of opening

At resting potential (–70 mV)

Open (activated)

From threshold to peak potential (–50 mV to +30 mV)

Closed and not capable of opening (inactivated)

From peak to resting potential (+30 mV to –70 mV)

Fig. 4-7a, p. 91

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Voltage-Gated Potassium Channel

At resting potential; delayed opening triggered at threshold; remains closed to peak potential (–70 mV to +30 mV)

From peak potential through after hyperpolarization (+30 mV to –80 mV)
I. RESTING MEMBRANE POTENTIAL:
“sets the stage for neural communication”
Inside the cell = __________________
Outside the cell = __________________

Outside of cell - positive

Inside of cell - negative

FORCES THAT MAINTAIN THE RESTING MEMBRANE POTENTIAL:

1. ______________________________________
   _________________________________________

2. ______________________________________
   _________________________________________

Summation of Resting Membrane Potential

Neurons are POLARIZED:: __________________
   _______________________________
Post-synaptic-potential (PSP)
Or Grade Potential (GP)
Excitable Cells

• All cells have a resting membrane potential due to differences in the distribution (concentration in the ECF vs. ICF) and permeability of Na$^+$, K$^+$ and A$^-$
• Nerve and muscle cells are excitable cells
• Excitable cells can undergo rapid, controlled, and transient changes in membrane potential that are used as electrical signals for communication
• These changes in membrane potential are orchestrated by membrane proteins and driven by the electrochemical gradients of the ions already discussed
II. GRADED POTENTIALS

- Normally takes place at synapses

1. **Hyperpolarization** = __________________________

2. **Depolarization** = __________________________

3. How are graded (synaptic) potentials produced?
   a. Neurotransmitter **binds** to neurotransmitter receptors on post-synaptic membrane.
   b. Binding of neurotransmitter **opens** ion channels in the post-synaptic membrane and produces:

   (i.) __________________________
   (ii.) __________________________
Cell membrane electrical states
Changes in Membrane Potential

- Changes in membrane potential are caused by changes in ion movement across the membrane.
- If positively charged ions flow into the cell (e.g., Na\(^+\)), the membrane becomes less negative (i.e., closer to zero and is depolarized).
- If positively charged ions flow out of the cell (e.g., K\(^+\)), the membrane becomes more negative (i.e., further from zero and is hyperpolarized).

Diagram:
- ECF and ICF compartments.
- Na\(^+\) and K\(^+\) ions move across the membrane.
- Membrane potential changes over time.
- Upward deflection = Decrease in potential.
- Downward deflection = Increase in potential.
**Excitatory** synapse triggers an **excitatory** (stimulatory) PSP that results in a slight **depolarization**.

**Inhibitory** synapse triggers an **inhibitory** PSP that results in a slight **hyperpolarization**.
**Hyperpolarization**

Hyperpolarization is due to an efflux of $K^+$, making the extracellular side of the membrane more positive.

An influx of $Cl^-$ also can produce hyperpolarization.

**Depolarization**

Depolarization is due to an influx of $Na^+$ through normally closed $Na^+$ channels.
Graded Potentials

- Small (10-20 mV) **local** changes in membrane potential
- **Short-lived** signals in a **small portion** of the membrane (the rest of the membrane remains at resting membrane potential)
- Triggering stimuli **opens gated ion channels** that cause a small outward flow of current around the initiating event

- Examples of triggering events:

![Diagram of graded potential](image)
Current Flow During a Graded Potential

Triggering event opens a closed Na+ channel (**Na+ rushes into the cell**) and changes the membrane potential in a small region of the membrane.

Current quickly dissipates due to the presence of leak channels near the initial *active* area.

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Change in membrane potential in mV relative to resting potential — i.e., magnitude of electrical signal.
Graded Potentials

• The magnitude of the change in membrane potential is proportional to the magnitude of the triggering stimulus.

• Triggering stimulus can result in depolarization (bringing MP closer to zero) or hyperpolarization (bringing MP further from zero).

• No ‘refractory (No resistances)’ period – 2nd graded potential can be initiated before the 1st has dissipated.

• Potentials can be ‘summed’ together.
Panel A: If an excitatory presynaptic input (Ex1) is stimulated a second time after the first EPSP in the postsynaptic cell has died off, a second EPSP of the same magnitude will occur.

Panel B: If, however, Ex1 is stimulated a second time before the first EPSP has died off, the second EPSP will add onto, or sum with, the first EPSP, resulting in temporal summation, which may bring the postsynaptic cell to threshold.

Panel C: The postsynaptic cell may also be brought to threshold by spatial summation of EPSPs that are initiated by simultaneous activation of two (Ex1 and Ex2) or more excitatory presynaptic inputs.

Panel D: Simultaneous activation of an excitatory (Ex1) and inhibitory (In1) presynaptic input does not change the postsynaptic potential, because the resultant EPSP and IPSP cancel each other out.
Question. According to the illustration below, this is an example of:
A. Temporal summation only.
B. Spatial summation only.
C. Could be either temporal and/or spatial summation.
D. Neither temporal nor spatial summation.
Action Potential (AP)
Neural Communication Signals

• Two kinds of rapid changes in membrane potential that neurons use to generate electrical signals
  – Graded potentials
  – Action potentials
An action potential is produced by changes in voltage-sensitive K⁺ and Na⁺ channels, ...

The opening of Na⁺ channels produces an Na⁺ influx ...

... which can be blocked by TEA and tetrodotoxin, respectively.

The opening of K⁺ channels produces a K⁺ efflux.

When neither chemical is used, a combined influx of Na⁺ and efflux of K⁺...

...results in a normal action potential that consists of the summed voltage changes due to Na⁺ and K⁺.
III. PRODUCTION OF ACTION POTENTIALS

1. INTEGRATION: ____________________________________
   ____________________________________

2. THRESHOLD: _______________________________________
   ____________________________________________________
   ____________________________________________________

**Key features of neuronal action potentials**

- AP is activated when membrane reaches a *threshold potential*
- *Voltage-gated channels* in the membrane open to allow ions to flow across the membrane (down their concentration gradients)
- Flow of *sodium ions into* the cell reverses the membrane potential from -70 mV to +30 mV
- Subsequent flow of *potassium ions out* of the cell restores the membrane potential to the resting state
III. PRODUCTION OF ACTION POTENTIALS

3. VOLTAGE (POTENTIAL) DEPENDENT ION CHANNELS:

- Na+ channels - snap open at threshold; close at the peak of the action potential.

- K+ channels - snap open near the peak of the action potential; close as membrane potential approaches the resting membrane potential

4. REFRACTORY PERIOD:
3) Na+ rushes into the cell down its concentration gradient, resulting in rapid depolarization

2) Membrane potential reaches the threshold potential (-50 mV)
Voltage-gated Na+ Channels open

1) Excitatory ‘triggering event’ causes slight depolarization of resting membrane potential (increases from -70 to -50 mV)

4) Membrane pot. reaches +30 mV; Voltage-gated Na+ Channels close
Voltage-gated K+ Channels open

5) K+ rushes out of the cell down its concentration gradient, resulting in rapid repolarization
Action Potentials

- Brief, rapid, large (55-100mV) changes in membrane potential during which potential actually reverses (transiently)
- An AP at one point in the plasma membrane triggers an identical AP at a neighboring point in the membrane
- Individual APs occur in only a small portion of the total excitable cell membrane, but ‘signal’ is propagated along the membrane
- AP signal does not decrease in strength as it travels from the site of initiation throughout remainder of cell membrane
IV. CONDUCTION OF ACTION POTENTIALS

1. All-or-none law:

2. Rate law:
3. Regenerative process

Refractory Periods

• Absolute refractory: period following AP in which it is impossible to fire another AP

• Relative refractory: cell can fire but it takes more stimulation

• These lead to 2 important characteristics:

1. Direction of conduction

   Na+ rushes in

   Na+ spreads downstream - starts to depolarize the next segment of axon

   AP occurring here

2. Refractory and hyperpolarized

3. Back to resting potential
Refractory Periods

- Limit AP *frequency* and ensure *unidirectional* impulse propagation

- Absolute Refractory period
  - Membrane is completely unresponsive to further stimulation
  - Another AP cannot be initiated
  - Lasts while Na+ channels are open (threshold to AP peak at ~+30 mV) until returning to RMP

- Relative Refractory period
  - Follows absolute refractory period
  - AP can be triggered by stronger than normal stimuli
  - Hyperpolarization of membrane necessitates greater depolarizing stimulus to reach threshold potential

- Hyperpolarization of membrane necessitates greater depolarizing stimulus to reach threshold potential
Action Potential Propagation

- **Unidirectional** AP propagation due to *refractory period*

- Two types of propagation
  - **Contiguous** conduction
  - **Saltatory** conduction
Contiguous Conduction

Previous active area returned to resting potential

New active area at peak of action potential

New adjacent inactive area into which depolarization is spreading; will soon reach threshold

“Backward” current flow does not re-excite previously active area because this area is in its refractory period

“Forward” current flow excites new inactive area

Direction of propagation of action potential

Unidirectional Impulse Conduction
Active area at peak of action potential

Adjacent inactive area into which depolarization is spreading; will soon reach threshold

Remainder of axon still at resting potential

Local current flow that depolarizes adjacent inactive area from resting to threshold

Direction of propagation of action potential

Fig. 4-11, p. 95
Previous active area returned to resting potential

Adjacent area that was brought to threshold by local current flow; now active at peak of action potential

New adjacent inactive area into which depolarization is spreading; will soon reach threshold

Remainder of axon still at resting potential

Fig. 4-11, p. 95
Saltatory Conduction

4. Saltatory conduction in myelinated axons

Depolarizing stimulus

- more rapid – saves time;
- requires less active process – saves energy.

Saltatory Conduction

• Propagates APs faster than contiguous conduction because APs do not have to be regenerated at myelinated section

• Myelinated fibers conduct impulses about 50 times faster than unmyelinated fibers of comparable size (↑diameter = ↑conduction velocity)

• Myelin

Myelin sheath

Decremental conduction under myelin sheath - no action potential

Action potential is regenerated at nodes of Ranvier
Restoration and maintenance ion gradients

• After an action potential depolarization (Na+ influx), the membrane repolarizes (K+ efflux) returning to resting potential (after a brief hyperpolarization)
• However, the distribution of Na+ and K+ ions (which are critical to maintaining resting membrane potential and ‘excitability’) is now disrupted
• The Na+/K+ pump gradually restores the concentration gradients disrupted by action potentials (but not after each individual AP)
  • Sodium is pumped out of the cell (into the ECF)
  • Potassium is pumped into the cell (ICF)
Summary of events in the neuronal action potential

Depolarization
Na+ rushes into cell

Repolarization
K+ rushes out of cell

“triggering” signal brings membrane to threshold potential (e.g., ‘summed’ excitatory graded potentials)

Summary of events in the neuronal action potential

Depolarization
Na+ rushes into cell

Repolarization
K+ rushes out of cell

“triggering” signal brings membrane to threshold potential (e.g., ‘summed’ excitatory graded potentials)
### Action vs. Graded Potentials

**Graded potentials**

- Result in **small** (10-15 mV) depolarization or hyperpolarization
- Magnitude of voltage change = magnitude of stimulus
- Signal **dissipates quickly**
- No refractory periods
- Can be ‘summed’ together

**Action potentials**

- Results in **large** (100 mV), rapid depolarization
- Activation is ‘all or none’
- Signal **strength is maintained**
- Refractory period prevents 2\textsuperscript{nd} AP from occurring
- Cannot be ‘summed’