By: Moe El-bagdady

Module One: Introduction to Physiology

1.1 – Objectives

- Define Physiology
- Define homeostasis
- Describe negative feedback control systems
- List levels of organization in human body

1.2 – Introduction

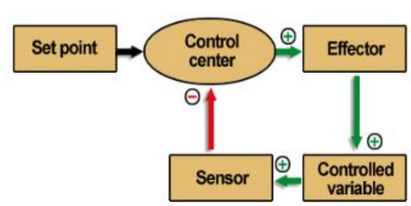
- **Key Problem for Body + Cells**: to surround themselves with barriers that allows wanted stuff to pass in and unwanted stuff to pass out.
- **Terms:**
  - Internal Environment
  - External environment
  - Homeostasis
- **Importance of Negative feedback control systems and their involvement in regulating internal environment?**
- **Physiology:**
  - Study of living organism functions.
  - Explores the mechanisms by which the organisms control their internal environment regardless of what happens in outside (external) environment.
  - Explain physical and chemical factors responsible for both function and disease (pathology).

1.3 – Homeostasis

- **Internal Environment**: fluids in which cells of body live in.
  - **Interstitial ("between") fluid/ Tissue fluid***:* the extracellular fluid bathing most tissues, excluding the fluid within the lymph and blood vessels. Found in the interstitial spaces.
    - It is the main component of ***Extracellular Fluid*** *(all body fluid outside of cells),* which also includes ***plasma*** and ***transcellular fluid*** *(portion of total body water contained within epithelial lined spaces. Smallest component of extracellular fluid)*.
  - **Blood plasma:** the yellow or gray-yellow, protein-containing fluid portion of blood in which the blood cells and platelets are normally suspended.
- **External Environment**: region outside body
  - Also includes: space/contents of digestive, repertory, and urogenital tracks (organ system of the reproductive organs and the urinary system).
- **Homeostasis:** maintenance of relatively stable conditions within internal environment regardless external environment events.
  - Allows our bodies to maintain a stable internal environment so cells can function regardless of what is happening in the external environment.
  - Maintains homeostasis using **Negative** and **Positive Feedback** control mechanisms.

1.5 – Negative Feedback Controls

- **Negative feedback controls: Controlled variable eventually shuts off its own production**
  - Examples: maintaining body temperatures, maintaining fluid volumes.
  - All operate same way:
    - Contain: Set point, control center (aka integrator), effector, controlled variable, and sensor (aka receptor).



Simple Example (1.6)

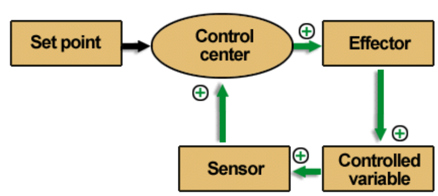
- Example: **"House"**
  - *Set Point* → Heat of 20° C
    - Predetermined "Set Point" to be maintained in environment.
  - *Sensor/Control center* → Thermostat (usually not both)
    - Sensor "Senses" alterations in environmental conditions
    - Control center "Controls" Effector which then controlled by "sensor" (ie. Sensor turns off Control center when condition is achieved).
  - *Effector* → Furnace (effects environment to achieve point)
    - Effector "affects" altered environmental conditions to achieve Set point.

Body Example (1.7)

- Example: **"Body Temperature"**
  - *Set Point* → Body Heat of 37° C
    - Predetermined "Set Point" to be maintained in body.
  - *Sensor* → Nervous system sensors detect heat changes,
    - "Senses" change in body temperature
    - Signals control center (ie. brain part hypothalamus)
  - *Control center* → Region in brain called the Hypothalamus
    - Control center notices temperature difference.
    - Activates organs/systems (ie. effector)
    - Control center "Controls" Effector and Control center is controlled by "sensor" (ie. Sensor turns off Control center when condition is achieved).
  - *Effector* → Organs/Bodily Systems (effects environment to achieve set point)
    - Generates heat (controlled variable) by shivering and conserving heat by decreasing blood flow to skin.
    - Once set point achieved, control center stops the shivering and would return the blood flow to the extremities.
    - If body temperature increased above the set point Hypothalamus (control center) would signal blood vessels in the skin to dilate and sweat glands to sweat. Heat dissipates and body temperature drops to normal.
    - Effector "affects" altered environmental conditions to achieve a control variable value.

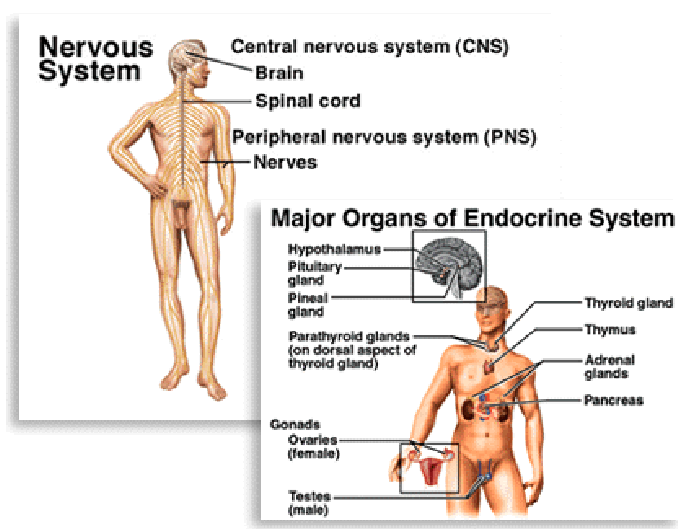
Control Variable → Body Heat

1.8 – Positive Feedback Controls (feed forward systems)



- The controlled variable actually stimulates its own production.
- Positive feedback systems are self-amplifying mechanisms that can produce a very rapid change in a physiological system.
- The controlled variable is detected by the sensor that signals the control center to activate the effector to produce more of the controlled variable. In this way, large amounts of the controlled variable are produced very rapidly.
  - Examples: Generation of the action potential in nerve cells and the surge of luteinizing hormone that causes the ovulation of the egg from the ovary.

1.9 – Negative and Positive Feedback Control Systems



- All body systems use negative or positive feedback to regulate functions and maintain homeostasis.
  - These feedback mechanisms rely on two control systems to function properly: the **nervous system** and the **endocrine system**.
- <u>Nervous system</u> (brain, spinal cord, and all of the nerves) is adapted for rapid communication through complex system of neurons and nerves.
- <u>Endocrine system:</u> responds slower, communicating by release and distribution of hormones in blood.

1.10 – The Body's Structural Hierarchy

- **Atoms** make up **molecules**. Molecules make up **macromolecules**, which **form cellular organelles**. Almost all **cells** of the body contain similar **organelles** like the nucleus, the cell membrane, proteins, and so on.

- Some cells have taken these basic structures and have turned them into highly specialized structures giving each cell specific purpose.
    - Example: muscle cells contain large quantities of special proteins that cause the muscle to contract.
- **Tissue**: Groups of cells with all the same specialization.
    - Example: muscle tissue is specialized because it contains cells that can contract.
- **Organs**: Two or more types of tissues combined to form a complex, functional unit.
    - Example, the heart is composed of connective tissue, muscle tissue, and specialized conducting tissue.
- **Organ systems**: when several organs cooperate for a common function.
- **Cardiovascular system**: combined blood vessels (veins, arteries, and capillaries) and the heart.
- **Organism**: when all of the organ systems are grouped together.

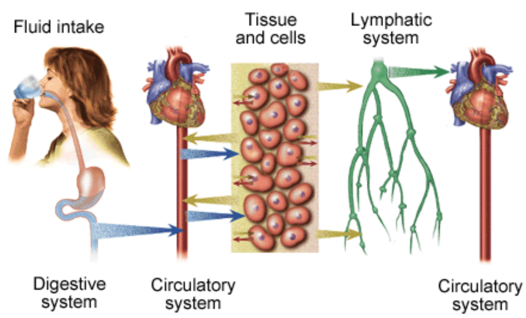
1.11 – A Quick Look Back

- In order for all of the cells and organ systems to function properly, the internal environment of the body must be maintained at relatively stable conditions, regardless of what is happening in the external environment.
    - Maintaining a relatively constant body temperature, water balance, salt concentrations, etc.
- The body achieves this by detecting changes then, through negative feedback control systems, correcting the change.
- Each organ system is made up of different organs working together for a common function. Each organ is made up of several different types of tissues, while each tissue is made up of cells with similar specializations.
    - Fluid and ion composition inside of the cell is different from that outside and how these differences come about.

Module Two: Body Fluids

2.1 – Objectives

- **Diagram:** 2 cells w/ a nearby capillary.
  - Label: intracellular and extracellular compartments, interstitial fluid compartment, plasma and cell membrane.
  - Indicate: relative size of each compartment in terms of % of total body water.
- **Describe composition of:** intracellular fluid, interstitial fluid, and plasma in terms of: Na^+, K^+, Cl^-, and proteins.
- **Explain** the reason in difference in compositions for intracellular fluid, interstitial fluid, and plasma.

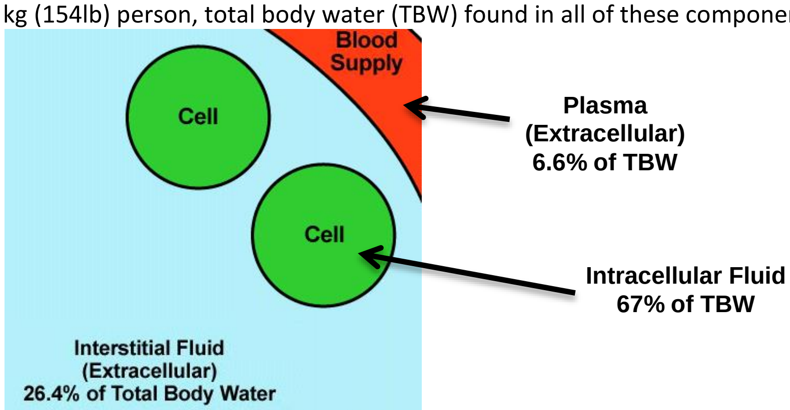


2.2 – Introduction

- Section outline: to look at these body fluids, their compartments, volumes, and chemical compositions.
- Remember: homeostasis is the maintenance of stable internal environment (ie. or body).

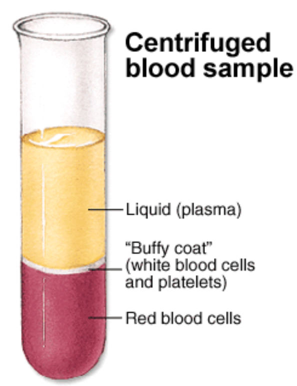
2.3 – Body Fluid Compartments

- Body has 2 main fluid components:
  - Intracellular fluid component (ICF) (within cells) –67% of TBW
  - Extracellular fluid component (ECF) (outside cells)
    - Makes up internal environment of body and can be further divided into:
      - Interstitial fluid component (fluid directly outside, bathing cells) –26.4% of TBW
      - Plasma (watery portion of blood) –6.6% of TBW
- For every avg. 70 kg (154lb) person, total body water (TBW) found in all of these components is 42 litres (L) or 11.1 gallons.



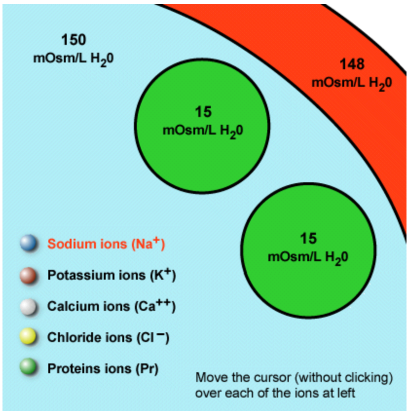
2.4 – A Quick Look at Plasma

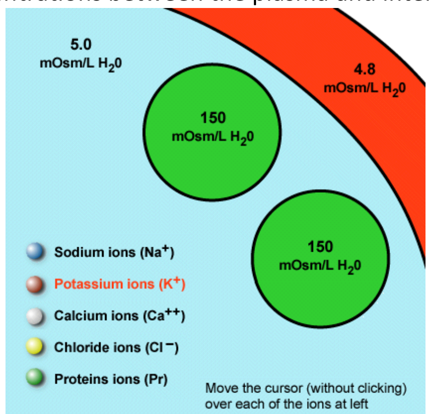
- **Plasma**: pale yellow fluid consisting of ~92% water & 8% other (ie. proteins, ions, nutrients, gases, and waste)
  - A colloidal solution (liquid with suspended, unsettling substances)
  - Most suspended substances are plasma proteins including: albumins, globulins, and fibrinogen.
- Plasma volume remains relatively constant.
- Digestive tract's water intake matches water loss through the kidneys, lungs, digestive tract, and skin.

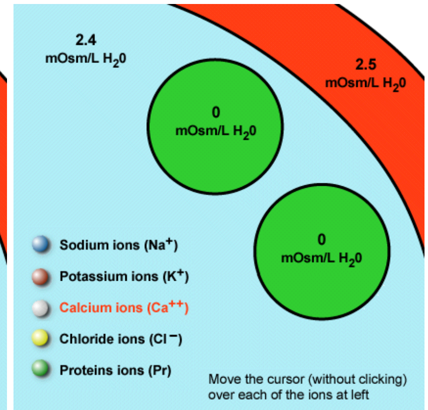


2.6 – Chemical Composition of the Body Fluids

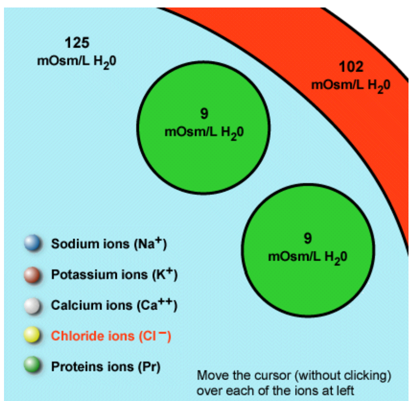
- *****KEY*** NOTE RELATIVE DISTRIBUTIONS OF ION CONSENTRATIONS BETWEEN:**
  - **INSIDE AND OUTSIDE OF CELL AND;**
  - **PLASMA AND INTERSTITIAL FLUID**
- Note:
  - Big difference in ion concentrations between the inside and outside of the cell.
  - Small difference in ion concentrations between the plasma and interstitial fluid.

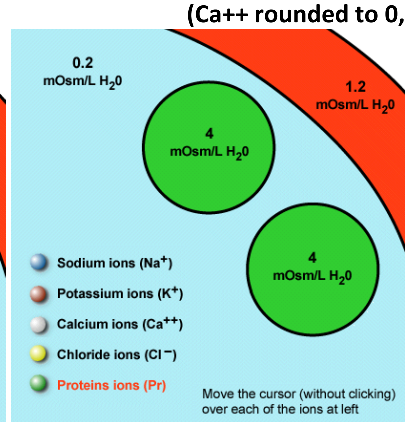






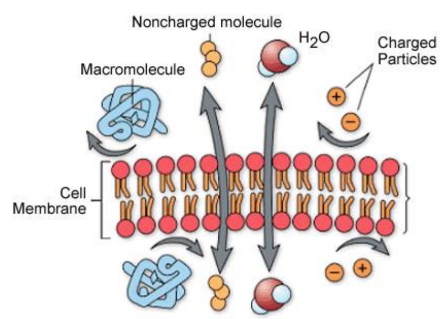
(Ca++ rounded to 0, actually just very low)





- **Key:** Note that most of the sodium ions (Na^+), chloride ions (Cl^-), and calcium ions (Ca^{++}) are found outside the cell and that most of the potassium ions (K^+) are found inside the cell.

– Chemical Composition of the Body Fluids (cont.)

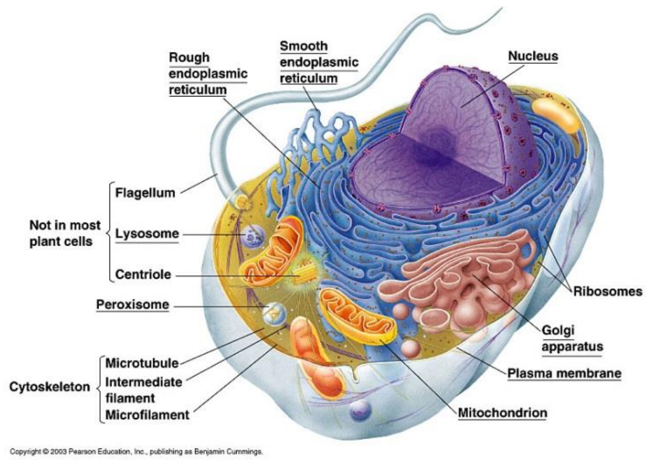


- Why is there a difference in the ionic composition between the inside and the outside of the cell?
- Why are there more sodium ions (Na+) outside the cell and more potassium ions (K+) inside?
  - Selectively permeable cell membrane (aka plasma membrane) between intracellular and extracellular fluid.
    - Some large macromolecules cannot cross at all
    - Does this due to: channels, pores, and special transport systems that regulate passage.

Module Three: Human Cell

3.1 – Objectives

- ★ Diagram: cell membrane, w/ parts of the phospholipid bilayer, positions of membrane proteins, cholesterol, and carbohydrate moieties.
- ★ Discuss permeability of the lipid bilayer.
- ★ Five functions of the membrane proteins.
- ★ Five major ways substances cross membranes.
- ★ Describe diffusion mechanism.
- ★ List four factors that affect substance movement rate through protein channels
- ★ Describe facilitated diffusion. How does it differ from simple diffusion?
- ★ Describe active transport. How does it differ from facilitated diffusion?
- ★ Define osmosis and describe the factors that affect the movement of water across membranes. Define osmotic pressure.
- ★ Define isotonic, hypotonic, and hypertonic. Describe the effect of such solutions on biological cells.
- ★ Describe how chemical and electrical gradients affect the movement of molecules across membranes.
- ★ Define a resting membrane potential and state its normal polarity and strength (voltage).
- ★ Describe the forces acting on ions and define equilibrium potential.
- ★ State the equilibrium potentials for K+, Na+, and Cl– in a nerve membrane.
- ★ Describe two functions of the Sodium/Potassium Pump.



3.2 – Introduction

- Functioning of organs/systems relies on complex cellular function.
- We will examine: cell structure, membrane and components, different ways chemical substances cross the cell membrane.

3.3 – Basic Cell Organelles

- **Mitochondrion:** Primary source of energy of cell.
  - Membranous organelle where most of the body's ATP is generated.
  - "Powerhouse of cell."
  - # of mitochondrion in a cell is determined by that particular cell's energy needs.
  - Can self-replicate without mitosis (occurs when energy is in high demand ie. 'Muscle cells')
- **Nucleus:** Location of all the cell's DNA
- **Nucleolus:** Contains specific DNA that codes for ribosomal RNA.
- **Centrioles:** Direct DNA movement in cell division.
- **Secretory Vesicle:** Transports proteins out of cells.
  - Produced by Golgi apparatus & used to transport protein out of cell to other parts of body.
  - Secretion: Process of releasing protein into extracellular environment.
- **Golgi apparatus:** Packages proteins into vesicles.
  - Packages proteins from rough ER into membrane-bound vesicles.
  - **2 Types of Vesicles:**
    - Secretory (protein to cell membrane into extra-cell environment),
    - Storage vesicles (lysosomes; contents stored for use within the cell).
- **Lysosome:** Digestive system of cell.
  - Storage vesicle produced by the Golgi apparatus.
  - Contain several enzymes to destroy organelles, kill bacteria, and break down other kinds of biomolecules.
- **Endoplasmic Reticulum:** Site of protein synthesis.
  - Continuation of nuclear membrane and site for synthesis, storage and transport of proteins/lipids.
  - 2 Types: rough/granular endoplasmic reticulum
- **Ribosomes:**
  - Dense granules of RNA and protein.
  - Make protein from a.a. under control of cells DNA.
  - **2 types Ribosomes:**
    - Fixed (attached to ER)
    - Free (float in the cytoplasm), often form in groups of 10-20 known as polyribosomes.

3.4 – The Cell Membrane

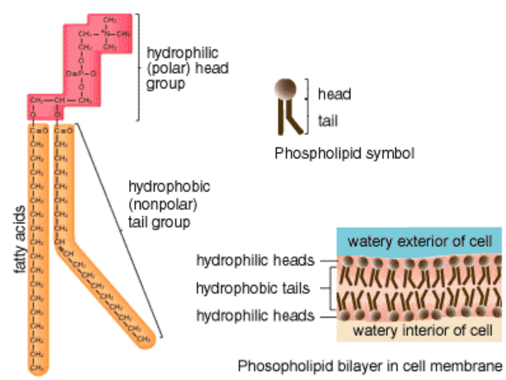
- Separates intracellular environment from extracellular environment.
- Proteins, nucleotides, and other large molecules for structure/function cannot pass through.
- Other molecules and many ions can pass through at varying degrees.
  - Ie. “**Selectively permeable”:** provides two-way traffic for nutrients and waste, and prevents other substances between the intracellular and extracellular compartments.

3.5 – The Cell Membrane: Structure

- Cell membrane made up of:
  - Proteins → Channels and Pores
    - **Associated Protein:** can be attached to either the intracellular or extracellular surface of the membrane.
      - **Enzyme:** act as catalysts for certain reactions on the inner or outer region of membrane.
      - **Structural:** attached to inside surface of cell membrane, support/strengthen membrane or anchor some cell organs to intracellular side of the membrane.
      - **Membrane Spanning Protein:** embedded in phospholipid bilayer (span entire width of membrane), can act as gates/channels to control movement of molecules.
  - Carbohydrate molecules → Cell Recognition
    - Associated with extracellular membrane proteins/lipids.
    - Form protective layer (**glycocalyx**) that is key in the immune response of the cell and in recognition of the other cells in the body.
  - Cholesterol → Stability.
    - In non-polar lipid layer of membrane.
    - Helps make membrane impermeable to some water soluble molecules and keeps membrane flexible over wide temp. range.
  - Phospholipid Molecule → Double layer of phospholipid molecules
    - **Hydrophobic Head:** face outside cell into water base solutions
    - **Hydrophilic Tail:** face away from aqueous and extra/intracellular solutions into the cell membrane.

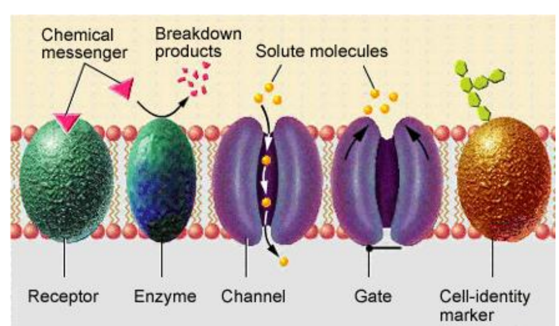
3.6 – Structure: Phospholipids

- Phospholipid molecule: phosphate “head” and fatty acid or lipid “tail.”
  - Fatty acid tail: Hydrophobic
    - Major barrier to water and water-soluble substances (anything that dissolves into water) such as ions, glucose, urea, and most other molecules found in living organisms.
    - Fat-soluble substances like oxygen, carbon dioxide, and steroid hormones can penetrate easily by dissolving through lipid region of the membrane.
  - Phosphate head: hydrophilic
- When thrown into water, automatically form lipid bilayer.



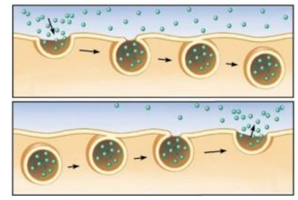
3.7 – Structure: Membrane Proteins

- **Functions of membrane proteins:**
  1. ***Receptors:*** for Chemical hormones and neurotransmitters to bind to
  2. ***Enzymes*** : carry out chemical reactions or breakdown
  3. ***Ion channels/pores***: allows water-soluble substances, like ions, into the cell
  4. ***Membrane-transport carriers:*** transport molecules across the membrane (ie. gated channels)
  5. ***Cell-identity markers***: ie. antigens or glycoproteins.
     a. Antigens are foreign particles that can stimulate the immune system.



- One of most important functions of the proteins is to transport substances across membrane.

- Some substances require protein to cross, and others do not.
- Membrane transport mechanisms include:
  - **(1) Endocytosis** (enter) / **Exocytosis** (exit) (pinocytosis for small molecules)
    - *Exocytosis:* a way for molecules unable to past through the lipid bilayer of the plasma membrane, to exit the cell.
      1. Molecule produced in the ER.
      2. Molecules packaged in vesicle and sent into Golgi apparatus.
      3. Molecules modified by Golgi.
      4. Golgi packages molecules into a vesicle and sends it off.
      5. Membrane of vesicle and plasma membrane merge and contents exit cell.
    - ***Endocytosis****:* a way for large molecules to enter cell (creates vesicle in cell in process).
  - ***Diffusion* through**:
    - **(2) Lipid bilayer** (ie. fat-soluble molecules)
    - **(3) Protein channels** (ie. water and water-soluble molecules)
  - **(4) Facilitated diffusion**
  - **(5) Active transport**



Membrane Transport Mechanisms

3.9 – Diffusion

- Movement of molecules from high to low concentration by random thermal motion.
  - Movement from high to low = **chemical concentration gradient.**
  - Will continue to transfer into [low] until **concentration is uniform** throughout.
  - At this point, transfer **reaches chemical equilibrium** and **net diffusion is zero** (*although still randomly moving*).
- Ions move toward opposite charged areas down their **electrical gradient.**
  - Therefore ions move down both **chemical** and **electrical gradient**.
  - Note: if chemical and electrical gradients are opposite in direction, movement will depend on balance of two gradients and will stop changing the net movement until **electrical equilibrium** is reached (when the electrical force is equal to and in opposite direction to the chemical force).

3.11 – Diffusion of Lipid-Soluble Substances

- Lipid soluble substances pass through cell membrane easily, yet water soluble molecules have a tougher time.
  - Lipid-soluble: oxygen, carbon dioxide, fatty acids, and some steroid hormones.

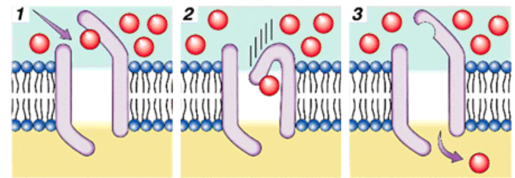
3.12 – Diffusion of Water-Soluble Substances

- Water soluble substances cannot pass through membrane through fatty-acid region, but can still pass through by other ways.
  - Water and many ions can pass through special protein channels and pores.
  - Each pore/channel is usually specific to one or two types of ions.

3.13 – Diffusion Factors

- **Size** of protein channel (approx. 0.8 nm).
  - Sugar molecules are too large for protein pores.
- **Charge** on the molecule since proteins that make up channels also make charges.
  - Ie. Positive ion won't pass through positive charged protein.
- **Electrochemical gradient** of molecule (greater gradient the faster the movement)
  - Opposite charges attract.
  - Substances move down both concentration and electrical gradients.
- **Number of channels** in the membrane
  - Without a channel there would be no diffusion of some substances

3.14 – Facilitated Diffusion



1 Particular molecules can bind to special protein channels in the plasma membrane.

2 The protein channel helps (facilitates) the diffusion process and does not require energy.

3 The molecule is released on the far side of the membrane.

- Other water-soluble substances (such as sugars) that can't pass through the lipid bilayer and are too large for protein channels can still pass through the cell at a fast rate.
- These molecules **attach to a specific protein carrier** and cause a change in protein shape.
  - **Result**: Either opens protein channel (molecule passes through), or protein rotates molecule into the membrane inner surface where it's released.
- **Similar** to simple diffusion in that it does not require energy and powered by concentration gradient.
- **Differs** to simple diffusion in that it is limited by the number of available proteins.
  - If all carriers are occupied, system becomes **saturated** and cannot operate faster.
  - Speed at which protein can change shape is also limited.
- Shows **chemical specificity** and may be **completely inhibited** by similarly shaped molecules.

3.16 – Active Transport

- Like facilitated diffusion by: Requires protein carriers, can be saturated, and shows chemical specificity and competitive inhibition.
- Unlike facilitated diffusion by: requires energy (ATP).
  - Moves molecules against concentration gradient.
  - ATP → ADP + PE
- Ex. Na/K Pump: 3 Na exits, 2 K enters, ATP → ADP + PE

3.17 – Osmosis

- Water transportation using special pores (cannot diffuse through hydrophobic portion of membrane)
  - Normally: water entering = water leaving. Therefore volume constant.
  - Other times: water movement down the concentration gradient (**Osmosis**).
    - Distribute the water molecules equally on both sides of a permeable membrane.
    - Addition of solute molecules that cannot cross membrane reduces number of free water molecules on that side, as they bind to that solute (ie. Salt).
    - Diffusion then causes free water molecules to move from side where there are more free water molecules to the side with solute (where there are less free water molecules).
- **Solute**: substance dissolved into liquid (ie. glucose, Na^+, honey).
  - **Higher [solute] = low [water]**
- **Solvent**: liquid doing the dissolving (ie. water).
- **Solution**: end product after dissolving.
- **Osmosis affected by**:
  - *Permeability* of membrane to the solutes in the intracellular/interstitial fluids
  - *Concentration* gradients of solutes in the intracellular/interstitial fluids
  - *Pressure* gradient.

3.21 – Units of Osmosis

- $[\text{solute}] \propto \frac{1}{[\text{water}]}$
- To know the direction of osmosis, we must know the concentration of each solution.
  - **Osmotically active particle**: particle that causes osmosis (ie. Na^+, Cl^-, K^+, glucose).
  - **Osmole**: unit for osmotically active particles in soluntion.
- **Two unit of osmosis concentration:**
  - **Osmolality**: osmoles per kilogram (kg) of water.
  - **Osmolarity**: osmoles per L of solution.

   - Assume these two units are the same.
- Examples:
   - What is the osmolality/concentration of a 1 molar solution of NaCl?
      - 1 mol NaCl per 1 kg H_2O = 1 mol Na^+ + 1 mol Cl^- = 2 osmotically active particles = 2 osmoles per kg H_2O
   - What is the concentration of a 1.5 molar solution of $CaCl_2$?
      - 1 mol $CaCl_2$ = 1.5 Ca^{++} + 3.0 Cl^- = 2 osmotically active particles = 4.5 osmoles per kg H_2O

3.22 – Isotonic, Hypotonic, and Hypertonic

- **Tonicity**: ability of solution to cause osmosis across biological cell membrane.
- Cell = 300 mOsm/kg of water
- **Isotonic solution**: same concentration as body fluids.
   - If human cell place into this solution, no osmosis would take place.
- **Hypotonic solution**: low concentration compared to cells (Osmosis into cell – cell swells)
- **Hypertonic solution**: high concentration compared to cells (Osmosis out of cell – cell shrinks)

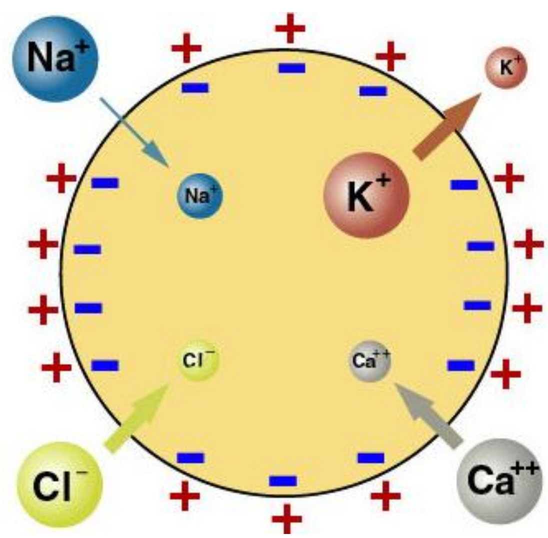
Which of the following solutions will cause a red blood cell to swell if the red blood cell were placed in that solution? Select the correct answer, then click the Check button.

Correct - you answered B

A) 100 mM solution of CaCl2
B) 100 mM solution of NaCl
C) 150 mM solution of KCl
D) 400 mM solution of glucose
E) 200 mM solution of NaCl

3.23 – Concentration Gradients and Membrane Permeabilities

- Na^+, Ca^{++}, and Cl^- have [higher] outside cell = move inside.
- K^+ has [lower] outside cell = move outside.
- **Just because they have a concentration gradient *does not* mean that they will diffuse in those directions.**
- Membrane determines ions passage.
   - Has permeability depending on the **ion** and **type of cell.**
- Most cells aren't very permeable to Na+
- Similar to Cl^- and Ca^{++}.
   - Few channels for them in membrane
- K+ is different -- the membrane is more permeable to K+. Some will leak down concentration gradient.



Note: Na+ line is thinner

__Important Key concepts:__

- **Relative ion concentrations** and **permeability** of membrane to each ion…
   - **This is a generalization**
   - **True for 'most' cells/circumstances**
      - Permeability varies.
      - Channels open/close due to stimuli (chemical or voltage).

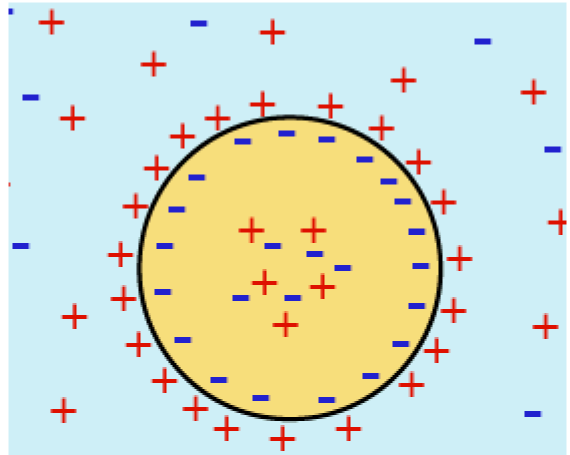
1. Understand diagram and concentration gradients
2. Know relative permeability of the membrane to ions
3. There are still different types of channels not discussed.

3.27 – Membrane Potentials

- Charged particles (ie. ions) are also affected by electrical gradients.
- **Electrical potential**: charge difference between two points.
- Relative permeabilities of the major intracellular and extracellular ions and their electrochemical gradients establish and maintain the membrane potential found in virtually all cells in the body.
- This section will be looking at different types of membrane potentials, including:
   1. **Equilibrium** Potentials
   2. **Resting membrane** potentials

3. **Action** Potentials

- Later modules will discuss:
    1. **Excitatory postsynaptic** potentials and **inhibitory post synaptic** potentials
    2. **Generator** potentials



3.28 – The Resting Membrane Potential

- Fluids in and out of cell are charged (electrolytic)
- **Negative (-) anions** accumulates immediately inside the cell along surface; and an equal amount of **positive (+) cations** accumulate immediately outside membrane.
    - **Effect:** establishment of electrical potential.
- **Resting membrane potential:** electrical potential difference across the membrane **(Inside – and Outside +)** that is present even in resting cells.
    - All cells in body have resting membrane potential.
- In most cases a microscopic coltmeter measuring rest potential would read: -70 millivolts (mV).
    - Varies depending on cell.
    - Negative because the inside (-) is being compared to the outside (+).
- Cell membranes are permeable to varying degrees (to both +/-)
- Diffusible ions influence resting membrane depending on degree of permeability and concentration gradient.

3.30 – Equilibrium Potential

- Ions have two forces acting on it:
    - Chemical Concentration Gradient
    - Electrical Gradient
- **Electrostatic equilibrium:** When these 2 forces are equal in magnitude and opposite in direction, there is no net movement and ion.
- **Equilibrium potential of ion**: electrical potential to be applied inside cell to stop movement of that ion down concentration gradient.
    - $Concentration\ gradient \propto equilibrium\ potential\ needed\ to\ stop\ the\ movement\ of\ the\ ion$
- Equilibrium potential varies on the animal species and type of cell.
    - Nerve cells might have different equilibrium potetients than other cells
- Approximate numbers for a vertebrate neuron to be applied inside cell to keep each ion from moving down its concentration gradient:
    - **$E(K^+)$ = –90 mV**
    - **$E(Na^+)$ = +60 mV**
    - **$E(Cl^-)$ = –70 mV**

Na+ has a strong concentration gradient pushing it into the cell. In order to keep it out, you must apply a positive charge (like charges repel) to the inside of the cell. Given the concentration gradient for Na+, this charge must be +60 mV. This is the charge that would be just strong enough to keep Na+ from moving into the cell. This is similar for K+, but K+ wants to move out of the cell. If you want to keep a positively charged ion from moving out you must apply a negative charge to the inside of the cell (unlike charges attract), and the strength of that charge will depend upon the size of the concentration gradient. The equilibrium potential for K+ therefore is –90 mV.

Our problem is that the resting membrane potential is –70 mV. This is the actual voltage on the inside of the cell.Therefore, some K+ will try and leave the cell, and some Na+ will try and enter. The Na+/K+ pump balances the leakage of these ions.

(Example)

3.32 – Sodium/Potassium Pump: an integral membrane protein

- 3 Na^+ ions out and 2 K^+ ions in
- Contributes to resting membrane potential by making inside more negative (ie. more + leave than enter)
- **Electrogenic pump:** pumps ions against concentration gradients, requires ATP, form of active transport.

Functions of the Sodium/Potassium Pump:

- Na+ leaks into cell and K+ leaks out, the pump acts to maintain the concentration gradient.

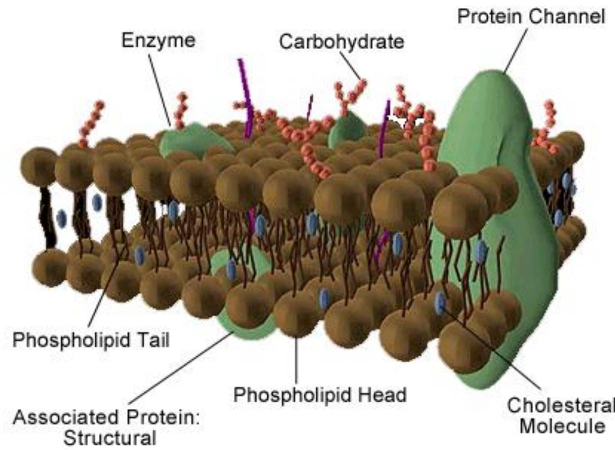
- Causes cell to become electronegative on the inside, contributing to some resting membrane potential
- Without pump, most cells would swell until they burst.
- Cells contain a lot of proteins and other compounds to which membrane is impermeable.
    - Many of these molecules contain negative (-) charge and attract (+) ions; increasing # of particles inside the cell, causing osmosis into cell.
- Since $3Na^+$ leave and $2K^+$ enter → reduction of particles inside cell
    - Causes osmosis of water out of cell and offsets the osmosis into the cell → cell volume is kept constant.

3.34 – Significance of the Resting Membrane Potential

- Significance of resting membrane potential = ENERGY! (ie. cell can do work)
- **Excitable cells** can use this potential to do work and then spontaneously regenerate elevtrical potentials at their membranes.
- **Two types of excitable cells:**
    1. Nerves.
    2. Muscles.

Quick Look Back:

Part 1:

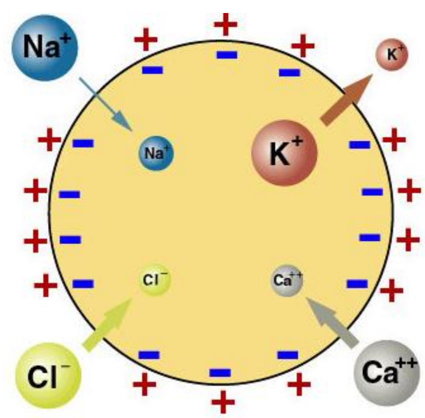


- Cell membrane = selectively permeable.
  - Some cross, some cross with difficulty, others do not cross at all.
- Due to bilayer of phospholipid molecules
  - Embedded within are proteins that act as: channels, pores, transport carriers, receptors, markers, and enzymes.

Part 2:

- Ways molecules cross membrane:
  1. Diffusion (through lipid bilayer or protein channel)
  2. Facilitated diffusion
  3. Active transport
- "diffusion" of water = *osmosis*
  - Need *semipermeable membrane* (permeable to water, but not solute) is required.
  - Factors affecting osmosis.
  - Result of placing a human cell into solution of different concentrations (ie. hypo-, iso-, and hypertonic solutions)

Part 3



- Memorize diagram→
- Relative permeability of the membrane to each ion (how easy the ion can move across when cell is at rest)
  - Ie. membrane is not very permeable to Na^+ is to K^+

Part 4

- Inside of cell has -70 mV voltage compared to outside (resting membrane potential)
- Equilibrium potentials: electric charge for ion on the inside of the cell that is necessary to stop an ion from moving down its concentration gradient.
  - Each ion has different equilibrium potential because each has a different concentration gradient
  - Know equilibrium potentials for major ions.

Part 5

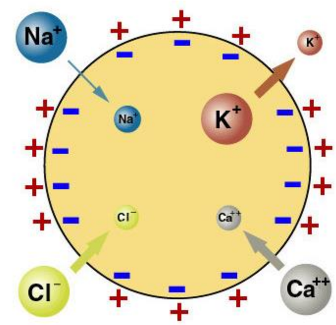
- At this point, we put the whole cell together and reviewed ionic concentration gradients, permeability of the membrane to each ion, and so on.
  - Some K^+ leak out and some Na+ leak in.
  - This leaking of ions is solved by the sodium/potassium pump.
  - This pump is also partly responsible for the resting membrane potential of the cell

Module Four: Nerve Cells

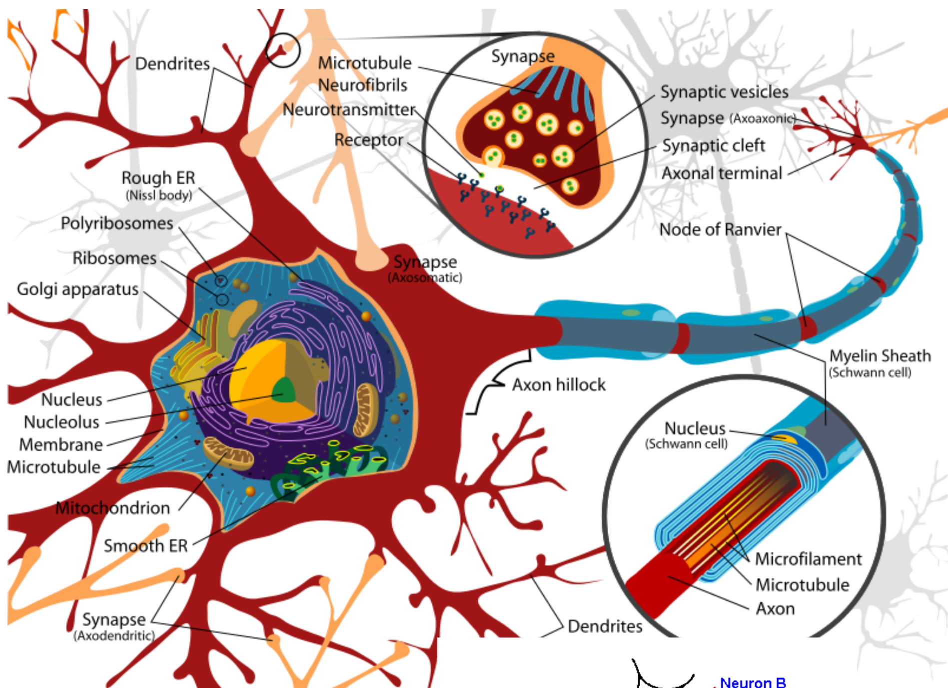
4.1 – Objectives

- ★ Explain the difference between excitable and nonexcitable cells.
- ★ Draw and label the soma, axon, dendrites, axon hillock, myelin sheath, nodes of Ranvier, and terminal boutons of a typical neuron.
- ★ Describe the "voltage-dependent" sodium and potassium channels.
- ★ Draw a diagram of an action potential and the permeability changes of sodium and potassium, and use it to describe the ionic mechanisms of the action potential.
- ★ Define depolarization, repolarization, threshold, overshoot, and hyperpolarization.
- ★ Answer the following questions about action potentials:
  - How many ions move through the membrane during one action potential?
  - What are two reasons for why the action potential does not reach the sodium equilibrium potential?
  - What mechanism returns the membrane potential from +35 mV during the peak of the action potential to resting levels?
- ★ Describe the conventional direction of current flow.
- ★ Describe how an action potential propagates down the membrane of an excitable cell.
- ★ Describe the saltatory conduction of action potentials in myelinated fibers. What are the advantages of saltatory conduction?
- ★ Describe what is meant by the all-or-nothing principle of action potential conduction.
- ★ Explain what determines the direction of the conduction of the action potential.

4.2 – Introduction

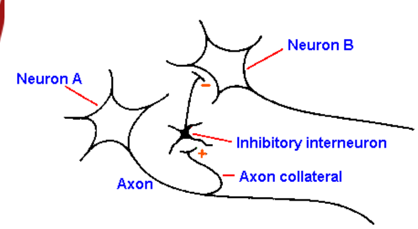


- Always keep this diagram in mind when you think about all of the different membrane potentials.
- **Excitable:** term used to describe cells that use their resting membrane potential to generate an electrochemical impulse called an **action potential**.
  - **Action potential:** language of nervous system. Necessary for muscle contractions.

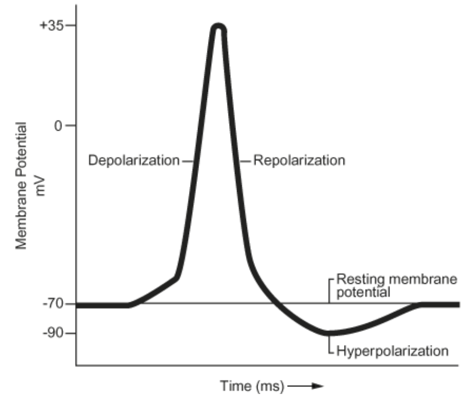


4.4 – Structure of a Nerve Cell

- There are several types of neurons.
- **Understand the following:**
  - **Dendrites:** thin branching processes of the cell body whose function is to receive incoming signals, increase overall surface area of the neuron to communicate to many other neurons, number of dendrites of a neuron will vary depending on where the cell is located.
  - **Cell body (soma):** control center of the cell, containing the nucleus and all necessary organelles for directing cellular activity.
  - **Axon:** projection of the cell body which carries the outgoing signal to the target cell in the form of an action potential. May or may not be myelinated (which refers to the presence of a layered phospholipid membrane sheath wrapped tightly around the axon). The
  - **Axon Hillock:** specialized region of the cell body from which the axon itself projects, point at which the action potential begins its generation in the nerve cell.
  - **Myelin sheath:** acts as a kind of insulator for the axon forcing the ionic changes that comprise the action potential to take place only at small exposed regions of the axon called the **Nodes of Ranvier**.



- Jumping of action potential from node to node results in significantly increased speed of transmission down the axon.
  - **Collaterals:** A collateral axon is a branch separated from the main axon that generally feeds back onto the soma. This occurs to facilitate the modulation of cell firing. The process of separation from the main axon is also known as axon collateral.
  - **Terminal Bouton or axon terminal:** end/terminal of the axon that forms a synapse with other another neuron to pass on information.



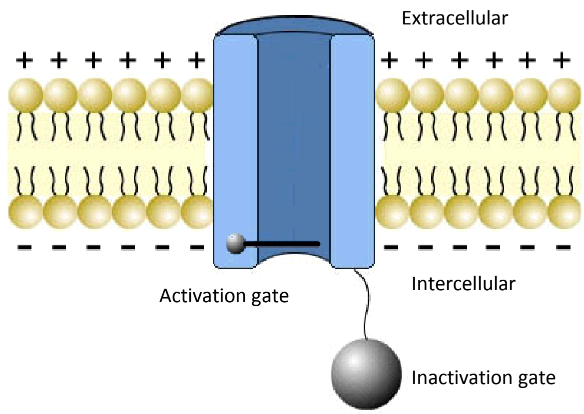
4.5 – A Quick Look at the Action Potential

- Action potential: rapid reversal of the resting membrane.
- **Depolarization**: membrane goes from resting voltage of -70 mV to roughly +35 mV.
- **Repolarization:** returns to -70 mV.
- **Hyperpolarization:** membrane then briefly becomes more negative to about -90 mV which then returns to -70 mV.
- Cause for rapid changes in membrane potential → movement of ions across membrane (ie. Na^+ and K^+)

4.6 – Voltage-Gated Channels

- Two special types of channels that are found in nerve/muscle cells:
  - Voltage-gated sodium
  - Voltage-gated potassium
- Channels are generally found on axon and are required for generating action potential.
- Sensitive to membrane potential changes and open when inside of cell becomes more positive (ie. -70 mV → -60 mV) (depolarization).

4.7 – Voltage-Gated Sodium Channels



- Open only when depolarization of membrane
- Summary of events:
  1. Depolarization of membrane
  2. Activation gate quickly opens
  3. Na+ flow into cell, down [gradient].
  4. Inactivation gate closes and Na+ no longer flows into cell; channel cannot open
  5. Channel returns to resting (inactivation gate open and activation gate closed)
  6. Channel is now ready to open again (waiting for depolarization)

- The Na+ channel has two gates:
  1. Activation gate
     - Closed at rest
  2. Inactivation gate
     - Open at rest

4.8 – Inactivation of Na+ Voltage-Gated Channel & the Absolute Refractory Period

- When the inactivation gate is closed, regardless of the strength, the channel does not open (ie. **Inactive**).
  - Time period of this inactivation: **Absolute refractory period.**

4.9 – Voltage-Gated Potassium Channel

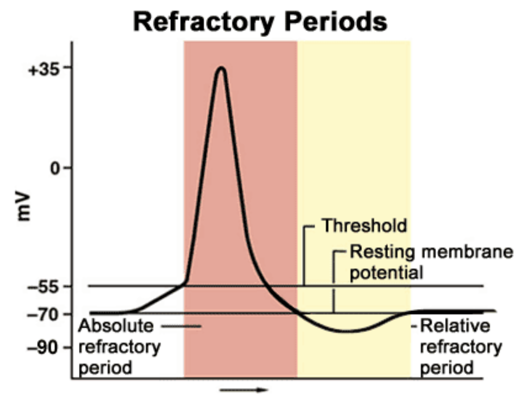
- Contain only one gate.
  - Opens when membrane depolarizes.
  - Doesn't open immediately like the Na+ voltage-gated channels.
  - **Begin opening when the Na+ voltage gated channels start to become inactivated.**
- Summary of events:

1. Depolarization of membrane
2. *After brief pause*, K+ voltage-gated channels open.
3. K+ flow out of the cell, down their electrical and chemical gradients.
4. Gate closes and channel returns to rest.
5. Channel ready to open again.

- Unlike Na+ voltage-gated channel, this channel does not have an inactivation period.
- ★ So what do these channels have to do with the electrical activity of the nerve cell?
  - Essential for generating **action potential**.
  - **Key**: Na+ channels open first and then become inactivated, producing the *absolute refractory period*.
  - K+ voltage-gated channels then begin to open as the Na+ channels begin entering the inactivated period.

4.11 – The Action Potential

- During action potential, membrane potential rapidly reverses from -70 mV to roughly +35 mV starting at axon hillock (axon hillock contains largest number of voltage-gated channels).
- Summary of events:
  1. Strong depolarization at axon hillock triggers opening of most Na+ voltage-gated channels.
  2. Na+ rushes down electrochemical gradient into cell.
  3. Membrane depolarizes rapidly to roughly +35 mV
  4. Na^+ channels become inactivated while K^+ channel begin opening.
  5. K^+ rushes out of cell, down electrochemical gradient.
  6. Membrane begins repolarizing back to normal (+35 mV back to -70mV).
  7. K^+ continues rushing out of cell and membrane hyperpolarizes (reaches -90 mV)
  8. Membrane potential slowly returns to rest value of -70 mV.

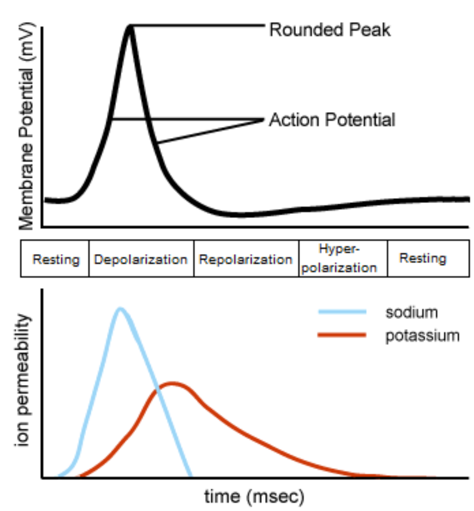


4.12 – Refractory Periods

- **Absolute refractory period:** contributed by inactivation of Na^+ channels in which regardless of depolarization strength, the Na^+ gates will not open to fire another action potential.
- **Relative refractory period:** period during action potential when membrane is hyperpolarized (ie. more negative than -70 mV)
  - Caused my K^+ channels (which are both slow to open and close)
    - Allows K^+ to continue to leave cell even after being repolarized to -70 mV.
  - Is possible to fire another action potential during this time, but requires a stronger stimulus to reach threshold.

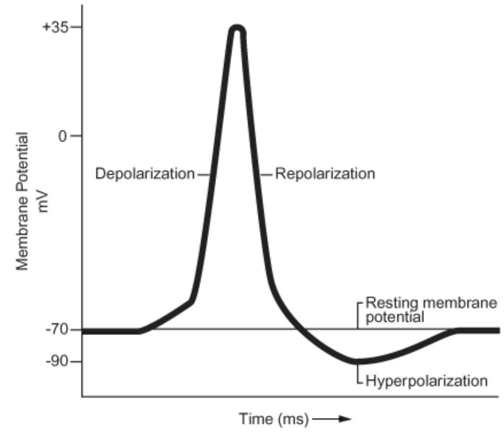
4.13 – Threshold for Starting an Action Potential

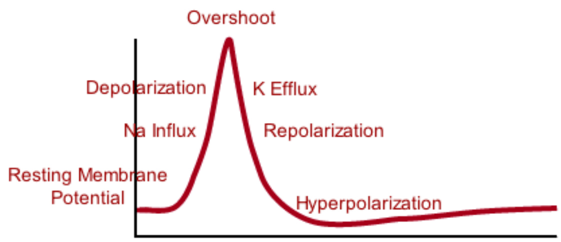
- Action potentials do not always occur.
  - Requires strong axon hillock depolarization to open many Na^+ channels.
- Consider:
  - Few Na^+ ions enter cell to change cause a depolarization, yet the cell attempts to maintain the resting potential of -70 mV.
  - The positive build up in the cell will strongly affect Cl^- and K^+ ions in and out of the cell.
    - The positive K^+ will wish to leave, while the Cl^- will wish to enter.
  - The movement of Cl^- and K^+ ions will **repolarize** the membrane back to -70 mV.
- To fire the action potential, the Na^+ depolarizing force must exceed the natural repolarizing forces of both K^+ and Cl^-.
- If enough Na^+ enters, then the movement of K^+ and Cl^- will not be sufficient to repolarize the cell, allowing the Na^+ voltage-gated channels to open.
  - Threshold for generating action potential: when most of the Na^+ channels will open with the membrane potential depolarization of -55 mV. Once reached, action potential is always achieved.



4.15 – Changes in Na+ and K+ Permeability/Conductance during an Action Potential

- Permeability of the membrane to each ion during an action potential:
  - Na^+ enters cell and Na^+ channels react quickly: rapid peak, depolarization (cell more +)
  - K^+ slowly leaves since channels react slow: repolarization (cell becoming more –) (back to -70 mV)
    - Rounded top/overshoot of the action potential caused by Na^+ moving in while K^+ moves out.





4.16 – Important Facts about Action Potentials

- Very few ions move through membrane during action potential.
  - 1/million of ions available participate in action potential.
    - Therefore no significant change in concentration gradient for the ions after one action potential.
- Thousands (1000s) of action potentials can be generated before the concentration gradients for Na^+ and K^+ break down enough to prevent further action potential generation.
- Sodium/Potassium pump is not required for repolarization
- Rest membrane potential is brought by continued increased conductance of K^+ when Na^+ permeability is normalized.

4.17 – Action Potential Propagation

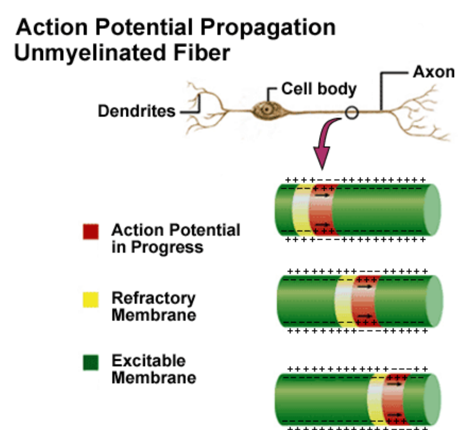
- **Propagation/Conduction:** Action potential generated at axon hillock will travel down axon to axon terminal of another neuron.
- General mechanism involved in propagation down Unmyelinated and Myelinated is similar, but there are important differences.
- Remember:
  - Ion movement sets up ionic current in and out of the axon.
  - Current is carried by positively charged ions (like Na^+) to areas that are negative (unlike charges attract).

4.18 – Propagation of the Action Potential down an Unmyelinated Nerve

- Steps of Unmyelinated axon action potential propagation (see video):
  1. Where action potential exits axon, inner region is more positive (~+35 mV) than outside since Na^+ has entered cell.
  2. Positive charge is attracted to and moves down to closest rest/negative region, creating a local current (+ → -)
  3. Positive charge buildup causes adjacent area of membrane to depolarize.
  4. Depolarization triggers Na^+ channels to open.
  5. Na^+ rushes in and depolarizes region to threshold, creating a new action potential.
  6. Repeat of this propagates action potential along membrane.

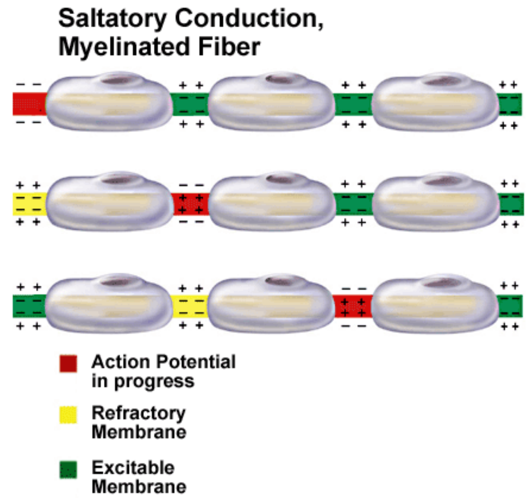
4.19 – Unidirectional Nature of the Action Potential

- After the action potential passed a spot on axon, membrane repolarizes and returns back to (-70 mV).
  - Why is it not possible for the positive area of action potential to draw back in, generating an action potential that could "back up" the axon
    - ANSWER: inactive voltage-gated channels, ie. State of absolute refractory.
    - These channels are inactivated and will not open, regardless of what you do to them.
    - Therefore this area cannot generate an action potential and by the time the voltage-gated channels are ready to open, the action potential has traveled too far down axon to be able to affect them.



4.20 – Propagation of the Action Potential down a Myelinated Nerve: Saltatory Conduction

- Myelinated axons are coated with fatty material called **myelin,** which is produced by special cells: Schwann cells of the peripheral nervous system (PNS) and oligodendrocytes in the central nervous system (CNS).
- Myelin is used to keep ions from leaking through membrane.
- Voltage-gated channels only exist at gaps between myelin (ie. **nodes of Ranvier**)
- Steps of **Myelinated** axon action potential propagation (see video):
    1. Positive charge from existing action potential is attracted/moves to adjacent negatively charged node of Ranvier.
    2. Node depolarizes.
    3. Depolarization triggers Na^+ channels to open.
    4. Na^+ rushes in and depolarizes region to threshold, creating a new action potential.
    5. Repeat of this propagates action potential along membrane.
- **Action potential on myelinated nerve jumps from one node to another** (ie. saltatory conduction).



4.21 – Important Facts about Saltatory Conduction

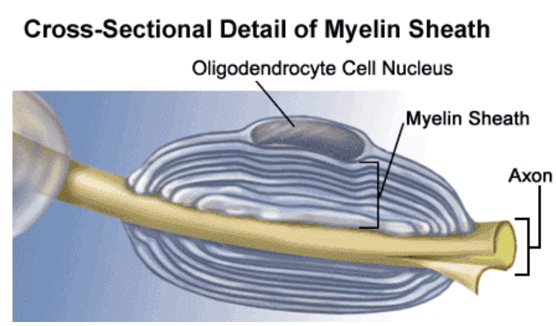
- Saltatory conduction is much faster than conduction of unmyelinated fibers.
- The action potential cannot back up the axon because the absolute refractory period of the Na^+ voltage-gated channels.
    - These channels are inactivated in the region behind the moving action potential.

4.22 – All-or-Nothing Principle of Action Potentials

- **All or nothing principle:** either full potential or none
    - If threshold is not reached, membrane natural repolarizing forces will return the potential to normal (-70 mV).
    - Once threshold is reached, an action potential will be generated and propagated down the axon at its full height without decreasing size!
- Due to the absolute refractory period of Na^+ channels, two action potentials cannot be fired one on top of the other.
    - Therefore, action potentials will almost always have a fixed height/amplitude (some exceptions, but don't worry).

4.23 – Multiple Sclerosis

- Myelination speeds up conduction of action potentials, yet this is the site of attack in multiple sclerosis disease (MS).
    - MS: disease in which body's natural immune system attacks the myelin around axons.
        - Can be so severe that it interrupts natural action potential flow so much that no transmission occurs.
        - If the nerve that is damaged is connected to a muscle, the muscle will not contract and the person will suffer paralysis.

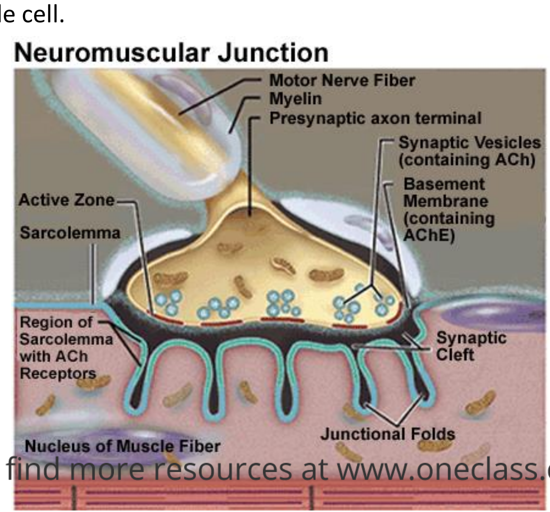


4.24 – Synaptic Transmission

- **Chemical synapse:** Where the neuron's axon terminal is almost in contact with another nerve cell, a muscle cell, or an organ like the heart.
- **Neuromuscular junction (NMJ)**: synapse between a neuron and a muscle cell.
    - Nerve cell action potential triggers action potential on the muscle cell, eventually leading to muscle contraction.

4.25 – The Structure of the Neuromuscular Junction

- **Motor nerve fiber**: neuron that contacts a muscle cell.
- The membrane of the **presynaptic axon terminal** contains **Ca^{++} voltage-gated channels**.

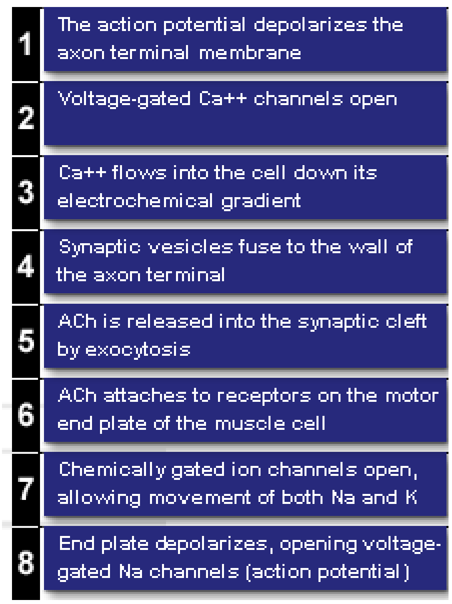


- These channels also open when the cell membrane depolarizes.

- Axon terminal of the motor cell/fiber contains synaptic vesicles containing **neurotransmitter acetylcholine (ACh)**.
- The basement of the membrane of the axon terminal contains the enzyme **acetylcholinesterase (AChE)**.
- **Sarcolemma**: folded muscle cell membrane directly under the axon terminal located in **end plate** region.
- **End plate:** region containing **receptors for acetylcholine**, which is associated with **ligand-gated channels**.
- **Synaptic cleft:** gap between motor fiber and muscle cell.

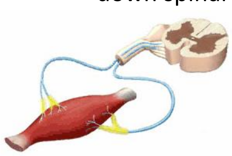
4.26 – Events at the Neuromuscular Junction (+Video)

1. Presynaptic motor nerve action potential triggers Ca^{++} voltage-gated channels to open and Ca^{++} ions flow into cell, down their concentration gradient.
2. Ca^{++} ions triggers fusing of synaptic vesicles to membrane and the release of neurotransmitter ACh into synaptic cleft by exocytosis.
3. ACh diffuses across synaptic cleft and attaches to receptors on muscle cell/fiber membrane.
4. Ligand-gated ion channels open. Lots of Na^+ flows into cell, and few K^+ leave, triggering local depolarization called **end plate potential (EPP)**.
   a. *NOTE:* there is no action potential yet!
5. Depolarization of the EPP spreads to adjacent cell membrane where voltage-gated channels are located and channels open (essential for action potential). Large amounts of Na^+ flows into the muscle cell and triggers the action potential.
6. ACh is broken down to acetic acid and choline by enzyme AChE in synaptic cleft, and choline is taken back into axon terminal to be recycled.

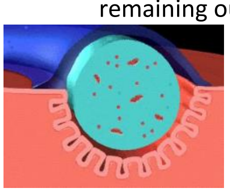


4.27 – The Neuromuscular Junction

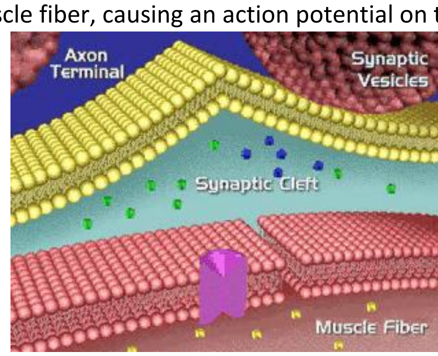
1. To activate skeletal muscle, the central nervous system sends an action potential down spinal cord to motor neurons.

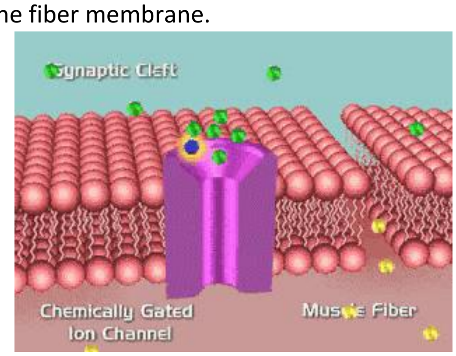


2. The action potential travels down each nerve fiber branch.
   - Each nerve fiber branches many times and stimulates several skeletal muscle fibers.
   - **Neuromuscular junction**: union of axon and muscle fiber.
3. Each branch of the neuron has a terminal that invaginates the muscle fiber, while remaining outside of the muscle fiber plasma membrane.



4. Action potential arrives at the axon terminal and causes the release of ACh from synaptic vesicles into the space between the axon terminal and muscle fiber called the synaptic cleft.
5. In synaptic cleft Ach binds with receptor on the fiber membrane, opening a chemically gated ion channel.
6. Na^+ then rushes through channel, into muscle fiber, causing an action potential on the fiber membrane.
7. Action potential spreads along the muscle fiber and as more nerves activate additional fibers, the action potential spreads over the entire muscle.
8. Upon activation, the muscle contracts.



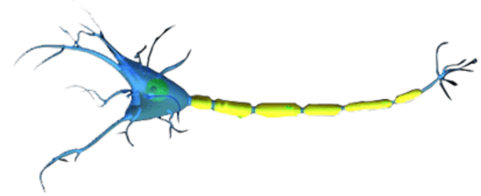


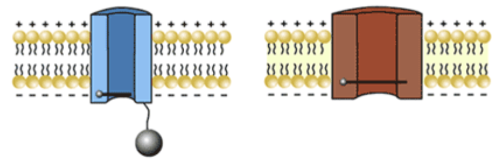
4.28 – Another Look at the Neuromuscular Junction

- Important things to note:
  - A motor nerve cell action potential will always generate an action potential on the muscle.
    - Assuming a healthy motor nerve and muscle cell.
    - One action potential on motor nerve will release enough acetylcholine (ACh), which will open enough.
  - The action potential on muscle will cause the muscle to contract.

Quick Look Back:

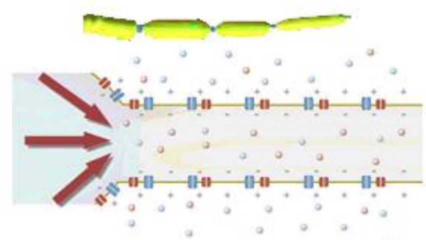
Part 1:

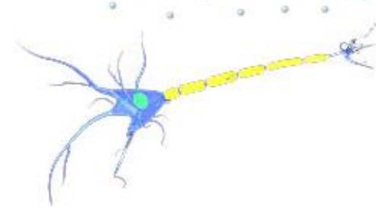




- Important ions involved in action potential: Sodium (Na^+) and potassium (K^+).
    - Each of these ions has its own special voltage-gated channel that opens in response to the depolarization of the cell membrane.
- The Na^+ channels open quickly, while K^+ channels open a little later.
- Ion movement across membrane changes membrane potential and produces the action potential at the axon hillock.

Part 2:





- Action potential is transmitted down axon in a domino effect in **unmyelinated** nerves.
    - One action potential stimulates the opening of adjacent voltage-gated channels, producing a new action potential.
- In **myelinated** fibers, the axon is insulated with a fatty sheath called myelin.
    - Voltage-gated channels are located only at the nodes of Ranvier (gaps between myelin).
    - **Saltatory conduction:** Action potential jumps from one node to another.
    - Much faster method of propagation.
- Once the action potential reaches the axon terminal, it will synapse with another nerve, or muscle, or some other organ.

Part 3:

- Review of events at the Neuromuscular Junction.

Module Five: Muscles

5.1 – Objectives

- ★ Describe the structural components of skeletal muscle, including muscle fibers, myofibrils, myofilaments, sarcomere, and the arrangement of the thin and thick myofilaments.
- ★ Describe the structure of the thin filament and its associated proteins.
- ★ Describe the structure of the thick filament.
- ★ Describe the sliding filament theory and the interaction of thin and thick filaments.
- ★ Define excitation-contraction coupling and describe the sequences involved.
- ★ Describe the complete series of events involved in muscle contraction, starting with the release of calcium from the sarcoplasmic reticulum.
- ★ List four functions of ATP in muscle contraction.
- ★ Describe the mechanism responsible for rigor mortis.
- ★ Describe how the grading of muscle contraction is accomplished.

5.2 – Introduction

- Muscles: biological machines that use chemical energy from metabolism to perform useful work.
- Three (3) types of muscle:
  1. **Skeletal**: primarily for voluntary motion
  2. **Smooth**: found within walls of blood vessels, airways, various ducts, urinary bladder, uterus, and digestive tract.
  3. **Cardiac**: found in heart.
- Body contains over 600 different muscles.
- Three (3) principle functions:
  1. **Movement**
  2. **Heat production**
  3. **Body support/ posture**
- This module only covers only **skeletal muscle** and the **mechanism of muscle contraction as it applies to movement**.

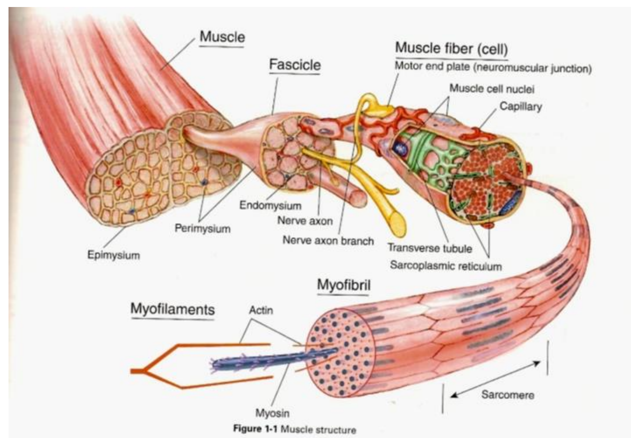
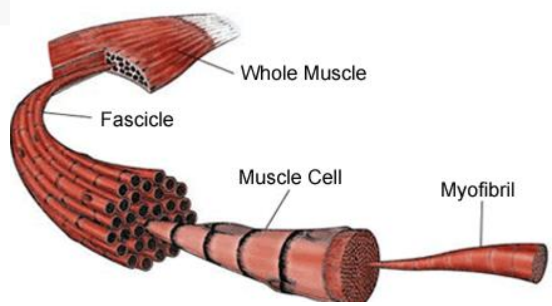


Figure 1-1 Muscle structure

5.3 – A Whole Look at the Structure of Muscle

- **Whole muscle**: made of bundles of fasciculi.
- **Fascicle**: made up of groups of muscle cells/fibers
- **Muscle fiber/cell**: contains many bundles of microfibrils.
- **Myofibril**: contains thin and thick myofilaments which are actual contractile elements of the cell.
- **Sarcomere**: section of myofibril
  - Thin myofilaments: contain mostly the protein **actin** along with troponin and tromyosin
  - Think myofilaments: contain the protein **myosin**
  - **Interaction of thin and thick myofilaments sliding past one another, results in muscle contraction.**

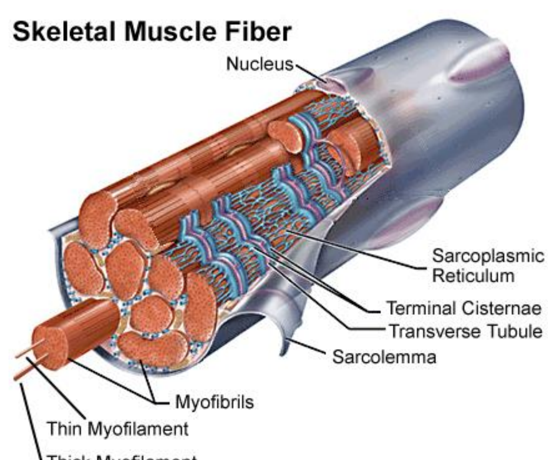


5.4 – Structure of a Skeletal Muscle

- **See 5.3**

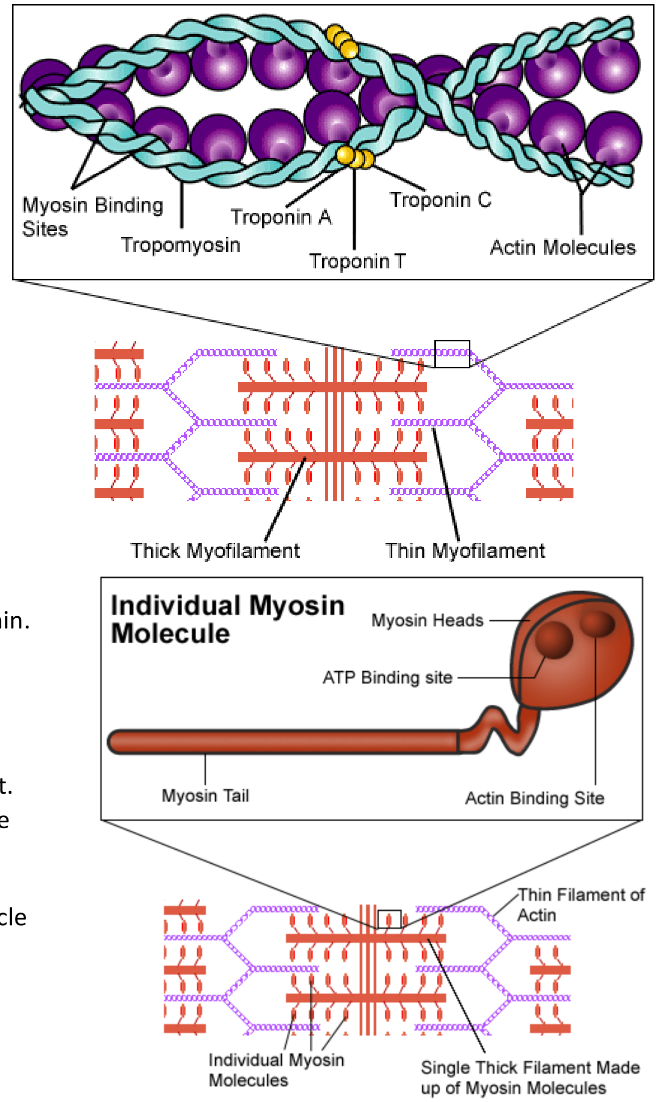
5.5 – Structure of a Muscle Cell

- Muscle cells/fibers one of few cells with more than one nucleus.
  - Surrounded by **sarcolemma,** muscle cell membrane, over which the action potential is transmitted.
    - **Transverse (T) tubules**: tube-like projections of the sarcolemma that extend down into cell and conducts action potential deep into cell to contractile proteins.
  - **Myofibrils**: long and cylindrical, within muscle cell and contain contractile proteins of the muscle (thin/think myofilaments).



- **Sarcoplasmic reticulum (SR)**: mesh –like network of tubes containing Ca^{++} (essential for contraction) that surround myofibrils.
- **Terminal cisternae**: at either end of and continuous with **Sarcoplasmic reticulum (SR)**; a membranous enlargement of the SR, which is close to the T tubule (where action potential travels).

5.6 – Thin Myofilament



- Composed of:
- **Actin**: globular protein.
  - Each **actin** molecule contains a **special binding site for** the other contractile protein **myosin** (of the **Think myofilaments**).
  - Many actin molecules are strung together like beads on string and twisted to form backbone of thin myofilaments.
- **Tropomyosin**: long protein strands.
  - When muscle at rest, these proteins cover binding site for myosin.
- **Troponin:**
  - Made of up three (3) subunits
    - **A:** binds to actin
    - **T:** binds to tropomyosin.
    - **C:** binds to Ca^{++}. When bound, tropomyosin is pulled off myosin binding sites by the troponin.
  - At rest this protein holds tropomyosin over the myosin binding sites.

5.7 – Thick Myofilament

- Many myosin molecules arranged to form one thick myofilament.
- Long bendable tail with two (2) heads that each can attach to the myosin binding site on actin.
  - Head also has site that binds/splits ATP.
    - ATP energy released to myosin, powering muscle contraction.

5.8 – Actin / Myosin Relationship

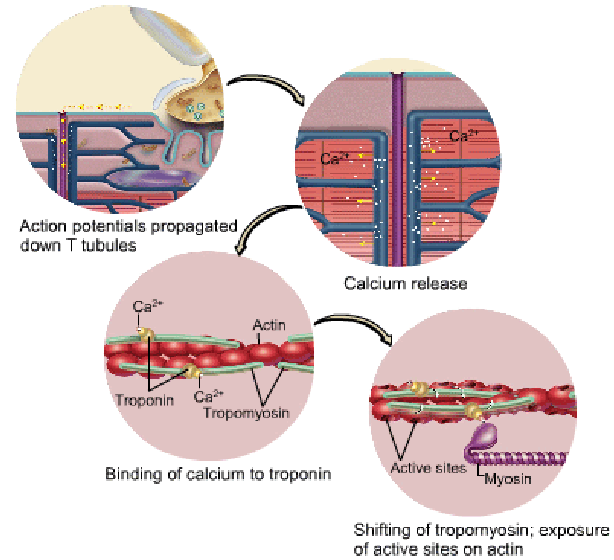
- Pattern: Thick, thin, thick, thin.
  - From one end of muscle to the other along myofibril
  - Gives muscle cell a banded/striated appearance (why skeletal muscle also referred to as striated muscle.
- **Thin myofilament groups:** extended outwards in opposite directions from a central **Z disk (Z line)**, where they are anchored.
  - Regions of Thin filaments: appear as light bands called **I bands**
- **Thick myofilament groups:** extended outward in opposite direction from central **M line,** where they are attached.
- Each myofilament is parallel to the myofibril and the muscle cell.
  - Regions of Thick filaments: appear as dark bands called **A bands.**
- **Sarcomere**: region from Z disk to Z disk; smallest functional contractile unit of muscle.

5.9 – Muscle Contraction—Sliding Filament Theory

- Interaction of actin and myosin.

1. Head of myosin binds to actin site, forming **crossbridge** and change in shape.
2. Change in shape causes myosin head to swing, producing **power stroke**.
3. Power stroke slides actin past myosin.
   - NOTE: neither thin nor thick filaments shorten during muscle contraction. Sarcomere 'shortens.'

Excitation-Contraction Coupling



5.10 – Excitation-Contraction Coupling and Muscle Contraction

- **Excitation-contraction coupling:** process of action potential exciting muscle cell, producing a contraction.
    1. Action potential is generated by neuromuscular junction, spread over the sarcolemma, and down **T-tubules** into muscle core.
    2. Action potential travels close to **sarcoplasmic reticulum (SR)**, opening Ca^{++} channels and releasing ions from **terminal cisternae** of the **SR**.
    3. Ca^{++} binds to **thin myofilament troponin C**, causing **tropomyosin** to uncover myosin binding sites found on actin.
    4. Myosin now able to attach to actin and a power stroke occurs.

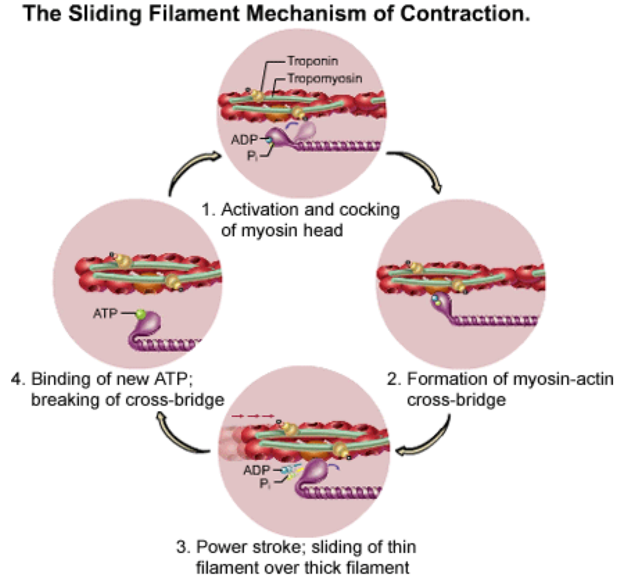
5.11 – Relaxation of Muscle

- When action potential stops, Ca^{++} stops diffusing and special Ca^{++} pumps rapidly pump the ions up concentration gradient (requires ATP), into SR.
    1. If no Ca^{++} in muscle cell cytoplasm, tropomyosin will cover myosin binding sites again.
    2. Myosin will be unable to bind to actin and power strokes will not occur.
    3. Muscle relaxed.
- Why muscles do not want to relax while working?
    - Because you are sending 1000s of action potentials down muscles to keep muscles contracted.
    - When continually sending action potentials, you are continually releasing Ca^{++} from SR, flooding the cell with them.
    - After action potential, to relax muscle all ions must be actively (use ATP) pumped back into SR.
        - **Important characteristic of active transport**: can be saturated ie. Pumps can overload and not work as fast, even with lots of ions around. Therefore muscles cannot relax even when action potentials stop since ions are still present.
    - If Ca^{++} is still floating around, muscle will contract.

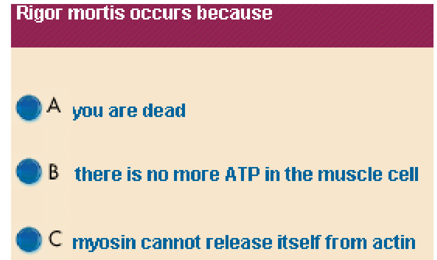
5.12 – Actin-Myosin and ATP Cycle

- Events of single cross bridge formation between actin and myosin:
    1. ATP split into ADP + Pi bind to myosin head, releasing energy to myosin and preparing/activating it for activity.
    2. Cross bridge formation when Ca^{++}, released from SR by action potential, binds to Troponin C, rolling tropomyosin off myosin binding sites found on actin.
    3. Powerstroke occurs and myosin head bends and slides thin myofilaments of actin over thick myofilaments of myosin. ADP and Pi are released from myosin head.
    4. New ATP binds to myosin head. Cycle repeats.
- Check point:
    1. AP travels down transverse (T) tubules into cell center.
    2. Ca^{++} released from sarcoplasmic recticulum binds to troponin
    3. Tropomyosin molecule moves and uncovers myosin binding site
    4. Myosin binds to actin and forms crossbridge
    5. Power stroke initiated
    6. Thin filaments slide over thick
    7. Z-lines move closer together.
    8. ADP and Pi released from myosin
    9. Myosin released from actin and crossbridge is broken
    10. ATP split and energy is transferred to myosin head.

The Sliding Filament Mechanism of Contraction.



5.13– Rigor Mortis

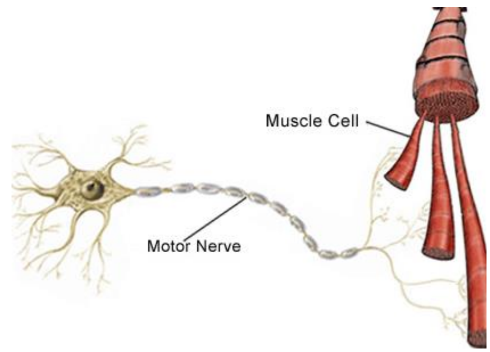


- Begins 3-4 hours after death, muscle become very stiff for about 12 hours, and slowly disappears over next 24-48 hours.
- Rigor mortis results directly from loss of ATP in dead muscle cells (dead cells do not produce ATP)
- Slow degradation of sarcoplasmic reticulum (SR) releases Ca^{++}.
- Myosin binds to actin, forming cross bridge between thin and thick filaments and produces rigid conditions of the muscle.
- Without ATP, bonds cannot be broken (stiffness) until further cell degradation/decomposition dissolves linkage.

5.14 – Altering the Force of Contraction

- Consider: Lifting weights, pick up one light and one heavy dumbbell and do bicep curls.
  - What happens in each bicep to allow pick up of different weight, yet control in same manner?
    - You are able to alter the force of contraction in muscle to adjust to weight being lifted.
    - Two (2) ways that muscle can alter force of contraction:
      1. **Recruit motor units**
      2. **Summation of twitch contractions**

5.15 – The Motor Unit



- **Motor unit**: motor neuron and all of muscle cells/fibers it causes to contract.
  - In almost all situations, one motor neuron contacts (or innervates) several muscle cells, but each cell is innervated by only one motor neuron.
  - The number of muscle cells innervated by a motor neuron.
  - **Large motor unit:** has motor nerve in contact with many muscle cells (up to ~200).
  - **Small motor unit:** has motor nerve in contact with few muscle cells.

5.16 – Recruitment of Motor Units

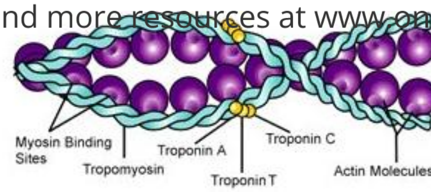
- Consider: standing at tap, holding a bucket while it fills (gets progressively heavier)
  - What happens in muscle?
    - **Motor unit recruitment: progressive activation of motor units.**
      - When bucket empty → few motor units (few muscle cells) contracted.
      - When bucket gets heavier → activation of more muscle cells.

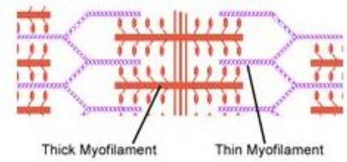
5.17 – The Muscle Twitch: simplest and smallest muscle contraction

- Result of one action potential in motor neuron, which excites the muscle cell, causing the release of enough Ca^{++} from SR to cause very small contraction of the muscle.
- Duration = 10 – 100 milliseconds (action potential = 2 milliseconds).
  - Difference in length of time important when we look at summation of these twitch contractions.
- **Latent period**: time delay from when AP occurred on the motor neuron to when muscle contracts.
  - Delay caused by all events at neuromuscular junction:
    - Generation of AP on muscle cell, and consequent interaction of the thin and thick myofilaments.

5.18 – Summation of Twitch Contractions

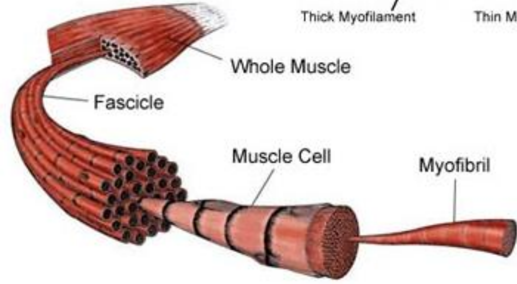
- Consider: simulating muscle with AP, causing a twitch, and then stimulated it again before muscle fully relaxed.
  - Would trigger another twitch that adds on first one → doubling tension in muscle.
  - Can take place because twitch is a type of mechanical event relying on protein interactions.
  - AP = all-or-nothing event that cannot be summed due to absolute refractory period caused by inactivation of Na^+ voltage gated channels.
  - Therefore: can increase force of contraction by increasing rate of AP that travels down nerve (increasing frequency).
    - High frequency = produces maximal tetanic contraction (muscles stay at contraction).
    - Higher voltage = stronger AP/contraction (ie. if low voltage then twitch, if higher then contraction).



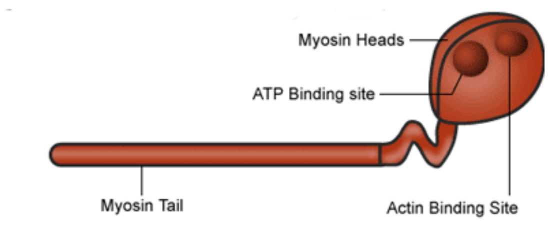


5.20 - 5.24 – A Quick Look Back

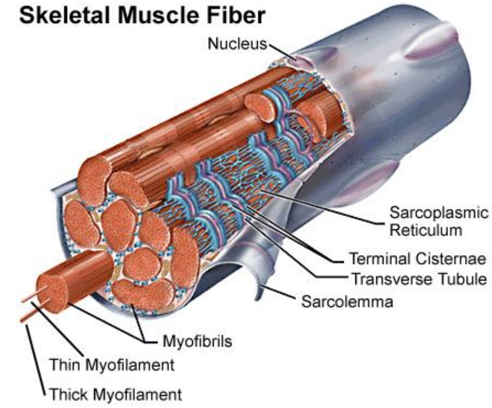
1. **Overall structure:**
   - Whole muscle → bundles of muscle cells → bundles of myofibrils → myofilaments of thin (actin/troponin/tropomyosin) & thick (myosin)
     - Actin of myosin filaments join o form crossbridges during contraction.



2. **Excitation-contraction coupling:** process of AP on muscle cell membrane causing contraction.
   a. AP generated by neuromuscular junction activity.
   b. Travels along muscle cell membrane and down transverse (T) tubules into center of cell.
   c. AP causes release of Ca^{++} from terminal cisternae of sarcoplasmic reticulum (SR).

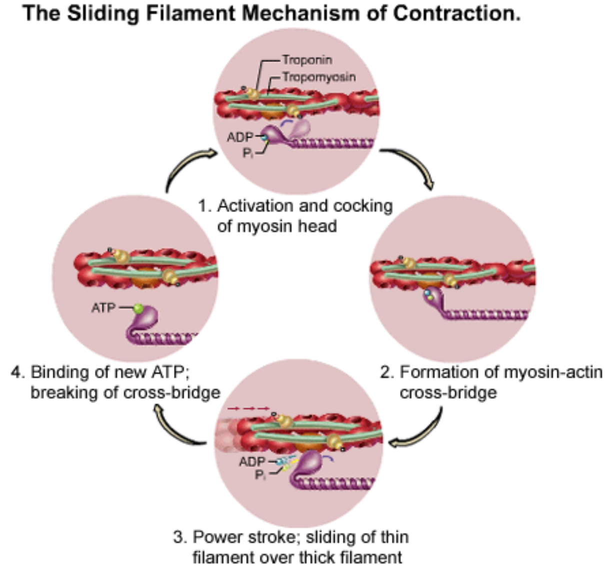


Skeletal Muscle Fiber



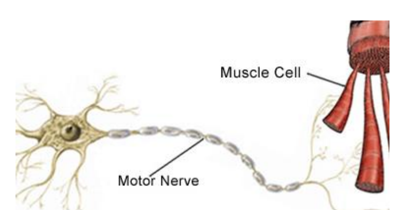
3. **Excitation-Contraction Coupling and Muscle Contraction:** takes place in sarcomeres in every muscle cell; consequently, whole muscle shortens during contraction.
   - For myosin to attach to actin, myosin binding site on actin must be uncovered.
   - Ca^{++} released from SR binds to troponin C complex of troponin molecule causes tropomyosin molecule to roll off the binding sites.
   - Myosin can now bind to actin, forming a cross bridge.
   - Sliding filament theory tells us that myosin molecules "bend" to slide thin filaments over thick filaments during a power stroke.
   - Sliding bridges bring Z lines closer.

The Sliding Filament Mechanism of Contraction.



4. **Actin-Myosin and ATP Cycle:**
   - ATP is split and energizes myosin head.
   - Although myosin head is ready to attach to actin, it can't until myosin binding site is revealed. Requires:
     - AP release Ca^{++} from SR.
     - Ca^{++} bind to troponin C
     - Tropomyosin rolls off myosin binding site.
   - Now myosin binds to actin and power stroke is initiated.
   - Old ADP + Pi released, new ATP binds to myosin, and myosin is now released from actin.
   - Cycle will continue as long as ATP and Ca^{++} are available.

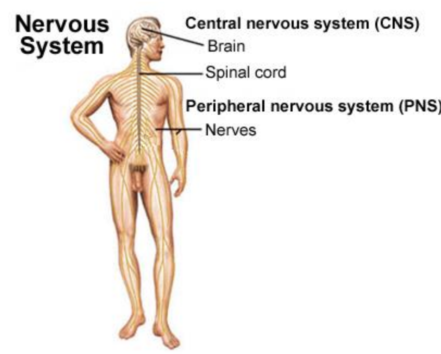
5. **Altering the Force of Contraction:** two ways
   1. **Recruit motor units**
   2. **Summation of Twitch Contractions**: Increase the frequency of AP traveling down the motor nerve.



Module Six: The Nervous System

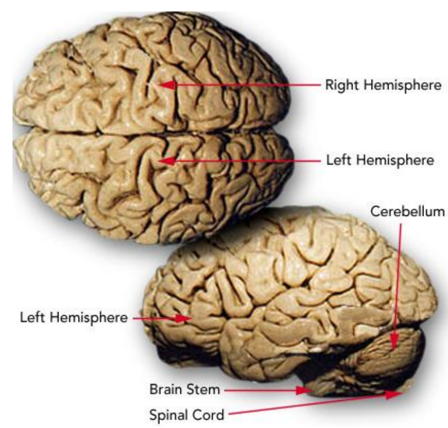
5.1 – Objectives

- ★ Draw and label a diagram of the human brain, showing all the major regions, important gyri and sulci, and the major functional areas of movements, sensory, vision, hearing, speech, and so on.
- ★ Name two main types of brain cells.
- ★ Draw and label a chemical synapse.
- ★ Describe the events underlying synaptic transmission.
- ★ Name the four classes of neurotransmitters.
- ★ Name the main excitatory and inhibitory neurotransmitters in the brain.
- ★ Describe the ionic mechanisms and the changes in membrane potential associated with an excitatory postsynaptic potential (EPSP) and an inhibitory postsynaptic potential (IPSP).
- ★ Define spatial and temporal summation.
- ★ Draw and explain the arrangement of the motor system.
- ★ Define the motor cortex.
- ★ Draw a simple diagram of the corticospinal tract.
- ★ Draw a simplified diagram of a muscle spindle.
- ★ Draw a diagram of the reflex arc for the stretch reflex (for example, knee jerk reflex), and describe the sequence of events in this reflex.
- ★ Describe alpha-gamma coactivation.
- ★ Name three specific functions of the cerebellum.
- ★ Name seven behaviors influenced by the limbic system.
- ★ Name seven major functions of the hypothalamus.
- ★ List the two divisions of the Autonomic Nervous System (ANS).
- ★ Describe the pathways of the Parasympathetic NS (PSYN) and Sympathetic NS (SYN).
- ★ List the functions of the PNS and SNS.



6.2-6.3 – Introduction

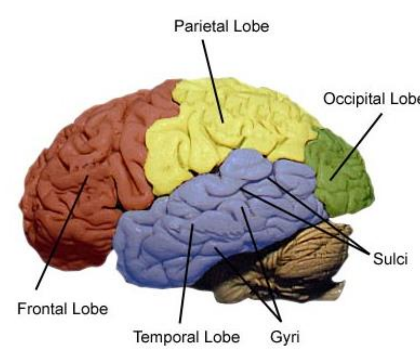
- Nervous system: composed of
  - **Central nervous system (CNS)**: brain & spinal cord.
  - **Peripheral nervous system (PNS)**: nerves outside CNS that go to muscles and organs.
    - **Somatomotor NS**: directed to skeletal muscles.
    - **Autonomic NS**: directed to other organs.
- Facts about brain:
  - Contains 10 – 100 billion cells and weighs ~1.5 kilos (3.5 lbs)
  - If all cells laid out in line = 1000km = 600 miles
  - Have more brain cells when born
  - Action potentials (brain language) travel up to 400 km/hr.



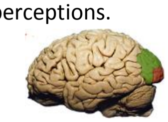
6.4-6.5 – Basic Structure of the Brain

- Has several large anatomical features.
- **Two (2) Cerebral hemispheres:**
  - **Left**: signals muscles on right.
  - **Right**: signals muscles on left.
- **Brain stem:** controls basic functions (ie. heart rate, respiration); midbrain.
- **Medulla:** cont. with spinal cord.
- **Cerebellum:** for coordinated movement; back/posterior and above brain stem.
- **Diencephalon:** consists thalamus & hypothalamus.

- **Surface of brain**
  - Consist of folds (most prominent in humans)
    - **Gyri:** bumps
    - **Sulci:** dips
  - Locations of Gyri and Sulci are very consistent between people (only minor differences with size & shape); given names.
  - Cerebral hemisphere are divided into 4 lobes based on "landmarks".
    - Each lobe has regions with specific functions.



6.6 – Functional Structure of the Brain

- Lateral View:
  - **Frontal Lobe**:
    
    - **Primary Motor Cortex:** processed input from skeletal muscles throughout body.
    - **(Premotor Cortex) Motor Association Area** & **Prefrontal Cortex:** integrate movement info with other sensory inputs to generate perception (interpretation) of stimuli.
  - **Temporal Lobe**:
    
    - **Primary Auditory Cortex** & **Auditory association areas:** receive/process signals from auditory nerve and integrate them with other sensory inputs.
      - **Other portions of Temporal lobe:** olfaction (smell) & mediating short-term memory storage and recall.
  - **Parietal Lobe**:
    
    - **Primary Somatosensory:** (anterior end of parietal lobe) receives input from major sense organs (skin, musculoskeletal system, taste buds)
      - Receives info from opposite sides of body.
      - Sensations of pain, temp., touch, and vibration processed here.
    - **Association areas:** integrate sensory info with other association areas of cortex to form meaningful perceptions.
  - **Occipital Lobe**: area of cerebral cortex for vision
    
    - **Primary visual cortex:** receives input from optic nerve.
    - **Visual Association Areas:** process visual info and integrate with other sensory inputs.
  - **Cerebellum** (structure with largest amount of neurons): processes sensory & coordinates execution of movement in the body
    
    - Receives input from somatic receptors, receptors for equilibrium, and balance and motor neurons from cortex.

- Medial:
  - **Corpus Callosum**: dense bundle of nerve fibers that serve as a pathway between two cerebral hemispheres.
    
    - Connection allows brain to integrate sensory/motor info from both sides of body, allowing coordination of whole-body movement/function.

  - **Diencephalon**: two major units.
    
    - **Thalamus**: receives sensory input as travels from spinal cord, and integrates sensory info before sending it to cortex.
    - **Hypothalamus**: controls a variety of endocrine functions (body temp, thirst, food intake, etc.) mainly by directing hormone release.

  - **Pituitary Gland:** 'regulated' by hypothalamus, and primarily 'regulates' other endocrine organs.
    
    - Anterior is derived from epithelial tissue of pharynx, while posterior derives from neural tissue of hypothalamus.
      - Anterior hormones: LH, FSH, ACTH, TSH, GH, and prolactin.
      - Posterior hormones: vasopressin and oxytocin.
  - **Midbrain** (mesencephalon): bridges lower brainstem to diencephalon; function is to control eye movement and auditory/visual motor reflexes.
    

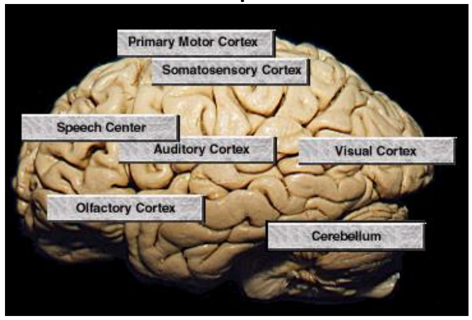
  - **Pons**: acts as a relay station for transferring information between cerebellum and cerebral cortex.
    
    - Along with centers in medulla, also coordinates/controls breathing.

  - **Medulla**: primary control over involuntary functions (ie. breathing, blood pressure & swallowing)
    
    - Fibers from corticospinal tract, which originates in motor cortex, crosses over to opposite side of spinal cord to innervate muscles on the opposite side of body.

- Ventral
  - **Optic chiasma**: optic nerves from both eyes meet here where they cross over and continue on as optic tracts to lateral geniculate bodies of thalamus. From there, axons extend to respective hemisphere on primary visual area of occipital lobe.
    
    - **Brain Stem**: extension of spinal cord, center for many involuntary functions and incorporates 9 cranial nerves; from left-→right on diagram, consist of three regions: **Midbrain, Pons, Medulla**

- Dorsal
  - **Language and Mathematical Area**: most often located in left hemisphere (even for left-handed people); serves as general interpretive center, enabling understanding of visual and auditory information and in turn generates written and spoken responses.
    

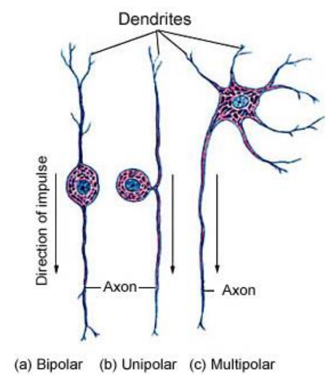
Check point:



6.7 – Neurons and Glial Cells

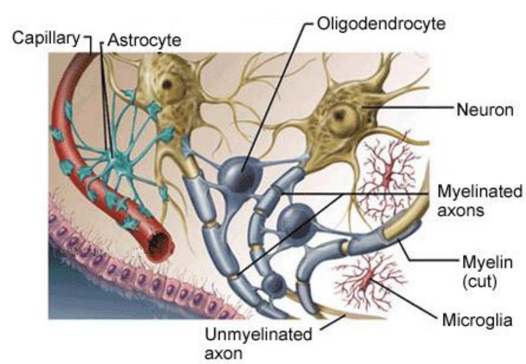
- Brain = 10s of billions of neurons & glial cells.
- **Neurons:** info transmitting and processing cells of the bod (small % of brain).
- **Glial cells:** make up about 90% of brain and provide environment for neurons to function properly

6.8 – Neurons



- Three types, based on number of cell body processes:
  - **Bipolar**: have 2 processes extending from cell body
    - Form of specialized neurons found in retina of eye.
  - **Unipolar**: have 1 process extending from cell body
    - Located outside CNS in peripheral nerves
    - Generally sensory in nature
    - Transmit signals to/from spinal cord
    - Body lies in middle and off to one side of axon
  - **Multipolar**:
    - contain many dendrite branching and 1 axon
    - most common in CNS (neurons seen in Nerve cell module)

6.9 – Glial Cells

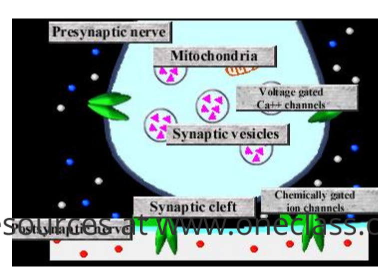


- Support cells of brain: maintain delicate internal environment of CNS.
- Five times as many glial cells as neurons.
- Roles:
  - Structural,
  - Regulate nutrients and specific interstitial environment of brain by regulating passage between blood and brain interstitial space.
- Types:
  - **Astrocytes**
  - **Microglia**
  - **Oligodendrocytes (produce myelin)**

6.10 – The Language of the Nervous System and Neural Coding

- Information travels down axons as action potential (action potential = language of nervous system).
  - Ex. How does brain know if you light vs. heavy object in hand?
    - Special receptors detect pressure on skin, sending AP to brain.
    - **Neural coding**: Weight of object coded in AP (ie. heavier = more AP/sec).
  - Info transmitted from hand along several neurons to brain (requiring neuron-neuron commination).

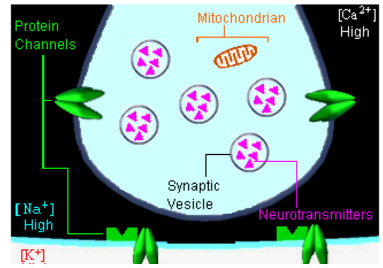
6.11 – Synaptic Transmission: The Chemical Synapse



- Nerve cells communicate by chemical synapse.
  - **Neurotransmitter**: chemical released by (chemical synapse) presynaptic nerve affecting postsynaptic nerve.
  - Structure & process similar to neuromuscular junction, however important differences.

6.12 – Structure of a Chemical Synapse

1. Axon terminal of presynaptic cell:
   - Voltage-gated Ca^{++} channels.
   - Synaptic vesicles containing neurotransmitter (which will have an effect on postsynaptic cell)
   - Mitochondria (production of ATP)
2. Synaptic cleft: forms a gap between two nerves (ie. between presynaptic and postsynaptic)
3. Postsynaptic cleft
   - Chemical receptors
   - Chemically gated ion channels (ligand-gated ion channels).
     - Open when chemical attaches (neurotransmitter in this case).

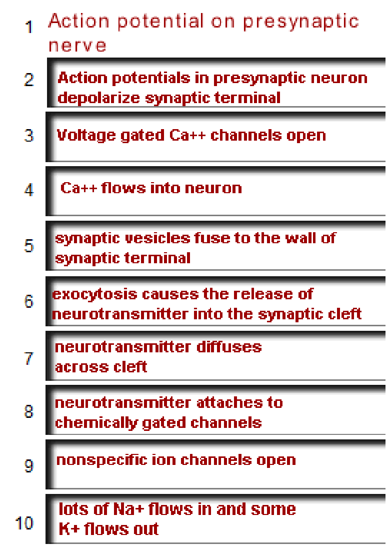


Remember concentrations

6.13 – Sequence of Events at a Chemical Synapse

1. **Presynaptic neurons** synthesize **neurotransmitters** and store in **synaptic vesicles**
2. AP in presynaptic neuron depolarizes membrane, activating **Voltage-gated Ca^{++} channels**; Ca^{++} flow into axon terminal (down gradient).
3. Ca^{++} cause synaptic terminal to fuse synaptic terminal, causing exocytosis and release of transmitter.
4. Neurotransmitter diffuses across cleft and act on postsynaptic cell membrane receptors.
5. Receptors open chemically gated ion channels.
6. Postsynaptic membrane potential changes: depolarization or hyperpolarization depending on neurotransmitter type.
   - Neurotransmitter then breaks down, taken by presynaptic cell to be used again and channels close.

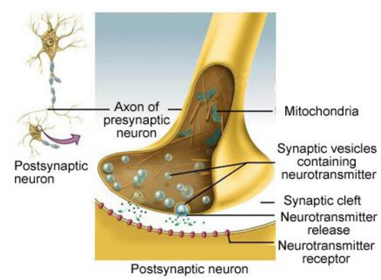
- ➢ Depolarization: increases probability of AP on postsynaptic Neuron
- ➢ Hyperpolarization: decreases probability of AP on postsynaptic Neuron.



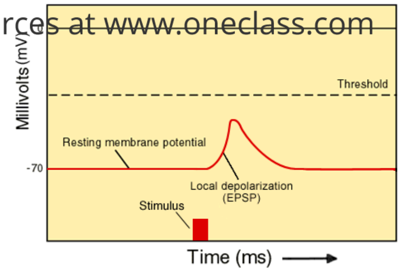
6.14-6.16 – Neurotransmitters

- Chemicals released by neurons at axon terminals.
  - Synthesized in neuron & stored in synaptic vesicles to be released in response to AP.
  - After release, neurotransmitter diffuses across synaptic cleft and produces response in postsynaptic neuron.
  - Depending on neurotransmitter, response may be **excitatory**, leading to **depolarization** of postsynaptic cell.
  - If strong enough, depolarization ***may*** fire AP.
  - Neurotransmitter could produce **inhibitory** response leading to **hyperpolarization** of the postsynaptic membrane, making the AP harder to generate.
- **Four (4) groups according to chemical makeup:**

1. **<u>Acetylcholine (ACh):</u>**
   - Seen before at neuromuscular junction.
2. **<u>Biogenic amines:</u>**
   - Catecholamines
     - Dopamine
     - Norepinephrine
     - Epinephrine
3. **<u>Amino acids:</u>**
   - Excitatory Amino Acids: turn on neuron
     - Glutamate
     - Aspartate
   - Inhibitory Amino Acids: turn off neuron
     - Gamma-amino-butyric Acid (GABA)
     - Glycine
4. **<u>Neuropeptides:</u>**
   - Endogenous opioids (ex. Endorphin)
   - Vasoactive Intestinal Peptide (VIP)

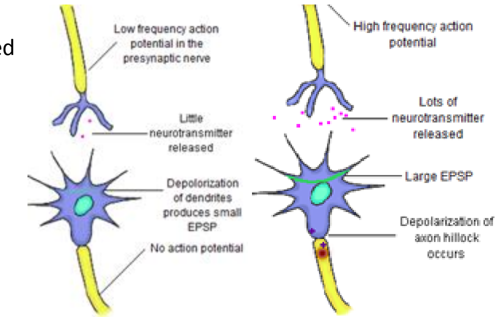


- Chemical synapse similar structure/function to neuromuscular junction (NMJ).
  - IMPORTANT DIFFERENCE:
    - At NMJ, single AP in motor neuron produced a single AP in muscle cell, causing contraction.
    - At Chemical synapse, single AP on presynaptic neuron will NOT produce AP on postsynaptic neuron.
    - How then, do you generate AP on postsynaptic nerve cell?



6.17-6.18 – Ionic Basis of Postsynaptic Potentials—EPSPs and IPSPs

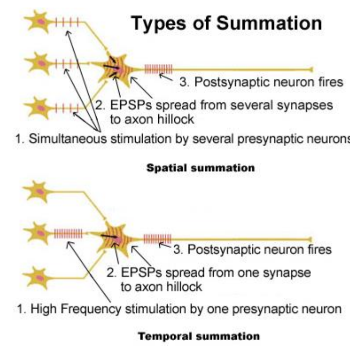
- Neurotransmitter will cause local change in membrane potential of postsynaptic cell.
  - Excitatory or inhibitory → depending on type of released neurotransmitter.
    - **Excitatory** neurotransmitter: cause chem. gated channel to open;
      - Gate selective for **(+) ions**, and will allow influx of predominantly **Na^+** into cell, causing **local depolarization** of membrane called **excitatory postsynaptic potential (EPSP)**
        - EPSP graded potential, is very local & diminishes with time/distance from its point of origin c.
- Na^+ influx depolarizes region of dendrite, but won't fire AP because no **voltage-gated channels** on neuron dendrites/cell body.
- **REMEMBER**: V-Gated channels are essential for production of AP.
  - Action potential begins at the axon hillock where highest concentration of V-Gated channels.
  - To generate AP, EPSP must depolarize axon hillock (see diagram on right).



6.19 – EPSPs

- EPSP gets smaller with travel distance thus to cause sufficient depolarization to open V-gated Na^{++} channels on axon hillock, positive current of EPSP must be strong enough to spread from synapse (origin) to axon hillock.
- Question: how do you make EPSP strong enough? (see dragram #2) →

6.20 – Spatial and Temporal Summation of Synaptic Potentials

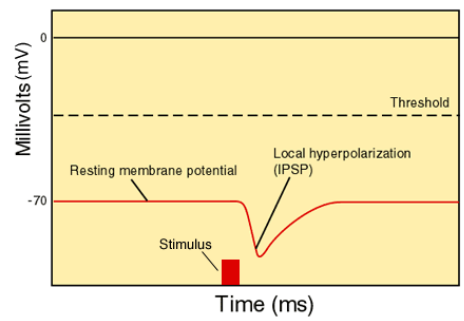


- Differences between EPSP & AP:
  - **EPSP:** occurs on dendrites and cell body, decrease with time/distance traveled.
    - Added one on top of the other, while AP cannot
  - **AP:** usually only found on axon, all-or-nothing.
- EPSP strength increases in two ways:
  - **Spatial summation of EPSPs:** additive effect produced by many EPSPs generated at many different synapses on the same postsynaptic neuron at same time.
  - **Temporal summation of EPSPs:** additive effect produced by many EPSPs generated at same synapse by series of high-frequency **AP** on presynaptic nerve.

6.21 – Spatial Summation

- Since postsynaptic nerves can receive 1000s of synapses from other nerves, EPSPs at different synapses can be simultaneously added to produce large depolarization.
  - When depolarization reaches axon hillock, V-gated channels reach threshold and fire AP.

6.22 – Temporal Summation



- Summing of series of consecutive EPSPs generated by set of high-frequency AP.
  - When depolarization reaches axon hillock, sufficient number of V-gated channels reach threshold and fire AP.
- **NOTE:** spatial and temporal summation possible in both IPSPs and EPSPs (rather than stronger depolarization's, summation of IPSPs produce larger hyperpolarization)

6.23-6.24 – Inhibitory Postsynaptic Potentials—IPSPs

- **Inhibitory neurotransmitters:** shuts off nerve cell.
  - Neurotransmitters create hyperpolarization called Inhibitory postsynaptic Potentials (**IPSPs**).
    - Hyperpolarization created by opening different chemically gated channels that, depending on neurotransmitter type, will either let Cl^- into cell or let K^+ out (same effect = make membrane potential negative).
    - Hyperpolarization moves membrane potential away from threshold, making less chance of firing AP (shuts off nerve).

6.25 – EPSPs and IPSPs—Synaptic Integration

- Any 1 postsynaptic nerve can receive 100,000s of synapses; some produce EPSPs, others IPSPs (ie. postsynaptic cell could have EPSPs and IPSPs occurring simultaneously)
  - Does cell depolarize and fire AP, or hyperpolarize and shut off?
    - Depends on # of postsynaptic potential. If EPSPs >> IPSPs, fires AP. If IPSPs >> EPSPs, cell shuts off.
    - "Battle" of postsynaptic potential is called **synaptic integration**.

Given the following situations, which one is likely to produce an action potential in the postsynaptic neuron? More than one box may be correct.

Correct - you answered DE

A) one action potential (AP) in a presynaptic nerve producing one EPSP in the postsynaptic neuron
B) 10 EPSPs and 10 IPSPs on the postsynaptic neuron
C) 100 IPSPs/second on the postsynaptic neuron
D) 100 EPSPs/second on the postsynaptic neuron
E) 100 APs/second in an excitatory presynaptic neuron

6.26 – Quick Review

- AP=language of nervous system; generated at axon hillock by strong depolarization opening V-gates.
- Initiated →Travel axon to axon terminal → AP triggers Ca^{++} influx into cell → synaptic vesicles release neurotransmitter
  - Excitatory NT opens Na^{++} channels = Depolarization of postsynaptic membrane → EPSP
  - Inhibitory NT = hyperpolarizes postsynaptic membrane → IPSP.
    - EPSP & IPSP can occur on same neuron and spatially or temporally summed.
    - Synaptic integration is the interaction of many IPSPs and EPSPs.
    - Summation of EPSPs = AP production at axon hillock of postsynaptic cell.

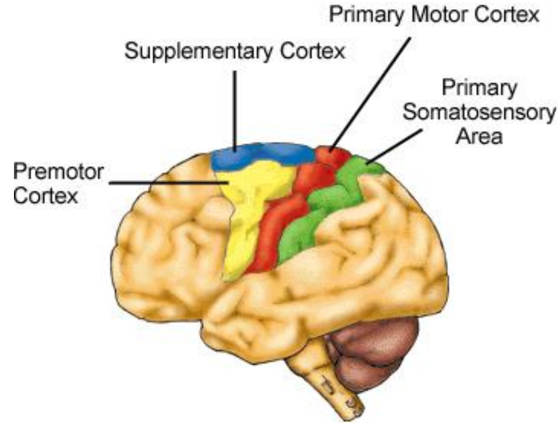
Which of the following characteristics are shared by both IPSPs (inhibitory postsynaptic potentials) and EPSPs (excitatory postsynaptic potentials)?

Correct - you answered E

A) Neurotransmitters are involved in their production.
B) They both can undergo temporal summation.
C) They will both decrease in size with time and distance from the point of production.
D) They both can undergo spatial summation.
E) All the above are shared by both EPSPs and IPSPs.

6.27 – The Somatic-Motor System: Introduction

- How brain controls muscles to perform voluntary movements; areas of brain responsible for activating muscles; spinal tracts that end info to muscles; and how muscles send sensory info back to brain about their position.
  - Key brain section: primary motor complex.



6.28 – Basic Structures and Organization

- Motor system includes:
  - <u>**Premotor area**</u>
  - <u>**Supplementary motor area**</u>
  - <u>**Primary motor cortex**</u>
  - **Basal ganglia**
  - **Spinal pathways**
  - **Motor nerves** going to muscles
  - **Muscle receptors**
- **Proprioception:** special receptors in muscles send info to brain concerning limb position.

6.29-6.31 – Structure and Organization of the Motor System

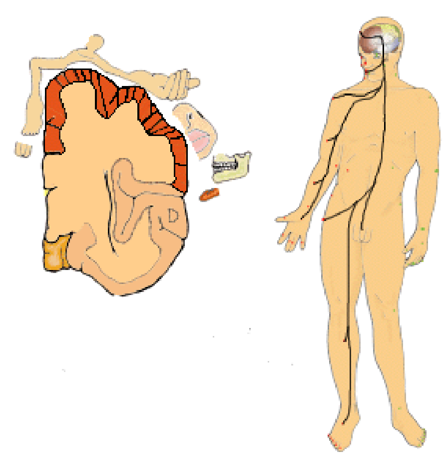
6.29– The Premotor Cortex

- ***Develops*** appropriate motor sequences.
- Example: picking up coffee
  - See coffee (Sensory info)
  - Wish to pick up coffee, ie. thought = **Prefrontal cortex**
  - Signal then passes through **premotor complex** in frontal lobe, which develops strategy for req. movements.
  - Ex. Arm must extend before the hand closes around handle.
- Damage to this area causes wrongful strategy for req. movements of a task.
- After sequence of muscle contractions developed, info travels to **Supplementary cortex**

6.30 – The Supplementary Motor Cortex

- ***Programs*** appropriate motor sequences.
  - Area important for programming muscles to open/close hand and for repetitious movement, since can be complex
    - More complex/repetitive = more supplementary motor area is needed.
  - People with lesions/damage to supplementary cortex try to pick something up, hand assumes awkward position ad it reaches.
    - They are unable to orient hands/digits properly.
  - After program is written, info travels to **Primary Motor Complex.**

6.31 – The Primary Motor Cortex



- **Activates neurons** that will eventually active the appropriate muscles.
- Located in a specific manner on **precentral gyrus** in **frontal lobe**.
  - Like entire body is projected on brain like map.
  - **Homunculus:** topographical representation of body on surface of cortex.
- Medial (midline) → lateral: foot, ankle, knee, thigh, trunk, shoulder, elbow, wrist, hand, fingers (lots of room), face, lips, jaw, tongue.
- Signals from primary motor complex travel down spinal cord through corticospinal tract.

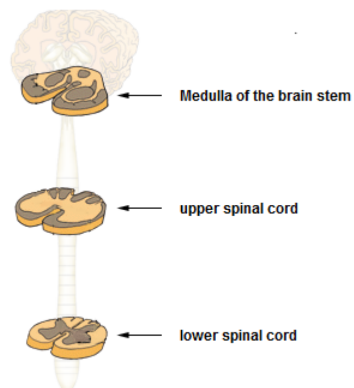
6.32 – Corticospinal Tract

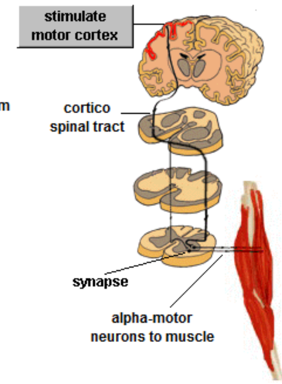
- **Major motor pathway from**: Primary Motor Cortex → Motor Neurons that innervate muscle cells.
    - Made up of millions of axons with cell bodies in primary motor cortex

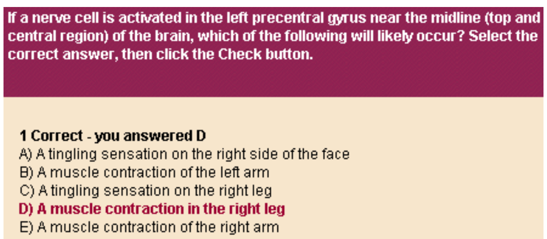
Fiber Pathway/Tract

Motor cortex → **Brain stem (medulla)** → **Spinal cord** and **Synapse w/ Motor neurons** → Innervates muscle

- In **medulla** of brain stem:
    - 80% of all nerve fibers cross to **contralateral** side of body
    - 20% on **Ipsilateral** side
- Once reach level of spinal cord where they synapse with motor neurons, fibers on **ipsilateral** side **cross to contralateral** side.
    - Directly innervates muscle.
        - Nerves that activate muscles in arm/upper-body end up in upper spinal cord.
        - Neurons that activate muscles in legs/lower-body end up in lower spinal cord



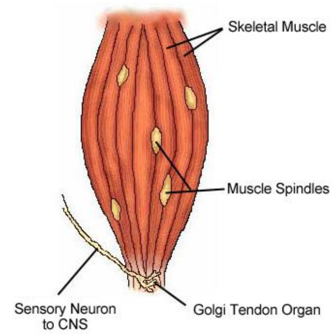



If a nerve cell is activated in the left precentral gyrus near the midline (top and central region) of the brain, which of the following will likely occur? Select the correct answer, then click the Check button.

1 Correct - you answered D
A) A tingling sensation on the right side of the face
B) A muscle contraction of the left arm
C) A tingling sensation on the right leg
D) A muscle contraction in the right leg
E) A muscle contraction of the right arm

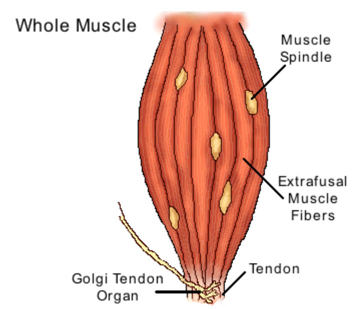
6.33 – Muscle Receptors

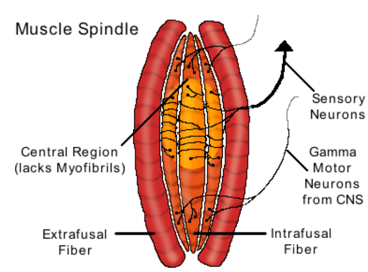
- **Proprioception** ("muscle sense"): Important for the brain to be aware of limb positions and extent of each muscle contraction at all times.
    - Almost all muscle movements are made without consciously following them with your eyes to make sure they are being performed accurately.
    - **Possible due to presence of special receptors in muscle** which send signals back to brain:
        1. **Muscle spindles**: detect muscle stretch, length, and the rate of change in length.
        2. **Golgi tendon organs**: detect muscle tension



6.34 – Muscle Spindles

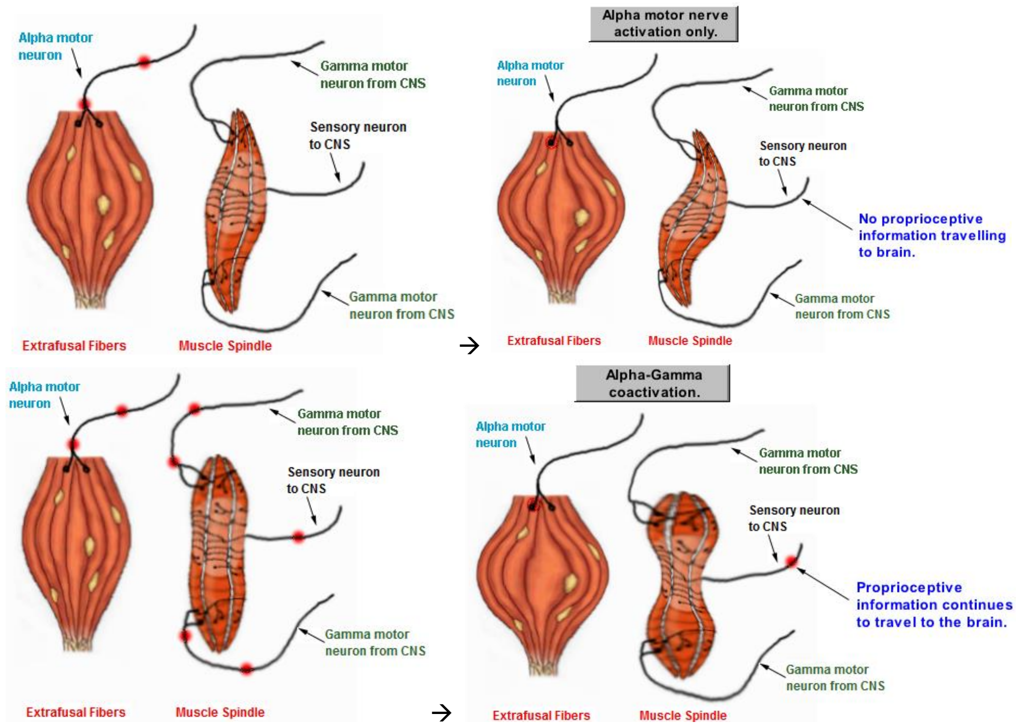
- In **whole muscle** and adjacent to the real contractile muscle cells (**extrafusal fibers),** are sensory organs/receptors called **Muscle Spindles**:
    - Sense the length/stretch of muscle.
    - Consists of:
        - **Intrafusal muscle fibers**
        - **Central sensory region**
        - **2 sets of gamma motor neurons**: activate the intrafusal fibers
        - **Sensory neuron**: originates in the sensory region.
- When whole muscle stretches, spindle sensory region stretches.
    - Sensory region is sensitive to changes in shape so:
        - Depolarizes → triggering AP in sensory nerve → signals brain
    - (Stretched Muscle) ∝ (Stretched Sensory) ∝ (Depolarization) ∝ (AP sent back to CNS)
    - Brain receives information and interprets how stretched muscle is and since attached to a limb, it will "know" position of the limb in space (**proprioception)**



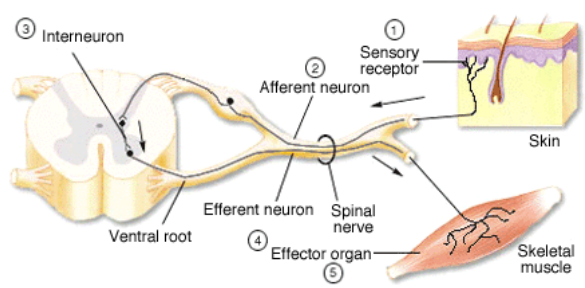


6.35 – Alpha-Gamma Coactivation

- Signals sent from spinal cord (through alpha motor neurons) → whole muscle (like the biceps), causing contraction.
  - **Extrafusal muscle fibers** contract.
  - Intrafusal muscle fibers within **muscle spindles** go slack and info from muscle spindle stop.
- To keep intrafusal muscle spindles operating (in sensitive range) during contraction, commands are simultaneously sent through **gamma motorneurons** to **intrafusal fibers**.
  - Causes contraction of intrafusal fibers, maintaining stretch on the central region (where stretch receptors are located) at same rate as whole muscle.
  - Therefore, during contraction, **alpha-gamma coactivation** ensures muscle spindles continue to send information to the brain about muscle and limb position.



6.36 – The Reflex Arc

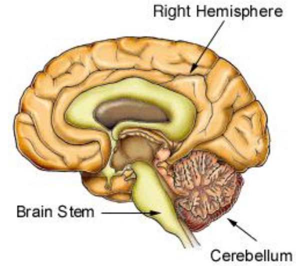


- **Reflex arc:** most basic integrated neural activity type.
  - Requires:
    - **Sensory receptor**
    - **Sensory/afferent neuron**
    - **Motor/efferent neuron**
    - **Effector organ** (like muscle)
    - 1+ **Synapses** (generally in the spinal cord)
    - and may contain 1+ **Interneurons**
  - Begins in **receptor** with a receptor potential producing AP in the **afferent neuron**, AP enters spinal cord producing APs on **interneurons** and, eventually, on **efferent neuron** which **activates effector** (ie. muscle).
  - **Note**: reflex arc does not require output by brain to cause the muscle (effector) to contract

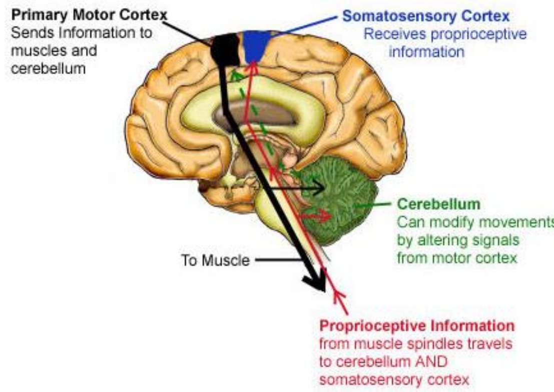
6.37– Stretch Reflex

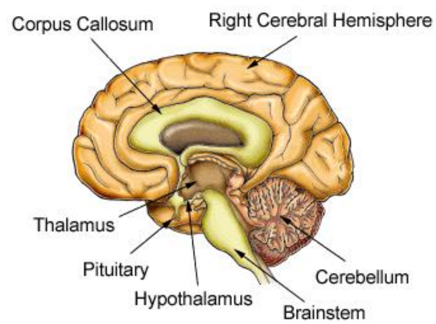
- Example of reflex arc: stretch reflex in the quadriceps muscle (can be found in all muscles)
  - **Sequence of events**:
    1. Tapping tendon produces very small stretch of the quadriceps muscle
    2. Stretching also stretches muscle spindles
    3. Muscle spindles trigger AP in the afferent neuron → enters spinal cord
    4. Quadriceps motor nerve activated, while hamstring muscles inhibited
    5. Quadriceps contract, hamstring relaxes; lower leg kicks out.

6.38-6.39 – Cerebellum



- Cerebellum ("little brain" = partly accurate): smaller than brain, contains more neurons than the rest of the brain combined.
    - **Functions**
        - Contributes to accurate limb movements
        - Corrects ongoing movement
        - Modifies reflex strength
        - Involved with classical Pavlovian conditioning, learning muscle movement, and **vestibular occular reflex** (VOR)—one of our important eye movements.
- How cerebellum generates accurate movements and corrects ongoing ones:
    - For cerebellum to assist and correct limb movement, it must receive info from two different sources:
        - Must receive same info from **motor cortex** that is traveling out to the muscles being activated; and
        - Must receive information with position of the limbs in space (**proprioception**).
    - Cerebellum compares actual signal from brain with proprioceptive info from muscle itself, making sure muscle is doing what it should
        - If incorrect, cerebellum modifies signals from primary motor cortex.

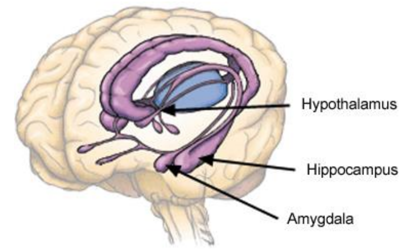




6.40-6.44 – The Limbic System and the Hypothalamus

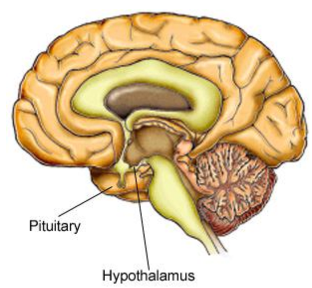
- Hypothalamus: component of limbic system.
- Limbic system's structure and function.
  - **Limbic system**: emotional center within brain
    - **Hypothalamus**: key role in homeostasis and the control and release of some hormones.
  - Stimulation of hypothalamus/limbic system may elicit normal behaviors:
    - ie. eating, drinking, locomotion, autonomic responses (including heart rate changes and blood pressure), attack responses, sexual behaviors, and memory.
  - Both regions together coordinate autonomic, hormonal, and motor effects associated with constant maintenance of internal environment and coordinating emotional behavior.

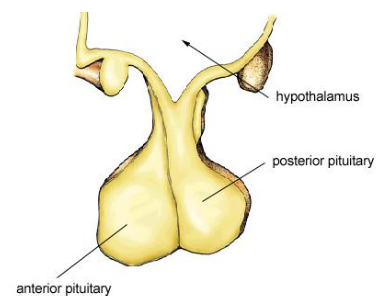
6.41 – Limbic System



- Limbic system composed of:
  - **hypothalamus**
  - **amygdala**
  - **hippocampus**
  - **cingulate cortex**
  - **septum**
- Most Limbic System structures found deep within brain forming ring around brain stem.
- **Key function**:
  - Link higher thought processes with primitive emotional responses (ie. fear, rage, and sexual pleasure).
  - Involved with behaviors dealing with feeding, drinking, pain, motivation, and learning.
  - Overall, limbic system allows us to correctly respond to changes in our environment.

6.41-6.42 – The Hypothalamus

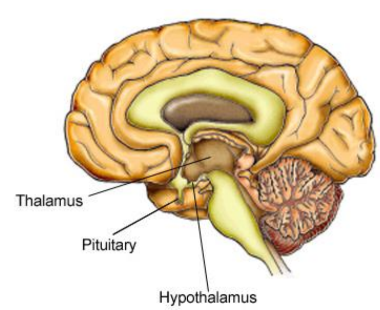




- Located at the base of brain, anterior to brain stem.
- Responsible for many important functions.
  - Temperature control
  - Body water regulation
  - Regulation of food intake
  - Cardiovascular regulation
  - Regulation of the circadian clock
  - Coordination of emotional behaviors
  - Control of hormones released from the anterior and posterior pituitary gland.
- **Performs most of these functions through negative feedback control**.
- Example: body temperature.
  - If the body temperature (set at 37°C, or 98.6°F) were to rise to 39°C (or 102.2°F), hypothalamus would detect change and initiate mechanisms to return the temperature to normal.
    - Mechanisms include diverting blood to the skin and sweating, both leading to cooling.

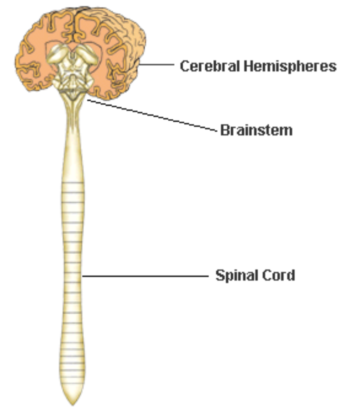
6.44 – The Pituitary Gland

- One of the smallest yet most important parts of the brain.
- In humans, roughly size of a large pea, hangs below the hypothalamus.
- Very important in control/release of hormones and is regulated by the hypothalamus.



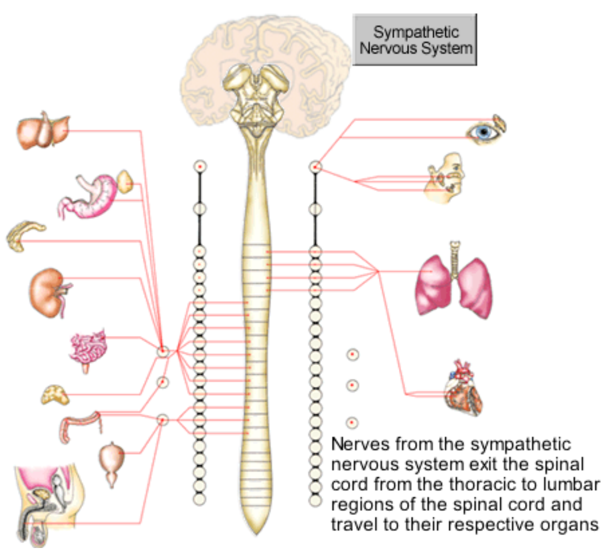
6.45-6.48 – The Autonomic Nervous System

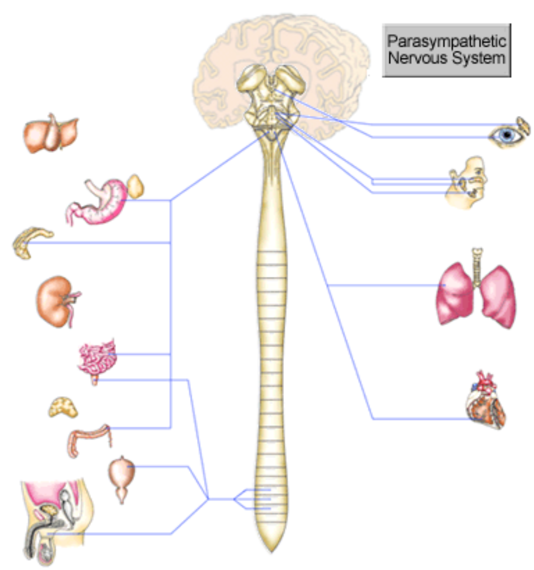
- Unlike the somatomotor system, not under voluntary control.
- Can be considered "automatic" system.
    - Controls heart rate, pupils, smooth muscle in walls of arteries/veins, glands like the adrenals, and many other organs.
- Two divisions of the ANS:
    - Sympathetic (SYN) nervous systems:
        - responsible for activating body functions involved in fight or flight situations.
        - when activated, will increase heart rate and blood pressure, dilate airways and blood vessels to the muscles, and shut down digestive system
    - Parasympathetic (PSYN) nervous systems
        - responsible for storage and conservation of energy
        - functions associated with rest and relaxation
        - system would slow heart rate and lower blood pressure



6.46 – Pathways of the ANS

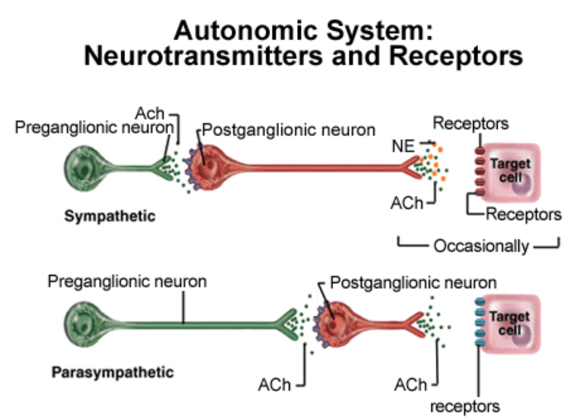
- Both SYN and PSYN send neurons to each of the organs shown (except adrenal, which only receives input from SYN).
- One division of the ANS excites organ, while the other inhibits.
- Nerves of the SYN exit spinal cord in thoracic and lumbar (central) regions of the cord.
    - These preganglionic neurons synapse in ganglia onto second postganglionic nerve that will travel to the effector/target organ of interest.
- Nerves of the PSYN exit at brain stem and very lower sacral region of the spinal cord.
    - These preganglionic nerves synapse onto postganglionic nerve very near effector organ of interest, nerve then synapses onto the target organ.





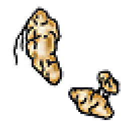
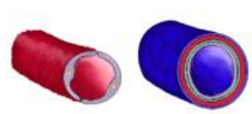
6.47 – Neurotransmitters of the ANS

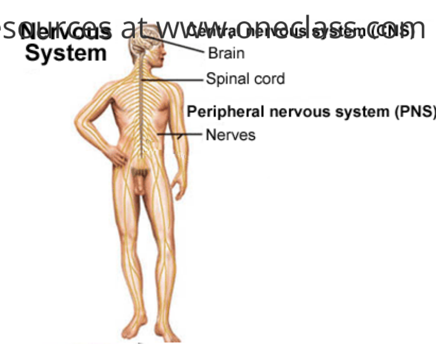
- Preganglionic neurons that leave spinal cord in SYN and PSYN release neurotransmitter acetylcholine (ACh).
    - axons of PSYN preganglionic fibers are longer since synapse occurs closer to the effector organ.
    - The ACh will then stimulate second postganglionic neuron.
- Neurotransmitter released by sympathetic postganglionic neuron onto target organ is usually norepinephrine (NE), but in some cases ACh.
- Neurotransmitter released by parasympathetic postganglionic neuron is always ACh.



6.48 – Functions of the ANS

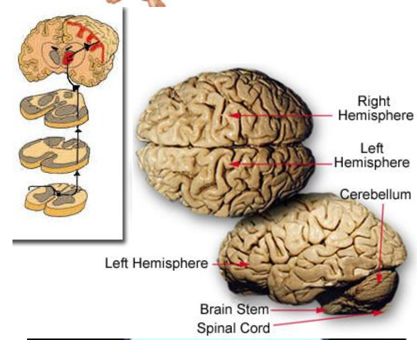
- SYN and PSYN effects on target organs are usually opposite.
- Where the SYN activates system, the PSYN will inhibit it—or vice versa.

Organ	ANS function		Picture
	Parasympathetic Response (PSYN)	Synpathetic Response (SYN)	
Adipose (fat) tissue	No effect	Stimulates lipolysis (fat breakdown) - Increases free fatty acids in blood to be used as a source of energy	
Adrenal Glands	No effect	Increased secretion of epinephrine (adrenaline) - increase cardiac output	
Lungs	Bronchioles constrict	Bronchioles dilate - lets more air into alveoli	
Salivary Glands	Watery saliva	Thick mucus saliva - dry mouth	
Pupils	Constrict	Dilate – lets more light in	
Heart	Heart rate slows	Heart rate and forse of contraction increase - cardiac output increases	
Kidney	No effect	Increased secretion of renin - stimulates RAS to increase blood pressure	
Bladder	Release of urine	Retention of urine	
Digestive system	Increased activity of igestive tract – motility and enzyme secreations	Decreases activity of digestive tract – motility and enzyme secreations - blood flow diverted to working muscles	
Blood Vessels, Arterioles, Veins	No sigificant changes	Constriction in non-exercising organs and dialation in skeletal and cardiac muscle - increase blood flow to working muscles	

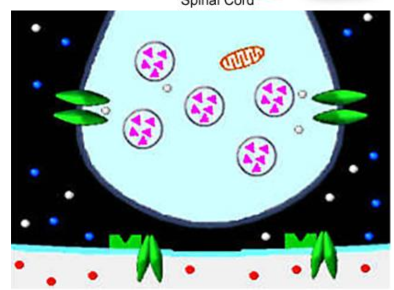


6.49-6.54 – A Quick Look Back

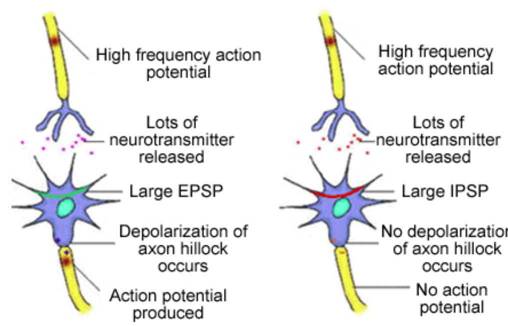
- Dealing with biological system that is constantly taking in external sensory information, processing it within the CNS, deciding what to do with that information, and then taking some form of action.
- Language of the CNS: action potential.
    - A strong sensory signal translated into high-frequency action potentials and not into larger action potentials (you will recall that APs are all or nothing—they cannot get bigger).



- Should be quite familiar with basic structure, lobes, and functional areas of the brain.
- Know the structure of the nerve and chemical synapse.
    - Chemical synapse is very similar to the neuromuscular junction. Review both of these.
    - Have a good understanding of all the ascending and descending pathways into and out of brain.



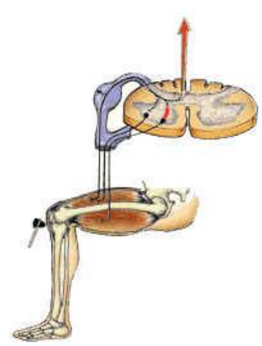
- Sequence of events at a chemical synapse:
    1. **Presynaptic neurons** synthesize **neurotransmitters** and store in **synaptic vesicles**
    2. AP in presynaptic neuron depolarizes membrane, activating **Voltage-gated Ca^{++} channels**; Ca^{++} flow into axon terminal (down gradient).
    3. Ca^{++} cause synaptic terminal to fuse synaptic terminal, causing exocytosis and release of transmitter.
    4. Neurotransmitter diffuses across cleft and act on postsynaptic cell membrane receptors.
    5. Receptors open chemically gated ion channels.
    6. Postsynaptic membrane potential changes: depolarization or hyperpolarization depending on neurotransmitter type.
        - Neurotransmitter then breaks down, taken by presynaptic cell to be used again and channels close.



- Excitatory neurotransmitter like acetylcholine causes depolarization that leads to excitatory postsynaptic potential (EPSP).
    - With spatial and temporal summation, many EPSPs can add together to produce an action potential at the axon hillock.
- Inhibitory neurotransmitter causes postsynaptic membrane to hyperpolarize and produce an inhibitory postsynaptic potential (IPSP).
    - Shuts off postsynaptic cell and not allowing it to produce an action potential.
- Only EPSPs and IPSPs will travel over the dendrites to the axon hillock, while action potentials only occur on the axon of a nerve.

Should be able to distinguish each and explain how and where each occurs:

- Resting membrane potentials are found on all excitable cells.
- Equilibrium potentials for each ion (Na, K, Cl) of a resting nerve cell.
- Action potentials occur on the axon of all nerve cells and over muscle cell membranes.
- EPSPs and IPSPs occur on the dendrites of neurons in the CNS.



- The motor system includes: supplementary motor cortex, premotor area, the motor cortex, basal ganglia, spinal pathways, motor nerves to the muscles, and muscle spindles.
- Its primary function activating muscles in well-coordinated and accurate manner to make specific voluntary movements.
- Portions of the motor system are also required for reflexes.
- Special muscle receptors responsible for detecting the stretch of the muscle (**muscle spindles**) and for determining the amount of tension that the muscle is generating (**Golgi tendon organs**).
    - Both of these receptors are involved with involuntary reflexes. Muscle spindles play an important role in the stretch (tendon tap) reflex.

Module Seven: The Nervous System

7.1 – Objectives

- ★ Define a sensory receptor and its adequate stimulus.
- ★ List four characteristics of generator potentials.
- ★ List the receptors responsible for touch, vibration, temperature, pain, and proprioception (limb position and movement).
- ★ Define receptive field of a neuron. Name the two major ascending sensory pathways and describe their anatomy and the information they carry.
- ★ List the somatotopic organization on the postcentral gyrus (somatosensory area), going from medial to lateral on the cortex.
- ★ Draw and label a picture of the visual system and the eye.
- ★ List the cell types in the retina and draw a diagram of their anatomical arrangement.
- ★ List the functional characteristics of the rod and cone systems.
- ★ Draw a flow diagram of the sequence of steps in the retina by which light is transduced to action potentials.
- ★ List four types of eye movements, describe when they occur, and describe their overall function.
- ★ Draw a simple diagram of the auditory system.
- ★ List three ways in which the outer and middle ear act to transmit pressure waves from air to fluid.
- ★ Describe how different frequencies of sound are transduced into action potentials.
- ★ Draw a simple diagram of a single semicircular canal with hair cells and cupula and the utricle and saccule with otoliths.
- ★ List the major functions served by the vestibular system.
- ★ Name the movement detected by the semicircular canal receptors and the two detected by the otolith organs.
- ★ Describe how angular motion of the head is transduced into action potentials.

7.2 – Introduction: Changes to the Sensory System

- Essential for body to maintain homeostasis (maintenance of relatively stable conditions in the internal environment).
  - To do this it is necessary for body to detect changes in external environment to react appropriately to maintain its internal environment.
- Human body has several sensory systems allowing it to detect external changes rapidly:
  - somatosensory (touch) system
  - visual system
  - auditory & vestibular system,
  - olfactory (smell) system
  - gustatory (taste) system
- Will look at how outside world events are
  - detected → action potentials → travel to brain → become consciously perceived
- Will examine most of sensory system of the body (with exception of smell/taste), structure, function, and pathways to the brain.

7.3 – Transduction of Environmental Information

- **Transduction of environmental** information: how information from external environment is turned into language the brain understands—action potentials.
- For brain to know what is happening outside, **environmental stimuli** (energy) like light, heat, touch, or sound is detected by **sensory receptors**, then info convert into action potentials.

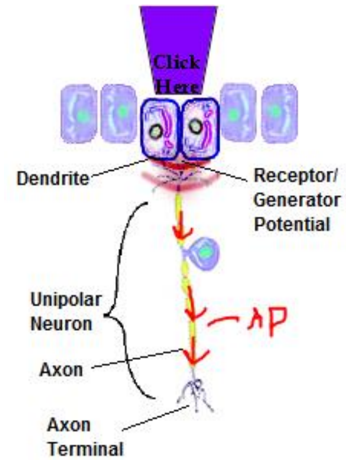
7.4 – Environmental Stimuli

- For the brain to consciously perceive **environmental stimulus**, stimulus must be detected by a **sensory receptor**.
- Environmental stimuli come in different forms, therefore, require different receptors.
  - Examples:
  - **Mechanical stimulus** (touch, vibrating, sound, pressure, proprioception/muscle sense):
    - Stretch **sensory receptors** in skin → open ion channels → depolarize S. neuron → AP
  - **Chemical stimulus** (sour taste or odor):
    - Binds with receptor → depolarization → AP.
  - **Light energy (EM)** absorbed by **photoreceptors** of the eye (rods and cones in the retina) and eventually produces action potentials.
  - **Gravity and motion** can also be detected by hair cells in vestibular system, which convert this form of external stimulus to action potentials.

7.5 – Adequate Stimulus for the Receptor

- Some receptors can detect more than one type of stimulus.
- **Adequate stimulus** is an **environmental stimulus** to which sensory receptor is **most sensitive**.
  - Adequate stimulus for rod/cone cells in retina = light.
- Sensory receptors respond to other forms of energy but not in an optimal way.
  - Example: rod/cone cells also respond to pressure on the eyeball

7.6-7.7 – Receptor (Generator) Potentials



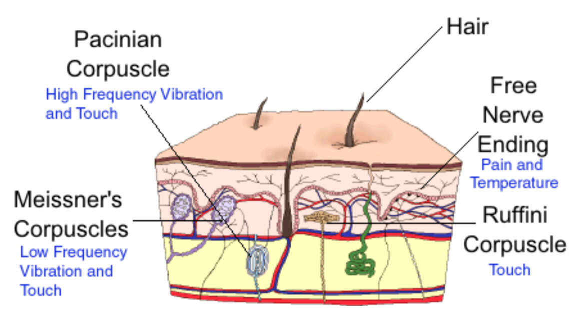
- Chemical synapse:
  - Excitatory neurotransmitter first produces EPSP that, if strong enough, *then* generates AP at the axon hillock. (Similar to events that take place at a sensory receptor)
- Once sensory receptor is stimulated by environmental stimulus, it will cause a change in ion permeability, leading to a local depolarization (**generator** or **receptor potential**).
  - Since receptor DOESN'T have voltage-gated ion channels to fire AP, receptor potential spreads to area on sensory neuron that does contain these channels (usually at **first node of Ranvier** on the axon).
  - AP is then generated/propagated along axon into spinal cord.
  - Depolarization in receptors with no axons (ie. hair cells in inner ear) must spread to synapse to release a neurotransmitter.
- Receptor potentials are similar to EPSPs and IPSPs and sharing some characteristics including:
  - Generally depolarizing but can hyperpolarize as well
  - Caused by increased permeability to Na^+/K^+ in case of hyperpolarizing stimulus.

7.8 – Receptor Potentials and Neural Coding

- **Neural coding** informs brain of weight of an object in hand.
  - Weight of the object "coded" into the Aps (heavier object = more AP per second).
  - How to generate large number APs: heavier trigger receptor to produce a large receptor potential.
    - Large receptor potential triggers many action potentials on sensory neuron's axon. This burst of high-frequency AP reach brain where you become consciously aware of weight.

7.9 – The Somatosensory System

- Somatosensory system detects/processes sensations of: touch, vibration, temperature, and pain (majority originates in skin).
  - Detecting each sensation requires several different sensory receptors within the skin, each developed to detect its adequate stimulus.
  - The receptors in the skin are collectively referred to as *cutaneous receptors*.
  - Include:
    1. **Hair follicle** receptors: fine touch/vibration
    2. **Free nerve endings**: pain/temperature (hot and cold)
    3. **Meissner's corpuscles**: low-frequency vibrations (between 30 and 40 cycles/sec) and touch
    4. **Ruffini's corpuscles:** touch
    5. **Pacinian corpuscles**: high-frequency vibrations (250 to 300 cycles/sec) and touch

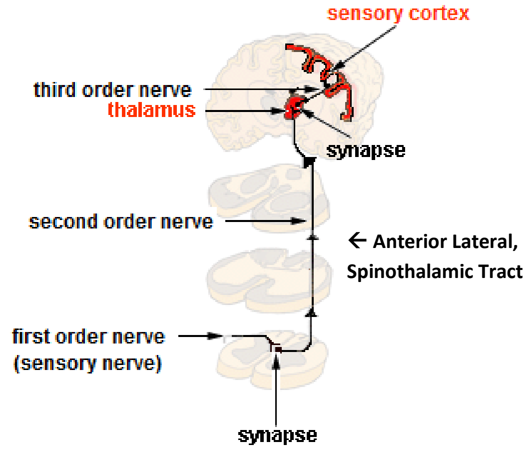


7.10 – Receptive Field

- Each receptor will only respond to a stimulus within a certain region on the skin.
- **Receptive field:** area on surface of the skin where adequate stimulus will activate a particular receptor to fire an AP in neuron.
  - Any stimulus applied outside the receptor field will not generate an action potential.
- Action potentials have been generated in the sensory nerve, they must be propagated to a specific area of the brain so that the individual becomes consciously aware of the stimulus.
- Action potentials reach the brain via two spinal tracts:
  - Spinothalamic (Anterolateral) Tract
  - Dorsal Column, Medial Lemniscal System

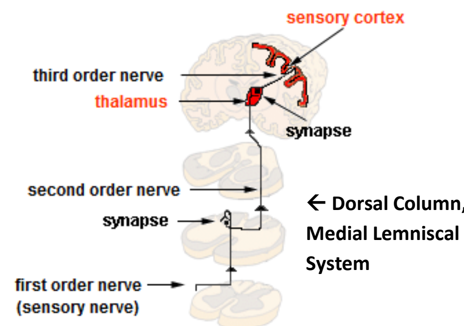
7.11-7.12 – Somatosensory Pathways from the Periphery to the Brain

7.11 – Spinothalamic (Anterolateral) Tract



- The spinothalamic (anterolateral) tract: transmits info of basic sensations (pain, temperature, crude touch).
  - **Sensory neuron (first order neuron)** info enters **spinal cord** where it synapses with **second order neuron**. Neuron **crosses** to opposite/contralateral side of spinal cord, ascends to region brain **thalamus** (acts as a **relay station** for sensory info except smell). **Second synapse** with **third order neuron** occurs here, then traveling to **somatosensory cortex**.
- NOTE: Sensory *information from the one side of the body goes to the opposite side of the brain*.

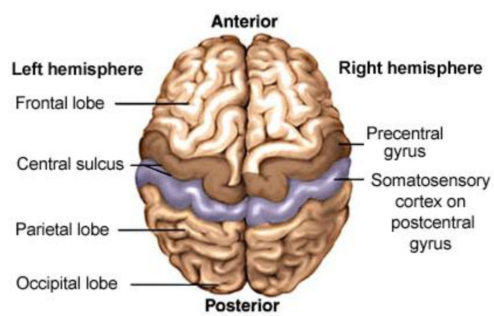
7.12 – Dorsal Column, Medial Lemniscal System



- The dorsal column, medial lemniscal system transmits info of advanced sensations/fine detailed touch, proprioception (muscle sense), and vibration.
- Info from **sensory neuron (first order neuron)** enters **spinal cord** and **immediately** travels up the spinal cord *before* crossing to contralateral side (unlike the spinothalamic system). In upper spinal cord, sensory neuron synapses with **second order neuron** and **crosses** to opposite side of spinal cord. Then continues to **thalamus** and **synapses** again onto **third order neuron** that travels to **somatosensory cortex**.

7.13 – Primary Somatosensory Cortex

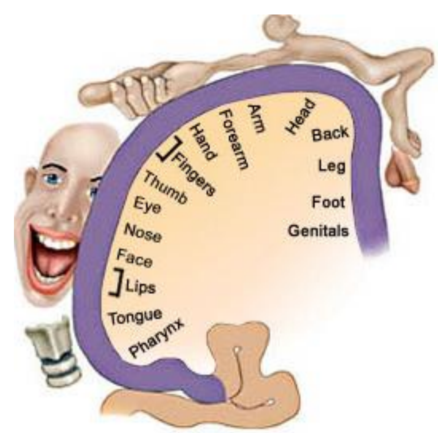
Primary Somatosensory Cortex, Superior View



- Once sensory info reaches brain, travels to **primary somatosensory cortex** (in **parietal lobe** on the **postcentral gyrus** behind the **central sulcus)**.

7.14-7.15 – The Somatosensory Homunculus

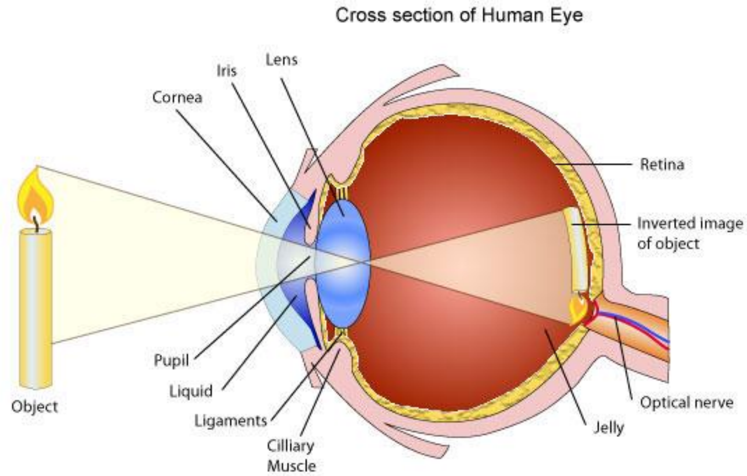
- Primary somatosensory cortex specific arrangement
  - The sensory information arriving at cortex is not randomly scattered around on surface;
    - Is "**geographically preserved**."
  - As if the entire body were projected onto the surface of the brain like a map.
  - **Somatosensory homunculus**: topographical representation of the body on the surface.
    - Some of the representative areas are out of proportion (much larger than should be = require more of the brain to process that information).
    - Hands, tongue, and lips = most sensitive = more sensory receptors than any other parts



7.16 – The Visual System

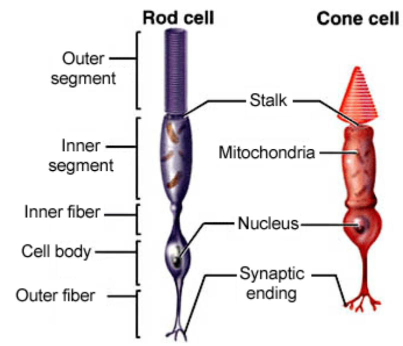
- Light Detection → Action potential → Primary visual areas for processing → Conscious interpretation.
  - **Eye** (photoreceptors: light → AP)
  - **Visual pathway** (transmits AP)
  - **Primary visual area** in **occipital lobe** of the brain (processes AP)

7.17 – The Eye



- Like a camera.
  1. Passes through **cornea**
  2. **Iris** regulates light (constrict in bright or dilate in dim)
  3. **Lens** flips light (upside down and backwards) and focuses it onto **retina** at back of the eye
     - Retina: photoreceptors (rods and cones) pointing toward back of head.
  4. Center of vision focused onto **fovea** (part of retina): highest concentration of cone cells.

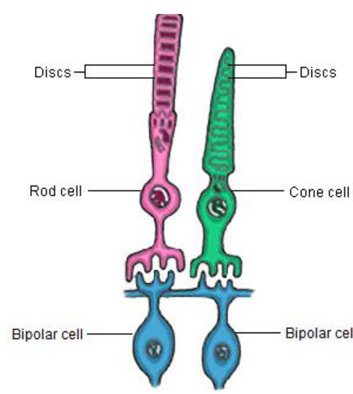
7.18 – The Photoreceptors of the Eye—Rod Cells and Cone Cells

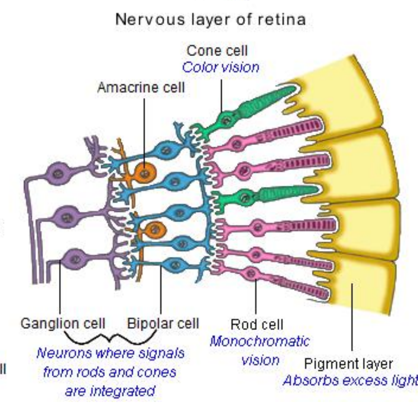


- **Rods**: extremely sensitive to light; function best under low light; contain one photopigment type and don't detect color; located mostly in region of retina (outside/around the fovea).
- **Cones**: function best under bright light; ideal for detail.
  - **Three different types** of cone cells, each with different photopigment (**one for every primary colour**). Principally located in region of fovea
- NOTE: rod and cone cells *do not* have axons (do not generate action potentials).
  - Generate receptor potentials that cause the release of ***inhibitory neurotransmitter*** from their synaptic ending.

7.19 – Other Cells of the Retina

- Retina contains pigment layer at very back of eye that absorbs excess light.
- Other cells in retina:
  - Bipolar cells
  - Ganglion cells
  - Horizontal cells
  - Amacrine cells.
- These cells are responsible for integration of info from rods/cones and production of AP.





7.20 – Transduction of Light to Action Potentials

- Visual system works "**backwards**."
  - Light striking retina flipped upside down and backwards from lens.
  - When depolarized, rod/cone cells release **inhibitory neurotransmitter** (shutts off bipolar cells)
  - When light strikes the retina, does *not* excite/depolarize rod/cone cells. **Light hyperpolarizes cells and shuts them off**.
  - Since cells release inhibitory neurotransmitter when **depolarized in dark**, they inhibit bipolar cells.
- Light strikes photoreceptors → hyperpolarizes → shuts off → stop releasing inhibitory NT → Bipolar cells (which can depolarize spontaneously by themselves) activate → depolarization of bipolar cells may lead to AP in ganglion cells

7.21 – How Light Is Transformed into Action Potentials

- In dark, Na^+ flows into photoreceptors, producing a **depolarization** leading to the inhibitory NT release.
- When light strikes cells, Na^+ channels close. Recall: [high of Na^+ outside]
  - Less Na^+ coming in / K^+ leaks out = **cell hyperpolarizes**
  - With hyperpolarization, no inhibitory NT is released and bipolar cell depolarizes.

7.22 – Types of Eye Movements

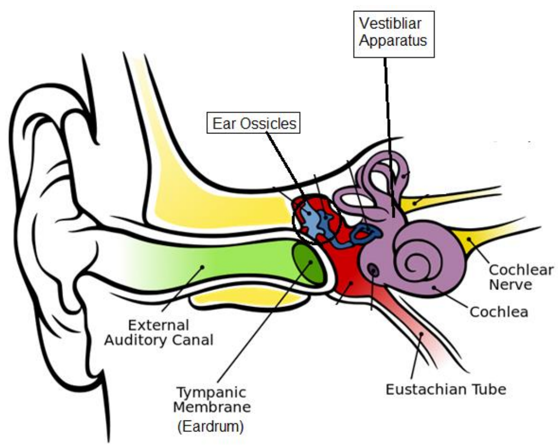
- To focus attention on an object, we must be able to direct our eyes to exactly the correct spot to focus image onto fovea (has highest concentration of cone cells).
- To do this, must be able to move eyes in a number of ways, depending on whether object is stationary or moving. Four primary eye movements:
  1. **Saccades**: rapid, jerky movements of the eye.
     a. Used to rapidly move eye to object of interest (gazing around while holding head).
  2. **Smooth pursuit**: smooth movement of the eyes to keep a moving object of interest focused
     a. Example: following flight of bird through sky keeping head still
  3. **Vestibular ocular reflex (VOR)**: focus attention on object and while moving head
  4. **Vergences**: made when object of interest approaches/moves away.
     a. moves away = eyes **diverge**;
     b. moves closer = eyes **converge**

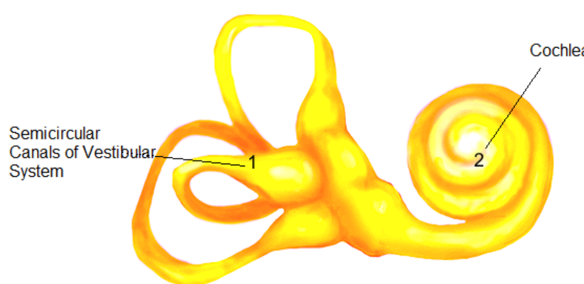
7.23 – The Auditory System

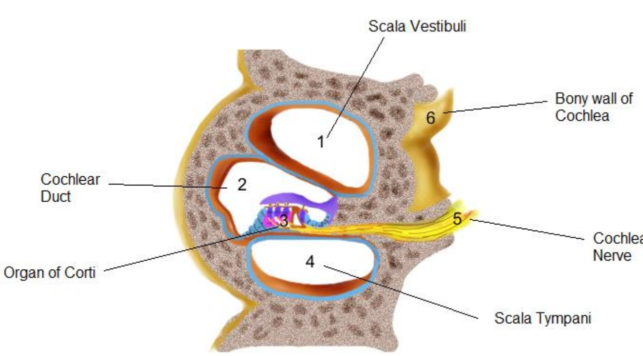
- Converts external environment sound waves → AP → travel to brain auditory system
- Typical, healthy human ear detect sound frequencies 20 Hz - 20,000 Hz.
  - Best, most acute: 1,000 - 3,000 Hz

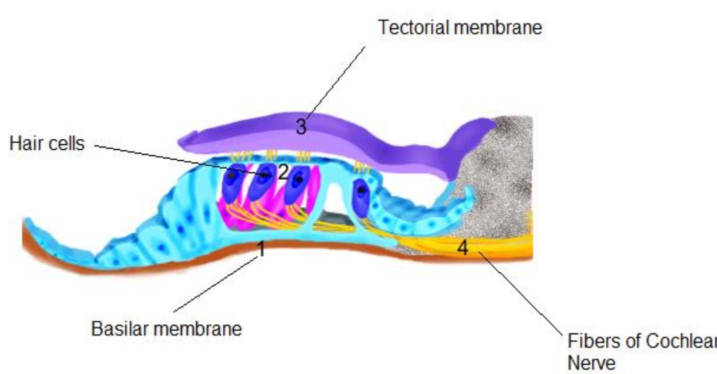
7.24 – The Auditory System—Structure

- Large, basic structural features of auditory system divided into three parts:
  1. **External/outer ear:**
     a. ear or **auricle**
     b. **external auditory canal**.
  2. **Middle ear:**
     a. **Eardrum** (or **tympanic membrane**),
     b. **Ear Ossicles** (made up of three bones—**malleus**, **incus**, and **stapes**),
     c. **Eustachian tube**.
  3. **Inner ear**:
     a. **Vestibular apparatus**: for sense of balance
     b. **Cochlea**: processes sound.

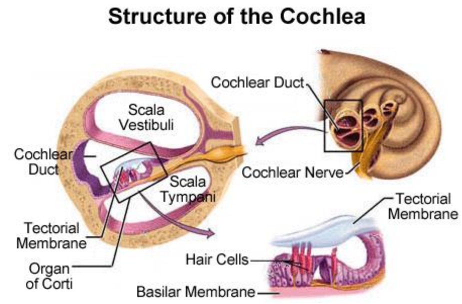








7.25 – Structures of the Cochlea

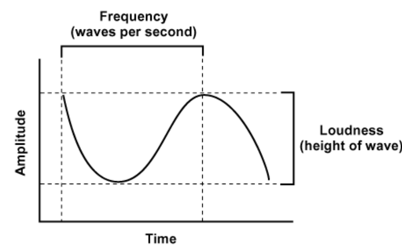


- **Cochlea** resembles shell of typical garden snail; hollow inside area divided into three compartments:
  - Upper **scala vestibuli** (aka vestibular duct)
  - Middle **cochlear duct**
  - Lower **scala tympani**.
- Separating cochlear duct and tympanic duct is **basilar membrane**, which contains **organ of Corti.**
  - Corti is converts sound waves to action potentials by special **hair cells**.
    - Hair cells embedded in **tectorial membrane**.
- Sound waves cause basilar membrane to vibrate, bending hair cells fixed in tectorial membrane.

7.26– What Is Sound?

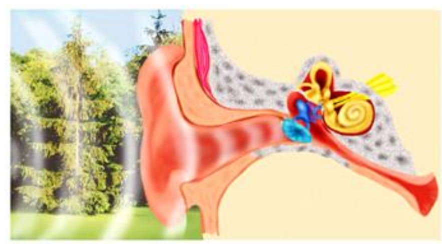
- When a tree falls in a forest and nothing is there to hear it, does it make a sound?
  - *NO*
- Sound is not created until this wave of air pressure hits parts of the ear (or microphone), turns into electrical information (action potentials in the CNS) and then interpreted as sound.

7.27 – Frequency and Intensity of Sound Waves

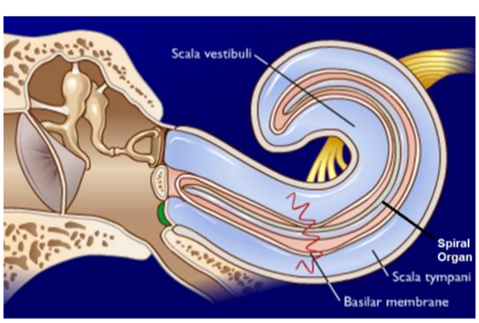


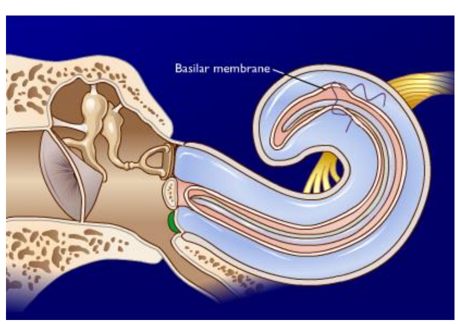
- Difference between sound frequency and sound intensity/loudness.
  - **Frequency**: number of waves (or cycles) per unit time.
  - **Intensity** (or loudness): height (or amplitude) of the sound wave.

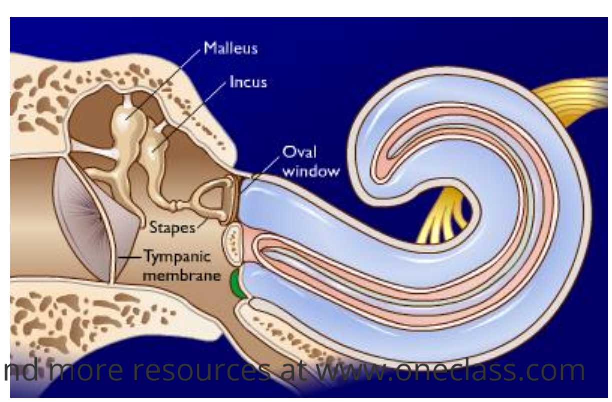
7.28-7.29 – Transfer and Amplification of Sound Vibrations



- Airwaves reach outer ear funnel into external auditory canal and strike tympanic membrane, causing it to flex back and forth.
- Levering action of the ear ossicles amplifies pressure waves that strike tympanic membrane.
- Ear ossicles vibrate oval window (small membrane-covered opening directly underneath the stapes; one of the ear ossicles).
  - Since ear ossicles amplify vibrations of tympanic membrane and since oval window is much smaller than this membrane →
    - waves are amplified 15 to 20 times original
- **Perilymph,** fluid inside cochlea transmit waves to hair cells embedded in basilar membrane, detect vibrations, and turn them into AP in auditory nerve.
- **Procedure:**
  - Sound waves strike tympanic membrane, causing vibration
  - Vibration causes vibration of 3 bones in middle ear
  - Vibration of foot plate causes perilymph in scala vestibule to vibrate, causing displacement of basilar membrane.
  - Short wavelengths cause displacement of basilar membrane near oval window
    - → movement is detected by hair cells of spiral organ (not visible in diagram)
  - Long wavelengths cause displacement of basilar membrane far from oval window
    - → movement is detected by hair cells of spiral organ
  - When vibrations reach perilymph in scala tympani, they travel to round window where they are dampened.



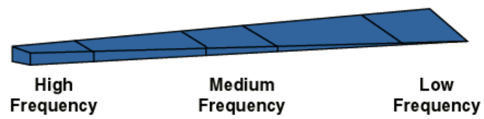




7.30 – Transduction of Sound to Action Potentials

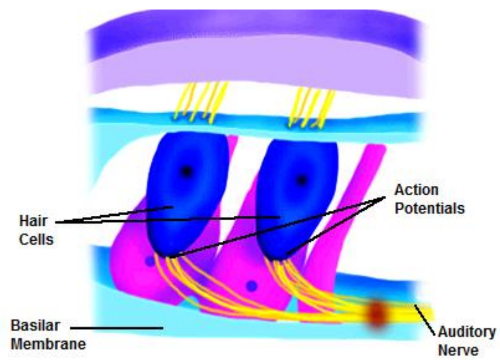
- "hearing" different frequencies of sound due to **basilar membrane (also called the basement membrane)** vibration located in the cochlea.
  - Recall basilar membrane is located between **cochlear duct/tympanic duct** and contains **organ of Corti**.
- The pressure waves in fluid created by vibrations of oval window produce traveling wave on basement membrane, reaching a peak at different regions of the membrane.
  - Happens because membrane is not consistent along its length.

7.31 – Basilar (Basement) Membrane

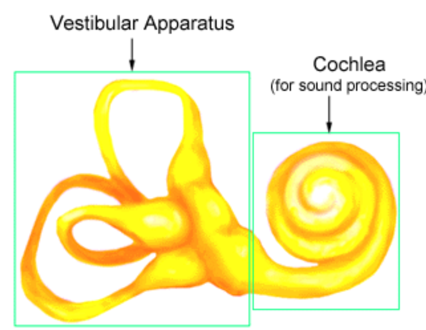


- Basilar membrane is wide/thin at top of cochlea, narrow/thick at base near the oval window.
- Shape not uniform + tension varies along length
  - "Tight" at base, "loose" at top.
- Depending on part of vibrating membrane, only certain hair cells activate by certain sounds:
  - Low frequencies will stimulate hair cells at apex (top) of cochlea,
  - High frequencies will stimulate hair cells on membrane near oval window.
- Hair cell length/stiffness differ along length of the membrane.
  - Another way of detect different frequencies.

7.32 – Sound



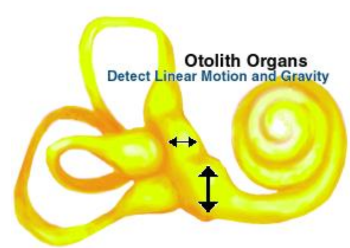
- When **basilar membrane vibrates**, **hair cells bend**, causing ion channels to open and the depolarization of the cells.
  - **Depolarization** causes **release of a neurotransmitter** from the hair cells → exciting neurons of auditory nerve **fire action potentials**.
    - Louder sound = stronger vibration of basilar membrane, the more bent the hair cells, the more neurotransmitter released, and the higher the frequency of action potentials produced.



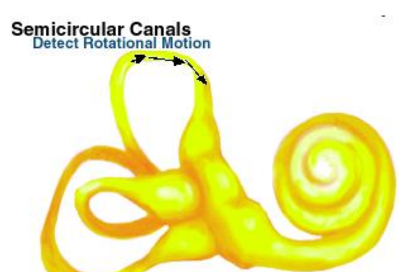
7.33 – The Vestibular System

- Inner-ear infection/really bad cold: may experience dizziness/disorientation.
  - Vestibular system is located in inner ear next to cochlea & responsible for maintaining balance, equilibrium, and postural reflexes.
- Performs these functions by detecting linear/rotational motion and position of head relative to body.
- The vestibular apparatus also responsible for vestibular ocular reflex (VOR).

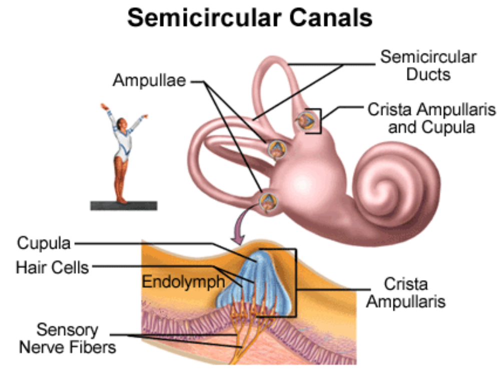
7.34 – Structure of the Vestibular Apparatus



- Each vestibular apparatus has two primary structures:
  - **Semicircular canals**: detect rotational or angular accelerations of head
    - Three semicircular canals in each apparatus.
      - Each detect movement in each plane of motion.
  - **Otolith organs**: detect linear accelerations.
    - Two Otolith organs:
      - one for detecting linear acceleration in the vertical plane (up and down)
      - one for accelerations on the horizontal plane.

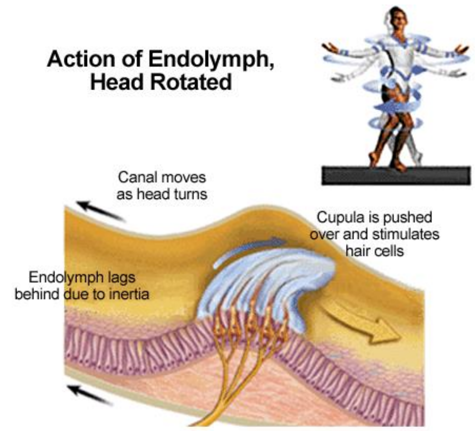


7.35-7.36 – Semicircular Canals

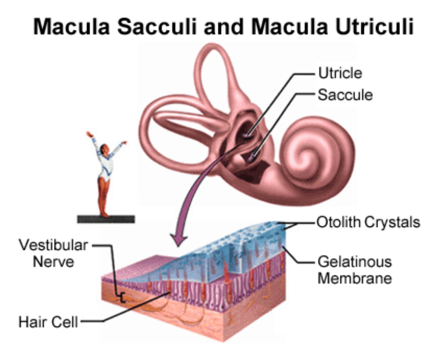


- Three semicircular canals in each vestibular apparatus: one for each plane of motion.
- **Endolymph:** fluid that fills semicircular canal.
- **Ampula**: swelling at the end of each canal.
- **Crista ampullaris**: sensory region inside ampula; contains **sensory hair cells**, which are fixed at their base, while their cilia are embedded in a gelatinous material called **cupula**.

- Semicircular canals only detect rotational accelerations and decelerations.
- For simplicity, consider accelerations/decelerations in horizontal plane.
  - When head is rotated to left, endolymph inside canals lags behind and seemingly moves right.
  - The endolymph hits cupula and bends hair cells embedded in it.
  - When hair cells are bent in a particular direction, they depolarize and fire action potentials, sending signals to the brain.
  - When bent in the opposite direction, they hyperpolarize, sending no signals to the brain.

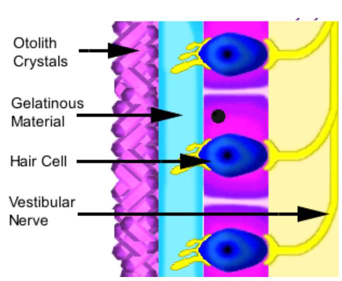


7.37-7.38 – Otolith Organ

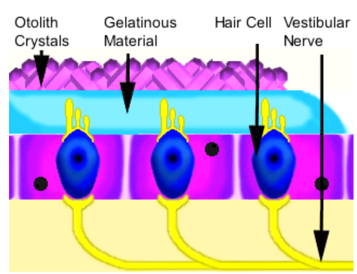


- Otolith organs detect **linear accelerations and decelerations** and **position of tilted head**.
- Two otolith organs in each vestibular apparatus.
  - **Utricle:** detects horizontal accelerations/decelerations (car)
  - **Saccule:** detects vertical accelerations/decelerations (elevator).
- Both organs act together to detect head tilts.
- Each otolith organ contains many **hair cells** anchored at their base and have their cilia embedded in a **gelatinous membrane**. The gelatinous membrane has **otolith crystals** embedded in it to give it weight and inertia during movements.

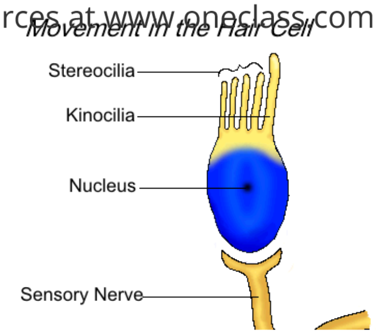
- When body is at rest, a series of action potentials is produced in vestibular nerve.
- When body accelerates, the otolith crystals initially lag behind and seem to move in opposite direction to acceleration.
  - bends cilia of the hair cells in the opposite direction, causing them to increase the frequency of action potentials in the vestibular nerve (the faster the acceleration, the higher the action potential frequency).
- When body is moving at a constant velocity, the hair cells return to "resting state" as do frequency of action potentials.
- When the body begins decelerates, hair cells bend in other direction, which causing frequency of action potentials to decrease further from the resting state (the more rapid the deceleration, the lower the action potential frequency).



Saccule



Utricle

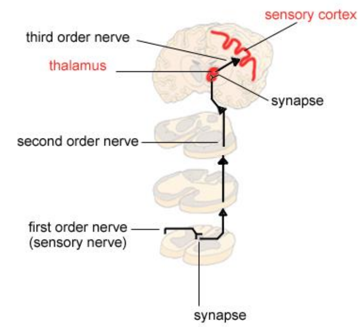


7.32 – The Incredible Hair Cell

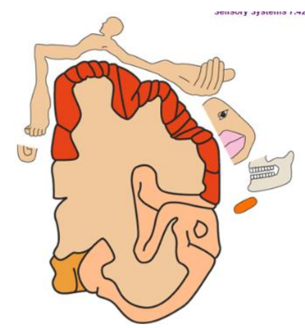
- How does one tiny cell perform such amazing functions in two widely different systems?
  - The secret lies in cilia at the top of the hair cells.
- When hair cells are at rest, they release a small resting level of neurotransmitter from base onto sensory nerve, firing action potentials.
- When smaller stereocilia bend toward larger kinocilium (during an acceleration, for example), hair cell releases more neurotransmitter, causing more action potentials in the sensory nerve.
- When the stereocilia bend away from the kinocilium (during a deceleration, for example), the hair cell releases less neurotransmitter, resulting in fewer action potentials.

7.33 – A Quick Look Back

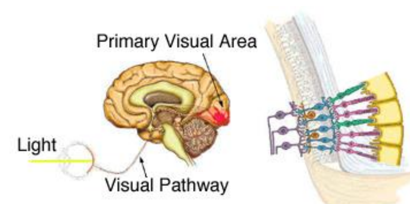
- Signal from outside → converted into AP → travels down nerves to brain → Brain interprets
- Outside signals converted to APs by *special receptors*, sensitive to 1 form of energy.
  - **Photoreceptors** = light
  - **Free nerve endings** = heat and pain
  - **Auditory hair cells** = sound waves
- Signal converted to Receptor Potentials (almost identical to EPSPs, but only found in sensory receptors) → converted to APs → travel along sensory neuron axon → other nerves → Somatosensory area of brain
- **Somatosensory system:** deals with sensations (touch, vibration, temperature, pain, and proprioception)
- Each sensations detected by one or many receptors.
  - **Touch**: Ruffini Corpuscles, Merkel's disks, Meissner's Corpuscles, and Pacinian corpuscles
  - **Low-frequency vibration**: Meissner's corpuscle
  - **High-frequency vibration**: Pacinian corpuscle
  - **Pain and temperature**: Free nerve endings
  - **Proprioception**: muscle spindles
- Two principal pathways that conduct somatosensory information to the brain:
  - (anterolateral) Spinothalamic tract
  - Dorsal column medial lemniscus.



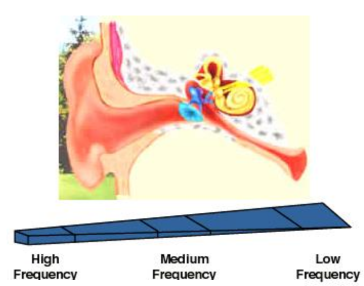
- Brain somatosensory area: arranged in topographical manner on the postcentral gyrus.
- This area of brain, called somatosensory homunculus, receives sensory information from body part.



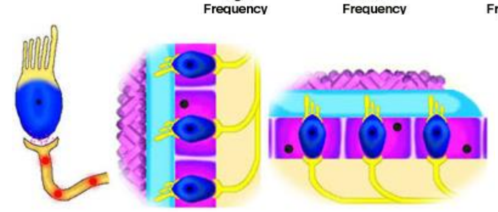
- Visual system processes light info, converts to APs → sent to brain for processing/form picture.
- Rods/cones: special light receptors (photoreceptors) that convert light into APs. Occurs by:
  1. Light causes photopigment in rods/cones to change shape.
  2. Causes decrease in Na+ permeability of rod/cone cell by closing Na+ channels.
  3. Less Na+ coming in/ same amount of K+ leaking out = cell hyperpolarizes (more negative).
  4. When hyperpolarizes, cell decreases release of inhibitory transmitter "shutting off" next cell in line.
  5. Bipolar cells now activated; in turn, activates ganglion cells and onward to visual cortex.



- Auditory system: converts sound waves → action potentials → to brain. Sound funneled down outer ear to eardrum, vibrating the ear ossicles in middle ear.
- Ear ossicles cause vibration of basilar membrane exciting hair cells resting on basilar membrane. Hair cells release neurotransmitter producing APs in cochlear nerve to brain.



- Vestibular system: helps maintain balance, equilibrium, and posture.
- Responsible for vestibular ocular reflex, (one of four eye movements)
- System located in inner ear next to cochlea. Vestibular system, like the auditory system, relies on special hair cells that detect the movement of the head.
- Two divisions of the vestibular system:
  - Semicircular canals: detect angular accelerations
  - Otolith organs: detect linear accelerations.
- Movement of head = movement of endolymph (fluid filling inner ear): fluid causes bending of hair cells, producing APs in vestibular branch of vestibular-cochlear nerve.



Module Eight: Circulatory System I: The Heart

8.1 – Objectives

- ★ State four main functions of cardiovascular system.
- ★ Describe different types of myocardial cells and explain their functions.
- ★ Explain origin of self-excitability and give two characteristics of sinoatrial node leading to self-excitability.
- ★ Describe sequence of events leading to an AP in the sinoatrial node.
- ★ Draw and label a cut-away of heart showing electrical conducting system.
- ★ Explain electrocardiogram (ECG) and what each peak represents.
- ★ Explain what ECG can tell you about the health of heart.
- ★ Describe in detail cardiac cycle and changes in ventricular and aortic pressure and volume during one complete cycle and be able to relate these changes to activity in valves and ECG events.
- ★ Explain how to calculate cardiac output and all controlling factors.
- ★ Describe in detail all factors controlling heart rate.
- ★ Describe in detail all factors controlling stroke volume.
- ★ Describe Frank-Starling Law of heart and explain how it works to normalize cardiac output.

8.2 – Introduction

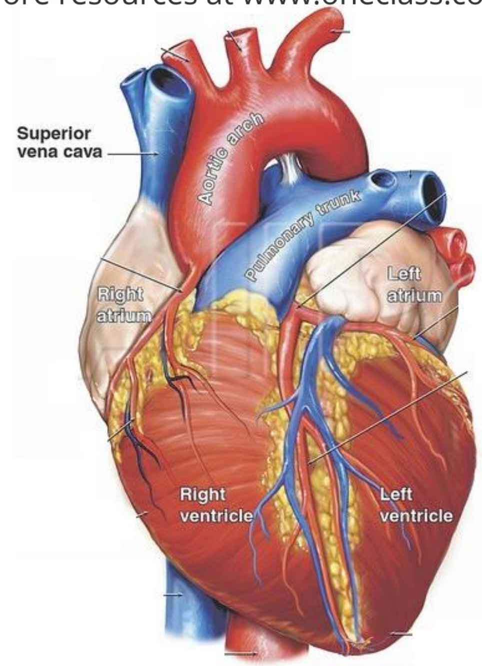
- One of most remarkable organs in body.
  - Begins beating long before birth and will not stop until death.
- About the size of fist, sits in chest cavity between your lungs.
- During average life, will beat roughly 2.5 billion times.
- Roughly 160,000 km (100,000 miles) of blood vessels transporting blood directly to almost every cell in body.

★ Four principal functions of the cardiovascular system:
1. Transports oxygen/nutrients to all cells.
2. Transports CO_2/waste products from cells.
3. Helps regulate body temperature and pH.
4. Transports/distributes hormones and other substances within body.

8.3 - Anatomy— the Heart

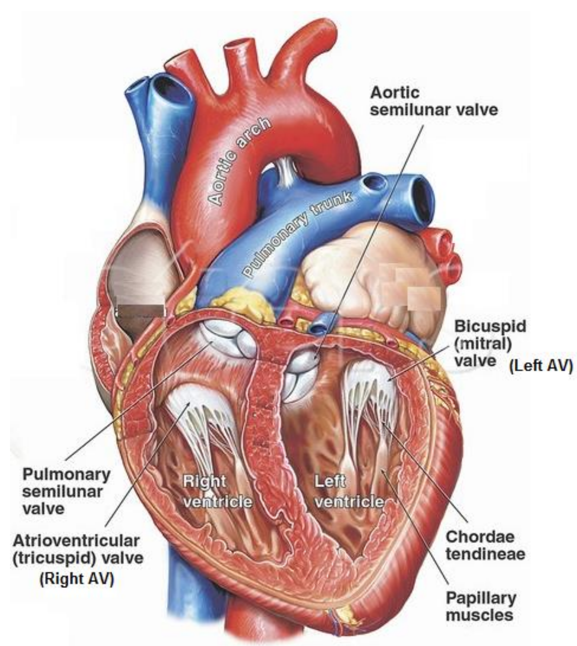
- Essentially consists of two side-by-side pumps:
  - Left atrium/ventricle pumps blood to rest of body
    - Wall of the left ventricle much thicker than wall of right ventricle.
    - The left ventricle must contract more forcefully to propel the blood through the entire systemic circulation.
  - Right atrium/ventricle pumps blood to lungs
    - The right ventricle only propels the blood to the nearby lungs, and does not need to contract as forcefully.
- Valves in heart, which ensure the one-way flow of blood through heart, may have several different names.
  - Right atrioventricular (AV) valve = **tricuspid valve**
  - Left atrioventricular (AV) valve = **bicuspid or mitral valve**

8.3.1 Anterior view

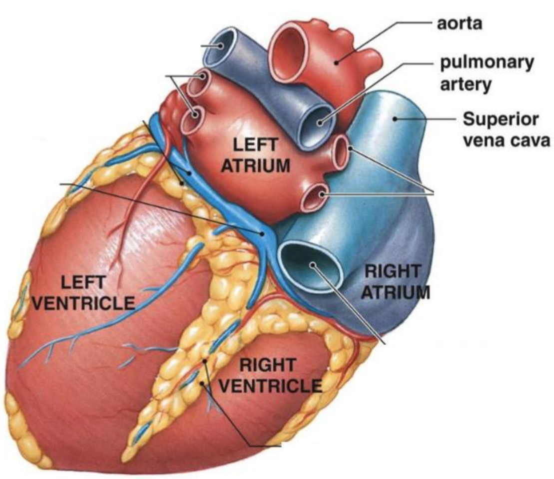


- **Superior Vena Cava**: Delivers blood from head/upper limbs to heart.
- **Pulmonary Artery:** Blood from right ventricle travels to lungs through pulmonary artery.
- **Aorta:** Blood leaving left ventricle travels through aorta and is distributed to entire body.
- **Right Atrium**: receives blood low in O_2/Co_2 concentration from entire body and pumps blood into right ventricle through right atrial-ventricular (AV or tricuspid) valve.
- **Left Atrium:** receives blood high in O_2/Co_2 concentration from lungs and pumps into left ventricle through left atrial-ventricular (AV or tricuspid) valve.
- **Right Ventricle:** pumps blood into pulmonary artery, which then delivers it to lungs for gas exchange.
- **Left Ventricle**: pumps blood into aorta, which then distributes the blood to body.

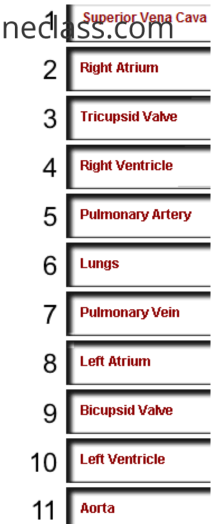
8.3.2 Anterior cutaway



- **Right AV (tricuspid) Valve:**
  - Ensures: blood travels from right atrium → right ventricle
  - Prevents: backup in atrium when ventricles contract.
- **Left AV (bicuspid) Valve:**
  - Ensures: blood travels from left atrium →left ventricle
  - Prevents: backup in atrium when ventricles contract.
- **Pulmonary Semilunar Valve:**
  - Ensures: blood travel from right ventricle → pulmonary artery,
  - Prevents: backup in right ventricle after relaxation.
- **Aortic Semilunar Valve:**
  - Ensures: blood travels from left ventricle → aorta
  - Prevents: backup in left ventricle after relaxation.
- **Chordae Tendineae:** cords of collagen attaching to valves at one end to papaillary muscles at other end.
  - Prevent AV valves from being pused into atria when ventricle pressure is high.
- **Papillary Muscles:** extensions of ventricular muscles attached to chordae tendineae.
  - Contract with ventricles and AV valves are held in place and don't fold backward into atria.



(b) Posterior (diaphragmatic) surface



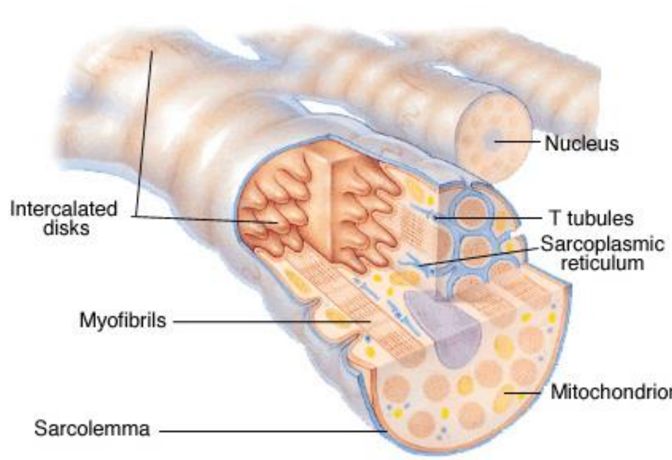
8.4 - Anatomy—Circulation through the Heart

- Flow through body → right atrium→ right atrioventricular valve → the right ventricle.
- When right ventricle contracts, it ejects blood out of heart → pulmonary valve → pulmonary artery → lungs.
- After passing through lungs, removing CO_2 and picking up O_2 → pulmonary vein → left atrium → left atrioventricular valve → left ventricle
- When the left ventricle contracts, blood ejected through aortic valve → aorta → body

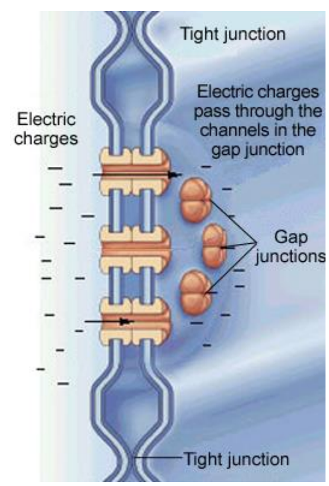
8.5 - Myocardial Cells

★ Two types of myocardial cells (myo = muscle, cardio = heart):
  - **Contractile cells:** similar features to skeletal muscle cells.
  - **Nodal/conducting cells:** similar features to nerve cells.

8.6-8.7 - Myocardial Cells—Contractile Cells

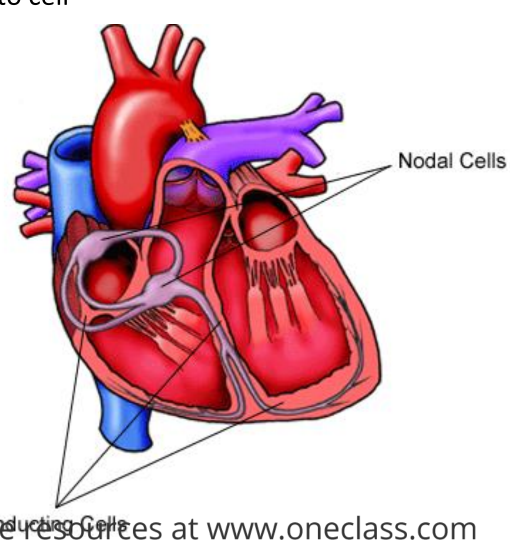


★ **Contractile cells:** real muscle cells of heart and form most walls of atria/ventricles.
  - Similar features/contract almost same ways as skeletal muscle fibers.
  - Contain same contractile proteins **actin and myosin** arranged in **myofibril** bundles and surrounded by a **sarcoplasmic reticulum**.
  - Differ from skeletal muscle by having only **one nucleus** and **more mitochondria**.
    - 1/3 volume is mitochondria.
  - Extremely efficient at extracting oxygen;
    - Extract ~80% of oxygen from passing blood—(twice amount of other cells).
  - Cells are much shorter, are branched, and are joined together by special structures called **intercalated discs**.
  - **Intercalated discs** contain **tight junctions** that bind cells together, while **gap junctions** allow for movement of ions/ion currents between myocardial cells.
  - Due to gap junctions, myocardial cells of heart **can conduct APs cell to cell** without nerves (extremely important feature of heart).
  - Intercalated discs contain tight junctions that bind cells together, while gap junctions allow for movement of ions/ion currents between myocardial cells.
  - Due to gap junctions, myocardial cells of heart can conduct APs cell to cell without nerves (extremely important feature of heart).



8.8 - Myocardial Cells—Nodal/Conducting Cells

★ **Nodal/conducting cells**: contract very weakly because they contain very few contractile elements (myofibrils).
  - Able to spontaneously generate APs without nervous input (neurons).
  - Can also rapidly conduct APs to atrial and ventricular muscle.
  - Provide self-excitatory system for heart to generate impulses and transmission system for rapid conduction of impulses throughout heart.

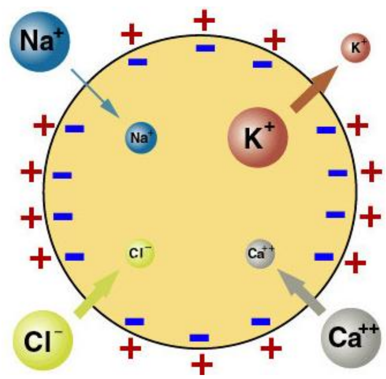


8.9 - Orgins of Self-Excitability

- ★ **Sinoatrial node** (or **SA node**): generally the origin site of AP in heart.
  - Located in upper posterior wall of right atrium, and is first area spontaneously depolarizing, producing an AP; this is why it is called the **pacemaker of the heart**.
- ★ Sequence of events for leading to AP in sinoatrial node:
  - **SA node/pacemaker→ Atria→ Atrial-ventricular node (AV node)→ Bundle of His→ Purkinje Fibers→ Ventricular muscle**

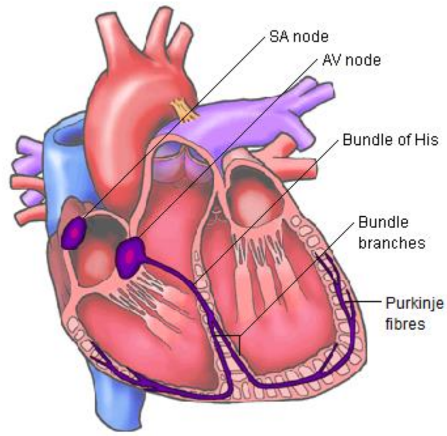
8.10 - Myocardial Cells—Remember!

- Responsible for AP in heart:



8.11-8.14 - SA Node Action Potential

- (Cause for spontaneously generated AP still controversial)
- ★ Characteristics of SA node are responsible for self-excitability:
  - Na^+ permeability is slightly higher here than in other cells.
    - Will make inside of cell more positive (depolarized) over time.
  - Ca^{++} are also trying to move into cell and will also depolarize cell.
  - Movement of Na^+ and Ca^{++} into an SA nodal cell, produces initial depolarization of membrane (Not yet created an action potential).
- ★ Main cause of spontaneous AP is K^+ movement.
  - K^+ trying to leave cell down concentration gradient causing inside to be more negative (a hyperpolarization).
    - Don't want this to happen if you want to depolarize cell.
  - Instead, potassium permeability of SA node cells decreases over time (less K^+ leak out).
  - Also, since Na^+/K^+ pump is always pumping K+ into cell, both of these factors cause cells to depolarize.
- ★ Since Na^+/Ca^{++} flow into cell and K^+ build up inside, membrane potential of SA nodal cells depolarizes from –60 mV to –40 mV (threshold).
  - SA nodal cells do not have a stable "resting" membrane potential like neurons or muscle cells.
  - Slow depolarization is completely spontaneous and is called the **pacemaker potential**.
    - Responsible for setting pace of heartbeat, and any alteration affects heart rate.
- ★ Once membrane potential depolarizes to threshold (–40 mV), special **voltage-gated Ca^{++} channels** open.
  - Ca^{++} rapidly flow in, producing **depolarization** phase of **SA node action potential**.
  - Ca^{++} channels begin closing roughly same times as **voltage-gated K^+ channels** begin to open, allowing K^+ out **to repolarize the cell**. Once cell returns to lowest value of roughly –60 mV, pacemaker potential begins depolarizing cell and sequence repeats.
  - This influx of Ca^{++} is important during heart contraction.
- Notice: sequence of events is similar to generation of a neuronal AP, yet there are some important differences in terms of ions and their movements.



★ 8.15-8.16 - Myocardial Cells—Conducting System of the Heart

- AP generated at SA node is highly coordinated throughout heart = Important = Conduction speed important
- From **SA node**, AP spreads throughout **Atrial muscle**, causing contraction.
- (Because atria is electrically isolated from ventricles by a fibrous tissue, AP cannot jump directly down to ventricles)
- With SA node at top of heart, AP/contraction moves top → down to ensure blood is forced down into ventricles

SA Node	= 0.05m/sec
Atrial Muscle	= 1m/sec
AV Node	= 0.03m/sec
Bundle of His	= 1m/sec
Purkinje Fibers	= 5m/sec
Vent. Muscle	= 1m/sec

SA node (depolarizes *slowly*)

↓

Atrial muscle
(***rapidly; ensuring*** simultaneous muscle contraction**)**

↓

Atrio-ventricular (AV) node
(***slows down AP;*** ensuring the atria has finished contracting before the ventricles contract)

↓

through **Bundle of His** & into **branches** (***rapidly)***
(For AP to reach apex of heart to contract first so blood can be forced up and out of valves at the top of ventricles)

↓ **RAPID**

Apex of Heart

↓ **VERY RAPID**

Propagates through **Purkinje Fibers**

↓ **RAPID**

Ventricular muscle

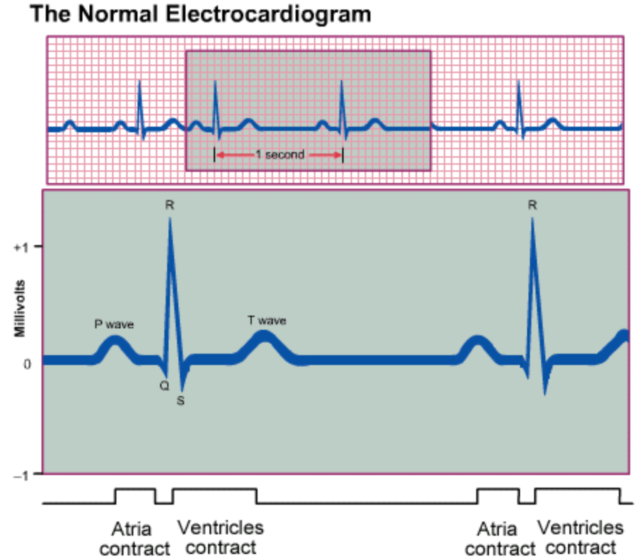
↓

Contraction from apex upward

8.17-8.18 - Electrocardiogram (ECG)

- ★ Because heart sits in middle of good conducting body fluid, as AP passes through various parts of heart, electrical current spreads over body surface.
  - Electrodes placed on skin around heart can record generated electrical potentials.
  - **Electrocardiogram (ECG)**: Recording during cardiac cycle (ECG).
- ★ **P wave**: heart electrical activity with **depolarization of atrial** muscle leading to contraction.
- ★ Large **QRS complex:** produced by **depolarization of ventricular** muscle prior to its contraction.
- ★ **T wave**: a result of **repolarization of ventricular** muscle as it relaxes.
  - Notice: no wave associated with the repolarization of atrial muscle. This is obscured by much larger QRS complex.

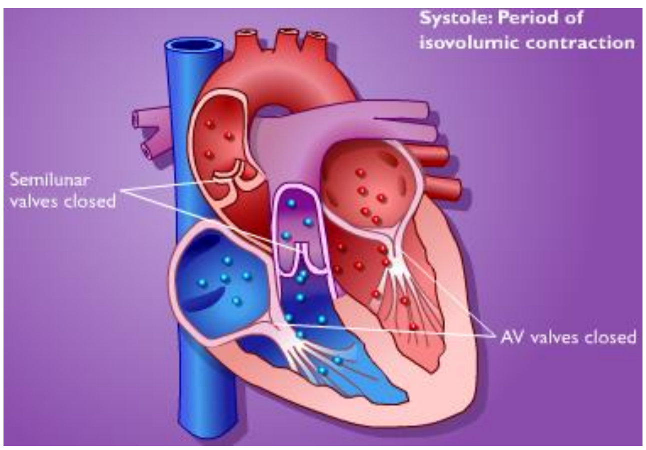
The Normal Electrocardiogram

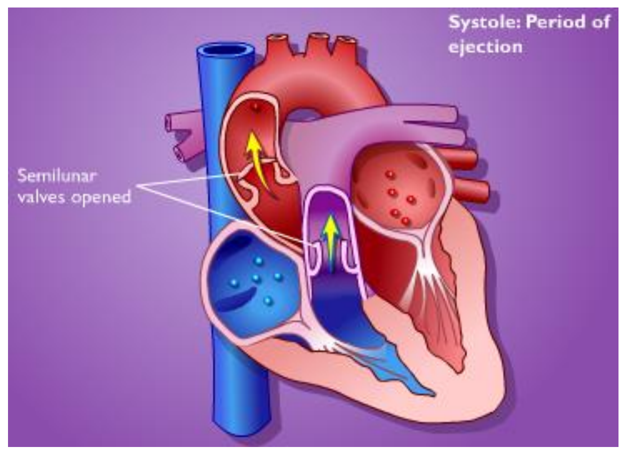


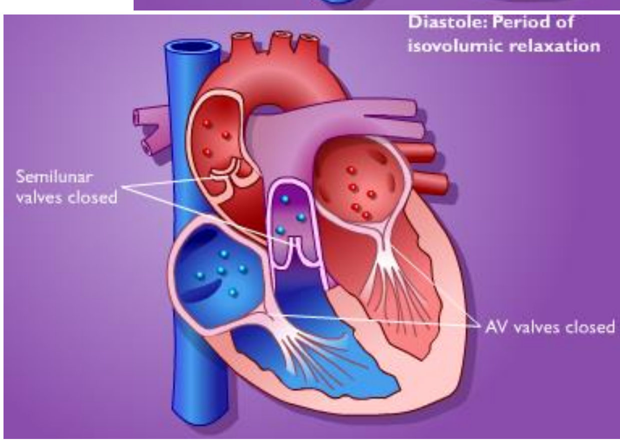
8.19-8.20 - The Cardiac Cycle

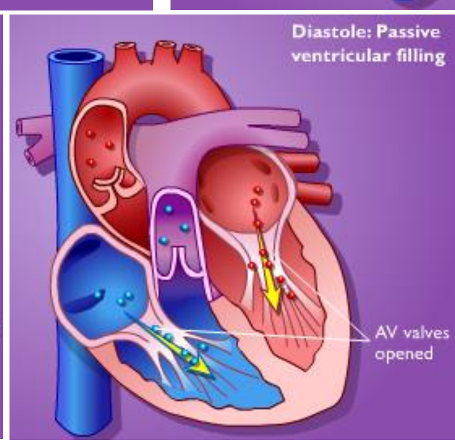
- The cardiac cycle consists: mechanical, electrical, and valvular events during a single contraction.
    - Relationship between events is important to understand how heart functions as a pump.
- Two (2) primary phases of Cardiac Cycle:
    1. **Systole**
    2. **Diastole**
    - For blood to flow, must be pressure gradient from high to low between two areas, volume in ventricle, and activity of valves.

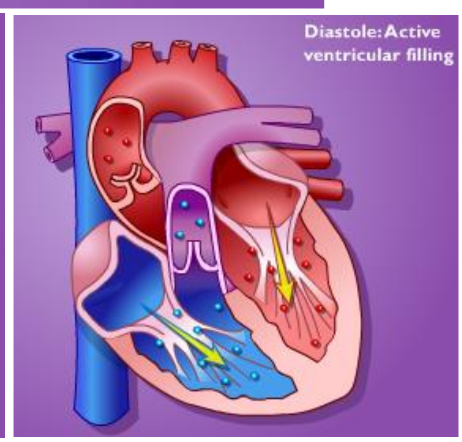
1. Ventricular contraction causes atrioventricular (AV) valves to close, signaling beginning of ventricular systole.
    a. Semilunar valves were closed during previous diastole and remain closed during this period.
2. Continued ventricular contraction increases pressure in the ventricles above the pressure in aorta and pulmonary trunk, causing semilunar valves to open
3. When ventricles relax and their pressures drop, blood flowing back toward relaxed ventricles cause semilunar valves to close, which is the beginning of ventricular diastole (note Atrioventricular valves remain closed).
4. When pressure in ventricles become lower than the pressure in the atria, atrioventricular valves open and blood flows into the relaxed ventricles (accounting for most ventricular filling).
5. Atria then contracts and completes ventricular filling.











8.21 - Contribution of Atrial Contraction to Ventricular Filling

Step 1—*Atrial systole*.

- Atria depolarizes (P wave in the ECG) → Atria contracts
  - Aorta pressure > Atrial pressure > Ventricular pressure
- AV (mitral) valve opens, blood flows into ventricle.
  - Ventricular volume increases slightly (this is the end diastolic volume)

Step 2—*Isovolumetric ventricular contraction (also called early ventricular systole)*.

- Ventricles depolarize (QRS complex) → Ventricles contract.
  - Ventricular pressure increases rapidly:
    - Aortic pressure > Ventricular pressure > Atrial pressure
- AV (mitral) valve closes.
- No ventricular volume change.

Step 3—*Ventricular systole (also called ejection period)*.

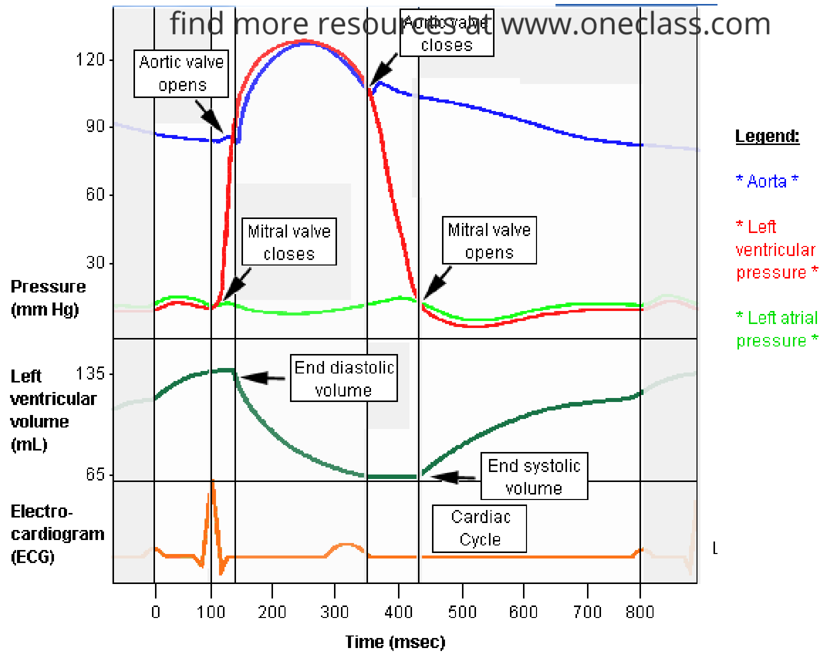
- Ventricles still contracting
  - Ventricular pressure > Aortic pressure > Atrial pressure
- Aortic valve open
  - Blood flows into aorta
  - Pressure increases
- Ventricular volume decreases
  - Ventricular pressure begins to fall.

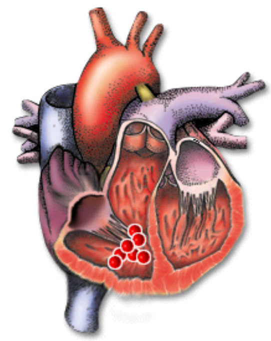
Step 4—*Early ventricular diastole (also called isovolumetric relaxation phase)*.

- Aortic valve closes.
  - Aortic pressure > Ventricular pressure
- Some blood remains in ventricles (end systolic volume).
- Ventricular pressure continues to fall.
- No change in ventricular volume.

Step 5—*Late ventricular diastole*.

- Aortic pressure > Atrial pressure > Ventricular pressure.
  - Mitral valve opens, blood flows into ventricle.
- Ventricular volume increases.
  - P wave begins, and
- Cycle repeats.

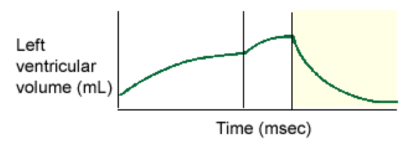




(1) When the ventricles relax, 70% of the blood flows into ventricles passively (ventricular diastole).

(2) The last 30% is pumped in by the atria contracting (atrial systole).

(3) The blood is then pumped out during ventricular systole.

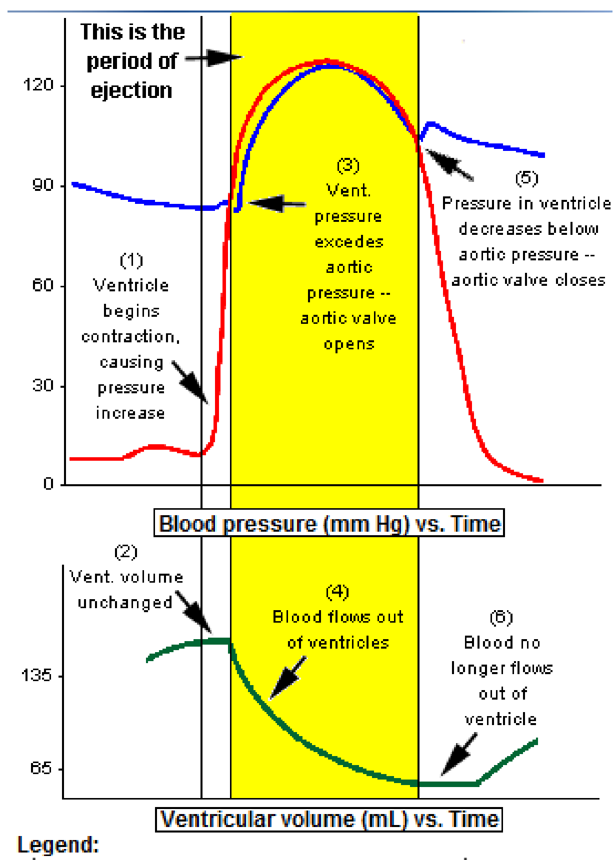


8.22 - Cardiac Cycle—Period of Ejection

- **Ventricular diastole**: ventricles relaxed 70–80% of blood enters ventricles (during late ventricular diastole).
- **Atrial systole**: atria contracts and 20–30% blood enters.
- When pressure of Atria > Ventricles: blood flows passively into ventricles.
- Pressure gradient begins during late ventricular diastole (ventricles relaxing), and continues until atria is finished contracting.

8.23 - Cardiac Cycle—Heart Sounds

- For blood to eject from heart:
  - Ventricle pressure > Aorta pressure
- If left ventricle pressure > 80 mmHg (pressure of aorta):
  - Aortic valve opens.
- Immediately, blood pours out of ventricles, while pressure continues to increase to 120 mmHg = **ejection period**.



8.24-8.36 - Mechanical Performance of the Heart

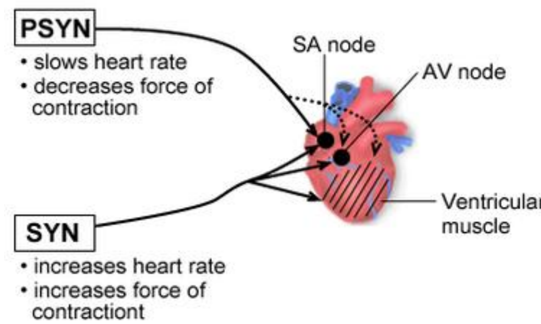
- **Cardiac output (CO):** ventricle blood pump/min.
  - *Rest* = ~5 liters (1.3 gallons)/min.
  - *Exercise*:
    - Average: ~20 L/min (5.2 gallons/min)
    - Athlete: ~35 - 40 L/min (10 gallons/min) (ie. small automobile gas tank in 1 min… same length of time as a gas pump).

8.25 - Cardiac Output

- **Heart rate (HR)**: beats/min
- **Stroke volume (SV)**: blood pumped by **one ventricle during one contraction/heartbeat.**
  - *Rest*:
    - Heart rate = 70 beats per minute (bpm)
    - Stroke volume is roughly 70 ml/beat.

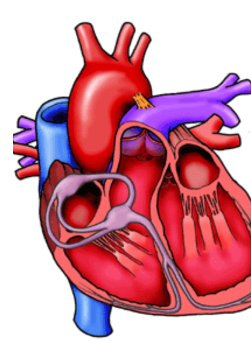
$$Cariac\ Output = Heart\ Rate\ (bpm)\ x\ Stroke\ volume\ (ml)$$

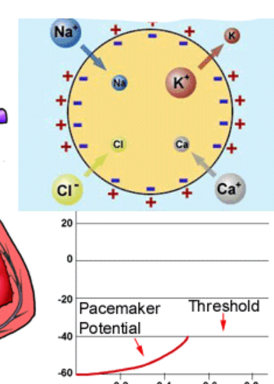
    - *CO = 70 x 70ml = 4900mL/min = 5 L/min.*
  - Exercise:
    - CO increases dramatically in order to supply the working muscles with more oxygen and nutrients. Increase in CO by increasing HR and/or SV.



8.26-8.28 - The Control of Heart Rate

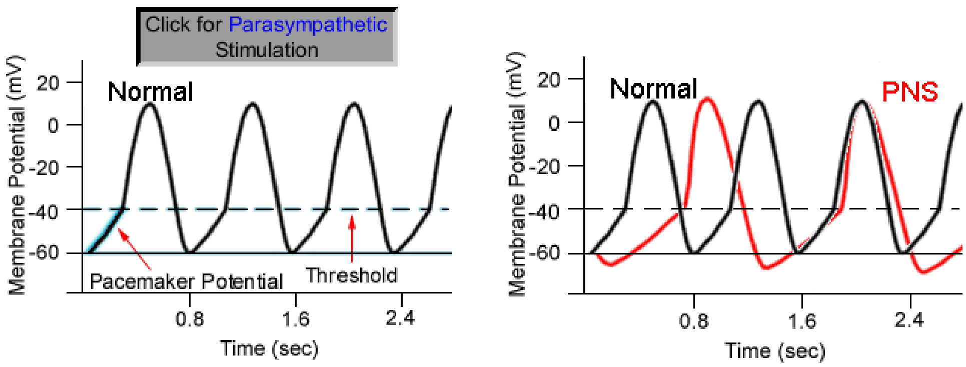
- Recall: ***Autonomic nervous system (ANS)*** exerts powerful control over heart rate and force of contraction.
  - Reason: heart is innervated by both:
    - **Parasympathetic nervous system (PSYN)**:
      - Parasympathetic nerves are distributed mainly to SA and AV nodes and to a lesser extent to atrial and ventricular muscles.
        - PSYN will decrease heart rate by affecting both SA node + AV node and will (to a lesser extent) decrease force of heart contraction.
    - **Sympathetic nervous system (SYN)**:
      - Sympathetic nerves are distributed to the same areas but with a stronger innervation to the ventricular muscle.
        - SNS will have opposite effect, increasing the heart rate and force of contraction.
  - If all ANS influences removed, heart would beat at its own natural rhythm of ≅ 100 bpm. Resting heart rate of a normal individual ≅ 70 bpm.
    - Why?
      - Constant activity from PSYN keeping heart rate slowed to roughly 70 bpm!
- **Vagal tone**: PSYN is continually activated at rest to keep heart beating at roughly 70 bpm
  - Vagus nerve transmits signals from PSYN to heart.
- If no activity from PSYN and SYN heart will beat at its intrinsic rate of 100 bpm.
  - **Increasing PSYN→ heart activity**: decreases heart rate from intrinsic rate.
  - **Increasing SYN→ heart activity**: increases heart rate from intrinsic rate.
- *Pacemaker potential* of SA nodal AP change → Heart rate change
  - Recall: pacemaker potential is result of Na+ and Ca++ leaking in + K+ permeability decreasing (gradual depolarization to threshold (–40 mV) and firing AP).
  - Rate of depolarization of pacemaker potential change → heart rate change





8.29-8.30 - Mechanical Performance—Parasympathetic Nervous System

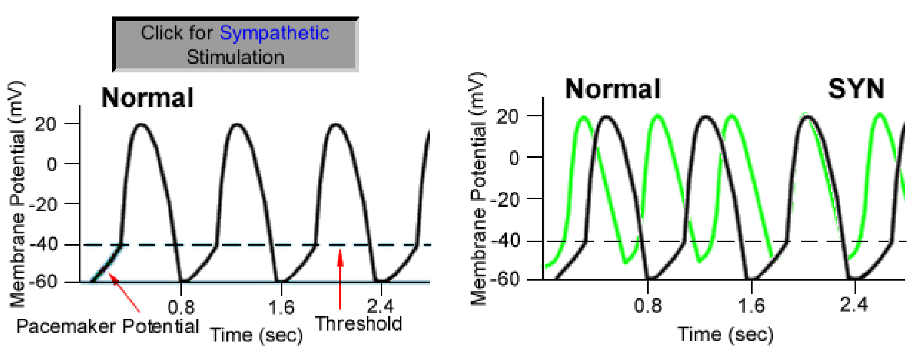
- Pacemaker potential altered by parasympathetic nervous system (PSYN).
  - When heart PSYN neurons activate → neurotransmitter acetylcholine (ACh) released onto SA and AV nodes.
  - ACh opens K+ channels → allowing more K+ out of cell.
    - Will do two things:
      - Membrane potential hyperpolarizes, pacemaker potential slope decreases.
      - This means membrane potential will take longer to reach threshold and heart rate slows.



- PSYN will also affect the AV node by release of acetylcholine onto cells in this region.
  - Why? After all, SA node is the pacemaker and it sets heart rate—right?
    - AP has to travel through AV node on to ventricles; and slows down here to ensure atria have finished contracting before ventricles begin contracting.
- If heart rate is decreased further → AP conduction through AV node must also decrease to ensure the atria finishes contracting before ventricles.

8.31 - Mechanical Performance—Sympathetic Nervous System

- Sympathetic nervous system (SYN) has opposite effect on SA and AV nodes; increases heart rate.
  - To increase heart rate, threshold must be reached faster, requiring an increased pacemaker potential slope.
    - Accomplished by neurotransmitter norepinephrine (and hormone epinephrine, AKA adrenaline).
      - Epinephrine, released by nerves of SYN onto SA node, causes opening of Na+ and Ca++ channels, allowing more of these ions to enter SA nodal cells causing rapid depolarization.
      - Consequently, pacemaker potential will reach threshold quicker and the heart rate will increase.



- Pacemaker potential altered by parasympathetic nervous system (PSYN).
  - When heart PSYN neurons activate → neurotransmitter acetylcholine (ACh) released onto SA and AV nodes.

8.32 - Mechanical Performance

- Recall: ANS can change heart rate, altering cardiac output (CO).

$$Cariac\ Output = Heart\ Rate\ (bpm)\ x\ Stroke\ volume\ (ml).$$

8.33-8.34 - Mechanical Performance—Stroke Volume

- *End Diastolic Volume (EDV)*: amount of blood in the ventricle at the end of diastole—or just before it contracts.
  - @ rest = 120 mL.
- *End Systolic Volume (ESV)*: amount of blood in the ventricle at the end of systole—or just after it contracts.
  - @ rest = 50 mL
- Difference of two values gives amount of blood ejected, or stroke volume.

$$Stroke\ Volume\ =\ EDV - ESV$$

  - EDV = 120 mL
  - ESV = 50 mL
    - SV = 120 mL – 50 mL = 70mL. ie. at rest hear pumps 70mL of blood during contraction.
- Both diastolic volume (EDV) and end systolic volume (ESV) affects stroke volume (SV).
  - Change to SV will change cardiac output (CO).
    - Since heart *force of contraction* determines SV, whatever factors can change force of contraction will change SV (and consequently cardiac output).
    - Three things can alter the stroke volume:
      1. Input from the autonomic nervous system—either the **PSYN** or the **SYN**
      2. EDV and preload
      3. ESV

8.35 - Mechanical Performance—Control of Stroke Volume by the Autonomic Nervous System

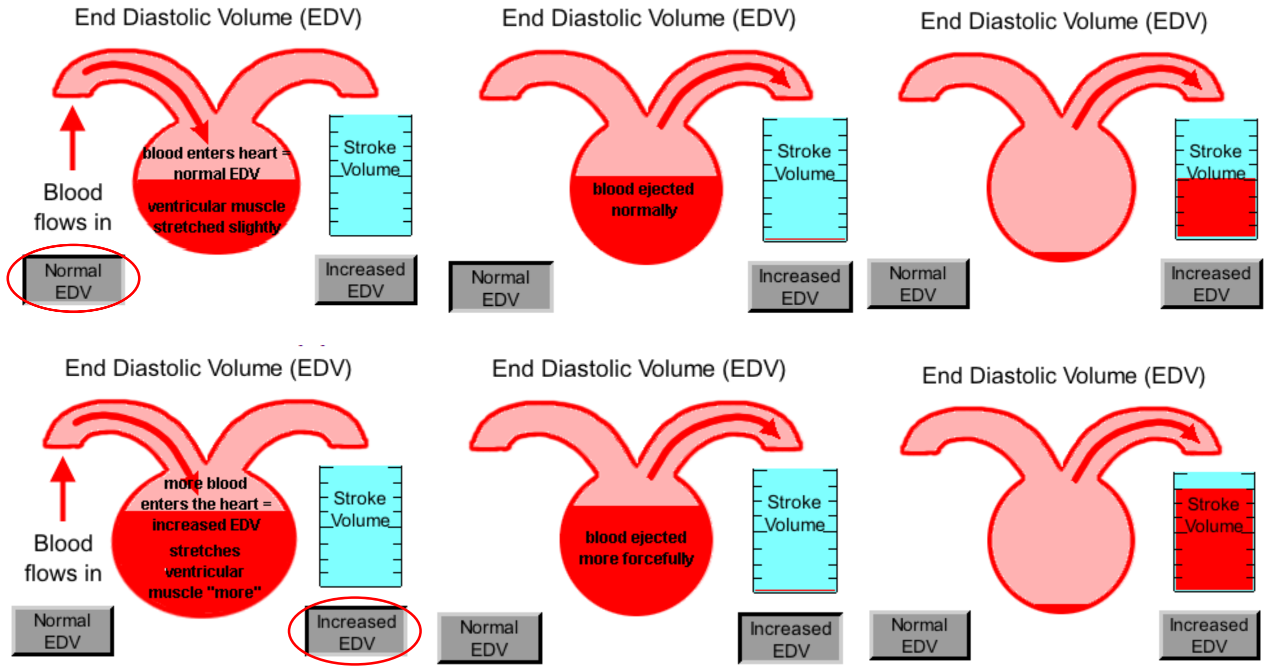
- **PSYN** decreases heart contraction force by releasing acetylcholine (ACh) onto cardiac muscle.
  - Will decrease amount of Ca^{++} entering muscle cells.
    - Since Ca^{++} are essential for muscle contraction, decrease in Ca^{++} decrease contraction force.
      - Will decrease the stroke volume.
- **SYN** will do opposite by releasing norepinephrine onto muscle cells.
  - Will increase amount of Ca^{++} entering cells, leading to a more forceful contraction and increased stroke volume.

8.36 - Control of Stroke Volume by Changing EDV and Preload

- **Preload**: "load" on heart just **before** contraction, directly related to diastolic volume (EDV) end.
  - This load comes from blood in ventricle that stretches heart muscle.
    - More blood in ventricle (the higher the EDV) = more "load" on heart muscle just before contraction.
    - This stretching will cause special Ca^{++} channels in cardiac muscle cells to open, allowing Ca^{++} into the cell.
    - More Ca^{++} in muscle cell = more forceful contraction during systole = more blood ejected.
      - More blood ejected = lower end systolic volume and higher stroke volume.
- **Frank-Starling Law of the Heart:** mechanism which occurs in heart even without nervous system input.

8.37 - Frank-Starling Law of the Heart

- **Law states that:** $\boldsymbol{End\ diastolic\ volume}\ (EDV) \propto \boldsymbol{Stroke\ volume}\ (SV)$

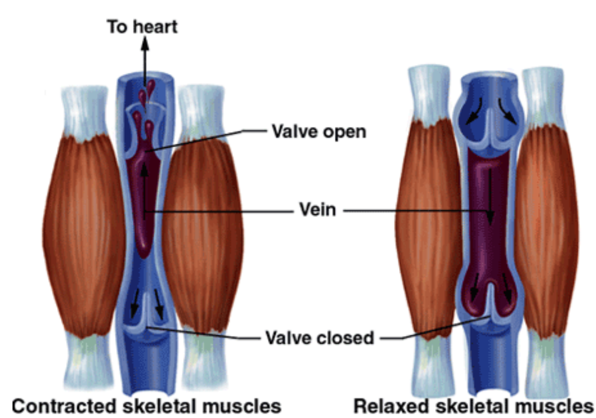


8.38 - Changing EDV

- Increasing end diastolic volume (EDV) = filling heart with more blood before contraction.
  - Since blood returns to heart by veins, one way to increase EDV is "squeezing".
  - Veins contain **70% of total body blood volume**.
  - Since veins have **valves**, which ensure blood flows in one direction, squeezing veins will increase **venous return** of blood to heart, which will increase EDV.
- One way to squeeze veins, to increase venous return, is by activating SYN.
  - SYN innervates smooth muscle located in vein walls.
    - Muscle forms ring around inside of vessel wall.
    - When muscle contracts → veins constrict + with help of valves → squeezes blood back to heart.
    - → increase venous return →increasing EDV → increase in SV → increase CO

8.39 - Changing EDV by Exercising

- Repeated contraction/relaxation of skeletal muscle can also squeeze veins.
  - Since many veins run between large groups of muscle, exercise can repeatedly squeeze veins, pumping the blood back to heart.
  - "Muscle pump" can consequently increase end diastolic volume (EDV) →(& by Frank-Starling Law) increase stroke volume → increase cardiac output.
- Activity of exercise increases cardiac output, helping to deliver more blood to exercising muscle.

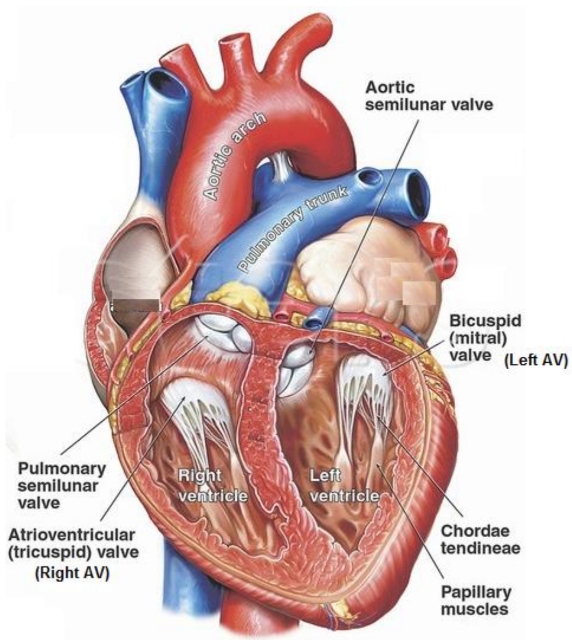


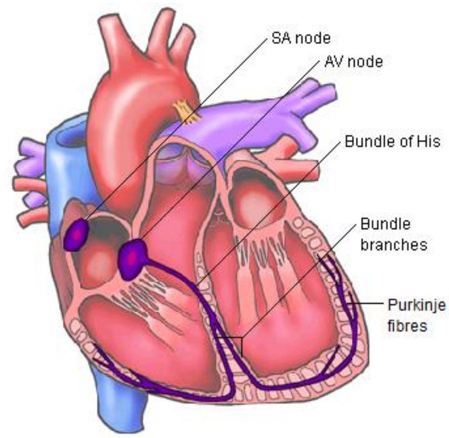
8.40 – 8.41 - A Short Review

- Heart = pump.

$$Cariac\ Output = Heart\ Rate\ (bpm) x\ Stroke\ volume\ (ml)$$

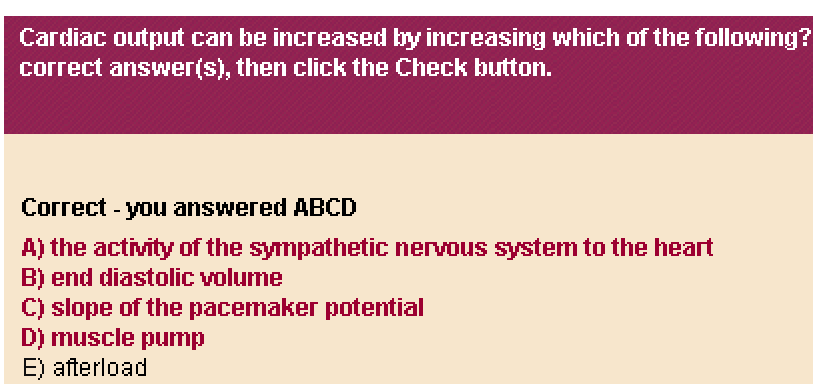
- Division of autonomic nervous system (ANS) can change heart rate.
- PSYN releases acetylcholine onto SA nodal cells, decreasing slope of pacemaker potential, which decreases heart rate.
- The SYN releases norepinephrine onto heart cells, increasing slope of pacemaker potential, which increases heart rate.





$$Stroke\ Volume\ = EDV - ESV$$

- Stroke volume, like heart rate, can be altered by **PSYN** and/or **SYN**, each of which alters Ca^{++} entry into ventricular muscle cells.
  - **PSYN** decreases entry of Ca^{++}, causing a decrease in force of contraction and decreasing stroke volume (SV).
  - **SYN** increases Ca^{++} entry into muscle cells, increasing force of contraction, causing increase in stroke volume.
- Increasing end diastolic volume and preload increases stroke volume.
  - By Frank-Starling law: Increasing venous return → Increase EDV → Increase stroke volume


Cardiac output can be increased by increasing which of the following? correct answer(s), then click the Check button.

Correct - you answered ABCD

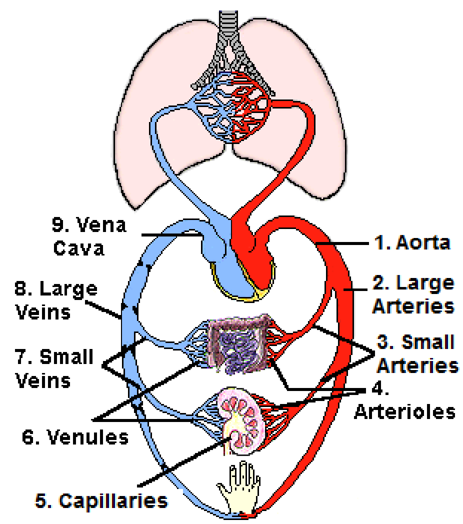
A) the activity of the sympathetic nervous system to the heart
B) end diastolic volume
C) slope of the pacemaker potential
D) muscle pump
E) afterload

Module Nine: Circulatory System Part II: Blood Vessels

9.1 – Objectives

- Describe and explain the general organization and anatomy of the cardiovascular system, including the heart and blood vessels.
- Describe the blood volume distribution within the different blood vessels and explain the significance of the different volumes.
- Describe and explain the relationship between pressure, flow, and resistance.
- Describe the changes to pressure and resistance throughout the circulatory system and explain why pressure and resistance are different in different vascular beds.
- Explain what would happen to blood pressure above and below a constriction.
- Calculate total peripheral resistance (TPR) in an individual and explain what would happen to blood pressure if the TPR changed.
- Describe the structural features (amount of muscle, elastic tissue, and fibrous tissue) of all the different blood vessels and how these features contribute to the specific characteristics of these vessels ("stretchability" and so on).
- Describe the lymphatic system and explain how it regulates the interstitial body fluid and how it is related to the Starling Forces.
- Describe and explain all of the Starling Forces that contribute to the movement of fluid across a capillary.
- List and explain the factors that contribute to edema.
- Describe and explain in detail the control of the cardiovascular system.
- Explain the (local) myogenic and metabolic theories as well as the humoral and neural control mechanisms.
- List the agents responsible for vasodilation and vasoconstriction.
- Describe the Baroreceptor reflex and how it regulates blood pressure.

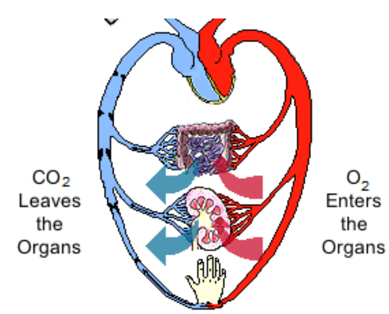
9.2 – Introduction



- Blood vessels: pumps and distributes blood to all areas of body.
- Circulatory system divided into:
  1. Pulmonary circulation
  2. Systemic circulation.

9.3-9.5 - Anatomy—General Organization

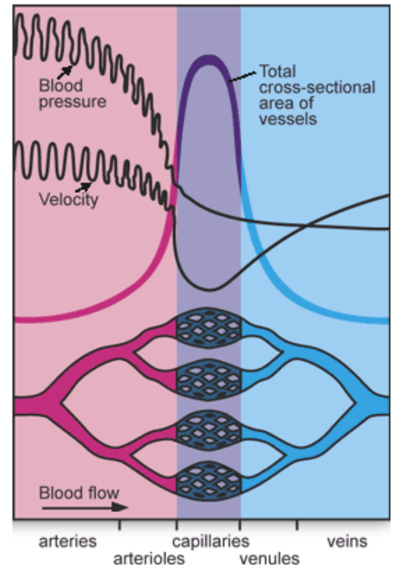
- **Circulatory system**: closed system of tubes (**blood vessels**) filled with fluid (**blood**) moved around by a central pump (**the heart**).
  - **Blood vessels:**
    - arteries + arterioles transport blood from heart
    - capillaries where gas exchange takes place
    - venules + veins return blood
- (See figure)
- Capillaries are the smallest of all the blood vessels and are functional units of circulatory system where substances enter/leave.
- Two principal loops blood takes through body:
  - **Pulmonary circulation**: begins on right side of heart and sending blood through arteries to lungs. These blood vessels continually branch into smaller and smaller blood vessels, eventually becoming capillaries. Gas exchange takes place in pulmonary capillaries. Oxygen diffuses into blood and carbon dioxide out. Blood enters venules and progressively larger veins eventually returning to left side of heart.



  - **Systematic circulation**: begins on left side of heart. Freshly oxygenated blood now pumped to rest of body; travels from left ventricle, through aorta, and into arteries. Arteries branch into smaller arterioles, branching into capillaries. Capillaries are the site of gas exchange. Oxygen, nutrients, hormones, etc. are delivered to cells, and carbon dioxide (CO_2) and waste picked up. Deoxygenated blood returns to right side of heart through venules and larger veins.
    - Two smaller circulatory loops within larger systemic circulation:
      - Hepatic portal loop that we will see in the digestive system
      - Hypothalamic-hypophyseal portal system found in brain

9.6 - Blood Volume Distribution

- Total blood volume (TBV) of average human = 5 liters (1.3 gallons).
  - Veins: 70%.
    - Largest because most "capacity," veins are often referred to as the capacitance vessels or blood "reservoir."
  - Arteries: 10% of TBV,
  - Heart and lungs: 15%.
  - Capillaries (gas exchange vessels): 5%

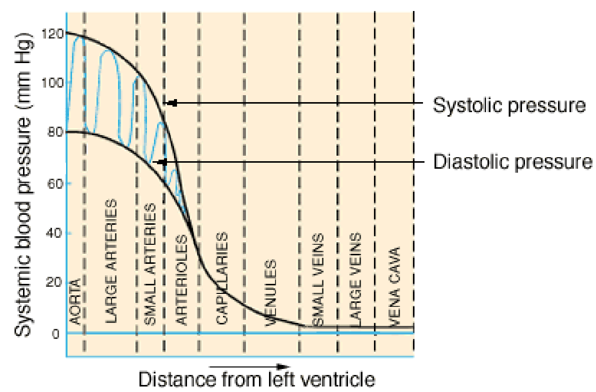


9.7 - Blood Velocity and Cross-Sectional Area of Vessels

- Blood volume, pressure, velocity, and cross-sectional areas of the blood vessels all vary throughout circulation.
  - Characteristics have important functional significance
  - **Arteries**: highest blood pressure & velocity, yet very low cross-sectional area
    - These vessels rapidly distribute blood throughout body
  - **Arterioles**: lower blood pressure & velocity, yet higher cross-sectional area.
    - These vessels are site of highest resistance in circulation and help regulate blood flow to organs
  - **Capillaries**: blood velocity is lowest, total cross-sectional area is highest in circulation.
    - Characteristics help maximize exchange of substances across blood vessels
  - **Venules and veins**: Blood pressure & cross-sectional area decrease, blood velocity increases
    - Return blood back to heart & store large percentage of total blood volume

9.8-9.9 - Pressure, Flow, and Resistance

- Recall: driving force **moving ions** during diffusion is a **concentration gradient**.
- **Pressure gradient**: force that **moves** blood through circulatory system.
  - Diagram shows large drop in pressure from high (in the aorta) to low (in the veins).
  - This pressure gradient causes blood to flow through both pulmonary and systemic circulation.
  - Higher pressure gradient = higher blood flow.



- Blood flows through vessels by pressure gradient.
  - Encounters resistance due to blood "dragging" along walls of vessels.
  - Higher blood resistance = lower flow.
    - Blood flow through vessel = **laminar (streamlined) flow**
      - There are thin "layers" of flow whose velocity varies across the vessel—flow is slower at edges and faster in center.
  - To examine blood flow through a vessel, consider pressure gradient and encountered fluid resistance.

$$Blood\ Flow\ (F) = \frac{P1 - P2}{R} = \frac{Pressure\ gradient}{Resistance}$$

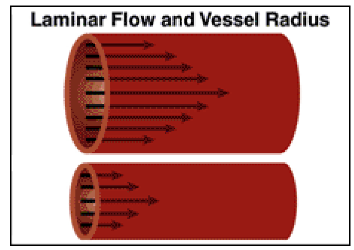
9.10-9.11 - Resistance to Blood Flow

- Several factors can affect resistance:
  1. **Thickness or viscosity of the fluid**: Thicker fluid = Higher resistance.
     a. Generally, viscosity of blood does not change.
  2. **Length of the vessel**: Longer blood vessel = Higher resistance.
     a. Since vessels in body are of constant length and do not change over short periods of time, length of the vessel is not a major factor.
  3. Most important factor, **diameter (or radius) of blood vessel**: Smaller inside diameter, higher

- Blood viscosity can be altered by dehydration or blood doping (removing blood, to allow more red blood cells to grow, and then replace their original blood = higher than normal. Dangerous (illegal) and puts too much strain on heart = death.

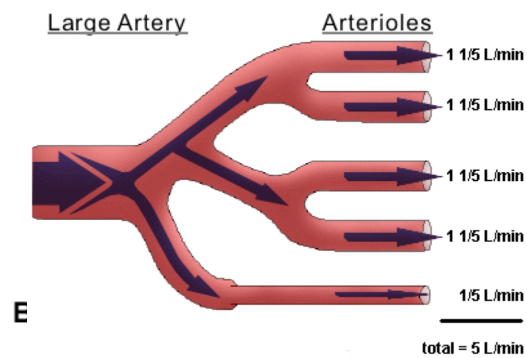
- Over long time, blood vessels can grow larger especially in overweight.
  - **L** = length of blood vessel
  - **n** = viscosity of the fluid
  - **r** = internal radius of the vessel
- To calculate blood vessel resistance, we take into account viscosity of fluid and length and radius of the blood vessel as shown in equation 2.
- Blood viscosity does not usually change and length of vessels generally remain constant over short periods of time. Therefore, simplify eq2 by removing viscosity and length, resulting in eq3.
  - States that if radius of a blood vessel decreases, resistance increases and vice versa.
  - Take equation 3 and combine with equation 1 from earlier, result is equation 4.
- According to equation 4, altering either pressure gradient or radius of the vessel, will alter blood flow.

- Equation 2:
  - $Resistance = \frac{Ln}{r^4}$
- Equation 3:
  - $Resistance = \frac{1}{r^4}$
- Equation 4:
  - $Blood\ flow = Pressure\ Gradient\ x\ r^4$



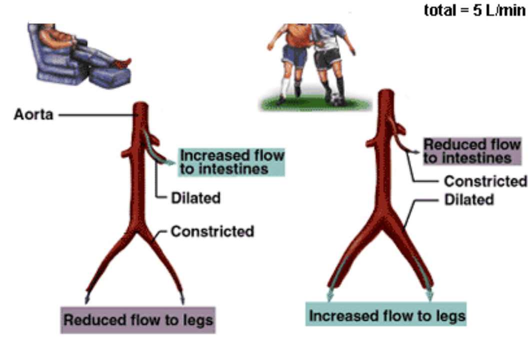
9.13 - Control of Blood Flow in the Body

- Two ways body can alter blood flow-by changing
  - **Pressure gradient**, or
  - **Radius** of vessel
- Since blood pressure is generally kept relatively constant, best way to regulate blood flow through an organ is by changing **radius** of vessels supplying it.
  - Decreasing radius of vessel feeding an organ, increases resistance in turn decreasing flow of blood into that organ.
- **Arterioles** are main vessels controlling organ blood flow.
  - Note: if blood flow decreases in one arteriole, blood flow in other arterioles increases to maintain a constant flow of 5 L/min



9.14 - Changing Blood Flow in Response to Needs of an Organ

- Changing diameter of blood vessel supplying an organ can alter blood flow to it.
  - Why? Blood flow to an organ depends on needs of that organ for oxygen or nutrients.
  - Example: after meal, blood flow is diverted away from muscle to intestine to help with the digestion of food. When exercising, blood is diverted away from the intestine to the working muscle to supply it with oxygen and nutrients while removing carbon dioxide.
- Diverting blood is achieved by altering radius of **arterioles**—by either **vasodilating** them (making them wider) or **vasoconstricting** them (making them narrower).
  - Recall: changing diameter either increases or decreases blood flow.
  - Equation 4: $Blood\ flow = (Pressure\ Change)\ x\ (r^4)$



9.15-9.16 - Blood Pressure and Resistance throughout the Systemic Circulation

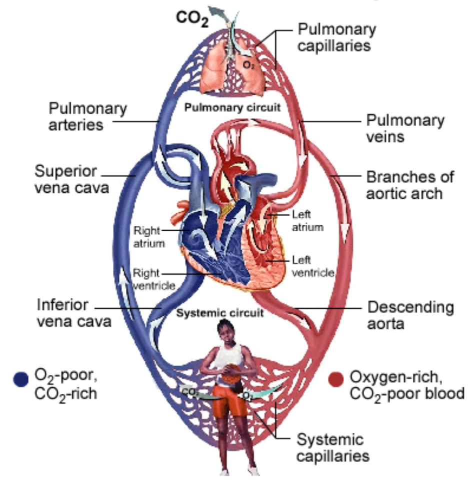
- When doctors measure blood pressure, they listen for specific tapping sounds: **Korotkoff's** sounds.
  - Blood produces these when flow becomes turbulent as it "squeezes" through blood vessels pinched off by pressure cuff as pressure is released.
    - **Systolic pressure**: Pressure when sound first appears.
    - **Diastolic pressure:** Pressure when sound disappears (flow becomes laminar again).
- Pressure in aorta and large arteries is pulsatile.
  - Normal healthy individual fluctuates between systolic pressure: 120 mmHg (heart contracts) and diastolic pressure: 80 mmHg (heart relaxes).
  - Since both aorta and large arteries are very elastic and have a large radius, very little blood resistance.
    - ∴ Pressure remains high in these vessels.
- Fall in pressure begins in small arteries where blood resistance begins to increase.
  - Greatest drop in pressure occurs in arterioles due to very large resistance (largest in entire systemic circulation).
    - Here, pressure decreases from roughly 80 mmHg – ~30 mmHg.

- Pressure continues to drop in capillary from 30 – 10 mmHg and then from 10 – 5 mmHg in veins.
  - Small but significant amount of resistance is present in venous circulation
    - By the time blood reaches the right atrium, the pressure is almost 0 mmHg.

9.17 - A Quick Review

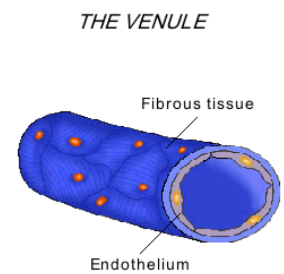
- Main purpose of cardiovascular system: to circulate blood, thereby delivering oxygen/nutrients to cells while removing carbon dioxide/waste.
  - To reach all cells, blood must flow through a series of ever-branching vessels that get smaller and smaller and then reconverge and get bigger.
- Driving force behind this flow of blood: **pressure gradient**, which is high at the beginning of the circulatory system and low at the end.
  - As blood flows through vessels, it encounters **resistance** slowing blood flow.
- Blood flow can be redirected to organs based on oxygen and nutrients needs by a combination of **vasoconstricting** and **vasodilating arterioles**.

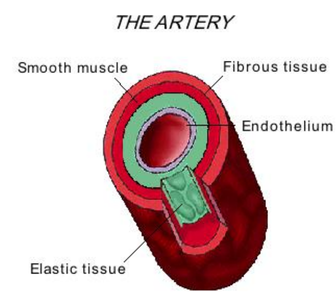
General Schematic of the Cardiovascular System

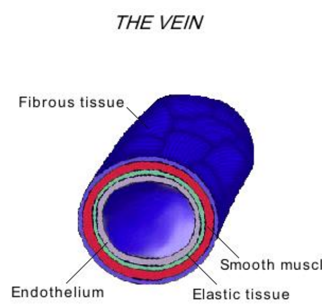


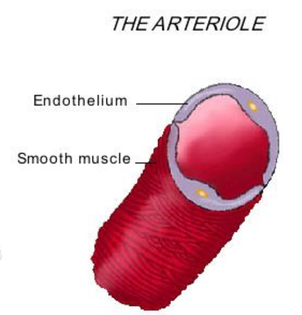
9.18-9.20 - Structure of Blood Vessels

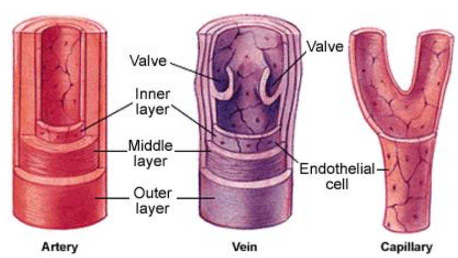
- Structure of blood vessels are responsible for the differences in pressure, resistance, and volume that can be found throughout the circulatory system.
- Arteries and veins contain three layers in their walls.
  - **Tunica externa**: outermost layer – composed mostly of **fibrous connective tissue**.
  - **Tunica media**: middle layer – consists of **smooth muscle and elastic tissue.**
  - **Tunica interna:** innermost layer – is composed of **endothelial cells**.
    - Along with these three layers, veins also contain **valves** to ensure blood flows in one direction—back to the heart.
- **Capillaries**, on other hand composed entirely of a **single layer of endothelial cells**.
  - These thin walls permit the diffusion of substances into and out of the blood.
- **Arteries** have walls with larger proportion of elastic tissue.
  - These vessels must be able to withstand/absorb the large pulsatile pressure changes during contractions of the heart.
- **Vein** walls are thinner than arteries. Contain some smooth muscle and a little elastic tissue.
  - Makes them more flexible and distensible; therefore, are able to contain 70% of total blood volume.
  - Small amount of muscle tissue and presence of valves allow these vessels to constrict, propelling blood back to the heart.
- **Arterioles** contain mostly smooth muscle and are able to constrict/dilate to redirect blood to and from organs.
- **Venules** contain no smooth muscle or elastic tissue since blood pressure is very low and their function is essentially to return blood to the veins.
- **Capillaries** are composed entirely of endothelial cells, facilitating diffusion of substances into and out of the blood.

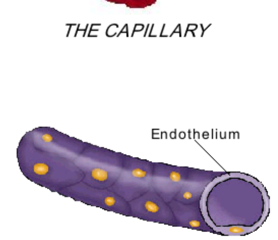


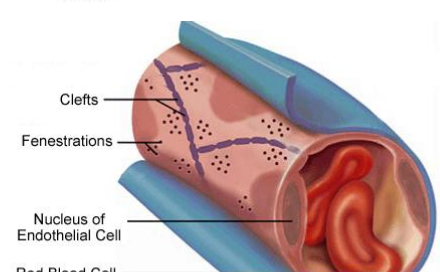








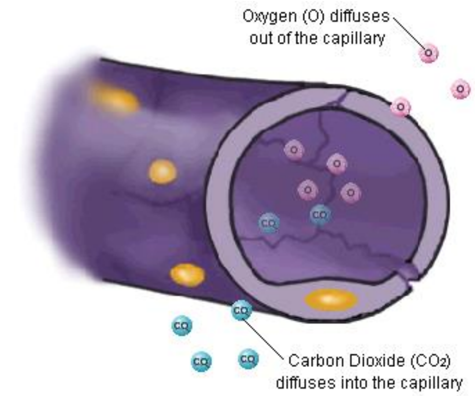




9.21 - Exchange of Substances across the Capillary

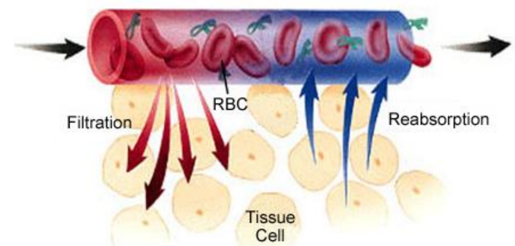
- Movement of oxygen, nutrients, water, carbon dioxide, and waste is enhanced by the very thin **endothelial cell** and also the presence of **clefts and fenestrations** in capillary.
  - These holes allow movement of water and most dissolved solutes (except large proteins) in/out of blood.
- Movement of dissolved substances across capillary occurs by diffusion, filtration, and reabsorption.

9.22 - The Capillary—Diffusion



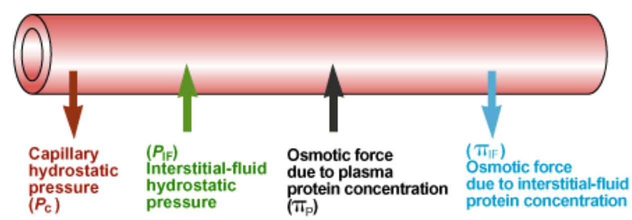
- Recall: diffusion is random movement of a solute down its concentration gradient.
  - Both oxygen and carbon dioxide are lipid soluble so they diffuse right through capillary endothelium.
    - Oxygen/nutrients = high in blood concentration and diffuse into interstitial fluid.
    - Carbon dioxide/waste = high in the tissue and diffuse into the blood.

9.23 - Filtration and Reabsorption (Starling Forces)



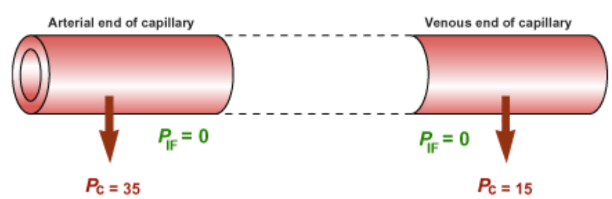
- Capillaries have small clefts and fenestrations that water and dissolved solutes can pass.
  - **Filtration:** process whereby fluid moves from capillary out to interstitial space.
  - **Reabsorption**: movement of fluid from interstitial space back into capillary.
- Four different "forces," called **Starling Forces**, acting on the fluid determine whether filtration or reabsorption occurs.
  - (*Do not* confuse these forces with the **Frank-Starling Law of the Heart**.)

9.24 - Starling Forces



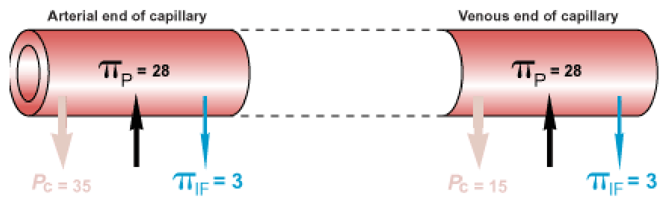
- Four Starling Forces can be broken into:
  - **Two hydrostatic pressures**:
    - **Capillary hydrostatic pressure** (P_c) – Filtration
    - **Interstitial-fluid hydrostatic pressure** (P_{IF}) – Absorption
  - **Two osmotic forces** (sometimes called colloid osmotic pressures, or COP):
    - **Osmotic force due to plasma protein concentration** (π_P) – Absorption
    - **Osmotic force due to interstitial-fluid protein concentration** (π_{IF}) – Filtration
- Each of these forces will cause either filtration or reabsorption.
- Important to realize each of these pressures and forces varies from tissue to tissue (and sometimes from textbook to textbook).

9.25 - Starling Forces—Hydrostatic Pressures



- **Capillary (blood) hydrostatic pressure** (or P_C for short): pressure on fluid forcing it outward on walls of capillaries.
  - Pressure ≅ 35 mmHg at arterial end of the capillary, and ≅ 15 mmHg at the venous end of capillary causing **filtration**.
  - Recall: resistance causes decrease in pressure along capillary.
- **Interstitial-fluid hydrostatic pressure** (or P_{IF} for short): pressure from fluid in interstitial compartment pushing back on capillary.
  - This pressure varies organ to organ, from –6 mmHg (in subcutaneous tissue) to +6 mmHg (in the brain and kidneys).
  - Assume that there is no hydrostatic pressure in the interstitial fluid.

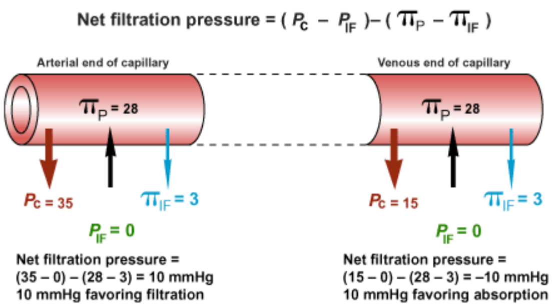
9.26 - Starling Forces—Osmotic Forces



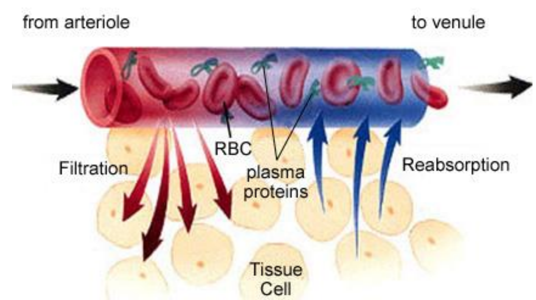
- **Osmotic forces** (or colloid osmotic pressures—COP): cause fluid to move into an area due to osmosis. Caused by presence of **large proteins** in **plasma** (generally albumin) and in **interstitial fluid**. These proteins are unable to move across capillary and causing osmosis.
  - **Osmotic force of plasma proteins** (or π_P): draws fluid back into capillary, causing **reabsorption**.
    - Since plasma contains a lot of proteins, this force is high at 28 mmHg.
  - **Osmotic force of proteins in the interstitial space** (or π_{IF}): pulls fluid out of capillary, causing **filtration**.
    - Since interstitial fluid contains little proteins, this force is low—around 3 mmHg.

9.27 - Starling Forces—Net Filtration Pressure

- Four forces battling to move fluid in/out of capillary: **Filtration (out)**, **Reabsorption (in)**.
  - To determine NET direction of fluid movement, calculate NET filtration pressure (NFP) using:
    - **NFP = $(P_c - P_{IF}) - (\pi_P - \pi_{IF})$**

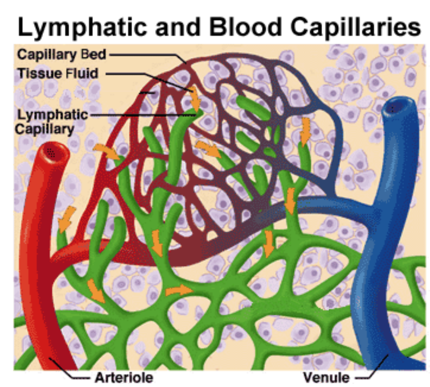


  - Substituting our values from the previous pages (using P_c from the arterial end = 35) into the above equation results in the following:
    - **NFP = [(35 – 0) – (28 – 3)] = +10 mmHg**
  - Because value is positive, there is a net filtration of fluid *out* of capillary into interstitial space with a pressure of 10 mmHg.
  - If we were to do this again using Pc from the venous end (15 mmHg), we would have a net filtration pressure of **–10 mmHg**
    - Reabsorbing fluid back into capillary. Therefore, fluid is moving out at arterial end of capillary and back in at venous end.



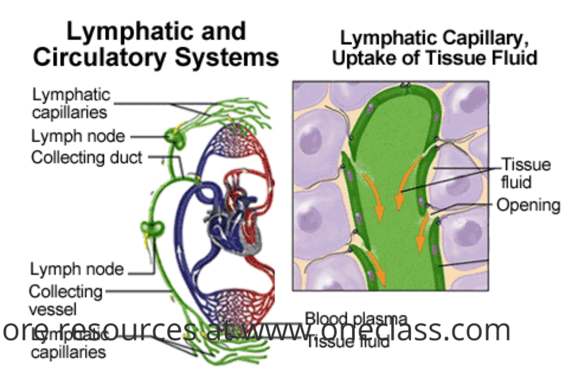
9.28 - Starling Forces and the Lymphatic System

- Had balance between filtration and reabsorption along length of capillary.
  - Should be pointed out, because four Starling Forces can vary between tissues and circumstances, this is not always the case.
  - Some situations where excess of fluid is filtered from capillaries, causing accumulation in interstitial space.
    - Example, subcutaneous tissue has negative hydrostatic pressure in interstitial space of roughly –6 mmHg.
    - Using previous values/equation → net filtration pressure = +16 mmHg at arterial end and –4 mmHg at venous end with an overall net filtration out of the capillary!
    - Where does all of this excess fluid go? **Lymphatic system**.



9.29-9.30 - The Lymphatic System

- **Lymphatic system:** Return **excess fluid** and other dissolved substances that enter interstitial space back into circulation through a system of vessels.
  - Large network of capillaries and vessels that returns excess fluid to systemic circulation.
- Consists of small blind-ended capillaries where excess fluid passes through openings.
  - Lymphatic capillaries return fluid to larger collecting vessels that pass through lymph nodes.
  - Lymph nodes filter/screen fluid for foreign particles before sending it back to venous circulation through collecting ducts.

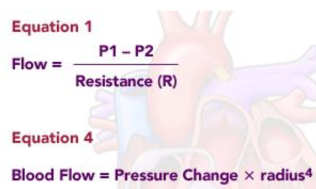


9.31 - Edema

- **Edema**: swelling in interstitial space caused by accumulation of fluid**.**
  - Under normal circumstances, does not occur because lymphatic system removes excess fluid.
  - Certain conditions such as the following, however, cause accumulation of fluid → producing edema:
    - An increase in the capillary hydrostatic pressure caused by increase in blood pressure.
      - Can occur during weight lifting when muscles contract long time without relaxing
        - Pinches off veins and causes blood pressure to increase in capillaries.
        - This edema in muscle causes "pumped up feeling" you get immediately after lifting weights.
        - Disappears once lymphatics pick up this excess fluid.
    - A decrease in plasma osmotic force
      - Occurs in cases of severe malnutrition leading to decrease in amount of plasma proteins.
        - With less water moving back into capillaries, fluid accumulates in interstitial space and can result in the bloated abdomen of malnourished children.
    - A blockage or disruption of the lymphatic system
      - Can occur after radical mastectomy that removes lymph nodes in and around the arms.
        - Because excess fluid in the arms cannot be removed by the disrupted lymphatic drainage, edema results in the hands and upper limbs.

9.32 - Control and Regulation of the Cardiovascular System

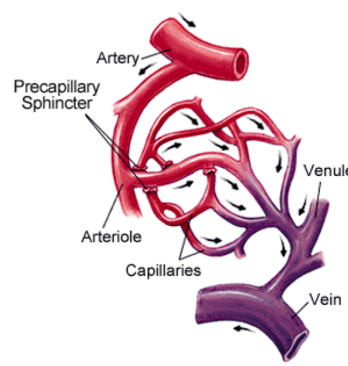
- Very important that cardiovascular system is regulated to maintain blood pressure at relatively constant levels.
  - Regulating cardiovascular system also ensures:
    - Cardiac output increases during exercise and decreases when at rest.
    - Blood flow to active tissues is increased while it is decreased to inactive tissues.
    - Most importantly, that there will always be adequate blood flow to vital organs.
- The three mechanisms that regulate the cardiovascular system:
  1. Local control mechanisms in the organs themselves
  2. Humoral mechanisms that rely on chemicals in the blood
  3. Autonomic nervous system (ANS), which alters the cardiac output and blood flow to organs



9.33 - Remember . . .

- To change blood flow to an organ, either:
  - Alter pressure change (P1 – P2)
  - Resistance
  - Radius of the vessel as shown by equations 1 and 4 at right

9.34 - Control of Blood Flow—Local Control Mechanisms (Autoregulation)

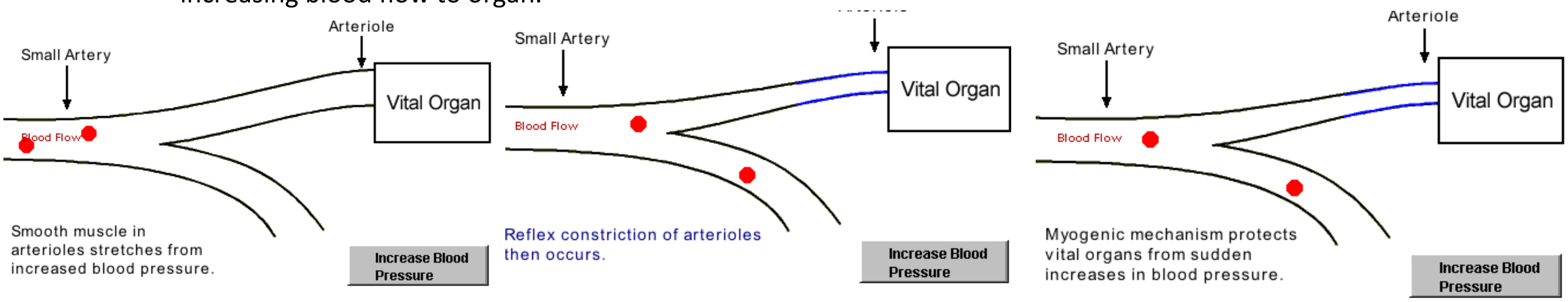


- Most tissues (especially brain, kidneys, heart, and skeletal muscle) have ability to control own blood flow by a process called **autoregulation.**
  - **Autoregulation**: process by which individual capillary beds maintain relatively constant blood flow when moderate changes occur in blood pressure.
  - The mechanisms responsible for local control are explained by two theories:
    - The **myogenic** theory
    - The **metabolic** theory
  - According to these theories, regulation of blood flow is achieved through changes in vessel radius—usually at arteriole or precapillary sphincter.

9.35 - Myogenic Theory

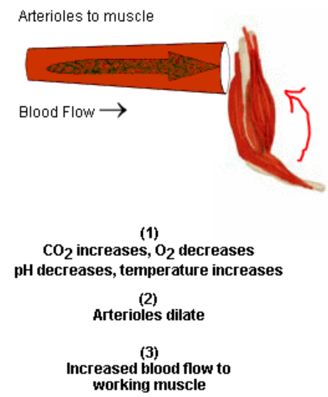
- **Myogenic theory**: refers to changes in blood flow produced by contraction/relaxation of **smooth muscle** in walls of the blood vessels.
  - Sudden increase in blood pressure to a vital organ causes blood vessels feeding that organ to briefly dilate.
  - This vasodilation causes reflex contraction of smooth muscle in walls of arterioles supplying organ.
  - Contraction of smooth muscle causes a vasoconstriction, decreasing blood pressure and flow.
  - This mechanism protects delicate capillary network in vital organs from sudden increases in pressure.

- The opposite can occur when there is a sudden drop in blood pressure ultimately producing a vasodilation, increasing blood flow to organ.



9.36 - Metabolic Theory

- Changing **metabolic activity** of an organ also **changes blood flow** to that organ.
  - Example: during exercise working muscle **heats up, uses oxygen, and produces carbon dioxide, lactic acid, and adenosine** (from the breakdown of ATP).
    - These metabolic by-products act locally on blood vessels, causing **vasodilation** and **increased blood flow** to active tissue.
    - Once exercise stops metabolites are washed out, vessel will return to its original size and blood flow decreases to normal.



9.37 - Humoral Regulation

- Humoral regulation involves regulation of blood flow **by chemical substances circulating in blood** (other than local metabolites).
  - Humoral regulators fall into two categories:
    1. **Vasoconstrictors**
       - **Agents include:**
         - **Epinephrine**: released from adrenal gland in response to a fight/flight situation, weak effect on blood vessels of intestine
         - **Angiotensin** (**Ang II**): one of most powerful vasoconstrictors in the body.
         - **Vasopressin**: (aka antidiuretic hormone/**ADH**) another hormone important in renal system
    2. **Vasodilators**
       - **Substrates include:**
         - **Epinephrine:** released during fight/flight, causes vasodilation of blood vessels in skeletal muscle and cardiac muscle.
         - **Kinins:** family of hormones formed in plasma and tissue.
         - **Histamine:** released from cells after damage.
         - **Atrial natriuretic factor (ANF):** produced by atrial muscle cells
- Note: hormone epinephrine (also called adrenaline), released from adrenal glands, can cause both vasoconstriction and vasodilation.
  - Can do this because it binds to different receptors in different organs.

9.38 - Neural Control Mechanisms

- Two divisions of the **autonomic nervous system** can also regulate blood flow because both divisions innervate the **smooth muscle** found in walls of the arterioles.
  - Contracting smooth muscle causes **vasoconstriction** (increasing resistance) leading to **decrease in blood flow**.
  - Relaxing smooth muscle produces **vasodilation** (decreasing resistance) leading to **increase in blood flow**.

The sympathetic nervous system, which is involved with the **fight or flight response**, causes an overall **vasoconstriction** by releasing **norepinephrine** onto the smooth muscle of blood vessels. However, it releases **acetylcholine** onto the blood vessels in skeletal **muscle** producing a **vasodilation**. By doing so, it redirects blood away from the digestive system, kidneys, and spleen and toward the muscle.

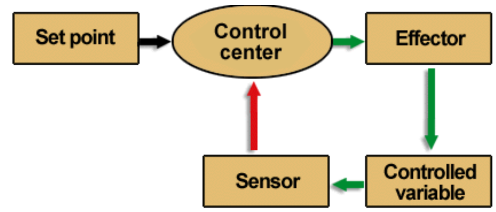
The parasympathetic nervous system, which is involved with **rest and relaxation**, does not strongly innervate the smooth muscle of blood vessels; where it does, however, it releases **acetylcholine** and produces a **vasodilation**.

9.39 - Regulating Blood Pressure by the Baroreceptor Reflex

- Extremely important that blood pressure is maintained at relatively constant levels.
  - The cardiovascular system uses **Baroreceptor reflex** to regulate blood pressure.
  - To better understand how, understand how to calculate blood pressure:
    - $Mean\ Arterial\ Pressure\ =\ Cardiac\ Output\ x\ Total\ Peripheral\ Resistance$
      - **Cardiac output**: amount of blood pumped by each ventricle in one minute
      - **Mean Arterial Pressure**: average pressure in arterial side of circulation.
      - **Total Peripheral Resistance**: sum of all resistance in all blood vessels in body throughout circulatory system.
- Notice: increasing cardiac output or total peripheral resistance increases pressure and vice versa.

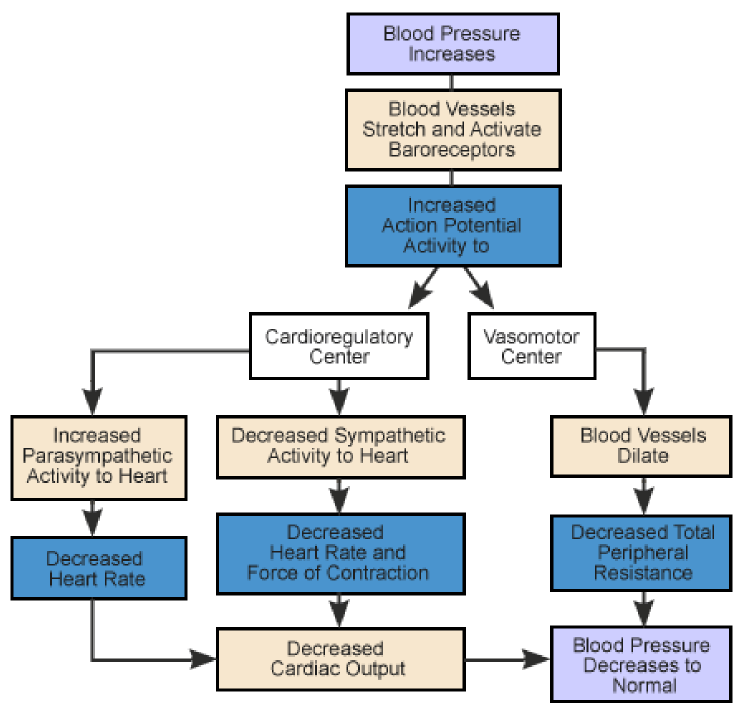
9.40-9.42 - The Baroreceptor Reflex

- Baroreceptor: perfect example of negative feedback mechanism.
    - Recall feedback loop relies on:
        - Set point (normal blood pressure value of 120/80)
        - Control center (cardiovascular center in the brain stem)
        - Effector (the heart and blood vessels)
        - Controlled variable (blood pressure)
        - Sensors (baroreceptors).



    - Baroreceptor reflex relies on special stretch receptors called **baroreceptors** located in walls of aortic arch and carotid sinuses.
        - Receptors are sensitive to stretching of blood vessel wall.
        - Increase in blood pressure stretches vessel walls (carotid arteries and aorta).
        - Activating receptors in these parts to increase basal rate of AP sent to cardioregulatory and vasomotor centers in medulla oblongata.
            - AP is conducted through:
                - Glossopharyngeal nerves (from carotid sinus) → Cardioregulatory center
                    - Cardioregulatory center increases parasympathetic stimulation (by Vagus nerve) to heart = decreases heart rate.
                - Vagus nerves (from Aortic arch) → Vasomotor center
                    - From center → signal travels to cardiovascular center which sends signal down Sympathetic nerves/chains:
                        - Decreases sympathetic stimulation to heart = decreases heart rate and stroke volume.
                        - Decreases sympathetic stimulation to blood vessels = vasodilatation
        - Vasodilatation + decrease in Blood pressure + decrease in Stroke volume
            - Bring elevatent blood pressure back to normal
        - If initial problem were decrease in blood pressure, activities + effects would be opposite

- Sudden increase in blood pressure dilates almost all blood vessels.
    - Walls of these vessels stretch, activating baroreceptors in arotic arch and carotid sinus.
    - As pressure increases, baroreceptors increases frequency of action potentials sent to cardioregulatory center and vasomotor center in brain stem.
    - To return blood pressure to normal, cardiac output and total peripheral resistance must be decreased.
- Recall:
    - Blood Pressure = CO TPR
    - Cardiac Output = HR Stroke Volume
- Cardioregulatory center activates parasympathetic nervous system shuting down sympathetic nervous system.
    - Result: drop in heart rate and force of contraction (decreasing stroke volume and, consequently, cardiac output).
    - Vasomotor center causes vasodilation of most blood vessels (decreasing total peripheral resistance).
    - Blood pressure will then return to normal.
- The opposite can occur if there was a sudden decrease in blood pressure.



9.43-9.46 - The Big Picture

- Keep in mind the entire cardiovascular systems main function is to deliver oxygen and nutrients while removing carbon dioxide and waste.
  - Essential that proper amounts of oxygen are delivered, while metabolic waste and carbon dioxide are removed.
    - Therefore, blood flow must be regulated precisely to each organ; this will depend on the organ's own requirements, which vary all the time.

Equation 1

$$\text{Flow} = \frac{P1 - P2}{\text{Resistance (R)}}$$

Equation 2

Blood Pressure = Cardiac Output (CO) × TPR

Equation 3

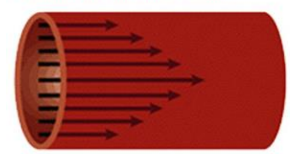
CO = Heart Rate (HR) × Stroke Volume (SV)

- Blood flow is dependent upon a pressure gradient and resistance the blood encounters in vessels.
  - Recall Equation 1.
- If you want to regulate blood flow, you can either change pressure or resistance.
  - Recall Equation 2.
- To change blood pressure, can change CO or TPR.
  - Recall Equation 3.

Equation 1

$$\text{Flow} = \frac{P1 - P2}{\text{Resistance (R)}}$$

Laminar Flow and Vessel Radius



- We know that ANS controls both
  - heart rate (HR)
  - stroke volume (SV)
- Parasympathetic branch decreases HR and SV, while sympathetic branch will do the opposite. Altering the end diastolic volume (EDV; that is, Starling's Law) can also change SV.
- Resistance that blood encounters in a vessel depends on several factors, but most important one is inside diameter or radius of blood vessel.
  - Recall the equation shown at right.

- Consider what an increase in total peripheral resistance (TPR) will do (Review the equation at right)
  - Increase TPR, will increase blood pressure.
    - But, do you want to increase blood pressure?
      - In normal circumstances you want to maintain a normal pressure around 120/80 mmHg.
      - You have a higher blood pressure so body will try and return it to normal by baroreceptor reflex.
        - Baroreceptor reflex will decrease heart rate and force of contraction to reduce the cardiac output; this will help to reduce blood pressure.
        - Reflex may also vasodilate blood vessels in order to reduce TPR in other organs other than the one we began with. Again, this will reduce blood pressure.

Blood Pressure = CO × Total Peripheral Resistance (TPR)