ANP Midterm 1 Comprehensive note

Structural organization of the body (Epithelial and Connective Tissue)

Keywords

- Organ: composed of 2-4 tissue types
- Organ system: Organs that work closely together to accomplish a common purpose
  - Ex// digestive system: process food/eliminate waste
- Organismal level: sum total of all structural levels working together to keep us alive
- Centriole: site of formation of microtubules
- Microtubules: form the mitotic spindle and moves around organelles within the cytoplasm. Units are tubulin subunits.
- Microfilament: strands made of spherical protein subunits called actin and can influence cell shape/muscle contraction
- Intermediate filaments: made up of tough fibers (insoluble protein fibers) that resemble woven ropes. Made up of tetramer subunits
- Cilia: many short projection from the cell surface that propel unwanted substances across it
- Flagellum: we are a single long projection that propels the cell
- Golgi apparatus: a stack of flattened membranes and vesicles close to the nucleus. Package, modify, and segregate proteins for secretion from the cell, inclusion in lysosomes, and incorporation into the plasma membrane
- Rough ER: studded with ribosomes and package the protein they make
- Smooth ER: make lipids, steroids, and detoxify drugs
- Peroxisomes: provide sacs of catalase and oxidase enzymes, and with these they inactivate free radicals
- Lysosomes: function as the cell's demolition crew, digesting bacteria, dead cells, and worn out organelles
- Nucleus: control center and facilitate activity of cells
- Nucleolus: made up of ribosomal RNA and proteins, Site of production of ribosomal subunits
- Histone protein: regulate DNA by compacting it into tightly wrapped chromatin when it is not dividing
- Red Blood Cell: Only type of body cell without a nucleus
- Cytoplasm: region of the cell between the plasma and nuclear membranes. Contain cytosol, cellular inclusions, and organelles.
- Organelle: metabolic machines of the cell
- Homeostasis: body's ability to dynamically maintain relatively stable internal conditions even though the outside world changes continuously

- Most diseases can be regarded as a result of a disturbance of homeosis
- Ex// Cancerous epithelial cells don't respect basal membrane: penetrate/invade underlying tissues

➢ Mucin: protein that dissolves in water to make a slimy coating that protects and lubricates

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HUMAN BODY ORIENTATION/ DIRECTIONAL TERMS

Term	Definition
Superior/Cranial	Towards the head
Inferior / Caudal	Away from the head
Ventral/Anterior	Front of the body
Dorsal/Posterior	Back of the body
Medial	Middle of the body (midline)
Lateral	Away from midline
Intermediate	Between medial and lateral
Proximal	Closer to origin of body part
Distal	Further from origin of body part
Superficial/External	Towards body surface
Deep / Internal	Away from body surface

DO NOT MEMORIZE ME

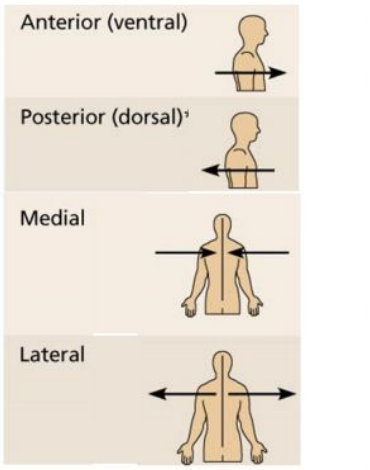

Table 1.1

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Concepts

Tissues: groups of cells similar structure that perform related and sophisticated functions

- Organize into organs that usually contain all four tissues

➢ Cellular organization: Atom to molecule to cell to tissue to organ to organ system to organismal level

➢ Four types
- Epithelial
- Connective
- Muscle
- Nervous

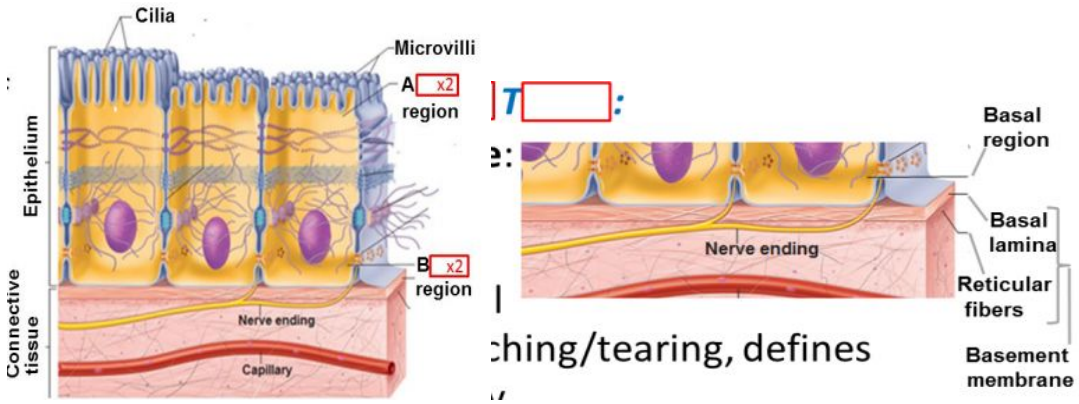
- Epithelial tissue
  - Come in two forms
    - Sheet: cover outside or line inside
      - Lines eg urogenital, digestive, respiratory systems
      - Covery body cavity walls, organs
    - Glandular
      - Fashions glands of body
  - Function
    - Protection
    - Absorption
    - Filtration
    - Excretion
    - Secretion
    - Sensory receptors

- Special characteristics of epithelium
  - Polarity
    - Upper apical surface exposed to exterior/organ cavity
      - Most have microvilli
        - Surface area up and brush up unwanted molecules or substances

    - Lower basal surface with basal lamina
      - Noncellular adhesive sheet
      - Selective filter
      - Scaffold during wound repair

  - Specialized contacts
    - Most (except glandular) as continuous sheets
    - Lateral contacts (tight junction and desmosomes)bind cells together
    - Maintain polarity: apical proteins can't drift basally

  - Supported by connective tissue
    - Basement membrane: basal lamina and reticular fibres reinforce epithelial sheet against stretching/tearing, defines epithelial boundary



- Supported by connective tissue
  - Basement membrane: basal lamina and reticular fibres reinforce epithelial sheet against stretching/tearing, defines epithelial boundary

- Epithelium are Avascular but innervated
  - Avascular: no blood vessels
    - Nourished by substances diffusing from underlying blood vessels
  - Innervated: supplied by nerve fibers

- Capable of regeneration
  - High regeneration capacity necessary
    - Exposure to friction/hostile environment environment
  - Triggers: loss of apical-basal polarity/lateral contacts (tight junction or desmosome)
  - Requirement: adequate nutrition
  - Occurs via cell division (meiosis and mitosis)

➢ Classification of epithelia
- Number of cells
  - Single epithelia
    - Single cell layer - thin
    - Absorption, filtration, secretion
  - Stratified epithelia
    - Greater than or equal to 2 stacked cell layers
    - High abrasion areas: eg skin surface, mouth lining
    - Reproduce from below, pushing apically, replacing less-nourished cells

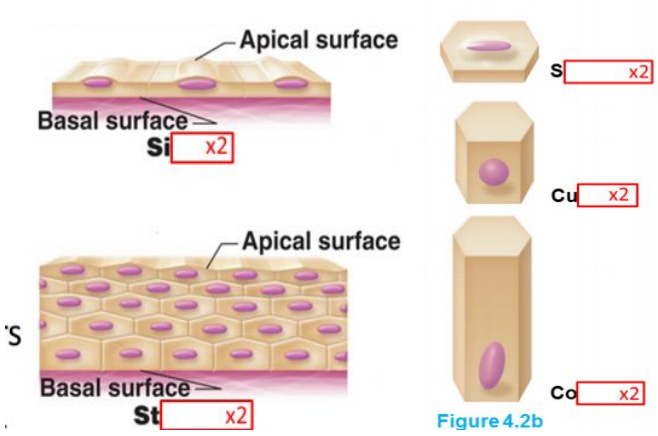
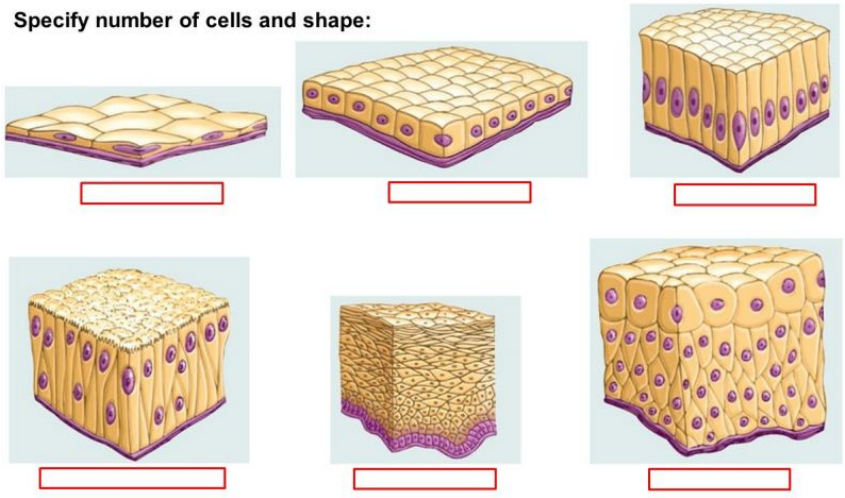


Figure 4.2b

- Shape of cells
  - All 6 sided (irregular)
  - Closely packed like honeycomb
    - Squamous: flat and scale-like
    - Cuboidal: boxlike
    - Columnar: tall columns
  - Nucleus shape conforms to cell shape



1. Simple squamous
2. Simple cuboidal
3. Simple Columnar
4. Pseudostratified columnar
5. Stratified squamous
6. Transitional
   - Shape of cells
     - All 6 sided (irregular)

        - Closely packed like honeycomb
            - Squamous: flat and scale-like
            - Cuboidal: boxlike
            - Columnar: tall columns
        - Nucleus shape conforms to cell shape

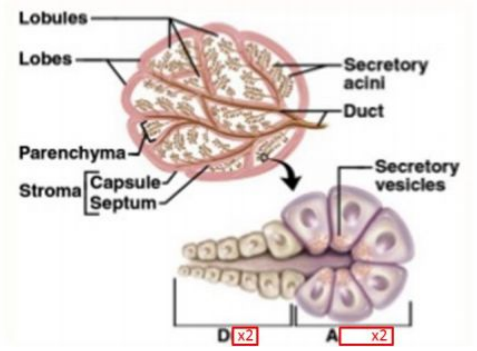
➢ Simple Squamous epithelium
    - Two simple squamous epithelia have special names
        - Endothelium
            - Cardiovascular & lymphatic systems, slick friction-reducing lining, exceptional thinness allows efficient exchange of nutrients and wastes between bloodstream and surrounding tissue
        - Mesothelium
            - Serous (double-layered) membranes that lie ventral body cavity and covers organs

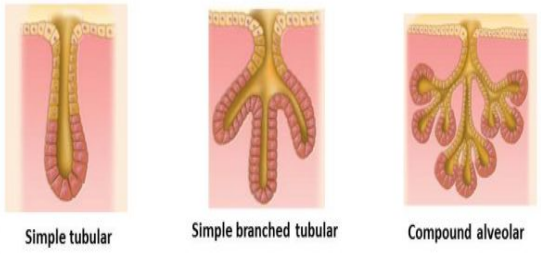
➢ Glandular epithelia
    - Made up of epithelial tissue (1 or more cells that make and secrete a particular product)
        - Product called a secretion [verb: secrete]
    - Types
        - Endocrine (ductless) glands
            - Balloon squirting out content
        - Exocrine glands
            - Secretion → body surfaces (skin)/body cavities
            - *Unicellular: directly via exocytosis don't need a duct*
            - *Multicellular: secretion via duct, eg sweat, oil, saliva, bile, digestive enzymes*

    - Unicellular exocrine glands
        - In epithelial linings of intestinal/respiratory tracts
            - Mucous cells
            - Goblet cells fill up at the top like a goblet, mucous cells do not
        - Both produce mucin (Mucin + H2O → mucous)

    - Multicellular exocrine glands
        - Two parts: epithelium derived duct and secretory acinus
        - Surrounded by fibrous capsule (connective tissue)
            - Supports gland structurally

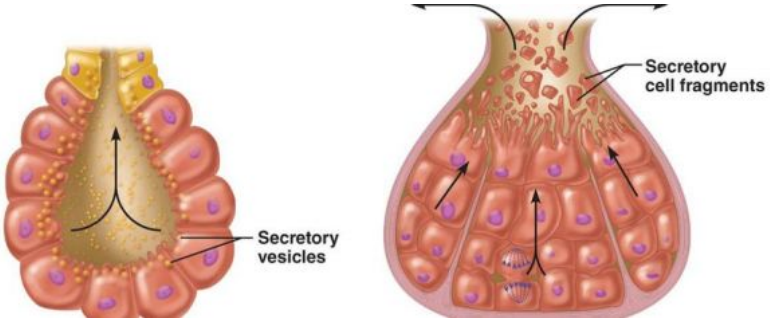
- Contains blood vessels and nerve fibers
- Divides glands into lobes





- Two ways of classifying by structure
  - Simple/compound: duct unbranched/branched
    - Simple : primary duct may branch, but no subsequent branching
    - Compound: primary duct has additional branches
  - Tubular/alveolar secretory units tubes/flasks

- Method of secretion
  - Merocrine: exocytosis (gland intact) eg pancreas, most sweat, salivary glands
  - Holocrine: gland ruptured and destroyed ‘die for their cause’



➢ Connective tissue
  - Function
    - Binding and support (bone, cartilage)
    - Protection (bone, cartilage, fat)
    - Store reserve fuel (fat)
    - Insulation (fat)

        - Transporting (blood)

- Common characteristics
    - Varying degrees of vascularity (none - rich)
    - Extracellular matrix
        - Nonliving part of tissue
        - Matrix allows CT to bear weight, withstand tension, endure abuse
    - Structural elements
        - 3 main ground substance, fibers (extracellular matrix), and cells
    - Ground substance
        - Fills space between cells
            - Composed of…
                - Cell adhesion proteins
                    - Arms used by migrating cells to haul themselves past each other
                    - Mechanical sensors - respond to changes in tension or fluid movement at cell surface by stimulating synthesis /degradation of tight junctions
                    - Transmit intracellular (cell-to-cell) signals that direct migration, proliferation, and specialization
                - Proteoglycans
                    - Glycosaminoglycans (GAGs) attached to protein core to trap water
                - Interstitial fluid

- Types of connective tissue fibers
    - Connective fibers
        - By far the most abundant
        - Thick, cross-linked collagen proteins
        - Tough, high tensile strength
        - Stronger than steel
    - Elastin fibers
        - Long, thin, branched
        - Rubber-band protein
        - Skin, lungs, blood vessels
    - Reticular
        - Short, fine, delicate, branched

- Continuous with collagen fiber - allowed more ‘give’
- Surround blood vessels, organs - fuzzy ‘nets’

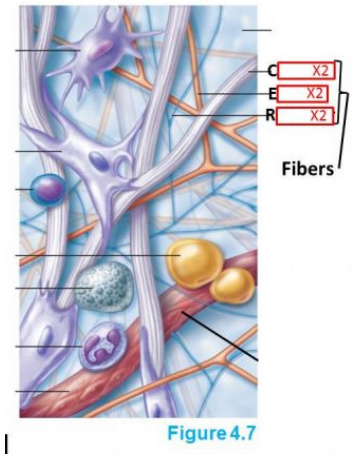
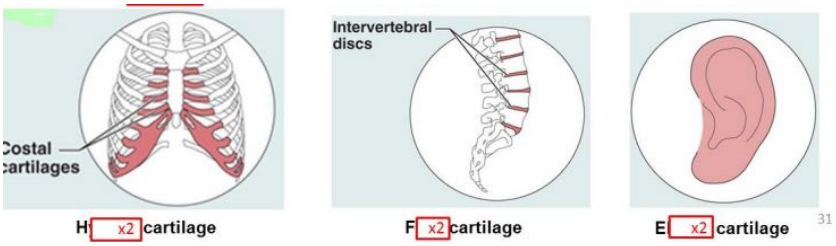


Figure 4.7

- Types of connective tissue cells
  - Macrophages (big eaters)
    - Phagocytize foreign matter
    - Remove dead cells
    - Immune system actors
  - Fibroblasts
    - Produce collagen fibres
  - Lymphocytes
    - White blood cell in immune system that is responsible for immune response
  - Neutrophils
    - Types of white blood cells
    - Also called eosinophils
    - Response to injury, infection
  - Fat cells
    - Stores nutrients
  - Mast cells
    - Detect foreign microorganisms (eg bacteria, viruses, fungi)
      - → inflammation for protective response
    - Have secretory granules: contents mediate response that mast cells put out
      - Heparin - anticoagulant
      - Histamine - makes capillaries leaky
      - Proteases - degrade protein

- Types of connective tissue
  - Loose connective tissue
    - Areolar - wraps/cushions, conveys/holds fluids, roles against bacteria/inflammatory response
    - Adipose (fat): supports/protects, reserve food fuel, insulates against heat loss
    - Reticular fibers: soft internal skeleton (stroma) supports other cells
  - Dense connective tissue
    - Dense regular: great strength (1 direction)
      - Tendons (cord, muscle-to-bone)
      - Ligament (cord, bone-to-bone)
      - Aponeuroses (sheets, muscle-to-muscle / muscle to bone)
    - Dense irregular: great strength (many directions)
    - Elastic: recoil after stretch, eg pulsatile blood flow in arteries, lung bronchial tubes post-inspiration
    - Cartilage: avascular, tough/flexible/no nerve fibers,
      - GAGs + collagen/elastin fibers + cells + 80% H2O
        - Chondroblasts: produce new matrix until skeleton stops growing at the end of adolescence
        - Chondrocytes- mature cartilage cells
      - Types of cartilage
        - Hyaline: supports/reinforces/cushions
        - Fibrocartilage: absorbs compressive shock, withstands pressure, supports
        - Elastic: maintains shape but allows flexibility



Diagrams

- Cellular organization: Atom to molecule to cell to tissue to organ to organ system to organismal level

Plasma membranes and membrane transport

Keywords

- Biological markers: every cell type has unique carbohydrate pattern in glycocalyx and glycoproteins can detect this.
    - With cancerous cells, glycocalyx is continually changing, thereby avoiding immune system destruction
- Cadherins: cell to cell joining (eg desmosomes)
- Integrins: attach cells to cytoskeleton and extracellular matrix
- Plaques
- Keratin filament
- Connexons: hollow tubes made up of transmembrane proteins
- Simple diffusion: passes through hydrophobic core of membrane
- [facilitated diffusion]: assisted by a carrier molecule
- aquaporin special membrane channels for water in red blood/kidney cells
- Symported - move in same direction

Concepts

- Homeostatic imbalance
- Phospholipid bilayer
    - Thin 7-10 nm
    - Proteins can move sideways and from one side to other
    - Separates body's two major fluid compartments intracellular and extracellular
- Lipids of the plasma membrane
    - Phospholipids 75%: 2 parallel sheets, molecules lying tail to tail
    - Glycolipids (5%) - lipids bonded to sugars
    - Cholesterol (20%) - stabilizes membrane
- Communication between outside/inside environments
    - Two distinct types
        - Integral Transmembrane protein: embedded within lipid bilayer
            - Protrude from one membrane face or are transmembrane
            - They are either channels, carriers, enzymes, or receptors for 'chemical messenger' hormones
        - Peripheral:
            - Loosely attached to membrane
                - Role: support membrane, link cells, change cell shape during cell division and muscle contraction, enzymes
- Cell junctions
    - A few types of cells (blood cells, sperm cells, immune system cells, certain cancer cells 'metastases' can move freely through bloodstream
    - Three factors involved in cells being held together tightly
        - Adhesive glycoproteins in glycocalyx

- ‘Tongue-in-groove’ fit between wavy contours of adjacent membranes (zig zaggy to fit together)
- Special junctions
    - Tight junction
        - Prevent passage of molecules and ions through extracellular space between adjacent cells
            - Eg cells of GI tract to keep digestive enzymes out of blood
            - Although “impermeable” some are leaky and allow small ions to pass

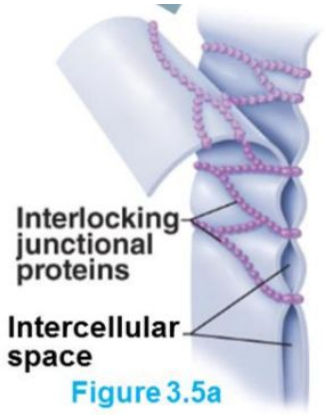


Figure 3.5a

    - Desmosomes
        - Mechanical anchoring junctions
            - Like rivets along sides of cells to prevent separation
            - Linker proteins (Cadherins) attach to plaques inside cell
            - Zipper-up adjacent cells in intercellular space
            - Keratin filaments attach to plaque inside wall and anchor to opposite wall

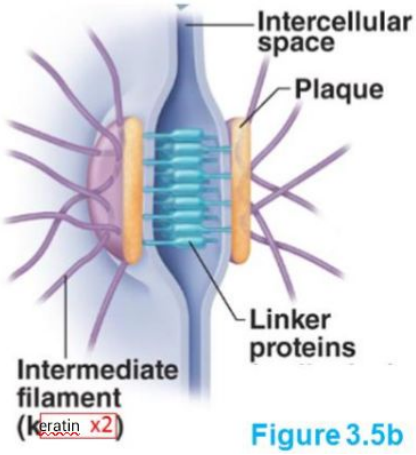
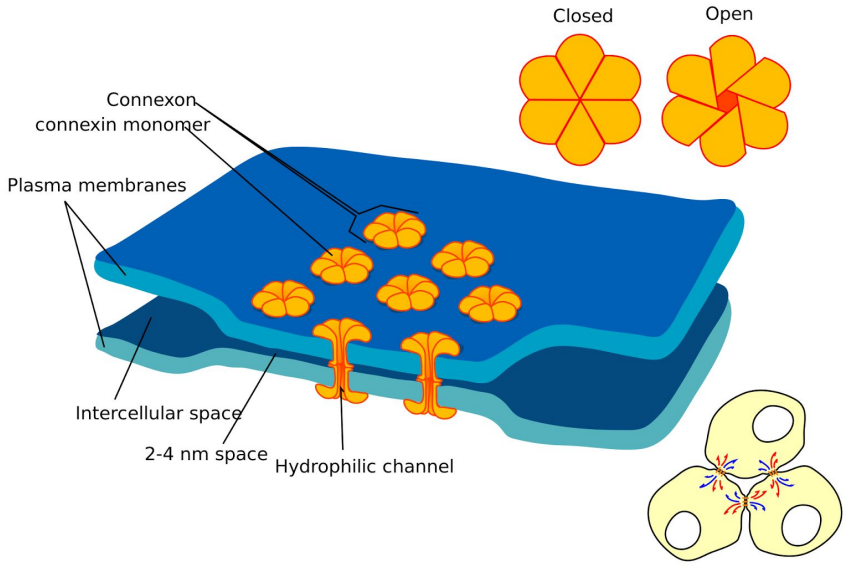


Figure 3.5b

- Gap Junction
  - Adjacent cells connected by channels (connexons) hollow tubes made up of transmembrane proteins
  - Selective because variety of connexon proteins
  - Channel allows passage of small size molecules (eg Na+, K+, small sugars)

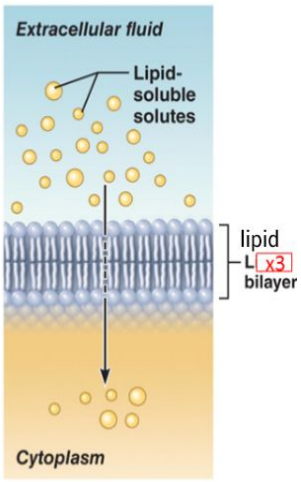


- Diffusion: movement of ions/molecules down a concentration gradient (high to low)
  - Kinetic energy
    - Constant, random motion
    - High speed motion
    - Scattered uniformly at equilibrium
    - Affected by concentration gradient direct proportionally

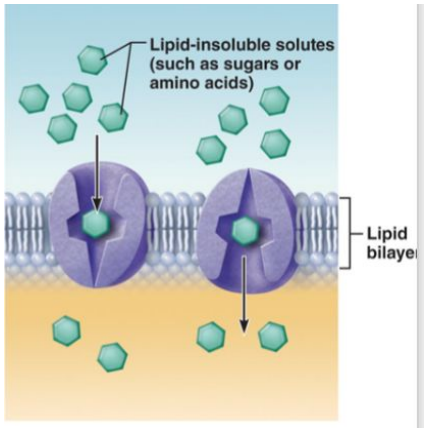
        - Affected by temperature directly proportionally \
        - Molecular size - inversely proportional

- Diffusion across plasma membrane
    - Selective/ differential permeability
        - Enter cell: nutrients (oxygen & glucose) yes*/ toxins - NO
        - Exit cell wastes yes*/ proteins - NO
    - *Ion/molecule will diffuse if it is:
        - Lipid soluble hydrophobic [Simple diffusion] passes through hydrophobic core of membrane
        - Small enough to fit through membrane channel, or assisted by a carrier molecule [facilitated diffusion].

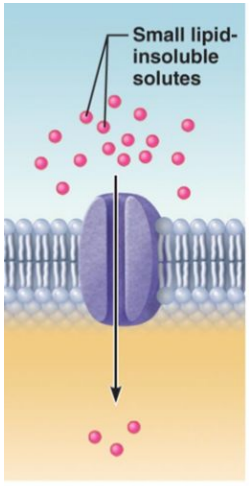
- Simple diffusion
    - Passively diffuse directly through lipid bilayer (plasma membrane)
        - Substances such as O2 and CO2



- Carrier-mediated facilitated diffusion
    - Passive diffusion via trans-membrane carrier proteins
        - Substances include
            - Polar, fat-insoluble molecules, eg sugars, amino acids
                - Too large to fit through membrane channels
            - As carriers change conformation (shape), solute passed through



- Channel-mediated facilitated diffusion
  - Passive diffusion via trans-membrane channel
    - Substances include: IONS (eg Na+, Ca2+)
    - Channel selective for pore size and charge (+ or -)
    - ‘Leakage channel’ so always open
    - ‘Gated channel’ controlled by chemical/electrical signals
    - Concentration gradient required

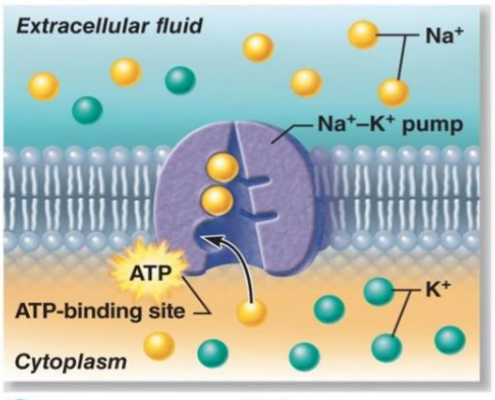


- Osmosis
  - Passive diffusion of water (or other solvent) through a semipermeable membrane
  - Water passes directly through plasma membrane and aquaporin special membrane channels in red blood/kidney cells
- Tonicity of a solution
  - Isotonic: static equilibrium

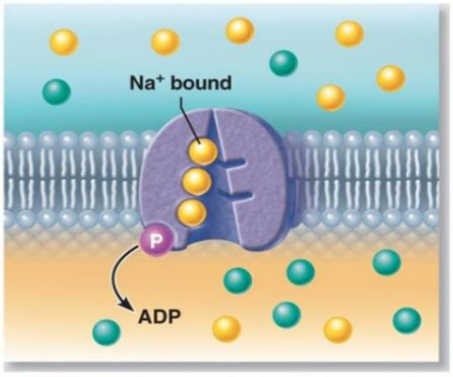
- Hypertonic: when particular solution that has a greater concentration of solutes on the outside of a cell when compared with the inside of a cell **Water rushes out of cell**
- Hypotonic: When particular solution has less concentration of solutes on the outside of a cell compared with the inside of a cell. **Water rushes into cell**
- Medical application: left leg edema, dehydration

- Active membrane transport
  - Cells need energy to move substances across membrane
    - Substances that are needed but too large for channel/ too polar for lipid bilayer and must be moved uphill against concentration gradient
  - Types of active transport
    - Primary active transport
      - Energy directly from hydrolysis of ATP
      - Works against conc gradient

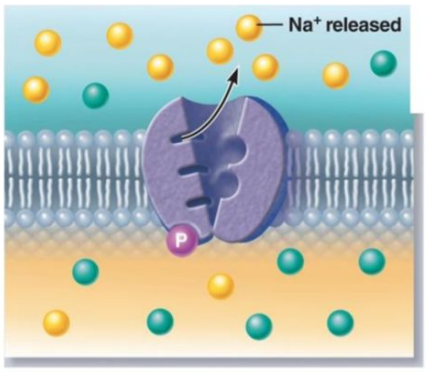
    - Secondary active transport
      - Driven indirectly by energy stored in ionic concentration gradients, created by primary active transport pumps
    - Vesicular transport
      - Solute transported inside membranous sacs
- Primary Transport: Transmembrane enzyme Na+-K+ATPase



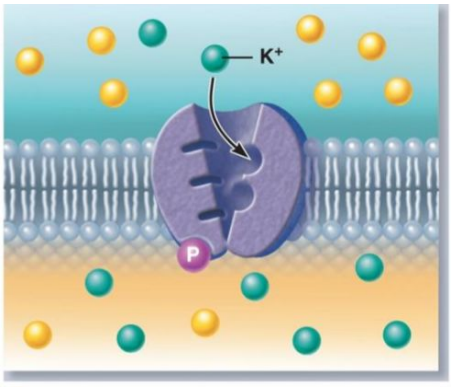
1 Three cytoplasmic X2 bind to pump protein.



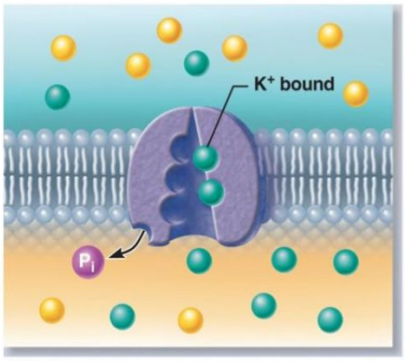
2 X2 binding promotes hydrolysis of ATP. The energy released during this reaction phosphorylates the pump.



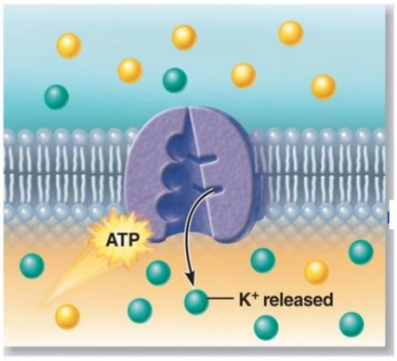
(3) Phosphorylation causes the pump to change shape, expelling Na^+ to the outside



(4) Two electrons K^+ bind to pump.

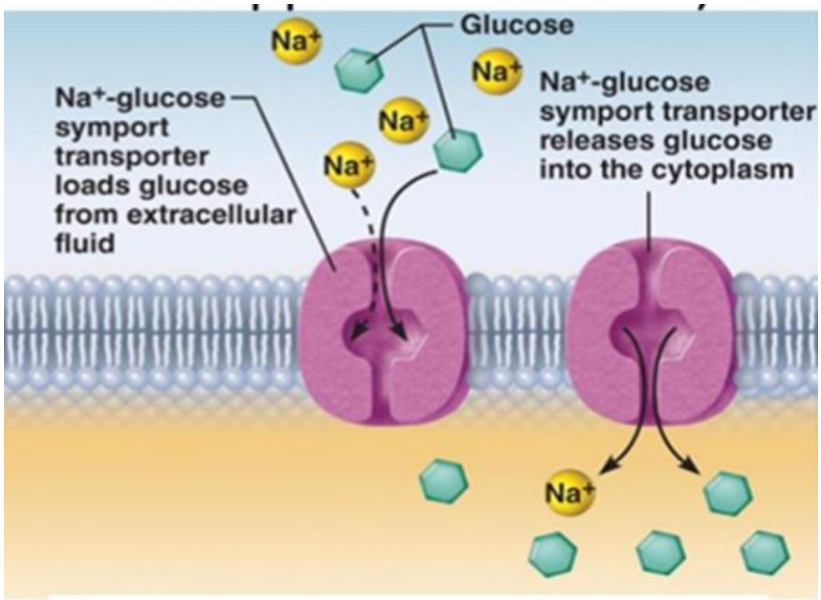


(5) K^+ binding triggers release of the phosphate. The dephosphorylated pump resumes its original conformation.



(6) Pump protein binds ATP; releases K^+ to the inside, and Na^+ sites are ready to bind Na^+ again. The cycle repeats.

- Secondary transport



② **Secondary active transport**
As Na^+ diffuses back across the membrane through a membrane cotransporter protein, it drives glucose against its concentration gradient into the cell.

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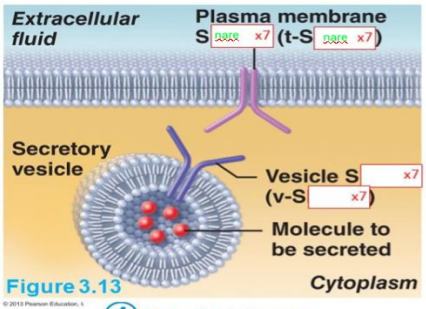
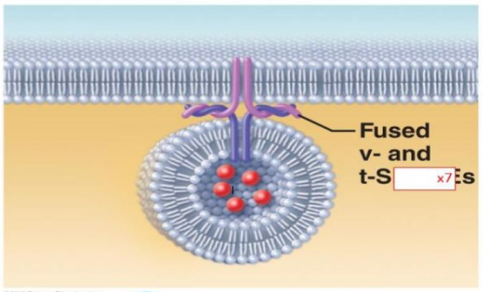
- Vesicular transport
    - Fluids containing large particles/macromolecules transported across plasma membrane <u>inside membranous sacs</u> called vesicles
        - Endocytosis: move substance into cell
            - Phagocytosis
                - Cell engulfs relative large solid material and brings it inside
                    - 1. Material binds to cell surface receptors
                    - 2. Pseudopod form and flow around material
                    - 3. Vesicle detaches. Phagosome moves into cell with material inside
                    - 4. Phagosome fuses with a lysosome and contents digested
            - Receptor-mediated endocytosis
                - Specific mechanism for endocytosis of most macromolecules
                    - Substance binds to specific receptor
                    - Exquisitely sensitive mechanism allows cells to concentrate material present in only small amounts of intracellular fluid

- Infectious pathogens (flu viruses, cholera toxin) can also enter cell through this mechanism
    - Once inside cell, material can be released for further action or digested with a lysosome.
- Pinocytosis
    - Cell ‘gulps’ a droplet of extracellular fluid containing dissolved molecules
    - 1. Vesicle forms
    - 2. Detaches, moves into cell, and fuse with an endosome
    - No receptor used, so process is relatively non specific
    - Pinocytosis is a routine activity of most cells compared to phagocytosis
    - Non specific way of sampling extracellular fluid
- Exocytosis: move substance out of cell

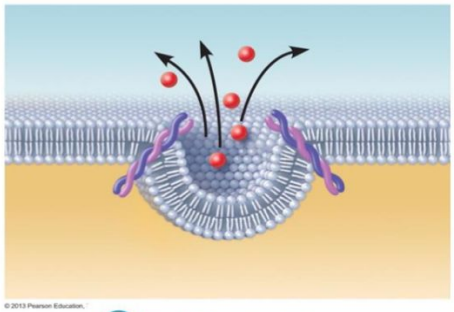


1 The membrane-bound vesicle migrates to the plasma membrane.



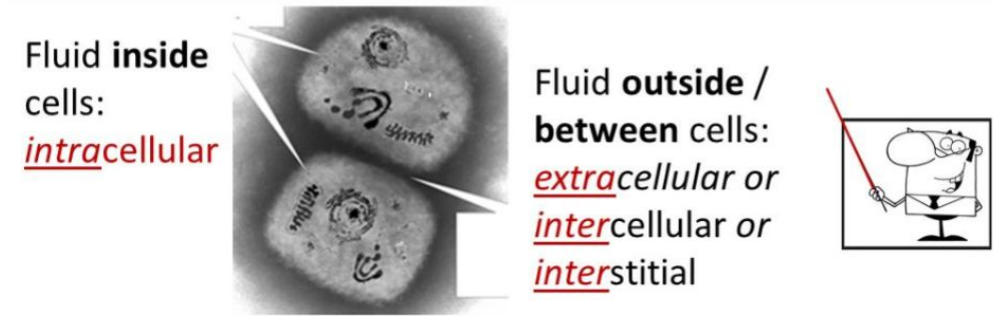
2 There, proteins at the vesicle surface (v-S s) bind with t-S s (plasma membrane proteins).

3 The vesicle and plasma membrane fuse and a pore opens up.

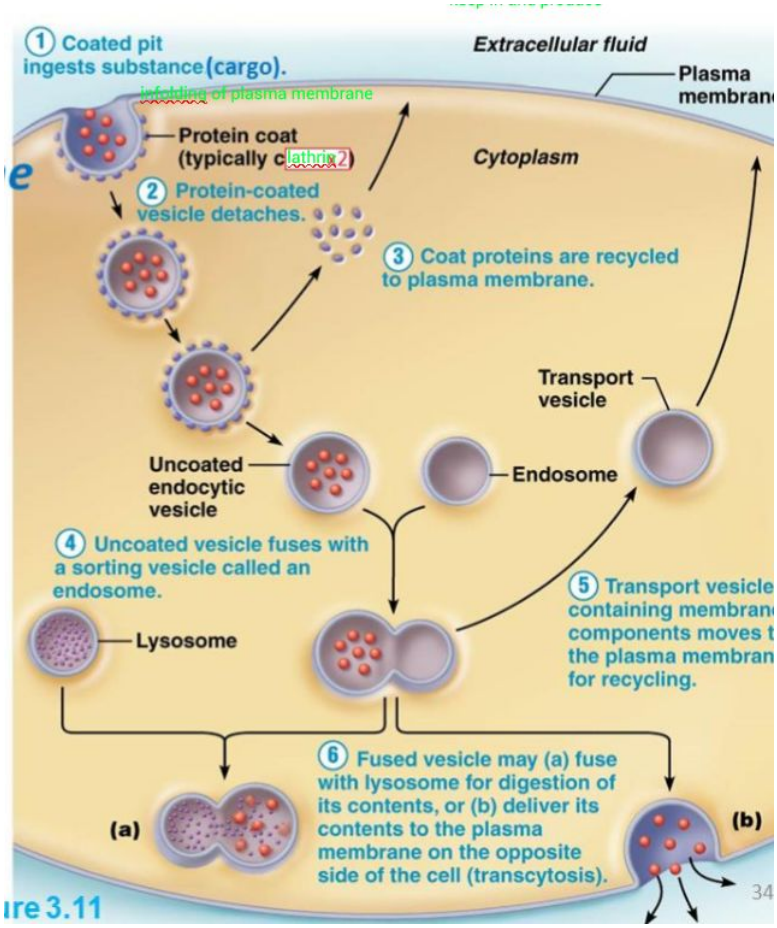

4 Vesicle contents are released to the cell exterior.

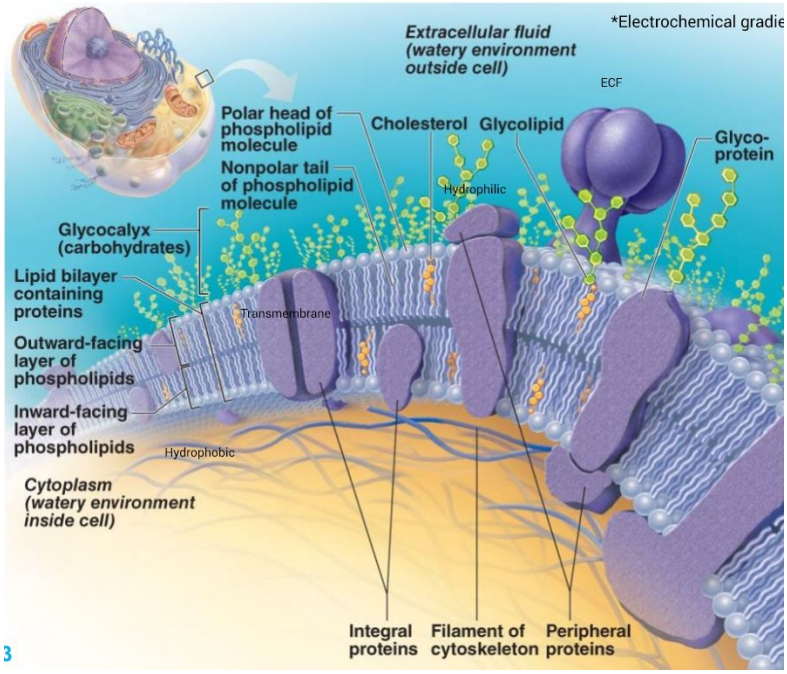
- Transcytosis: move substance in, across, and out of cell
- Vesicular trafficking: move substance around within cell

Diagrams



Endocytosis





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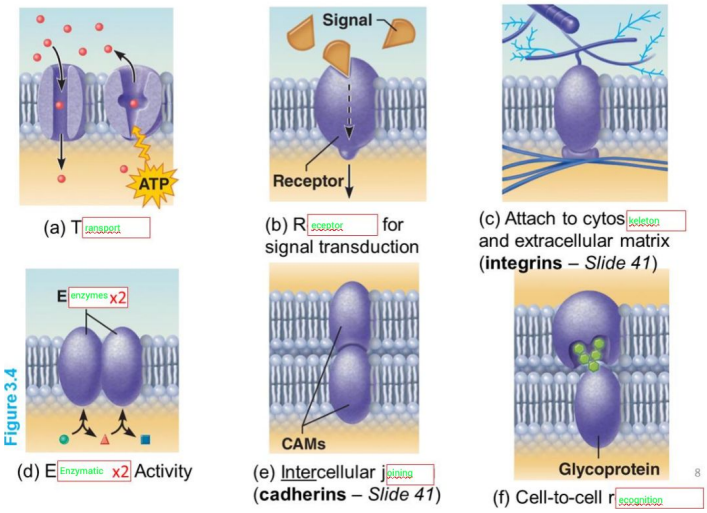


(a) T ransport

(b) R eceptor for signal transduction

(c) Attach to cytos keleton and extracellular matrix (**integrins** – *Slide 41*)

Figure 3.4

(d) E Enzymatic x2 Activity

(e) Intercellular j oining (**cadherins** – *Slide 41*)

(f) Cell-to-cell r ecognition

8

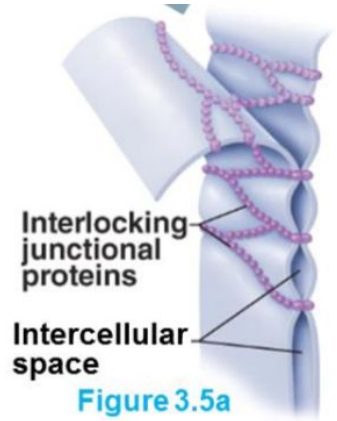


Figure 3.5a

Nervous system & Nervous Tissue

Keywords

- Neuron: highly specialized structural units of nervous system that conduct messages-nerve impulses-through body
- Nuclei: cluster of cell bodies in CNS
- Ganglia: cluster of cell bodies in PNS
- Axodendritic
  - Information between axon of one nerve and dendrite of next nerve
- Axosomatic
  - Info between axon and effector cell (eg nerve/muscle/gland)
- Axoaxonal (rare)
  - Info between axon of one nerve and axon of next nerve
- Dendrodendritic (rare)
  - Info between dendrite of one nerve and dendrite of next nerve
- Somatodendritic (rare)
  - Info between dendrite and effector cell (nerve/muscle/gland)

Concepts

- Homeostatic imbalance: neurofibrillary tangles from collapsed microtubules: biomarker for alzheimer's. Collapsed cell structure neurons.
- Homeostatic imbalance: retrograde transport 'hijacked' because bad viruses (herpes viruses), tetanus toxin reach and destroy cell body via retrograde transport
- Homeostatic imbalance: multiple sclerosis body's immune system attacks myelin sheath proteins
  - Symptoms visual disturbance, blindness, weakness/clumsiness. Paralysis, speech impairment
- Homeostatic imbalance: chemical/physical factors can impair nerve propagation
  - Local anaesthetics (lidocaine used by dentists) block voltage-gated Na+ channels
    - No Na+ entry, no action potential, therefore no pain
  - Cold/local pressure
    - Interrupt blood flow to neuron processes
      - Reduced ability to conduct nerve impulses
- Homeostatic imbalance: muscle dystrophy
  - Degenerate muscle atrophy/ fat up and connective tissue
  - Most common: duchenne muscular dystrophy
    - Sex linked, recessive
    - Defective gene for dystrophin
      - Stabilize scarlemma

        - Muscle contractions tear
        - Contractile fibers/CT sheath damaged by immune attack
    - No cure
    - Current treatment: prednisone and other immunosuppressants
    - Injection of myoblasts

➔ Effects of aging on muscle

- Muscle cells/fibers decrease, connective tissue increase
- Sarcopenia begins by age 30 in healthy
- 50% loss by age 80
- Intermittent claudication
    - From atherosclerotic blocking of extremity arteries
    - Reduced blood flow to leg muscle

➔ Neuron

- Three special properties
    - Extreme longevity - can function optimally overtime if free of disease
    - Amitotic - cannot divide/ be replaced if destroyed
        - Exception: olfactory epithelium, hippocampus (memory) have stem cells
    - Exceptionally high metabolic rate
        - Demand O2/Glucose continuously
- Nerve cell body
    - Cell body, nucleus, nucleolus, cytoplasm
        - Ribosomes, rough ER, golgi apparatus most active/best developed in body: protein and membrane making machinery
        - Mitochondria scattered throughout
    - Dendrites
        - Short, tapering, diffusely branched
        - Typically hundreds per neuron
            - Bristle with tiny dendritic spikes
                - Where dendrite synapses with other neurons
        - Main receptive or input region for neuron
            - Convey incoming messages toward cell body
                - Signals travel via graded potential, NOT ACTION POTENTIALS
            - All organelles in cell body are also in dendrite
    - Axon structure
        - Each neuron has a single axon (and many dendrites)
            - Branches called axon collaterals
    - Axon functional characteristics

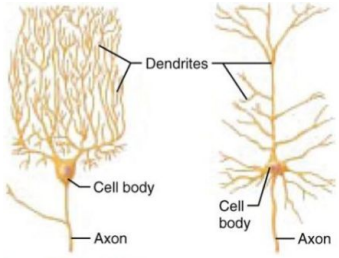
        - Conducting region of neuron
        - Generates/transmits nerve impulses away “typically”, from cell
            - Along plasma membrane ‘axolemma’
            - From trigger zone to terminal secretory region

- Transport along the axon
    - Moving molecules along the axon length may appear difficult, however through the cooperation efforts of motor proteins and cytoskeletal elements (microtubules and actin filaments), substances travel continuously along the axon in both directions
    - Anterograde movement away from cell body
        - Mitochondrial, membrane components used to renew the axon plasma membranes, and enzymes
    - Retrograde movement towards cell body: organelles for recycling, signalling molecules
        - Organelles returning to the cell body to be degraded or recycled.
    - Use ATP=dependent motor proteins kinesin/dynein
        - Components move along microtubules at speeds up to 40 cm/day
- Myelin sheath
    - Many nerve fibers in CNS/PNS, especially larger and longer ones, covered with segmented myelin sheath
    - Composition lipids + proteins
    - Function
        - Protection
        - Electrically insulates
        - Increases speed of nerve transmission

- Structural/functional classifications
    - (Structurally Bipolar
        - 1 axon/ 1 dendrite
        - Rare only in special organis (nose, eye, ear)
    - All sensory functional class

    - Structural: multipolar
        - 1 axon/many dendrites

- Most common 99%



- Functional class
  - Most are interneurons - connect sensory (afferent) input with motor (efferent) output
  - Some are motor neurons from CNS to muscle/gland

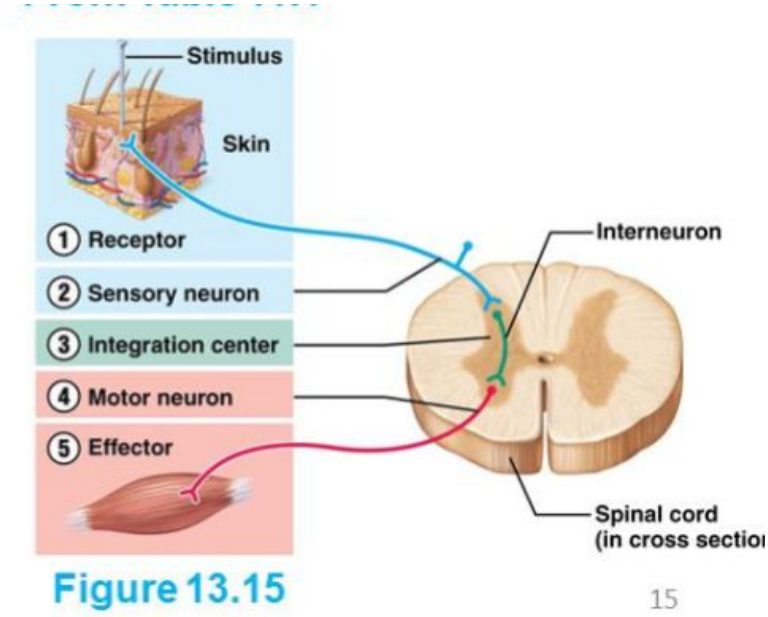


Figure 13.15

15

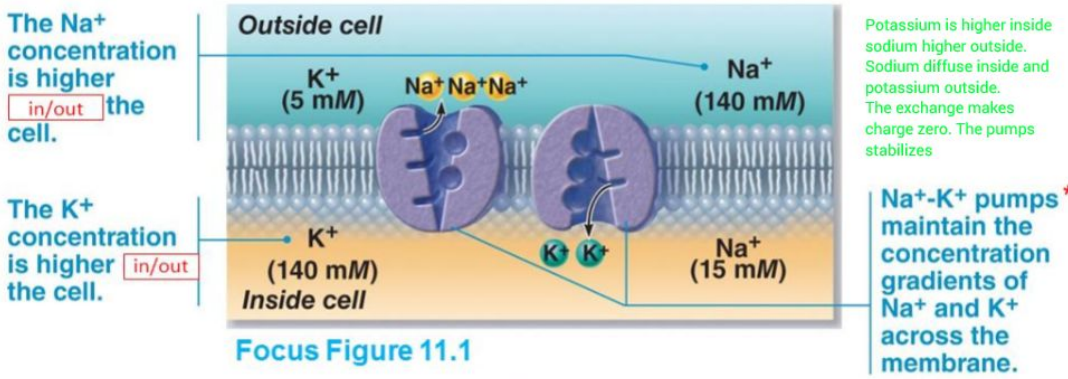
- Structural - unipolar
  - Single short process emerges from cell body, divides T-like into:
    - Central process conducts impulses away from cell body
    - Peripheral process "perplex" the impulse
      - Generates/conducts impulses, myelinated, microscopic appearance: 'axon'
      - Conducts impulses toward cell body: dendrite
  - Functional classes: Most sensory → CNS

➔ Membrane ion channel
- Gated - open or closed
  - Leakage - always open

- Chemically - gated: chemical (eg neurotransmitter binds)
- Voltage - gated: change in membrane potential
- Mechanically gated - deformation, eg by touch

➔ Resting membrane potential -40 to -90 mV

- Cytoplasm inside negatively charted to outside positively charged
- Membrane 'polarized'
- Two factors that generate resting potentials
  - Difference in ionic compositions of the intracellular and extracellular fluids → concentrations and amount
    - ***[1] Differences in Ionic Concentration***
      - Concentrations of Na^+ and K^+ on each side of the membrane are different



Focus Figure 11.1

      - Without Na+-k+ pumps, concentration gradients and resting potential/all neuronal signaling would disappear.
  - Differences in plasma membrane permeability ie changes in number of channels open to Na + and K+

    Case 1: leaky
    - Ions flow down their concentrations gradients, k+ is more leaky and more permeable to the membrane. It establishes a negatively charged inner membrane surface.
    - Na+ in because offset of charge inside.
    - Result: net -ve inside/resting membrane potential of -90 mV

    Case 2: adding na+ channel
    - Adding a Na+ channel through leakage balances to -70 mV more positive ions inside

    Case 3: adding a Na+-K+pump

        - Maintains the concentration gradients resulting in a consistent -70 mV

➔ Changing resting membrane potential
- ◆ Change produced by altering permeability of membrane
    - Give rise to two types of signals
        - Graded potentials (GPs)
        - Action potentials (APs)
- ◆ Depolarization: Decrease in potential towards positive zero, but increased probability of nerve signals
- ◆ Hyperpolarization charge becomes more negative and decreases probability of nerve signals

➔ Graded potentials
- ◆ Brief, short-distanced signals within neurons
- ◆ Magnitude/distance vary with stimulus strength, hence 'graded'
- ◆ Current dies out within a few mm of its origin, but GPs are essential in initiating long distance APs

➔ Action potential
- ◆ Transmit nerve signals over LONG distances
    - From trigger zone at axon hillock through entire length of axon (few mm to over a meter)
- ◆ Begins with a brief - but more intense- depolarization of short patch of membrane
- ◆ **Do not decay with distance**
- ◆ Typically seen only in axons part of neurons
    - Axon hillock and axon
- ◆ Begin as Graded potentials in dendrites/cell bodies

➔ Changes in membrane potential
- ◆ As AP moves down axon, voltage changes occur
    - 1. Resting state (-70 mV)
    - 2. Depolarization (+30 mV)
    - 3. Repolarization (-70 mV)
    - 4. Hyperpolarization (~ -80 mV)
        - Na +channels close/inactivated after

➔ Voltage gated channels

- AP with changes in membrane potential will open/close channels

➔ Action potential: All or none phenomenon
- Depolarization must reach a threshold value or axon will not fire
  - When matches become hot enough (Enough Na+ enters cell), they reach a flash point (threshold)
  - Flames will consume all the matches even if original removed (AP propagated even if stimulus removed)

➔ Graph terminology

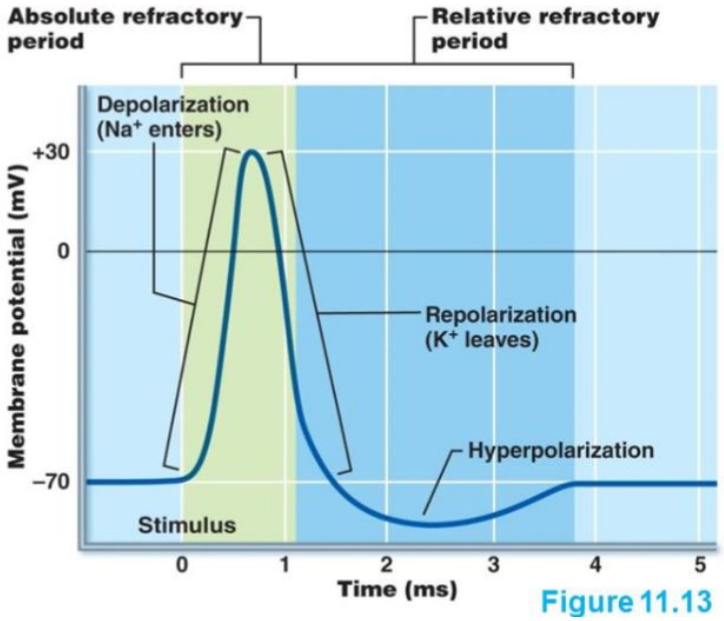


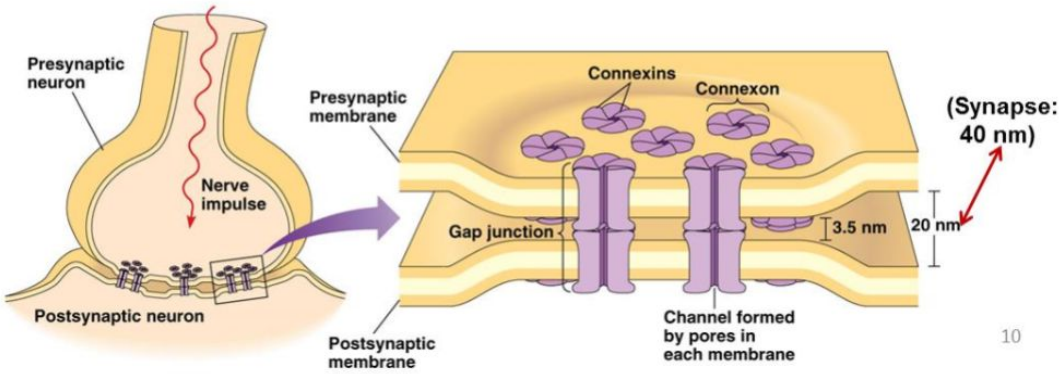
Figure 11.13

- Absolute refractory period: threshold for new AP prohibitively high
- Relative refractory period: most Na+ and K+ channels reset. Very strong stimulus can make AP
- Enforce one way transmission of AP

➔ Conduction velocity
- Depends on axon diameter
  - Larger = faster
- Depends on degree of myelination
  - More = faster

➔ The synapse
- Presynaptic neuron
  - Sends information and conducts impulse towards synapse
- Postsynaptic neuron
  - Receives information and conducts impulses away synapse

- Two kinds
  - Chemical synapse
    - Separated by synaptic cleft
  - Electrical synapse
    - Direct cell-to-cell
    - Presynaptic and postsynaptic neurons direct contact
    - Gap junction with connexon protein channels - connect cytoplasm
    - Chemical messengers flow through channels (Cl-, small molecules)
    - Can be uni/bidirectional



    - Can be uni/bidirectional
    - Communication between cells is very RAPID
    - Quite rare
      - hippocampus in brain (memory/emotion)
      - Responsible for stereotyped (repeating pattern movement, eg normal jerky eye movements
      - Very common in embryo build CNS development

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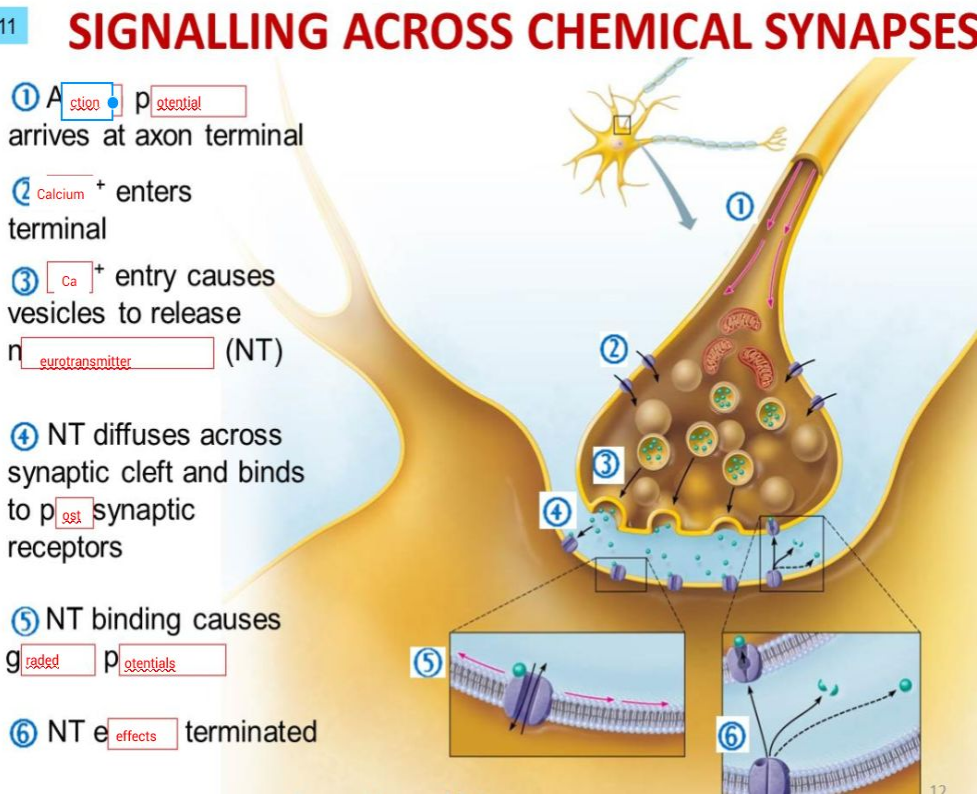


- The effect of calcium
  - Interacts with snare proteins on vesicles/axon membrane
  - Vesicles fuse with membrane
  - Neurotransmitters empty into synaptic cleft
    - 300 vesicles/nerve impulse
    - Stimulus up, impulse up
  - Ca2+ taken out by mitochondria or pumped out of axon

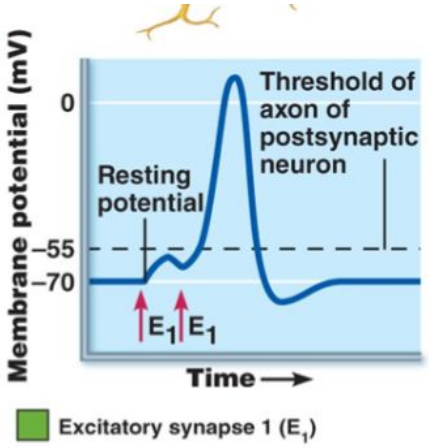
- Termination of neurotransmitter effects
  - Binding of NT (eg norepinephrine, serotonin) to its receptor is reversible (bind, come off-, rebind)
  - Outcomes
    - Reuptake
      - Back into presynaptic terminal, will be reused/destroyed
    - Degradation
      - Degradation by enzymes from presynaptic membrane or in synapse (eg acetylcholine)
    - Diffusion
      - Away from synapse

- Synaptic delay
    - Speed of nerve impulse down axon 150 m/s
    - Neural transmission across synapse
        - 0.3-5.0 milliseconds
        - Rate - limiting step
- Postsynaptic potentials
    - After NT binds to dendrite/neural cell body membrane,
        - Chemically gated ion channels open and differ from voltage-gated that cause action potentials
            - Chemically gated… no self-generating/amplifying channel opening
            - Graded potentials result
                - Vary in strength depending on amount of NT
- Excitatory and inhibitory synapses
    - Excitatory synapses, NT binding depolarizes membrane
        - Causes graded potential as chemically-gated ion channels open and Na+ flows in/K+ out, but since Na+ in > K+ out there is net depolarization but not enough depolarization to generate an action potential
        - Excitatory postsynaptic potential (EPSPs) are local graded potentials
            - Can turn into action potential if there are enough EPSPs, then axonal voltage gated channels open, action potential generated
                - Short-lived but can reach axon hillock

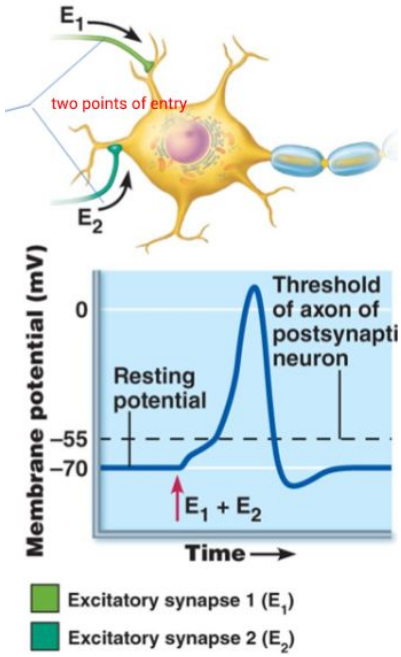
    - Inhibitory synapses and IPSPs (inhibitory postsynaptic potentials)
        - NT binds to dendrite/neural cell body membrane, opening chemically-gated ion channels
        - Cl- flows in or K+ flows out, either causing hyperpolarization more neg
        - As potential driven further from axon's threshold value, postsynaptic neuron is Less likely to fire, causing inhibitory effects

    - No effective summation
        - A single excitatory postsynaptic potential can't induce an AP in the postsynaptic neuron if its membrane potential does not reach threshold value
        - 2 excitatory stimuli separated in time cause subthreshold EPSPs that do not add together, no action potential results
        - ONLY if many EPSPs fire on same postsynaptic membrane, or smaller number fire rapidly, summation may cause the AP threshold to be reached

- Temporal summation of EPSPs

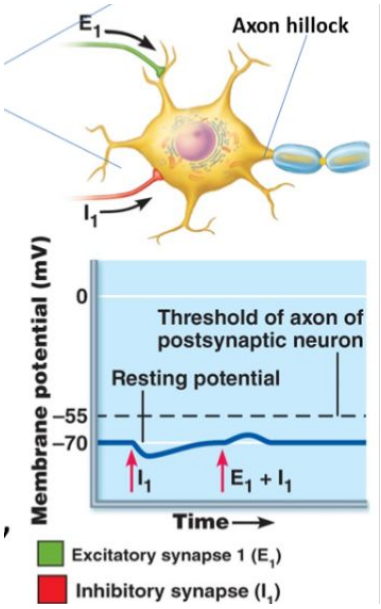


  - One or more presynaptic neurons transmit impulses in rapid-fire order
    - Bursts of NT released in quick succession
    - Before EPSP from 1st impulse dissipates, next impulse triggers another EPSP
    - EPSPs summate (cumulative), threshold reached, AP produced
- Spatial summation of EPSPs



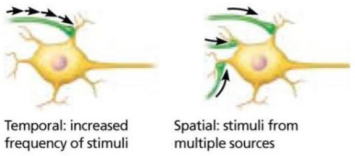
  - Postsynaptic neuron stimulated at the same time by large number of terminals
    - Many of its receptors bind NT - all simultaneously initiate EPSPs
  - EPSPs summate and dramatically enhance depolarization

- Spatial summation of EPSPs and IPSPs



  - Changes in membrane potential can cancel each other out
  - Excitatory synapse is on dendrite, inhibitory synapse is on cell body
- Synaptic potentiation
  - Repeated use of synapse increases presynaptic neuron's ability to excite postsynaptic neuron; larger-than-expected EPSPs ('long term potentiation)
  - Learning process increases efficiency of transmission along certain pathway
    - Eg hippocampus - key learning/memory center
      - An instant of synaptic plasticity
- Presynaptic inhibition
  - When release of an excitatory NT by one neuron is inhibited by activity of another

Comparison	Graded potential	Action potential
Location	Cell body, dendrite	Axon hillock and axon
Distance travelled	SHORT: across cell body to axon hillock (0.1 - 1.0 mm)	LONG: 1mm to 1 meter
Amplitude (size)	-Graded, depends on stimulus And amount of NTs -Decays with distance	-Stays at the same potential throughout when travelling -Always same (all-or-nothing)

		-Doesn't decay with distance
Ion channels opened by	-Chemical (neurotransmitter) -Sensory stimulus (light)	-voltage - depolarization, triggered by GP reaching threshold
Summation	-yes stimulus responses can summate  Temporal: increased frequency of stimuli Spatial: stimuli from multiple sources	No, (all or none phenomenon)

Comparison	Graded action potential	Action potential
Function	Short-distance signalling that can spread to axon hillock, moving membrane potential either towards EPSP or away from threshold (IPSP), generating an AP	Long distance signally - constitutes the nerve impulse
Initial effect on stimulus	-EPSP: opens chemically gated channels for simultaneous NA+and K+ influx	-Opens voltage gated channels-first for NA+ than for K+
Peak membrane potential	ESPS Moves → 0 mV IPSP Moves → -90 mV	+30 to +50 mV

- Classification by structure
    - Acetylcholine (Ach)
        - CNS - memory

        - PNS - neurons that stimulate skeletal muscle and autonomic nervous muscle
    - Biogenic amines
        - Norepinephrine, dopamine, serotonin, histamine…
        - Movement, emotion, and behaviour (Mood disorders, schizo)
    - Amino acids
        - GABA: principle inhibitory NT in CNS - role in anxiety disorder
        - Glutamate - principle excitatory NT in CNS
        - Glycine - principle inhibitory NT in spinal cord
    - Neuropeptides
        - Endorphins and enkephalins - brain's natural opiates
        - Pain mediator
    - Purines
        - ATP
        - Adenosine
    - Gases
        - Nitric oxide, carbon monoxide
        - Small, short lived, toxic
        - NO relaxes smooth muscle
    - Lipids
        - Endocannabinoids - brain's natural marijuana

- **<u>Function of a NT determined by receptor it binds to</u>**
    - Classification by function - effects
        - Excitatory
        - Inhibitory
    - Classification by function -action
        - Directly (bind to open ion channels - rapid response)
        - Indirectly (via G protein 2nd messenger - long lasting)
        - Neuromodulator - indirectly affects synaptic transmission strength
            - Presynaptic: effects synthesis/release/reuptake/degradation of NTs
            - Postsynaptic: alters membrane NT sensitivity
            - Release from one cell, acts on many other

- Neurotransmitter receptors
    - Channel-linked (ionotropic receptors)
        - Direct, simple, and fast
        - Receptor protein includes a chemically-gated ion channel

        - NT/ligand binding → conformation change
        - CHannel opens/ions flow
        - Membrane potential changes → GP/AP if excitation
    - At excitatory receptors, channels for Na+,K+,Ca++ depolarize
    - At inhibitory receptors, channels for Cl- cause hyperpolarization
- G protein-linked (metabotropic receptors)
    - Indirect, complex, FAST (hundreds of msec)/prolonged
    - G protein receptors are also transmembrane but contain no channels
        - NT/Ligand (1st messenger) binding
        - G protein conformational change
        - An enzyme is activated
        - Leads to production of a 2nd messenger
        - 2nd messenger changes membrane permeability by opening or closing ion channel

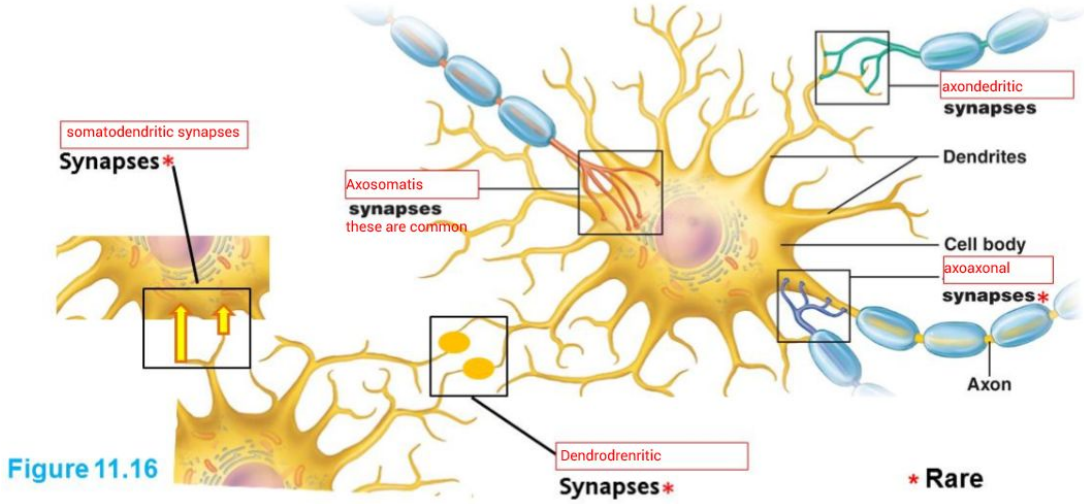


Figure 11.16

Cellular Physiology of Muscles

Keywords

- ➢ Skeletal muscle
- ➢ Cardiac muscle
- ➢ Smooth muscle
- ➢ Origin: point of attachment to immovable/less movable bone
- ➢ Insertion: point of attachment to bones that move
- ➢ Homeostatic imbalance: NMJ - myasthenia gravis
    - Antibodies to ACh receptor (autoimmune)

        - Symptoms: Ptosis upper eyelid droops, weak smile
        - Neck muscle weak
        - Diplopia (slurred speech,m general weakness late in day)
        - Slows down removal of ACh from synapse: attempt to make up for destruction of its receptors
- ➢ Homeostatic imbalance: stiffness of death: dying cells unable to pump out Ca++ against concentration so it stays in muscle.
    - Troponin and tropomyosin cannot act as inhibitory muscle constriction cause Ca 2+ is present. Troponin is the site of calcium regulation
    - Promotes formation of myosin cross bridges
    - Muscle begins to stiffen 3-4 hours after death

Concepts

- ➢ Special characteristics of muscle tissue
    - Excitability (Responsiveness)
        - Receives/responds to stimuli
            - Typically a neurotransmitter or a change in pH
        - Electrical impulse generated along cell membrane
    - Contractility
        - Shorten forcibly when stimulated
        - Unique to muscle tissue
    - Extensibility
        - Ability to stretch
        - Shorten when contracting but can stretch, even beyond their resting lengths when relaxed
    - Elasticity
        - Recoil to resting length after stretching
- ➢ Function
    - Produce movement
        - Skeletal: movement and manipulation
        - Cardiac: blood circulation
        - Smooth: maintains BP, propels food/urine/semen
    - Maintain posture/body position (unconscious action)
        - Skeletal muscles constantly counteract gravity
    - Stabilize/strengthen joints of the skeleton
    - Skeletal muscles generate heat (as they contract)
        - 40% of body mass - vital to maintain normal temp

- Smooth muscle forms valves, dilates/constricts pupils, moves hair follicles (piloerection)

	Skeletal	Cardiac	Smooth
Location	Attach to/cover bony skeleton	Walls of heart	Walls of hollow visceral organs (stomach, uterus)
Cell shape and appearance	-Single very long -Cylindrical, multinucleate cells with striations	-Branching chain of cells, uni/binueacleated -striated	-single, uninucleate, no striations
Voluntary	YES	NO	No
Contractions	Rapid and powerful, but tires easily. Light - heavy objects	Steady, controlled by internal pace maker, no need for nervous system	Slow and sustained
Function	For locomotion, manipulation of environment	Propels blood in circulation	Propels objects (eg food, urine, a baby_ Heart valves Pupil size

➢ Nerve and blood supply
- In general: one nerve, one artery, and one or more vein serve each muscle
- Nerve endings in muscle fibers control it activity
- Rich blood supply essential for contracting muscles
  - Huge amounts of energy, O2, nutrients consumed/quantity of metabolic waste
- Long networks of capillaries (smallest blood vessels) wind through muscle
  - Able to straighten when muscle stretches, control when muscle relaxes without affecting blood flow

➢ Connective tissue sheath
- Wrap muscle fibers, prevent bursting with contractions

- Three sheaths

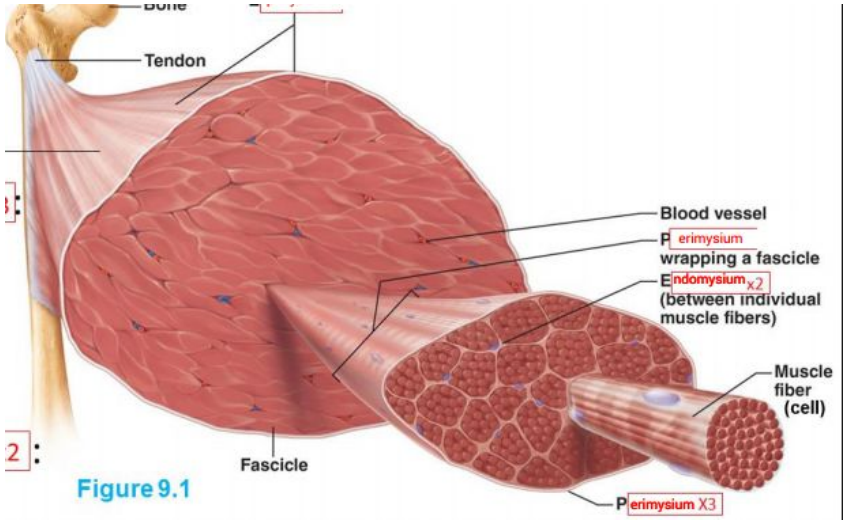
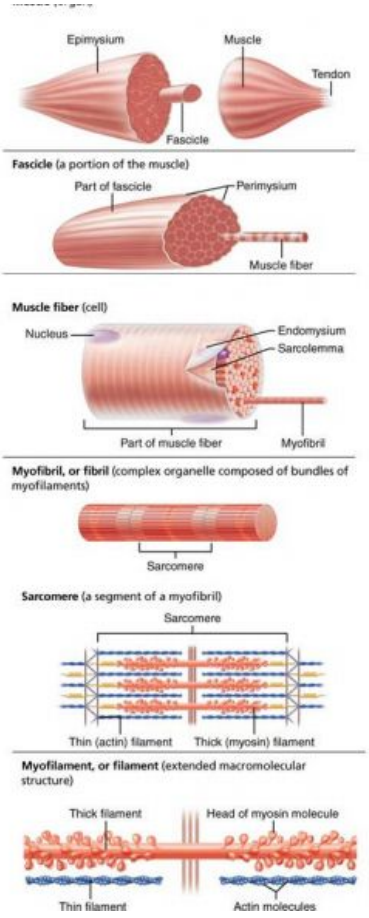


Figure 9.1

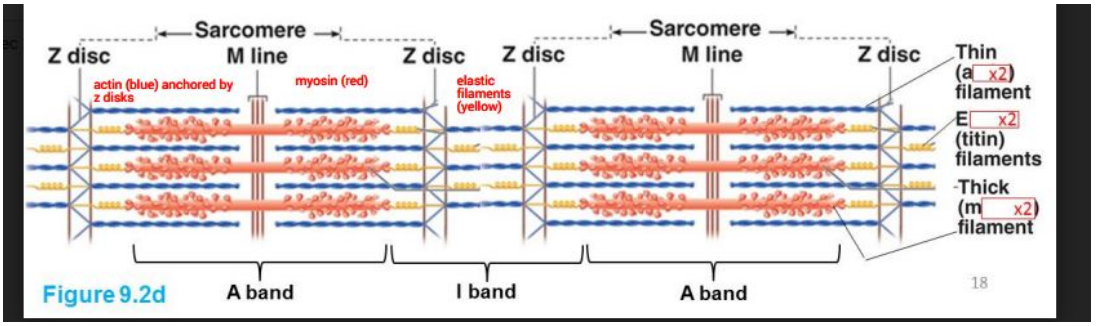
  - Epimysium: surround whole muscle
  - Perimysium: surround bundles of fibers (fascicles)
  - Endomysium: surrounds each muscle cell

➢ Muscle attachments and common terms
- Brachii example
  - Humerus is the origin stays put (bicep part)
    - Origin stays
  - Ulna is the insertion (moves)
    - Insertion is the movement of the attached bone
- Two types of attachments
  - Direct/fleshy: epimysium fused to bone/cartilage
  - Indirect: epi museum extends beyond muscle as rope (tendon) / sheet (aponeurosis) that attaches to bone/cartilage
- Muscle (organ): hundreds of thousands of muscle fibers (cell)
- Fascicle: a portion of the muscle: discrete bundle of muscle cells
- Muscle fibers (cell): elongated multinucleate cell
- Myofibril or fibril (organelle): rodlike contractile elements composed of sarcomere
- Sarcomere: the contractile unit made up of contractile thick and thin myofilaments
- Contractile myofilaments: actin bundles (thin myofilaments) and myosin bundles (thick myofilaments)

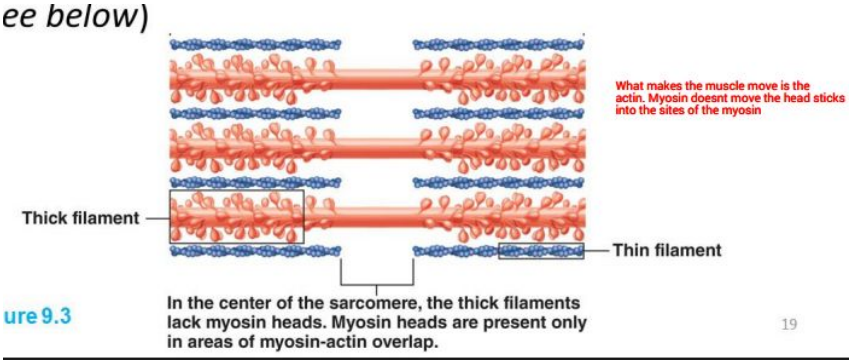


- Microscopic anatomy
  - Skeletal muscle cell/fiber
    - Long, cylindrical cells
    - Multiple nuclei
    - Plasma membrane sarcolemma
      - Under endomysium
    - Cytoplasm-special features
      - Many glycosomes
        - Glycogen granules
      - Large amounts of myoglobin
        - Red pigment that stores oxygen
      - Myofibrils
      - Sarcoplasmic reticulum, T tubules
- Myofibrils
    - Hundreds-thousands of rods, 80% cell volume.
    - Striation of dark and light band
- Striations and sarcomeres

        - Dark A band: H zone midsection with M line in centre
        - Light l band: z disc in center
        - Sarcomere: region between two z discs
            - Smallest contractile unit of a muscle fiber
            - Line up end-to-end along muscle
        - Note thick filaments inside sarcomere and thin filaments running between sarcomere
    - Myofilaments (aka filaments)
        - Lie side to side, connected by sarcolemma
            - Thin actin filaments anchored by Z discs (but not connected at M line)
            - Thick Myosin filaments connected at M line in middle of sarcomere
            - Elastic (titin) filaments run between z disc and M line and through centre core of myosin filament

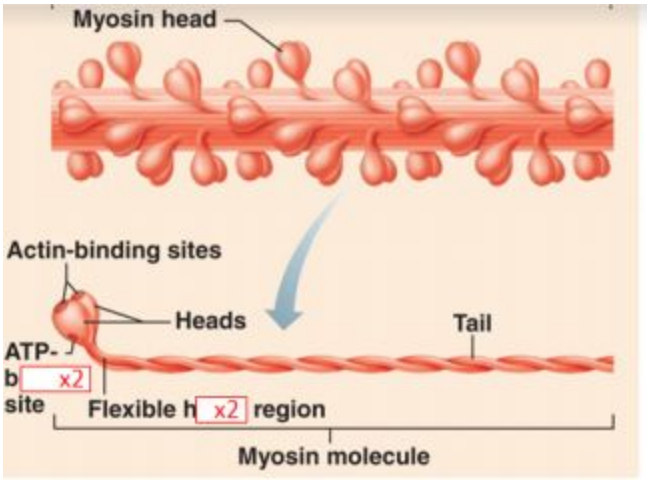


    - Myosin and Actin filaments setup to overlap
        - Each myosin molecule has head and tail
            - Thick myosin filament bundles ~300 myosin molecules together: tails intertwine centrally/head face out
        - Actin studded with sites into which myosin heads can fit



    - Myosin filaments
        - Myosin heads: ‘Business end’ of myosin

        - Contains actin binding sites at the end of a flexible hinge region
        - Also have ATP binding sites with ATPase activity
            - Can split ATP → ADP to generate energy for muscle contraction

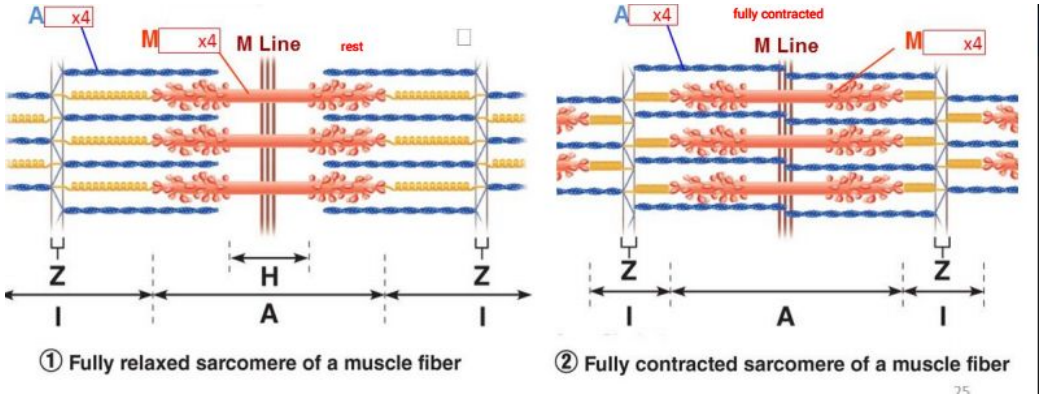


- Actin filament
    - Two strands of kidney-shaped actin subunits (globular actiné G actin) twisted into double helix
        - Contain active sites for myosin head attachment during muscle contraction
    - Contain three regulatory proteins
        - Tropomyosin
            - Spirals about actin core - stabilize/stiffens
        - Troponin
            - binds to actin, tropomyosin and Ca++, site of calcium regulation
        - Dystrophin
            - Links thin filaments to proteins in sarcolemma
- Sarcoplasmic reticulum
    - Sets of intracellular tubes vital to muscle contraction
        - Sarcoplasmic reticulum (SR) smooth endoplasmic reticulum of muscle cells, surround all myofibrils
            - Some are known as terminal cisterns
            - Stores/releases intracellular Ca+
            - Associated with glycogen granules and mitochondria
                - Produce energy needed for contraction
- T Tubules
    - Continuations of the sarcolemma

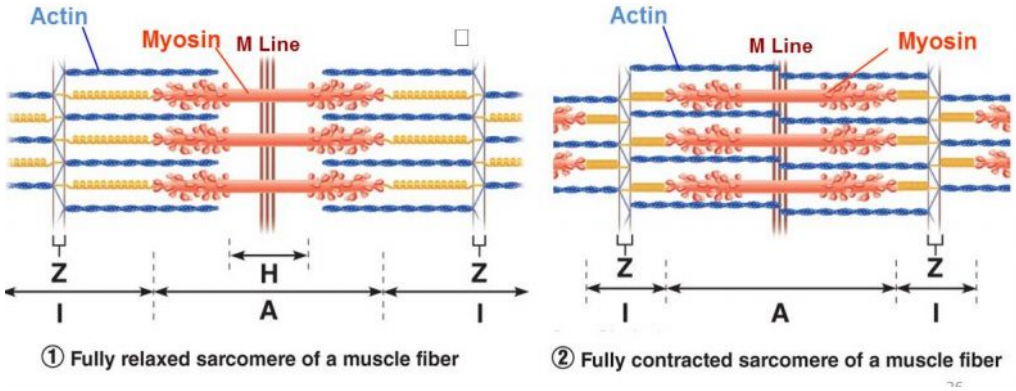
- Conducts nerve impulses/Ca++ to every sarcomere
- Triad 2 SRs + 1 T Tubule

➢ Molecular mechanism of skeletal muscle contraction

- 1. Relaxed sarcomere of muscle fiber
  - Actin (thin) and myosin (thick) filaments overlap only at the A band

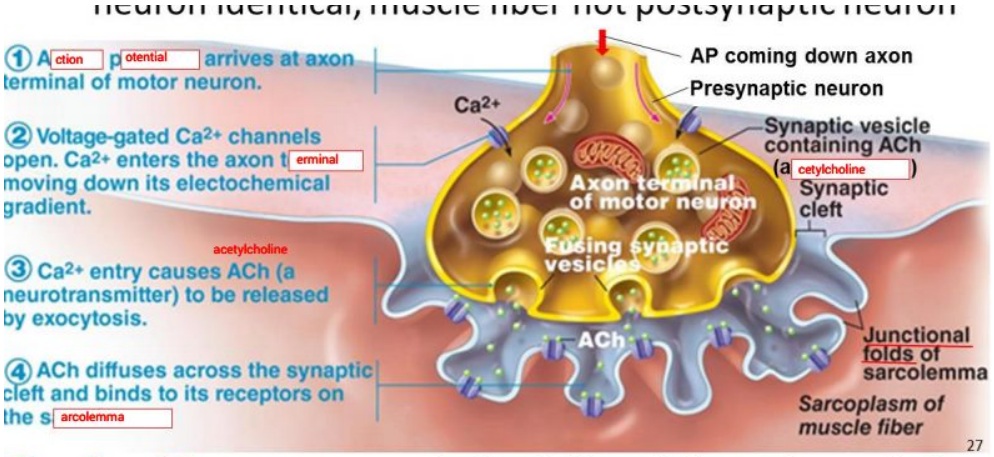


- 2. Contracted sarcomere of muscle fiber
  - Actin filaments have slide laterally. FUll overlap with myosin filaments. Attached Z discs pulled toward M line
  - L band shortens
  - Distance between z discs shortens
  - H zones disappear
  - A bands move closer together, length doesn't change



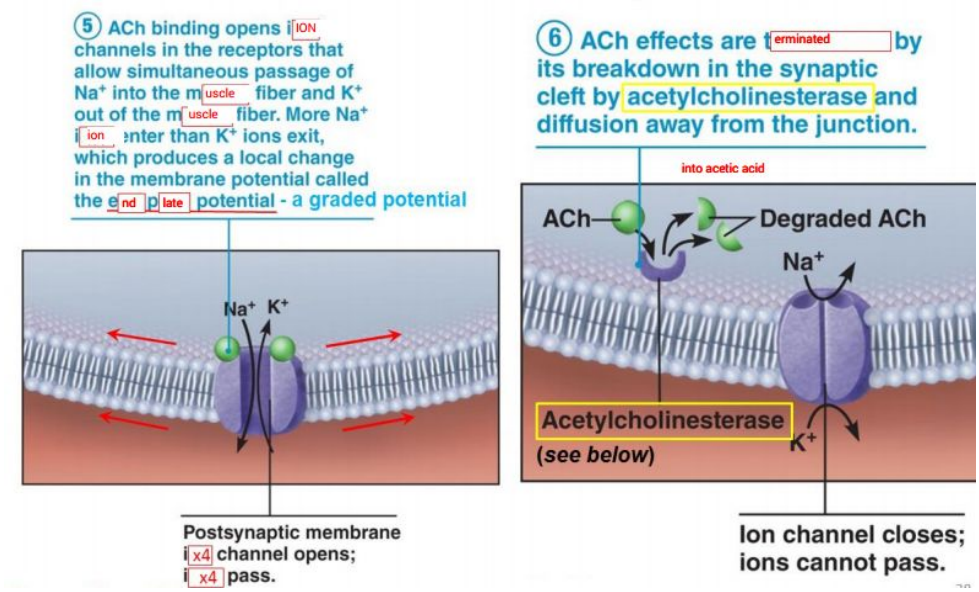
- Neuromuscular junction events
  - Stimulation of muscle fiber at neuromuscular junction
    - Action potential arrives at axon terminal of motor neuron
    - Voltage-gated Ca2+ channels open, CA2+ enters the axon terminal moving down the electrochemical gradient
    - Ca2+ entry causes acetylcholine to be released by exocytosis

- ACh diffuses across synaptic cleft and binds to its receptor on the sarcolemma
- ACh binding opens (ION channel) in the receptors that allow simultaneous passage of Na+ into the muscle fiber and K_ out of the muscle fiber. More Na+ ion enter than K+ ions exit, which produces a local change in the membrane potential called the end plate potential (graded potential)
- ACh effects are terminated by its breakdown in the synaptic cleft by acetylcholinesterase and diffusion away from the junction



Focus Figure 9.1

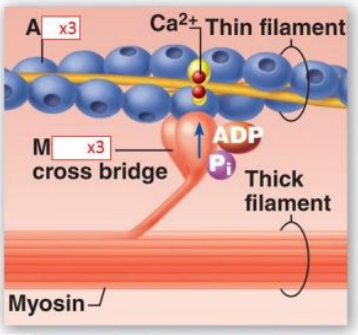
Junctional folds provide large surface area for the millions of ACh receptors located along sarcoplasm



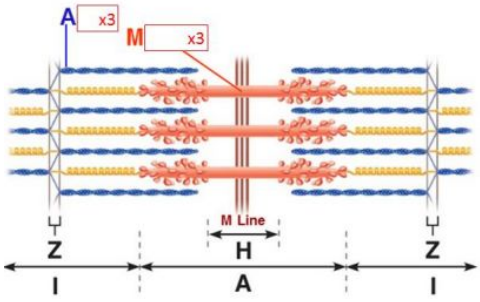
- Action potential results from end plate potential (5)
  - Depolarization: end plate potential ignites AP: spread to adjacent membrane areas and opens Na+ channels

- Repolarization/hyperpolarization: Na+ channels close and K+ channels open
    - Muscle fiber refractory: cant’ be restimulated
- As AP spreads in one direction (few ms), → contraction of entire muscle fiber (> or equal to 100ms)

- ➢ Excitation - contraction coupling
    - The action potential (AP) propagates along the sarcolemma and down the T tubules
    - Calcium ions are released because the T tubule causes voltage-sensitive tubules proteins to change shape, this change of shape opens the Ca2+ channel in the terminal cisterns of the sarcoplasmic reticulum.
        - The reticulum stores calcium
    - Calcium binds to troponin and removes the blocking action of tropomyosin. When Ca2+ binds, troponin changes shape, exposing the binding site for myosin (active sites) on the thin filament actin
        - Troponin and Tropomyosin are regulator inhibitors for actin/myosin contraction, however in the presence of Ca2+, it is removed
    - Contraction begins as myosin binding to actin forms cross bridges and contraction begins.
- ➢ Cross bridge formation

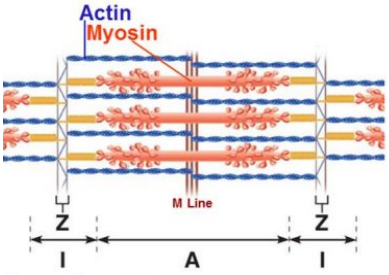


1] **Cross bridge formation.**
Energized m yosin head attaches to an a ctin myofilament, forming a cross bridge. ATP → ADP supplies energy
Myosin head is in high-energy, pre-stroke, 'c ocked' position

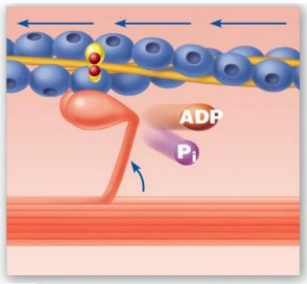


Focus Figure 9.3

    - Energized myosin head attaches to an actin myofilament, forming a crossbridge. ATP → ADP supplies energy and myosin is in high energy, prestroke, 'cocked' position

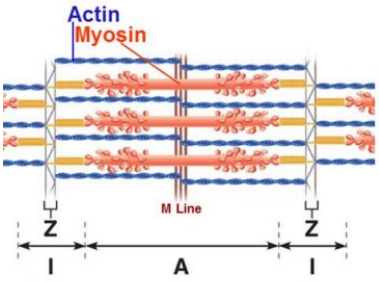


Focus Figure 9.3

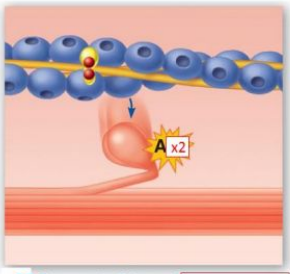


2] **The power (working) stroke.** ADP and P_i are released and the myosin head p[ivots] and bends, changing to its bent low-energy state. As a result it p[ulls] the actin filament toward the M line.

- The release of ADP and Pi makes the myosin change into a low-energy state, producing a bend. As a result since the myosin head is attached to the actin, this movement pulls the actin filament toward the M line



Focus Figure 9.3



3] **Cross bridge d**[etach x2]**. After A**[TP] attaches to myosin, the link between myosin and actin weakens, and the myosin head d[etaches] (the cross bridge "breaks").

During this step – which does not require energy – there is Ca^{++} reuptake from the cytosol/sarcoplasm back into the sarcoplasmic reticulum. (See Step 2, slide 22)

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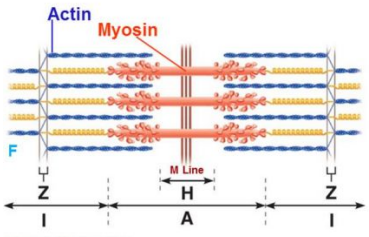
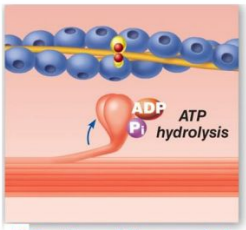
- Myosin head detaches from actin myofilament



Focus Figure 9.3



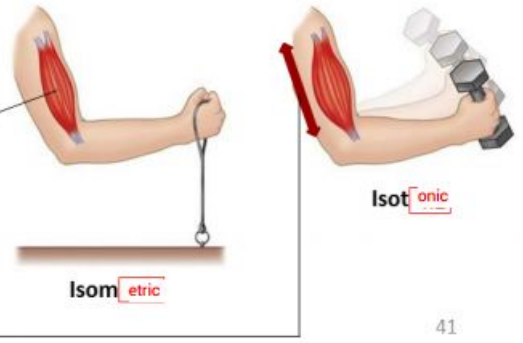
4] **Cocking of the myosin head.** As ATP is hydrolyzed to ADP and P_i, the myosin head returns to its pres[troke] high-e[nergy] or "cocked," position.*

* This cycle will continue as long as ATP is available and Ca^{++} is bound to troponin

- Returns to original state when gets energized

Contraction	Load Moves	Muscle Shortens	Measure
Isometric	No	No	Muscle tension
Isotonic	Yes	Yes**	Muscle shortening

**Or lengthens – (*See below*)



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- Motor unit (one motor neuron and all muscle fibers)
  - Each muscle served by 1 or more motor nerve
  - Each motor nerve contains axons from hundreds of motor neurons
  - At muscle, each axon has many terminals, forming neuromuscular junctions with muscle fibers within muscle

- Muscle twitch
  - Latent: Excitation - contraction / cross bridging begin, but no muscle tension
  - Contraction: Actin fibers pull together, if tension greater than load, muscle shortens
  - Relaxation: CA2+ reenters sarcoplasmic reticulum.
    - Cross bridge declines
    - Contractile force declines
    - Tension → 0. Muscle length returns to normal

- Graded muscle responses
  - Wave or temporal summation
    - Second contraction occurs before muscle has completely relaxed. Because the muscle is already partially contracted and more calcium is being squirted into the cytosol to replace that being reclaimed by the SR, muscle tension produced during second contraction causes more shortening than the first.
      - The contraction are added together
      - Relaxation time between twitches become shorter and shorter
      - The [Ca2+] in cytosol rises higher and higher
      - **Unfused or incomplete tetanus** occurs when quivering contraction

                - **Fused or complete tetanus** occurs when stimulation frequency continues to increases to reach maximum tension
        - Subthreshold stimulus (no contraction)
            - More precisely controls force of contraction
        - Threshold stimulus (1st observable stimulus)
            - Further increases 4-6 more and more motor units recruited
        - Maximal stimulus - strongest that increases contractile force
            - Further strength increases give no greater contractile force
- Stimulus effects on contraction
    - Motor units with smallest fibers are recruited first
    - As motor units with larger fibers excited, contractile strength increases
    - Largest motor unit with largest muscle fibers (50 x contractile force) excited only if most powerful contractile force necessary
- Muscle tone
    - ALthough skeletal muscles 'voluntary' they are even when relaxed, slightly contracted
    - Due to spinal reflexes activating successful groups of motor units
    - Keeps muscle firm, healthy, and responsive
    - ALso stabilizes joints and maintains posture

- Isotonic (TONE)
    - Muscle length changes and load is moving
    - Tension constant once enough to move load
    - Two flavours
        - Concentric (shortens) bicep curls and shortened contracted biceps. Feels bunched up.
        - Eccentric (lengthens) but still have load

- Isometric contraction
    - Tension may build to peak capacity but no change in length
        - MORE LOAD NO LENGTH CHANGE
        - Eg pushing a wall with all force or squat position
        - Holding a glass of water with straight arm
- Energy for muscle contraction
    - Direct phosphorylation
        - ATP-PC creatine phosphate
            - NO oxygen
            - 1 ATP per CP
            - Duration 15 seconds good for heavy lift

- Anaerobic
  - Glycolysis and lactic acid formation
    - No oxygen used up
    - 2 ATP per glucose
    - 30-40 seconds
      - More than this will start the build up of lactic acid
- Aerobic
  - Cellular respiration
    - Oxygen required
    - 32 ATP per glucose
    - Hours of aerobic exercise

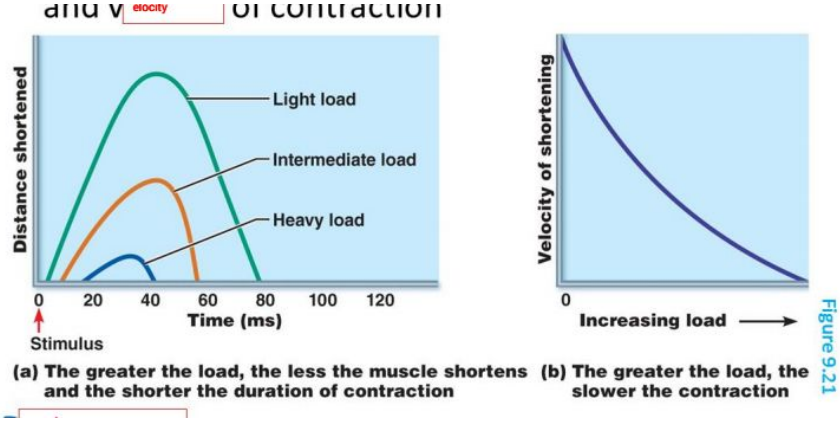
➢ Muscle fatigue
- State of physiologic inability to contract from stimulus
  - Many factors
    - (NOT running out of ATP - available during fatigue)
    - Excitation - contraction coupling problem
    - Problems at neuromuscular junction (rarely)
    - Ionic imbalances
    - Buildup of inorganic phosphate from ATP breakdown
      - Interferes with Ca+ release from SR
    - Lactic acid lowering pH long assumed, however can be possibly helpful

➢ Muscle strength
- Depends on number of myosin crossbridges
  - Affect four factors
    - Number of muscle fibers recruited
    - Size of muscle fibers
    - Frequency of stimulus
    - Degree of muscle strength

➢ Size of muscle fibers
- The bulkier the muscle (the greater its cross-sectional area), the more tension it can develop
- Regular resistance exercise leads to muscle hypertrophy (increase in size)

➢ Factors affecting contraction
- Velocity of contraction (type)
- How fast myosin ATPases split ATP
- Speed: Ca 2+ → SR
- Pattern of electrical activity of motor neurons

- Pathways for forming ATP
    - Muscle fiber types
        - Slow fibers
            - Oxidative fibers: (aerobic path)
                - Contractions slow and so is rate of fatigue.
                - Good for endurance activities
                - Requires a lot of O2 aerobic respiration
                    - HIgh myoglobi red
                    - Many mitochondria
                    - Many capillaries
                    - THIN: in general
                    - LOW: Doesn't require glycogen stores
        - Fast fibers
            - Glycolytic fibers: Anaerobic path
                - Contraction are fast but so is rate of fatigue
                - Suited for short-term intense/powerful activities
                    - Requires NO Oxygen
                    - Low myoglobin (pale)
                    - Few mitochondria
                    - Few capillaries
                    - Thick glycogen stores and high amount
        - Fast oxidative fibers
            - In Between slow/fast
                - SUited for sprinting and walking
- Load
    - Load affects duration, amount of muscle shortening and velocity of contraction



- Recruitment
    - The more motor units, the faster and more prolonged the contraction

- Smooth muscle
  - Single, uninucleate, no striation
  - Connective tissue components - endomysium
  - No T Tubules and site of invagination; only caveolae
  - Equivalent to cardiac muscle; some SR contacts the sarcolemma
  - There is a gap junction unitary muscle
  - Cells do not exhibit individual neuromuscular junction
  - Regulation of contraction is involuntary: hormones, local chemicals, stretch
  - Both excitation and inhibition
  - Very slow speed of contractions
  - Mainly aerobic metabolism
- What happens when muscle layers contract involuntary:
  - Longitudinal layer (fibers parallel to long axis)
    - Organ shortens
  - Circular layer (around circumference)
    - Lumen constricts
  - Peristalsis: alternating contraction/relaxation of layers of digestive tract
    - Squeezes or propels organ's contents along
  - Asthmatic wheeze
    - Constricted airways
  - Stomach cramps
    - Constricted arteries
- Neuromuscular junction
  - Instead of neuromuscular junction it's *diffuse junctions*
    - Nerves swell into bulbous varicosities
    - Neurotransmitters released from these into wide synaptic cleft in general area of smooth muscle cell
    - Skeletal muscle gets priority mail, smooth muscle gets bulk mails [Fast/direct v slow/untargeted]
    - Involuntary ACTION
- Entry of CA2+ into smooth muscle
  - Similar but diff
  - Sarcoplasmic reticulum is much smaller and less developed
  - Caveolae replaces T tubules
    - Both inpockets-shallow v deep- of sarcolemma
    - Both have Ca2+ channels
    - Most Ca2+ via channel from extracellular space
  - In both contraction begins when Ca+ enters cytoplasm, ends when it is pumped back into SR

- ➢ Thick/thin filaments in smooth
  - Both myosin and actin are present but differences:
    - No sarcomere - so no striation
    - Myosin (thick filaments) are
      - Much shorter than actin thin filaments
      - Relatively fewer myosin: actin= 1:13 v 1:2
    - In skeletal muscle, Ca2+ initiates cross-bridge by binding to troponin on actin, removing tropomyosin and then revealing myosin binding sites. Myosin is thereby 'activated' and its head can attach to actin
    - In smooth muscle, Ca2+ activates myosin by interacting with calmodulin in the cytoplasm
      - Calmodulin causes myosin kinase to activate myosin
- ➢ Synchronous contraction
  - Entire sheet of muscle responds to the stimulus: unison
  - Why? Gap junctions electrically coupled smooth muscle cells
    - Skeletal muscle cells electrically independent. Individual neuromuscular junctions contractions
  - In Gi Tract, some smooth cells are pacemaker cells
    - Set the pace of contraction for entire muscle sheet
- ➢ Similarities
  - Actin and myosin filaments interact by sliding past each other
    - Final trigger for contraction:L rise in intracellular Ca2+ conce
    - ATP energizes the sliding process
    - Muscles rest when intracellular Ca 2+ drops
- ➢ Mechanism of contraction
  - 1. Calcium ions enter the cytosol from the ECF via voltage dependent or voltage-independent Ca2+ channels, or from the Scant SR
  - 2. Note involvement of intermediate protein, calmodulin, not seen. The Ca2+ binds to and activates calmodulin
  - 3. Activated calmodulin activates the myosin light chain kinase enzyme
  - 4.The activated kinase enzymes catalyze transfer of phosphate to myosin, activating the myosin
  - 5. Activated myosin forms cross bridge with actin and thin filaments. Shortening begins
- ➢ Energy efficiency of contraction
  - Smooth muscle takes 30x longer to relax/contract than skeletal muscle
  - More efficient: maintain same tension for long periods of time a less than 1% energy cost
    - Why?

                - ATPases in step 4 above sluggish/need energy
                - Myofilaments in step 5 stay together in a latch state
        - Smooth muscle in body remains moderately contracted day in/day out: smooth muscle tone

➢ Chemical regulation of contraction
    - Some smooth muscle cells also respond to hormones or local chemical factors
    - Other only respond to chemicals - no nerve supply\
    - Response to chemicals ultimately same as to nerve stimulation
        - Mediated by release of Ca2+ into sarcoplasmic
            - Ex/ Gastrin contracts stomach muscles

➢ Special features of contraction
    - Stress-relaxation response
        - Smooth muscle contracts when stretched
        - Then adapts to new length, relaxes
        - Retains ability to contract on demand
        - Hollow organ can expand slowly to accommodate contents without contracting/expanding them
            - Stomach can digest a meal/absorb nutrients
            - Urinary bladder can store urine
➢ Types of smooth muscle
    - Unitary/visceral smooth muscle
        - In walls of hollow organs except heart
        - Far more common
        - Innervated by autonomic nerves
        - OFten exhibit rhythmic spontaneous action potentials
        - Electrically coupled (gap junctions) contract as unit
        - Response to various chemical stimuli
    - Multi-unit smooth muscle
        - In lung airway, large arteries, eye muscles
        - Similar to skeletal muscle
        - Richly supplied with nerves that form motor unit
        - No spontaneous action potentials
        - NOT electrically coupled- fibers independent
        - Respond to neural stimuli