Fundamentals of the Nervous System and Nervous Tissue: Part B

Neuron Function
• Neurons are highly irritable
• Respond to adequate stimulus by generating an action potential (nerve impulse)
• Impulse is always the same regardless of stimulus

Principles of Electricity
• Opposite charges attract each other
• Energy is required to separate opposite charges across a membrane
• Energy is liberated when the charges move toward one another
• If opposite charges are separated, the system has potential energy

Definitions
• Voltage (V): measure of potential energy generated by separated charge
• Potential difference: voltage measured between two points
• Current (I): the flow of electrical charge (ions) between two points

Definitions
• Resistance (R): hindrance to charge flow (provided by the plasma membrane)
• Insulator: substance with high electrical resistance
• Conductor: substance with low electrical resistance

Role of Membrane Ion Channels
• Proteins serve as membrane ion channels
• Two main types of ion channels
  1. Leakage (nongated) channels—always open

Role of Membrane Ion Channels
2. Gated channels (three types):
   • Chemically gated (ligand-gated) channels—open with binding of a specific neurotransmitter
   • Voltage-gated channels—open and close in response to changes in membrane potential
   • Mechanically gated channels—open and close in response to physical deformation of receptors

Gated Channels
• When gated channels are open:
  • Ions diffuse quickly across the membrane along their electrochemical gradients
    • Along chemical concentration gradients from higher concentration to lower concentration
    • Along electrical gradients toward opposite electrical charge
  • Ion flow creates an electrical current and voltage changes across the membrane

Resting Membrane Potential (Vr)
• Potential difference across the membrane of a resting cell
  • Approximately –70 mV in neurons (cytoplasmic side of membrane is negatively charged relative to outside)
• Generated by:
  • Differences in ionic makeup of ICF and ECF
  • Differential permeability of the plasma membrane

Resting Membrane Potential
• Differences in ionic makeup
  • ICF has lower concentration of Na\(^+\) and Cl\(^-\) than ECF
  • ICF has higher concentration of K\(^+\) and negatively charged proteins (A\(^-\)) than ECF

Resting Membrane Potential
• Differential permeability of membrane
  • Impermeable to A\(^-\)
  • Slightly permeable to Na\(^+\) (through leakage channels)
  • 75 times more permeable to K\(^+\) (more leakage channels)
  • Freely permeable to Cl\(^-\)
• Negative interior of the cell is due to much greater diffusion of $K^+$ out of the cell than $Na^+$ diffusion into the cell
• Sodium-potassium pump stabilizes the resting membrane potential by maintaining the concentration gradients for $Na^+$ and $K^+$

**Membrane Potentials That Act as Signals**
• Membrane potential changes when:
  • Concentrations of ions across the membrane change
  • Permeability of membrane to ions changes
• Changes in membrane potential are signals used to receive, integrate and send information

**Membrane Potentials That Act as Signals**
• Two types of signals
  • Graded potentials
    • Incoming short-distance signals
  • Action potentials
    • Long-distance signals of axons

**Changes in Membrane Potential**
• Depolarization
  • A reduction in membrane potential (toward zero)
  • Inside of the membrane becomes less negative than the resting potential
  • Increases the probability of producing a nerve impulse

**Changes in Membrane Potential**
• Hyperpolarization
  • An increase in membrane potential (away from zero)
  • Inside of the membrane becomes more negative than the resting potential
  • Reduces the probability of producing a nerve impulse

**Graded Potentials**
• Short-lived, localized changes in membrane potential
• Depolarizations or hyperpolarizations
• Graded potential spreads as local currents change the membrane potential of adjacent regions
Graded Potentials
• Occur when a stimulus causes gated ion channels to open
  • E.g., receptor potentials, generator potentials, postsynaptic potentials
• Magnitude varies directly (graded) with stimulus strength
• Decrease in magnitude with distance as ions flow and diffuse through leakage channels
• Short-distance signals

Action Potential (AP)
• Brief reversal of membrane potential with a total amplitude of ~100 mV
• Occurs in muscle cells and axons of neurons
• Does not decrease in magnitude over distance
• Principal means of long-distance neural communication

Generation of an Action Potential
• Resting state
  • Only leakage channels for Na⁺ and K⁺ are open
  • All gated Na⁺ and K⁺ channels are closed

Properties of Gated Channels
• Properties of gated channels
  • Each Na⁺ channel has two voltage-sensitive gates
    • Activation gates
      • Closed at rest; open with depolarization
    • Inactivation gates
      • Open at rest; block channel once it is open

Properties of Gated Channels
• Each K⁺ channel has one voltage-sensitive gate
• Closed at rest
• Opens slowly with depolarization

Depolarizing Phase
• Depolarizing local currents open voltage-gated Na⁺ channels
• Na⁺ influx causes more depolarization
• At threshold (~55 to ~50 mV) positive feedback leads to opening of all Na⁺ channels, and a reversal of membrane
polarity to +30mV (spike of action potential)

**Repolarizing Phase**
- Repolarizing phase
  - $\text{Na}^+$ channel slow inactivation gates close
  - Membrane permeability to $\text{Na}^+$ declines to resting levels
  - Slow voltage-sensitive $\text{K}^+$ gates open
  - $\text{K}^+$ exits the cell and internal negativity is restored

**Hyperpolarization**
- Hyperpolarization
  - Some $\text{K}^+$ channels remain open, allowing excessive $\text{K}^+$ efflux
  - This causes after-hyperpolarization of the membrane (undershoot)

**Role of the Sodium-Potassium Pump**
- Repolarization
  - Restores the resting electrical conditions of the neuron
  - Does not restore the resting ionic conditions
  - Ionic redistribution back to resting conditions is restored by the thousands of sodium-potassium pumps

**Propagation of an Action Potential**
- $\text{Na}^+$ influx causes a patch of the axonal membrane to depolarize
- Local currents occur
- $\text{Na}^+$ channels toward the point of origin are inactivated and not affected by the local currents

**Propagation of an Action Potential**
- Local currents affect adjacent areas in the forward direction
- Depolarization opens voltage-gated channels and triggers an AP
- Repolarization wave follows the depolarization wave
- (Fig. 11.12 shows the propagation process in unmyelinated axons.)

**Threshold**
- At threshold:
  - Membrane is depolarized by 15 to 20 mV
• Na\(^+\) permeability increases
• Na influx exceeds K\(^+\) efflux
• The positive feedback cycle begins

**Threshold**
- Subthreshold stimulus—weak local depolarization that does not reach threshold
- Threshold stimulus—strong enough to push the membrane potential toward and beyond threshold
- AP is an all-or-none phenomenon—action potentials either happen completely, or not at all

**Coding for Stimulus Intensity**
- All action potentials are alike and are independent of stimulus intensity
  - How does the CNS tell the difference between a weak stimulus and a strong one?
- Strong stimuli can generate action potentials more often than weaker stimuli
- The CNS determines stimulus intensity by the frequency of impulses

**Absolute Refractory Period**
- Time from the opening of the Na\(^+\) channels until the resetting of the channels
- Ensures that each AP is an all-or-none event
- Enforces one-way transmission of nerve impulses

**Relative Refractory Period**
- Follows the absolute refractory period
  - Most Na\(^+\) channels have returned to their resting state
  - Some K\(^+\) channels are still open
  - Repolarization is occurring
- Threshold for AP generation is elevated
- Exceptionally strong stimulus may generate an AP

**Conduction Velocity**
- Conduction velocities of neurons vary widely
- Effect of axon diameter
• Larger diameter fibers have less resistance to local current flow and have faster impulse conduction
• Effect of myelination
  • Continuous conduction in unmyelinated axons is slower than saltatory conduction in myelinated axons

Conduction Velocity
• Effects of myelination
  • Myelin sheaths insulate and prevent leakage of charge
  • Saltatory conduction in myelinated axons is about 30 times faster
    • Voltage-gated Na⁺ channels are located at the nodes
    • APs appear to jump rapidly from node to node

Multiple Sclerosis (MS)
• An autoimmune disease that mainly affects young adults
• Symptoms: visual disturbances, weakness, loss of muscular control, speech disturbances, and urinary incontinence
• Myelin sheaths in the CNS become nonfunctional scleroses
• Shunting and short-circuiting of nerve impulses occurs
• Impulse conduction slows and eventually ceases

Multiple Sclerosis: Treatment
• Some immune system–modifying drugs, including interferons and Copazone:
  • Hold symptoms at bay
  • Reduce complications
  • Reduce disability

Nerve Fiber Classification
• Nerve fibers are classified according to:
  • Diameter
  • Degree of myelination
  • Speed of conduction

Nerve Fiber Classification
• Group A fibers
  • Large diameter, myelinated somatic sensory and motor fibers
• Group B fibers
  • Intermediate diameter, lightly myelinated ANS fibers
• Group C fibers
  • Smallest diameter, unmyelinated ANS fibers