An overview of the nervous system

- The **nervous system** (which is one of the two organ systems that function to control or adjust the activities of many other systems simultaneously) provides swift and brief responses to stimuli
  - Compare this to the **endocrine system** (the body’s other major controlling organ system), which adjusts metabolic operations and directs slower and more long-term changes

- The nervous system includes all of the neural tissue of the body, which has two main types of cells:
  - The supporting cells of the nervous system are called **neuroglia** (or **glial cells**)  
  - The basic **functional** cells of the nervous system are **neurons**
The organization of the nervous system

- **I. Central nervous system (CNS)** = the brain and spinal cord; it functions to integrate, process, and coordinate sensory data and motor commands; the brain also provides higher functions such as intelligence, memory, learning, and emotion

- **II. Peripheral nervous system (PNS)** = neural tissue (mostly spinal nerves and cranial nerves) that is located outside the CNS
  - A. **Afferent division**: brings sensory information from receptors to the CNS
  - B. **Efferent division**: carries motor commands from the CNS to effectors
    - 1. **Somatic nervous system (SNS)** (Ch. 15): mostly voluntary control of skeletal muscle
    - 2. **Autonomic nervous system (ANS)** (a.k.a. the visceral motor system) (Ch. 16): involuntary control of smooth muscle, cardiac muscle, glands, and adipose tissue
      - a. Sympathetic division
      - b. Parasympathetic division

A nervous system organizational chart

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**Organization of the Nervous System**

- Central Nervous System (CNS) (brain and spinal cord)
  - Sensory information within afferent division
  - Motor commands within efferent division
  - Integrate, process, and coordinate sensory data and motor commands

- Peripheral Nervous System (PNS) (neural tissue outside the CNS)
  - Includes Somatic nervous system (SNS), Autonomic nervous system (ANS), Parasympathetic division, Sympathetic division

**Receptors**
- Special sensory receptors: monitor smell, taste, vision, balance, and hearing
- Visceral sensory receptors: monitor internal organs
- Somatic sensory receptors: monitor skeletal muscles, joints, and skin surface

**Effectors**
- Skeletal muscle
  - Smooth muscle
  - Cardiac muscle
  - Glands
  - Adipose tissue

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Fig. 12-1, p. 387
The basic anatomy of a neuron

- Consists of the **cell body**, **dendrites**, **axon**, and **telodendria**
  - The **cell body** contains the nucleus and other organelles
  - **Dendrites** – receive information (often from other neurons) and carry it **toward** the cell body
  - The dendrites and cell body are capable of generating **graded (local) potentials**, but **not** **action potentials** (nerve impulses)
    - More on this later!

- **Axon**
  - Carries information **away** from the cell body
    - The **initial segment** of the axon is where **action potentials** (APs) are generated
    - It may have major side branches called **axon collaterals** (not shown here)
  - “Fast stream” **axoplasmic transport** = proteins called kinesin and dynein actively (via ATP) move materials along the axon
    - **Anterograde flow** = the movement of neurotransmitters and organelles away from the cell body (performed by kinesin)
    - **Retrograde flow** = the movement of certain chemicals toward the cell body (performed by dynein)
      - So the presence of certain chemicals at the synapse may affect gene activity in the presynaptic neuron’s nucleus

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[Image: Color-coded figure showing the four general regions of a neuron.]

[Image: Diagram illustrating the axon and its components.]
Synapses

- **Telodendria** = small branches at the end of an axon
- **Axon terminals** (a.k.a. synaptic terminals or synaptic knobs) = the swollen ends of the telodendria, which...
  - Store chemicals called **neurotransmitters (NTs)** in synaptic vesicles, and...
  - Release NTs in response to electrical activity (such as the arrival of an incoming AP)
- **Terminology note** – the neurons that communicate at synapses are referred to as **presynaptic** cells/neurons and **postsynaptic** cells (which are often neurons, but may also be muscle fibers, secretory [gland] cells, or adipocytes)

Neuron classification by structure

- Is based on the number and type of processes attached to the cell body
  - **Anaxonic neurons** – lack an axon
    - They are found in the brain and some special sensory organs
    - Their functions are poorly understood
  - **Bipolar neurons** – have two distinct processes
    - They are relatively rare
    - They are special sensory and found in the eye, ear, and nose

<table>
<thead>
<tr>
<th>Anaxonic neuron</th>
<th>Bipolar neuron</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image1.png" alt="Anaxonic neuron" /></td>
<td><img src="image2.png" alt="Bipolar neuron" /></td>
</tr>
</tbody>
</table>

- Anaxonic neurons have more than two processes, and they are all dendrites.
- Bipolar neurons have two processes separated by the cell body.
More neuron classification by structure

- **Unipolar neurons**
  - have one process (that connects to a continuous axonal fiber)
  - E.g. sensory neurons
- **Multipolar neurons**
  - have more than two processes
  - They are the most common type of neuron
  - E.g. motor neurons and interneurons

<table>
<thead>
<tr>
<th>Unipolar neuron</th>
<th>Multipolar neuron</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dendrites</td>
<td>Dendrites</td>
</tr>
<tr>
<td>Initial segment</td>
<td>Axon</td>
</tr>
<tr>
<td>Axon</td>
<td>Cell body</td>
</tr>
<tr>
<td>Axon terminals</td>
<td>Axon terminals</td>
</tr>
</tbody>
</table>

Unipolar neurons have a single elongated process, with the cell body located off to the side. Multipolar neurons have more than two processes; there is a single axon and multiple dendrites.

Neuron classification by function

- **1. Sensory (afferent) neurons** – carry information from sensory receptors to the CNS
  - The main sensory receptor types:
    - *Interoceptors* – monitor (detect changes in the conditions of) internal organ systems
      - E.g. sensing heart rate, blood pressure, deep pressure/pain, etc.
    - *Exteroceptors* – monitor the external environment
      - E.g. sensing ambient temperature, light, touch, sound, etc.
    - *Proprioceptors* – monitor the position and movement of muscles and joints
- **2. Motor (efferent) neurons** – carry information away from the CNS to effectors (muscles, glands, and adipose tissue)
- **3. Interneurons (association neurons)** – most carry information *within* the CNS
Neuron classification by function

An introduction to neuroglia

- General function: support and protect neurons
Neuroglia in the CNS

- Myelinated vs. unmyelinated peripheral axons

Schwann cells

A diagrammatic view of neural tissue in the CNS, showing relationships between neuroglia and neurons

Fig. 12-6, p. 394

A myelinated axon, showing the organization of Schwann cells along the length of the axon.

The enclosing of a group of unmyelinated axons by a single Schwann cell. A series of Schwann cells is required to cover the axons along their entire length.

Fig. 12-7, p. 396
Neural responses to injuries

- **IMPORTANT**: for repair to occur, the neuron cell body must remain alive!

- **CNS repair of axons** is very limited:
  - 1. An injury to the CNS would destroy many axons at once
  - 2. Astrocytes produce scar tissue, which blocks axon regrowth
  - 3. Astrocytes release axon growth inhibitors

- **PNS repair of axons** involves Schwann cells (see the figure shown here)...

Neuron membrane physiology: an overview
The membrane potential (in general)

- Is caused by a separation of electrical charges (ions) across a cell membrane (e.g. Na\(^+\) and K\(^+\) ions, among others)
  - “Potential” = an electric voltage difference
    - The membrane potential is usually reported in millivolts (mV)
    - At rest, the inside of a cell is more negative than the outside of a cell (more on this soon)
- Is influenced by:
  - Electrochemical gradients = both the chemical [concentration] and electrical forces acting on each ion
  - The movement of ions across the membrane, both by active transport (e.g. the Na\(^+\)-K\(^+\) exchange pump) and by diffusion through membrane channels…
    - 1. Passive (leak) channels – are always open
      - These channels are important for establishing the resting potential
    - 2. Active (gated) channels – may be open (activated) or closed
      - Note that “active” does not refer to ATP use in this case
      - These channels are important for generating graded (local) potentials and action potentials (APs)
      - There are 3 main subtypes of gated channels (see the next three slides):
        » a. Chemically (ligand-) gated channels
        » b. Voltage-gated channels
        » c. Mechanically gated channels

Chemically (ligand-) gated channels

- Open after binding to a specific chemical (ligand)
- Are most abundant on the cell body and dendrites of neurons, and the motor end plate of muscle fibers
- Are important for the generation of graded (local) potentials
- E.g. ACh receptors
  - The binding of ACh changes the shape of the receptor, opening the channel, allowing small ions like Na\(^+\) and K\(^+\) to diffuse through

Fig. 12-11a, p. 403
Voltage-gated channels

- Open in response to changes in the membrane potential (voltage)
- Are important for the generation and propagation (spread) of action potentials (nerve impulses), the release of Ca\(^{2+}\) from the sarcoplasmic reticulum during muscle contraction, and the release of neurotransmitter from axon terminals
- E.g. voltage-gated K\(^+\), Na\(^+\) and Ca\(^{2+}\) channels
- Can exist in 3 different states:
  - Closed, but can be opened
  - Open (activated)
  - Closed, and cannot be opened (inactivated)

Mechanically gated channels

- Open or close in response to physical distortion of the membrane
- E.g. sensory receptors such as touch and pressure receptors
- We will discuss these in more detail in Ch. 15
Types of membrane potentials

1. The resting potential
   - = the voltage difference across the cell membrane for an unstimulated ("resting") cell; it's about -70 mV for most neurons

2. Graded (local) potentials
   - = temporary, local changes in the membrane potential that occur when the cell body and dendrites are stimulated
   - Do not self-regenerate or spread over long distances (their intensity decreases with distance from the stimulus site)

3. Action potentials ("nerve impulses")
   - = self-regenerating changes in the membrane potential that occur when the initial segment of the axon reaches a specific membrane potential value called threshold (due to stimulation by a graded potential)
   - Spread over long distances (their intensity does not decrease as they travel down the axon)

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The resting potential

Keys:
- Intra-cellular negatively charged proteins
- K⁺ leak channels are much more permeable than Na⁺ leak channels
- The Na⁺-K⁺ pump exchanges 3 Na⁺ for every 2 K⁺
Changes in the resting membrane potential

- The membrane at rest is polarized: i.e., the inside is slightly negative (about \(-70\) mV) compared to the outside
- The diffusion of ions through the membrane can cause changes in the resting membrane potential:
  - When gated Na\(^+\) channels open, more Na\(^+\) enters the cell, and the inside of the membrane becomes more positive = **depolarization**
  - When gated Na\(^+\) channels close after depolarization, Na\(^+\) is pumped back out, returning the membrane to the resting potential = **repolarization**
    - More rapid repolarization occurs when gated K\(^+\) channels open immediately after depolarization, such as during an action potential (more on this coming soon)
  - When gated K\(^+\) channels open in a resting membrane, more K\(^+\) leaves the cell, and the inside of the membrane becomes more negative = **hyperpolarization**

![Diagram of membrane potential changes](image)

Graded (local) potentials

- = **local** changes in the membrane potential that decrease in intensity with distance from the site of stimulation
- Are caused by ions entering the dendrites or cell body through open (activated) chemically gated or mechanically gated membrane ion channels
- Results in local depolarization or hyperpolarization
  - Whether depolarization or hyperpolarization occurs depends on which specific ion channels are opened (see the previous slide)
  - This **local current** does not spread very far from the site of the stimulus
  - The stronger the stimulus, the greater the change in membrane potential and the larger the area affected
- See the next slide for a visual representation of a graded potential…
Graded potentials

Action potentials (nerve impulses)

- = sudden, major changes in the membrane potential that propagate (travel) down the membrane of an axon
- Occur when the local currents from graded potentials cause the membrane at the initial segment of the axon to reach a specific membrane potential called **threshold** (= between -60 mV and -55 mV for a typical axon)
- Exhibit the **all-or-none principle**:  
  - Either an AP **happens all the way at full intensity** if threshold is reached, or it **doesn’t happen at all** if threshold isn’t reached
- Do not decrease in intensity over long distances (unlike graded potentials)
- The key to APs: **voltage-gated Na⁺ and K⁺ channels** (see the next few slides…)
Generation of an AP

Steps in the formation of an action potential at the initial segment of an axon. The first step is a graded depolarization caused by the opening of chemically gated sodium ion channels, usually at the axon hillock. Note that when illustrating action potentials, we can ignore the leak channels and the chemically gated channels, because their properties do not change. The membrane colors in steps 1-4 match the colors of the line graph showing membrane potential changes.

1. Depolarization to Threshold
   - The stimulus that initiates an action potential is a graded depolarization large enough to open voltage-gated sodium channels. The opening of the channels occurs at a membrane potential known as the threshold.

2. Activation of Sodium Channels and Rapid Depolarization
   - When the sodium channel activation gates open, the plasma membrane becomes much more permeable to Na⁺. Driven by the large electrochemical gradient, sodium ions rush into the cytoplasm, and rapid depolarization occurs. The inner membrane surface now contains more positive ions than negative ones, and the membrane potential has changed from -60 mV to a positive value.

3. Inactivation of Sodium Channels and Activation of Potassium Channels
   - As the membrane potential approaches +30 mV, the inactivation gates of the voltage-gated sodium channels close. This step is known as sodium channel inactivation, and it coincides with the opening of voltage-gated potassium channels. Positively charged potassium ions move out of the cytosol, shifting the membrane potential back toward resting levels. Repolarization now begins.

4. Closing of Potassium Channels
   - The voltage-gated sodium channels remain inactivated until the membrane is repolarized to near threshold levels. At this time, they regain their normal status: closed but capable of opening. The voltage-gated potassium channels begin closing as the membrane reaches the normal resting potential (about -70 mV). Until all of these potassium channels have closed, potassium ions continue to leave the cell. This produces a brief hyperpolarization.

FIG. 12-14, p. 408

Generation of an AP, continued
Summary: the generation of an AP

1. The incoming AP on the motor neuron depolarizes the axon terminal, causing the release of ACh into the synaptic cleft of the NMJ.
2. The motor end plate contains ACh receptors that are chemically gated Na\(^+\) channels.
3. A graded (local) potential (depolarization) is generated at the motor end plate.
4. The local Na\(^+\) current from the graded potential depolarizes the adjacent sarcolemma, where voltage-gated Na\(^+\) channels are found and, if threshold is reached, a new AP is generated, which propagates along the entire sarcolemma and deep into the T tubules, where excitation-contraction coupling occurs.

A brief look back at Ch. 10: APs and muscle fibers

- The incoming AP on the motor neuron depolarizes the axon terminal, causing the release of ACh into the synaptic cleft of the NMJ.
- The motor end plate contains ACh receptors that are chemically gated Na\(^+\) channels.
- A graded (local) potential (depolarization) is generated at the motor end plate.
- The local Na\(^+\) current from the graded potential depolarizes the adjacent sarcolemma, where voltage-gated Na\(^+\) channels are found and, if threshold is reached, a new AP is generated, which propagates along the entire sarcolemma and deep into the T tubules, where excitation-contraction coupling occurs.
Back to Ch. 12 and more neuron membrane physiology...

- Action potential propagation speed is influenced by:
  - 1. The presence of electrical insulation (myelin)
    - ↑ Electrical insulation (such as in a myelinated axon) → ↑ speed
  - 2. Axon (fiber) diameter
    - ↑ Fiber diameter → ↑ speed

Continuous propagation of an AP

- If no myelin is present, **continuous propagation** of an AP occurs
  - Which, as you’ll see on the next slide, is slower than saltatory propagation of an AP
Saltatory propagation of an AP

- If myelin is present: **saltatory propagation** of an AP occurs
  - Which is faster than continuous propagation of an AP

Axon classification

- Is based on diameter, myelination, and AP propagation speed:
  - **Type A fibers**:
    - Largest
    - Myelinated
    - Speed = up to 120 m/sec (268 mph!)
  - **Type B fibers**:
    - Medium sized
    - Myelinated
    - Speed = about 18 m/sec (40 mph)
  - **Type C fibers**:
    - Smallest
    - Unmyelinated
    - Speed = about 1 m/sec (2 mph)
- *Type A fibers* carry sensory info on fast pain, body position, balance, and delicate touch, as well as somatic motor commands
- *Type B and C fibers* carry sensory info on temperature, slow pain, general touch, as well as visceral (autonomic) motor commands
Information flow and synaptic activity

- Information in the form of an action potential (nerve impulse) travels along the axon of a neuron
- At a synapse, the signal passes from a **presynaptic** neuron to a **postsynaptic** cell (neuron, muscle fiber, glandular cell, or adipocyte)

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<table>
<thead>
<tr>
<th>Table 12–3 A Comparison of Graded Potentials and Action Potentials</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Graded Potentials</strong></td>
</tr>
<tr>
<td>Depolarizing or hyperpolarizing</td>
</tr>
<tr>
<td>No threshold value</td>
</tr>
<tr>
<td>Amount of depolarization or hyperpolarization depends on intensity of stimulus</td>
</tr>
<tr>
<td>Passive spread from site of stimulation</td>
</tr>
<tr>
<td>Effect on membrane potential decreases with distance from stimulation site</td>
</tr>
<tr>
<td>No refractory period</td>
</tr>
</tbody>
</table>

Table 12-3, p. 412
Types of synapses

1. **Electrical synapses** are fast; the pre- and postsynaptic membranes are fused, with gap junctions connecting the two
   - This type of synapse is extremely rare in the nervous system; it’s only found in certain brain regions
   - Each individual incoming action potential is always propagated to the postsynaptic cell

2. **Chemical synapses** are a bit slower; the membranes do not touch each other; neurotransmitter is used to “bridge the gap”
   - This is by far most abundant type of synapse
   - E.g. cholinergic synapses (see the next two slides)
   - Each individual incoming AP releases one “dose” of neurotransmitter, which *may or may not* be sufficient to cause a new AP in a postsynaptic neuron

Cholinergic synapses

- Use acetylcholine (ACh) as the neurotransmitter
- Are the most common type of chemical synapse
Neurotransmitters (NTs) and neuromodulators

- **Neuromodulators** are other chemicals released by axon terminals that can change 1) the rate of NT release by the presynaptic neuron, and/or 2) the postsynaptic cell’s response the NT

- Some examples of NTs and neuromodulators (see Table 12-4 for a lot more FYI detail)...
  - **Acetylcholine**
  - **Biogenic amines:**
    - E.g. epinephrine, norepinephrine, dopamine, serotonin, histamine
  - **Amino acids:**
    - E.g. glutamate, aspartate, glycine, GABA
  - **Neuropeptides:**
    - E.g. enkephalins, endorphins, substance P
  - **Purines:**
    - E.g. ATP, adenosine, GTP
  - **Gases:**
    - E.g. nitric oxide (NO), carbon monoxide (CO)

How neurotransmitters work (part 1)

- IMPORTANT: the mechanism of action (and effect—either excitatory or inhibitory) of a specific neurotransmitter (NT) ultimately depends upon the receptor type, not necessarily what the specific NT is
  - I.e., the same NT may be excitatory at one synapse while it is inhibitory at a different synapse, depending upon whether the NT binding to a receptor at the synapse causes the opening of, for example, a Na⁺ channel (causing depolarization toward threshold) or a K⁺ channel (causing hyperpolarization away from threshold), respectively

- **A. Direct effects**
  - The receptor is an ion channel
  - The binding of the NT directly opens or closes the ion channel
B. **Indirect effects via G proteins**
- The receptor is not an ion channel
- **Mechanism of action:**
  - 1. NT binds to the receptor
  - 2. A G protein is activated
  - 3. The activated G protein may activate a **second messenger** (e.g. cAMP), which may:
    - Open ion channels
    - **AND/OR** -
    - Activate intracellular enzymes, which change the metabolism of the cell

C. **Indirect effects via intracellular enzymes**
- E.g. lipid-soluble gases like nitric oxide (NO) and carbon monoxide (CO)
- There is no receptor; these NTs are small and lipid-soluble, and thus easily diffuse into the cell and bind to intracellular enzymes, producing secondary messengers, which may:
  - Open ion channels - **AND/OR** -
  - Change the metabolism of the cell
• A single postsynaptic cell may receive many inputs
• The effect of a presynaptic neuron’s NT on a postsynaptic cell’s membrane causes a **postsynaptic potential (PSP)**
  - These are graded (local) potentials and can be:
    • **Excitatory (EPSP),** which is a graded...
      - *Depolarization* – a postsynaptic neuron’s membrane potential moves closer to threshold (**facilitation**)
        - So a postsynaptic neuron is more likely to produce an action potential
        - E.g. when postsynaptic gated Na⁺ channels open
    • **Inhibitory (IPSP),** which is a graded...
      - *Hyperpolarization* – a postsynaptic neuron’s membrane moves further away from threshold (**inhibition**)
        - So a postsynaptic neuron is less likely to produce an action potential
        - E.g. when postsynaptic gated K⁺ channels open

---

**Summation**

• Postsynaptic potentials are added together to produce a net (overall) postsynaptic membrane potential
  - If the initial segment of the axon of a postsynaptic neuron reaches threshold, then an action potential is produced
  - If the initial segment of the axon of a postsynaptic neuron does not reach threshold, then an action potential is not produced
• **Temporal summation:** a single synapse (e.g. from presynaptic neuron A below) is stimulated repeatedly and rapidly
• **Spatial summation:** multiple synapses (e.g. from presynaptic neurons A and B below) are stimulated at the same time
Temporal and spatial summation

Temporal Summation. Temporal summation occurs on a membrane that receives two depolarizing stimuli from the same source in rapid succession. The effects of the second stimulus are added to those of the first.

Spatial Summation. Spatial summation occurs when sources of stimulation arrive simultaneously, but at different locations. Local currents spread the depolarizing effects, and areas of overlap experience the combined effects.

Interactions between EPSPs and IPSPs

Fig. 12-18, p. 422

Fig. 12-19, p. 423
Presynaptic inhibition and facilitation

- May occur at **axoaxonic synapses**

The rate of generation of APs

- Information (such as the magnitude or intensity of stimulation) is often encoded by the nervous system on the basis of **action potential frequency** (i.e., APs per second)
  - E.g. treppe vs. a tetanic contraction in a skeletal muscle fiber
  - E.g. a few APs/sec along a sensory neuron may be interpreted as light touch, while many APs/sec along the same sensory neuron may be interpreted as painful pressure
- Remember, the initial segment of an axon can produce frequent, consecutive APs if it remains above threshold (due to continuous excitatory stimulation):
  - The next AP is produced when the **absolute** refractory period of the previous AP is done
    - **AND**
    - If there is enough excitatory stimulation during the **relative** refractory period of the previous AP to overcome the brief hyperpolarization that occurs during this period
- The highest AP frequencies recorded from axons in the body are 500-1,000 AP/sec