The Nervous System
-The master controlling and communicating system of the body

Functions:
- Sensory input
- Integration
- Motor output

Organization of the Nervous System

Central nervous system (CNS)
- Brain and spinal cord
- Integration and command center

Peripheral nervous system (PNS)
- Paired spinal and cranial nerves
- Carries messages to and from the spinal cord and brain

Peripheral Nervous System (PNS): Two Functional Divisions

Sensory (afferent) division
- Sensory afferent fibers – carry impulses from skin, skeletal muscles, and joints to brain
- Visceral afferent fibers – transmit impulses from visceral organs to the brain

Motor (efferent) division
- Transmits impulses from the CNS to effector organs

Motor Division: Two Main Parts

Somatic nervous system (SNS)
- Conscious control of skeletal muscles

Autonomic nervous system (ANS)
- Regulates smooth muscle, cardiac muscle, and glands
- Divisions – sympathetic and parasympathetic

Histology of Nerve Tissue
There are two types of nerve cells:
- Neurons – excitable cells that transmit electrical signals
- Supporting cells – cells that surround and wrap neurons
Neuroglia/Glial Cells: Supporting Cells
- Segregate and insulate neurons
- Guide young neurons to the proper connections
- Promote health and growth

Astrocytes: Most abundant, versatile, and highly branched glial cells
- cling to neurons and their synaptic endings
- cover capillaries
- Functions:
  - Support and brace neurons
  - Anchor neurons to their nutrient supplies
  - Guide migration of young neurons
  - Control the chemical environment

Microglia: small, ovoid cells with spiny processes
- phagocytic
- monitor the health of neurons

Ependymal cells: range in shape from squamous to columnar
- line the central cavities of the brain and spinal column

Oligodendrocytes: branched cells that wrap CNS nerve fibers

Schwann cells (neurolemmocytes): surround fibers of the PNS

Satellite cells: surround neuron cell bodies with ganglia

^All of the above cell types are SUPPORTING CELLS

Neurons: (Nerve Cells)
- Structural units of the nervous system
  - Composed of a body, axon, and dendrites
  - Long-lived
  - amitotic (mostly)
  - have a high metabolic rate
- Plasma membrane functions:
  - Electrical signaling
  - Cell-to-cell signaling during development
**Nerve Cell Body** (the Soma)
- Contains nucleus and nucleolus
- Is the major biosynthetic center
- Is the focal point for the outgrowth of neuronal processes
- Has no centrioles (That’s why it’s amitotic!)
- Has well-developed rough ER
- Contains an axon hillock – cone-shaped area from which axons arise

**Processes: Axons and Dendrites**
- Armlike extensions from the soma
- Called tracts in the CNS and nerves in the PNS
- There are two types: axons and dendrites

**Dendrites**
- Short, tapering, and diffusely branched
- Receptive/ input regions
- Convey electrical signals as graded potentials (not action potentials)

**Structure of Axons**
- Slender processes of uniform diameter
- Arise from the hillock
- Long axons are called nerve fibers
- Usu. only one unbranched axon per neuron
- Rare branches called axon collaterals
- Axonal terminal – branched terminus of an axon

**Functions of Axons**
- Generate and transmit action potentials
- Secrete neurotransmitters from terminals
- Impulse travel can be:
  - Anterograde — toward axonal terminal
  - Retrograde — away from axonal terminal

**Myelin Sheath**
- Whitish, fatty (protein-lipoid), segmented sheath around most long axons
- Functions:
  - Protects the axon
  - Electrically insulate fibers from one another
  - Increase the speed of nerve impulse transmission
**Nodes of Ranvier** (Neurofibral Nodes)
- gaps in the myelin sheath between adjacent Schwann cells
- sites where axon collaterals can emerge

**Axons of the CNS**
- Both myelinated and unmyelinated fibers
- Myelin sheaths are formed by oligodendrocytes
- Nodes of Ranvier are widely spaced

**Regions of the Brain and Spinal Cord**
- White matter – dense collections of myelinated fibers
- Gray matter – mostly soma and unmyelinated fibers

**Neuron Classification**
- Structural:
  - Multipolar — three or more processes
  - Bipolar — two processes (axon and dendrite)
  - Unipolar — single, short process
- Functional:
  - Sensory (afferent) — transmit impulses toward the CNS
  - Motor (efferent) — carry impulses away from the CNS
  - Interneurons (association neurons) — shuttle signals through CNS pathways

**Neurophysiology**
- Neurons are highly excitable
- Action potentials, or nerve impulses, are:
  - Electrical impulses
  - Carried along the length of axons
  - Always the same regardless of stimulus
  - The underlying functional feature of the nervous system

**Electrical Current in the Body**
- Reflects the flow of ions (not electrons)
- There is a potential on either side of membranes when:
  - The number of ions is different across the membrane
  - The membrane provides a resistance to ion flow
The Role of Ion Channels
Types of plasma membrane ion channels:
- Passive, or leakage, channels – always open
- Chemically gated channels – opened by a specific neurotransmitter
- Voltage-gated channels – opened and closed by membrane potential
- Mechanically-gated channels – opened and closed by physical deformation of receptors

Operation of a Chemically-Gated Channel Protein
- Example: Na⁺-K⁺ gated channel
  Closed when a neurotransmitter is not bound to the extracellular receptor
    - Na⁺ cannot enter the cell and K⁺ cannot exit the cell
  Open when a neurotransmitter is attached to the receptor
    - Na⁺ enters the cell and K⁺ exits the cell

Operation of a Voltage-Gated Channel Protein
- Example: Na⁺ channel
  Closed when the intracellular environment is negative
    - Na⁺ cannot enter the cell
  Open when the intracellular environment is positive
    - Na⁺ can enter the cell

Gated Channels
When gated channels are open:
- Ions move quickly across the membrane
- Movement is along their electrochemical gradients
- An electrical current is created
- Voltage changes across the membrane (usually depolarization)

Electrochemical Gradient
- Chemical gradient: Ions move from an area of high chemical concentration to an area of low chemical concentration
- Electrical gradient: Ions move toward an area of opposite charge
- Electrochemical gradient – the electrical and chemical gradients taken together
Resting Membrane Potential ($V_r$)
-The potential difference (~70 mV) across the membrane of a resting neuron
-It is generated by different concentrations of Na$^+$, K$^+$, Cl$^-$, and protein anions (A$^-$)
  -Ionic differences are the consequence of:
    -Differential permeability of the neurilemma to Na$^+$ and K$^+$
    -Operation of the sodium-potassium pump

Membrane Potentials: Signals
-Used to integrate, send, and receive information
-Membrane potential changes are produced by:
  -Changes in membrane permeability to ions
  -Alterations of ion concentrations across the membrane
-Types of signals – graded potentials and action potentials

Changes in Membrane Potential
-Changes are caused by three events
  -Depolarization – the inside of the membrane becomes less negative
  -Repolarization – the membrane returns to its resting membrane potential
  -Hyperpolarization – the inside of the membrane becomes more negative than the resting potential

Graded Potentials
-Short-lived, local changes in membrane potential
-Decrease in intensity with distance
-magnitude varies directly with the strength of the stimulus
-strong graded potentials can initiate action potentials
-Voltage changes are decremental
-Current is quickly dissipated (leaky plasma membrane)
-Can only travel over short distances

Action Potentials (APs) (aka nerve impulses)
-A brief reversal of membrane potential
-total amplitude of 100 mV
-generated by muscle cells and neurons
-do not decrease in strength over distance
-principal means of neural communication
Phases of the Action Potential
1 – resting state
2 – depolarization phase
3 – repolarization phase
4 – hyperpolarization

Threshold and Action Potentials
- Weak (subthreshold) stimuli are not relayed into action potentials
- Strong (threshold) stimuli are relayed into action potentials
- All-or-none phenomenon

Action Potential: Resting State
- Na\(^+\) and K\(^+\) channels are closed
- Leakage accounts for small movements of Na\(^+\) and K\(^+\)
- Each Na\(^+\) channel has two voltage-regulated gates
  - Activation gates – closed in the resting state
  - Inactivation gates – open in the resting state

Action Potential: Depolarization Phase
- Na\(^+\) permeability increases; membrane potential reverses
- Na\(^+\) gates are opened; K\(^+\) gates are closed
- Threshold – a critical level of depolarization (-55 to -50 mV)
  - At threshold, depolarization becomes self-generating

Action Potential: Repolarization Phase
- Sodium inactivation gates close
- Membrane permeability to Na\(^+\) declines to resting levels
- As sodium gates close, voltage-sensitive K\(^+\) gates open
- K\(^+\) exits the cell and internal negativity of the resting neuron is restored

Action Potential: Hyperpolarization
- Potassium gates remain open, causing an excessive efflux of K\(^+\)
- This efflux causes hyperpolarization of the membrane (undershoot)
- The neuron is insensitive to stimulus and depolarization during this time

Action Potential: 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 sodium-potassium pump

Coding for Stimulus Intensity
- All action potentials are alike and are independent of stimulus intensity
- Strong stimuli can generate an action potential more often than weaker stimuli
- The CNS determines stimulus intensity by the frequency of impulse transmission

Absolute Refractory Period
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-Time from the opening of the $\text{Na}^+$ activation gates until the closing of inactivation gates
  -Prevents the neuron from generating an action potential
  -Ensures that each action potential is separate
  -Enforces one-way transmission of nerve impulses

Relative Refractory Period
-The interval following the absolute refractory period when:
  -Sodium gates are closed
  -Potassium gates are open
  -Repolarization is occurring
-The threshold level is elevated, allowing strong stimuli to increase the frequency of action potential events

Conduction Velocities of Axons
-Conduction velocities vary widely among neurons
-Rate of impulse propagation is determined by:
  -Axon diameter – the larger the diameter, the faster the impulse
  -Presence of a myelin sheath – myelination dramatically increases impulse speed

Saltatory Conduction
-Current passes through a myelinated axon only at the nodes of Ranvier
-Voltage-gated $\text{Na}^+$ channels are concentrated at these nodes
-Action potentials are triggered only at the nodes and jump from one node to the next
-Much faster than conduction along unmyelinated axons

Synapses
-A junction that mediates information transfer from one neuron:
  -To another neuron
  -To an effector cell
-Presynaptic neuron – conducts impulses toward the synapse
-Postsynaptic neuron – transmits impulses away from the synapse

Electrical Synapses
-Electrical synapses:
  -Are less common than chemical synapses
  -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

Synaptic Cleft
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- Fluid-filled space separating the presynaptic and postsynaptic neurons
- Prevents nerve impulses from directly passing from one neuron to the next
- Transmission across the synaptic cleft:
  - Is a chemical event (as opposed to an electrical one)
  - Ensures unidirectional communication between neurons

**Synaptic Cleft: Information Transfer**
- Nerve impulses reach the axonal terminal of the presynaptic neuron and open Ca\(^{2+}\) channels
- Neurotransmitter is released into the synaptic cleft via exocytosis in response to synaptotagmin
- Neurotransmitter crosses the synaptic cleft and binds to receptors on the postsynaptic neuron
- Postsynaptic membrane permeability changes, causing an excitatory or inhibitory effect

**Termination of Neurotransmitter Effects**
- Neurotransmitter bound to a postsynaptic neuron:
  - Produces a continuous postsynaptic effect
  - Blocks reception of additional “messages”
  - Must be removed from its receptor
- Removal of neurotransmitters occurs when they:
  - Are degraded by enzymes
  - Are reabsorbed by astrocytes or the presynaptic terminals
  - Diffuse from the synaptic cleft

**Neurotransmitters** - Chemicals used for neuronal communication
- 50 different neurotransmitters have been identified
- Classified chemically and functionally

**Chemical Neurotransmitters** - Acetylcholine (ACh)
- Biogenic amines
- Amino acids
- Peptides
- Novel messengers: ATP and dissolved gases NO and CO

**Acetylcholine** - First neurotransmitter identified, released at the neuromuscular junction

**Biogenic Amines** - Examples:
- Catecholamines – dopamine, norepinephrine (NE), and epinephrine
- Indolamines – serotonin and histamine
- Play roles in emotional behaviors and our biological clock

**Amino Acids**
- Include:
  - GABA – Gamma (g)-aminobutyric acid
  - Glycine
  - Aspartate
  - Glutamate
-Found only in the CNS

**Peptides**
-Include:
  - Substance P – mediator of pain signals
  - Beta endorphin, dynorphin, and enkephalins
-Act as natural opiates, reducing our perception of pain
-Bind to the same receptors as opiates and morphine

**Functional Classification of Neurotransmitters**-Two classifications: excitatory and inhibitory
- Excitatory neurotransmitters cause depolarizations (ex: glutamate)
- Inhibitory neurotransmitters cause hyperpolarizations (ex: GABA and glycine)

-Some neurotransmitters have both excitatory and inhibitory effects
- Determined by the receptor type of the postsynaptic neuron
- Example: acetylcholine
  - Excitatory at neuromuscular junctions with skeletal muscle
  - Inhibitory in cardiac muscle