How Do Neurons Transmit Information?

Important parts of the process:

Biological Membranes

- The membrane of a neuron is a lipid bilayer.
- The membrane is semi-permeable - this is critical for producing a difference in potential (electrical charge) across the membrane
- This potential difference is produced by ions
  - Cations: positively charged ions (ex. Sodium = Na+, Potassium = K+)
  - Anions: negatively charged ions (ex. Chloride = Cl-)

Biological Membranes

- The neuronal membrane has proteins embedded in it:
  - Ion Channels (channel proteins = doorways): allow selected ions to pass in and out of a cell (ex. Na+, K+, Ca++, Cl-)
  - Receptors: site where neurotransmitter binds, causing an immediate (ion channels open) or delayed (intracellular signaling is activated as with a signal protein) effect
  - Active transporters: pull certain substances into the cell (ex. glucose, reuptake of neuro-transmitters)

The Resting Membrane Potential

- Membrane Potential
  - the difference in electrical charge between the inside and outside of a membrane
- Resting Membrane Potential
  - In the resting state:
    - more Na⁺ and Cl⁻ ions are outside
    - more K⁺ ions and negatively charged proteins are on the inside

The Resting Membrane Potential

- It’s between -60 and -70mV for most neurons
  - The inside of the neuron is negative relative to the outside
Forces That Maintain the Resting Membrane Potential:

- **Concentration Gradient:** Na\(^+\) more concentrated outside the cell, tends to drive it into the cell. What about K\(^+\)?
- **Electrical gradient:** more positive charge outside the cell tends to drive Na\(^+\) into the cell. What about K\(^+\)?

Forces That Maintain the Resting Membrane Potential:

- **Differential (selective permeability):** In resting neurons, K\(^+\) and Cl\(^-\) ions pass through the membrane easily, Na\(^+\) with difficulty, and proteins not at all.
- **Sodium-potassium pumps (use cellular energy):** 3 Na\(^+\) ions are pumped out for every 2 K\(^+\) ions pumped in.

Passive and Active Forces Maintain the Resting Potential

- **Passive -** There is a small, passive leak of K\(^+\) out of the cell (K\(^+\) 20X more concentrated inside the cell); there are large numbers of negatively charged amino acids/proteins that can’t move out of the cell (about 100X more concentrated inside the cell – this is a large reserve of negative charge).
- **Active (uses cellular energy) -** Sodium-potassium pump actively maintains the unequal distribution of positive ions across the membrane: 3 Na\(^+\) ions out / 2 K\(^+\) ions in

The Resting Membrane Potential

- A very nice web-based animation showing how this comes about can be found at:
  - http://bcs.whfreeman.com/thelifewire/content/chp44/4402001.html (for PC)
  - http://bcs.whfreeman.com/thelifewire/content/chp44/4401s.swf (for MAC)

Graded Potentials

- Neurons release chemicals called neurotransmitters when they fire
- Neurotransmitters diffuse across the synaptic clefts and bind to receptors on the post-synaptic side
**Graded Potentials**

- **Excitatory Postsynaptic Potentials (EPSPs)**
  - depolarizations (ex. -71 to -68 mV) - increase the likelihood that the neuron will fire

- **Inhibitory Postsynaptic Potentials (IPSPs)**
  - hyperpolarizations (ex. -68 to -71 mV) - decrease the likelihood that the neuron will fire

**Postsynaptic Potentials Are Graded Potentials**

- Their amplitude is proportional to the intensity of the input
  - Stronger stimuli produce bigger EPSPs or IPSPs

- Neurons combine together (integrate) individual potentials - the total determines whether the neuron will fire an action potential

- Neurons integrate incoming signals in two ways:
  - Over space
  - Over time

**Postsynaptic Potentials and Action Potentials**

- The sum of the postsynaptic potentials reaching the axon hillock (the axon potential trigger-zone) determines whether an action potential will occur.

**Elements of The Action Potential**

- **Voltage-dependent Ion Channels**
  - opened by a change in membrane potential

- **Absolute Refractory Period**
  - brief period after initiation of an action potential when another one cannot be fired (Na⁺ channels temporarily inactivated)

- **Relative Refractory Period**
  - action potential can be fired, but it requires a greater than normal degree of stimulation

**The Firing Of An Action Potential Is An All-or-none Process**

**The Rate Law:**
The Action Potential

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http://bcs.whfreeman.com/thelifewire/content/chp44/4402002.html

Propagation of an Action Potential Is a Regenerative Process

Postsynaptic Potentials and Action Potentials

- Postsynaptic potentials (PSP) are graded potentials
  - Their amplitude is proportional to the intensity of the input stimulus and decreases with distance from the source (they are generally decremental)
- The sum of the postsynaptic potentials reaching the axon hillock (the axon potential trigger-zone) determines whether an action potential will occur.
- Action potentials are not graded potentials
  - The size of an action potential does not vary with stimulus intensity, only the rate of firing
- Action potentials are non-decremental
  - They arrive at the terminals of the axon the same size that they left the axon hillock

Local Anesthetics

- Produce loss of sensation in limited area of body
- Many act by blocking Na\(^+\) channels, and thus blocking action potentials in the affected area
  - Examples: Lidocaine (Xylocaine) and Novocain

General Anesthetics

- Produce unconsciousness
- Some decrease brain activity by opening some types of potassium channels wider than usual
- Thus, when a stimulus starts to excite a neuron by opening sodium channels, K\(^+\) ions exit about as fast as the Na\(^+\) ions enter, preventing most action potentials
Fun with Fugu?

- Puffer fish (fugu) is considered a delicacy in Japan
- Some species contain tetrodotoxin (blocks voltage-sensitive sodium channels)
- Very small amounts can shut down signaling to a fatal degree
- A recipe for fishy revenge!

Mechanisms for Increasing the Speed an Action Potential

- Increasing Size of Axon
  - Giant axon of the squid can reach a diameter of 1 mm
- Insulating the Axon
  - Myelination

Saltatory Conduction in Myelinated Axons

- Ions can pass through the axonal membrane only at the nodes of Ranvier
  - Current diminishes as it travels rapidly, but passively along the axon between the nodes of Ranvier, but it is still strong enough to open voltage-gated channels clustered at the next node
  - Action potentials are actively regenerated at the nodes

Saltatory Conduction in Myelinated Axons

- Conduction along the myelinated section of the axon is extremely rapid
  - The active regeneration of the action potential at the nodes introduces a slight delay (Latin: saltare “to skip or jump”)
  - Saltatory conduction is more energy efficient

Synapses: How Neurons Communicate

- Synthesis, packaging and transport of neurotransmitter molecules
- Release of neurotransmitters
• Deactivation of neurotransmitters
• Action of neurotransmitters at receptor sites
• Classes of neurotransmitters

31 Synapses: How Neurons Communicate
32 Synthesis, Packaging And Transport Of Neurotransmitter (NT) Molecules
• Small-molecules NTs — (ex. amino acids, monoamines, acetylcholine)
  — Typically synthesized in synaptic button
  — Packed into small vesicles by button’s Golgi
  — Stored in clusters next to the presynaptic membrane

33 Synthesis, Packaging And Transport Of Neurotransmitter (NT) Molecules
• Large-molecules NTs - (neuropeptides) synthesized in soma (ex. endorphins)
  — Assembled on ribosomes in the cell body
  — Packaged in larger vesicles by the soma’s Golgi
  — Transported by microtubules to terminal buttons
  — Stored farther from presynaptic membrane that small-molecule neurotransmitters

34 Electron Micrograph: Cross Section Of A Synapse
35 Electron Micrograph: Cross Section Of A Synapse
36 Electron Micrograph: Cross Section Of A Synapse
37 Release of Neurotransmitters
38 Release of Neurotransmitters
• Action potential arrives
• Voltage-sensitive calcium channels open
• Ca++ enters the presynaptic button
• Induces the “docking” and fusion of synaptic vesicles to membrane
• Exocytosis: neurotransmitter is released into the synaptic cleft
EXOCYTOSIS

Halting Synaptic Transmission - Deactivation of Neurotransmitters

RECEPTORS AND RECEPTOR SUBTYPES

• Any molecule that binds to a receptor is a ligand of that receptor.
• Thus, neurotransmitters are ligands of their receptors.

RECEPTORS AND RECEPTOR SUBTYPES

• Receptors are proteins embedded in the membrane that bind neurotransmitters
• They are specific for particular neurotransmitters: a “lock and key” arrangement (ex. acetylcholine won’t bind to a glutamate receptor)

RECEPTORS AND RECEPTOR SUBTYPES

• Receptor subtypes: Several different receptor proteins can bind the “same” neurotransmitter (ex., acetylcholine binds both “nicotinic” and “muscarinic” acetylcholine receptors)

Neurotransmitters Can Influence A Postsynaptic Neuron In Fundamentally Different Ways By Binding To Either Ionotropic Or Metabotropic Receptors

• Ionotropic Receptors
  – Binding of neurotransmitter opens, or closes, an ion channel
• Metabotropic Receptors
  – Binding of neuro-transmitter activates signal proteins and G proteins
  • G protein subunit breaks off and binds to an ion channel, or stimulates production of an second messenger

Major Classes of Neurotransmitters

• Small-molecule Neurotransmitters
• Large-molecule (peptide) Neurotransmitters
• Soluble gases

Small-molecule Neurotransmitters

• Monoamines
1. Dopamine
   - movement, attention, learning, reward
   - degeneration of Substantia Nigra in midbrain = Parkinson’s disease (loss of DA)
   - schizophrenia (too much DA release)
2. Norepinephrine and Epinephrine (Adrenaline)
   - released by sympathetic n.s. and adrenals
   - control alertness/wakefulness; alarm
3. Serotonin
   - control of eating, sleep, and arousal
   - inhibits dreaming (LSD blocks serotonin)

Small-molecule Neurotransmitters

• Acetylcholine
  – contracts skeletal muscles (neuromuscular junction)
  – parasympathetic nervous system

• Amino Acids
  – Excitatory amino acids
    • (ex., glutamate, aspartate)
    • excitatory neurotransmitters producing EPSPs
  – Inhibitory amino acids
    • 1. Gamma-aminobutyric acid (GABA)
      » inhibitory neurotransmitter producing IPSP
      » degeneration in basal ganglia
    • 2. Glycine
Glycine is an inhibitory neurotransmitter normally inhibits motor neuron activity in spinal cord.

Large-molecule (peptide) Neurotransmitters
- Very diverse types and functions
  - Examples:
    - endorphins (endogenous opiates; pain)
    - cholecystokinin (gut peptide; food intake)
    - vasopressin (fluid regulation)

Soluble gases
- Small molecules with very different neurotransmitter characteristics
- Produced in cytoplasm by enzymes and diffuses freely across lipid bilayers to neighboring neurons
  - Examples:
    - Nitric oxide
      - regulates vascular relaxation
      - involved in learning and memory
    - Carbon monoxide
      - also regulates vascular relaxation
      - regulates peristaltic relaxation

Many Drugs and Toxins Act By Mimicking Or Blocking The Action Of A Neurotransmitter
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- The tetanus toxin blocks the receptors for the inhibitory neurotransmitter GABA.
- As a result, the disease causes extreme muscle spasms that may lead to the ripping of muscles and the breaking of bones.
Many Drugs and Toxins Act By Mimicking Or Blocking The Action Of A Neurotransmitter

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- There are about 100 cases of tetanus per year in the US.
- There are about a million deaths per year worldwide due to tetanus.
- Even in a well equipped hospital 30-40% die.