Nervous Systems:
Neuron Structure and Function
Integration

- An animal needs to function like a coherent organism, not like a loose collection of cells.

- **Integration** = refers to processes such as summation and coordination that produce coherency and result in harmonious function.
Integration

- **Cellular integration** = processes within cells

- **Whole-animal integration** = selective combination and processing of sensory, endocrine, and central nervous system (CNS) information in ways that promote harmonious functioning of the whole organism within its environment.
  - This includes its all its cells, tissues, and organs
Integration

- Nerve cells are specialized for control and coordination.

- Integration ensures that an animal’s responses are smooth and coordinated rather than clashing or disjointed.
Excitable Cells

- **Neurons** are a type of *excitable cell*
  - Specially adapted to generate an electrical signal

- Can rapidly alter their membrane potential in response to an incoming signal.

- Vary in structure and function but use the same basic mechanism to send signals.
Neuron Function – Main Points

- Specialized for processing and conveying information.

- Information is coded into changes in electrical potential across cell membranes.

- Neurons use action potentials to transmit these signals across long distances.

- Neurons allow animals to sense and respond to their environment.
Benefits of Neurons

- Plants (no neurons):
  Action potentials travel @ 1-3 cm/sec

- Animals (neurons):
  Action potentials travel @ 100m/sec or 10,000cm/sec
CNS to Muscles

- Signal Reception
- Signal Integration
- Signal Conduction
- Signal Transmission
- Dendrites & Cell Body
- Axon Hillock
- Axon
- Axon Terminals
Signal Reception

- **Dendrites** sense and convert incoming signals into electrical signals by changing membrane potential.

- **Cell Body** = routine metabolic functions
Signal Integration

- Incoming signals are conducted to the axon hillock

- If signal is sufficiently large an electrical signal, or action potential, is initiated.
Signal Conduction

- **Axon**: One per neuron. Vary in length.

- Wrapped in myelin sheath that aids in the conduction of nerve impulses.
Signal Transmission

- **Axon terminals** form synapses with target skeletal muscle cells.

- Electrical signal results in the release of chemical neurotransmitters.
Motor Neuron Overall Process

1. Receive incoming signal
2. Convert to change in membrane potential
3. Trigger action potentials that conduct signals across long distances
4. Transmit signals to target cells in the form of a neurotransmitter
Electrical Signals in Neurons

- Average resting membrane potential is approximately -70mV.

- **Depolarization** = the charge difference between the inside & outside of the cell membrane decreases.

- **Hyper-polarization** = membrane potential becomes more negative.

- **Repolarization** = cell membrane potential goes back to resting levels.
Membrane potential (mV)

- **Threshold depolarization**
  - **Action potential**
  - **Threshold potential**
  - **Resting membrane potential**

Time (msec)
Membrane Potential

3 factors contribute to membrane potential:

- Distribution of ions across the membrane
- Permeability of the membrane to these ions
- The charge of the ions
Membrane Potential

- Neurons selectively alter permeability of their membranes to ions (ex. Na$^+$ & K$^+$).

- Opening and close gated ion channels.
  - Na$^+$ influx
  - K$^+$ efflux
Ligand Gated Ion Channels

- Open and close in response to a stimulus, such as the binding of a neurotransmitter.
Membrane Potential

- Changes in permeability alters membrane potential and generates electrical signals.

- Opening Na$^+$ channels results in depolarization

- Opening K$^+$ channels results in hyperpolarization
Electrochemical Driving Force

(a) Opening of Na⁺ channels depolarizes the membrane
Electrochemical Driving Force

(b) Opening of $K^+$ channels hyperpolarizes the membrane
**Electrochemical Driving Force**

- **Equilibrium point** = membrane potential at which electrical and chemical gradients favoring movement of an ion exactly balance each other.

- no NET movement across membrane.

- Therefore, at equilibrium, there is no electrochemical driving force.
Signals in Dendrites & Cell Body

- Cell body (soma)
- Dendrites
- Nucleus
- Endoplasmic reticulum
- Mitochondrion
- Signal reception
- Incoming signal
Signals in Dendrites & Cell Body

- Incoming Signal = Neurotransmitter
- Binds to membrane bound receptor = Ligand Gated Ion Channel
- Changes in permeability alter membrane potential.
In the dendrites and cell bodies of neurons electrical signals are called graded potentials.

**Graded potentials** vary in magnitude depending on the strength of the stimulus.
No Neurotransmitter
Low [Neurotransmitter]

(b) Low concentration of neurotransmitter
High [Neurotransmitter]

Neurotransmitter bound to most receptors

Many ions can cross the membrane

Most ion channels in “open” conformation

(c) High concentration of neurotransmitter
Depolarization v. Hyperpolarization

Most important ion channels in the dendrites and cell body of a neuron are:
- $\text{Na}^+$, $\text{K}^+$, $\text{Cl}^-$, and $\text{Ca}^{2+}$

Open $\text{Na}^+$ or $\text{Ca}^{2+}$ = depolarization

Open $\text{K}^+$ or $\text{Cl}^-$ = hyperpolarization
Graded Potential

1. Neurotransmitter binds to a ligand-gated Na⁺ channel.
2. Na⁺ enters cell through the open channel.
3. Current spreads through the cell.
4. The strength of the signal decreases with distance.
Graded Potentials

- Short distance signals due to:
  - leakage of charged ions
  - electrical resistance of the cytoplasm

- Cannot travel long distances without dying away.
Signals at the Axon Hillock

- “Trigger Zone”
Signals at the Axon Hillock

• Action potentials are triggered by the NET graded potential at the membrane of the axon hillock.

• Action potentials are “fired” when the net graded potential is beyond the threshold potential.
Signals at the Axon Hillock

- The net graded potential at the axon hillock membrane can be a:
  - Subthreshold Potential
  - Suprathreshold Potential
Subthreshold Potential

- Subthreshold depolarization
- Threshold potential
- Resting membrane potential
Suprathreshold Potential

![Diagram showing membrane potential changes over time](image)

- **Membrane potential (mV)**: The vertical axis represents the membrane potential in millivolts, ranging from -90 to +30 mV.
- **Time (msec)**: The horizontal axis represents time in milliseconds, ranging from 0 to 7 msec.
- **Action potential**: A rapid change in membrane potential that triggers the generation of an action potential.
- **Threshold depolarization**: A gradual increase in membrane potential towards the threshold level.
- **Threshold potential**: The critical point at which the membrane potential reaches the threshold level, triggering an action potential.
- **Resting membrane potential**: The baseline membrane potential, typically around -70 mV.
Signals at the Axon Hillock

- **Excitatory potential =**
  - Depolarizing graded potential
  - Brings the membrane potential closer to threshold potential

- **Inhibitory potential =**
  - Hyperpolarizing graded potential
  - Moves membrane potential farther away from threshold potential.
Multiple Graded Potentials

- Neurons can generate many graded potentials at once

- **Spatial summation:**
  Sum of multiple potentials

- **Temporal summation:**
  Potentials may build on each other as long as they are not too far apart in time.
Spatial Summation
Temporal Summation

![Graph showing membrane potential over time with stimuli at E₁ and E₂. The graph illustrates the concept of temporal summation where multiple stimuli can lead to an action potential if their timing is appropriate.](image)
Temporal Summation

![Diagram showing membrane potential and action potential.](image)

The diagram illustrates the concept of temporal summation, showing a membrane potential that rises above the threshold potential (E2) after two stimuli (1 and 2). The rise in potential above the threshold results in an action potential (purple line). The resting membrane potential is indicated as approximately -90 mV.
**Signals in the Axon**

- AP is triggered when membrane potential at the axon hillock reaches its threshold.

- Action Potentials have 3 phases:
  - Depolarization – reaches +30 mV
  - Repolarization – returns to -70 mV
  - After-hyperpolarization – overshoots
3 Main Phases of Action Potentials

- **Depolarization phase of action potential**
- **Repolarization phase of action potential**
- **After-hyperpolarization**
Voltage Gated Ion Channels

- Changes in membrane potential cause structural changes in voltage gated channels, resulting in changes in permeability.
Voltage Gated Na\(^+\) Channels

- Voltage Gated Na\(^+\) Channels have 2 gates:
  - Activation gate
  - Inactivation gate
1. When the neuron is at the resting membrane potential, the activation gate closes voltage-gated Na⁺ channels, preventing Na⁺ entry.

2. A suprathreshold depolarizing graded potential causes the activation gate to open, allowing Na⁺ to enter the cell.

3. Increased Na⁺ entry further depolarizes the cell, opening even more voltage-gated Na⁺ channels in a positive feedback loop, causing the rapid depolarization phase of the action potential.

4. The inactivation gate of the channel closes as the membrane approaches +30 mV, preventing Na⁺ entry.

5. Over time, in response to the rapid repolarization of the membrane, the channel returns to its original state.
Refractory Periods

- **Absolute refractory period** =
  - axon is incapable of regenerating a new action potential no matter how strong the stimulus

- **Relative refractory period** =
  - new action potential can be generated, but only by a very large stimulus
Refractory Periods

- Due to the opening and closing of voltage gated ion channels

- Opening $\text{Na}^+$ channels = depolarization

- Opening $\text{K}^+$ channels = repolarization
Refractory Periods

![Graph showing relative membrane ion permeability over time](image)

- **Relative membrane ion permeability**
- **Time (msec)**
- **Stimulus**

- **Na⁺**
- **K⁺**

(b)
Refractory Periods

- Opening Na\(^+\) Channels

  - Positive feedback loop of Na\(^+\) entry results in extremely rapid changes in Na\(^+\) permeability

  - Before reaching Na\(^+\) equilibrium (+60mV), Na\(^+\) channels close, terminating depolarization
Refractory Periods

- Opening $K^+$ channels:
  - open more slowly
  - only open in substantial numbers just before $Na^+$ channels close.
  - $K^+$ moves out of the cell, cell becomes more negative, and causes repolarization.
  - $K^+$ channels close slow, explaining why there is the after-hyperpolarization phase.
<table>
<thead>
<tr>
<th><strong>Table 4.1</strong> Differences between graded potentials and action potentials.</th>
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<tbody>
<tr>
<td><strong>Graded potentials</strong></td>
</tr>
<tr>
<td>Vary in magnitude</td>
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<tr>
<td>Vary in duration</td>
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<tr>
<td>Decay with distance</td>
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<tr>
<td>Occur in dendrites and cell body</td>
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<tr>
<td>Caused by opening and closing of many kinds of ion channels</td>
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</table>
“Traveling” Along the Axon

Axon

Schwann cells of myelin sheath

Integration

Signal conduction

Direction of signal

Axon terminal
“All-or-None”

- Axons conduct action potentials unidirectionally.

- Travel along axon in an “All-or-None” fashion.
  - Reach threshold potential and fire, or don’t.
“Traveling” Along the Axon

- Action potentials in one part of the axon trigger action potentials in adjacent areas of axonal membrane.
  - Dominoes.

- Therefore, action potentials are conducted across long distances without decaying.
1. When an action potential occurs at A on the membrane, Na⁺ enters the axon through opened voltage-gated Na⁺ channels. This action potential depolarizes the membrane at A to +30 mV.

2. The depolarization due to the action potential at A spreads electrotonically by local current flow through the axon, depolarizing adjacent areas of the membrane toward threshold (~55 mV).
When the depolarization at B reaches threshold, voltage-gated Na⁺ channels at B open, initiating an action potential that depolarizes B to +30 mV.

The depolarization due to the action potential at B spreads electrotonically by local current flow through the axon, depolarizing adjacent areas of the membrane toward threshold (−55 mV), triggering an action potential at C. Voltage-gated Na⁺ channels at A are inactivated (and thus refractory), so a new action potential is not initiated at A.
Myelinated Axons

- Vertebrate motor nerves are **myelinated**:
  - Wrapped in an insulating layer of myelin

- **Schwann cells** = specialized lipid-rich cells that form a myelin sheath by wrapping in a spiral pattern around a single axon.
Myelinated Axons

- Several Schwann cells may wrap long axons.

- Myelinated regions = internodes.

- **Nodes of Ranvier** = exposed sections of axonal membrane in between internodes.
  - contain high densities of voltage-gated ion channels.
Saltatory Conduction

- Action potentials only occur in nodes of Ranvier.
- Current spreads electrically through internodes
Saltatory Conduction

- Action potentials appear to “jump” from one node to another along the axon.
- Conduction occurs faster and with less degradation along myelinated axons than along unmyelinated axons.
Saltatory Conduction
Unidirectional Conduction

- If you electrically stimulate an axon halfway along its length, APs will be generated in both directions.

Why do action potentials only occur in the downstream direction?
In a natural action potential, the stimulus is initiated at the axon hillock.

As the action potential travels along the axon, the region just upstream has just produced an action potential.

Voltage gated Na$^+$ channels there are in a conformation unable to open in response to changes in membrane potential.
Unidirectional Conduction

- Voltage gated channel (A): corresponds to the absolute refractory period.
Unidirectional Conduction

- Together, absolute refractory periods and relative refractory periods prevent **retrograde** (backwards) transmission of action potentials.
Action potentials carry information about the strength of a graded potential by changing frequency rather than amplitude.

- Remember “all-or-none”
Action Potential Frequency

(a) A weak stimulus triggers a low frequency of action potentials
Action Potential Frequency

(b) A suprathreshold stimulus triggers a high frequency of action potentials
Signals Across the Synapse

- Synapse is made up of 3 parts:
  - Presynaptic cell – cell that transmits the signal
  - Postsynaptic cell – cell that receives the signal
  - Synaptic cleft – space in between
Types of Synapses

- Neurons can form synapses with many types of cells including:
  - Neurons
  - Muscles
  - Endocrine cells

- **Neuromuscular junction** = Synapse between a motor neuron and a skeletal muscle cell.
Neuromuscular Junction

- Neurotransmitter release is regulated by intracellular Ca$^{2+}$ levels.
Synaptic Vesicles

- 2 pools of synaptic vesicles:
  - Ready Releasable Pool
    - Located at active zone of synapse
    - Bound to docking proteins
    - Ready to release contents by exocytosis
  - Storage Pool
    - Bound to cytoskeleton
    - Not docked to membrane
Synaptic Vesicles

- Increases in $\text{Ca}^{2+}$ concentration in the axon terminal act as a signal to neurotransmitting synaptic vesicles:
  - Vesicles from readily releasable pool fuse with plasma membrane and release contents by exocytosis.
  - Vesicles from storage pool move to active zone and bind to docking proteins.
Vesicles & Neurotransmitters

- Many neurotransmitters in one vesicle

- The number of neurotransmitters per vesicle is similar for all vesicles.

- Increasing action potentials increases the number of vesicles moving to the membrane and releasing their contents.
Vesicles & Neurotransmitters

- When action potentials arrive at high frequencies, cellular removal of Ca\(^{2+}\) cannot keep up with the influx of Ca\(^{2+}\) through activation channels.

- Resulting in:
  - ↑ intracellular [Ca\(^{2+}\)]
  - Results in a stronger signal for exocytosis.
Vesicles & Neurotransmitters: “Take Home Process”

↑ Frequency Action Potentials

↑ Intracellular $[\text{Ca}^{2+}]$

↑ Signal Intensity

↑ Neurotransmitter Release
Acetylcholine (ACh)

- Primary neurotransmitter at the vertebrate neuromuscular junction.

- ACh is packaged into synaptic vesicles and released into the synapse by exocytosis.
Acetylcholinesterase (AChE)

- Signalling between a ligand, such as a neurotransmitter, and its receptor must be terminated in order to be effective.

- AChE = specific enzyme in synapse that removes Ach from its receptor.
  - Breaks Ach down
Acetylcholinesterase (AChE)

- Important role in regulating the strength of the signal to the post synaptic cell by regulating the concentration of neurotransmitter in the synapse.
Recycling of Acetylcholine (ACh)

1. Acetyl CoA is synthesized in the mitochondria.
2. Choline acetyl transferase catalyzes the conversion of choline and acetyl CoA to acetylcholine (ACh).
3. The ACh is packaged into synaptic vesicles.
4. ACh is released into the synapse.
5. ACh binds to its receptor on the postsynaptic cell.
6. Acetylcholinesterase (AChE) breaks down ACh into choline and acetate, terminating the signal in the postsynaptic cell.
7. The presynaptic cell takes up and recycles the choline, and the acetate diffuses out of the synapse.
Postsynaptic Reception

- Postsynaptic cells detect neurotransmitters using specific cell-surface receptors.

- **Nicotinic Ach receptors** = ligand gated ion channels in muscle cells.
Nicotinic ACh receptors contain a relatively non-selective channel.
- Permeable to Na$^+$, K$^+$, and to a lesser extent Ca$^{2+}$

Resulting graded potential in post-synaptic cells is dominated by Na$^+$ ions.
ACh binding to nicotinic receptors on skeletal muscle always results in a rapid excitatory postsynaptic potential because of the resulting influx of Na⁺ → depolarization of the muscle cell.
Postsynaptic Reception

- The amount of neurotransmitter and the number of receptors on the post synaptic cell influence the strength of signal in the target cell.
Postsynaptic Reception

[Neurotransmitter] in the synapse = balance of release (presynaptic) and removal (postsynaptic)

Removal can depend on:

1. diffusion
2. surrounding cells
3. enzymes present in the synapse (ex. Acetylcholinesterase)
Outline of Postsynaptic Reception

1. Neurotransmitter (Ach) binds to receptor (Nicotinic receptors).

2. Receptor changes shape, acting as a signal in the target cell.

3. A pore opens in the middle of the receptor allowing ions to cross the membrane.

4. Rapid influx $\text{Na}^+$ influx depolarizes the postsynaptic muscle cell. (contraction)