Chapter 48
Neurons, Synapses, and Signaling
Overview: Lines of Communication

- The cone snail kills prey with venom that disables neurons
- **Neurons** are nerve cells that transfer information within the body
- Neurons use two types of signals to communicate: electrical signals (long-distance) and chemical signals (short-distance)
• Interpreting signals in the nervous system involves sorting a complex set of paths and connections
• Processing of information takes place in simple clusters of neurons called **ganglia** or a more complex organization of neurons called a **brain**
Concept 48.1: Neuron organization and structure reflect function in information transfer

- The squid possesses extremely large nerve cells and has played a crucial role in the discovery of how neurons transmit signals
Figure 48.2

- Ganglia
- Nerves with giant axons
- Brain
- Arm
- Eye
- Mantle
- Nerve
Introduction to Information Processing

- Nervous systems process information in three stages: sensory input, integration, and motor output
- Sensors detect external stimuli and internal conditions and transmit information along **sensory neurons**
- Sensory information is sent to the brain or ganglia, where **interneurons** integrate the information
- Motor output leaves the brain or ganglia via **motor neurons**, which trigger muscle or gland activity
• Many animals have a complex nervous system that consists of
  – A central nervous system (CNS) where integration takes place; this includes the brain and a nerve cord
  – A peripheral nervous system (PNS), which carries information into and out of the CNS
  – The neurons of the PNS, when bundled together, form nerves
Neuron Structure and Function

- Most of a neuron’s organelles are in the **cell body**
- Most neurons have **dendrites**, highly branched extensions that *receive* signals from other neurons
- The **axon** is typically a much longer extension that transmits signals to other cells at synapses
- The cone-shaped base of an axon is called the **axon hillock**
• The **synaptic terminal** of one axon passes information across the synapse in the form of chemical messengers called **neurotransmitters**

• A **synapse** is a junction between an axon and another cell

• Information is transmitted from a **presynaptic cell** (a neuron) to a **postsynaptic cell** (a neuron, muscle, or gland cell)

• Most neurons are nourished or insulated by cells called **glia**
Figure 48.5

- **Dendrites**
- **Axon**
- **Cell body**
- **Portion of axon**

- **Sensory neuron**
- **Interneurons**
- **Motor neuron**
Figure 48.6

Cell bodies of neurons

Glia

80 μm
Concept 48.2: Ion pumps and ion channels establish the resting potential of a neuron

- Every cell has a voltage (difference in electrical charge) across its plasma membrane called a **membrane potential**
- The **resting potential** is the membrane potential of a neuron not sending signals
- Changes in membrane potential act as signals, transmitting and processing information
Formation of the Resting Potential

• In a mammalian neuron at resting potential, the concentration of $K^+$ is highest inside the cell, while the concentration of $Na^+$ is highest outside the cell.

• Sodium-potassium pumps use the energy of ATP to maintain these $K^+$ and $Na^+$ gradients across the plasma membrane.

• These concentration gradients represent chemical potential energy.
• The opening of **ion channels** in the plasma membrane converts chemical potential to electrical potential

• A neuron at resting potential contains many open $\text{K}^+$ channels and fewer open $\text{Na}^+$ channels; $\text{K}^+$ diffuses out of the cell

• The resulting buildup of negative charge within the neuron is the major source of membrane potential
Table 48.1 Ion Concentrations Inside and Outside of Mammalian Neurons

<table>
<thead>
<tr>
<th>Ion</th>
<th>Intracellular Concentration (mM)</th>
<th>Extracellular Concentration (mM)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Potassium (K⁺)</td>
<td>140</td>
<td>5</td>
</tr>
<tr>
<td>Sodium (Na⁺)</td>
<td>15</td>
<td>150</td>
</tr>
<tr>
<td>Chloride (Cl⁻)</td>
<td>10</td>
<td>120</td>
</tr>
<tr>
<td>Large anions (A⁻) inside cell, such as proteins</td>
<td>100</td>
<td>(not applicable)</td>
</tr>
</tbody>
</table>
Figure 48.7

Key

- Na\(^+\)
- K\(^+\)

- Sodium-potassium pump
- Potassium channel
- Sodium channel

OUTSIDE OF CELL

INSIDE OF CELL
Modeling the Resting Potential

- Resting potential can be modeled by an artificial membrane that separates two chambers
  - The concentration of KCl is higher in the inner chamber and lower in the outer chamber
  - $K^+$ diffuses down its gradient to the outer chamber
  - Negative charge ($Cl^-$) builds up in the inner chamber
- At equilibrium, both the electrical and chemical gradients are balanced
Figure 48.8

(a) Membrane selectively permeable to K⁺

\[ E_K = 62 \text{ mV} \left( \log \frac{5 \text{ mM}}{140 \text{ mM}} \right) = -90 \text{ mV} \]

(b) Membrane selectively permeable to Na⁺

\[ E_{Na} = 62 \text{ mV} \left( \log \frac{150 \text{ mM}}{15 \text{ mM}} \right) = +62 \text{ mV} \]
(a) Membrane selectively permeable to $K^+$

$$E_K = 62 \text{ mV} \left( \log \frac{5 \text{ mM}}{140 \text{ mM}} \right) = -90 \text{ mV}$$
The equilibrium potential \((E_{\text{ion}})\) is the membrane voltage for a particular ion at equilibrium and can be calculated using the Nernst equation

\[
E_{\text{ion}} = 62 \text{ mV} \left( \log [\text{ion}]_{\text{outside}} / [\text{ion}]_{\text{inside}} \right)
\]

The equilibrium potential of K\(^+\) \((E_K)\) is negative, while the equilibrium potential of Na\(^+\) \((E_{Na})\) is positive.
• In a resting neuron, the currents of $K^+$ and $Na^+$ are equal and opposite, and the resting potential across the membrane remains steady.
Membrane selectively permeable to $\text{Na}^+$

\[
E_{\text{Na}} = 62 \text{ mV} \left( \log \frac{150 \text{ mM}}{15 \text{ mM}} \right) = +62 \text{ mV}
\]
Concept 48.3: Action potentials are the signals conducted by axons

- Changes in membrane potential occur because neurons contain gated ion channels that open or close in response to stimuli.
Hyperpolarization and Depolarization

- When gated $K^+$ channels open, $K^+$ diffuses out, making the inside of the cell more negative.
- This is **hyperpolarization**, an increase in magnitude of the membrane potential.
(a) Graded hyperpolarizations produced by two stimuli that increase membrane permeability to $K^+$

(b) Graded hyperpolarizations produced by two stimuli that increase membrane permeability to $Na^+$

(c) Action potential triggered by a depolarization that reaches the threshold
Figure 48.10a

(a) Graded hyperpolarizations produced by two stimuli that increase membrane permeability to $K^+$.
• Opening other types of ion channels triggers a **depolarization**, a reduction in the magnitude of the membrane potential

• For example, depolarization occurs if gated Na\(^+\) channels open and Na\(^+\) diffuses into the cell
(b) Graded depolarizations produced by two stimuli that increase membrane permeability to Na⁺
Graded Potentials and Action Potentials

- **Graded potentials** are changes in polarization where the magnitude of the change varies with the strength of the stimulus.
- These are not the nerve signals that travel along axons, but they do have an effect on the generation of nerve signals.
• If a depolarization shifts the membrane potential sufficiently, it results in a massive change in membrane voltage called an **action potential**

• Action potentials have a constant magnitude, are all-or-none, and transmit signals over long distances

• They arise because some ion channels are **voltage-gated**, opening or closing when the membrane potential passes a certain level
Figure 48.10c
(c) Action potential triggered by a depolarization that reaches the threshold.
Generation of Action Potentials: A Closer Look

- An action potential can be considered as a series of stages
- At resting potential
  1. Most voltage-gated sodium ($\text{Na}^+$) channels are closed; most of the voltage-gated potassium ($\text{K}^+$) channels are also closed
Figure 48.11-1

Key
- Na⁺
- K⁺

Membrane potential

Time

Threshold
Resting potential

OUTSIDE OF CELL
INSIDE OF CELL

Sodium channel
Potassium channel
Inactivation loop

Resting state
• When an action potential is generated
  2. Voltage-gated Na\(^+\) channels open first and Na\(^+\) flows into the cell
  3. During the *rising phase*, the threshold is crossed, and the membrane potential increases
  4. During the *falling phase*, voltage-gated Na\(^+\) channels become inactivated; voltage-gated K\(^+\) channels open, and K\(^+\) flows out of the cell
Figure 48.11-2

Key
- **Na⁺**
- **K⁺**

1. **Resting state**
2. **Depolarization**

**OUTSIDE OF CELL**
- Sodium channel
- Potassium channel

**INSIDE OF CELL**
- Inactivation loop

<table>
<thead>
<tr>
<th>Membrane potential (mV)</th>
</tr>
</thead>
<tbody>
<tr>
<td>+50</td>
</tr>
<tr>
<td>0</td>
</tr>
<tr>
<td>-50</td>
</tr>
<tr>
<td>-100</td>
</tr>
</tbody>
</table>

Time

**Threshold**

**Resting potential**
Figure 48.11-3

1. **Resting state**

2. **Depolarization**

3. **Rising phase of the action potential**

Key:
- **Na⁺**
- **K⁺**

<table>
<thead>
<tr>
<th>Time (ms)</th>
<th>Membrane potential (mV)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>-70</td>
</tr>
<tr>
<td>40</td>
<td>-50</td>
</tr>
<tr>
<td>90</td>
<td>0</td>
</tr>
<tr>
<td>100</td>
<td>+50</td>
</tr>
</tbody>
</table>

**OUTSIDE OF CELL**

- Sodium channel
- Potassium channel

**INSIDE OF CELL**

- Inactivation loop

**Key**
- **Na⁺**
- **K⁺**

**Graph**
- **Action potential**
- **Threshold**
- **Resting potential**
- **Time**
Inactivation loop

Sodium channel

Potassium channel

Action potential

Threshold

Resting potential

Membrane potential (mV)

Time

Key

Na⁺

K⁺

Resting state

Depolarization

Rising phase of the action potential

Falling phase of the action potential

Figure 48.11-4
5. During the *undershoot*, membrane permeability to $K^+$ is at first higher than at rest, then voltage-gated $K^+$ channels close and resting potential is restored.
Figure 48.11-5

1 **Resting state**

2 **Depolarization**

3 **Rising phase of the action potential**

4 **Falling phase of the action potential**

5 **Undershoot**

**Key**
- **Na⁺**
- **K⁺**

**Membrane potential (mV)**
- **Resting potential**
- **Threshold**
- **Action potential**

**Time**

**OUTSIDE OF CELL**
- Sodium channel
- Potassium channel

**INSIDE OF CELL**
- Inactivation loop

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Figure 48.11a

- **Membrane potential (mV)**
  - Resting potential: -100 to -50 mV
  - Action potential: +50 mV

- **Time**
  - Steps:
    1. Resting potential
    2. Threshold
    3. Peak of action potential
    4. Recovery phase
    5. Return to resting potential
During the **refractory period** after an action potential, a second action potential cannot be initiated.

The refractory period is a result of a temporary inactivation of the Na\(^+\) channels.
Animation: Action Potential
Right-click slide / select “Play”

Cell body
Dendrites
Axon

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Conduction of Action Potentials

• At the site where the action potential is generated, usually the axon hillock, an electrical current depolarizes the neighboring region of the axon membrane
• Action potentials travel in only one direction: toward the synaptic terminals
• Inactivated Na\(^+\) channels behind the zone of depolarization prevent the action potential from traveling backwards
Figure 48.12-1

Na\(^{+}\)

Action potential

Axon

Plasma membrane

Cytosol

1
Figure 48.12-2

Axon

Action potential

Plasma membrane

Cytosol

1. Na⁺

2. K⁺
Figure 48.12-3

Action potential

Axon

Plasma membrane

1

Na⁺

2

K⁺

3

Na⁺

K⁺

Action potential

Axon

Plasma membrane

Cytosol
Evolutionary Adaptation of Axon Structure

• The speed of an action potential increases with the axon’s diameter
• In vertebrates, axons are insulated by a myelin sheath, which causes an action potential’s speed to increase
• Myelin sheaths are made by glia—oligodendrocytes in the CNS and Schwann cells in the PNS
Figure 48.13

Axon
Myelin sheath
Schwann cell
Nodes of Ranvier

Node of Ranvier
Layers of myelin
Axon
Schwann cell
Nucleus of Schwann cell

Axon
Myelin sheath
Schwann cell
Nodes of Ranvier

0.1 μm
• Action potentials are formed only at nodes of Ranvier, gaps in the myelin sheath where voltage-gated Na$^+$ channels are found.

• Action potentials in myelinated axons jump between the nodes of Ranvier in a process called saltatory conduction.
Cell body

Schwann cell

Depolarized region (node of Ranvier)

Myelin sheath

Axon

Figure 48.14
Concept 48.4: Neurons communicate with other cells at synapses

- At electrical synapses, the electrical current flows from one neuron to another.
- At chemical synapses, a chemical neurotransmitter carries information across the gap junction.
- Most synapses are chemical synapses.
The presynaptic neuron synthesizes and packages the neurotransmitter in **synaptic vesicles** located in the synaptic terminal.

The action potential causes the release of the neurotransmitter.

The neurotransmitter diffuses across the **synaptic cleft** and is received by the postsynaptic cell.
Presynaptic cell

Postsynaptic cell

Axon

Synaptic vesicle containing neurotransmitter

Postsynaptic membrane

Synaptic cleft

Voltage-gated Ca\(^{2+}\) channel

Ligand-gated ion channels

Ca\(^{2+}\) channel

Ligand-gated ion channels

K\(^+\) channel

Na\(^+\) channel

Figure 48.15
Generation of Postsynaptic Potentials

- Direct synaptic transmission involves binding of neurotransmitters to **ligand-gated ion channels** in the postsynaptic cell.
- Neurotransmitter binding causes ion channels to open, generating a postsynaptic potential.
• Postsynaptic potentials fall into two categories
  – **Excitatory postsynaptic potentials (EPSPs)** are depolarizations that bring the membrane potential toward threshold
  – **Inhibitory postsynaptic potentials (IPSPs)** are hyperpolarizations that move the membrane potential farther from threshold
After release, the neurotransmitter
  – May diffuse out of the synaptic cleft
  – May be taken up by surrounding cells
  – May be degraded by enzymes
Summation of Postsynaptic Potentials

• Most neurons have many synapses on their dendrites and cell body
• A single EPSP is usually too small to trigger an action potential in a postsynaptic neuron
Figure 48.16

Postsynaptic neuron

Synaptic terminals of presynaptic neurons

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Figure 48.17

Terminal branch of presynaptic neuron

Postsynaptic neuron

Axon hillock

Membrane potential (mV)

Threshold of axon of postsynaptic neuron

Resting potential

(a) Subthreshold, no summation

(b) Temporal summation

(c) Spatial summation

(d) Spatial summation of EPSP and IPSP

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If two EPSPs are produced in rapid succession, an effect called **temporal summation** occurs.
Terminal branch of presynaptic neuron

Postsynaptic neuron

E\_1 \quad E\_2

Resting potential

Membrane potential (mV)

Threshold of axon of postsynaptic neuron

Action potential

(a) Subthreshold, no summation

(b) Temporal summation

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• In **spatial summation**, EPSPs produced nearly simultaneously by different synapses on the same postsynaptic neuron add together

• The combination of EPSPs through spatial and temporal summation can trigger an action potential
Figure 48.17b

(c) Spatial summation

(d) Spatial summation of EPSP and IPSP
• Through summation, an IPSP can counter the effect of an EPSP
• The summed effect of EPSPs and IPSPs determines whether an axon hillock will reach threshold and generate an action potential
Modulated Signaling at Synapses

- In some synapses, a neurotransmitter binds to a receptor that is metabotropic
- In this case, movement of ions through a channel depends on one or more metabolic steps
• Binding of a neurotransmitter to a metabotropic receptor activates a signal transduction pathway in the postsynaptic cell involving a second messenger

• Compared to ligand-gated channels, the effects of second-messenger systems have a slower onset but last longer
Neurotransmitters

- There are more than 100 neurotransmitters, belonging to five groups: acetylcholine, biogenic amines, amino acids, neuropeptides, and gases
- A single neurotransmitter may have more than a dozen different receptors
Table 48.2 Major Neurotransmitters

<table>
<thead>
<tr>
<th>Neurotransmitter</th>
<th>Structure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acetylcholine</td>
<td>[\text{H}_3\text{C} - \text{C} = \text{O} - \text{CH}_2 - \text{CH}_2 - \text{N}^+ - \text{CH}_3]</td>
</tr>
<tr>
<td><strong>Amino Acids</strong></td>
<td></td>
</tr>
<tr>
<td>GABA (gamma-aminobutyric acid)</td>
<td>[\text{H}_2\text{N} - \text{CH}_2 - \text{CH}_2 - \text{CH}_2 - \text{COOH}]</td>
</tr>
<tr>
<td>Glutamate</td>
<td>[\text{H}_2\text{N} - \text{CH}_2 - \text{CH}_2 - \text{CH}_2 - \text{COOH}]</td>
</tr>
<tr>
<td>Glycine</td>
<td>[\text{H}_2\text{N} - \text{CH}_2 - \text{COOH}]</td>
</tr>
<tr>
<td><strong>Biogenic Amines</strong></td>
<td></td>
</tr>
<tr>
<td>Norepinephrine</td>
<td>[\text{HO} - \text{CH} - \text{CH} - \text{CH}_2 - \text{NH}_2]</td>
</tr>
<tr>
<td>Dopamine</td>
<td>[\text{HO} - \text{CH} - \text{CH} - \text{CH}_2 - \text{NH}_2]</td>
</tr>
<tr>
<td>Serotonin</td>
<td>[\text{HO} - \text{CH} - \text{CH} - \text{CH}_2 - \text{NH}_2]</td>
</tr>
<tr>
<td><strong>Neuropeptides</strong> (a very diverse group, only two of which are shown)</td>
<td></td>
</tr>
<tr>
<td>Substance P</td>
<td>[\text{Arg} - \text{Pro} - \text{Lys} - \text{Pro} - \text{Gln} - \text{Gln} - \text{Phe} - \text{Phe} - \text{Gly} - \text{Leu} - \text{Met}]</td>
</tr>
<tr>
<td>Met-enkephalin (an endorphin)</td>
<td>[\text{Tyr} - \text{Gly} - \text{Gly} - \text{Phe} - \text{Met}]</td>
</tr>
<tr>
<td><strong>Gases</strong></td>
<td></td>
</tr>
<tr>
<td>Nitric oxide</td>
<td>[\text{N} = \text{O}]</td>
</tr>
</tbody>
</table>
Acetylcholine

- **Acetylcholine** is a common neurotransmitter in vertebrates and invertebrates.
- It is involved in muscle stimulation, memory formation, and learning.
- Vertebrates have two major classes of acetylcholine receptor, one that is ligand gated and one that is metabotropic.
Amino Acids

• Amino acid neurotransmitters are active in the CNS and PNS
• Known to function in the CNS are
  – Glutamate
  – Gamma-aminobutyric acid (GABA)
  – Glycine
Biogenic Amines

- Biogenic amines include
  - Epinephrine
  - Norepinephrine
  - Dopamine
  - Serotonin
- They are active in the CNS and PNS
Neuropeptides

• Several **neuropeptides**, relatively short chains of amino acids, also function as neurotransmitters
• Neuropeptides include substance P and **endorphins**, which both affect our perception of pain
• Opiates bind to the same receptors as endorphins and can be used as painkillers
**EXPERIMENT**

1. Radioactive naloxone and a test drug are incubated with a protein mixture.

2. Proteins are trapped on a filter. Bound naloxone is detected by measuring radioactivity.

**RESULTS**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Opiate</th>
<th>Concentration ThatBlocked Naloxone Binding</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morphine</td>
<td>Yes</td>
<td>$6 \times 10^{-9} \text{ M}$</td>
</tr>
<tr>
<td>Methadone</td>
<td>Yes</td>
<td>$2 \times 10^{-8} \text{ M}$</td>
</tr>
<tr>
<td>Levorphanol</td>
<td>Yes</td>
<td>$2 \times 10^{-9} \text{ M}$</td>
</tr>
<tr>
<td>Phenobarbital</td>
<td>No</td>
<td>No effect at $10^{-4} \text{ M}$</td>
</tr>
<tr>
<td>Atropine</td>
<td>No</td>
<td>No effect at $10^{-4} \text{ M}$</td>
</tr>
<tr>
<td>Serotonin</td>
<td>No</td>
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Radioactive naloxone and a test drug are incubated with a protein mixture. Proteins are trapped on a filter. Bound naloxone is detected by measuring radioactivity.
## RESULTS

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</tr>
</tbody>
</table>
Gases

• Gases such as nitric oxide and carbon monoxide are local regulators in the PNS