Lecture 1

Anatomy

- Scientific study of the structure of body parts and their relationship to one another

Physiology

- Scientific study of how the body functions i.e. the biochemical process involved; describes how things work in terms of biochemical processes

Liver

- An anatomist is concerned with the shape, size, position, blood supply and innervation (supply an organ or other body part with nerves) of the organ
- A physiologist is interested in the production of bile, the role of the liver in nutrition and the regulation of bodily functions

Subdivisions of Anatomy

- Gross/macroscopic anatomy:
    - the study of large visible structures
- Regional Anatomy
    - Looks at all structures in a particular area of the body
- System anatomy
    - Looks at just one system (CV, nervous, muscular ect)
- Surface Anatomy
    - Looks at internal structures as they relate to overlying skin (visible muscle masses or veins seen on surface)
- Microscopic anatomy
    - Deals with structures too small to be seen by naked eye
        - Cytology: microscopic study of cells
        - Histology: microscopic study of tissues
- Developmental anatomy
    - Studies anatomical and physiological development throughout life
        - Embryology: study of developments before birth.

NOTE: to study anatomy one must know anatomical terminology and be able to observe, manipulate, palpate and auscultate

Subdivisions of physiology

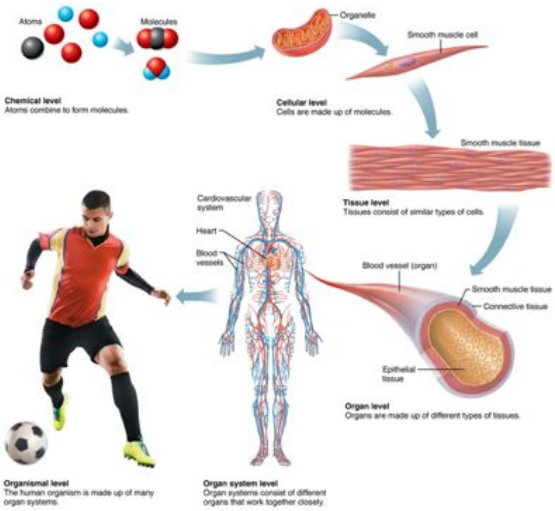
- Based on organ systems (renal or CV physiology)
- Often focuses on cellular and molecular levels of the body
    - Looks at how the body's abilities are dependent on chemical reactions in individual cells

NOTE: to study physiology, one must understand basic physical principles (e.g., electrical currents, pressure and movement) as well as basic chemical principles

Principle of Complementarity of structure and Function

- Anatomy and physiology are inseparable
    - Function always reflects structure
    - What a structure can do depends on its specific form
- Examples
    - Bones can support body organs because they contain hard mineral deposits
    - Blood flows in one direction through the heart because the heart has valves that prevent backflow
    - Lungs can serve as a site for gas exchange because the walls of their air sacs are extremely thin

Structural organization of the Human Body



- Atoms
  - The building blocks of matter. Different parts are protons, electrons and neutrons
- Molecule
  - a combination of atoms
- Organelle
  - Molecules associate in specific ways to form organelles
  - Basic components of cells
- Cells
  - Fundamental structural and functional unit of a living thin
  - Smallest unit that can maintain and perpetuate life
  - Cells vary in size/shape reflecting unique functions

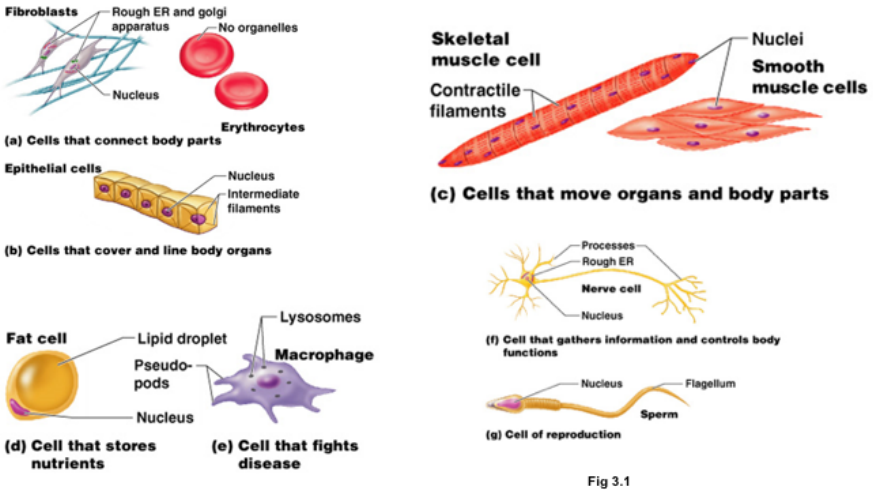
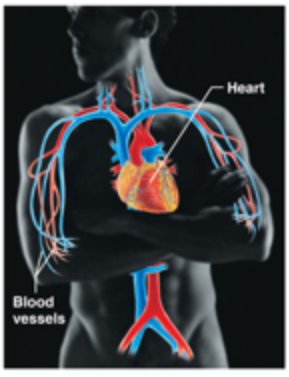
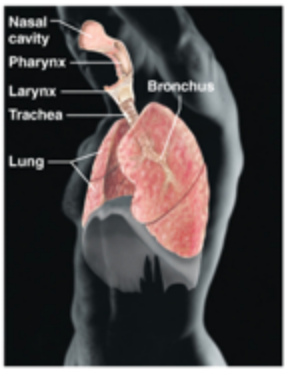


Fig 3.1

- Tissue
  - Groups of cells that are similar in structure and function
    - Connective - support, protect and transport
    - Nervous transmits - electrical impulses
    - Epithelial - form boundaries b/t different environments and secrete things
    - Muscle - contracts (produces force)
- Organ
  - Structure composed of at least 2 (but usu. 4) tissue types that performs a specific function for the body. (composed of more than one tissue)
  - ***Give an example of an organ and describe how each of its tissue types contributes to its overall role or function in the body***
- Organ system
  - Organs that work closely with one another to accomplish a common purpose. Eg nervous system



(f) Cardiovascular System
Blood vessels transport blood, which carries oxygen, carbon dioxide, nutrients, wastes, etc. The heart pumps blood.



(h) Respiratory System
Keeps blood constantly supplied with oxygen and removes carbon dioxide. These exchanges occur through the walls of the air sacs of the lungs.

Cells: The smallest living units

- Cell diversity
    - Over 250 different types of human cells
    - Types differ in size, shape, and subcellular components; these differences lead to differences in functions
- Eukaryotic cells have three basic parts
    - Plasma membrane
        - Flexible outer boundary
    - Cytoplasm
        - Intracellular fluid containing organelles
    - Nucleus
        - DNA containing control centre

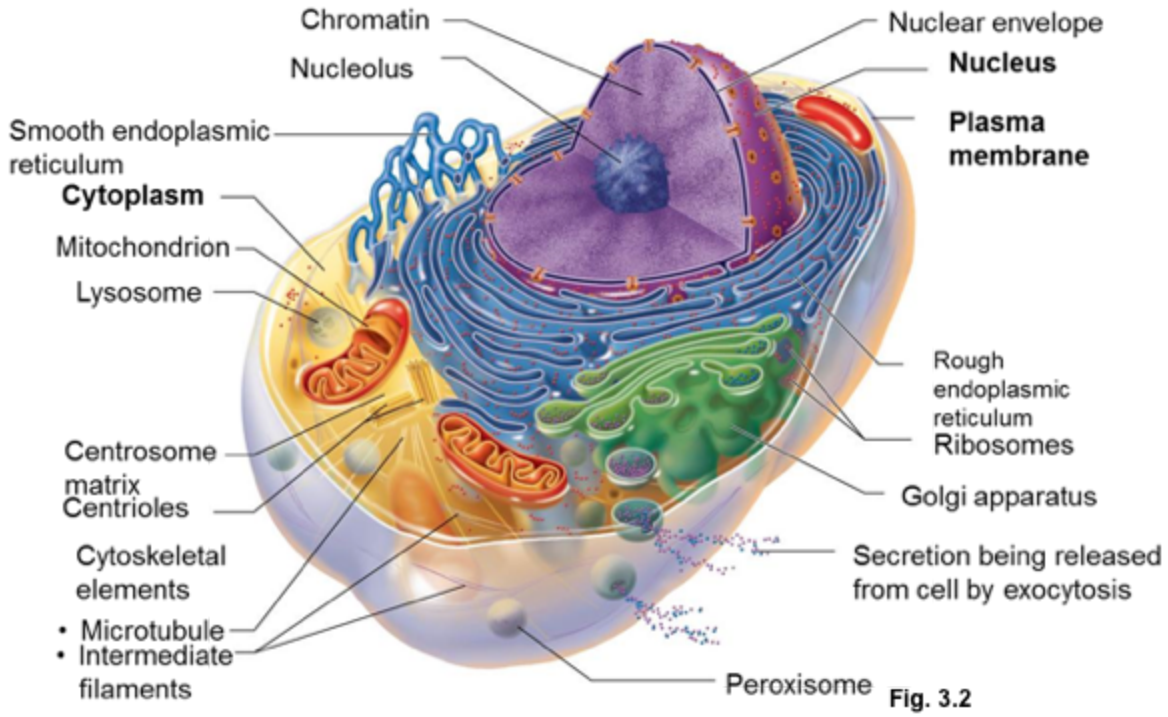


Fig. 3.2

Structure and functions of organelles

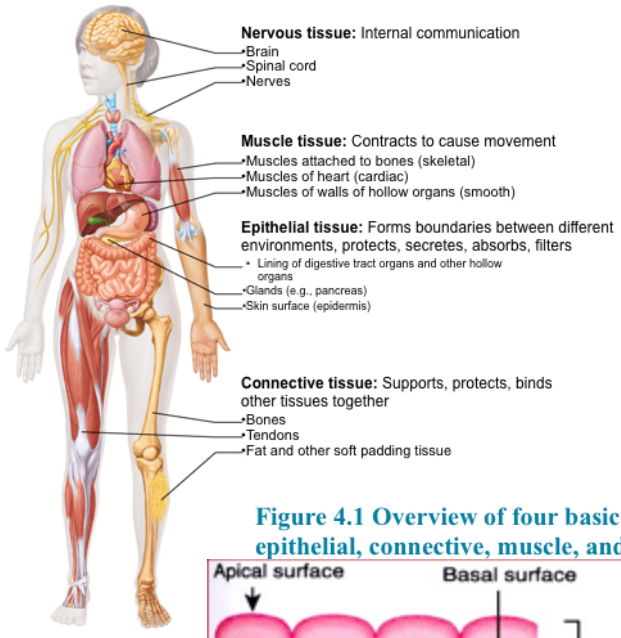
- Plasma membrane
    - Double phospholipid bilayer barrier embedded with proteins; provides boundary and shape
- Cytoplasm
    - Area outside the nucleus and inside the PM; includes the cytosol, dissolved solutes and organelles; site of most cellular activities
- Mitochondria
    - ‘Powerhouses” of the cell; Carry out reactions where O_2 is used to break down food to make ATP
- Ribosomes
    - Made of protein & RNA; site of protein synthesis
- **??????**
    - A network of interconnected tubes and parallel membranes that coils and twists throughout the cytoplasm. Continuous with the outer nuclear membrane. Functions like a little circulatory system within the cell for the transport of molecules.

- Rough ER
    - Membranous system enclosing a cavity
    - Studded with ribosomes; prepare protein for transport to Golgi apparatus
- Smooth ER
    - Membranous system of sacs and tubules; free of ribosomes
    - Site of lipid and steroid (cholesterol) synthesis, fat metabolism, and detoxification of drugs
- Golgi apparatus
    - A stack of flattened membranous sacs
    - Modifies and packages proteins for secretion
- Lysosome
    - Membranous sacs of acid hydrolases: enzymes that digest unusable materials within the cel (intracellular digestion)/ abundant in phagocytes
- Peroxisomes
    - Membranous sacs of catalase and oxidase enzymes detoxify harmful substance/ neutralize free radicals
- Cytoskeleton
    - Network of protein structures throughout the cytoplasm; provides internal framework of the cell. Made up of 3 types of protein
- Microfilaments
    - Fine filaments composed of actin; involved in muscle contraction
- Intermediate filaments
    - Protein (keratin) fibers of various compositions
- Microtubules
    - Cylindrical structures made of tubulin supports the cell and gives it shape
    - Anchored at one end near the nucleus called centrosome (cell centre)
- Centrosome
    - Microtubule organizing centre.
    - Contains paired cylindrical bodies called centrioles
- Cillia
    - numerous, fine, contains microtubules, hair like projections; coordinated movement creates current that propels substances across cell surface
- Flagella
    - Whip like tail; propels the cell
- Vicrovilla
    - Finger like extensions of the PM; bundle of actin filament; increases surface area for absorption
- Nucleus
    - Largest organelle; control center of the cell; contains the genetic information that provides instructions for protein synthesis
- Nuclear membrane
    - double phospholipid membrane barrier punctuated by pores that allow passage of substances to and from the nucleus; separates nucleoplasm and cytoplasm
- Nucleolus
    - Dense spherical bodies made of ribosomal RNA & proteins; site of ribosome synthesis
- Chromatin
    - Composed of DNA and histone protein/ encodes the genes

Lecture 2

Tissues the living fabric

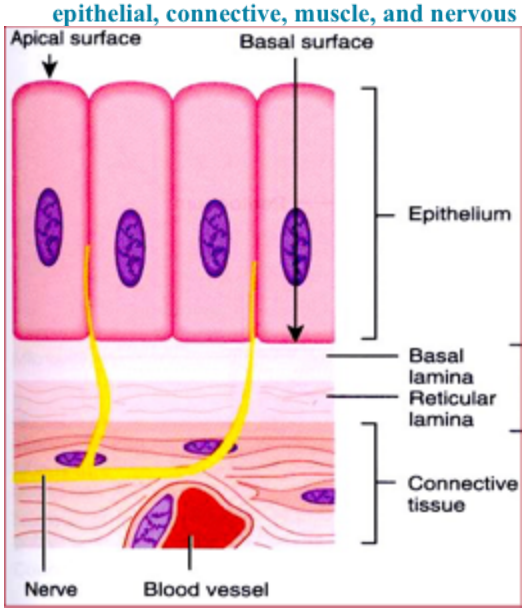
- Individual body cells are specialized
    - Each type performs specific functions that maintain homeostasis
- Tissues
    - Groups of cells similar in structure that perform a common or related function
- Histology
    - Study of tissues and their cellular organization
- Four basic tissue types: epithelial, connective, muscle, and nervous tissue



Epithelial TIssue

- Epithelial tissue (epithelium) is a sheet of cells that covers body surfaces or cavities
- Two main forms:
    - Covering and lining epithelia
        - On external and internal surfaces (example: skin)
    - Glandular epithelia
        - Secretory tissue in glands (example: salivary glands)
- Main functions of epithelial tissue: 1)protection, 2)absorption, 3)filtration, 4)excretion, 5)secretion, and 6)sensory reception
- Epithelial tissue has five distinguishing characteristics:
    - Polarity
        - apical and basal surfaces; apical surface often specialized including microvilli or cilia
    - Specialized contacts
        - Tight junctions and desmosomes
    - Supported by connective tissues
        - Supported by a basement membrane composed of a basal lamina and reticular lamina
    - Avascular, but innervated
        - where do nutrients come from?
    - Regeneration
        - has a high regenerative capacity

Figure 4.1 Overview of four basic tissue types: epithelial, connective, muscle, and nervous



Indicate the 2 criteria used to classify epithelial cells

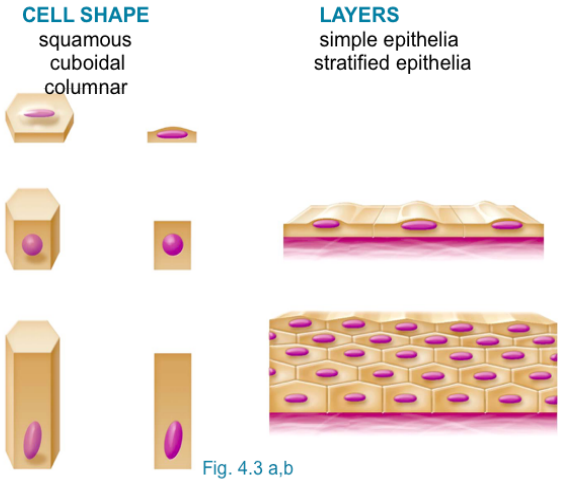


Fig. 4.3 a,b

Examples of Simple Epithelia: (function-absorption, secretion, filtration)

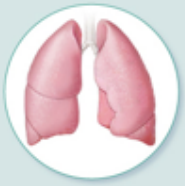
1. simple squamous epithelium: thin & permeable - filtration, diffusion - eg: endothelium & in kidney, lungs
2. simple cuboidal epithelium: secretion & absorption - eg: kidney tubules, small glands
3. simple columnar epithelium: also digestion & secretion – eg. digestive tract
4. pseudostratified columnar epithelium: a single layer - eg: respiratory tract where cilia and mucus secretion are local specializations

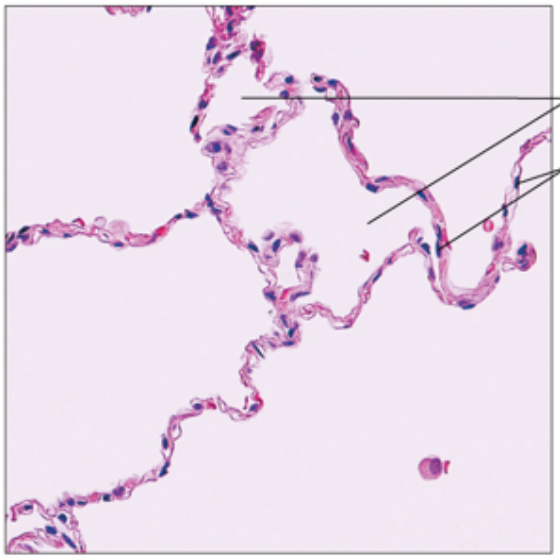
(a) Epithelium: simple squamous

Description: Single layer of flattened cells with disc-shaped central nuclei and sparse cytoplasm; the simplest of the epithelia.

Function: Allows materials to pass by diffusion and filtration in sites where protection is not important; secretes lubricating substances in serosae (linings of ventral body cavity).

Location: Kidney glomeruli; air sacs of lungs; lining of heart, blood vessels, and lymphatic vessels; serosae.

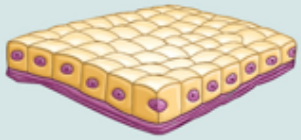




Photomicrograph: Simple squamous epithelium forming part of the alveolar (air sac) walls (140×).

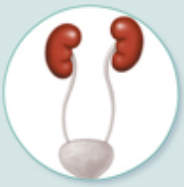
(b) Epithelium: simple cuboidal

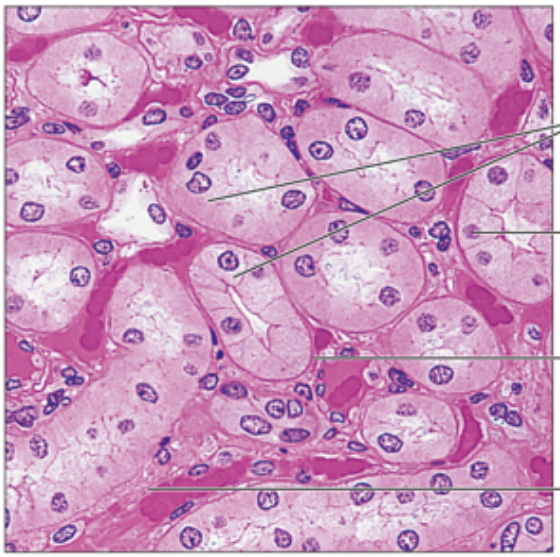
Description: Single layer of cubelike cells with large, spherical central nuclei.



Function: Secretion and absorption.

Location: Kidney tubules; ducts and secretory portions of small glands; ovary surface.

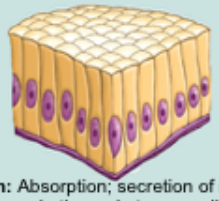




Photomicrograph: Simple cuboidal epithelium in kidney tubules (430×).

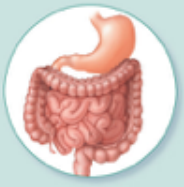
(c) Epithelium: simple columnar

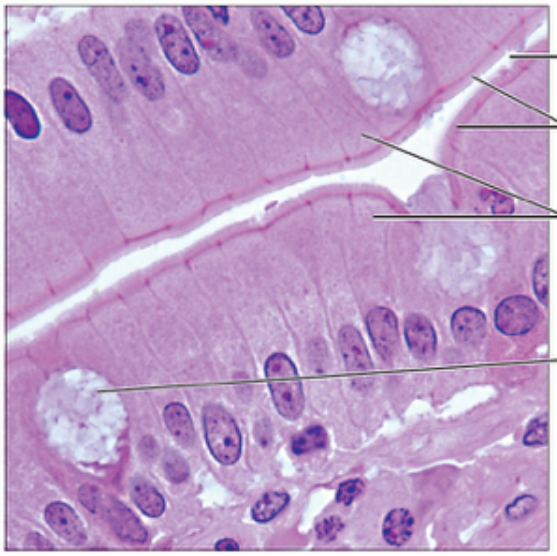
Description: Single layer of tall cells with *round* to *oval* nuclei; many cells bear microvilli, some bear cilia; layer may contain mucus-secreting unicellular glands (goblet cells).



Function: Absorption; secretion of mucus, enzymes, and other substances; ciliated type propels mucus (or reproductive cells) by ciliary action.

Location: Nonciliated type lines most of the digestive tract (stomach to rectum), gallbladder, and excretory ducts of some glands; ciliated variety lines small bronchi, uterine tubes, and some regions of the uterus.





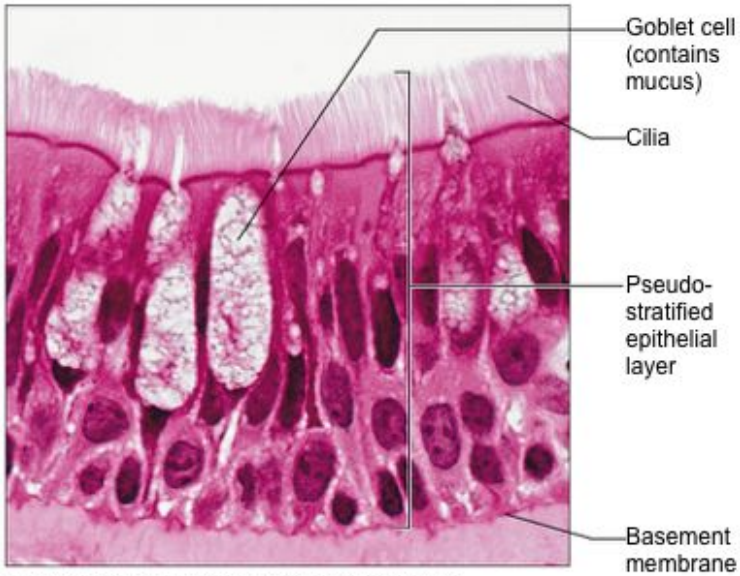
Photomicrograph: Simple columnar epithelium of the small intestine mucosa (640×).

(d) Epithelium: pseudostratified columnar

Description: Single layer of cells of differing heights, some not reaching the free surface; nuclei seen at different levels; may contain mucus-secreting cells and bear cilia.

Function: Secrete substances, particularly mucus; propulsion of mucus by ciliary action.

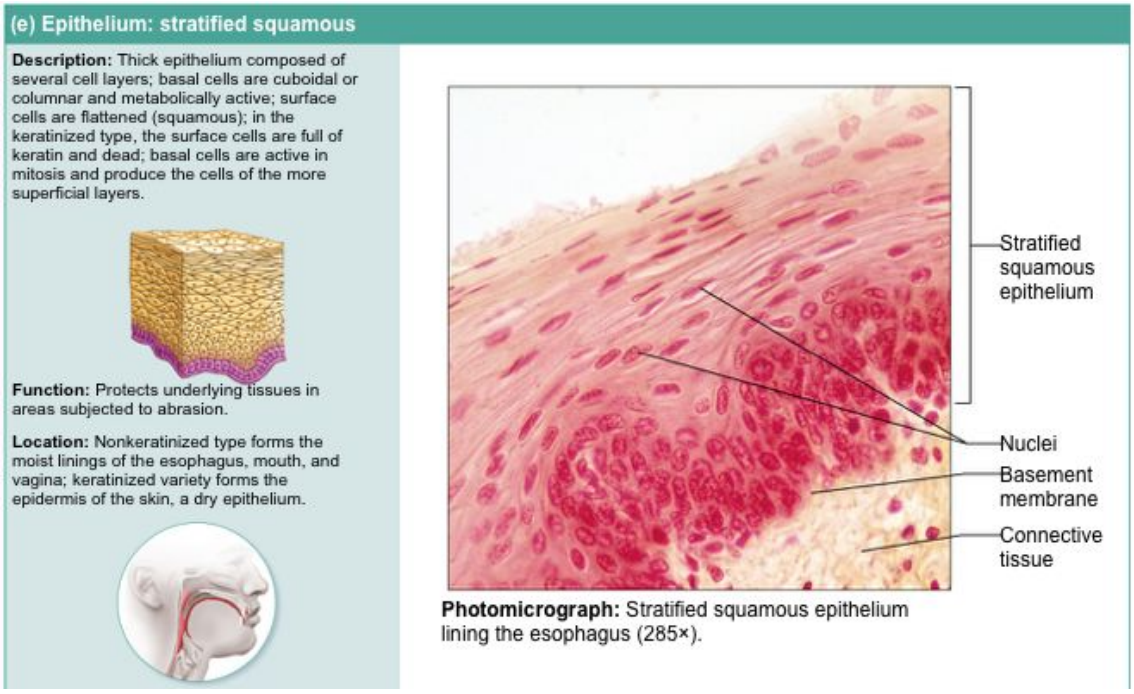
Location: Ciliated variety lines the trachea and most of the upper respiratory tract; nonciliated type in males' sperm-carrying ducts and ducts of large glands.



Photomicrograph: Pseudostratified ciliated columnar epithelium lining the human trachea (780×).

Stratified epithelial tissues

- Involve two or more layers of cells
- New cells regenerate from below
  - Basal cells divide and migrate toward surface
- More durable than simple epithelia because protection is the major role
- Stratified squamous epithelium
  - Most widespread of stratified epithelia
  - Free surface is squamous, with deeper cuboidal or columnar layers
  - Located in areas of high wear and tear (example: skin)
  - Keratinized cells found in skin; nonkeratinized cells are found in moist linings



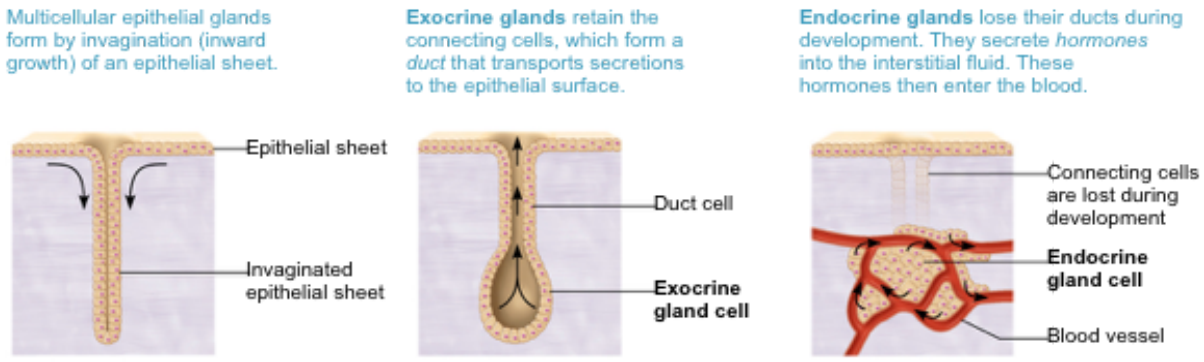
Classification of Epithelia

- Stratified epithelial tissues (cont.) Stratified cuboidal epithelium
  - Quite rare
  - Found in some sweat and mammary glands
  - Typically only two cell layers thick
- Stratified columnar epithelium
  - Also very limited distribution in body
  - Small amounts found in pharynx, in male urethra, and lining some glandular ducts
  - Usually occurs at transition areas between two other types of epithelia
  - Only apical layer is columnar
- See atlas for pictures of these two rare types
- Stratified epithelial tissues (cont.)
  - Transitional epithelium
    - Forms lining of hollow urinary organs
      - Found in bladder, ureters, and urethra
    - Basal layer cells are cuboidal or columnar
    - Ability of cells to change shape when stretched allows for increased flow of urine and, in the case of bladder, more storage space

Glandular Epithelia

- Gland
    - One or more cells that makes and secretes an aqueous fluid called a secretion
- Classified by:
    - Site of product release:
        - Endocrine: internally secreting (example: hormones)
        - Exocrine: externally secreting (example: sweat)
    - Relative number of cells forming the gland
    - Unicellular (example: goblet cells) or multicellular (example: salivary)

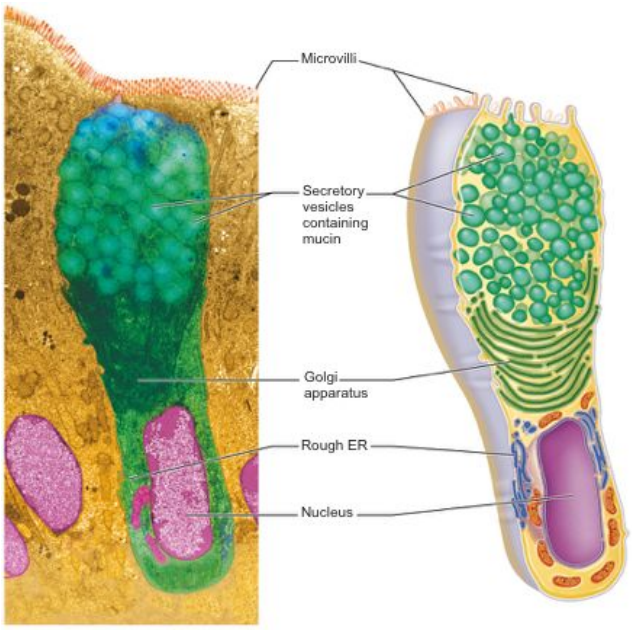
Figure 4.5 Formation of multicellular exocrine and endocrine glands.



Glandular Epithelia

- Endocrine glands
    - Ductless glands
        - Secretions are not released into a duct; are released into surrounding interstitial fluid, which is picked up by circulatory system
    - Secrete (by exocytosis) hormones, messenger chemicals that travel through lymph or blood to their specific target organs
    - Target organs respond in some characteristic way
- Exocrine glands
    - Secretions are released onto body surfaces, such as skin, or into body cavities
    - More numerous than endocrine glands
    - Secrete products into ducts
    - Examples include mucous, sweat, oil, and salivary glands
    - Can be: Unicellular or Multicellular
- Unicellular exocrine glands
    - The only important unicellular glands are mucous cells and goblet cells
    - Found in epithelial linings of intestinal and respiratory tracts
    - All produce mucin, a sugar-protein that can dissolve in water to form mucus, a slimy protective, lubricating coating

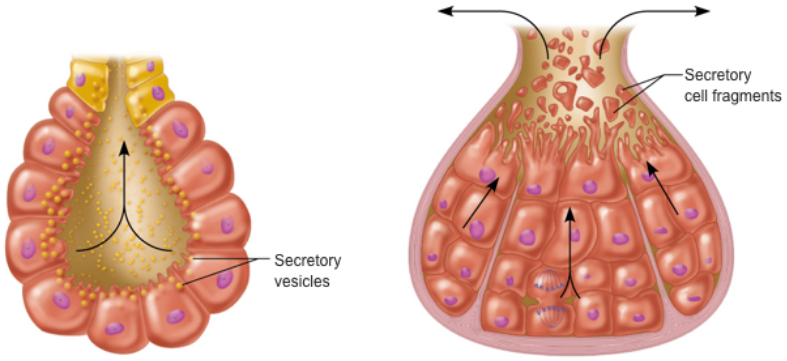
Figure 4.6 Goblet cell (unicellular exocrine gland).



Glandular Epithelia

- Multicellular exocrine glands
    - Multicellular exocrine glands are composed of a duct and a secretory unit
    - Usually surrounded by supportive connective tissue that supplies blood and nerve fibers to gland
        - Connective tissue can form capsule around gland, and also extend into gland, dividing it into lobes
    - Classified by:
        - Structure
        - Mode of secretion
    - Mode of secretion
        - Merocrine: most secrete products by exocytosis as secretions are produced (sweat, pancreas)
        - Holocrine: accumulate products within, then rupture (sebaceous oil glands)
        - Apocrine: accumulate products within, but only apex ruptures; whether this type exists in humans is controversial (maybe mammary cells?)

Figure 4.8 Chief modes of secretion in human exocrine glands.



(a) Merocrine glands secrete their products by exocytosis.

(b) In holocrine glands, the entire secretory cell ruptures, releasing secretions and dead cell fragments.

4.3 Connective Tissue

- Connective tissue is the most abundant and widely distributed of primary tissues
- Major functions: binding and support, protecting, insulating, storing reserve fuel, and transporting substances (blood)
- Four main classes: Connective tissue proper, Cartilage, Bone, Blood

Overview of types of connective tissue.

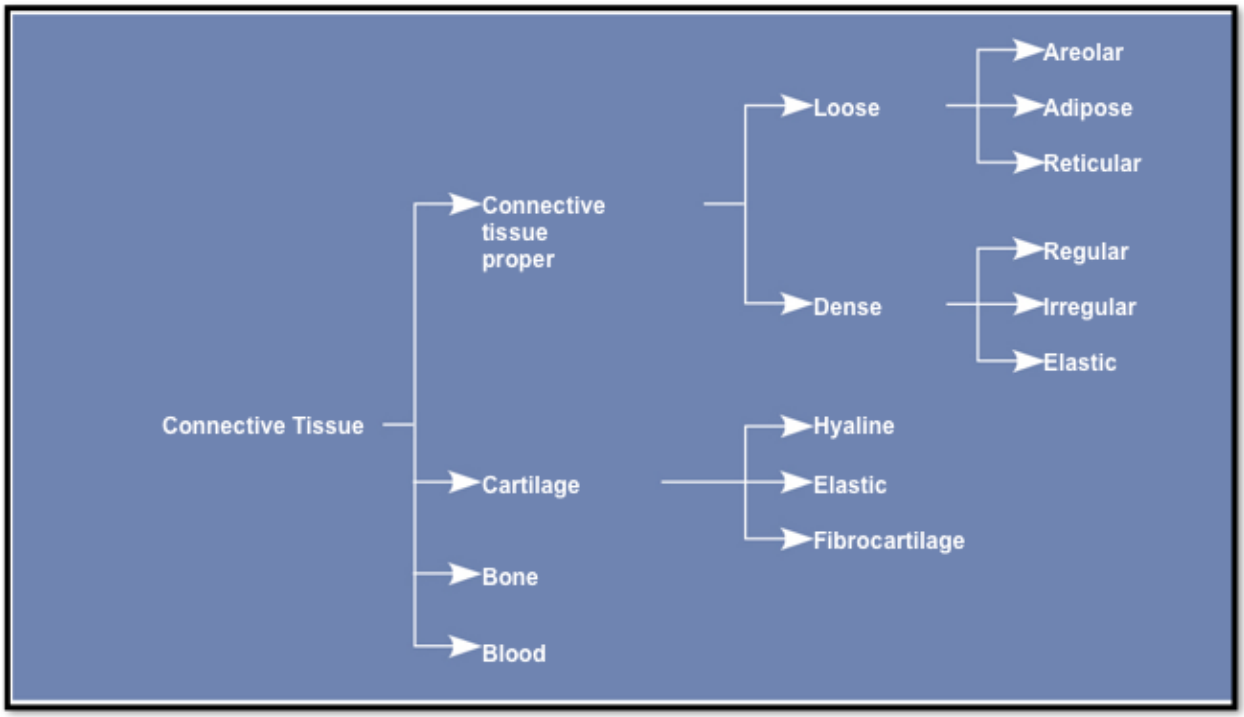


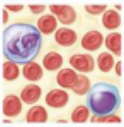
Table 4.1-1 Comparison of Classes of Connective Tissues

Table 4.1 Comparison of Classes of Connective Tissues

TISSUE CLASS AND EXAMPLE	SUBCLASSES	COMPONENTS: CELLS	COMPONENTS: MATRIX	GENERAL FEATURES
Connective Tissue Proper  *Dense regular connective tissue*	1. Loose connective tissue • Areolar • Adipose • Reticular 2. Dense connective tissue • Regular • Irregular • Elastic	Fibroblasts Fibrocytes Defense cells Adipocytes	Gel-like ground substance All three fiber types: collagen, reticular, elastic	Six different types; vary in density and types of fibers Functions as a binding tissue Resists mechanical stress, particularly tension Provides reservoir for water and salts Energy (fat) storage
Cartilage  *Hyaline cartilage*	1. Hyaline cartilage 2. Elastic cartilage 3. Fibrocartilage	Chondroblasts (found in growing cartilage) Chondrocytes	Gel-like ground substance Fibers: collagen, elastic fibers in some	Resists compression because of the large amounts of water held in the matrix Functions to cushion and support body structures

Table 4.1-2 Comparison of Classes of Connective Tissues

Table 4.1 Comparison of Classes of Connective Tissues

TISSUE CLASS AND EXAMPLE	SUBCLASSES	COMPONENTS: CELLS	COMPONENTS: MATRIX	GENERAL FEATURES
Bone Tissue  *Compact bone*	1. Compact bone 2. Spongy bone (See Chapter 6 for details)	Osteoblasts Osteocytes	Gel-like ground substance calcified with inorganic salts Fibers: collagen	Hard tissue that resists both compression and tension Functions in support
Blood 	(See Chapter 17 for details)	Red blood cells (RBCs) or erythrocytes White blood cells (WBCs) or leukocytes Platelets	Plasma No fibers	A fluid tissue Functions to carry O_2, CO_2, nutrients, wastes, and other substances (such as hormones)

Types of CT:

1) **Mesenchyme:** first tissue formed from mesoderm germ layer - mesenchymal cells + fluid ground substance & fine fibrils ➢ source of all other CTs
2) **CT Proper:** 2 subclasses ➢➢
   A. **Loose CT** (areolar, adipose, reticular)
   B. **Dense CT** (dense regular, dense irregular, elastic)

Common Characteristics of Connective Tissue

- Three characteristics make connective tissues different from other primary tissues:
- All have common embryonic origin: all arise from mesenchyme tissue as their tissue of origin
- Have highly variable degrees of vascularization (cartilage is avascular, bone is highly vascularized)
- Cells are suspended/embedded in **extracellular matrix (ECM)**
- ECM supports cells so they can bear weight, withstand tension, endure abuse

1.3.10 describe the structural organization of CT in general; distinguish between collagen, elastic & reticular fibers; distinguish between “blast” and “cyte” types of CT cells

Structural Elements of CT:

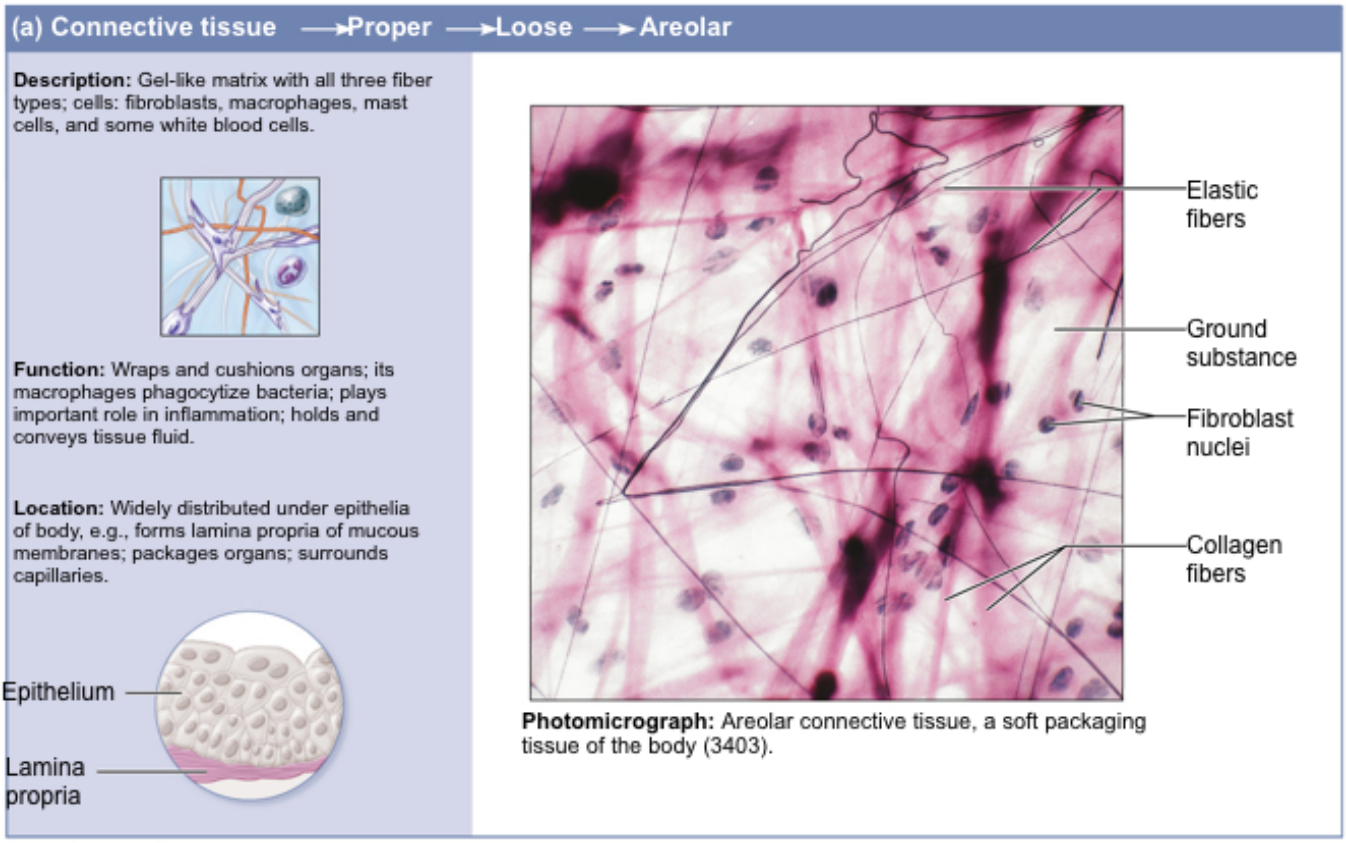
- ground substance: interstitial fluid + cell adhesion proteins & proteoglycans: molecular sieve
  - fibronectin, laminin - help cells attach to CT elements
  - proteoglycans - What are these? What do they do?
- Fibers:
  - collagen fibers: high tensile strength
  - elastic fibers: elastin has coiled structure to allow stretch + recoil
  - reticular fibers: thin collagen protein; fine network to support blood vessels, soft tissues
  - Cells:

Structural Elements of Connective Tissue

- Ground substance
  - Unstructured gel-like material that fills space between cells
    - Medium through which solutes diffuse between blood capillaries and cells
  - Components
    - Interstitial fluid
    - Cell adhesion proteins (“glue” for attachment)
    - Proteoglycans (sugar proteins), made up of protein core + large polysaccharides
    - Water also is trapped in varying amounts, affecting viscosity of ground substance

- Connective tissue fibers
- Three types of fibers provide support
- Collagen
  - Strongest and most abundant type
  - Tough; provides high tensile strength
- Elastic fibers
  - Networks of long, thin, elastin fibers that allow for stretch and recoil
- Reticular
  - Short, fine, highly branched collagenous fibers (different chemistry and form from collagen fibers)
  - Branching forms networks that offer more “give”
- Cells
  - “Blast” cells
  - Immature form of cell that actively secretes ground substance and ECM fibers
  - Fibroblasts found in connective tissue proper
  - Chondroblasts found in cartilage
  - Osteoblasts found in bone
  - Hematopoietic stem cells in bone marrow
- “Cyte” cells
  - Mature, less active form of “blast” cell that now becomes part of and helps maintain health of matrix

Connective tissues proper: i) loose-areolar.



ADIPOSE TISSUE: areolar CT modified to store nutrients; adipocytes

- Description: fat-filled adipocytes with displaced nuclei; do not reproduce; scanty matrix
- Location: under the skin, around kidneys & eyeballs, in bones & within abdomen, in breasts; 18% of average wt (15% ♂ & 22% ♀)
- Function: fuel reservoir, insulation, supports & protects organs

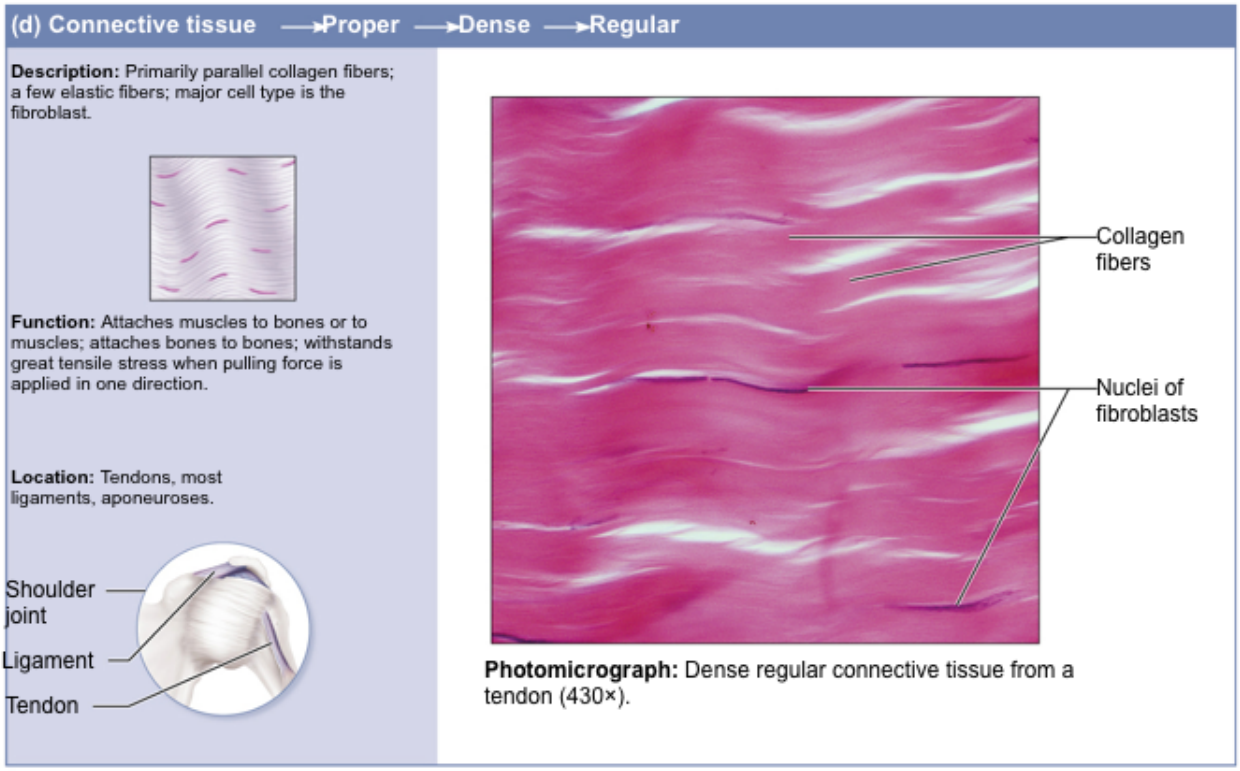
RETICULAR CT: like areolar CT, but only reticular fibers

- Loc: lymphoid organs (lymph nodes, bone marrow, spleen)
- Fcn: fibers form soft internal skeleton that supports free blood cells

Types of Connective Tissues (6 of 13)

- CT proper: dense connective tissues
    - Three varieties of dense connective tissue
        - Dense regular
        - Dense irregular
- Dense regular connective tissue
    - Very high tensile strength; can withstand high tension and stretching
    - Closely packed bundles of thick collagen fibers run parallel to direction of pull
        - Fibers appear as white structures
            - Great resistance to pulling
        - Fibers slightly wavy, so stretch a little
    - Fibroblasts manufacture collagen fibers and ground substance
    - Very few cells and ground substance, mostly fibers
    - Poorly vascularized
    - Example: tendons and ligaments

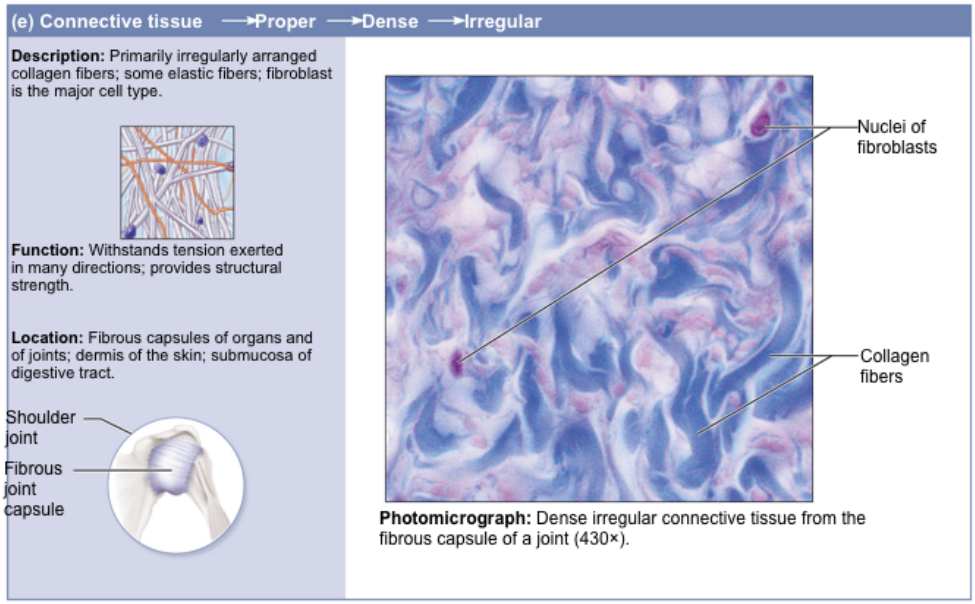
Connective tissues proper: Dense-regular



Types of Connective Tissues

- Dense irregular connective tissue
    - Same elements as dense regular, but bundles of collagen are thicker and irregularly arranged
    - Forms sheets rather than bundles
    - Resists tension from many directions
    - Found in:
        - Dermis
        - Fibrous joint capsules
        - Fibrous coverings of some organs

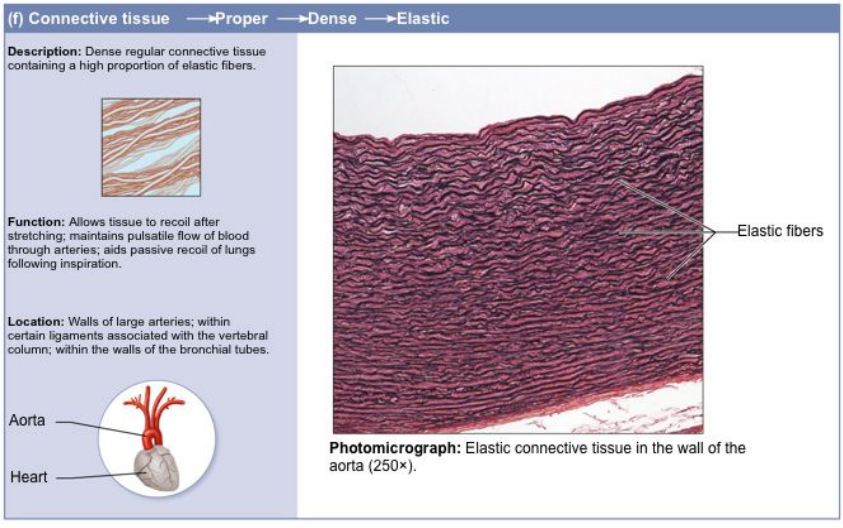
Connective tissues proper: Dense-irregular.



Types of Connective Tissues

- Elastic connective tissue
    - Some ligaments are very elastic
        - Example: ligaments connecting adjacent vertebrae must be very elastic
    - Also found in walls of many large arteries
        - Arteries need to stretch when blood enters and recoil to push blood out

Connective tissues proper: Dense Elastic.



Types of Connective Tissues: Cartilage

- Cartilage
    - Matrix secreted from chondroblasts (during growth) and chondrocytes (adults)
        - Chondrocytes found in cavities called lacunae
        - 80% water, with packed collagen fibers and sugar proteins (chondroitin and hyaluronic acid)
    - Tough yet flexible material that lacks nerve fibers
    - Avascular: receives nutrients from membrane surrounding it (perichondrium)
        - Periochondrium gives rise to chondroblasts and chondrocytes

Types of Connective Tissues: Cartilage

- Three types of cartilage:
    - Hyaline cartilage
        - Most abundant; Appears as shiny bluish glass
        - Found at tips of long bones, nose, trachea, larynx, and cartilage of the ribs
    - Elastic cartilage
        - Similar to hyaline but with more elastic fibers
        - Found in ears and epiglottis
    - Fibrocartilage
        - Properties between hyaline and dense regular tissue
        - Strong, so found in areas such as intervertebral discs and knee

NOTES

- Histology - study of tissue (dies can be used to show tissues)
- Epithelial tissue is useful for separation of instance in our guts
- Apical -apex and basal (think base)
    - Imagine a mountain you have a top and a bottom
- Most cancers originate from epithelial because of its regenerative capacity.
- Polarity of the tissue always tiesto its function
    - Ex. the way it allows things to transport
- Avascular - low blood level
- When naming start at the top layer (refer to textbook for more info)
    - Naming based on shape and number of layers.
- All cells touch the apex 9there may be a thin line for the ones at the bottom
- Nutrients diffuse from extracellular fluid to the epithelial cell
- Keratinized cells are generally dry.
- Non keratinized cell example: inside of your cheek (if you touch its wet)
- Anything that is secreted into the digestive tract is exocrine because its like releasing outside the body

Answers

1. D
2. B
3. C
4. C

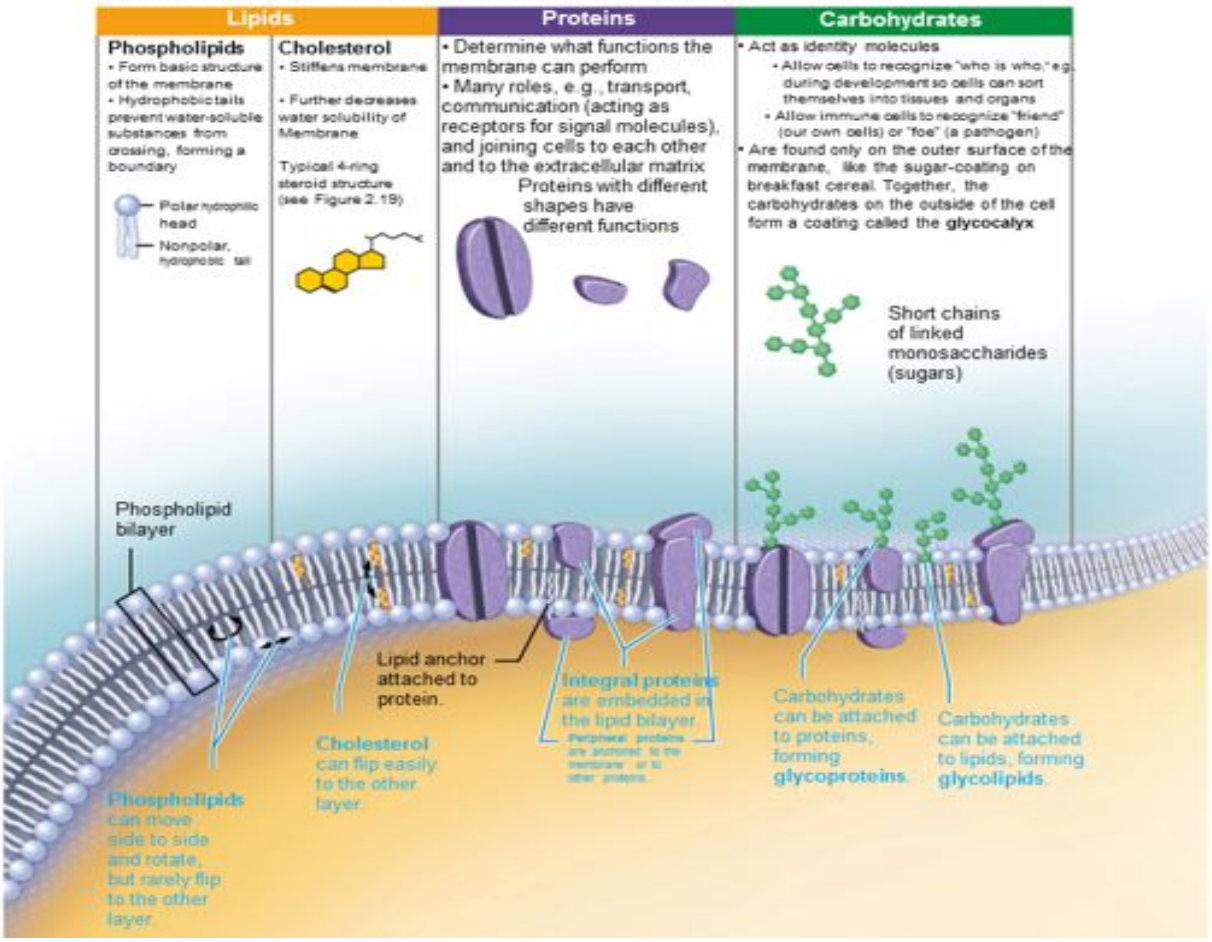
FOR EXAM:

- know the different types of epithelial tissue and know how to label them. In class diagram had four.
- KNOW THE DIFFERENT GLANDS and give examples of exocrine and endocrine (very important)
- Define endocrine and exocrine
- everything on the exam is gonna be in the slides (couple comprehension)
- On mastering AP there is a quiz on every chapter

Lecture 3

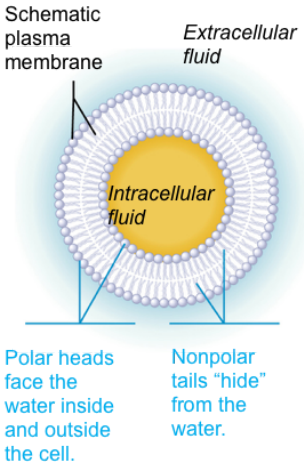
Plasma membrane (aka cell membrane)

- Acts as an active barrier separating intracellular fluid (ICF) also known as cytoplasm from extracellular fluid (ECF) in other words outside separate from outside
- The plasma membrane is selectively permeable (determine what comes in/out)
- Plays a dynamic role in cellular activity by controlling what enters and leaves the cell
- ECF determines what enters and leaves, brings oxygen and glucose and releases waste, creates semipermeable membrane
- Consists of membrane lipids that form a flexible lipid bilayer
- Specialized membrane proteins float through this fluid membrane, resulting in constantly changing patterns
    - Referred to as **fluid mosaic** (made up of many pieces) pattern
- Surface sugars form glycocalyx (the carbohydrate on the membrane)
    - Glycocalyx tells other cells what the cell is (it's technically is an antigen)
- Membrane structures help to hold cells together through cell junctions
- **Lipid rafts** are subdomains of the plasma membrane that contain high concentrations of cholesterol (makes it rigid) and glycosphingolipids
- Communication : Plasma membrane proteins interact with specific chemical messengers and relay messages to the cell interior



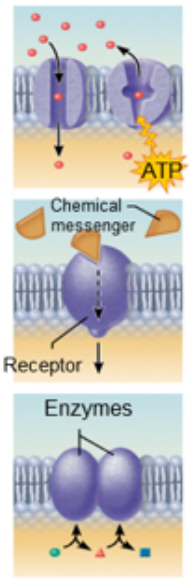
Phospholipids

- Polar hydrophilic head (includes the phosphate group)
- Non polar hydrophobic tail (fatty acids) which is why hydrophobic (fat soluble) molecules can enter
- PM lipid bilayer is made of: 75% phospholipids, 5% glycolipids, and 20% cholesterol
- Orient themselves to prevent water from interacting with non polar tails



Membrane proteins (2 types)

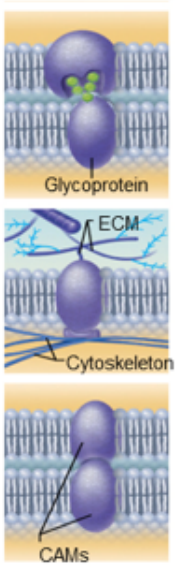
- Allow cell communication with environment
- Make up about half the mass of plasma membrane
- Most have specialized membrane functions
- Some float freely, and some are tethered to intracellular structures
- How is this info helpful in medicine? Drugs are not hydrophobic, if you want to target a cancer cell tries to target integral proteins so it can target a specific cell.
- **Integral proteins**
  - Firmly inserted into membrane
  - Most are transmembrane proteins (span membrane - go out and come in multiple times)
  - Have both hydrophobic and hydrophilic regions
    - Hydrophobic areas interact with lipid tails
    - Hydrophilic areas interact with water
  - Function as transport proteins (channels and carriers), enzymes, or receptors
- **Peripheral proteins**
  - Loosely attached to integral proteins
  - Include filaments on intracellular surface used for plasma membrane support
  - Function as: Enzymes, motor proteins for shape change during cell division and muscle contraction, Cell-to-cell connections



(a) **Transport**
- A protein (left) that spans the membrane may provide a hydrophilic channel across the membrane that is selective for a particular solute.
- Some transport proteins (right) hydrolyze ATP as an energy source to actively pump substances across the membrane.

(b) **Receptors for signal transduction**
- A membrane protein exposed to the outside of the cell may have a binding site that fits the shape of a specific chemical messenger, such as a hormone.
- When bound, the chemical messenger may cause a change in shape in the protein that initiates a chain of chemical reactions in the cell.

(c) **Enzymatic activity**
- A membrane protein may be an enzyme with its active site exposed to substances in the adjacent solution.
- A team of several enzymes in a membrane may catalyze sequential steps of a metabolic pathway as indicated (left to right) here.



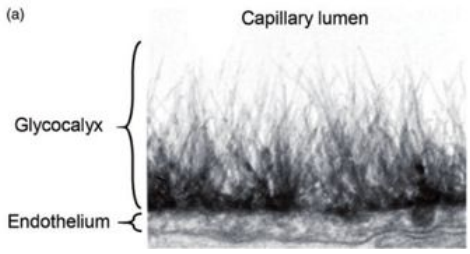
(d) **Cell-cell recognition**
- Some glycoproteins (proteins bonded to short chains of sugars which help to make up the glycocalyx) serve as identification tags that are specifically recognized by other cells.

(e) **Attachment to the cytoskeleton and extracellular matrix (ECM)**
- Elements of the cytoskeleton (cell's internal framework) and the extracellular matrix (fibers and other substances outside the cell) may anchor to membrane proteins.
- Helps maintain cell shape, fixes the location of certain membrane proteins, and plays a role in cell movement.

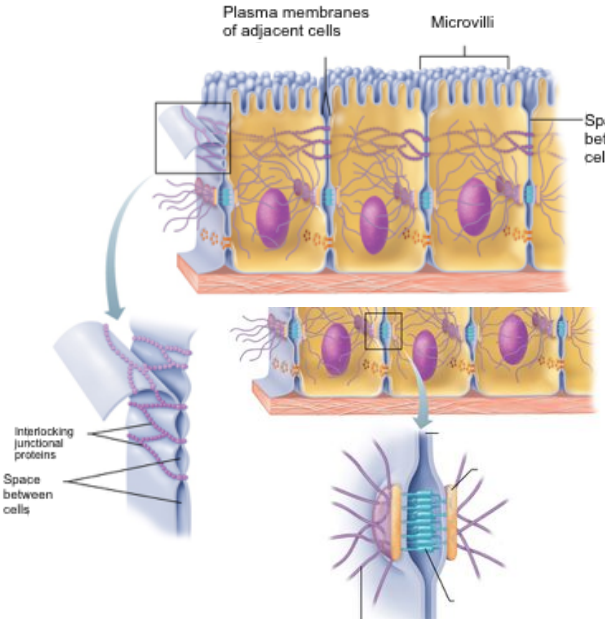
(f) **Cell-to-cell joining**
- Membrane proteins of adjacent cells may be hooked together in various kinds of intercellular junctions.
- Some membrane proteins (cell adhesion molecules or CAMs) of this group provide temporary binding sites that guide cell migration and other cell-to-cell interactions.

Glycocalyx

- Consists of sugars (carbohydrates) sticking out of cell surface
  - Some sugars are attached to lipids (glycolipids) and some to proteins (glycoproteins)
- Every cell type has different patterns of this "sugar coating"

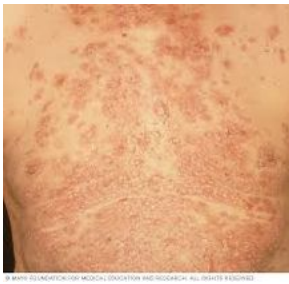


- Functions as specific biological markers for cell- to-cell recognition
- Allows immune system to recognize “self” vs. “nonself”

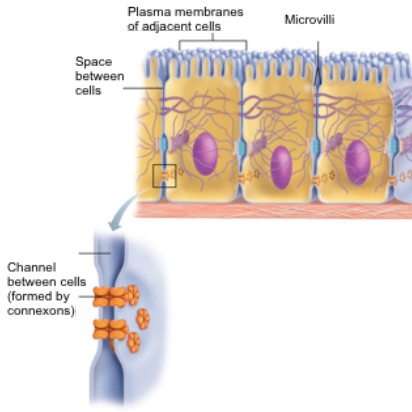


Cell junctions

- Tight junctions
  - Impermeable junctions
  - Form continuous seals around the cell kind of like a ziploc. It’s a continuous set of proteins that bond two cells together, does not allow anything through
  - Prevent molecules from passing between cells
  - Epithelial must form a watertight surface
- Desmosomes
  - Rivet-like cell junction formed when linker proteins (cadherins) of neighboring cells interlock like the teeth of a zipper
  - Desmosomes allow “give” between cells, reducing the possibility of tearing under tension.
  - Gets strength by being anchored to cadherins
  - What would happen if we didn’t have enough desmosomes?
    - Ex. In pemphigus foliaceus, the immune system damages skin cells called keratinocytes causing rashes.



- Gap junctions
  - Transmembrane proteins (**connexons**) form tunnels that allow small molecules to pass from cell to cell
  - Used to spread ions, simple sugars, or other small molecules between cells
  - Allows electrical signals to be passed quickly from one cell to the next cell
  - Used in cardiac and smooth muscle cells



Summary: The 4 functions of plasma membranes

- effective barrier between the intracellular & extracellular fluids
- selectively permeable (some things get through)
- allows the cell to respond to changes in the extracellular fluid
- site of cell-to-cell interaction and recognition

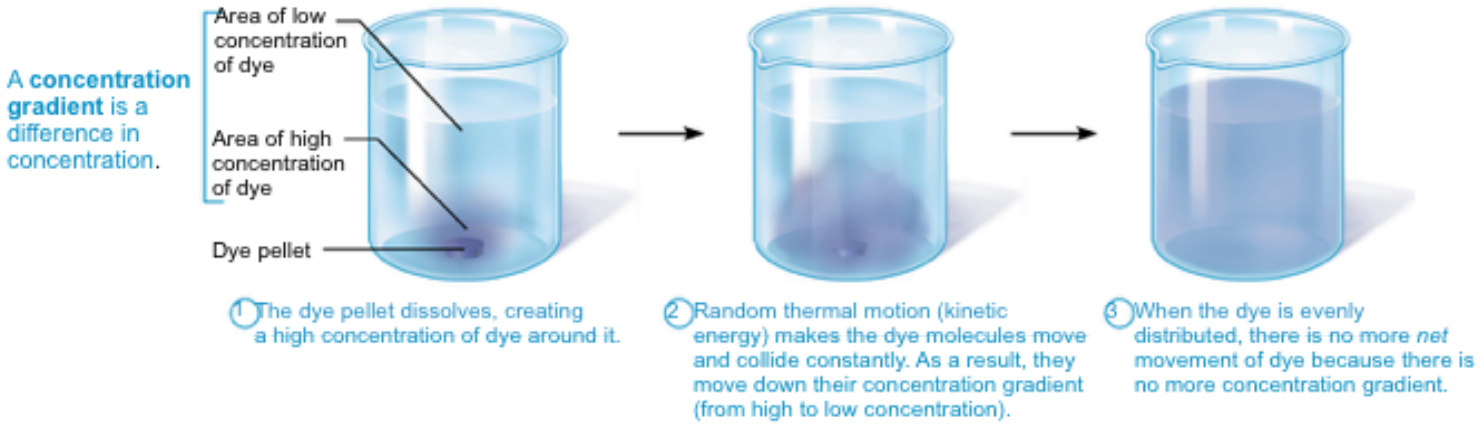
Cell Junctions Maintain Selective Permeability of PM

- Many substances must constantly move across the plasma membrane
  - Some molecules pass through easily; some do not
- The plasma membrane is selectively permeable allowing only certain molecules to cross
- Two essential ways substances cross plasma membrane:
  - Passive transport: no energy is required
  - Active transport: energy (ATP) is required

Passive Membrane Transport

- Passive transport requires no energy input (gets energy from concentration gradient)
- Three types of passive transport: Simple Diffusion, Facilitated diffusion, Osmosis
- All types involve diffusion – natural movement of molecules from areas of high concentration to areas of low concentration
  - Also referred to as moving down a concentration gradient

- All molecules have random, high-speed movement due to their intrinsic kinetic energy
- Movement results in collisions between molecules
- Molecules in higher concentration areas collide more resulting in molecules being scattered to lower concentration areas
- Brownian motion - random collision - solute has many collisions at high concentration and reduces the amount of collision in low concentration area

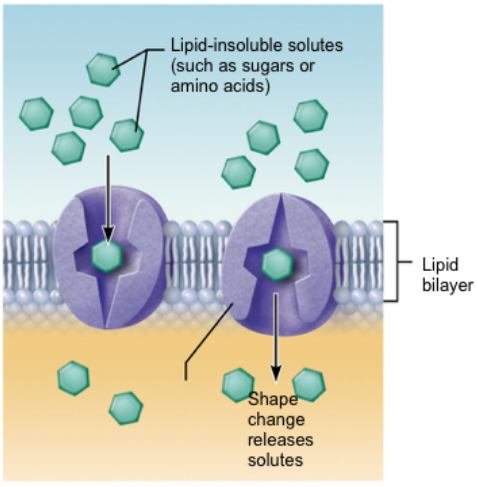


Diffusion

- Speed of diffusion influenced by 3 factors:
  - Concentration
    - The greater the difference in concentration between two areas, the faster diffusion occurs
  - Molecular Size
    - Smaller molecules diffuse faster
  - Temperature
    - Higher temps increase kinetic energy which results in faster diffusion
- **Equilibrium** is reached when there is no net movement of molecules in one direction only
- Molecules have a natural drive to diffuse down concentration gradients that exist between extracellular and intracellular areas
  - Move down their concentration gradient means high to low
- Nonpolar, hydrophobic lipid core of plasma membranes stop diffusion and create concentration gradients by acting as selectively permeable barriers
  - Also called “differentially permeable” barrier
- Membrane limits diffusion, you can get work out of a concentration gradient which is what makes it important.
- Molecules that are able to passively diffuse through membrane include:
  - Lipid-soluble and nonpolar substances
  - Very small molecules that can pass through membrane or membrane channels
  - Referred to as **simple diffusion** (goes through plasma membrane)
- Simple diffusion
  - nonpolar, lipid-soluble: O_2, CO_2, fats, urea, alcohol
  - O_2 & CO_2 follow gradients into and out of cells, respectively
  - molecule is moving down its concentration gradient!!
- Larger or non-lipid soluble or polar molecules can cross membrane but only with the assistance of carrier molecules
  - Referred to as facilitated diffusion
- Osmosis is a special name for movement of solvent (usually water), not molecules

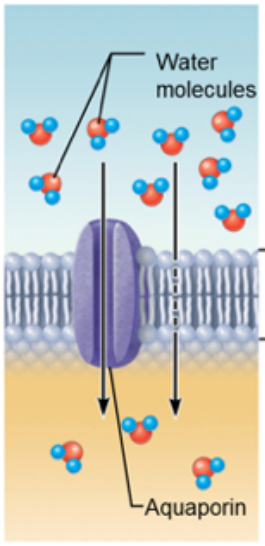
Facilitated diffusion

- Certain hydrophobic molecules (e.g., glucose, amino acids, and ions) are transported passively down their concentration gradient by:
    - Carrier-mediated facilitated diffusion
        - Substances bind to protein carriers
    - Channel-mediated facilitated diffusion
        - Substances move through water-filled channels



(b) Carrier-mediated facilitated diffusion via protein carrier specific for one chemical; binding of solute causes transport protein to change shape

- Carrier-mediated facilitated diffusion
    - Carriers are transmembrane integral proteins
    - Each carrier transports specific polar molecules, such as sugars and amino acids, that are too large for membrane channels
    - Binding of molecule causes carrier to envelope it and change shape that results in molecule being moved across membrane in process
    - Binding is limited by number of carriers present
        - Carriers are saturated when all are bound to molecules and are busy transporting
- Glucose is higher on the outside so required facilitated diffusion to enter the cell
- Channel-mediated facilitated diffusion
    - Channels with aqueous-filled cores are formed by transmembrane proteins
    - Amount of carriers determines rate of diffusion
    - Channels transport molecules such as ions or water (osmosis) down their concentration gradient
        - Specificity based on pore size and/or charge
        - Water channels are called aquaporins
    - Two types:
        - Leakage channels: Always open
        - Gated channels: Controlled by chemical or electrical signals

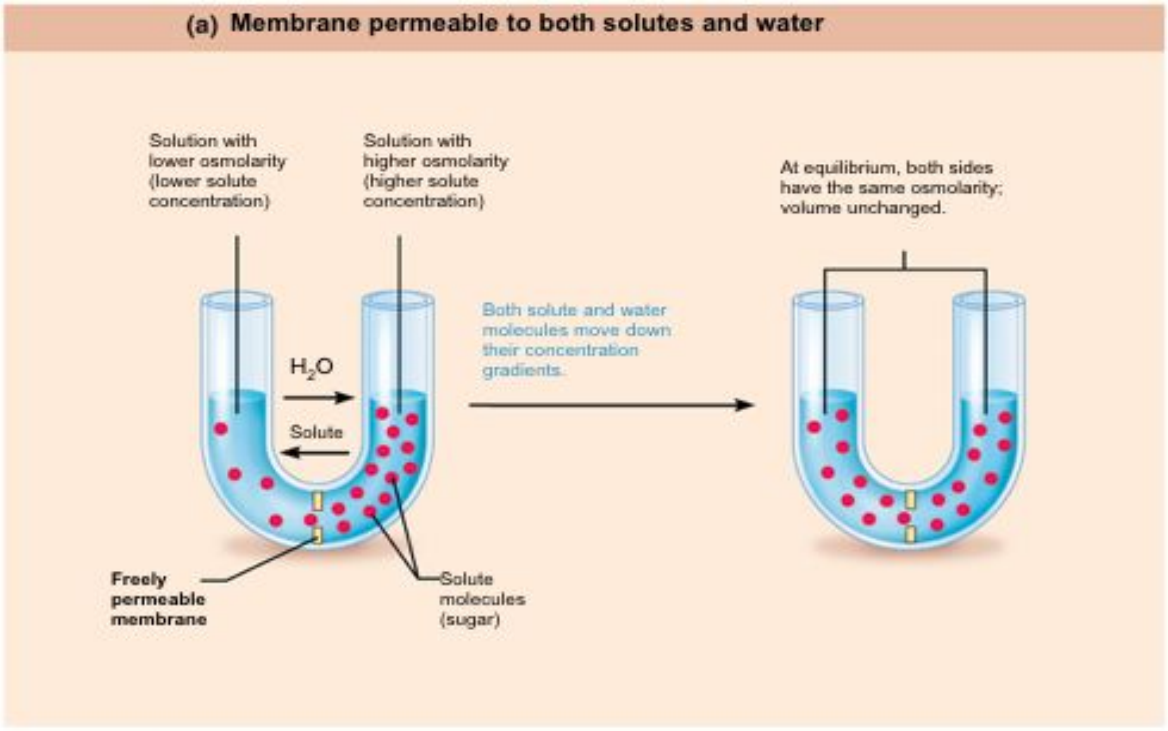


(d)

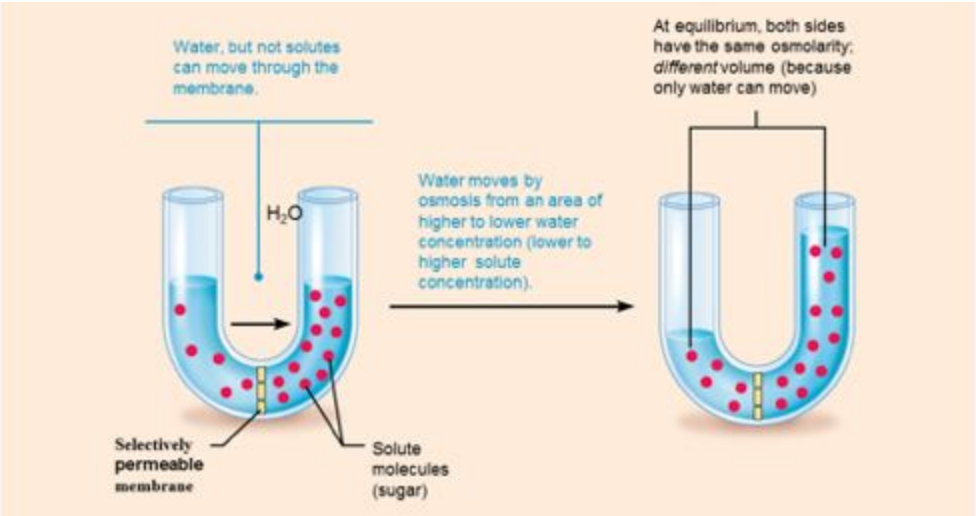
Osmosis

- Movement of solvent (not molecules), such as water, across a selectively permeable membrane
- Water diffuses across plasma membranes
    - through lipid bilayer (even though water is polar, it is so small that some molecules can sneak past nonpolar phospholipid tails)
    - through specific water channels called aquaporins (AQPs)
- Flow occurs when water (or other solvent) concentration is different on the two sides of a membrane
- Osmolarity: measure the concentration of the total number of solute particles in solvent (water goes to an area of high osmolarity.)
- Water concentration varies with number of solute particles because solute particles displace water molecules
    - When solute concentration goes up, water concentration goes down, and vice versa
- Water moves by osmosis from areas of low solute (high water) concentration to high areas of solute (low water) concentration
- When solutions of different osmolarities are separated by a membrane permeable to all molecules, diffusion of solutes and osmosis of water occur cross membrane until equilibrium of solutes and water is reached
    - Equilibrium: Same concentration of solutes and water molecules on both sides, with equal volume on both sides

- Influence of membrane permeability



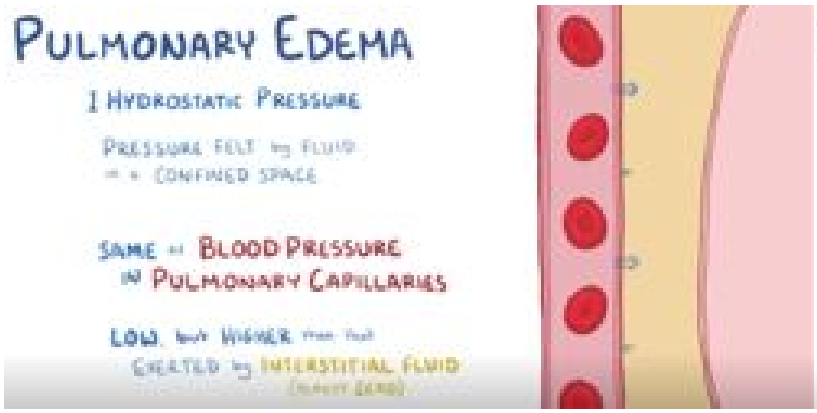
- When solutions of different osmolarities are separated by a membrane that is permeable only to water, only osmosis will occur until equilibrium is reached
    - Water will have net movement across membrane until osmolarity is the same on both sides
    - Results in volume changes on both sides
        - Low solute side volume decreases
        - High solute side volume increases

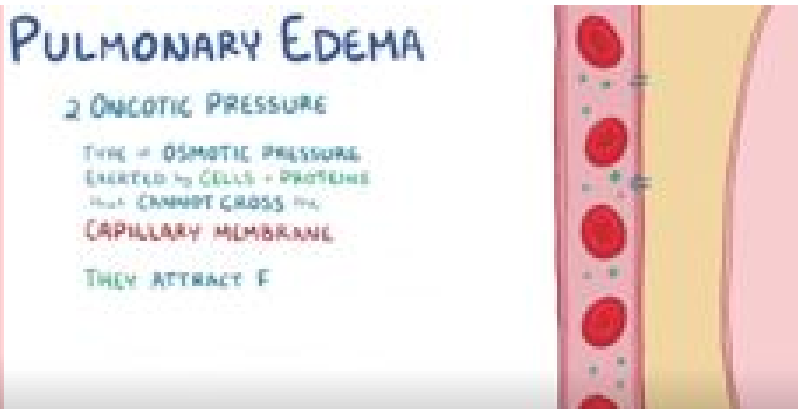


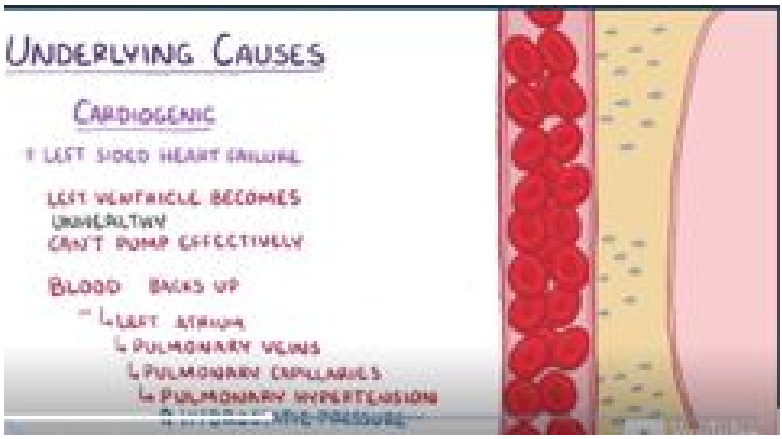
Membrane permeable to water.

- Movement of water involves pressures:
    - Hydrostatic pressure: outward pressure exerted on cell side of membrane caused by increases in volume of cell due to osmosis
        - Also referred to as “back pressure”
    - Osmotic pressure: inward pressure due to tendency of water to be “pulled” into a cell with higher osmolarities
        - The more solutes inside a cell the bigger the pull on water to enter, resulting in higher osmotic pressures inside the cell
- When hydrostatic pressure equals osmotic pressure, no further net movement of water occurs
    - Water trying to get out equals water trying to get in
- Plant cells are surrounded by strong cell walls that act to limit hydrostatic pressure levels which in turn limit osmotic pressure
    - Plant cell will fill with only so much water then stop
- Animal cells do not have cells walls, therefore they cannot limit hydrostatic and osmotic pressures
    - Animal cells will burst if too much water is taken in
- Water can also leave a cell, causing it to shrink
- Changes in cell volume can disrupt cell function
- Animal cells don't have a wall so we can add water till it ruptures where as plant cells only fill a certain amount because of its cell wall

Health relevance







- When you're healthy you have a somewhat leaky capillary, hydrostatic pressure is slightly healthy. nothing expands b/c there is a good balance

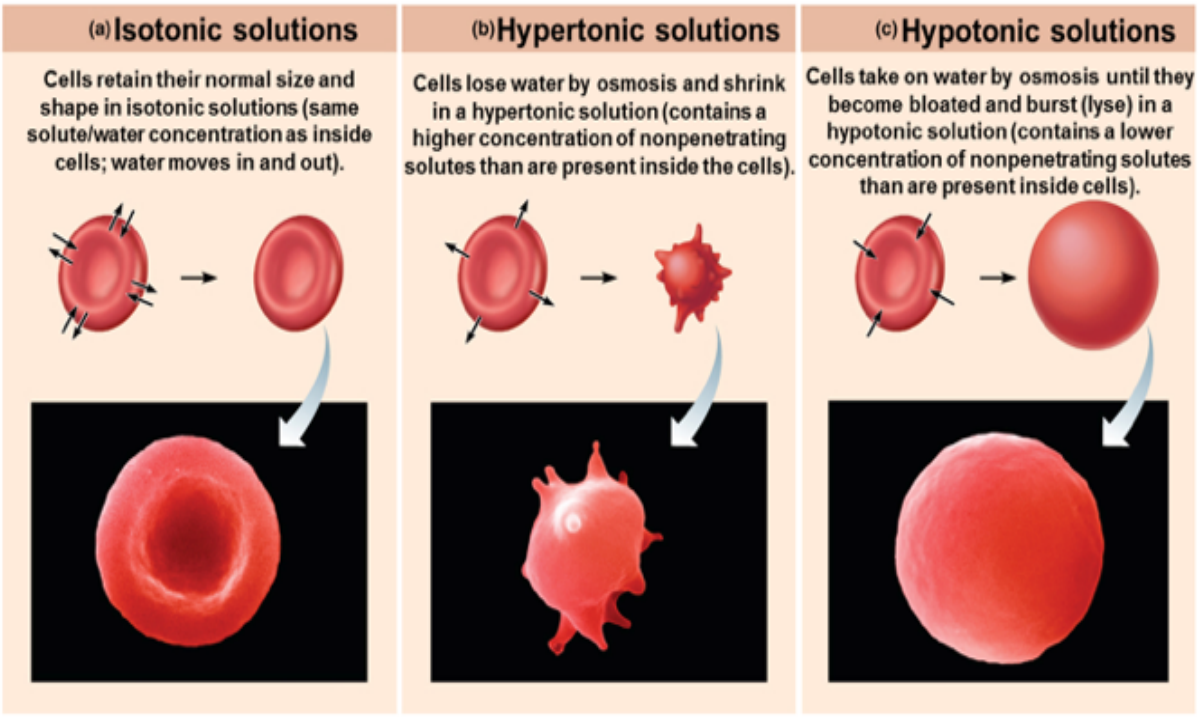
Tonicity

- Ability of a solution to change the shape or tone of cells by altering the cells' internal water volume
    - Isotonic solution has same osmolarity as inside the cell, so volume remains unchanged
    - Hypertonic solution has higher osmolarity than inside cell, so water flows out of cell, resulting in cell shrinking
        - Shrinking is referred to as crenation
    - Hypotonic solution has lower osmolarity than inside cell, so water flows into cell, resulting in cell swelling
        - Can lead to cell bursting, referred to as lysing

Osmosis

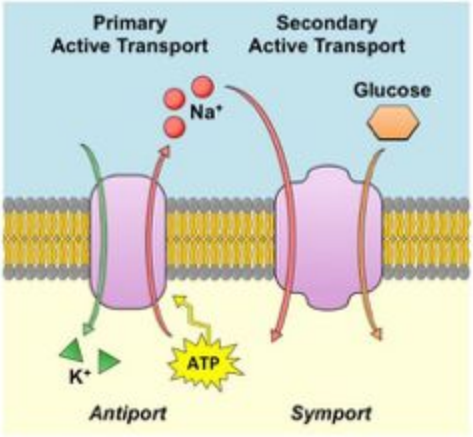
- Osmolarity is equal to molarity times the number of ions (particles)
    - Example: (1 particle) ionizes to and (2 particles)
    - Thereore, 1 M solution of equals a 2 Osm solution
- Osmolarity is expressed in osmoles/liter (osmol/L)

The effect of solutions of varying tonicities on living red blood cells:



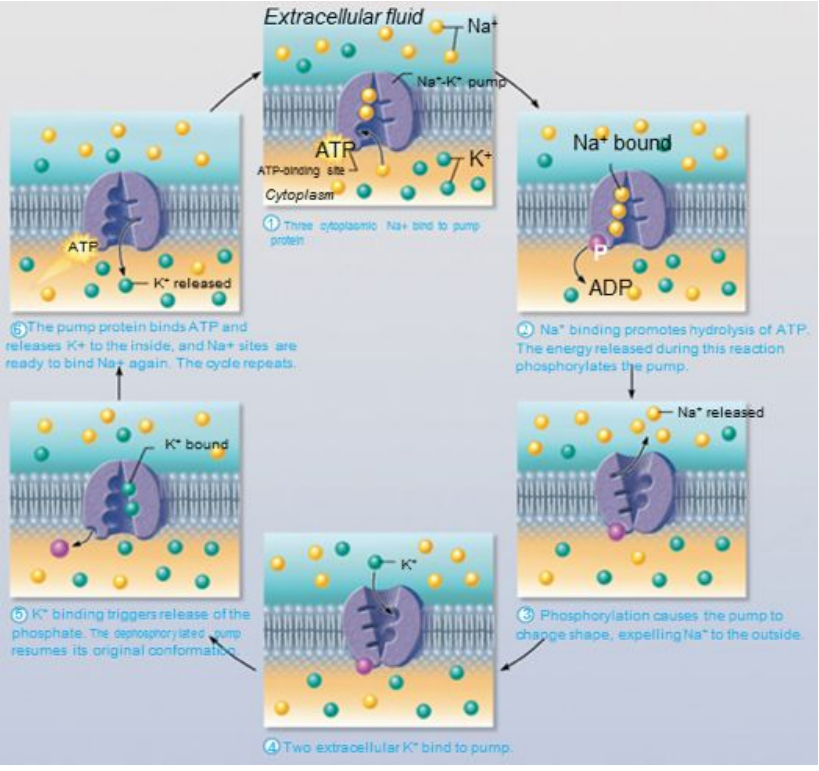
Active Membrane transport

- Two major active membrane transport processes
    - Active transport
    - Vesicular transport
- Both require ATP to move solutes across a plasma membrane for any of these reasons:
    - Solute is too large for channels, or



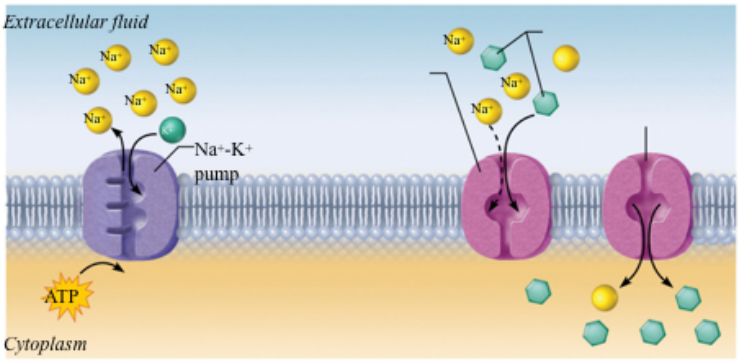
    - Solute is not lipid soluble, or
    - Solute is not able to move down concentration gradient
- Requires carrier proteins (solute pumps)
    - Bind specifically and reversibly with substance being moved
    - Some carriers transport more than one substance
        - Antiporters transport one substance into cell while transporting a different substance out of cell
        - Symporters transport two different substances in the same direction
- Moves solutes against their concentration gradient (from low to high)
    - This requires energy (ATP)
- Two types of active transport:
    - Primary active transport
        - Required energy comes directly from ATP hydrolysis
    - Secondary active transport
        - Required energy is obtained indirectly from ionic gradients created by primary active transport
- Primary active transport
    - Energy from hydrolysis of ATP causes change in shape of transport protein
    - Shape change causes solutes (ions) bound to protein to be pumped across membrane
    - Example of pumps: calcium, hydrogen (proton), pumps
- Sodium-potassium pump
    - Most studied pump
    - An enzyme called ATPase, that pumps out of cell and back into cell
    - Located in all plasma membranes, but especially active in excitable cells (nerves and muscles)
- Leakage channels located in membranes result in leaking into the cell and leaking out of cell
    - Both travel down their concentration gradients
- pump works as an antiporter that pumps out of cell and back into cell against their concentration gradients
- Maintains electrochemical gradients, which involve both concentration and electrical charge of ions
    - Essential for functions of muscle and nerve tissues

Primary active transport is the process by which solutes are moved across cell membranes against electrochemical gradients using energy supplied directly by ATP.



- Secondary active transport
    - Depends on ion gradient that was created by primary active transport system
        - Energy stored in gradients is used indirectly to drive transport of other solutes
        - Low concentration that is maintained inside cell by pump strengthens sodium's drive to want to enter cell
        - can drag other molecules with it as it flows into cell through carrier proteins (usually symporters) in membrane
    - Some sugars, amino acids, and ions are usually transported into cells via secondary active transport

- Secondary active transport is driven by the concentration gradient created by primary active transport



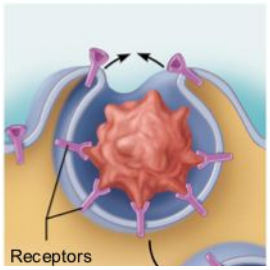
1 Primary active transport
The ATP-driven Na^+-K^+ pump stores energy by creating a steep concentration gradient for Na^+ entry into the cell.

Lecture 4

Vesicular Transport

- Involves transport of large particles, macromolecules, and fluids across membrane in membranous sacs called vesicles
- Requires cellular energy (usually ATP)
- Vesicular transport processes include:
    - Endocytosis: transport into cell
        - 3 different types of endocytosis: phagocytosis, pinocytosis, receptor-mediated endocytosis
    - Exocytosis: transport out of cell
    - Transcytosis: transport into, across, and then out of cell
    - Vesicular trafficking: transport from one area or organelle in cell to another
- Endocytosis
    - Involves formation of protein-coated vesicles
    - Usually involve receptors; therefore can be a very selective process
        - Substance being pulled in must be able to bind to its unique receptor
    - Some pathogens are capable of hijacking receptor for transport into cell
    - Once vesicle is pulled inside cell, it may: • Fuse with lysosome or
    - Undergo transcytosis
- Phagocytosis: type of endocytosis that is referred to as "cell eating"
    - Membrane projections called pseudopods form and flow around solid particles that are being engulfed, forming a vesicle which is pulled into cell
    - Formed vesicle is called a phagosome
    - Phagocytosis is used by macrophages and certain other white blood cells
        - Phagocytic cells move by amoeboid motion where cytoplasm flows into temporary extensions that allow cell to creep

Comparison of three types of endocytosis



- Phagocytosis: The cell engulfs a large particle by forming a projecting pseudopod. The phagosome combines with a lysosome and its contents are digested. The vesicle has receptors capable of binding to microorganisms or solid particles.
    - Phagocytosis: type of endocytosis that is referred to as “cell eating.
    - Membrane projections called pseudopods orm and flow around solid particles that are being engulfed, forming a vesicle which is pulled into cell
    - Formed vesicle is called a phagosome
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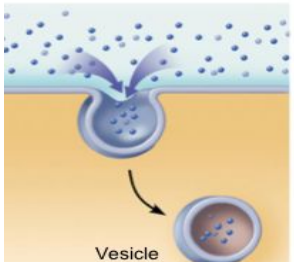
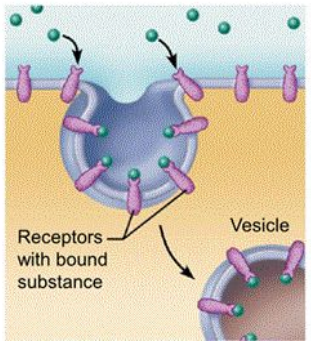
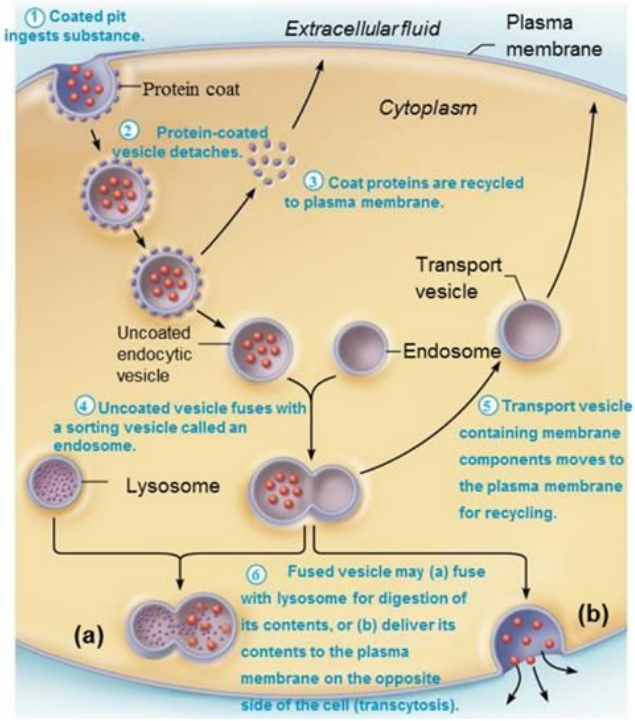


- Pinocytosis: The cell “gulps” a drop of extracellular fluid containing solutes into tiny vesicles. No receptors are used, so the process is nonspecific.
    - type of endocytosis that is referred to as “cell drinking” or fluid-phase endocytosis
    - Plasma membrane infolds, bringing extracellular fluid and dissolved solutes inside cell
    - Fuses with endosome
        - Used by some cells to “sample” environment
    - Main way in which nutrient absorption occurs in the small intestine
    - Membrane components are recycled back to membrane



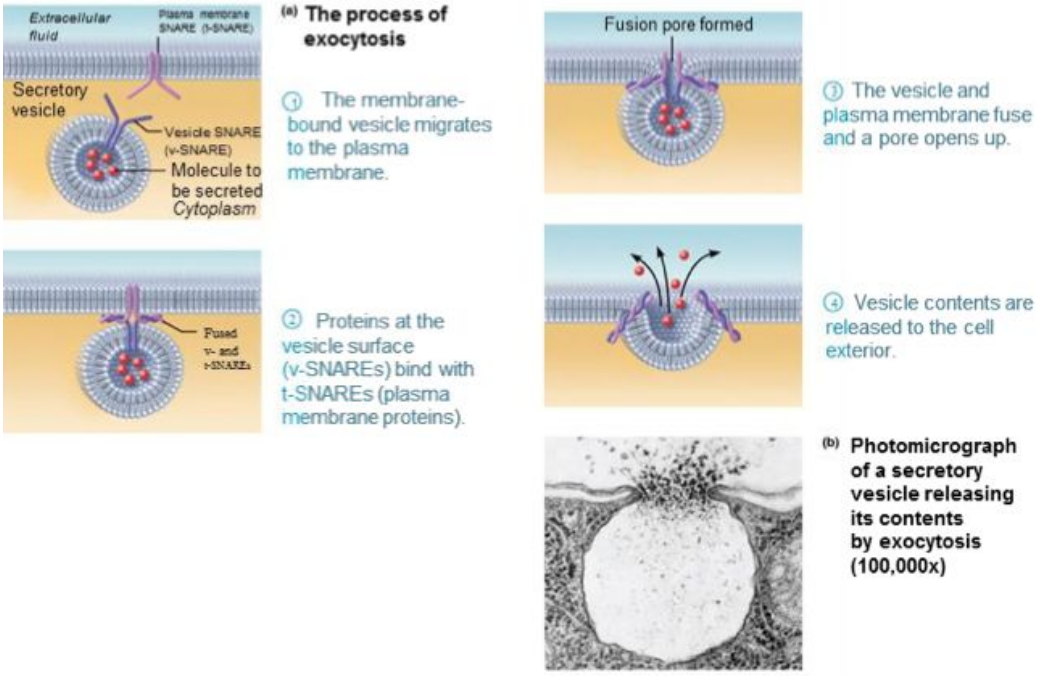
- Receptor-mediated endocytosis involves endocytosis and transcytosis of specific molecules
    - Extracellular substances bind to specific receptor proteins, enabling the cell to ingest and concentrate specific substances in protein-coated vesicles. Substances may be released inside the cell or digested in a lysosome.
    - Many cells have receptors embedded in clathrin-coated pits, which will be internalized along with the specific molecule bound
    - Examples: enzymes, low-density lipoproteins (LDL), iron, insulin, and, unfortunately, viruses, diphtheria, and cholera toxins may also be taken into a cell this way
    - Caveolae have smaller pits and different protein coat from clathrin, but still capture specific molecules (folic acid, tetanus toxin) and use transcytosis



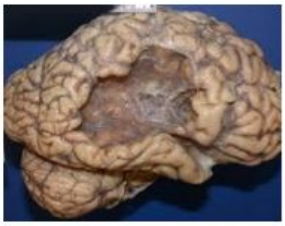
Endocytosis by protein coated pits by the numbers

Exocytosis

- Process where material is ejected from cell
    - Usually activated by cell-surface signals or changes in membrane voltage
- Substances being ejected are enclosed in secretory vesicles
- Protein on vesicle called v-SNARE finds and hooks up to target t-SNARE proteins on membrane
    - Docking process triggers exocytosis
- Some substances exocytosed: hormones, neurotransmitters, mucus, cellular wastes



2.2.1 Identify the different regions of the neuron and associate each region with the functions of reception, propagation and transmission
2.2.1.1 justify 3 special properties of neurons that set them apart from most other cells in the body
2.2.1.2 label and indicate the functions of the receptive, conducting and secretory regions of the neuron structural units of NS: conduct electrical impulses from one body part to another



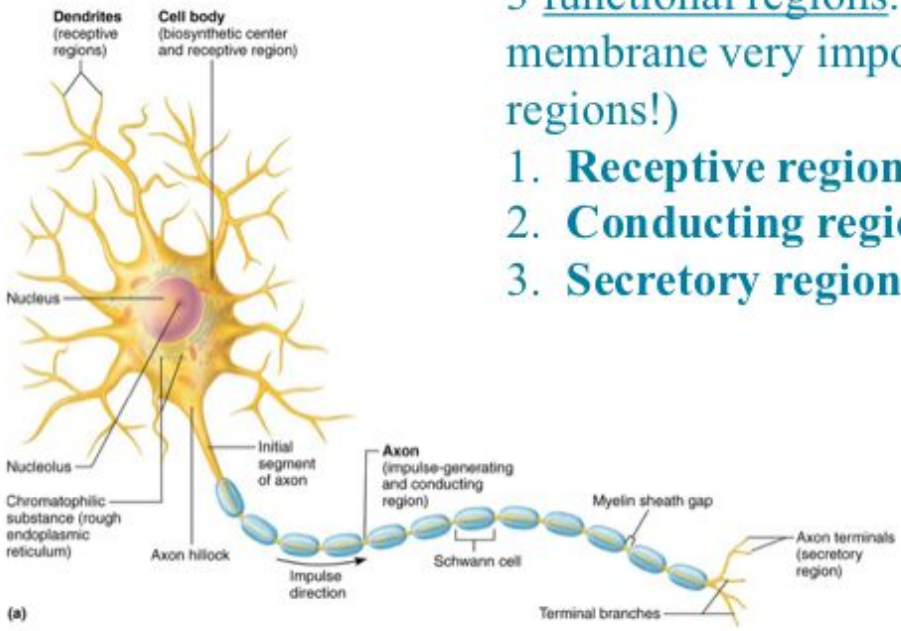
Special features:
1. Extreme longevity: adequately nourished 100 yr+
2. Amitotic: why? what does this mean if neurons are damaged? 3. High metabolic rate: O2/glucose requirements?
large, complex cells: all have a cell body + one or more processes

"There are perhaps about one hundred billion neurons, or nerve cells, in the brain, and in a single human brain the number of possible inter-connections between these cells is greater than the number of atoms in the universe." (Robert Ornstein and Richard Thompson, The Amazing Brain. Boston: Houghton Mifflin Company. 1984, 21)

Neuron Processes

- Armlike processes that extend from 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
    - Axon

Structure of a Motor Neuron



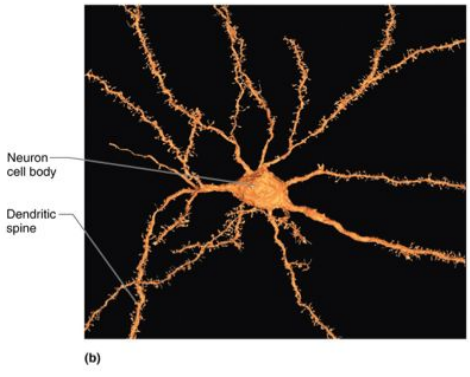
3 functional regions: (plasma membrane very important in all regions!)

1. **Receptive region**
2. **Conducting region**
3. **Secretory region**

Neuron 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

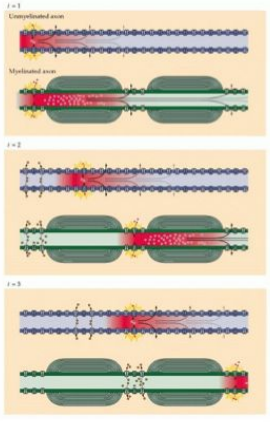
Structure of a Motor Neuron



Neuron Processes

- The 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 entire length of cell
  - 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 boutonn**
- The axon: 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 same time
  - Axons rely on cell bodies to renew proteins and membranes
  - Quickly decay if cut or damaged
  - 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
      - Examples: mitochondria, cytoskeletal elements, membrane components, enzymes
    - Retrograde: toward cell body
      - Examples: organelles to be degraded, signal molecules, viruses, and bacterial toxins
- Myelin sheath
  - Composed of myelin, a whitish, protein-lipid substance
  - Function of myelin
    - Protect and electrically insulate axon
    - Increase speed of nerve impulse transmission
  - Myelinated fibers: segmented sheath surrounds most long or large-diameter axons
  - Nonmyelinated fibers: do not contain sheath
    - Conduct impulses more slowly

Myelin sheaths increase the speed of AP travel

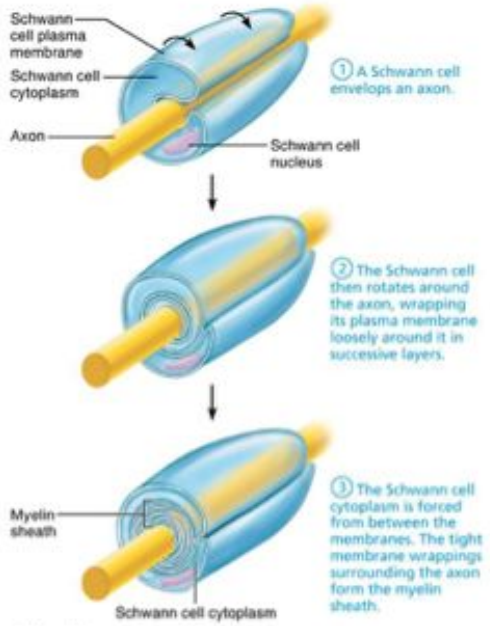


- **Myelinated axon ~150m/s**
- **Unmyelinated axon 0.5-10m/s depending on diameter**

Fig 3.14 (https://www.ncbi.nlm.nih.gov/books/NBK10921/)

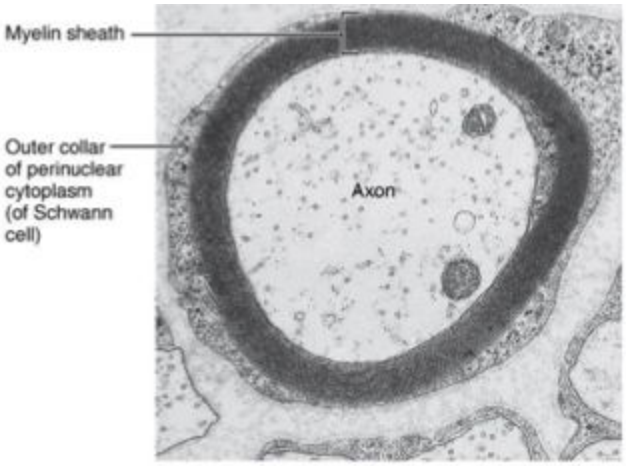
- Myelination in the PNS
    - Formed by Schwann cells
        - Wraps around axon in jelly roll fashion
        - One cell forms one segment of myelin sheath
    - Outer collar of perinuclear cytoplasm (formerly called neurilemma): peripheral bulge containing nucleus and most of cytoplasm
    - Plasma membranes have less protein
        - No channels or carriers, so good electrical insulators
        - Interlocking proteins bind adjacent myelin membranes

PNS Nerve Fiber Myelination



(a) Myelination of a nerve fiber (axon)

PNS Nerve Fiber Myelination



(b) Cross-sectional view of a myelinated axon (electron micrograph 24,000×)

- Myelination in the PNS (cont.)
    - Myelin sheath gaps
        - Gaps between adjacent Schwann cells
        - Sites where axon collaterals can emerge
        - Formerly called nodes of Ranvier
    - Nonmyelinated fibers
        - Thin fibers not wrapped in myelin; surrounded by Schwann cells but no coiling; one cell may surround 15 different fibers
- Myelin sheaths in the CNS
- Formed by processes of oligodendrocytes, not whole cells
- Each cell can wrap up to 60 axons at once
- Myelin sheath gap is present
- No outer collar of perinuclear cytoplasm
- Thinnest fibers are unmyelinated, but covered by long extensions of adjacent neuroglia
- White matter: regions of brain and spinal cord with dense collections of myelinated fiber
    - Usually fiber tracts
- Gray matter: mostly neuron cell bodies and nonmyelinated fibers

11.4 Membrane Potentials

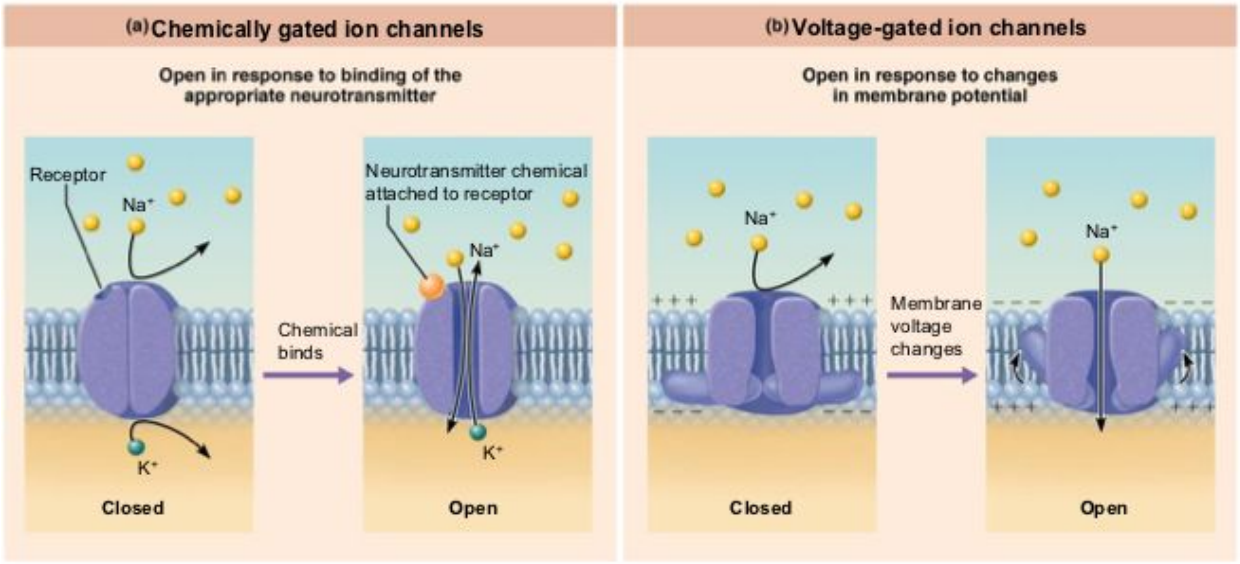
- Like all cells, neurons have a resting membrane potential
- Unlike most other cells, neurons can rapidly change resting membrane potential
- Neurons are highly excitable

Basic Principles of Electricity

- Opposite charges are attracted to each other
- Energy is required to keep opposite charges separated across a membrane
- Energy is liberated when the charges move toward one another
- When opposite charges are separated, the system has potential energy
- Voltage: a measure of potential energy generated by separated charge
    - Measured between two points in volts (V) or millivolts (mV)
    - Called potential difference or potential
        - Charge difference across plasma membrane results in potential
    - Greater charge difference between points = higher voltage
- Current: flow of electrical charge (ions) between two points
    - Can be used to do work
    - Flow is dependent on voltage and resistance
- Resistance: hindrance to charge flow
    - Insulator: A substance with high electrical resistance
    - Conductor: a substance with low electrical resistance
- Role of membrane ion channels
    - Large proteins serve as selective membrane ion channels
        - K+ ion channel allows only K+ to pass through
    - Two main types of ion channels
        - Leakage (nongated) channels, which are always open
        - Gated channels, in which part of the protein changes shape to open/close the channel
            - Three main gated channels: chemically gated, voltage−gated, or mechanically gated

- Chemically gated (ligand-gated) channels
    - Open only with binding of a specific chemical (example: neurotransmitter)
- Voltage-gated channels
    - Open and close in response to changes in membrane potential
- Mechanically gated channels
    - Open and close in response to physical deformation of receptors, as in sensory receptors

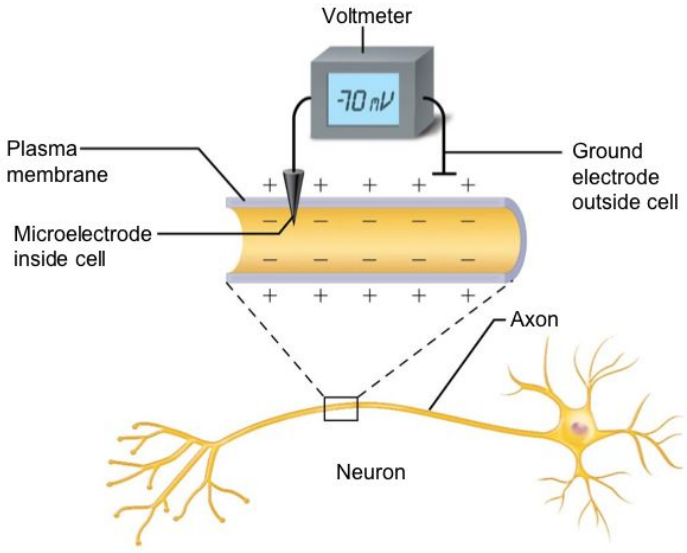
Operation of gated channels



Generating the Resting Membrane Potential

- A voltmeter can measure potential (charge) difference across membrane of resting cell
- Resting membrane potential of a resting neuron is approximately –70 mV
    - The cytoplasmic side of membrane is negatively charged relative to the outside
    - The actual voltage difference varies from –40 mV to –90 mV
    - The membrane is said to be **polarized**
- Potential generated by:
    - Differences in ionic composition of Intracellular fluid (IFC) and Extracellular Fluid (ECF)
    - Differences in plasma membrane permeability

Measuring membrane potential in neurons



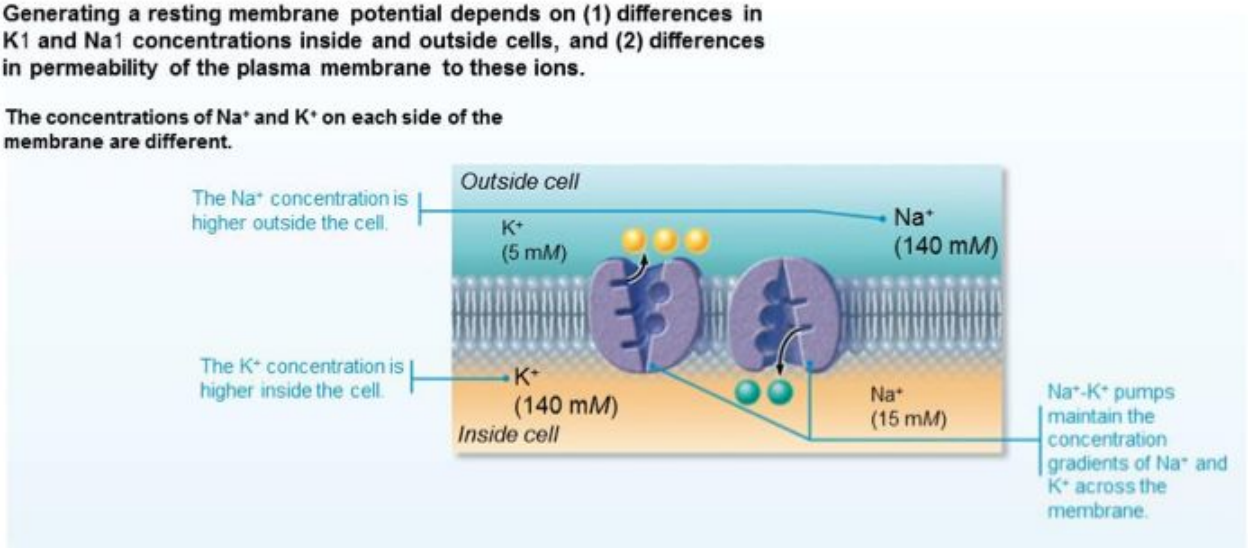
Lecture 5

Generating the Resting Membrane Potential

- Differences in ionic composition
  - ECF has higher concentration of Na + than ICF
    - Balanced chiefly by chloride ions (Cl)
  - ICF has higher concentration of K+ than ECF
    - Balanced by negatively charged proteins
  - K+ plays the most important role in membrane potential

Resting Membrane Potential

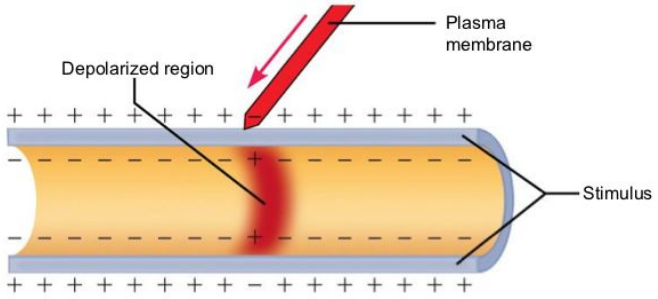
- Generating a resting membrane potential depends on (1) differences in K+and Na + concentrations inside and outside cells, and (2) differences in permeability of the plasma membrane to these ions.



11.5 Graded Potentials

- Short-lived, localized changes in membrane potential
  – The stronger the stimulus, the more voltage changes and the farther current flows
- Triggered by stimulus that opens gated ion channels
  – Results in depolarization or sometimes hyperpolarization
- Named according to location and function
  - Receptor potential (generator potential): graded potentials in receptors of sensory neurons
  - Postsynaptic potential: neuron graded potential

The spread and decay of a graded potential

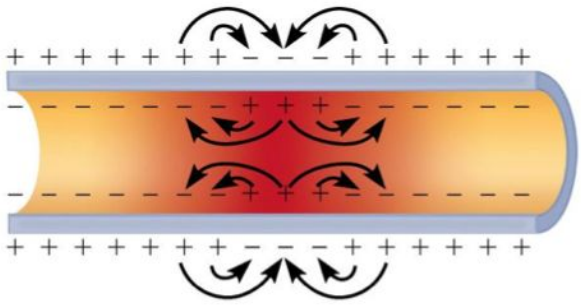


(a) Depolarization: A small patch of the membrane (red area)depolarizes.

Graded Potentials

- Once gated ion channel opens, depolarization spreads from one area of membrane to next

The spread and decay of a graded potential



(b) Depolarization spreads: Opposite charges attract each other. This creates local currents (black arrows) that depolarize adjacent membrane areas, spreading the wave of depolarization.

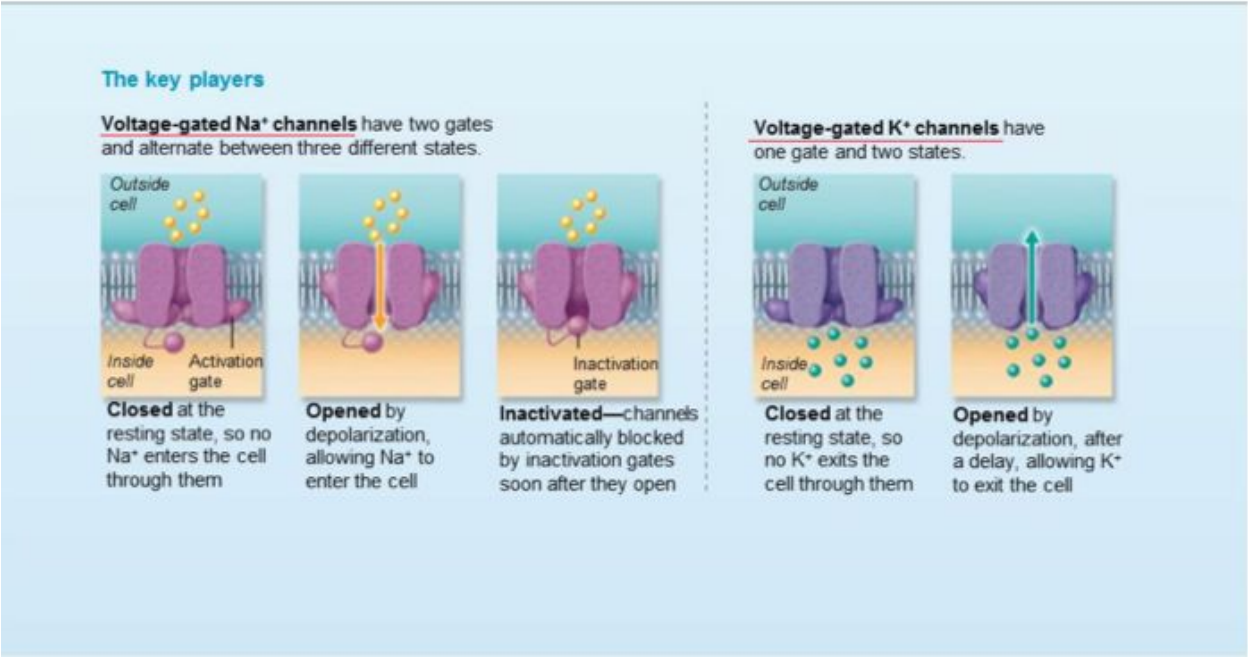
Graded Potentials

- Current flows but dissipates quickly and decays
    - Graded potentials are signals only over short distances

11.6 Action Potentials

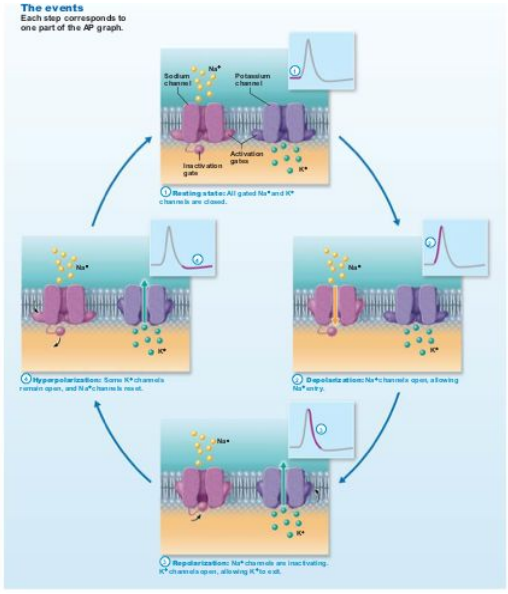
- Principal way neurons send signals
  – Means of long-distance neural communication
- Occur only in muscle cells and axons of neurons
- Brief reversal of membrane potential with a change in voltage of ~100 mV
- Action potentials (APs) do not decay over distance as graded potentials do
- In neurons, also referred to as a nerve impulse
- Involves opening of specific voltage-gated channels

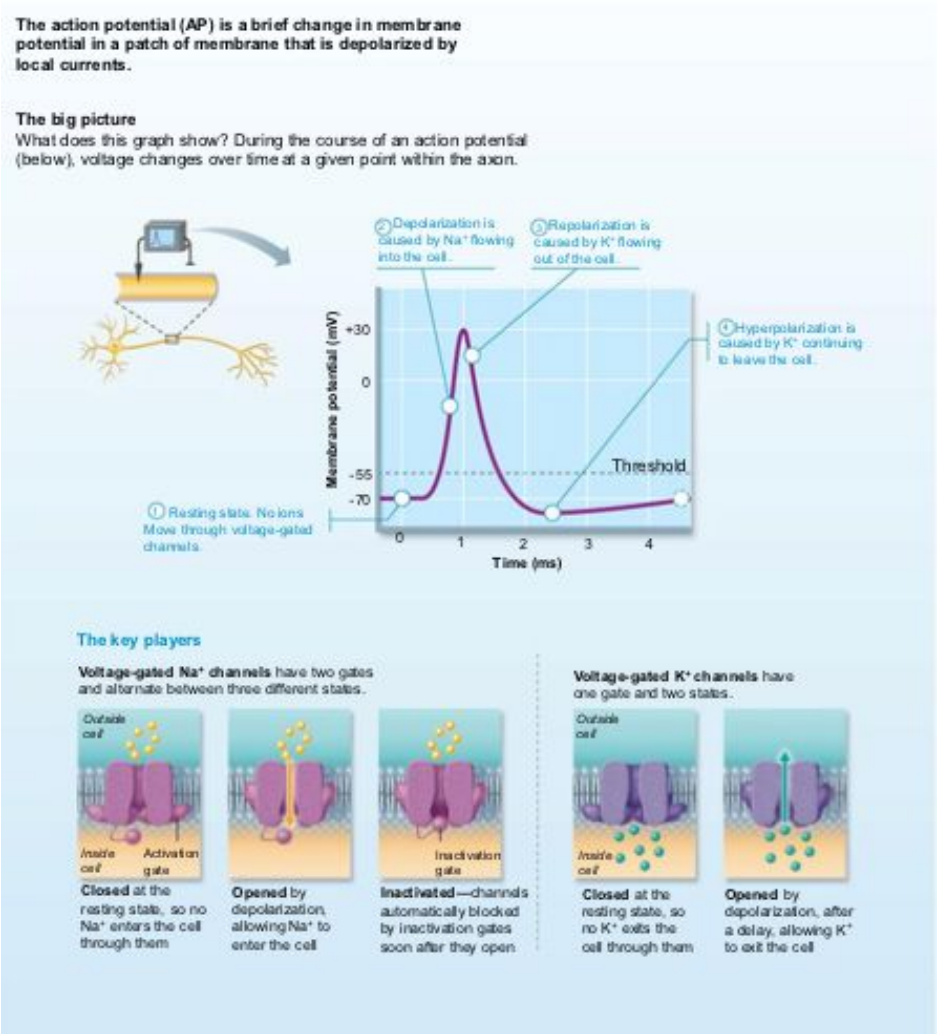
Action Potential



Generating an Action Potential

- Four main steps +
    a. Resting state: All gated Na and K+ channels are closed +
        - Only leakage channels for Na and K+ are open
            - Maintains the resting membrane potential
        - Each Na+ channel has two voltage-sensitive gates
            - Activation gates: closed at rest; open with depolarization, allowing Na+ to enter cell
            - Inactivation gates: open at rest; block channel once it is open to prevent more Na + from entering cell
        - Each K+ channel has one voltage-sensitive gate
            - Closed at rest
            - Opens slowly with depolarization
    b. Depolarization: Na+ channels open
        - Depolarizing local currents open voltage-gated Na + channels, and Na + rushes into cell
        - Na + activation and inactivation gates open
        - Na + influx causes more depolarization, which opens more Na + channels
            - As a result, ICF becomes less negative
        - At threshold (–55 to –50 mV), positive feedback causes opening of all Na + channels
            - Results in large action potential spike
            - Membrane polarity jumps to +30 mV
    c. Repolarization: Na + channels are inactivating, and K+ channels open
        - Na+ channel inactivation gates close
            - Membrane permeability to Na + declines to resting state
            - AP spike stops rising
        - Voltage-gated K+ channels open
            - K+ exits cell down its electrochemical gradient
        - Repolarization: membrane returns to resting membrane potential
    d. Hyperpolarization: Some K+ channels remain open, and Na + channels reset
        - Some K channels remain open, allowing excessive K efflux
            - Inside of membrane becomes more negative than in resting state
        - This causes hyperpolarization of the membrane (slight dip below resting voltage)
        - Na + channels also begin to reset





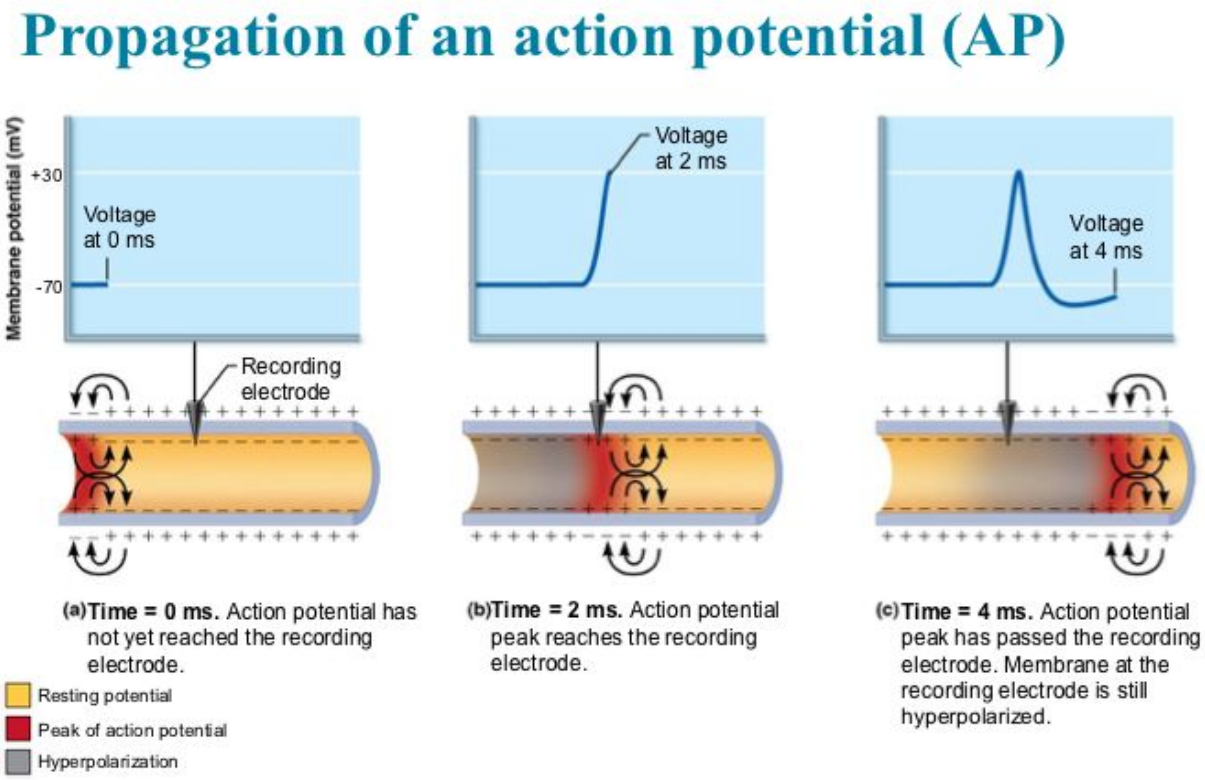
Threshold and the All-or-None Phenomenon

- Not all depolarization events produce APs
- For an axon to “fire,” depolarization mustreach threshold voltage to trigger AP
- At threshold:
    - Membrane is depolarized by 15 to 20 mV
    - Na + permeability increases
    - Na + influx exceeds K+ efflux
    - The positive feedback cycle begins
- All-or-None: An AP either happens completely, or does not happen at all

Propagation of an Action Potential (see right)

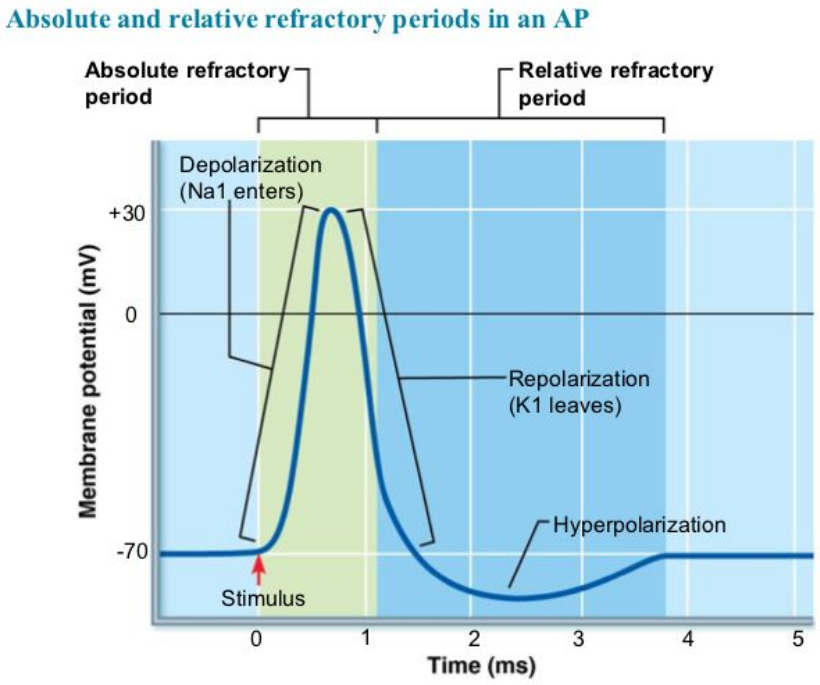
- Propagation allows AP to be transmitted from origin down entire axon length toward terminals
- Na+ influx through voltage gates in one membrane area cause local currents that cause opening of Na + voltage gates in adjacent membrane areas
    - Leads to depolarization of that area, which in turn causes depolarization in next area
- Once initiated, an AP is self-propagating
    - In nonmyelinated axons, each successive segment of membrane depolarizes, then repolarizes
    - Propagation in myelinated axons differs
- Since Na + channels closer to the AP origin are still inactivated, no new AP is generated there

- AP occurs only in a forward direction



Refractory Periods

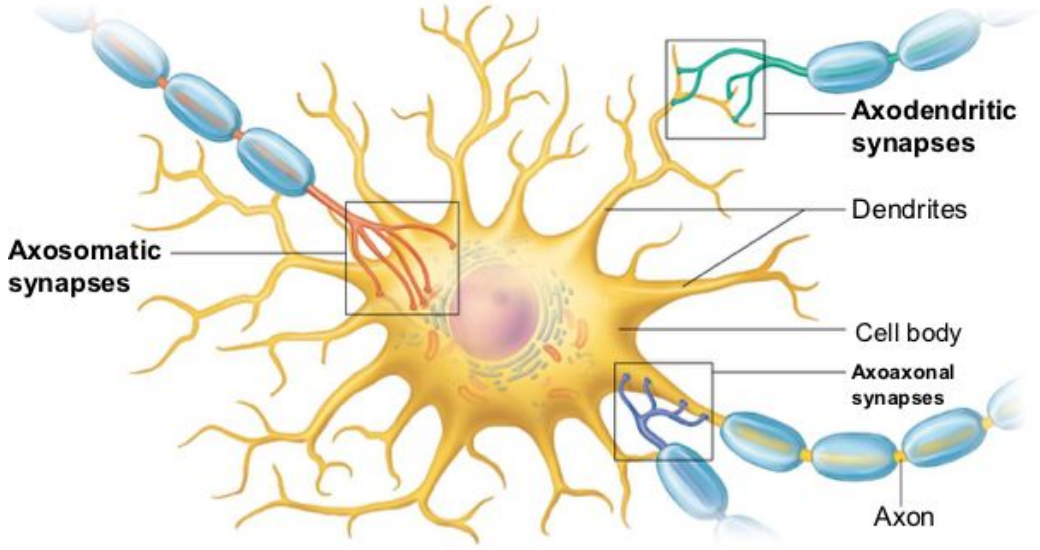
- Refractory period: time in which neuron cannot trigger another AP
  - Voltage-gated Na + channels are open, so neuron cannot respond to another stimulus
- Two types
  - Absolute refractory period
    - Time from opening of Na + channels until resetting of the channels
    - Ensures that each AP is an all-or-none event
    - Enforces one-way transmission of nerve impulses
  - Relative refractory period
    - Follows absolute refractory period
      - Most Na + channels have returned to their resting state
      - Some K+ channels still open
      - Repolarization is occurring
    - Threshold for AP generation is elevated
    - Only exceptionally strong stimulus could stimulate an AP
  - Think of a disobedient (refractory) dog – if he is absolutely refractory he will never come when called, but if he is relatively refractory, he may come but only if you call loud enough



11.7 The Synapse

- Nervous system works because information flows from neuron to neuron
- Neurons are functionally connected bysynapses, junctions that mediate information transfer
    - From one neuron to another neuron
    - Or from one neuron to an effector cell
- Presynaptic neuron: neuron conducting impulses toward synapse (sends information)
- Postsynaptic neuron: neuron transmitting electrical signal away from synapse (receives information)
    - In PNS may be a neuron, muscle cell, or gland cell
- Most function as both

Synapses



(a) Axodendritic, axosomatic, and axoaxonal synapses.

Synaptic connections

- Axodendritic: between axon terminals of one neuron and dendrites of others
- Axosomatic: between axon terminals of one neuron and soma (cell body) of others
- Less common connections:
    - Axoaxonal (axon to axon)
    - Dendrodendritic (dendrite to dendrite)
    - Somatodendritic (dendrite to soma)
- Two main types of synapses:
    - Chemical synapse
    - Electrical synapse

Chemical Synapses

- Most common type of synapse
- Specialized for release and reception of chemical neurotransmitters
- Typically composed of two parts
    - Axon terminal of presynaptic neuron: contains synaptic vesicles filled with neurotransmitter
    - Receptor region on postsynaptic neuron's membrane: receives neurotransmitter
        - Usually on dendrite or cell body
    - Two parts separated by fluid-filled synaptic cleft
- Electrical impulse changed to chemical across synapse, then back into electrical

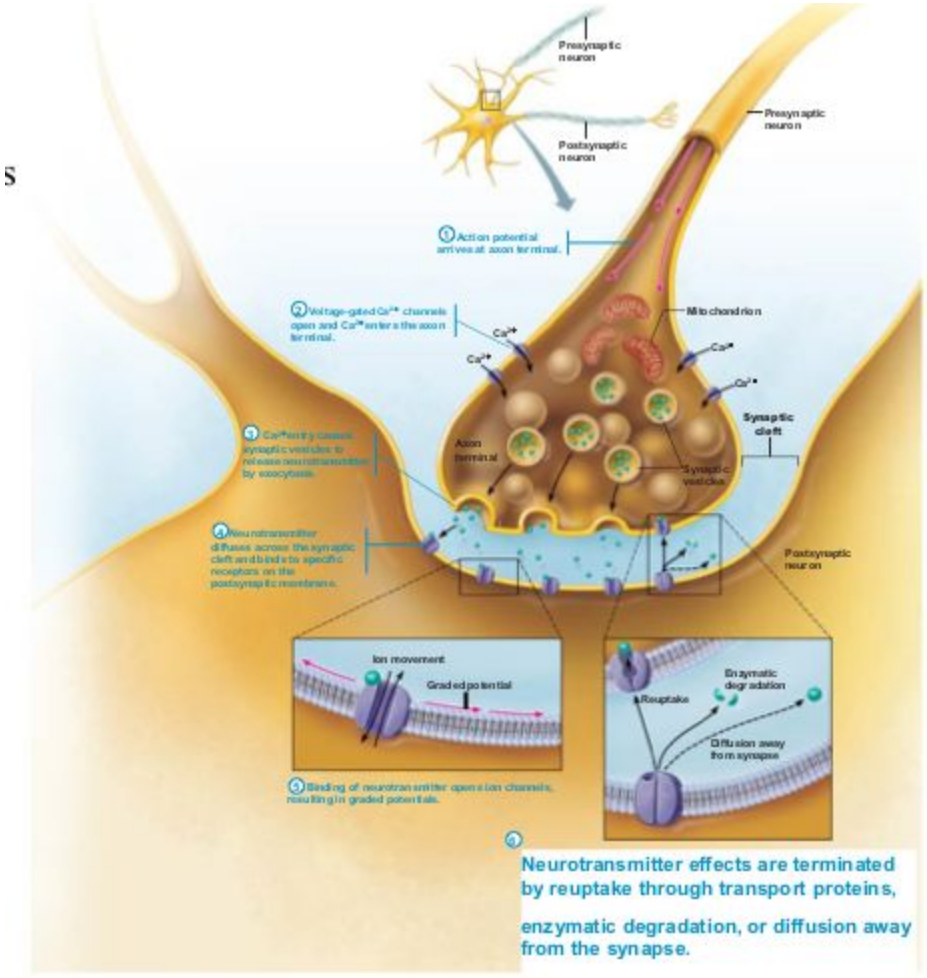
Transmission across synaptic cleft

- Synaptic cleft prevents nerve impulses from directly passing from one neuron to next
- Chemical event (as opposed to an electrical one)
- Depends on release, diffusion, and receptor binding of neurotransmitters
- Ensures unidirectional communication between neurons

Chemical Synapses

- Information transfer across chemical synapses
- Six steps are involved:
    a. AP arrives at axon terminal of presynaptic neuron
    b. Voltage-gated $Ca2+$ channels open, and $Ca2+$ enters axon terminal
        - $Ca2+$ flows down electrochemical gradient from ECF to inside of axon terminal
    c. $Ca2+$ entry causes synaptic vesicles to release neurotransmitter
        - $Ca2+$ causes synaptotagmin protein to react with SNARE proteins that control fusion of synaptic vesicles with axon membrane
        - Fusion results in exocytosis of neurotransmitter into synaptic cleft
        - The higher the impulse frequency, the more vesicles exocytose, leading to a greater effect on the postsynaptic cell
    d. Neurotransmitter diffuses across the synaptic cleft and binds to specific receptors on the postsynaptic membrane
        - Often chemically gated ion channels
    e. Binding of neurotransmitter opens ion channels, creating graded potentials
        - Binding causes receptor protein to change shape, which causes ion channels to open
            - Causes a graded potential in postsynaptic cell » Can be an excitatory or inhibitory event
            - Some receptor proteins are also ion channels
    f. Neurotransmitter effects are terminated

- As long as neurotransmitter is binding to receptor, graded potentials will continue, so process needs to be regulated
- Within a few milliseconds, neurotransmitter effect is terminated in one of three ways
    - Reuptake by astrocytes or axon terminal
    - Degradation by enzymes
    - Diffusion away from synaptic cleft



Chemical Synapses

- Synaptic delay
    - Time needed for neurotransmitter to be released, diffuse across synapse, and bind to receptors
        - Can take anywhere from 0.3 to 5.0 ms
    - Synaptic delay is rate-limiting step of neural transmission
        - Transmission of AP down axon can be very quick, but synapse slows transmission to postsynaptic neuron down significantly
        - Not noticeable, because these are still very fast

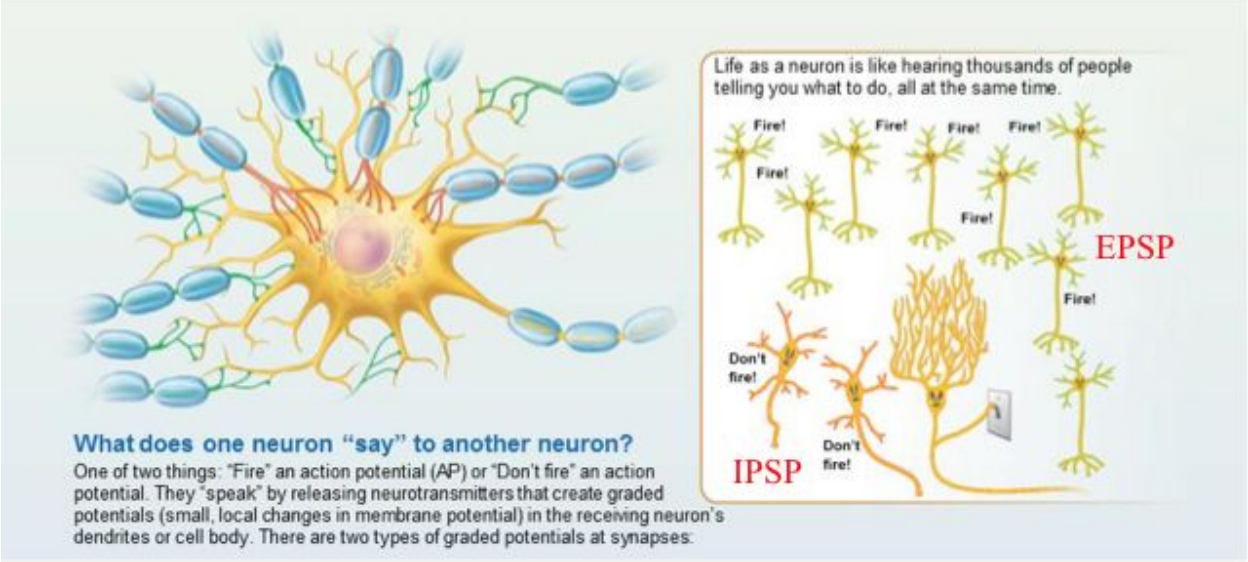
Electrical Synapses

- Less common than chemical synapses
- Neurons are electrically coupled
    - Joined by gap junctions that connect cytoplasm of adjacent neurons
    - Communication is very rapid and may be unidirectional or bidirectional
    - Found in some brain regions responsible for eye movements or hippocampus in areas involved in emotions and memory
    - Most abundant in embryonic nervous tissue

11.8 Postsynaptic Potentials

- Neurotransmitter receptors cause graded potentials that vary in strength based on:
    - Amount of neurotransmitter released
    - Time neurotransmitter stays in clef
- Depending on effect of chemical synapse, there are two types of postsynaptic potentials
    - EPSP: excitatory postsynaptic potentials
    - IPSP: inhibitory postsynaptic potentials

Postsynaptic Potentials and Their Summation



Excitatory Synapses and EPSPs

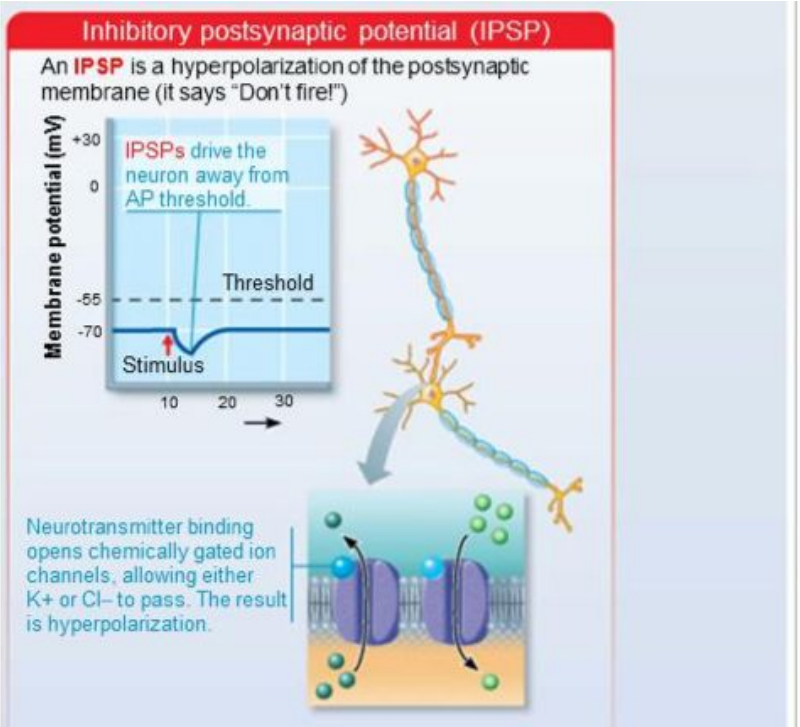
- Neurotransmitter binding opens chemically gated channels
    - Allows simultaneous flow of Na + and K+ in opposite directions
- Na+ influx greater than K+ efflux, resulting in local net graded potential depolarization calledexcitatory postsynaptic potential (EPSP)
- EPSPs trigger AP if EPSP is of threshold strength
    - Can spread to axon hillock and trigger opening of voltage-gated channels, causing AP to be generated

Inhibitory Synapses and IPSPs

- Neurotransmitter binding to receptor opens chemically gated channels that allow entrance/exit of ions that cause hyperpolarization
    - Makes postsynaptic membrane more permeable to K+ or Cl–
        - If K+ channels open, it moves out of cell
        - If Cl– channels open, it moves into cell

- Reduces postsynaptic neuron's ability to produce an action potential
    - Moves neuron farther away from threshold (makes it more negative)

Postsynaptic Potentials and Their Summation



2.2.4.5 define (in terms of EPSPs & IPSPs): temporal summation, spatial summation; justify the role of the axon hillock as the neural integrator

C1. Summation by Postsynaptic Neuron

- single EPSP cannot generate an AP
- 2 types of summation (EPSPs & IPSPs):
    - Temporal
    - Spatial:
- axon hillock = neural integrator (numerous EPSPs & IPSPs)
- most effective synapses: closest to axon hillock – why??