So now, let’s look at another EXAMPLE: What accounts for \textit{causes} singing \textit{behavior} in songbirds?

**Physiological Account:**
What are the neural underpinnings of this behavior?

\textit{Two nuclei in the hypothalamus:}
- caudal nucleus of the hyperstriatum ventrale (CNHV)
- robust nucleus of the archistriatum (RNA)

**Size of these two nuclei**
- male vs. female songbirds
- sparrows and finches vs. chickens and pigeons

\textit{Inject testosterone} into a female, which \textit{increases the size of these two nuclei} \rightarrow female starts to sing

\textit{Damage the nuclei}
\rightarrow Male birds stop singing
Lecture 3 (Jan 15th):
NEURONS AND NERVE IMPULSES

Lecture Outline

1) CNS vs. PNS
2) Structure of Neurons
   parts of a neuron: soma, dendrites, axons
3) Glial Cells
4) Mitosis and Regeneration in Neurons
5) Neuronal Communication
6) The Nerve Signal (Electrical)
   - A Neuron at Rest
   - Graded Potentials and Action Potentials (we skip the yellow)
7) Multiple Sclerosis

Blood Brain Barrier (you learn from book/my one slide, just the very basics)
THE NERVOUS SYSTEM

1) **Central** Nervous System (CNS): Brain and Spinal Cord

2) **Peripheral** Nervous System (PNS): The Rest

Two types of cells in the Nervous System:

1) **Neurons** (100 billion, $10^{11}$):
   communicate through electrical signals

2) **Glia** ($10^{12}$, but 1/10th the size of neurons)
   form the myelin sheath of neurons

...... will come back to later today
The NEURON
Components common to all cells of the body:
cytoplasm, nucleus
membrane
  H₂O, O₂, CO₂, urea pass freely across membrane
  Large or Electrically charged molecules do NOT
  -> Need ionic “channels” for: K⁺, Na⁺, Cl⁻
mitochondria (energy from metabolism)
ribosomes (synthesis of new proteins)
lysosomes (break things down -> recycle)
Golgi complex (secretion of waste)
How Neurons are like other cells:

- **Nucleus**
  - (membrane-enclosed region containing DNA; hereditary control)
  - **Endoplasmic reticulum**
    - (isolation, modification, transport of proteins and other substances)

- **Plasma membrane**
  - (control of material exchanges, mediation of cell-environment interactions)

- **Mitochondrion**
  - (aerobic energy metabolism)
Components *unique* to NEURONS:
soma (sometimes called “cell body”)  
dendrites (one or many): receive signals  
axon: sends electrical signal to next neuron  
presynaptic (“before the synapse”) terminals  
synapse  
myelin sheath (glia): Not found in invertebrates  
nodes of Ranvier (will come back to later today)
GLIAL CELLS (support cells)

1) Form the MYELIN SHEATH
   CNS: Oligodendrocytes
   PNS: Schwann Cells

2) Microglia & Astrocytes (CNS)
   remove waste material, dead neurons
   (Astrocytes?)

3) Radial Glia
   direct neurons during *development*
NEURON: Mitosis (Make New Neurons) and Regeneration (Repair Injured Neurons)
NEURON: Mitosis (Make New Neurons)

After development, neurons in both the CNS and PNS lose their ability to undergo mitosis……

which is a bummer if there is an injury (e.g., stroke)!

Why is it this way? (we’ll come back to in a couple of slides)

Exceptions: Some neurons that DO undergo Mitosis (adults)

1) Olfactory neurons
2) Isolated parts of bird, rodent and PRIMATE brain
   (e.g., hippocampus involved in memory)

QUESTION: As we age… don’t brain cells die and are not replaced? (uh-oh!)

No, they just shrink and are less functional. Phew! ??!
And what about BRAIN CANCER?

*Isn’t cancer when mitosis has gone wild??!!*

Well… brain cancer is usually GLIA, not NEURONS.

**Glial cells in both the CNS and PNS undergo mitosis.**
Regeneration (Repair Injured Neurons)

of cut AXONS in the PNS … not the CNS

In PNS, there are mechanisms for creating collagen around the injury to act as a “bridge” for axons to grow along.

Questions to Mother Nature:
“Why is there no regeneration in the CNS?”
“Why is there no MITOSIS in adulthood, in both the CNS and PNS?”

(especially important to know for spinal cord injury)
Electrical signal sent from one neuron to the next
(from the “presynaptic” -> “postsynaptic” neuron, or muscle)

Neuromuscular Junction
Overview of Events:
1) Electrical signal starts in the presynaptic neuron and travels down the axon to the presynaptic terminals.
2) Causes release of neurotransmitter into the synapse
3) Neurotransmitter binds to receptors \( (R) \) on postsynaptic neuron’s dendrites
4) Triggers an electrical signal in postsynaptic neuron, and so on…..

MORE LATER TODAY AND NEXT LECTURE
Some “Relative” Terms about Neuronal Connections:

1) PRESYNAPTIC vs. POSTSYNAPTIC

2) AFFERENT vs. INTRINSIC vs. EFFERENT
Speed of Transmission:

- electricity (electrons): $6 \times 10^6$ m/sec
- myelinated: 100 m/sec
- thick unmyelinated: 10 m/sec
- thin unmyelinated: 1 m/sec

DEMO of the “Nerve Impulse”
How Do Electrical Signals Travel Along a Neuron?

Let’s Learn this as a Story, **yellow text is extra info (you don’t have to know)**

**What is a “Membrane Potential”?**

Voltage/Electrical Difference between IN and OUTside of neuron

At **“REST”**: the Membrane Potential = -70 mV

i.e., the inside of the neuron is more NEGATIVE than outside (large, negatively-charged molecules trapped inside!)

- \( \text{H}_2\text{O}, \ \text{O}_2, \ \text{C}_0\text{O}_2, \) -> *pass freely* across cell membrane

- Electrically Charged “IONS”:
  - \( \text{K}^+ = \text{Potassium} \)
  - \( \text{Na}^+ = \text{Sodium} \)
  - also... \( \text{Cl}^- = \text{Chloride} \) (next lecture)

  can *only* cross membrane through
  “ION CHANNELS” (or “pores”)

---

---

...
- **ION CHANNELS** are *SELECTIVE* for different ions

- **ION CHANNELS** are relatively OPEN or CLOSED depending on the VOLTAGE of membrane

  This is called a **“VOLTAGE-GATED”** Ion Channel

  At Rest (i.e., -70 mV):
  
  $K^+$ (and $Cl^-$) channels are (relatively) OPEN
  
  $Na^+$ channels are CLOSED (*this will be important later*)

- **CONCENTRATION DIFFERENCE** across MEMBRANE

  At Rest (i.e., -70mV):
  
  $K^+$: Inside > Outside
  
  $Na^+$: Outside > Inside (*this will be important later*)
3 forces across membrane (red is what happens at -70 mV)

1) **Na⁺/K⁺ PUMP** (**K⁺ in, Na⁺ out**), (not through ion channels!), relies on ATP

2) **Electrical Gradient** (**K⁺ in, Na⁺ in**)

3) **Concentration Gradient** (**K⁺ out, Na⁺ in**): “diffusion”

Remember, forces (2) and (3) want Na⁺ to go IN, but WHY does Na⁺ stay OUTside at REST (-70 mV)???
The Membrane Potential (Voltage) can CHANGE from $-70\text{mV}$ = an electrical signal!

**Depolarization:** membrane potential *less* negative (i.e., more +)

**How does the Membrane Potential get depolarized to begin with?**
(I mentioned this earlier today and we’ll return to in the next lecture)

-> Neurotransmitters bind to receptors on neuron

Hey! What about the 1st neuron in the chain?  
(*Stimulus* -> more on this in a few weeks)

**Hyperpolarization:** membrane potential becomes *more* negative  
(which makes it harder to create an Action Potential)
Electrical signal travels along the axon:

1) Graded Potentials, or
2) Action Potential

1) **Graded Potential:**

   The strength of the depolarization diminishes over time and distance (as it travels down the axon), and can only survive for a short distance along the axon.

   - Fine for short neurons (e.g., in the retina).

2) **ACTION POTENTIAL**

   Occurs when membrane depolarization gets to $-55 \, \text{mV} = \text{threshold}$.

   Then, big depolarization signal (to $+30 \, \text{mV}$), which does not diminish as it travels down axon. “ALL-OR-NONE”,...
Let’s Go Through this FAST….. You go over it carefully later

What happens at -55 mV? (8 steps)

1) **Voltage-Gated Na⁺ Channels** (which were closed at -70 mV) start to OPEN at -55 mV (i.e., they start to open when the membrane potential gets more +)

2) **Na⁺** ions rush **INSIDE** the neuron down the *concentration* and *electrical gradient* -> membrane potential gets more positive (+), i.e., more depolarized

   -> therefore Na⁺ channels open even *more*, etc. (positive feedback loop)

3) **K⁺** channels are *also* voltage-gated. Although already open in the resting state (-70 mV), K⁺ open *even more* when the neuron becomes depolarized.
4) $K^+$ rushes OUT of the neuron
   Down the *concentration gradient*
   Hey, but what about the *electrical gradient??*
   Concentration Grating beats Electrical Gradient
   And…. once membrane potential is a POSITIVE number (+),
   $K^+$ also goes down the *electrical gradient*.

(4) is what starts to make the inside of the neuron go back towards being negative!

5) So, Membrane potential heads back towards its *resting state* (i.e., -70 mV).

6) And, voltage-gated Na$^+$ (and K$^+$) channels start to close.

7) $K^+$ “exit” onsets more slowly and lasts longer than Na$^+$ “entry”. Therefore K$^+$ continues to leave the neuron, which *hyperpolarizes* the neuron briefly (more negative than −70mV)
After an action potential, the membrane potential is back to resting state (i.e., ~ -70 mV), but….

… Na\(^+\) and K\(^+\) concentrations (inside/outside) have changed and need to be “put back”!

How? Na\(^+\)/K\(^+\) pump! Na\(^+\) \textit{OUT}, K\(^+\) \textit{IN}
Nodes of Ranvier / Saltatory Conduction

Action Potential JUMPS from Ion Channel to Ion Channel at the Nodes of Ranvier

Myelin Sheath
Nodes of Ranvier / Saltatory Conduction
What goes wrong in Multiple Sclerosis (MS)?

1) Early in development, when no myelin yet

2) Later, you develop myelin, and the ion channels underneath the myelin go away

3) MS: myelin gets destroyed by own immune system
BLOOD BRAIN BARRIER (BBB)

purpose: keep out viruses, bacteria in CNS

How the BBB works:
- in all body parts, endothelial cells line the inside of blood vessels
- in all body parts except the CNS, there exist gaps between these endothelial cells, so substances in the blood can move out of the blood vessels to the body parts
- in the CNS, there are “tight junctions” between cells, which disallow this movement

Fuel for the CNS (glucose and O₂) get through the BBB:
- with an “active transport” system (glucose)
- with “diffusion” (O₂).

Drugs that get through the BBB:
Fat-soluble substances, e.g., heroin, nicotine, cannabinoids ->
dissolve through fats of blood vessel walls