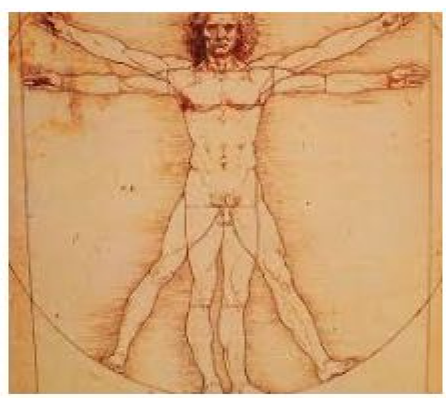
LECTURE 1
- Skeletal, neurons, cardic, kidneys, immune
- Blood classified as a tissue because it has cells and can form clots (solidifies)

Themes in Physiology
- 5 themes (#1 and #4 most important!)
    1. Structure and function are closely related across all levels of organization
    2. Energy - storage, transfer, use
    3. Information flow coordinates body functions
    4. Homeostasis and the control systems that maintain it
    5. Evolution

In a living system, form (anatomy) will always fit with function (physiology)
- All living things perform the same functions
    1. Respond to changes in their immediate environment
        a. Ex. sweating in the heat, it is your body responding to elevated temp
    2. Show adaptability
        a. Your body will adapt and be ready to handle it if you work outside for most of the day
    3. Grow and reproduce
        a. Offspring can adapt to environment
    4. Capable of some degree of movement
        a. To run to avoid danger or capture food
    5. Life functions require energy
        a. ATP
- Organisms are physical beings, and as such physiological process must *obey laws of chemistry and physics*

The Vitruvian Man
- Proportions of the human body according to Vitruvius
- Depics the idea human proportions
- Early origins in the study of anatomy and physiology

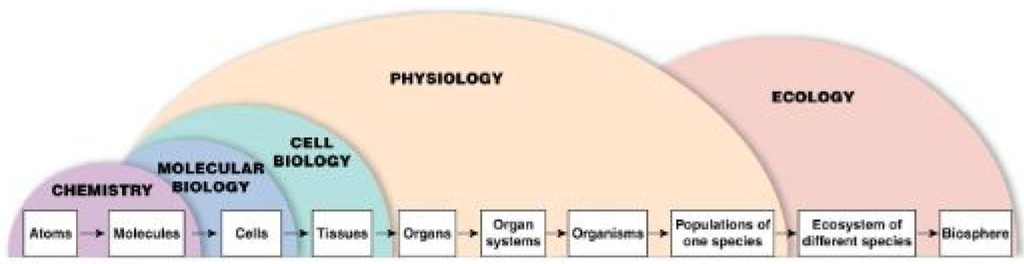


Human Body Can Be Broken Into A Series of Related Groups or Systems
- The study of an organism:
    - Broken down to series of groups or sections
        - One part cannot function alone however
    - Can see how each group/section works within itself
        - And in conjunction with other groups and sections as a whole

How the body is organized

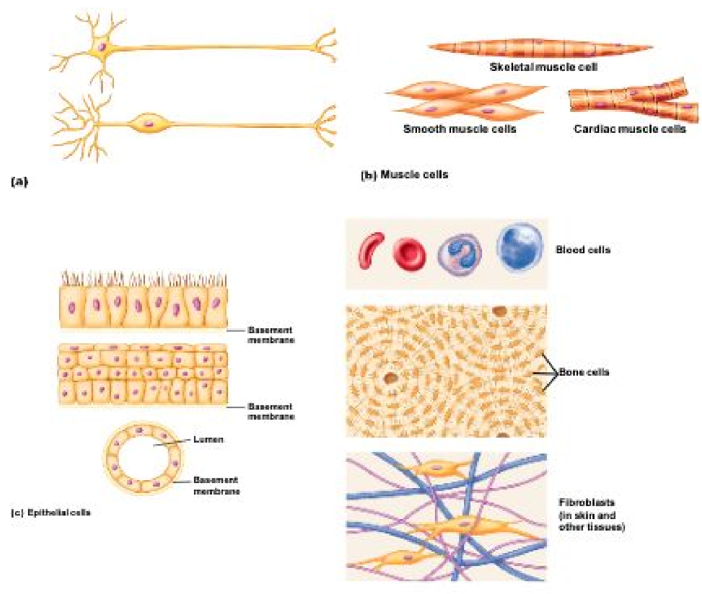
- We are made of *organ systems (*11 types)
- Organ systems are made of *organs*
- Organs are made of *tissues*
- Tissues are made of *cells*
- Cells are made of *cellular structures*

Body Functions are Integrated

- Parts of the body work together - a meaningful context
- Proper functioning and support of one part depends on the function of a different part(s)
- Ex:
    - Muscle requires oxygen provided by erythrocytes in blood that are manufactured in bone marrow
    - Erythrocyte synthesis requires the hormone erythropoietin, which is secreted by the kidneys
    - Oxygen is extracted from air breathed in by the lungs
    - Lung expansion is controlled by the nervous system
    - Blood is pumped by the heart
    - 

Overview of major cell types in body

- There are over 200 cell types in the body
    - 4 major classes
        - Neurons
        - Muscle cells
        - Epithelial cells
        - Connective tissue cells
    - Together these make the four main types of tissues in the body



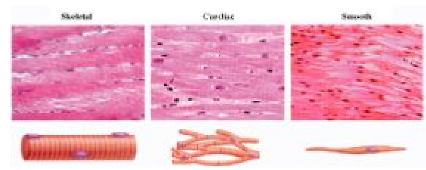
Neurons and Neural Tissue

- Specialized to carry information or instructions within the body
- Two basic types of cells

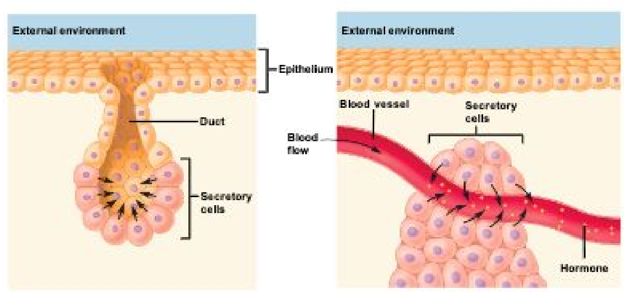
1. Neurons (nerve cells)
    - Transmit information in form of electrical impulses
2. Neuroglia (supportive cells)

- Isolate and support neurons
- Form supporting framework
- Two locations within the body
  1. Central Nervous System
     - Brain and spinal cord
  2. Peripheral Nervous System
     - Nerves connecting central nervous system with other tissues and organs
- Neural tissue:
  - Conducts electrical impulses
  - Carries information

<u>Muscle cells and Muscle Tissue</u>
- Contract to generate mechanical force and movement
- Electrical signals → mechanical force
- Voluntary - skeletal muscles (arms, legs)
- Non-voluntary - cardiac, smooth muscle (blood vessels), responds to the rest of the body



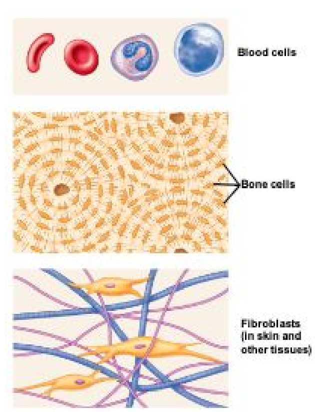
<u>Epithelial cells and Epithelial Tissue</u>
- *Epithelium*: sheet-like layer of cells
- Forms lining of internal body surfaces and cavities
- Forms lining of hollow organs
  - Blood vessels have specialized epithelium called endothelium
  - Lumen = interior
- Major function - a protective barrier (ultimately maintain homeostasis)
- Forms glandular tissue
  - Produce compounds
  - Exocrine glands: products collect and release into ducts
    - Sweat, salivary, tears
  - Endocrine glands: direct release into the bloodstream, no ducts
    - Pituitary, thyroid, adrenal, hypothalamus



Exocrine glands
Products collect and released into duct
Eg. sweat, saliva, tears

Endocrine glands
Direct release into bloodstream
Pituitary, thyroid, hypothalamus

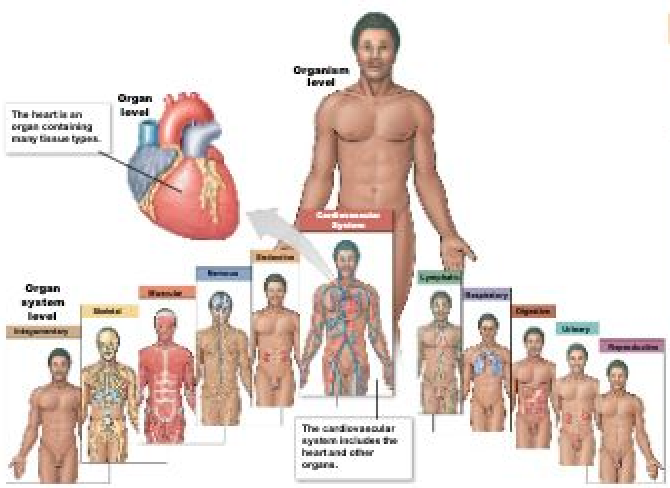
<u>Connective cells and connective tissue</u>
- Most diverse of the four cell types
- Has extracellular matrix

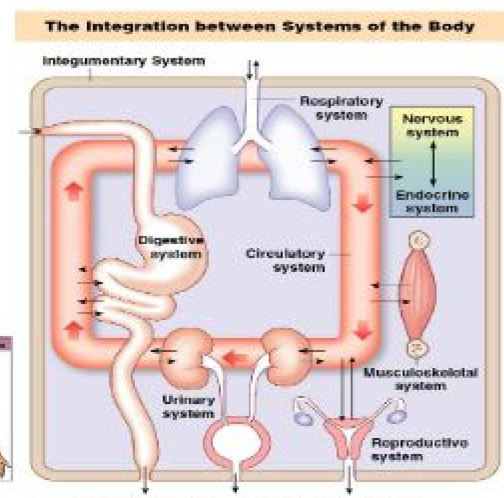


- Functions to anchor, attach body structures
- Bone, tendons, fat, blood (blood is connective!!)
    - Blood forms the fibrous network (fibroblasts)

<u>Organs and Organ Systems</u>

- *Organs*: have at least two tissue types and perform specific functions
- *Organ system*: collection of organs performing a particular task
    - 11 organ systems (sometimes 10 in some sources)
        - **Integumentary**, **skeletal**, **muscular**, **nervous**, **endocrine**, cardiovascular, **lymphatic**, **respiratory**, **digestive**, **urinary**, **reproductive**
        - **MR. SLICED, RUN!**
    - All are vital but none function in isolation
    - Some are physically connected (ex. Gastrointestinal, cardiovascular, urinary)
    - Some are not connected but widely scattered (ex. Endocrine, lymphatic (immune) system
    - All systems are interdependent
    - All systems strive to maintain homeostasis





This schematic figure indicates relationships between systems of the human body. The interiors of some hollow organs (shown in white) are part of the external environment.

    -

<u>Overall Body Plan</u>

- Overall plan of the body can be broken down into a very simplistic model
- Consists of:
    1. External environment
    2. Internal environment
        - Must have a source to exchange air (O_2/CO_2)
        - Must have a way of taking in nutrients and sending out waste
        - Must have a way of moving the components from air exchange and nutrients around to the rest of the body

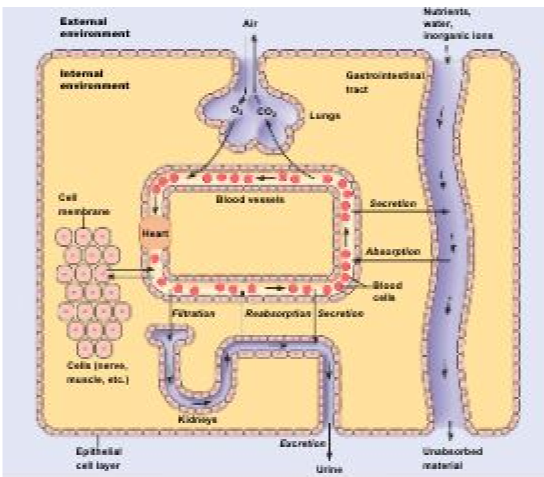
- You don't need to have movement as a critical function of the body!

GOALS/OBJECTIVES

- Understand and describe the big themes in physiology (two big ones = homeostasis, form & function)
- Understand and describe the concept of 'form fits function'
- List major components of body
- Describe and give examples of major cell types found in the body
- Know 11 organ systems - provide detailed examples of how they're related

LECTURE 2 - Homeostasis, cell structure, and function

Reductionist View of the Body

- 

- What's wrong with this picture?
    - It is missing limbs (arms legs head)
    - GI tract isnt a straight line
    - Lungs is single sac here with nothing surrounding it
    - Heart is square...its not that simple
    - Not all cells look like that

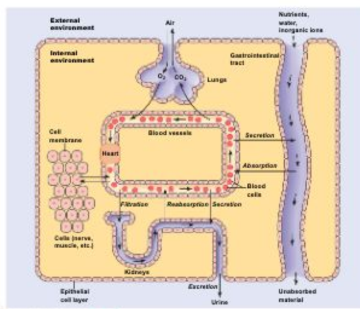
Internal and External Environments are Separated

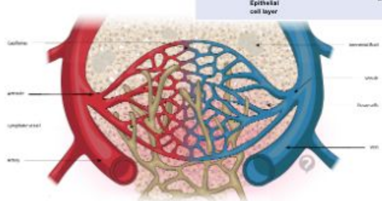
- Epithelial cells form a layer that separates the external environment from the inside of the body
- Skin, linings of the lungs, GI system, kidney tubules - *all are continuous with the external environment*
- Examples of how body is connected to external environment:
    - Surroundings external to the skin
    - Air in the lungs
    - Food in the stomach
    - Urine in the bladder

    - Things generated inside can get outside, but the key to maintaining homeostasis is protecting the internal from the external

<u>Internal Environment</u>

- Immediate environment of most cells
- Includes tissue fluid and plasma
    - *Tissue fluid* (interstitial fluid) is fluid around all other cells
    - *Plasma* is fluid around/surrounds blood cells
    - In to cell: → nutrients O_2
    - Out of cell: ← waste CO_2
        - Always exchanging waste and nutrients, it can tell us what the tissue is doing
        - Anything that is alive uses energy, and anything using energy produces waste



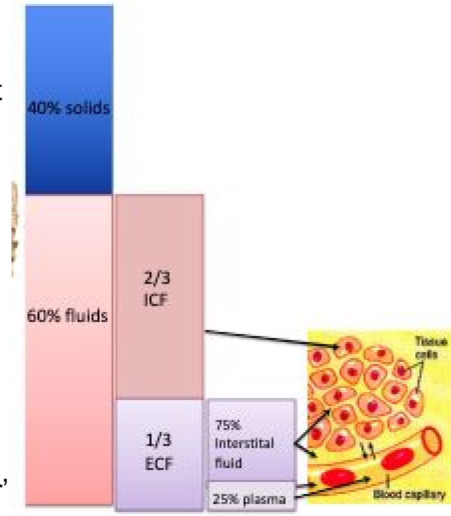
    - 

<u>Exchange Between Internal and External Environment</u>

- Cells exchange nutrients and wastes between internal and external environment
- But most cells are not in direct contact with the external environment
- Material is exchanged between blood (plasma)
    - Ex. lungs, GI tract, kidneys
    - *Across gastrointestinal tract*
        - Absorption
        - Secretion
    - *Across kidneys* (critical for homeostasis!!)
        - Filtration
        - Reabsorption (kidneys filter everything but then reabsorbs things like glucose)
        - Secretion

<u>Body Fluids and Compartments</u>

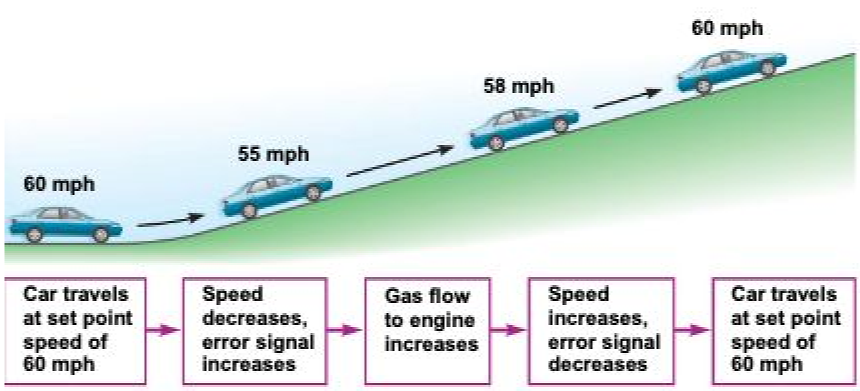
- Body is divided into (fluid) compartments
- Compartments contain fluids
- Compartments are separated by *epithelial membranes*
- Membranes are semipermeable (means sometimes can go across but not always...it allows things to cross membrane but not everything)
- Transport occurs between compartments
- Breakdown of compartments →
    - ICF = intracellular
    - ECF = extracellular



<u>Homeostasis - Began as a Concept</u>
- Claude Bernard
    - Described how internal environment is separate and different from the external environment 'milieu interieur'
- Walter Cannon
    - 'Homeostasis'
    - Underlying principle of physiology

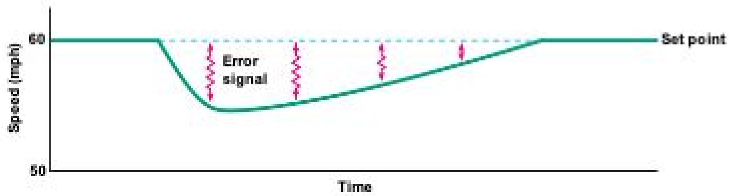
<u>Homeostasis</u>
- Defined as the *ability to maintain a relatively constant internal environment despite changes in the external environment*
- Components of the internal environment that are regulated include:
    - Temperature
    - Volume
    - Composition
- Homeostasis requires different organ systems to integrate and work together
- Disruption of homeostasis → disease and death

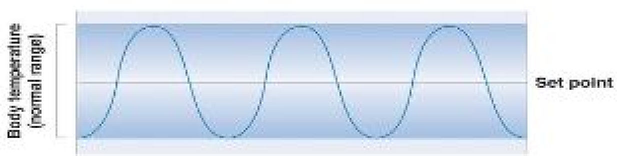
<u>Modeled after car on cruise control</u>



-
- The signals turn off after returning to set point
- This is about a set point and a feedback/monitor, a responds/action

Operates within a range

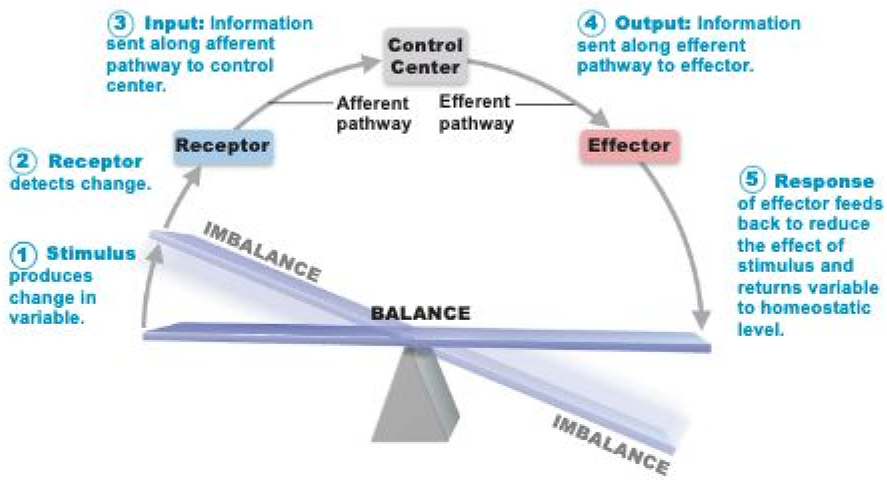
- Homeostatic set point is a series of variances around the normal operating range
- Serves as an error sensing function
- Minor adjustments are continually made to maintain normal operating range
    - We can see the error signals are strong at the start, but starts to become weaker as you return towards the set point again
- 

- 

Terms

- *Regulated variable*: variable that is maintained or is the set-point
    - Ex. speed of car, body temperature, blood pH
- *Negative feedback*: if a regulated variable decreases, system responds to increase it (negative effect) and vice versa
- *Set point*: normal operating range of a regulated variable
    - Ex. core body temp 37 deg
- *Error signal*: difference between the value of the set point and value of the regulated variable

Elements of a Homeostatic Control System



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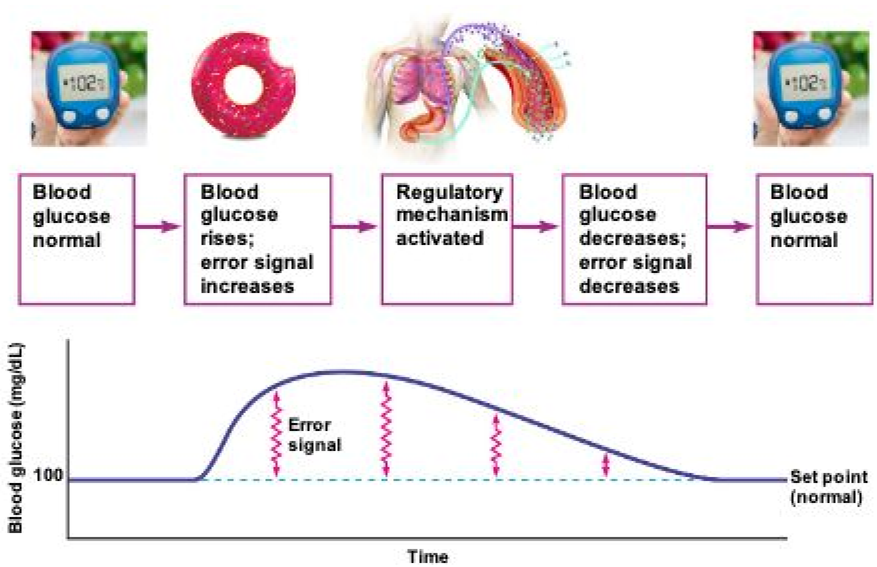
- Afferent (what **a**rrives to control center (CNS)) pathway & Efferent (what **e**xists) pathway

<u>Biological Example</u>



<u>Homeostasis in reality</u>

- Homeostasis of biological variables
    - Fluctuates around a set point
        - Dependent on the individual
        - Individual's adaption to environment
    - Maintained by *multiple* control mechanisms that generate *multiple* simultaneous effects
- Ex. it is hot outside
    - We sweat to regular core temperature
    - We're thirsty, we drink fluids to cool down and replenish the fluids lost via sweat

- Blood vessels open near skin to cool down, other blood vessels contract (ex near digestive system, we don't care about digesting when we're hot)
- There are many things that happen at the same time

CHAPTER 2 REVIEW

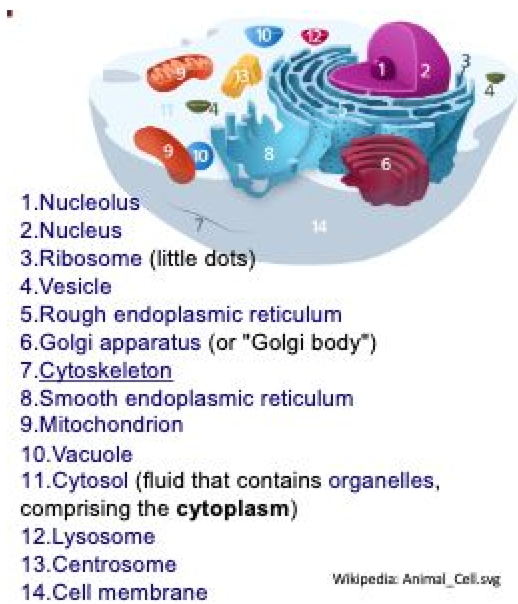
- Biomolecules
- Carbohydrates
- Lipids
- Amino acids and proteins
- Nucleotides and nucleic acids

Cell Structure and Function

- Over 100 trillion cells in the body
- All derived from the fertilized ovum
- 200 different cell types
    - 4 categories
- All cells have the same basic components

Cell Components

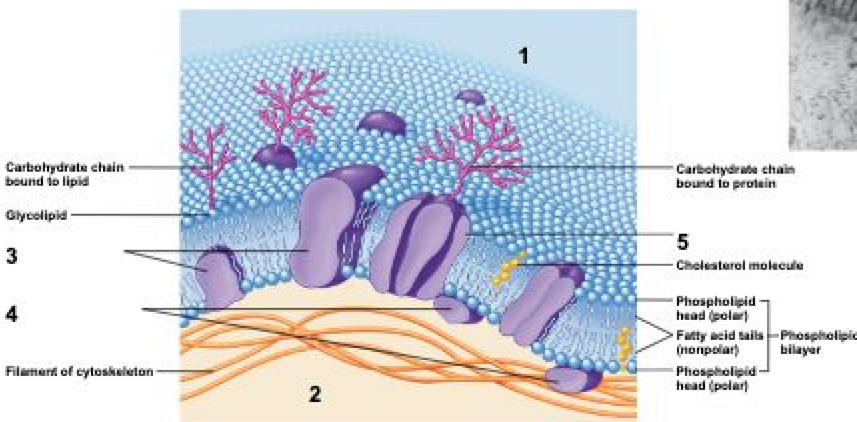
- Plasma membrane
    - Acts as barrier betwen cell and the external environment
    - Fluid inside the cell → ICF
    - Fluid outside the cell → ECF
- Internal compartments of cell
    - Nucleus
    - Cytoplasm (everything but the nucleus)
        - Cytosol - gel component of the cytoplasm
        - Organelles - structural component of the cytoplasm



Cell Structure

- Structure of the Plasma (Cell) Membrane
    - Described as a fluid mosaic model
    - Phospholipid bilayer - lipids form two layers, forms barrier between ECF and ICF
    - Water soluble proteins can't pass easily
    - Moves through channels formed by proteins called aquaporins (water channels)
- Cholesterol
    - Adds fluidity (mobility) to membrane
- Membrane proteins
    - Integral - embed within the bilayer
    - Peripheral - loosely bound

- Membrane carbohydrates
    - Covalently bound membrane lipids or proteins (glycolipids/glycoproteins)
    - Form a protective layer called glycocalyx - holds cells together
    - Help in cell recognition, self-immune function
        - Distinguish our cells from foreign cells

- 

<u>Structure and Function of the Nucleus</u>
- Structure:
    - Nuclear envelope
    - Nuclear pores
    - Nucleolus: site of ribosomal RNA (rRna) synthesis
- Function:
    - Transmission and expression of genetic information
        - Contains DNA: stores the genetic code
        - DNA transcribed to RNA: necessary to express genetic code

<u>Cytosol</u>
- Cytoplasm
    - Cytosol and organelles
- Functions of cytosol (fluid of cell)
    - Location of specific chemical reactions
    - Storage of fat and carbohydrates as inclusions
    - Storage of secretory vesicles
- Focus on:
    - Endoplasmic reticulum (ER)
    - Cytoskeleton
    - Cell-cell adhesions

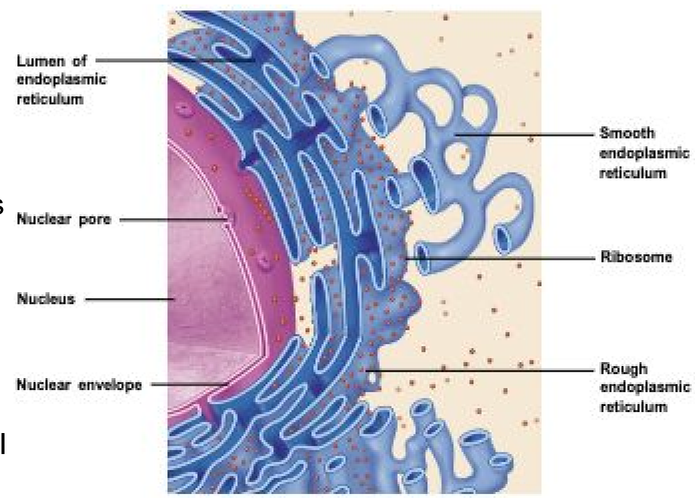
<u>Organelles</u>

- Membranous organelles
    - Membrane separates the structure from the cytosol
        - *Endoplasmic reticulum*
        - Golgi apparatus
        - *Mitochondria*
        - Lysosomes
        - Peroxisomes

Cytosol Components

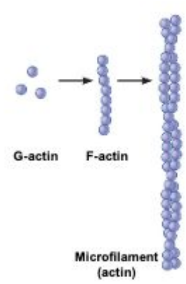
Endoplasmic reticulum

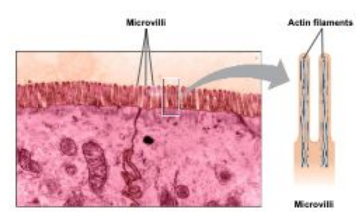
- Endoplasmic reticulum
    - Rough ER
    - Flattened sacs
    - Rich in ribosomes - granular/rough
- Smooth ER
    - Tube like structure, contains things
    - Smooth in appearance
    - Both have a lumen (body) that is continuous

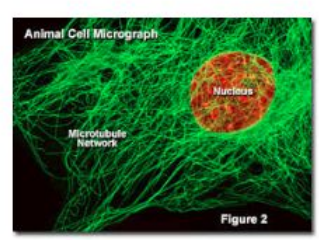


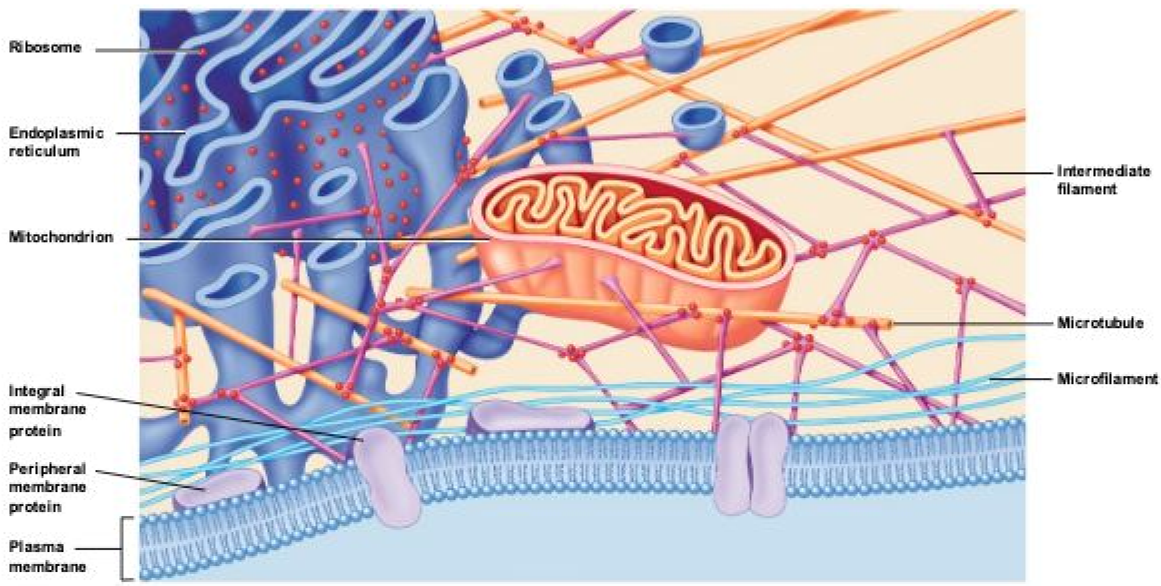
Cytoskeleton

- Makes a lattice protein structure within cell body
- Provides mechanical support, structure, rigidity
- Moves proteins within cell (protein transport)
- Supports and suspends organelles
- Attaches with other cells (cell-cell contact)
- Cellular contraction
- Cellular movement (motility)
- *know the functions of cytoskeleton*
- Three main cytoskeletal filaments:
    - Microfilaments
        - Actin (type of protein) most common
        - Involved in cell movements
    - Intermediate filaments
        - Slightly larger than microfilaments
    - Microtubules
        - Mitotic spindle (cell division)
        - Main part of cilia and flagella









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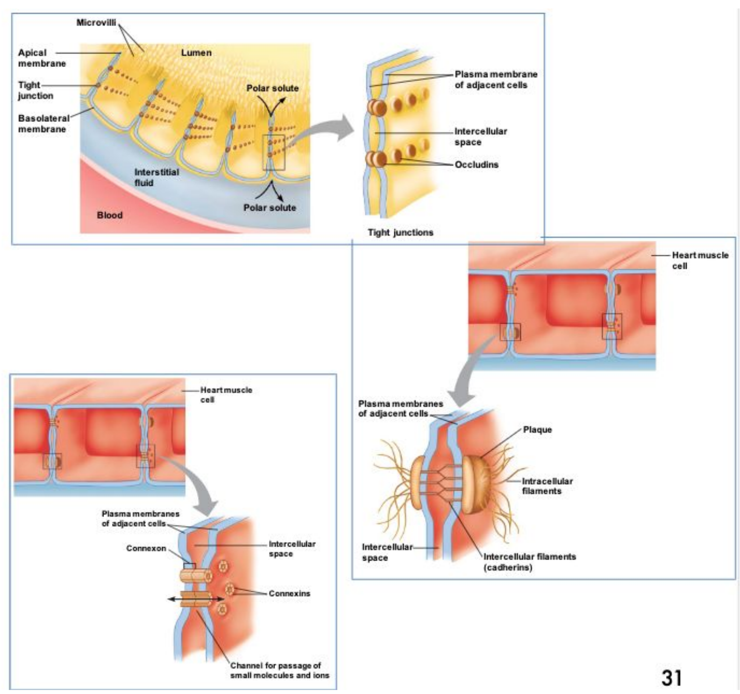
<u>Cell Adhesions</u>

- Cells like to hang out in groups
- Allows cells to function individually, as a group (tissue) and as a unit organ
- Most cell adhesions act to hold cell-cell together
- Other cell adhesions have more specialized roles
- Three main types of specialized junctions**:
    - Tight junctions
        - Hold cells together
        - Surrounds organs
    - Desmosomes
        - Filamentous junction between cells
        - Binds cells together - additional strength
        - Important where cells have *high mechanical stress* (weight lifting)
    - Gap junctions
        - Link (tubes) cytosol of two adjacent cells
        - → allows exchange of cellular components like ions, proteins, signaling molecules, nutrients, etc
        - Provides a direct way for cells to *communicate*
        - How organs are held together



Ricin
- Comes from beans used to make castor oil
- Is a lectin (carbohydrate binding protein)
- LD50 approx 22 mg/kg body weight
- Gets into cells by binding to carbohydrates on cell surface
- *Interferes with ribosomes and prevents protein synthesis*
- Protein synthesis is not a fast process - takes days for toxic effect to show
- Overtime cells need protein and if it doesn't get protein, the cells dies
    - Cells dies - tissue dies - organs die - organ system dies - you die
    - Body is not in homeostasis

OBJECTIVES/GOALS
- Put together the human body from a reductionist view
- Identify and define different components of body fluid
- Define and provide examples of homeostasis
    - Key terms used to describe homeostatic mechanisms
    - Why in reality is homeostasis not as simple as we learn it
- Biomolecules (chapter 2)
- Major cellular components - the big three for us

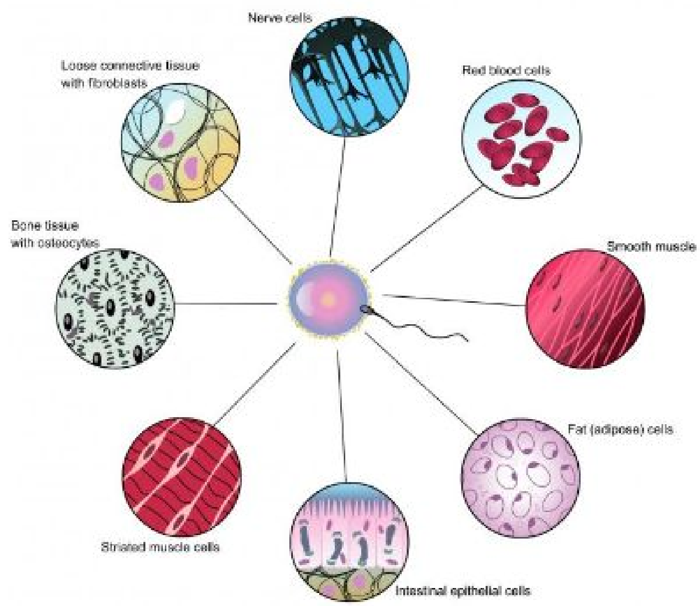
LECTURE 3 - Biomolecules
Organs and Organ Systems
- 11 organ systems
    - System: multiple organs make up function of body
- Principles:
    - All are vital but none function in isolation; interdependent
    - All systems are interdependent
    - All systems strive to maintain homeostasis

11 Organ Systems and Their Main Roles
1. Integumentary: protects from environment, helps with temperature control (skin, hair, nails, hooves, feathers)
2. Skeletal: support, protection, mineral storage, blood production
3. *Muscular: locomotion, support, heat
4. *Nervous: response to stimuli, coordination of other systems
5. Endocrine: long term changes and maintenance of all other systems
6. *Cardiovascular: internal transport of materials, gases, nutrients
7. Lymphatic: defense against infection and disease
    a. Immune system isn't actually a system → its called 'immune function'
8. Respiratory: delivery of air to sites of gas exchange
9. Digestive: processing of food and absorption of organic nutrients
10. *Urinary: elimination of excess H_2O, salts, wastes, pH control

11. Reproductive: production of sex cells and hormones

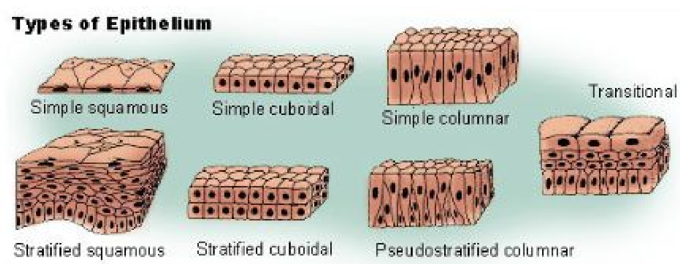
<u>Four Main Classes of Cells</u>

- Four main cell types:
    - All come from embryonic origin (you start out as a single cell)
    - “A nerve cell, is a nerve cell, is a nerve cell”
        - True or false? Why
        - False; *form fits function* they all serve different purposes
    - “A muscle cell; they’re all the same”
        - True or false? Why
        - We have smooth muscles, skeletal muscles, cardiac muscles

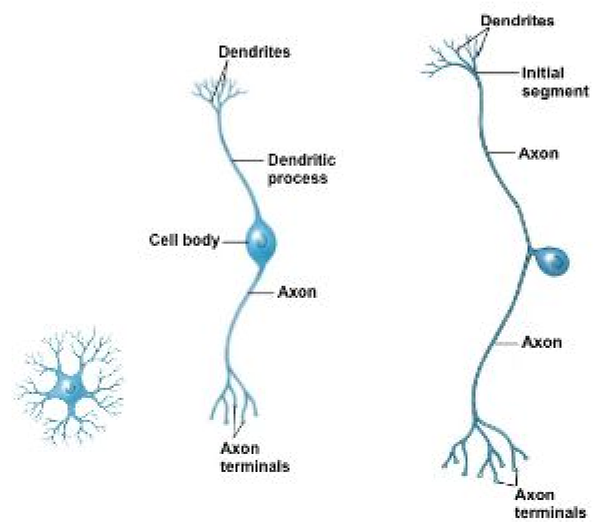


<u>Neurons and Epithelial Cells</u>

- Different types; some line various organs, some are involved in secretion, involved in protection

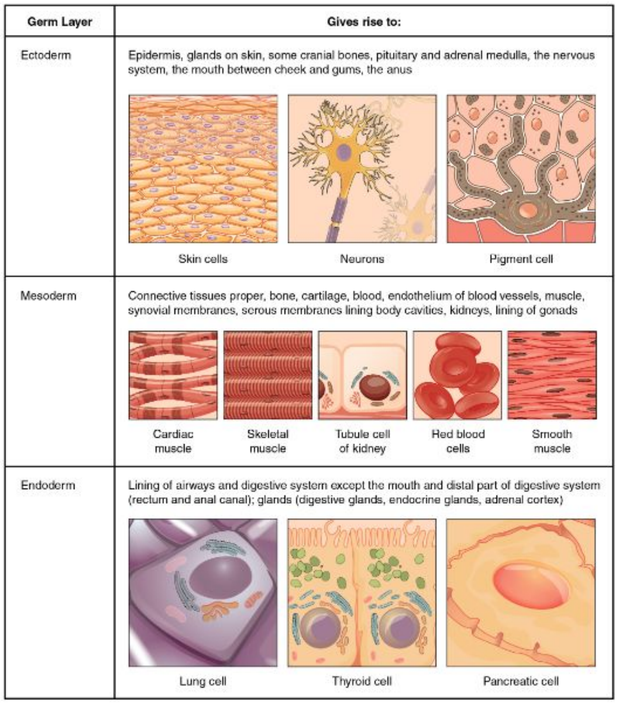


- Anaxonil neuron: not long enough to communicate to limbs, but it can make connections to face (proximal)



<u>Developmental Specialization of Cells</u>

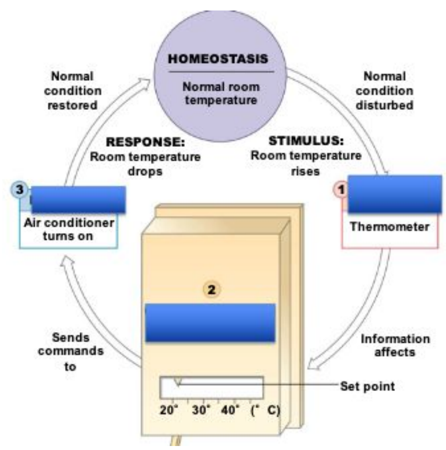
- Sperm cell enters an ovum
- Fertilization gives rise to the zygote
    - Over time, zygote specializes into three main ‘germ layers’
    - Over time, germ layers further specialize into a variety of different tissue types

- 

Germ Layer	Gives rise to:
Ectoderm	Epidermis, glands on skin, some cranial bones, pituitary and adrenal medulla, the nervous system, the mouth between cheek and gums, the anus
Mesoderm	Connective tissues proper, bone, cartilage, blood, endothelium of blood vessels, muscle, synovial membranes, serous membranes lining body cavities, kidneys, lining of gonads
Endoderm	Lining of airways and digestive system except the mouth and distal part of digestive system (rectum and anal canal); glands (digestive glands, endocrine glands, adrenal cortex)

don't need to learn this stuff

Critical Points in the Regulation of Homeostasis



- Three components of a homeostatic regulatory mechanism
    1. *Receptor* (detects through senses)
    2. *Control Centre* (processing and responds to what receptor is telling it based on the set point)
    3. *Effector* (effecting/causing the change)
- Similar example to the call on the slope
- Midterm question: why are analogies such as temperature thermostat and automobile cruise control not truly representative of homeostasis in humans
    - We are complex, not simple as a cruise control system, we are sensitive to many environments
    - What happens when things change in our bodies?
    - There are many systems, our control centre feeds to many different systems. We have many regulators to regulate set points
    - We are also very different individually - olympic athletes have a lower resting heart rate than us
    - Classic example is sweating when walking outside from AC

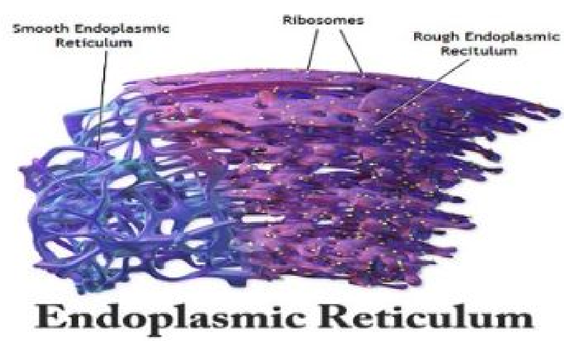
Key Organelles (3)

- Cytoskeleton
    - Found in *all* human cells (every cell has a cytoskeleton)

- Most significant in skeletal muscle tissue, cardiac tissue, intestine
- Three main elements: microfilaments, intermediate filaments, microtubules

Structure	**Function**
Microfilaments	Strength, alter shape, contraction, bind cytoskeleton to PM and other cells, cellular extensions - flagella
Intermediate Filaments	Strength, move materials through cytoplasm
Microtubules	Strength, move organelles
Centrioles, cilia, flagella, thick filaments	

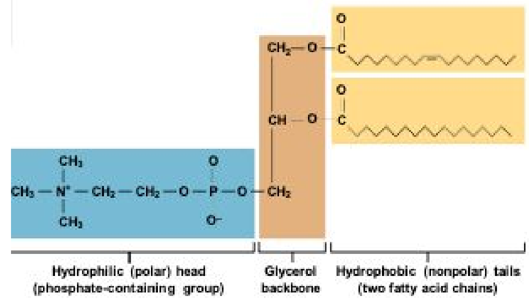
- Endoplasmic reticulum
    - Important in neurons, cardiomyocytes, skeletal muscle
    - Inside space of ER is called the lumen
    - *Rough ER*
        - Protein synthesis (occur in ribosomes): cells that involve secretion of hormones, antibodies, synaptic communication
            - Proteins function in groups
    - *Smooth ER*
        - Store cell compounds and solutes (calcium)

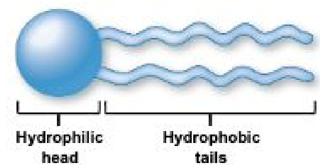


- Cell adhesion molecules (cell-cell junctions) ***p54***
    - Cardiac tissue, skeletal muscle, kidney, liver, small intestine, lung, etc
    - *Tight junctions*
        - Found in epithelial cell layers
        - Fuse (tightly bind) the cells together
            - Ex. in heart, cells are held together tightly
    - *Desmosomes*
        - Found in skeletal and cardiac muscle, uterus, skin - mechanical stress
        - Forms filamentous junction between two cells
        - Keeps cells from tearing apart under stress
    - *Gap junctions*
        - Abundant in many cell types
        - Allow electrical and nutrient coupling

Plasma Membrane

- Plasma membrane is a *lipid bilayer* (phospholipid)
    - Phospholipid made of glycerol backbone, two fatty acid chains (tail), phosphate-containing group (head)
    - Lipid bilayer helps maintain homeostasis!





Plasma Membrane Forms From Phospholipids in Aqueous Environment

- Reaction of phospholipids with water creates unique structures
- *Surfactant*: phospholipid layer in the lungs that prevents lung collapse
    - Premature babies haven't developed this surfactant...lungs collapse

know structures/proteins in membrane

Proteins Associated with the Plasma Membrane

- Membrane proteins are found within and along the plasma membrane
    - Anchoring proteins
        - Attach PM to surrounding structures
        - Provides stability
    - Recognition proteins
        - Receptors, immune system recognition
    - Enzymes
        - Integral or peripheral
    - Receptor proteins
        - Bind to extracellular molecules (ligands)
    - Carrier proteins
        - Binds solutes and carries them across membrane
    - Channels
        - Forms completely through the PM
        - Passive flow of solutes

- membranes allow things to pass through, proteins make the channel

Basics of Biomolecules

Biomolecules

- Molecules synthesized by living things
- Contain carbon
- Four types:

    - Carbohydrates
    - Lipids
    - Amino acids and proteins
    - Nucleotides

<u>Common Functional Groups on Biomolecules</u>

Functional group	Chemical formula	Structure	Chemical property
Hydroxyl	—OH	—O—H	Polar
Sulfhydryl	—SH	—S—H	Polar
Phosphate	$—HPO_4^-$	O X ± O± P± OH W O–	Polar
Carboxyl	—COOH	O O ± C T OH	Acid
Amino	$—NH_2$	H S ± N T H	Base

- Only look at the functional group
- They have attachments which allows it to change shape and have different activities

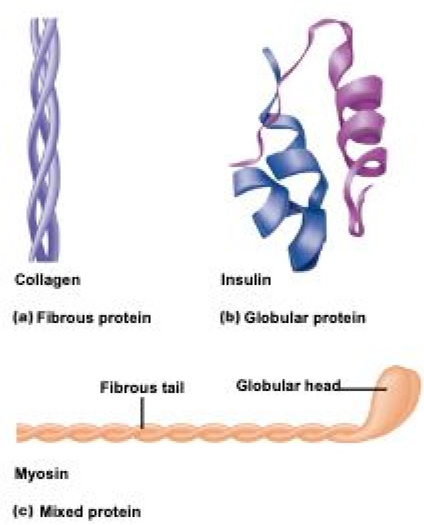
<u>Carbohydrates</u>
- Composed of carbon, hydrogen, and oxygen
- $C_n(H_2O)_n = (CH_2O)_n$
- Monosaccharides
- Disaccharides
- Polysaccharides

<u>Lipids</u>
- Composed primarily of hydrogen and carbon atoms
    - Nonpolar covalent bonds
    - Hydrophobic
- *5 classes*:
    - Triglycerides
        - Glycerol + three fatty acids
            - Glycerol: three carbon alcohol
            - Fatty acid: long carbon acid chain
                - Saturated fatty acids (no double carbon bonds)
                - Unsaturated fatty acids
                    - Trans or cis
            - Fatty acid chains

            - Nonpolar
            - hydrophobic
    - Ketones
    - Phospholipids
        - Amphipathic molecules
            - Polar head
            - Nonpolar tail
    - Eicosanoids
    - Steroids (hormones)

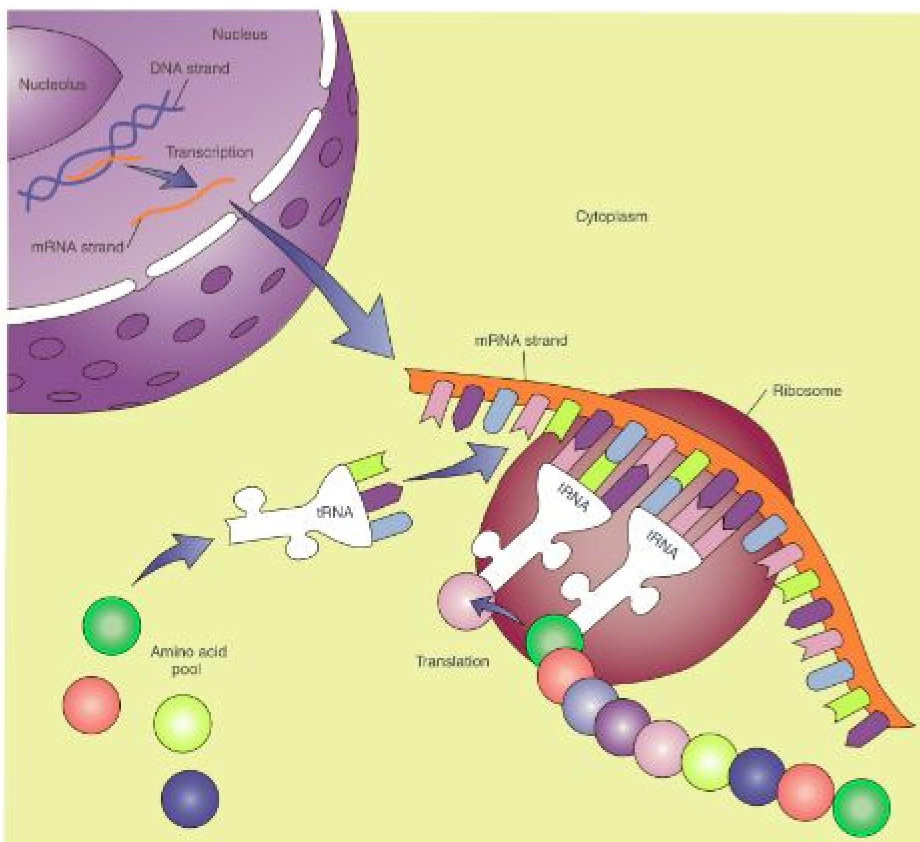
Proteins

- Polymers (chemical chain) of amino acids
- Basic unit of a protein contains a *carbon in the centre, an amino group, a carboxyl group, a hydrogen, and a residual group (R-group)*
- The R-group can vary (20 different variations of R exist from the genetic code)
- Amino acids
    - Building blocks of proteins
    - 20 different kinds of amino acids
        - We can make *11* of the amino acids required to make various proteins
        - The other *9* amino acids (essential amino acids) must come from food sources
    - Polymers of amino acids - peptides and protein
        - Polymers
            - Several amino acids linked together are needed to make functional molecules
            - 2-50 amino acids creates peptides
            - More than 50 amino acids creates a protein
        - Protein
            - Proteins are the functional units of the cell
            - Proteins have a number of different shapes or conformations which gives them activity and specificity for a particular functional process
            - *Four major conformations of proteins are:*
                - Primary
                - Secondary (folding)
                - Tertiary (standing on eachother)
                - Quaternary (hemoglobin structure)
            - Function of proteins relies on its conformation
- Three dimensional proteins are either fibrous or globular
    - Fibrous proteins: strands, contraction
    - Globular protein: bulky, irregular
    - Some can have both



    - Some proteins can have carbohydrate molecules attached (glycoprotein)
    - Some proteins can have lipids attached (lipoprotein)
- Many proteins in the cell form protein complexes
- Several proteins (at least two or more) interact and work together to bring about a specific function(s)
- The function of the protein complex is usually more complex than the function of a single protein within that complex
- Adds diversity and complexity to protein function
- Allows more sophisticated control mechanisms for the cell

Overview of Protein Synthesis

- Nucleus
    - DNA strand is transcribed to a message sequence (mRNA) → called *transcription*
    - mRNA strand leaves the nucleus through a *nuclear pore*
- Cytosol
    - mRNA strands binds with a ribosome associated on a RER
    - Transfer RNA (tRNA) finds three corresponding nucleotides (codon)
    - Binds with the codon and brings with it, the corresponding amino acid that's specific for the codon
    - The mRNA strand is translated into protein
    - 

QUESTIONS

- From the point of protein structure, what allows a protein to have complexity in the way it functions?
- In what ways could a single protein have multiple functions?
    - Can bind to one protein and have one function, bind with another protein and have another function

LECTURE 4

OBJECTIVES

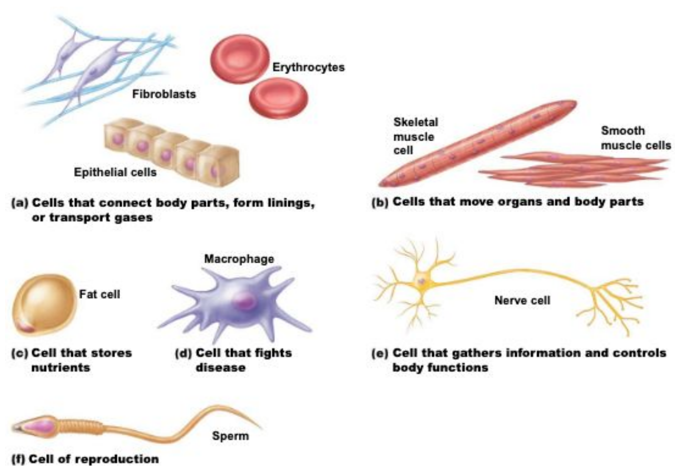
1. How is cellular diversity achieved?
2. What are the different types of epithelial cells and their functional roles
3. Describe the dynamic nature of cells in tissues and organs
4. Describe key components of the plasma membrane that regulate the transport of substances
5. Describe the factors (forces) that regular transport across the PM
6. Apply knowledge about membrane transport to clinically relevant issue

Developmental Specialization of Cells

- Sperm cell enters an ovum
- Fertilization gives rise to the zygote
    - Over time, zygote specializes into three main 'germ layers'
    - Over time, germ layers further specialize into a variety of different tissue types

Cell Diversity

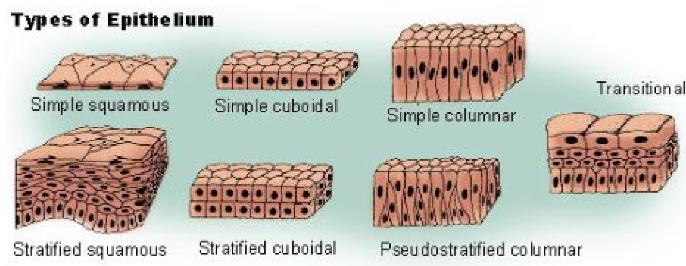
- Many different cell types
- All arise from the same totipotent stem cell - the zygote
- Form and function!



Epithelial Cells

- Naming convention
    - All epithelial cells have two names
    - First indicates number of cell layers (simple of stratified)
    - Second indicates shape (squamous, cuboidal, columndar)
    - Shape can vary in a stratified layer
    - Just need to know when they're useful
- Epithelial cells lines every organ
- Two surfaces
    - Apical surface faces the external environment
    - Basal surface faces the internal environment

Epithelial Cells - Squamous



- Simple epithelia
    - Important in absorption, secretion, filtration
- Simple squamous epithelium
    - Cells flatten laterally, thin cytoplasm (because lung deals with transport of gases, so they need to pass quickly (form fits function))
    - Important where rapid diffusion of cellular material is needed (ex. Kidney, lung)
- Two types of simple squamous epithelia are named based on location
    - Endothelium - lining of vessels, lines heart
    - Mesothelium - lines serous membranes in ventral body cavity
        - Parietal mesothelium lines body walls
        - Mesothelium lining internal organs is visceral mesothelium

Epithelial Cells - Cuboidal
- Simple cuboidal epithelium
    - Single layer of cells
    - Involved in secretion and absorption
    - Forms walls of smallest ducts of glands and many kidney tubules

Epithelial Cells - Columnar
- Simple columnar epithelium
    Single layer of tall, closely packed cells
        - Some cells have microvilli (little extensions to increase surface area - like if you need to absorb more), and some have cilia
        - Some layers contain mucus-secreting goblet cells
    - Involved in absorption and secretion of mucus, enzymes, and other substances
        - Ciliated cells move mucus
    - Found in digestive tract, gallbladder, ducts of some glands, bronchi, and uterine tubes

Epithelial Cells - Pseudostratified
- Pseudostratified columnar epithelium
    - Cells vary in height, thickness
    - Appear multi-layered but is actually a single layered simple epithelium
    - Cells are often ciliated
    - Involved in secretion, movement via ciliary action
    - Found in upper respiratory tract, ducts of large glands

Epithelial Cells - Stratified

- Stratified epithelial tissues
    - Consists of two or more layers of cells
    - New cells regenerate from the basal surface, migrate toward apical surface
    - More durable than simple epithelia….function is?
- Stratified squamous epithelium
    - Most common type of stratified epithelia
    - Apical surface is squamous, deeper layers are cuboidal or columunar
    - Found in tissues prone to wear and tear (skin)

Epithelial Cells - Transitional

- Forms lining of hollow urinary organs
    - Ex. bladder, ureters, urethra
- Has basal layer of cuboidal or columnar cells
- Cells can change shape when stretched - accommodates tissue function
    - Ex. bladder expansion

A hospital lab assistant accidentally loses the labels of two prepared slides she is studying. One slide is from a sample of intestinal tissue; the other slide is from a sample of esophageal tissue. You decide to help her sort them out. How would you decide which slide is which? Hint: they're both a type of epithelial tissue but with different forms

- Intestinal should be simpler - for absorption
- Esophageal should be stratified/stacked, thicker - needed for protection and rigidity when swallowing food

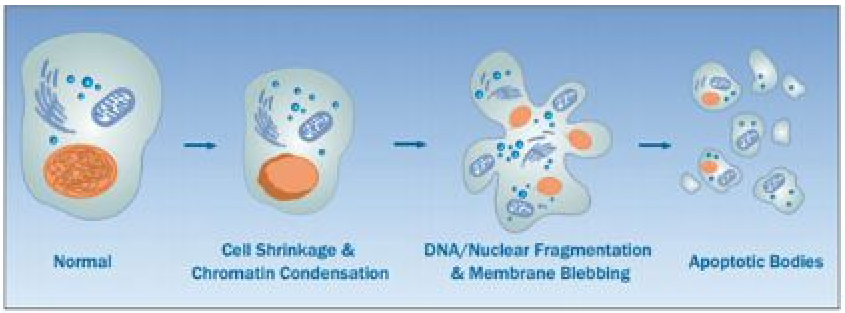
<u>Cell Death</u>

- Cells are constantly under stress; causing homeostatic imbalance
- If a cell cannot recover quickly from a stress insult, it will eliminate itself - programmed cell death/apoptosis
    - If you put it under non homeostatic environment it will want to die
- An overwhelming insult will cause the cell to rupture and undergo uncontrolled cell death - necrosis
- Cells in the stomach and small intestine - constantly die and new cells are made
- Cells in the heart (myocytes) do not readily die but if so, they do not easily renew
    - Renewal in the heart is limited - implications for heart disease

<u>Apoptosis</u>

- Programmed cell death
- Proteins are continually cycled throughout the lifespan of a cell
- Proteins can be marked for degradation
- When a cell can no longer maintain homeostasis, its proteins become marked to trigger a cell death response
- Controlled elimination of a cell is called programmed cell death or apoptosis

- In some instances, the cell does not have time or is unable to ‘quietly’ kill itself
- It undergoes an uncontrolled (unintentional) death response (lysis, cell disruption, cell damage)
    - Called cellular necrosis, which activates many things like inflammatory processes
    - Not going without a fight

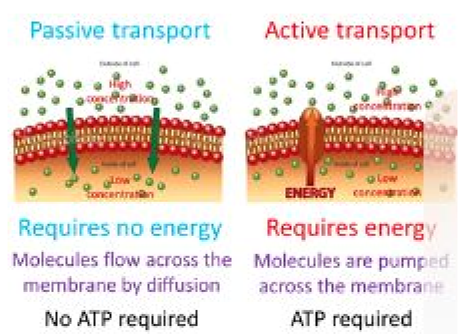


-
- *know the difference between apoptotic and necrosis death* - MC que

<u>Biological Membranes (Plasma Membrane)</u>

- Plasma membrane
    - Fluid mosaic
    - Barrier between internal cell and external environment
        - Protein = gandalf of the cell
    - Separate the ICF and ECF
    - Obtain nutrients (such as O_2)
    - Allow cellular waste to be removed
    - Essentially a gateway into and out of the cell

<u>Factors Affecting Transport Across the Membrane</u>



- Transport across → requires permission to cross
    - Passive transport (diffusion)
        - Spontaneous, slow
        - Nothing is forcing it in/out, but still needs ‘permission’
        - “Downhill” movement (high to low)
    - Active transport
        - Not spontaneous, takes energy
        - Things can push and pull molecules into/out the membrane
        - “Uphill” movement (against concentration gradient)
    - ATP = cellular energy
- Transport across → requires motion (force)
    - Chemical forces (high to low concentration) + electrical forces = electrochemical force

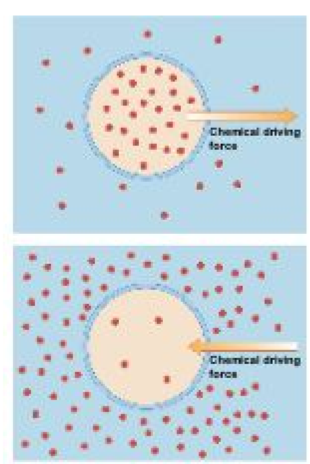
    - *Every cell has a charge (neutral, pos, neg) but not every cell will use that electric charge* !! (ex. Kidney cells, not super necessary vs cardiac cells, charge is super important)

Passive Transport (Diffusion)
- Membrane presents a barrier to free movement of molecules by diffusion
    - Some can pass easily
    - Others can pass by passing through a membrane channel (integral protein)
- Channel is not energy dependent (no ATP required)

Active Transport
- Form of carrier mediated transport
    - Requires ATP
    - Concentration gradient - not relevant
    - Often referred to as *ion pumps* - move NA^+, K^+, Mg^2 Ca^{2+}
- Other types of carrier mediated transport are
    - Facilitated diffusion
    - Secondary active transport

Vesicle-Mediated Transport
- Vesicle
    - Membrane bound organelle containing cell specific molecules and fluid
    - Processed in golgi apparatus
- Vesicle transport
    - Vesicles combine with the cell membrane to exocytose (exo = out) vesicular components
    - Can also endocytose (endo = within) components from the ECF

<u>Driving forces that occur across a membrane</u>
- Chemical forces
    - Concentration of particles is different outside vs inside the cell
    - Gradient pushes particles from region of *higher to lower concentration!*
    - Force is generated from higher to lower regions (high concentration to low conc)
    - Direction is 'down' the chemical gradient

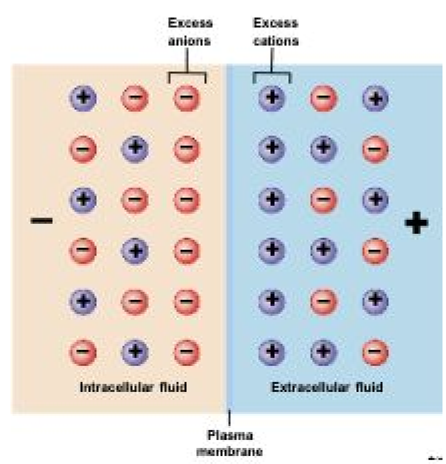


- Electrical forces
    - Come from charged particles (ions): anion/cation
        - *Cation*: a positively charged ion (plussy cat)
        - *Anion*: a negatively charged ion
        - Where are they coming from? Food sources!!
          They come from what we digest, called electrolytes! The kidneys regulate

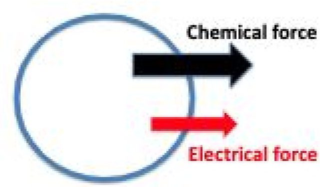
the concentration of ions in our body, based on how much we need or get rid of
- Minerals that we intake via diet are broken down into ionic species
- Important components around most membranes:
  - Na^+ (sodium) it *enters* the cell passively (because it has higher concentration outside and lower conc inside)
  - K^+ (potassium) it *leaves* the cell passively (because it has high conc outside and lower conc inside)
  - Cl^- (chloride) it *enters* the cell passively (high concentration on outside and low conc inside)
  - Ca^{2+} (calcium) it *enters* the cell passively (high conc outside and lower conc inside)
  - Proteins
- Every cell has these cation and anions around them (but not every cell uses them!! ← important)

- Is represented by the membrane potential (V_m)
- V_m is measure of force caused by unequal distribution of anions (neg) and cations (pos) across membrane
  - If difference was zero = it means there's no charge...it is in equilibrium. There is no flow, no movement of ions. Doesn't mean that there aren't ions around them, but they are in an equilibrium state
- Usually measured in millivolts - mV
- Measures difference in charge between inside and outside of the cell
  - At rest, inside of cell is more negative than outside
- Separation of charge gives energy, which then the energy is turned into the electrical force
- Direction of force depends on
  - Polarity of the cell
  - Charge of the particule

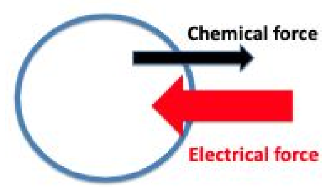
- Separation of charge across membrane
  - When positive and negative charges (originating from electrolytes which generate those ions)are unequally distributed across a membrane → separation of charge is generated
    - Electrolytes:
      - Minerals
      - Na+ K+ Cl- CA2+
      - Proteins (most carry neg charge) majority are inside the cell which makes sense why we have so much neg inside the cell (-70mV)
  - Separation of charge measured in voltage



  - *Charges surround the membrane* (everyone taking the aisle set), they are not dispersed throughout the cytoplasm (ICF)
  - ICF is slightly more negative than the ECF
    - -70mV = ICF more negative than ECF
    - -90mV - ICF more negative than ECF
    - +30mV = ICF less negative han ECF
  - Sodium on outside (salt on fries is on the outside) (blue)
  - Potassium on inside (peach)
  - Protein on inside of cells
- Electrical driving force
  - Negative particles are driven to more positive areas
  - Positive charges are driven to more negative areas
  - Conceptually - think regions of positivity and regions of negativity
    - Highest region of negativity on inside of cell
    - Highest region of positivity on outside of cell

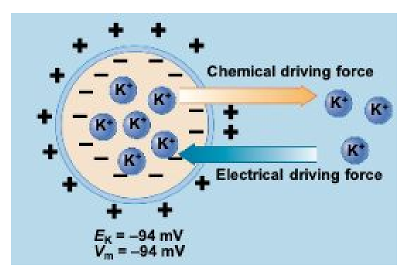


- Electrochemical force
  - Total force acting on particles
  - Sum of chemical and electrical forces
- Electrochemical force acting in the same direction
  - Chemical force and electrical force acting in same direction:
    - Electrochemical force will follow that direction
    - Magnitude = sum of chemical and electrical force



- Chemical and electrical forces acting in opposite directions
  - Electrochemical force will be in direction of stronger force
  - Magnitude = (larger force) - (smaller force)

<u>Equilibrium Potential</u>



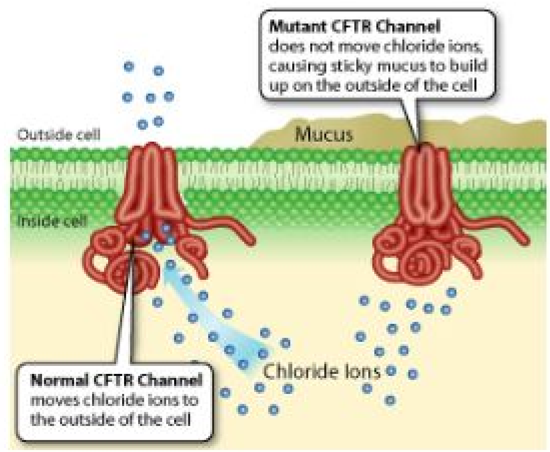
- Differs from cell to cell
- Membrane potential (Vm)
  - Exists when electrical force = chemical force
  - Forces act in opposite direction
  - Created by the uneven distribution of ions across the membrane, can change when ion concentration gradients change, or changes in permeability
    - If permeability to an ion increases, resting membrane potential will move toward that ion's equilibrium potential
      - Ex. if sodium channels open, then membrane potential will move from rest to something more positive, since sodium's equilibrium potential is pos
    - If permeability to an ion decreases, then resting membrane potential will move away from that ion's equilibrium potential

- Ex. if potassium channel closes, membrane potential will move from rest to something more positive, since potassium's equilibrium potential is neg

Facts to remember:
- All cells have a charge
- Ions will flow all the time, they are subjected to electrostatic forces
- Proteins function as a group - they are on the inside of cell
- Sodium is on the outside, but stick mostly to the membrane (cells have a lot more sodium than any other ion) - carries equilibrium potential of -70mV (the sum of both charge - the electrochemical charge)
- Potassium is on the inside, resides close to membrane
- Chloride resides on inside

Fainting goats
- During contraction (not homeostasis) ions can move but don't rebalance properly

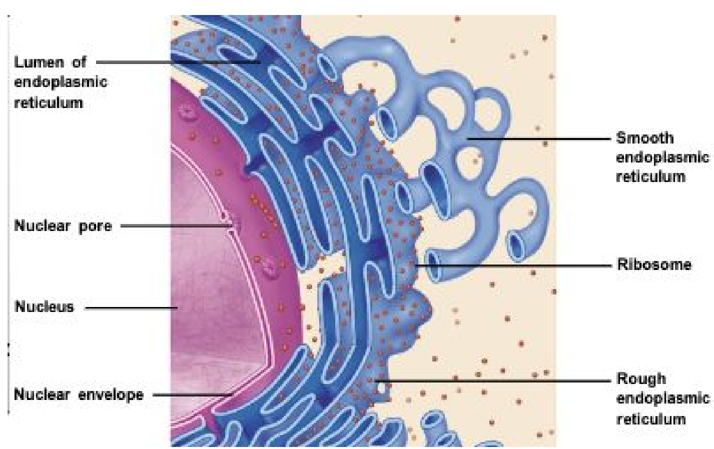
Cystic Fibrosis
- Genetic disorder that affects mostly lungs
- Difficulty breathing; mucous build up; frequent lung infections
  - Diseases are called channelopathys (something wrong with the channels in the membrane)
  - Problems with chloride channels - it breaks down resulting in accumulation of fluid
- Mutation to the cystic fibrosis transmembrane conductance regulator (CFTR) protein
- CFTR protein is a membrane protein (chloride ion channel protein) found on lung epithelial layer



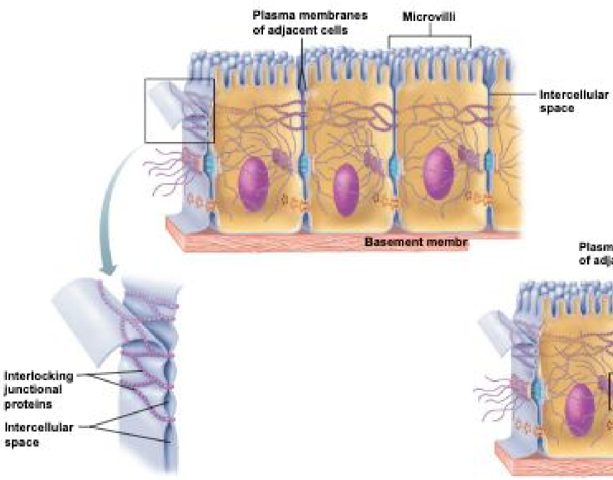
- CFTR regulates water and chloride ion flow into and out of lung epithelial cells
- Blocked channel caused by non-functional CFTR protein leads to build-up of mucous in the lungs

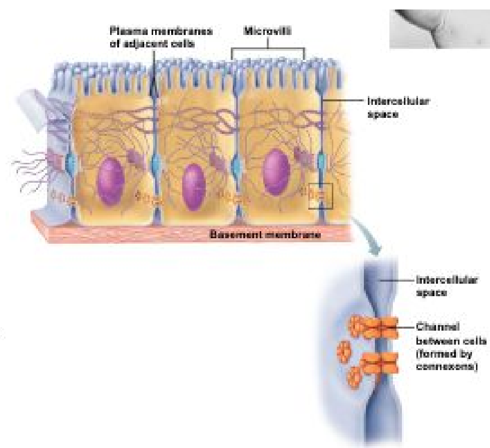
LECTURE 6 - NERVOUS SYSTEM I

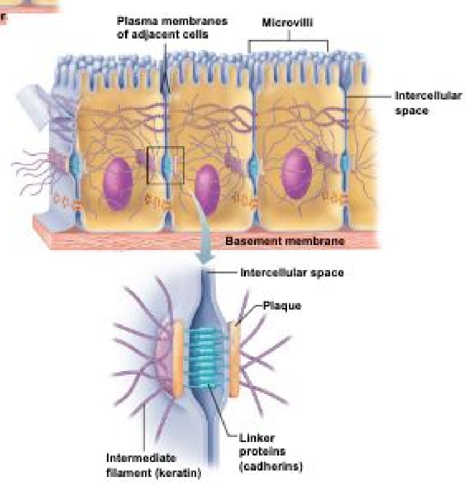
Cytosol Components - Endoplasmic Reticulum
- Endoplasmic reticulum
  - Rough ER
  - Flattened sacs
  - Rich in ribosomes - granular/rough
- Smooth ER
  - Tube like structure



- Smooth in appearance
- *Both have a lumen (body) that is continuous*
    - *Lumen:* any cavity that forms in an organelle that has an open space







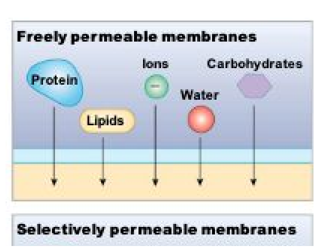
<u>First</u>: tight junction

Ex. in body: most critical is blood-brain barrier (really difficult to get things across, its so protective mech of brain)

<u>Second</u>: desmosomes

Difference: desmosomes hold cells together but also holds everything else together, tight only holds cells together

<u>Third</u>: gap (forms tunnels in between)

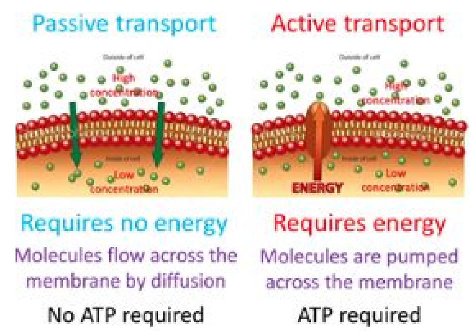


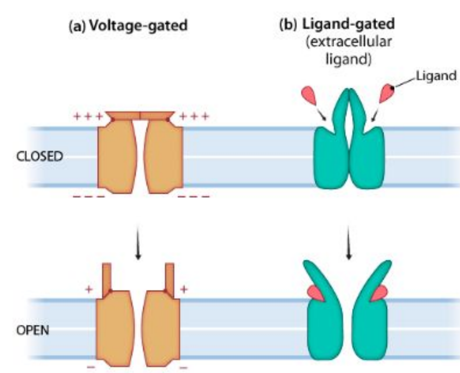
(recap from lecture 4)

Plasma membrane is selectively permeable

- Permeability
    - Property of plasma membrane that determines what substances can enter and what can leave the cytoplasm
    - Selectively permeable membrane will allow some material to pass freely and restrict others
    - Selectivity is based on size, charge, shape, lipid solubility and other factors
    - Components in the PM will give membranes different permeability characteristics
    - Most cells are selectively permeable - allows lipids through (membrane is made of lipids), ions are selectively passed. Most ions have a channel (their own person tunnel, it can be open or regulated (allows certain things through at certain times, a mechanism called ATP to function)

Factors that affect transport across membrane

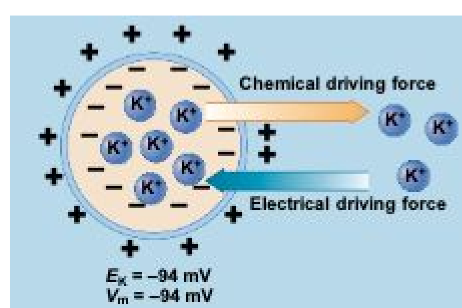




- Chemical forces + electrical forces = electrochemical force
- Passive transport (diffusion)
    - Spontaneous
    - Downhill movement (high conc to low conc)
    - Through an open channel (K+ has passive transport through a K+ channel)
    - Ion channels only allow passive transport
        - *Ligand-gated ion channels*: channels that are gated by a chemical messenger (a ligand) on the inside or outside of cell
        - *Voltage-gated ion channels*: channels gated by a change in the charge of their surrounding environment inside the cell
- Active transport
    - Not spontaneous
    - Uphill movement (against conc gradient)
        - Essentially goes against their concentration gradients
    - Can't occur through channels, only occurs through transporters and pumps

Equilibrium Potential and Membrane Potential

- Resting membrane potential (Vm)
    - A cell at rest is not active (neuron → no activity exists when electrical force = chemical force
    - Forces act in opposite direction
- Equilibrium is reached when there is no NET movement of ions into or out of cell
    - So when the cell is just resting, its in 'equilibrium'



- Figure on the right shows potassium at equilibrium
- Potassium moves both in and out of the cell
- But movement is not favoured in any one direction
- Chemical driving force = electrical driving

THE NERVOUS SYSTEM

Top hat chapter 5,7 (follow the text info that compliments the course notes - we don't focus on anatomy of nervous system)

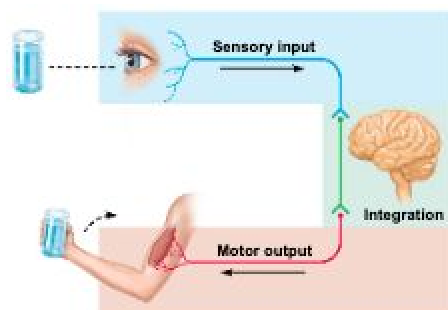
Objectives

1. Provide an overview of the nervous system
2. Describe the features of the neurons that facilitate its function
3. Describe the neurophysiology of a neuron - ions and the nerve cell membrane
4. What are some general functions of the nervous system? How do these features compare to those of other organ systems?
5. Describe the different types of cells found within the nervous system. What functions are served by each cell type?
6. What are the five main components of a neuron? How does the form of each component suit the function of the neuron as an excitable cell?
7. What are the different classes of a neuron and where are they relevant?

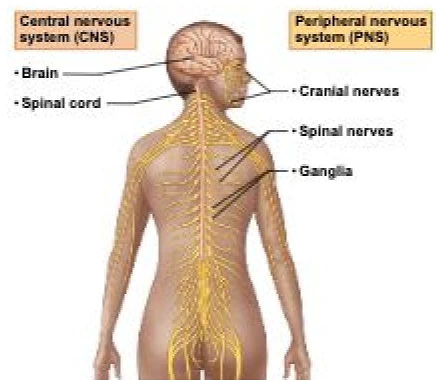
Functions of the Nervous System

- NS is the master controlling and communicating system of body
- Cells communicate via electrical and chemical signals
- Rapid and specific (key! Hormones can take days to communicate)
- Causing immediate response
- Three overlapping functions:
    - Sensory input
    - Integration
    - Motor output

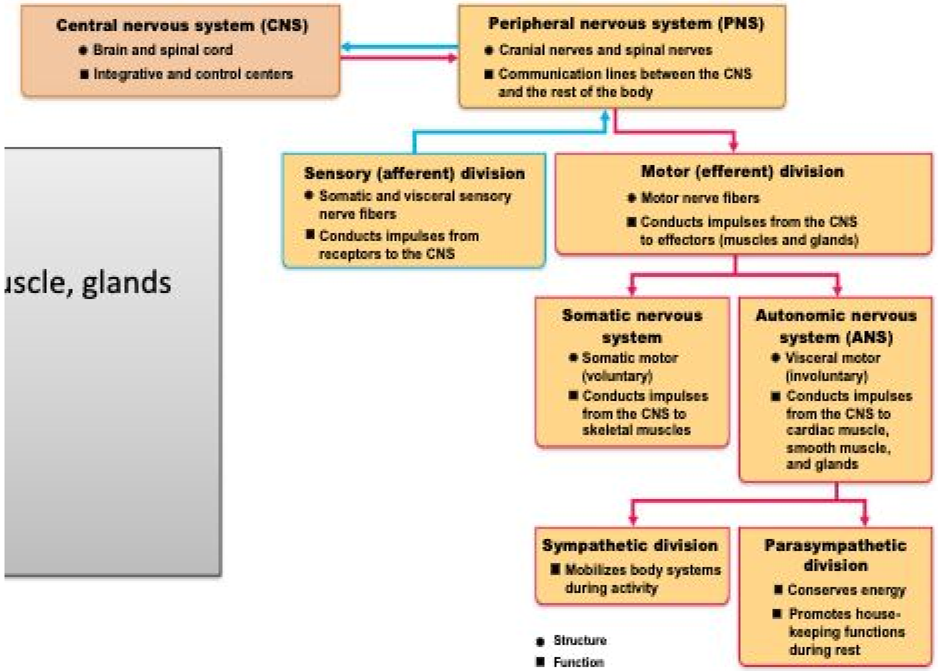
    = Helps provides and maintains homeostasis!



- Two components:
    - Central NS
        - Brain and spinal cord
        - Contained in dorsal body cavity
        - Serves as integration and control center
    - Peripheral NS
        - Outside the CNS
        - Nerve extensions from brain (cranial nerves)



- Nerve extensions from spinal cord (spinal nerves
- Has two divisions:
    - Sensory (afferent - a for arrives, it brings it to CNS)
        - Somatic sensory fibers - brings impulses from sensory organs, skeletal muscles, joints to CNS
        - Visceral sensory fibers - bring impulses from visceral organs to CNS
    - Motor (efferent)
        - Impulses from CNS to effector organs
        - Muscles and glands
        - Two divisions:
            - Somatic nervous system
                - Somatic motor neurons send impulses from CNS to skeletal muscle
                - Voluntary nervous system
                    - Conscious control of skeletal muscles
            - Autonomic nervous system
                - Consists of visceral (outside of central core) motor neurons
                - Regulates smooth muscle (ex blood vessels, digestive), cardiac muscle, glands
                - Involuntary nervous system
                - Two functional divisions:
                    - Sympathetic (flight or fight)
                    - Parasympathetic (rest and digest)
                    - Work opposite each other



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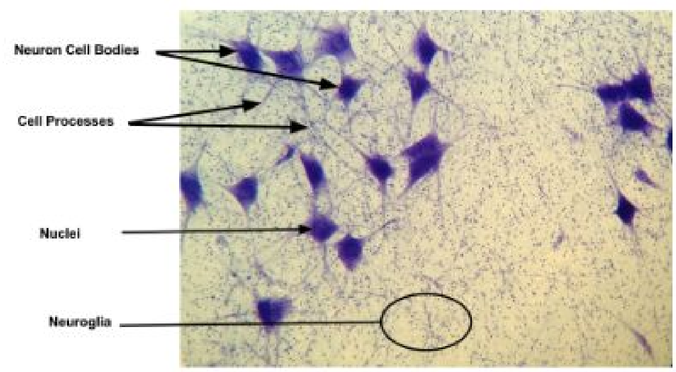
Cells of the Nervous System

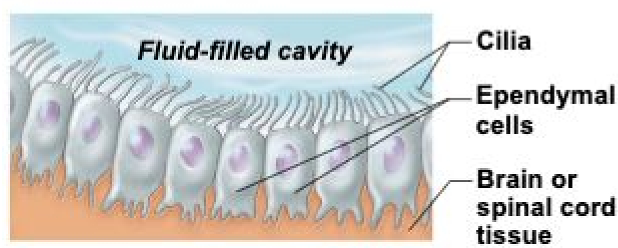
- Two main types of neuronal cells:
  - Neurons
    - Excitable cells
  - Neuroglia
    - Support cells of the NS
    - Different types of neuroglia
      - Ependymal cells
      - Oligodendrocytes
      - Astrocytes
      - Microglia
      - Satellite cells
      - Schwann cells



Types of CNS Neuroglia*

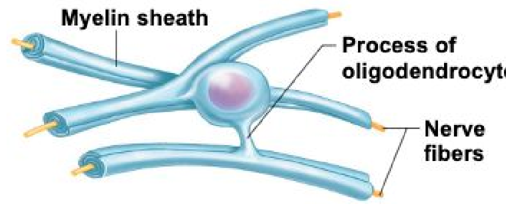
Ependymal cells

- Line vessels that surround CSF in brain and central spinal cord
- Range in shape; squamous → columnar
- May be ciliated
- L***ine central cavities of brain and spinal column***

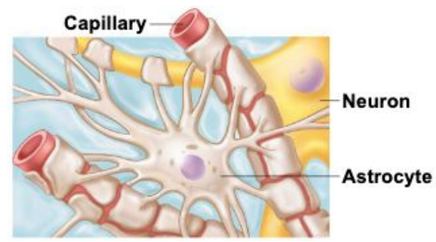


- Forms a permeable barrier between CSF in cavities and tissue fluid CNS cells - this is why they are thick...for protection

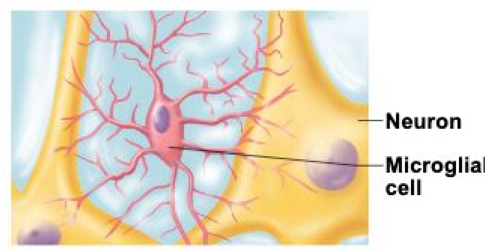
Oligodendrocytes
- Branched cells
- Processes wrap CNS nerve fibers, forming insulating myelin sheaths in thicker nerve fibers
    - ***Essentially they make the myelin sheath***
- Critical in nerve impulse (action potential) propagation in the CNS



Astrocytes
- Most abundant, versatile, and highly branched of glial cells
- Cling to neurons, synaptic endings, and capillaries
- Functions include:
    - ***Support and brace neurons, holding them together***
    - Play role in exchanges between capillaries and neurons
    - Guide migration of young neurons
    - Control chemical environment around neurons
    - Respond to nerve impulses and neurotransmitters
    - Influence neuronal functioning
    - Participate in information processing in the brain
- Important in the blood brain barrier



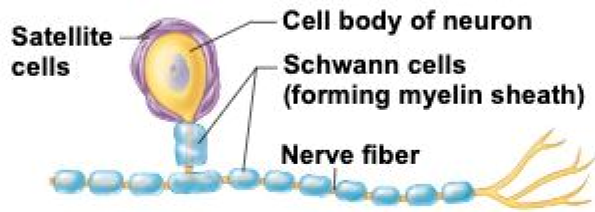
Microglial Cells
- Small, ovoid cells with thorny processes that touch and monitor neurons
- Migrate toward injured neurons
    - We want the NS to be protected and risk free from the immune system, ***they are defensive.***
    - They are big and able to grab invading organisms
- Can transform to phagocytize microorganisms and neuronal debris



(b) Microglial cells are defensive cells in the CNS.

<u>Types of PNS Neuroglia</u>

Satellite cells
- Cover and surround cell bodies of nerves in PNS
- Function similar to ***astrocytes*** of CNS



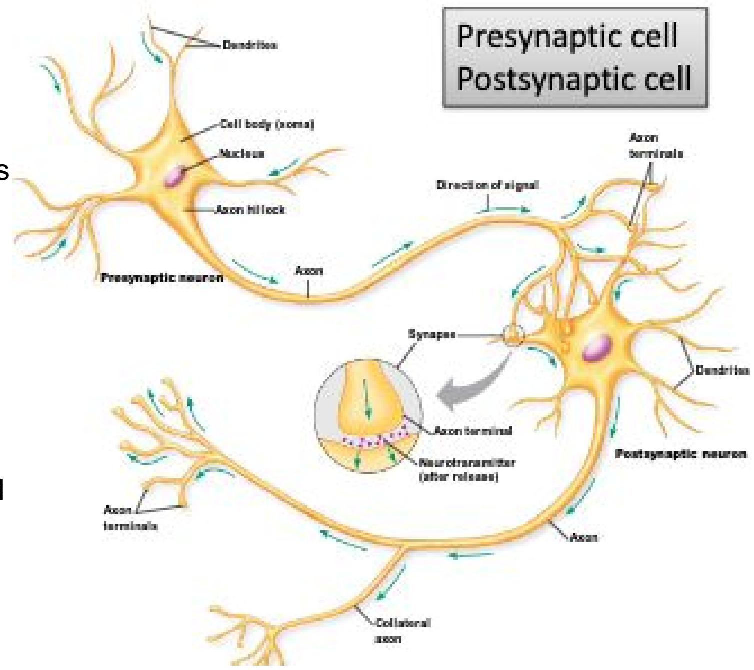
Schwann cells
- Forms myelin sheath around axons in the PNS
- Similar function as ***oligodendrocytes***
- Needed for regeneration of damaged peripheral nerve fibers

Neurons

- Neurons (nerve cells) are structural units of nervous system
- Large, highly specialized cells that conduct impulses
- Special characteristics
    - Extreme longevity (lasts a person's lifetime)
    - Amitotic (don't undergo cell division), with a few exceptions
    - High metabolic rate: requires continuous supply of oxygen and glucose (cell energy or ATP, and if they use this they will produce a lot of waste)
- All have cell body and one or more processes (dendrites, axon terminals)

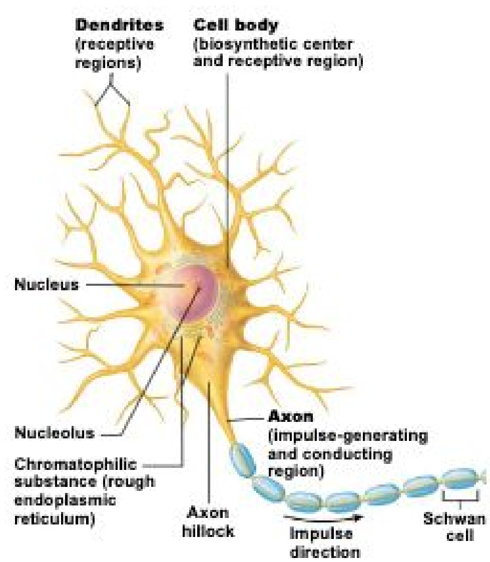
Components of a Neuron (know the basic structure and label it** THERE ARE 5)

- Dendrites
    - Reception of incoming information
    - Branch to junctions called synapses
- Soma (cell body)
    - Contains nucleus and most organelles
- Axon hillock
    - Where axon originates
    - Where potentials are initiated
- Axon
    - Transmits electrical impulses called action potentials
- Axon terminal (telodendria)
    - Releases neurotransmitter



Neuron Cell Body

- Called the perikaryon or soma
- Biosynthetic center of neuron
    - Synthesizes proteins, membranes, chemicals
    - Rough ER (chromatophilic substance, or Nissl bodies)
- Contains spherical nucleus with nucleolus
- Some contain pigments
- In most, plasma membrane is part of receptive region that receives input info from other neurons
- Most neuron cell bodies are located in CNS
    - *Nuclei*: clusters of neuron cell bodies in CNS
    - ~~*Ganglia*: clusters of neuron cell bodies in PNS~~



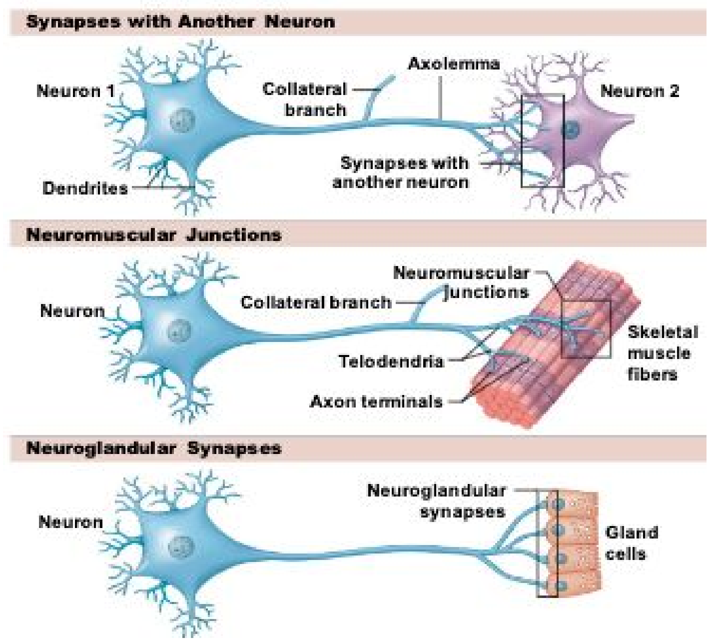
Neuron Processes

- ~~Armlike processes that extend from the cell body~~
    - ~~CNS contains both neuron cell bodies and their processes~~
    - ~~PNS contains chiefly neuron processes~~
- ~~*Tracts*: bundles of neuron processes in CNS~~
- ~~*Nerves*: bundles of neuron processes in PNS~~
- Two types of processes:
    - Dendrites
        - Motor neurons can contain 100s of these short, tapering, diffusely branched processes
            - Contain same organelles as in cell body
        - Receptive (input) region of neuron
        - Convey incoming messages toward cell body as *graded potentials* (short distance signals)
        - In many brain areas, finer dendrites are highly specialized to collect information
            - Contain *dendritic spines*, appendages with bulbous or spiky ends
    - Axon
        - *Structure:*
        - Each neuron has one axon that starts at cone-shaped area called *axon hillock*
        - In some neurons, axons are short or absent; in others, axon comprises almost the entire length of cell
            - Some axons can be over 1 meter long
        - Long axons are called *nerve fibers*
        - Axons have occasional branches called *axon collaterals*
        - Axons branch profusely at their end (terminus)
            - Can number as many as 10,000 terminal branches
        - Distal endings are called *axon terminals* or *terminal boutons*
        - *Functional Characteristics:*
        - Axon is the conducting region of neuron
        - Generates nerve impulses and transmits them along *axolemma* (neuron cell membrane) to *axon terminal*
            - *Terminal*: region that secretes neurotransmitters, which are released into extracellular space
            - Can excite or inhibit neurons it contacts
        - Carries on many conversations with different neurons at the same time
        - Axons rely on cell bodies to renew proteins and membranes
        - Axons have efficient internal transport mechanisms
            - Molecules and organelles are moved along axons by motor proteins and cytoskeletal elements
        - Movement occurs in both directions
            - *Anterograde*: away from cell body to the rest of the cell

- Ex. mitochondria, cytoskeletal elements, membrane components, enzymes
- *Retrograde*: toward cell body
  - Ex. organelles to be degraded, signal molecules, viruses, and bacterial toxins

Cellular products need to move in neurons
- Neuron length 1mm to > 1m**
- Entire cell must be ‘satisfied’ as a *cellular entity*
- *Energy, waste products* need to be transported between cell body and axon terminals
  - Anterograde and retrograde transport***
  - Slow axonal transport
  - Fast axonal transport
  - Rely on network of microtubule transport*** (this is how they move! Understand this)

Neural Communication: Synapse
- Site of communication between two neurons (neuronal synapse) or between a neuron and an effector organ
- Types:
  - Synapses are typically named/categorized by the type of post-synaptic cell they communicate with
  - Presynaptic cell is almost always a neuron
  - ***know these three***



Neuron Classification - Overview
- Neurons classified based on structure/anatomic class, how they look (don’t need to know this! just be aware of it)
  - Anaxonic
  - Bipolar
  - Unipolar
  - Multipolar
- **Neurons are also classified based on their function
  - Sensory neurons (through senses)
  - Interneurons (each other)
  - Motor neurons (muscle)
- **Synapses are classified by the post-synaptic cell thats innervated
  - Neuronal

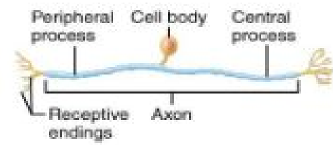
        - Neuromuscular
        - Neuroglandular

Neuron Classification

- 4 anatomical classes
    - Anaxonic neurons
        - Small neurons, lacking distinguishing features in axons vs dendrites (all cell processes look alike)
        - Located in the brain and in special sense organs
        - Functions are poorly understood
    - Bipolar neurons
        - Two distinct processes
        - One dendritic process that branches at its tip
        - One axon
        - Occur in special sense organs
        - Small (largest is less than 30 um in length)
    - Unipolar neurons (pseudo-unipolar)
        - Dendrites and axons are continuous (fused)
        - Cell body lies off to one side
        - Most sensory neurons in peripheral nervous system are unipolar
        - Axons may extend a meter or more
        - Longest carry sensory information from the tips of the toes to the spinal cord
    - Multipolar neurons
        - Have two or more dendrites and single axon
        - Most common neurons in the CNS
        - All motor neurons controlling skeletal muscles
        - Can be as long as unipolar neurons
        - Longest carry motor commands from spinal cord to small muscles that move the toes
- 3 functional classes of neurons

Table 11.1 Comparison of Structural Classes of Neurons

NEURON TYPE		
MULTIPOLAR	**BIPOLAR**	**UNIPOLAR (PSEUDOUNIPOLAR)**
Structural Class: Neuron Type According to the Number of Processes Extending from the Cell Body		
Many processes extend from the cell body. All are dendrites except for a single axon.	Two processes extend from the cell body. One is a fused dendrite, the other is an axon.	One process extends from the cell body and forms central and peripheral processes, which together comprise an axon.



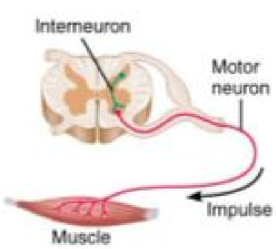
Relationship of Anatomy to the Three Functional Regions

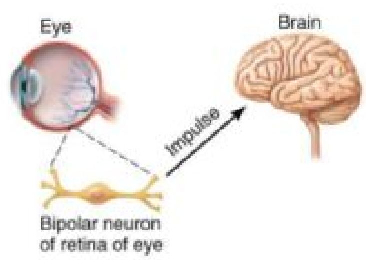
- Receptive region (receives stimulus).
- Conducting region (generates/transmits action potential).
- Secretory region (axon terminals release neurotransmitters).

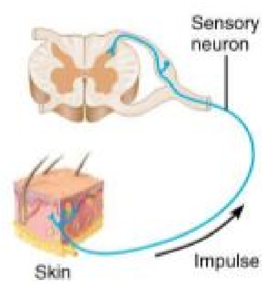
(Many bipolar neurons do not generate action potentials. In those that do, the location of the trigger zone is not universal.)

Table 11.1 Comparison of Structural Classes of Neurons *(continued)*

NEURON TYPE		
MULTIPOLAR	**BIPOLAR**	**UNIPOLAR (PSEUDOUNIPOLAR)**
Functional Class: Neuron Type According to Direction of Impulse Conduction		
1. Most multipolar neurons are **interneurons** that conduct impulses within the CNS, integrating sensory input or motor output. May be one of a chain of CNS neurons, or a single neuron connecting sensory and motor neurons. 2. Some multipolar neurons are **motor neurons** that conduct impulses along the efferent pathways from the CNS to an effector (muscle/gland).	Essentially all bipolar neurons are **sensory neurons** that are located in some special sense organs. For example, bipolar cells of the retina are involved with transmitting visual inputs from the eye to the brain (via an intermediate chain of neurons).	Most unipolar neurons are **sensory neurons** that conduct impulses along afferent pathways to the CNS for interpretation. (These sensory neurons are called primary or first-order sensory neurons.)

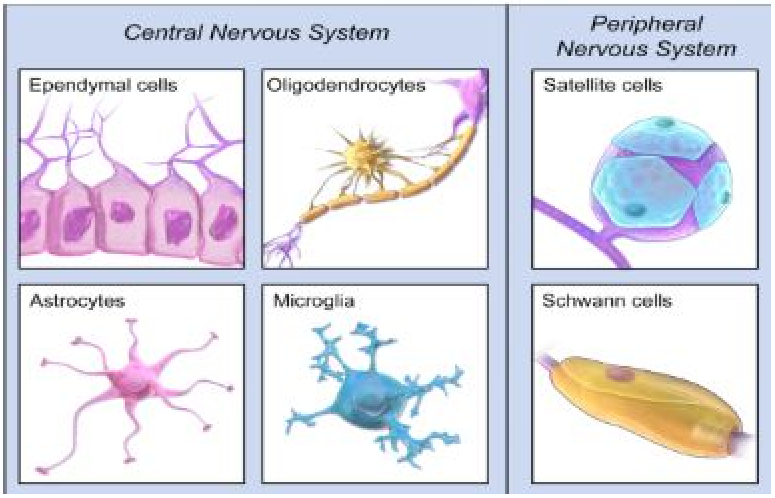






LECTURE 7 - NERVOUS SYSTEM II: RESTING MEMBRANE POTENTIAL

Types of Neuroglia



review the anatomy of a neuron, types of synapses

GOALS/OBJECTIVES

- Describe how the resting potential of a neuron is established and maintained
- Describe how molecules get across the neuron membrane via channels and pumps to help maintain resting potential
- Discuss the significance of the resting membrane potential - clinical implications
    - https://www.youtube.com/watch?v=O7eQKSf0LmY - venus fly trap takes 10 days to reset, we reset a billion times per millesecond
- How would you define resting membrane potential?
    - What's happening to the concentration of ions?
    - What electrical forces are generated by those ions?
    - Are the ions moving?
- What are some key features of the resting membrane potential?
- What happens when the resting membrane potential is disrupted?

Resting Membrane Potential

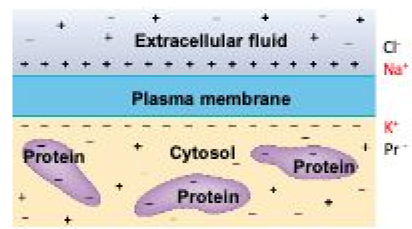
- All cells including neurons have a resting membrane potential (but not all cells use it!!)
- Cell is at rest
    - *Signals are not received or transmitted*
    - -70mV (for most neuronal cells)
        - Smooth muscle cell resting membrane potential is -90mV
        - Red blood cell's resting membrane potential is -12mV
        - Astrocytes resting membrane potential is -80/-90mV
        - Skeletal cell rmp is -90mV

Resting Membrane Potential Can Be Thought of as Bioelectricity

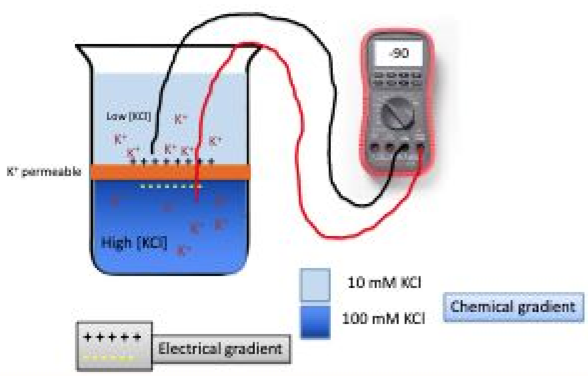
- Membrane potential (Vm)
    - All cells have a voltage difference across their membrane
    - The changes in Vm is used by cells to communicate (cell-cell signaling)
- Vm is measured with a voltmeter or microelectrode
- Two things needed to establish a potential (voltage)
    - 1. Concentration gradient of ions
    - 2. Membrane that is selectively permeable (permission to move)

<u>Signal Reception - Resting Membrane Potential</u>

- What does the neuronal membrane look like at rest?
    - Unequal charge distribution across the membrane
        - Inside of membrane is slightly negative
        - Slight excess of negatively charged ions and proteins in cytosol (ICF)
    - Outside of membrane is slightly positive
        - Slight excess of positively charged ions in the ECF



<u>Establishing the Membrane Potential of a Cell (experiment)</u>

- 

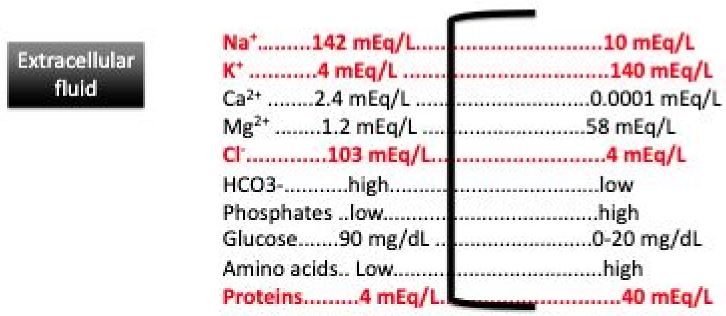
- Conclusions
    - The principles we demonstrated in the beaker can be directly applied to a biological membrane with two important things to remember:
        - Very few ions are required to generate Vm
        - Separation of charge to generate Vm is *localized to the membrane*
            - They don't need to travel long distances and they don't need to travel in large numbers = this allows us to reset so fast

<u>Membrane potential - electro-chemical gradients</u>

- Electrical gradient
    - Gradients that are based on charge
    - Attraction between opposite charges (+/-) or repulsion between like charges (-/-, +/+)

- Chemical gradient
    - Gradients based on concentration of ions across a plasma membrane
    - They tend to move downwards
- ***Equilibrium potential
    - When electrical and chemical gradients are equal and opposite, resulting in no net movement across the membrane (net = 0), but ions are still moving!
        - Why is resting potential -70? Because there are no big movement of one ion vs the other, there is equal movement on both sides
        - Nothing is happening but they are still moving

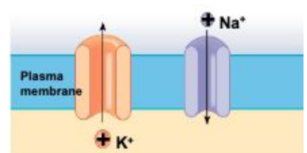
Establishing the resting potential of cells - ICF and ECF

- Some of the components residing in the ECF and ICF (don't need to know):
    - 

Extracellular fluid		Intracellular fluid
Na^+	142 mEq/L	10 mEq/L
K^+	4 mEq/L	140 mEq/L
Ca^{2+}	2.4 mEq/L	0.0001 mEq/L
Mg^{2+}	1.2 mEq/L	58 mEq/L
Cl^-	103 mEq/L	4 mEq/L
HCO3-	high	low
Phosphates	low	high
Glucose	90 mg/dL	0-20 mg/dL
Amino acids	Low	high
Proteins	4 mEq/L	40 mEq/L

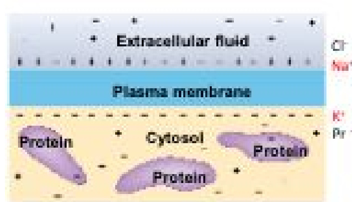
Resting Membrane Potential of Cells: Leak channels help establish the RMP

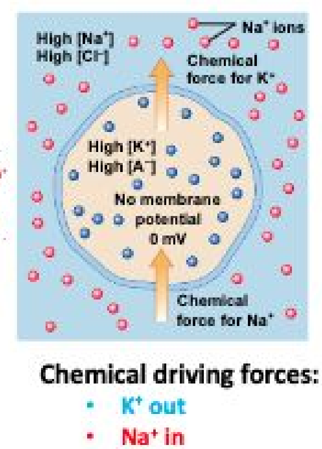
- All plasma membranes have selectively permeable channels (they are in the membrane!)
- Ions must move across the PM via channels or can be transported across
- Leak channels are always open; unique in size and shape makes them selective for their ion

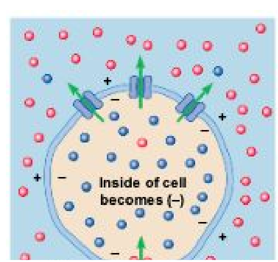


Resting Membrane Potential of a Neuron

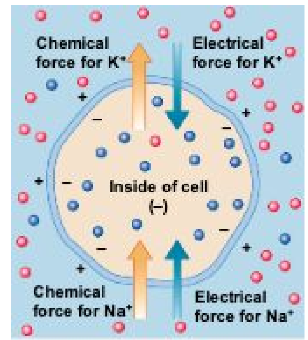
- Neuron is permeable to both sodium and potassium (and other ions)
    - Na+ and K+ selective leak channels allow the membrane to be permeable
    - But there are more K+ leak channels that Na+ channels
        - Membrane is more permeable to K+
- Ions are distributed
    - Outside cell: sodium and chloride
    - Inside cell: potassium and organic anions (proteins)
- K+ selective leak channels allow K+ to move



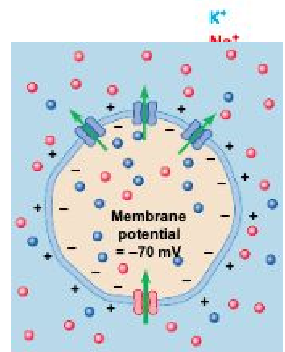




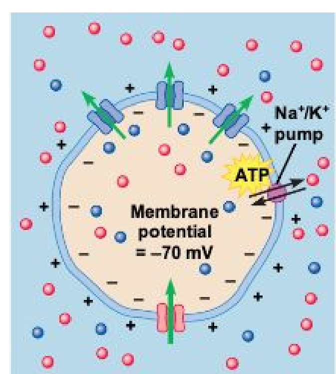
out of cell
- Membrane is more permeable to K+
- More K+ leaves the cell than Na+ enters the cell
- Inside of cell becomes negative ***p115***
    - As this happens…
    - Electrical forces develop:
        - Negative force inside cell pulls Na+ into cell
        - Negative force inside cell pulls K+ into cell
    - Electrical forces cause:
        - K+ outflow to slow down
        - Na+ inflow to speed up
        - *Steady state of forces develop*
            - Inflow of Na+ is balanced by outflow of K+



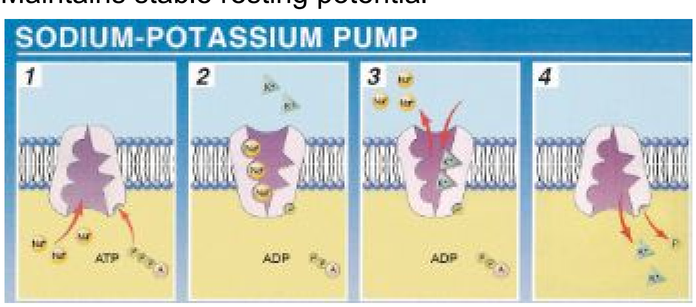
    - *Resting membrane potential = -70mV*
    - But during steady state there is *steady leakage*
    - *Electrochemical* forces cause Na+ to continually leak into cell, and K+ to continually leak out of cell via…
        - Equilibrium > membrane pot = chem wins
        - Equilibrium < membrane pot = elec wins
        - Electrochemical gradient goes in favour of who wins



    - Eventually the ion concentrations would change
        - Inside cell higher in sodium
        - Outside cell higher in potassium
    - Membrane potential is at risk of approaching zero mV
    - Another type of transport mechanism is required
        - Sodium-potassium pump maintains the resting potential
        - Pump is absolutely critical for neuron function



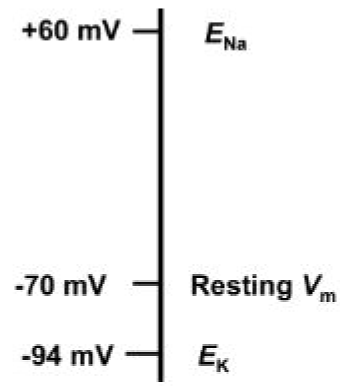
- Sodium-potassium exchange pump (Na-K-ATPase)
    - Ejects 3 sodium ions from the ICF and brings in 2 potassium ions from the ECF back into the cell
    - *Ratio of 3:2*
    - Maintains stable resting potential



    -
- Resting membrane potential must re-set very quickly (to re-function)

LECTURE 8 - NERVOUS SYSTEM III: ACTION POTENTIAL

Resting Membrane Potential



- The resting membrane potential is closer to the potassium equilibrium potential
    - A resting membrane at -70mV
    - Potassium membrane potential is -94mV, 24mV away from equilibrium
    - Sodium membrane potential is +60mV, 130 mV away from equilibrium
        - Electrochemical force for Na+ >>> K+ (it's far greater than potassium)

A Neuron at Rest

- Net electrical force on an ion will move the ion across the membrane so that the membrane potential is closer to that ion's equilibrium potential
- Small Na+ leaks at rest (high force, low permeability)
- Small K+ leak at rest (low force, high permeability)
- Sodium pump returns Na+ and K+ to maintain gradients

<u>Goldman Equation</u>

$$V_m = \frac{RT}{F} \ln \left(\frac{P_{Na^+}[Na^+]_{out} + P_{K^+}[K^+]_{out} + P_{Cl^-}[Cl^-]_{in}}{P_{Na^+}[Na^+]_{in} + P_{K^+}[K^+]_{in} + P_{Cl^-}[Cl^-]_{out}} \right)$$

-
- Describes the physical calculation for determining the voltage at the membrane (membrane potential)
- Equation accounts for the major ions that affect membrane potential (Na+, K+, Cl-)
- R is gas constant
- T is temperature (Kelvin; 37 degreeC = 310.5K)
- F is Faraday constant - charge per mode of electrons
- *P is permeability (for each ion)**** - we change P, we ultimately change Vm

GOALS/OBJECTIVES

- Describe electrical signaling through changes in membrane potential
- Ion channels and their roles in determining the action at the neuronal membrane and function of the neuron
- Describe graded potentials and action potentials
- Refractory periods of an action potential
- **What molecular features of the neuron allow it to respond to ionic changes at the membrane? (think of different channels, gated channels and pumps and where they are found throughout the neuron. Relate their localization with regional functionality of the neuron)**
- How does a graded potential differ from an action potential?

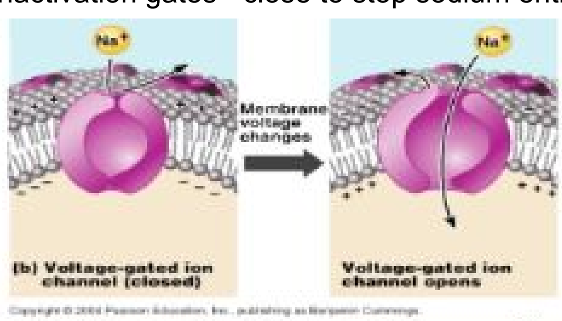
- What would happen if our neurons lost sensitivity to graded potentials
- How is the neuron designed to allow an AP to proceed in a forward direction? What keeps the AP from flowing backwards

Action Potential

For Action Potential - P needs to change (equation)

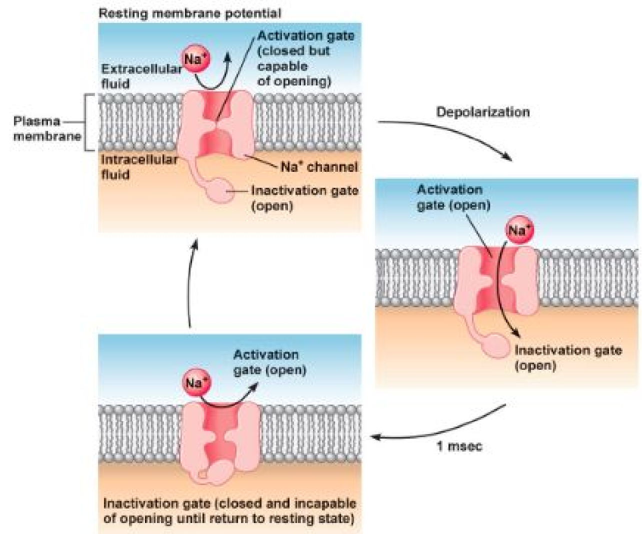
- The neuron
    - As a cell, primary characteristic of a neuron is to send and receive signals (to do this permeability needs to change)
    - Signals come in form of changes in membrane potential
        - Resting membrane - there are no changes in membrane potential
        - Active membrane - there are changes in membrane potential → action of *gated channels*
- Gated channels
    - Open or close in response to stimuli (compare this to the function of leak channels, leak channels are always open)
        - They are mostly *closed* at resting potential
        - Two important consequences:
            - Rate of movement of ion changes (P increases)
            - When P changes, there is an ultimate change in the voltage
    - Affect movement of ions → translates to an electrical signal and possible action potential
    - Three types of gated channels:
        - Voltage-gated channels
        - Chemically gated channels (ligand-gated channels)
        - Mechanically gated channels

Voltage Gated Channels

- Concentrated on excitable membranes
    - Open or close in response to changes in membrane potential
    - Voltage gated Na+, K+ and Ca+ channels are most important for neuron function
    - More complex in function - channel has two gates that operate independently (picture)
    - Activation gates - open upon stimulation
    - Inactivation gates - close to stop sodium entry
    - 

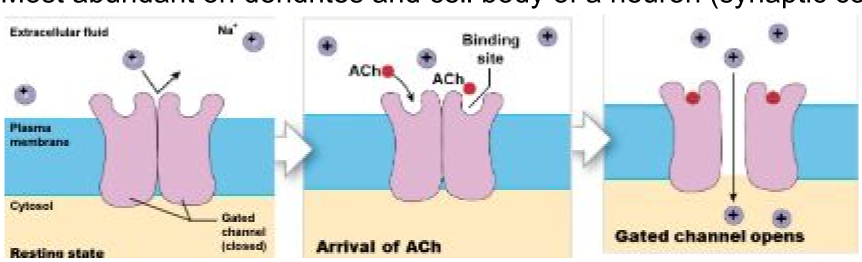
Voltage Gated Sodium Channel

- Two gates:
  - Activation and inactivation
- When unstimulated:
  - Activation gate is normally closed but able to open
  - Inactivation gate is open
- When depolarized
  - Inactivation gate opens; activation gate opens
- Immediately after depolarization is initiated (+30mV)
  - Some activation gates start closing
  - Inactivation gate closes
- Essentially it allows sodium to go through or not go through

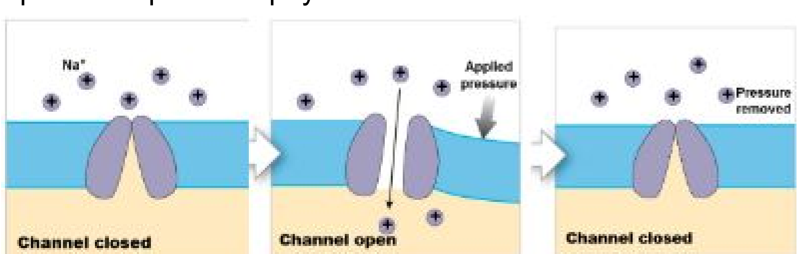


<u>Chemically/Ligand Gated Channels</u>

- Open when they bind to specific chemicals ex. ACh (ligand are binders). Think of a key
- Most abundant on dendrites and cell body of a neuron (synaptic communication)



<u>Mechanically Gated Channels</u>

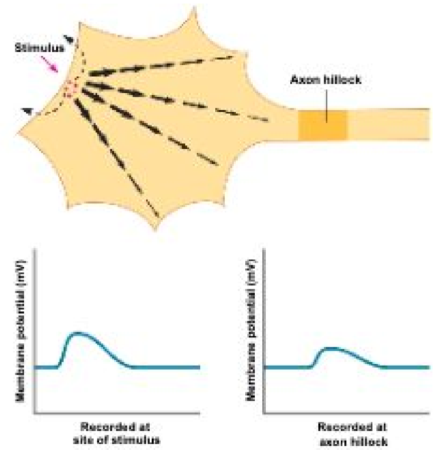
- Important in sensory receptors
- Open in response to physical distortion of membrane surface
- 

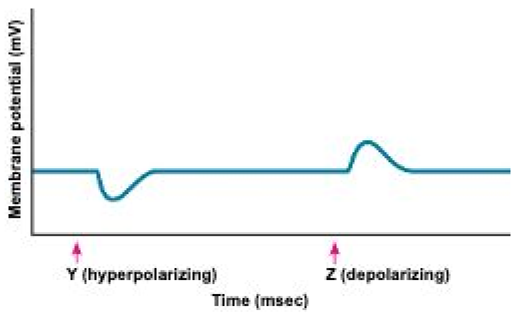
<u>Types of Electrical Signals</u>

- Graded potentials (small, communicate over short distances) - every potential is a graded potential, and some graded potentials are action potentials
- Action potentials (large, communicate over long distances)

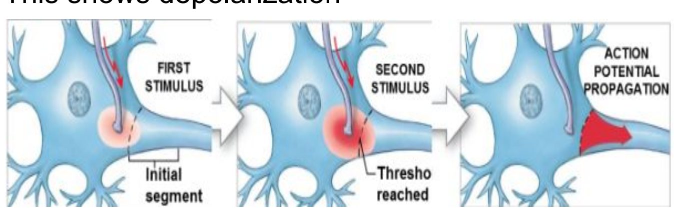
<u>Graded Potentials</u>

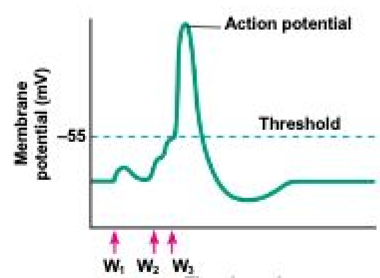
- Initiated by a stimulus (stimulus needs to be strong to reach the threshold to actually produce action)
- Small change in membrane potential
- Magnitude varies (graded)
- Magnitude of the potential decays as it spreads (electrotonic conduction)



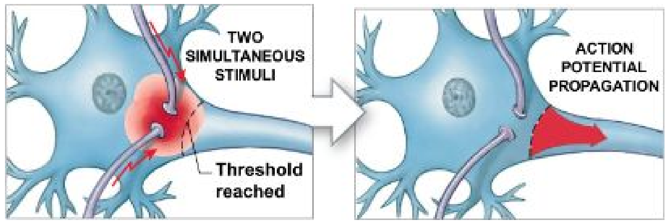
- Why do we have graded potentials?
    - It determines if an action potential will occur
    - Threshold
        - Level of depolarization needed to start an action potential
    - Excitatory → depolarization (becomes more positive in your membrane potential)
    - Inhibitory → hyperpolarization (not everything we do produces excitation)
    - 

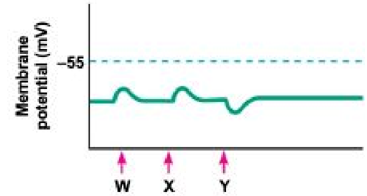
- Graded potentials can sum together over time
    - Temporal summation (temporal = time)
        - Same stimulus
        - Repeated close together in time
        - This shows depolarization



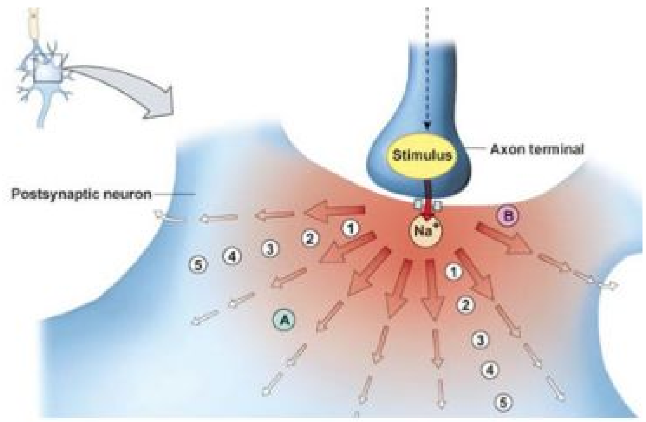


- Spatial summation
    - Different stimuli come in together
    - Overlap in time
    - They can also show inhibitory...graded potentials can do everything

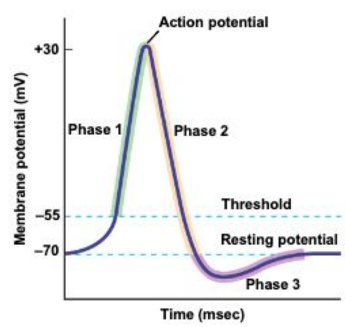
- 



<u>Graded potential vs action potential</u>

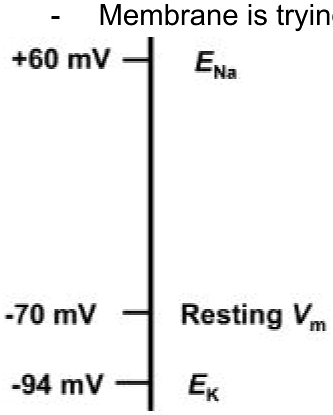


- Graded:
    - Graded potentials are localized and affect only a small area
    - But signal must travel the length of the neuron - cell must communicate between cell body and axon terminal (telodendria)
    - Excitable membranes (neuron) can generate action potentials
    - The force must be stronger or frequent so its able to travel to meet the hillock
        - The biggest force is at the point of ‘contact’, it fades out as it travels
- Action:
    - Rapid large depolarization is used for communication
- In neurons:
    - AP travels along axons from cell body to axon terminal



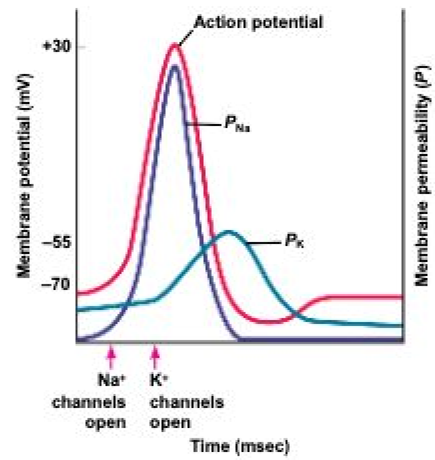
<u>Phases of an Action Potential</u>

- Phase I: Depolarization
    - travels to more positive → hits max +30mV, this is because of Na+ flooding in, voltage channels are open. K+ pulls back the charge
- Phase II: Repolarization
- Phase III: After-hyperpolarization
    - Membrane is trying to maintain homeostasis



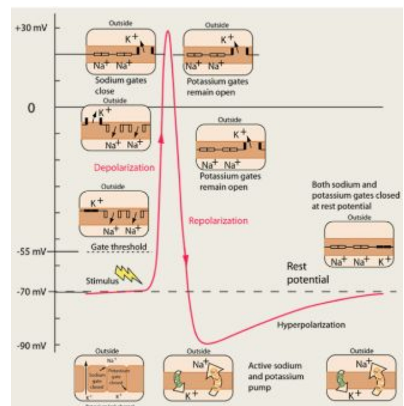
Changes in Na+ and K+ Permeability During Action Potential

- Movement of ions across the neuron membrane depends on its permeability for that membrane
- Sodium has a high permeability during the depolarization phase of AP
- Potassium has high permeability during the repolarization phase of AP
    - Its slower to get up, its delayed and slow to close (causes the major dip in mV momentarily)
- Permeability for each ion is determined by time-dependent opening and closing of voltage gated sodium and potassium channels



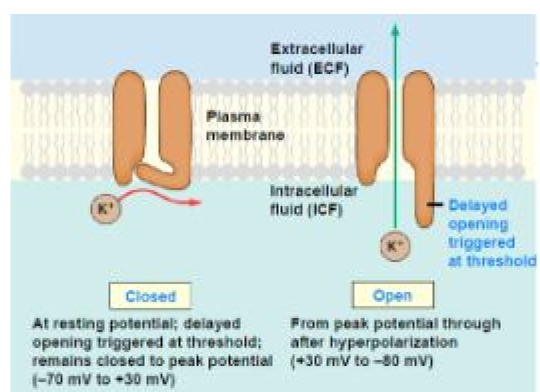
Steps of the Action Potential

- -70mV
    - VG channels are closed; only influence in Vm comes from ion specific leak channels
- Depolarization
    - Causes sodium inactivation gate to open temporarily; sodium rushes in
    - Potassium VG channel is a little slower and opens after the Sodium VG channel
    - This limits the Vm from reaching sodium ion equilibrium potential (ex. +60mV)
- Repolarization
    - Sodium inactivation gate closes; potassium activation gate remains open
- Hyperpolarization
    - Potassium gate remains open but eventually closes
    - Na+/K+ pump resets the concentration of Na+ and K+



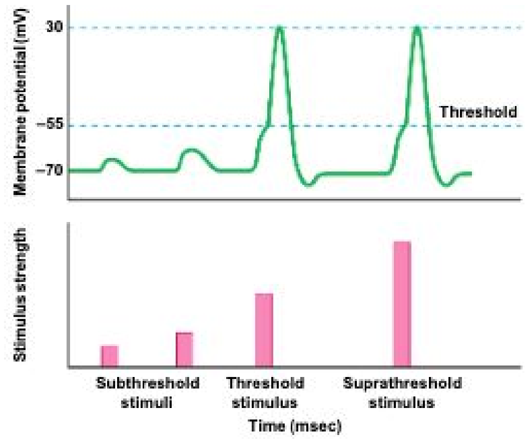
Role of Voltage Gated Potassium Channel during AP

- Voltage gated potassium channel
    - Has one gate
    - Is a slow moving channel - when triggered it does not close for a few milliseconds
    - When VG-K+ channel is closed, Vm goes from -70 to +30mV → K+ can't leave cell
    - When VG-K+ channel opens, Vm goes from +30mV to -80mV → K+ leaves cell



Threshold Stimulus

- Minimum amount of membrane depolarization is needed to initiate an AP
- Referred to as the threshold stimulus
- Stimulus less than threshold will not generate an AP
- Stimulus greater than threshold will generate an AP
- Strength of stimulus does not influence the degree of depolarization for an AP



All-Or-None Principle

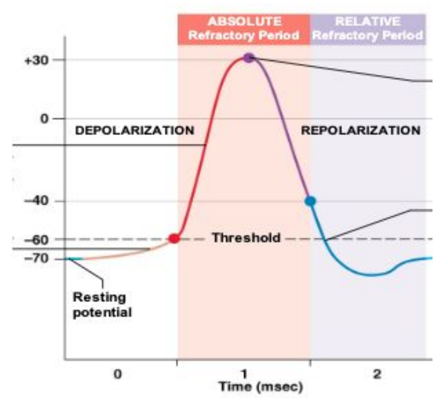
- The action potential either fires (all) or does not (none)
- The limiting factor in all-or-none principle is if the stimulus hitting the axon hillock reaches threshold voltage
- Ex. firing a gun, once it passes its threshold, the gun will fire

Threshold

- Minimum depolarization
- Threshold depolarization → action potential (all)
- Subthreshold depolarization → no action potential (none)
- Suprathershold depolarization → action potential
- Action potentials from threshold and supra-threshold stimuli are the same magnitude
    - 100 mV (-70mV → +30mV)

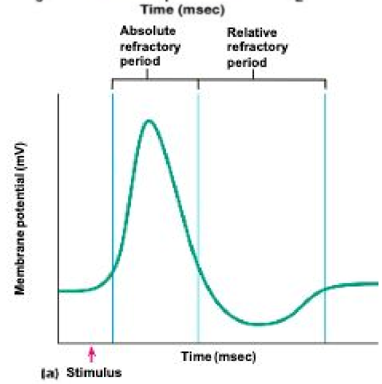
Two Important Periods of an Action Potential

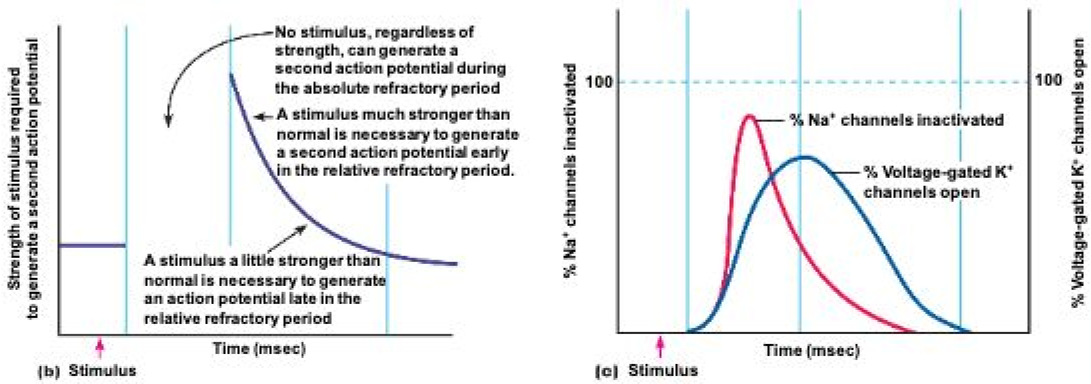
- *Absolute refractory period*: period where membrane can't respond to stimulus, no matter how strong
- *Relative refractory period*: period where membrane can respond to stimulus but only if stronger than normal



Refractory period - following an AP

- Absolute refractory
    - *Spans all of depolarization, most of repolarization*
    - Second AP cannot be generated
    - Na+ channels are open and can't be opened anymore
    - Most of sodium inactivation gates are closed and Na+ channel can't be opened when in this position
- Relative refractory
    - Spans last part of repolarization phase and hyperpolarization period
    - *Second AP can be generated* but stronger stimulus is required
    - *Some sodium inactivation gates are closed; some are open*



- 

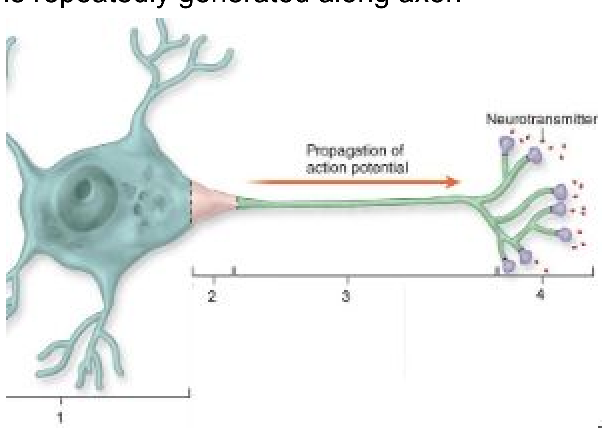
LECTURE 9 - NERVOUS SYSTEM IV: THE SYNAPSE

OBJECTIVES/GOALS

- Why is the refractory period needed for propagating the AP?
- Describe how the AP is propagated along the axon
- Describe the molecular events (ions, chemicals) during a synapse
- **Describe the types of information processing within a neuron**
- **What keeps AP moving in one direction? What would happen if the refractory periods (absolute and relative) were shifted to the left or right of the action potential wave? → would it stop and go the other way? Does it move L to R?**
- What role does myelin have with respect to the action potential?
- If acetylcholinesterase was inhibited, what would be the effect at the synapse? For the neuron?

Action Potential Propagation

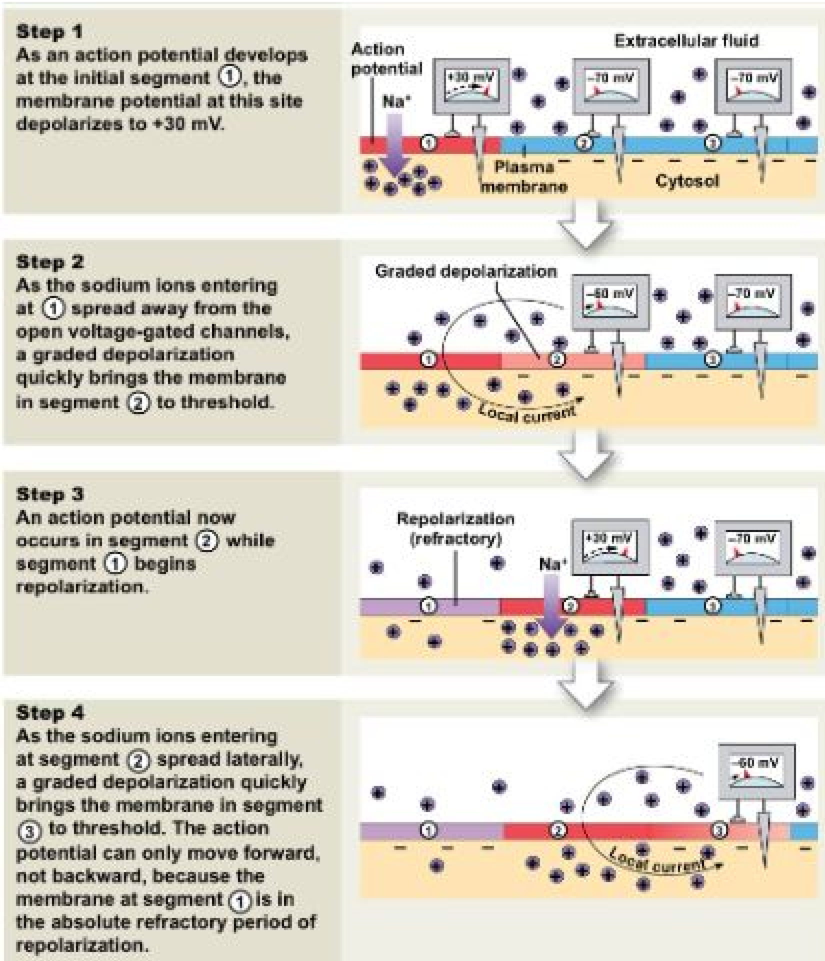
- AP is generated at the initial segment (near axon hillock)
- But doesn't actually move along axon
    - Is repeatedly generated along axon

- 

Continuous Propagation

- Continuous propagation occurs along unmyelinated axons
- Appears to smoothly move along axolemma but actually is a series of *tiny steps*

- Each step about 1.0 millisecond
- Sodium important in depolarization
- Potassium important in repolarization



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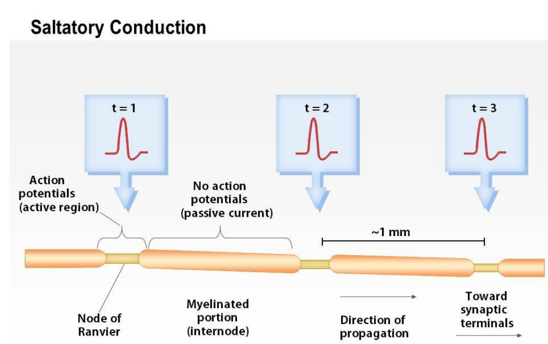
<u>Myelin is important for action potential</u>

- Myelin is key player in *saltatory* propagation (saltatory = jump/leap)
- Myelin quickens and enhances AP propagation
- But myelin blocks the flow of ions
    - Therefore ions need to ‘jump’ across the myelin
- AP can only cross the axon membrane at unmyelinated regions



<u>Saltatory Propagation</u>

- Because myelin prevents the flow of ions, AP skips to myelin-free regions along the axon membrane
    - Nodes of Ranvier
- AP skips the internode and depolarizes at the closest node

- Type of movement is called *saltatory* propagation
- Much faster than continuous propagation 10m/s vs 150m/s

Continuous Propagation	Saltatory Propagation
Unmyelinated axons	Myelinated axons
AP moves along the length of axon in tiny steps	Ions cross at unmyelinated nodes (Nodes of Ranvier)
Each step is only 1.0 millisecond	AP begins at initial segment, skips internode and depolarizes at closest node
Must be repeated along entire length of axon (0.5-10 m/s)	Faster than continuous (up to 150 m/s)
	Speed varies with diameter of myelin coating Larger diameter = less resistance

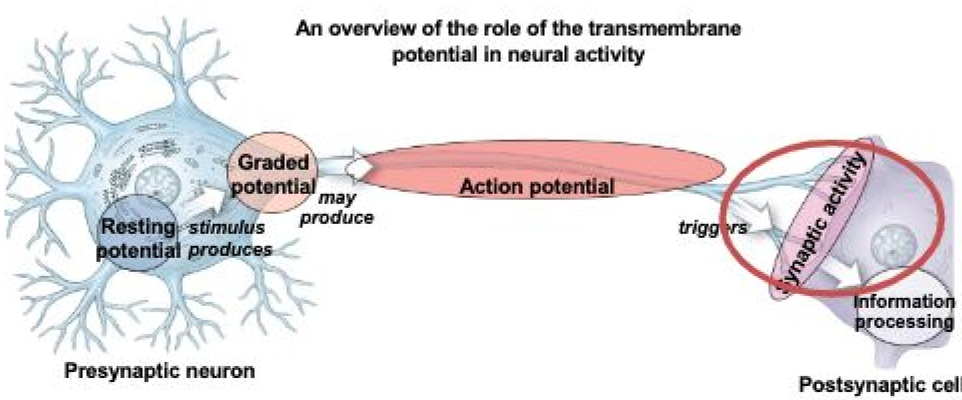
-

<u>Clinical Role of Myelin in the CNS - Multiple Sclerosis</u>

- MS is a progressive demyelinating disease (autoimmune disease)
- Immune cells attach the oligodendrocytes that cover the axons with myelin in CNS neurons
- T cells cross the BBB; recognize myelin as a forein antigen (invader) on the oligodendrocytes and attack it
- Regions of local inflammation (scars - axonal sclerosis) are left
- Action potential propagation (saltatory propagation) is disrupted
- We can see here the significance of myelin***

<u>Transmission at the Synapse</u>

- A nerve impulse needs not only to be propagated along an axon but must also be transmitted or transferred to another neuron or effector cell (ex. Muscle, gland - neuromuscular synapse, neuroglandular synapse, neuronal synapse))
- Transmission occurs at the synapse



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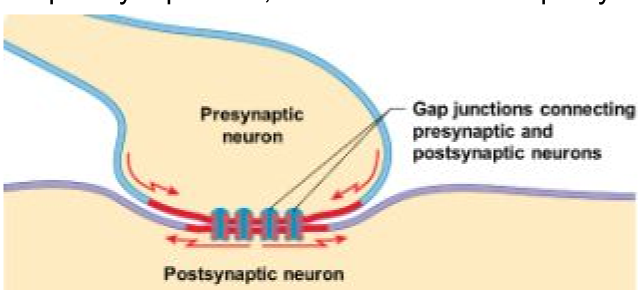
The Synapse

- Two types

Chemical synapse	Electrical synapse
Rely on neurotransmitters	Rely on gap junctions – joining of membranes
'Large' distance between pre- and post-synaptic cells 30-40 nm	Very short distance between pre- and post synaptic cells (approx 3-4 nm)
Most abundant	Fast but simple conduction of nerve impulse
Found in all synapses from neuron to cell	Not able to amplify the electrical impulse; lack gain
Found in most synapses from neuron to neuron	Bi-directional transmission of impulse
Cholinergic synapase (ACh) is common	more efficient but less versatile
Can amplify the electrical impulse	

- In chemical, it is more complex and tries for finesse
- Electrical is more simple, black and white

Electrical Synapse - Gap Junctions

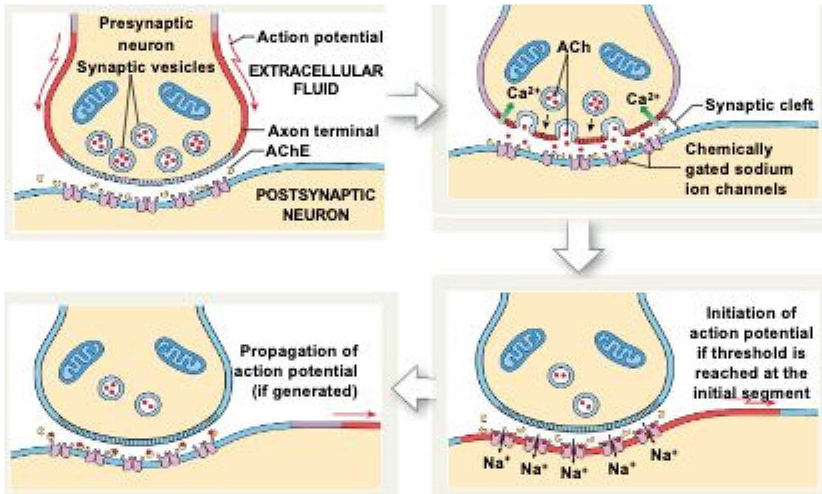
- Electrical synapses involve gap junctions to bridge the pre- and post-synaptic membrane
- The changes in the membrane potential of one cell produce local currents that affect the adjacent cell
- Signaling is efficient but there's no versatility in the signal. The signal does not vary in the postsynaptic cell, it's the same as the presynaptic cell
- 

Chemical Synapse

Neurotransmitters

- More than 100 exist and work in different ways
- Main goal is to alter postsynaptic cell activity

Bridging from Pre to Post synaptic cell

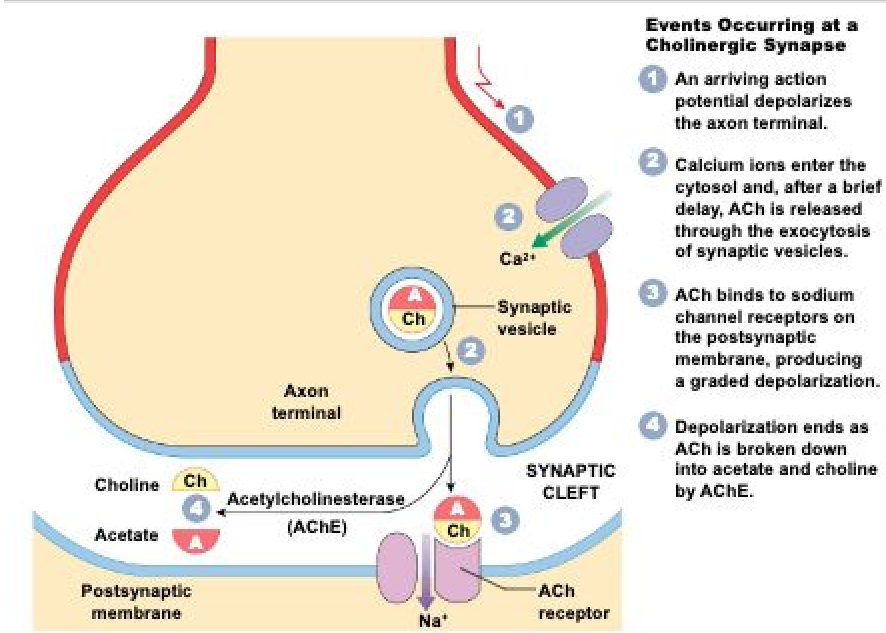


****know basic steps****

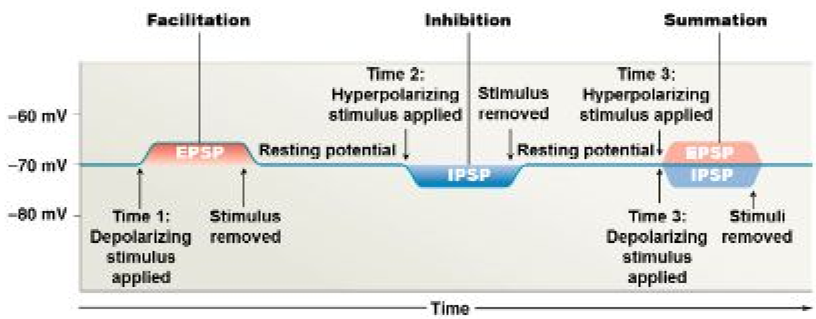
Voltage gated channels for Ca2+ opens up, and calcium allows these vesicles (organelle with lipid membrane that has Ach) to move towards membrane of presynaptic cell and melt with it, thereby letting out the Ach into the synaptic cleft, which goes and binds to receptors on the post synaptic cell. Those receptors are chemically gated sodium channels, AP is generated. ACh needs to come off receptor otherwise it will keep going and going (synaptic fatigue).

1. Signal (depolarization) down to synapse
2. VG Ca2+ channels sense and open
3. Ca2+ enters synapse (cell)
4. Vesicles (contains AChe) fuse with synaptic membrane → releases ACh
5. ACh → receptor (CG sodium channel… ligand = ACh)
6. Sodium enters → depolarization

ACh gets recycled back into the cell



Information Processing within a Neuron

- Excitatory and inhibitory post synaptic potentials
- 

Information Processing is by Post Synaptic Potentials

- Thousands of synapses hit a single neuron
- Neurotransmitters arriving at the postsynaptic cell can be excitatory and some can be inhibitory
- Axon hillock is summing the signals
    - Summation can be temporal or spatial

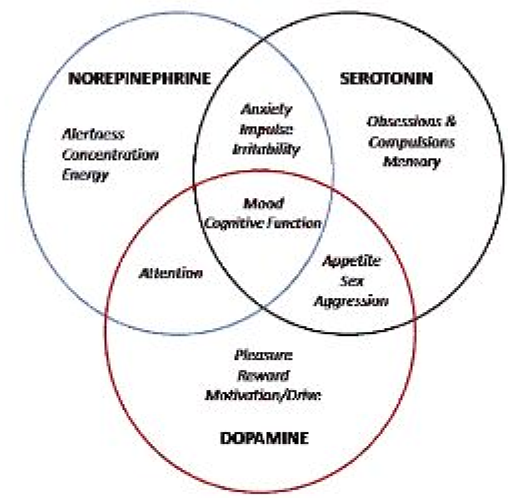
LECTURE 10 - SKELETAL MUSCLE 1: MUSCLE STRUCTURE

OBJECTIVES/GOALS

- Discuss the significance of the neuro-muscular junction and its relation to skeletal muscle tissue
- Describe the role of skeletal muscle as an organ system
- Describe the process of myogenesis (development)
- Describe the macroscopic and microscopic structure of skeletal muscle
- Describe the components and assembly of the thin and thick filaments of the sarcomere

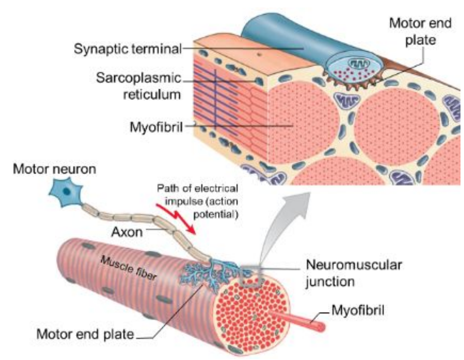
- Describe the process of muscle contraction
- What are some key roles of skeletal muscle? What role is likely to be the most important and why?
- Define and detail skeletal muscle myogenesis
- Is the myogenic program (muscle development) fails-proof?
- Where can muscle development go wrong and what are the consequences?

Neurotransmitters



Neuromuscular junction (NMJ)

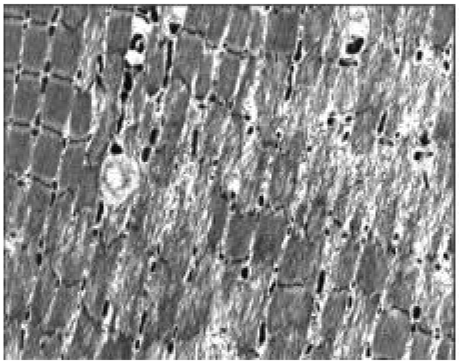
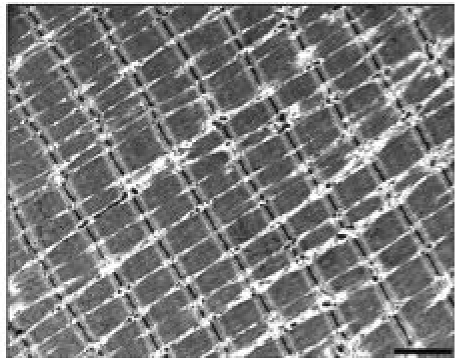
- NMJ
    - Connection between motor neuron and sk. m fiber → forms region called the motor end plate
    - One NMJ per muscle fiber
    - Telodendria (axon extensions) allows axon body to hit multiple muscle fibers
- Picture: this is one muscle cell, they are elongated fibers



Important of the motor neuron at the neuromuscular junction

- Spinal muscular atrophy (SMA) - disease of the neuromuscular junction
    - Muscle starts to degrade because it is not stimulated

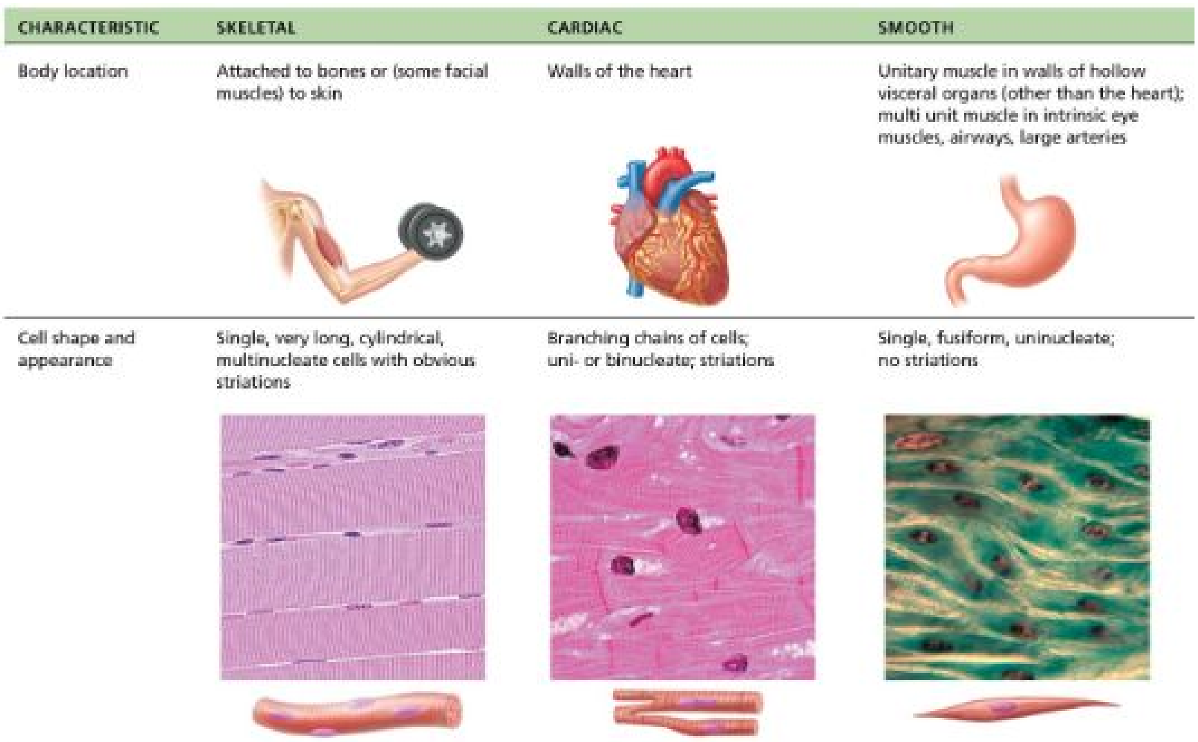
Skeletal Muscle is a Dynamic Tissue

After the gym Before the gym

- It changes, recovers, regenerates
- We can damage it and rest and repair, and it will be better

<u>Three Types of Muscle in our Bodies</u>

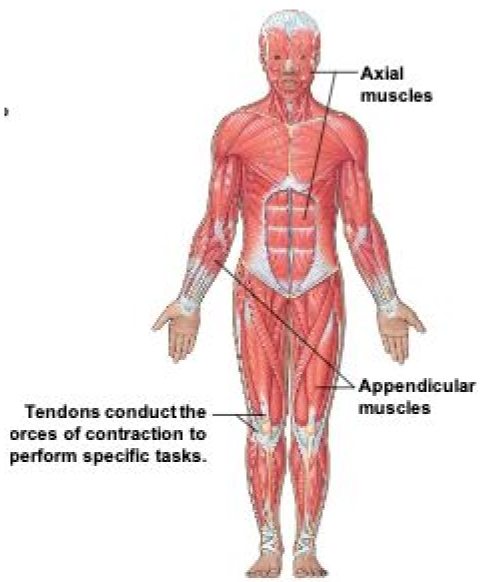
- 

CHARACTERISTIC	SKELETAL	CARDIAC	SMOOTH
Body location	Attached to bones or (some facial muscles) to skin	Walls of the heart	Unitary muscle in walls of hollow visceral organs (other than the heart); multi unit muscle in intrinsic eye muscles, airways, large arteries
Cell shape and appearance	Single, very long, cylindrical, multinucleate cells with obvious striations	Branching chains of cells; uni- or binucleate; striations	Single, fusiform, uninucleate; no striations

- Skeletal, cardiac, smooth
- **be aware of their characteristics**

<u>Muscular System - Majority of Body Tissue</u>

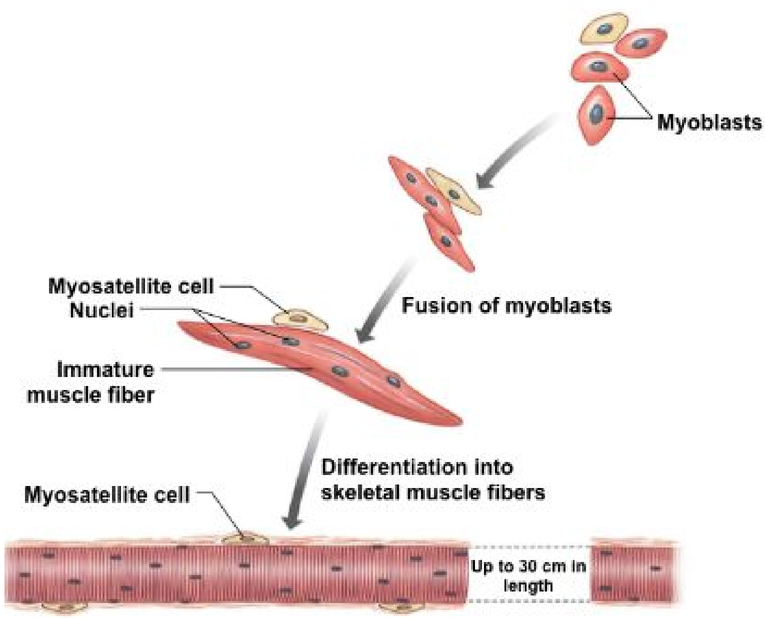
- Muscular system 44%
- Skeletal system 20%
- Integumentary (skin) system 16%

- 

<u>Role of Skeletal Muscle as an Organ System***</u>

- Movement of skeleton
- Maintain posture and body position
- Support soft tissues
- Protection - guard entrances and exists to the body
- Thermoregulation (generate heat = muscles start to shiver, burning ATP which releases heat)
- Provide nutrient reserves

<u>Skeletal Muscle Development - Satellite Cells and Myogenesis</u>

- 

Single cell

Nuclei cells

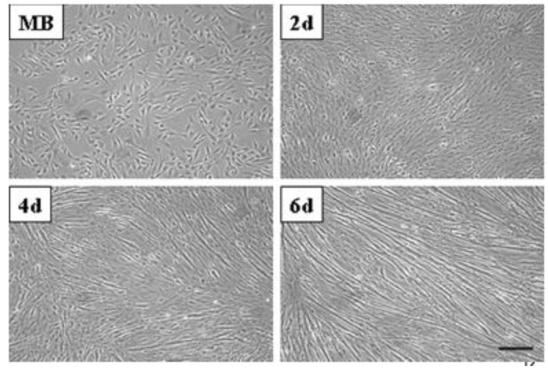
Elongate

Myosatellite cells stay

Myofiber

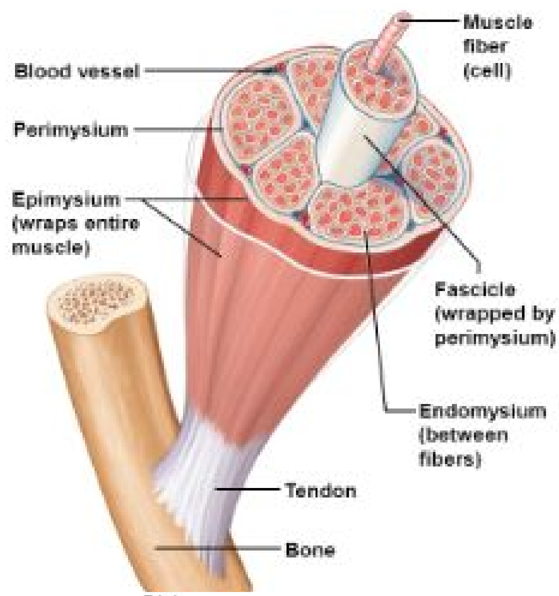
So essentially, myoblasts fuse together (myo = muscle, blast = cell)

Skeletal Muscle Cells



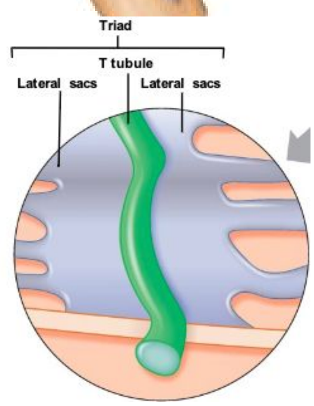
- A muscle fiber is really several muscle cells that have joined together to make a single cell
    - Start as cells with a single nucleus (mono nucleated)
    - Enlarge
    - Align
    - Fuse (multinucleated)
    - Elongate
        - Become individual fibers

Gross Structure of Skeletal Muscle **know the three layers**



- Skeletal muscle
    - Covered by 3 main layers of *connective tissue*
    - Each layer groups the skm into subsequently smaller divisions
- Epimysium (mysium = muscle)
    - Surrounds entire muscle tissue; continuous with tendon
- Perimysium
    - Extends into skm, divides into later bundles - fascicles
- Endomysium
    - Thin sheath, covers individual muscle fibers

Structure of Skeletal Muscle at Cellular Level



- Major components of muscle fiber:
    - Many myofibrils
    - Sarcoplasmic reticulum
        - Smooth ER
    - Many mitochondria
    - Transverse tubules
        - T-tubules
    - Lateral sacs (terminal cisternae)
        - Ca2+
        - Triad: T-tubule + two lateral sacs

Common Terminology Specifico Skeletal Muscle

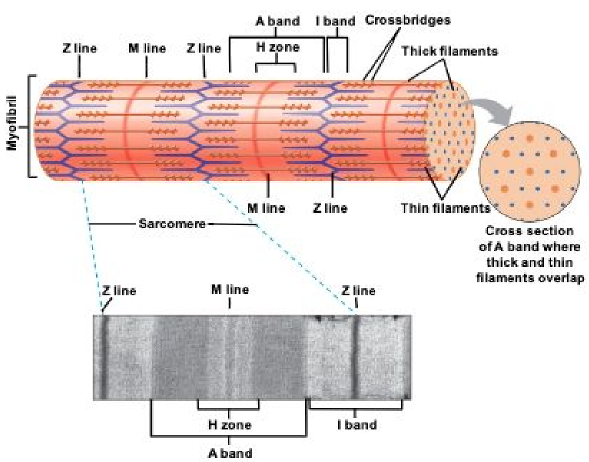
- Muscle cell is a *muscle fiber*
- Cell membrane is the *sarcolemma*
- Cytoplasm is a *sarcoplasm*

- Endoplasmic reticulum (ER) is the s*arcoplasmic reticulum* (SR)

<u>The Sarcolemma</u>

- Sarcolemma separates the sarcoplasm from surrounding interstitial fluid
- *Negative charges on inside surface, positive on external surface* - like a neuron
- Sarcolemma allows for the selective permeability of electrical charges - uneven distribution
- Blue = lateral sacs (Ca2+)
- 

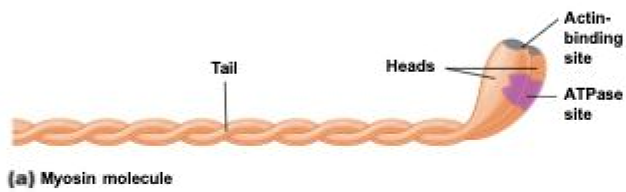
Contractile Apparatus - Structure at the molecular level

- *regions have different zones*
- H zone - thick filaments only
- I band - thin filaments only
- A band - thick and thin filaments overlap
- M line - region that links the thick filaments
- Z line - region that links the thin filaments
- Sarcomere: function unit of skeletal muscle - from Z line to Z line
- 

Thin Myofilament - Actin

- Contractile protein
- Each globular actin has a binding site for myosin
- *Associates with tropomyosin*
    - Regulatory protein
    - Covers active site on G actin
    - Prevents actin-myosin interaction
- Attaches to *troponin*

- Regulatory protein complex
- Complex of three proteins
    - Attaches to actin
    - Attaches to tropomyosin
    - Binds Ca2+ reversibly
- Ca2+ binding to troponin regulates skeletal muscle contraction
- TnC binds two calcium ions during contraction
- Displaces tropomyosin and allows actin-myosin interaction

Thick Myofilament - Myosin
- Myosin tail points towards M line
- Myosin head is towards I band
- Myosin head has two main features:
    - Actin binding site
    - Nucleotide binding site for ATP and ATPase
    - 

Thick Myofilaments are Connected by Titin
- Titin
    - Thick myosin filament attaches to titin
    - Titin is a huge MF
    - Supports protein in muscle
    - Very elastic protein
    - Anchor thick filaments between M line and Z line
    - Provides structural support and elasticity

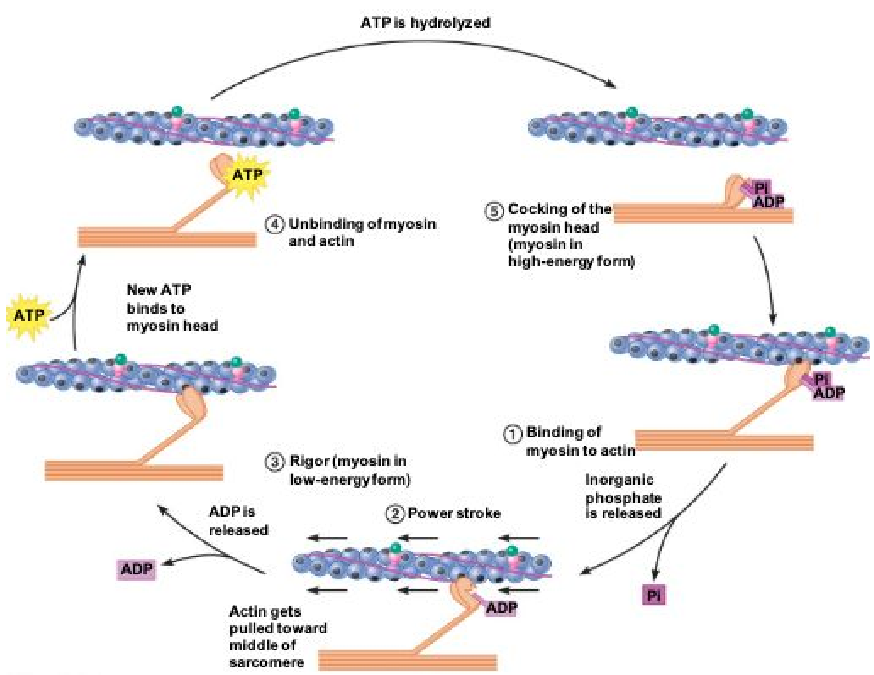
Sarcomeric Complex - not just actin and myosin
- The muscle sarcomere is a complex of multiple proteins
- Interaction, association and binding is specific - the proteins must assemble
- Functional (clinical) issues arise when components of the sarcomere are not expressed properly or do not assemble correctly

<u>Force Generation in Skeletal Muscle</u>
- Terminology to know:
    - Generating force in skeletal muscle relies on the *sliding filament model* - the physical mech to generate force
    - The *crossbridge cycle* describes how muscle generate force - molecular mech to generate force

- *Excitation-contraction coupling* describes how muscle contractions are turned on and off - the elec to mech conversion to generate force
- Muscle cell metabolism provides muscle cells with ATP that drives the crossbridge cycle

<u>Cross-Bridge Cycling</u>

- Cross-bridge cycling is analogous to rowing a boat through water
    - Power stroke: myosin head moves, propelling thin filament toward center of muscle = movement of oar propelling a boat
    - Thick and thin filaments detach = oar beaks contact with water
    - Myosin head returns to the initial position = oar moved to a new position, cycle starts again
        - Myosin head high energy state vs low energy state
        - The hydrolysis of ATP is what gives the energy
        - ADP and Pi moves the head up
        - ADP released = pivoting of myosin head 'stroke'
- Cross-bridge formation is asynchronous
    - Muscle cell generates force continually; cross bridges form in cycles continuously but out of synch (not coordinated to cycle together)
    - Some cross bridges start while others are finished while other cross bridges are at stages in between
    - If they were all in synch:
        - Cross bridges all form, then they all detach...thin filaments will passively slide back...all at the same time → contraction inefficient



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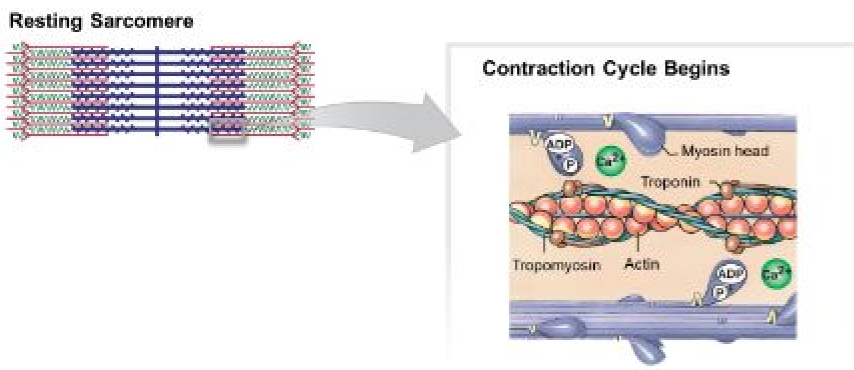
Muscle Fiber Contraction

- At rest, myosin heads are ‘energized’
- CA++ is released close to the thick and thin filaments (zone of overlap)
- Binds TnC, causes Tropomyosin to displace, revealing the active binding site for myosin on the actin thin filament



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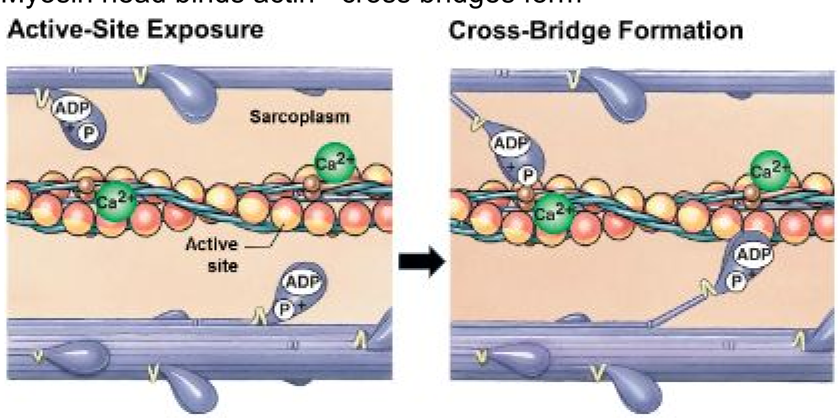
- Active site for myosin is exposed
- Myosin head binds actin - cross bridges form



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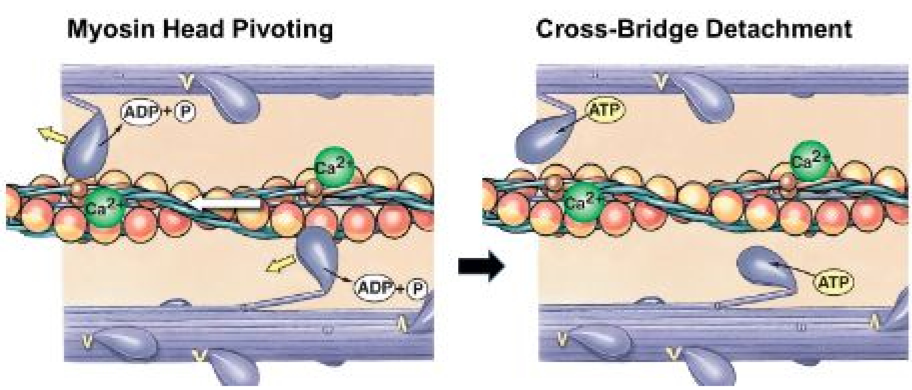
- Myosin head pivots towards M line - power stroke
- This releases the bound ADP and inorganic phosphate (Pi)
- Myosin head remains bound to actin binds a new ATP molecule
- New ATP molecule binds the myosin head and releases myosin from actin - detachment



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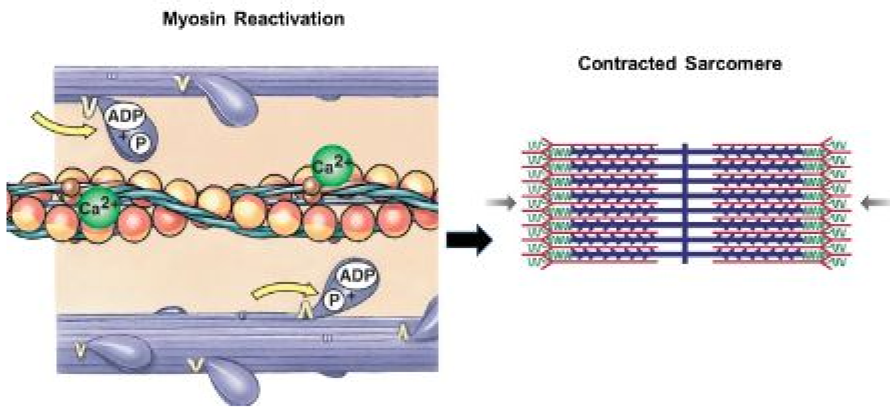
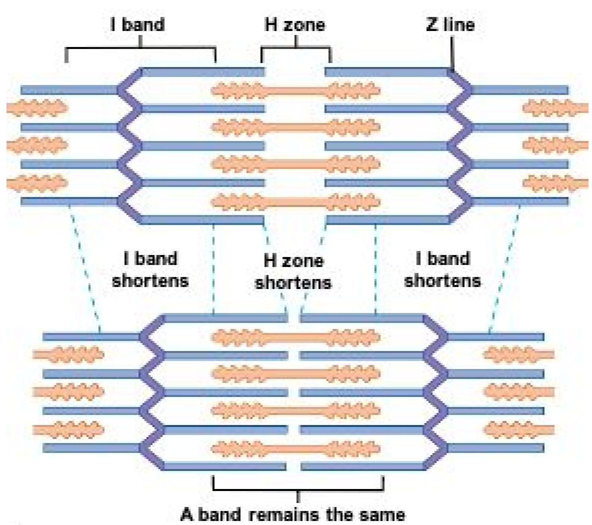
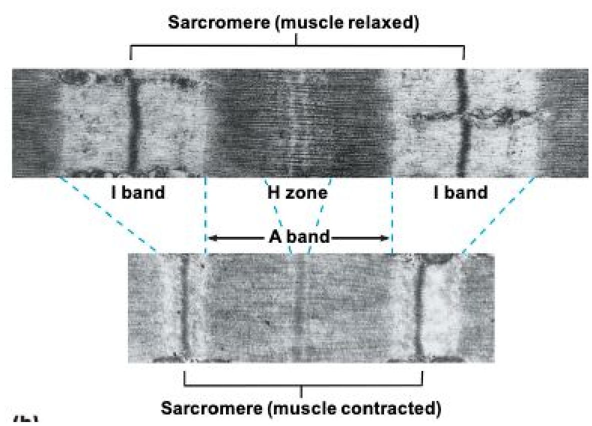
- Myosin head (now free) immediately hydrolyzes ATP to ADP and Pi
- This re-energizes the myosin head making it ready to bind an actin molecule

- Cycle continues as long as calcium ions are available
- Calcium is available as long as action potential passes along the T-tubule
- 

Muscle Contraction - Sliding Filament Model

- As muscle contracts, it shortens
- Thick and thin filaments overlap but neither of the filaments change in length
  - A band stays same length
  - I band shortens - move into H zone
  - H zone shortens
  - Sarcomere shortens
- Filaments slide past each other
- Z- lines move closer together and entire sarcomere shortens
- Sarcomere shortens = myofibril shortens = muscle fiber shortens = entire muscle shortens
- Sliding creates a cycle of forming and breaking between cross-bridges → *cross-bridge cycle*



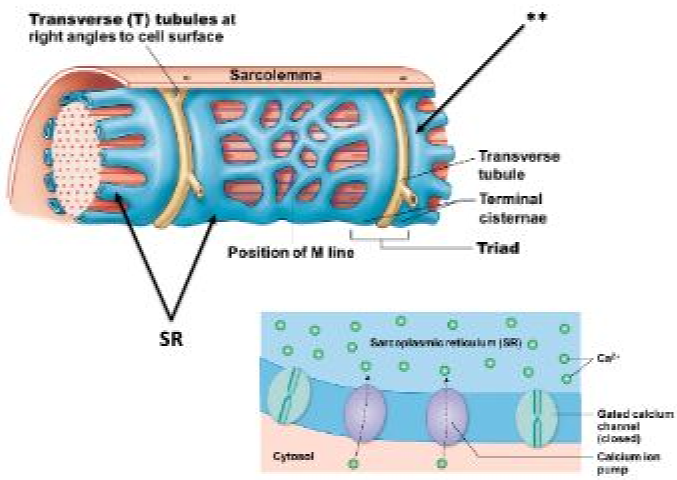


How do we turn muscle contractions on and off?

- Excitation-Contraction Coupling:
    - Defined as sequence of events whereby an AP in the sarcolemma causes contraction
    - Requires neural input from motor neuron to neuromuscular junction
    - Requires Ca2+ release from the sarcoplasmic reticulum

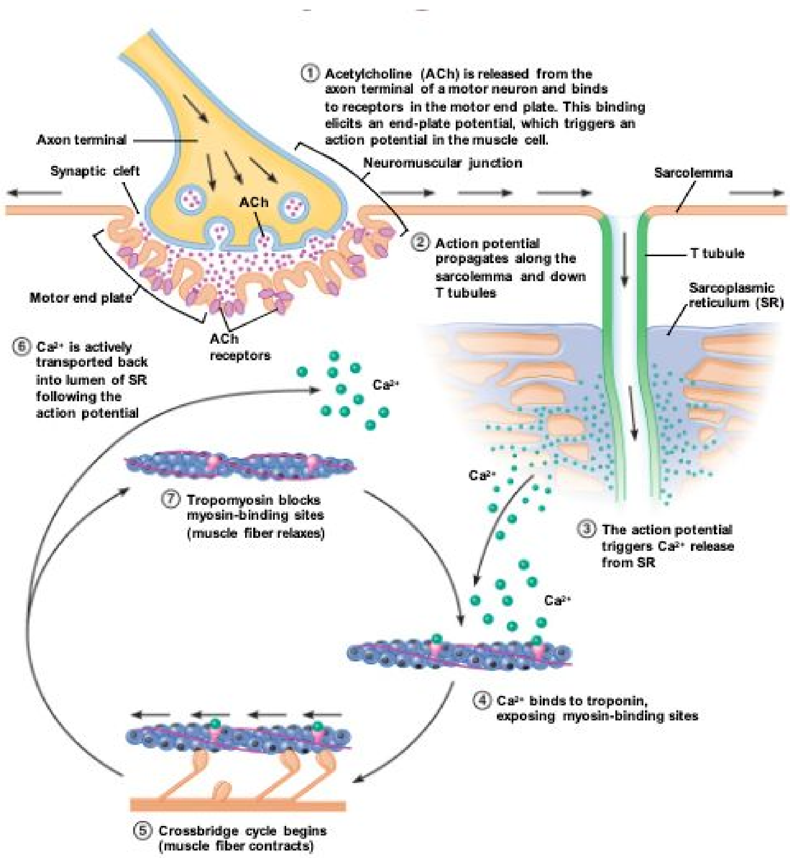
<u>Excitation Contraction coupling - role of SR and T Tubules</u>

- Sarcoplasmic Reticulum
    - Is the smooth endoplasmic reticulum of skeletal muscle
    - SR is a storage vat for calcium ions
    - Forms a tubular network around the myofibril
- Terminal cisternae
    - Flanks the T-tubules
    - Fuses with SR and expands into chambers
- Transverse tubule
    - Narrow tubes that connect all around sarcolemma
    - Extend into sarcoplasm at the right angles to cell surface
    - Forms tunnel like passages through muscle fiber
    - Situated at the region of overlap (at the sarcomere)

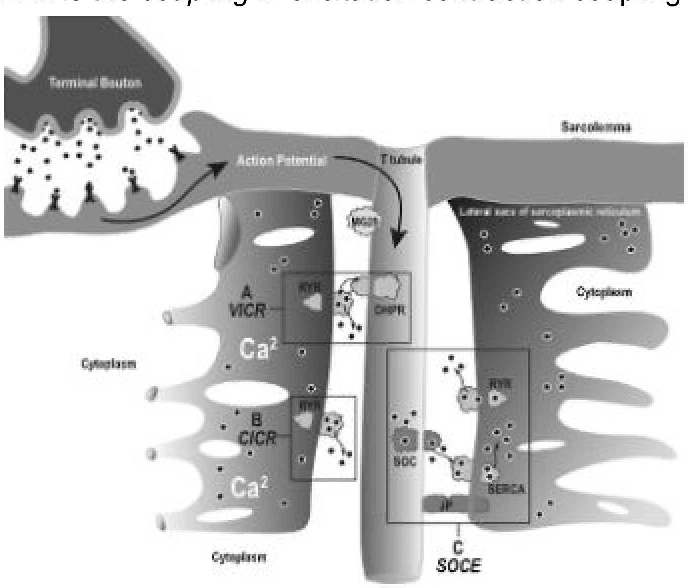


<u>NMJ, SR, and EC Coupling (Excitation Contraction coupling)</u>

1. AP arrives and depolarizes sarcolemma
2. AP travels down T tubules and activate DHP receptors
3. DHP receptors of T tubules trigger ryanodine receptors in lateral sacs of SR to open calcium ion channels
    a. A electrical signal couples with DHP, which pulls open the RYR
4. Ca2+ released into sarcoplasm
5. Ca2+ binds troponin, causes tropomyosin to shift
6. Cross-bridge cycling occurs



- Dihydropyridine receptor (DHPR) lies on T tubules
- Is physically linked to ryanodine receptor (RyR) on SR membrane
- Link is the *coupling* in excitation contraction coupling



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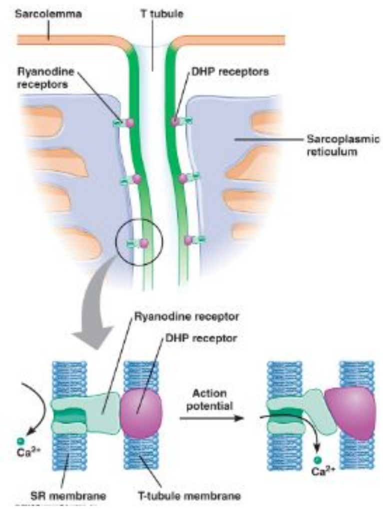
The Voltage Sensor and Voltage Gated Calcium Channel

- Dihydropyridine receptor (DHPR) is the *voltage senso*r on the T tubule membrane
- Ryanodine Receptor (RyR) is the *voltage gated Ca2+ channel* on the SR membrane (lateral sac)



EC Coupling - Contraction on/off switch - SUMMARY

Role of neuromuscular junction

- Each motor innervates several muscle cells
- Each muscle fiber receives input from a single motor neuron
- Similar to a neuronal synapse (ordinary synapse)
- Acetylcholine released
- Motor end plate has high density of ACh receptor
- End plate potential
- Motor neuron AP always creates a muscle cell AP

Role of Ca2+, troponin, and tropomyosin

- If no Ca2+ then troponin holds tropomyosin over myosin binding site on actin
    - No cross-bridge formation
    - Muscle relaxed
- If Ca2+ present then binds to troponin, causes tropomyosin to move and binding sites for myosin on actin is exposed
    - Cross-bridge form
    - Muscle contracts
- DHPR and RyR together allow Ca2+ release into the sarcoplasm to turn on contraction

Calcium and the SR → removal of Ca2+

- SR is like a big vat for holding calcium ions
- **Ca2+ is quickly pumped into the SR by SERCA (sarco/endoplasmic reticulumCa2+-ATPase)**
- Ca2+ concentration in SR will quickly increase and generate a concentration gradient - must be kept from diffusing out passively
- *Calsequestrin* holds Ca2+ in the SR (stops it from following the concentration gradient)
    - Sequester = to have forceful possession

LECTURE 11 - SKELETAL MUSCLE II: FORCE GENERATION

MIDTERM INFO:

- Wednesday
- 40 MC (40 marks)
- 5 short answers (28 marks)
- Sample ques:
    - Compare a graded potential to an action potential
        - Graded potential is a type of action potential. Graded potentials can be inhibitory or excitatory - caused by a stimulus. There are two types of summations - temporal (rapid succession of stimuli) and spatial (two +

stimuli hitting at different parts). These summations can be built up in strength to reach the threshold, as it is strongest at the point of contact and it diffuses. Once it reaches the threshold of -55, it becomes an action potential, with the all-or-none principle, which has three phases: depolarization, repolarization, and hyperpolarization. They propogate, depolarization will continue with equal intensity (-70 - +30)

- Which of the following is not a function of the cytoskeleton?
  - Contraction
  - **Energy synthesis**
  - Cellular movement
  - Suspension of organelles
  - Mechanical support
- Draw a multipolar neuron
  - Indicate where the voltage gated sodium channels are located **Focus on axon...but everywhere. This is for propagation**
  - Where are the voltage gated calcium channels found? **terminal/synapse**
  - In terms of voltage gated channels, how does the form of the myelinated axon fit with its function? **We want voltage gated channels where we have depolarization**
- Compare continuous and saltatory propagation
  - **Continuous: slower, unmyelinated,**
  - **Salt: fast, myelinated**
- What is the criteria needed to be a neurotransmitter?
  - **Synthesized in neuron** (part of autonomic ns)
  - **Must be released following depolarization**
  - **Must bind with post-synaptic receptor and must then be inactivated**
- Draw the steps that occur as the action potential arrives at the synapse from the axon terminal
  1. AP arrives & open VG Ca2+ channels
  2. CA2+ enters cell
  3. Release of vesicles (Ach)
  4. Ach joins with membrane release through exocytose and into the cleft
  5. Binds to CG sodium channels
  6. Sodium channels open, sodium rushes in and causes depolarization in post synaptic cell
  7. Ach inactivates via Ache (breaks down Ach)
- What are the three types of muscle in our bodies? Smooth, cardiac, skeletal
- Describe the process of myogenesis - how a muscle fiber is formed
- List 3 key components found in skeletal muscle cells
  - **T tubules**
  - **thick/thin filament**
  - **SR**

GOALS/OBJECTIVES

- What would happen if all the cross bridges cycled in synchrony in a muscle fiber?
- What would happen if ATP is no longer available in the muscle cell?
- What would be the effect of functional mutations (genetic mutations) in troponin or tropomyosin on force generation
- Based only on the key contractile proteins in a muscle cell (troponin, tropomyosin, actin, myosin), why are some muscle types able to generate more force than others?
- What does the *coupling* in EC-coupling refer to?
- Describe the steps in skeletal muscle contraction from the time an action potential reaches the neuromuscular junction

******* MIDTERM CUT OFF*******