BIOLOGY "CRACK" MASTER NOTES

- Transcription
  - mRNA composition and structure (RNA nucleotides, 5' cap, poly-A tail)
  - tRNA and rRNA composition and structure (e.g., RNA nucleotides)
  - Mechanism of transcription (RNA polymerase, promoters, primer not required)
- Translation
  - Roles of mRNA, tRNA, rRNA
  - Role and structure of ribosomes

Molecular Biology: Eukaryotes – Page 41

- Eukaryotic chromosome organization
  - Chromosomal proteins
  - Telomeres, centromeres
- Control of gene expression in eukaryotes
  - Transcription regulation
  - DNA binding proteins, transcription factors
  - Cancer as a failure of normal cellular controls, oncogenes
  - Post-transcriptional control

Genetics – Page 47

- Mendelian concepts
  - Phenotype and genotype
  - Gene
  - Locus
  - Allele: single and multiple
  - Homo- and heterozygosity
  - Wild type
  - Recessiveness
  - Complete dominance
  - Co-dominance
  - Incomplete dominance, leakage, penetrance, expressivity
  - Gene pool
- Meiosis and genetic variability
  - Significance of meiosis
  - Important differences between meiosis and mitosis
  - Segregation of genes
    - Independent assortment
    - linkage
    - recombination
    - single crossovers
    - double crossovers
  - Sex-linked characteristics
    - very few genes on Y chromosome
    - sex determination
    - cytoplasmic inheritance
  - Mutation

        - general concept of mutation-error in DNA sequence
        - types of mutations: random, translation error, transcription error, base substitution, inversion, addition, deletion, translocation, mispairing
        - advantageous vs. deleterious mutation
        - inborn errors of metabolism
        - relationship of mutagens to carcinogens
- Analytic methods
    - Hardy-Weinberg Principle
    - Test cross: back cross, concepts of parental, F1 and F2 generations

Microbiology – Page 57

- Fungi
    - General characteristics
    - General aspects of life cycle
- Virus structure
    - General structural characteristics (nucleic acid and protein, enveloped and nonenveloped)
    - Lack organelles, nucleus
    - Structural aspects of typical bacteriophage
    - Genomic content RNA or DNA
    - Size relative to bacteria and eukaryotic cells
- Viral life cycle
    - Self-replicating biological units that must reproduce within specific host cell
    - Generalized phage and animal virus life cycles:
        - attachment to host, penetration of cell membrane or cell wall, and entry of viral genetic material
        - use of host synthetic mechanism to replicate viral components
        - self-assembly and release of new viral particles
    - Retrovirus life cycle: integration into host DNA
    - Transduction: transfer of genetic material by viruses
- Prokaryotic cell: structure, bacteria
    - Lack of nuclear membrane, mitotic apparatus
    - Lack of typical eukaryotic organelles
    - Major classifications of bacteria by shape: bacilli (rod-shaped); spirilli (spiral shaped); cocci (spherical); eubacteria; archaea
    - Presence of cell wall in bacteria
    - Flagellar propulsion, mechanism
- Prokaryotic cell: growth and physiology
    - Reproduction by fission
    - High degree of genetic adaptability, acquisition of antibiotic resistance
    - Exponential growth
    - Existence of anaerobic and aerobic variants
    - Parasitic and symbiotic
- Prokaryotic cell: genetics
    - Existence of plasmids, extragenomic DNA, transfer by conjugation

    - Transformation: incorporation into bacterial genome of DNA fragments from external medium
    - Regulation of gene expression, coupling of transcription and translation

Generalized Eukaryotic Cell – Page 64

- Nucleus and Other Defining Characteristics
    - Defining characteristics (membrane bound nucleus, presence of organelles, mitotic division)
    - Nucleus (compartmentalization, storage of genetic information)
    - Nucleolus (location and function)
    - Nuclear envelope, nuclear pores
- Membrane-bound Organelles
    - Mitochondria
        - site of ATP production
        - self-replication; have own DNA and ribosomes
        - inner and outer membrane
    - Lysosomes (vesicle containing hydrolytic enzymes)
    - Endoplasmic reticulum
        - rough (RER) and smooth (SER)
        - RER (site of ribosomes)
        - role in membrane biosynthesis: SER (lipids), RER (transmembrane proteins)
        - RER (role in biosynthesis of transmembrane and secreted proteins that cotranslationally targeted to RER by signal sequence)
    - Golgi apparatus (general structure; role in packaging, secretion, and modification of glycoprotein carbohydrates)
- Plasma Membrane
    - General function in cell containment
    - Protein and lipid components, fluid mosaic model
    - Osmosis
    - Passive and active transport
    - Membrane channels
    - Sodium-potassium pump
    - Membrane receptors, cell signaling pathways, second messengers
    - Membrane potential
    - Exocytosis and endocytosis
    - Cell-cell communication (General concepts of cellular adhesion)
        - gap junctions
        - tight junctions
        - desmosomes
- Cytoskeleton
    - General function in cell support and movement
    - Microfilaments (composition; role in cleavage and contractility)
    - Microtubules (composition; role in support and transport)
    - Intermediate filaments (role in support)
    - Composition and function of eukaryotic cilia and flagella

    - Centrioles, microtubule organizing centers
- Cell Cycle and Mitosis
    - Interphase and mitosis (prophase, metaphase, anaphase, telophase)
    - Mitotic structures and processes
        - centrioles, asters, spindles
        - chromatids, centromeres, kinetochores
        - nuclear membrane breakdown and reorganization
        - mechanisms of chromosome movement
    - Phases of cell cycle: G0, G1, S, G2, M
    - Growth arrest
- Apoptosis (Programmed Cell Death)

Specialized Eukaryotic Cells and Tissues – Page 75

- Nerve Cell/Neural
    - Cell body (site of nucleus and organelles)
    - Axon (structure, function)
    - Dendrites (structure, function)
    - Myelin sheath, Schwann cells, oligodendrocytes, insulation of axon
    - Nodes of Ranvier (role in propagation of nerve impulse along axon)
    - Synapse (site of impulse propagation between cells)
    - Synaptic activity
        - transmitter molecules
        - synaptic knobs
        - fatigue
        - propagation between cells without resistance loss
    - Resting potential (electrochemical gradient)
    - Action potential
        - threshold, all-or-none
        - sodium-potassium pump
    - Excitatory and inhibitory nerve fibers (summation, frequency of firing)
- Muscle Cell/Contractile
    - Structural characteristics of striated, smooth, and cardiac muscle
    - Abundant mitochondria in red muscle cells (ATP source)
    - Organization of contractile elements (actin and myosin filaments, cross bridges, sliding filament model)
    - Calcium regulation of contraction, sarcoplasmic reticulum
    - Sarcomeres ("I" and "A" bands, "M" and "Z" lines, "H" zone - General structure only)
    - Presence of troponin and tropomyosin
- Other specialized cell types
    - Epithelial cells (cell types, simple epithelium, stratified epithelium)
    - Endothelial cells
    - Connective tissue cells (major cell types, fiber types, loose vs. dense, cartilage, extracellular matrix)

Nervous and Endocrine Systems – Page 88

- Endocrine system: Hormones
  - Function of endocrine system (specific chemical control at cell, tissue, and organ level)
  - Definition of endocrine gland, hormone
  - Major endocrine glands (names, locations, products)
  - Major types of hormones
- Endocrine system: Mechanisms of hormone action
  - Cellular mechanisms of hormone action
  - Transport of hormones (bloodstream)
  - Specificity of hormones (target tissue)
  - Integration with nervous system (feedback control)
- Nervous System: Structure and Function
  - Major functions
    - high-level control and integration of body systems
    - response to external influences
    - sensory input
    - integrative and cognitive abilities
  - Organization of vertebrate nervous system
  - Sensor and effector neurons
  - Sympathetic and parasympathetic nervous systems (functions, antagonistic control)
  - Reflexes
    - feedback loop, reflex arc, effects on flexor and extensor muscles
    - role of spinal cord, brain
    - efferent control
- Nervous System: Sensory Reception and Processing
  - Skin, proprioceptive, and somatic sensors
  - Olfaction, taste
  - Hearing
    - ear structure
    - mechanism of hearing
  - Vision
    - light receptors
    - eye structure
    - visual image processing

Circulatory, Lymphatic, and Immune Systems – Page 102

- Circulatory System
  - Functions (circulation of oxygen, nutrients, hormones, ions, and fluids; removal of metabolic waste)
  - Role in thermoregulation
  - Four-chambered heart (structure, function)
  - Systolic and diastolic pressure
  - Pulmonary and systemic circulation

    - Arterial and venous systems (arteries, arterioles, venules, veins)
        - structural and functional differences
        - pressure and flow characteristics
    - Capillary beds
        - mechanisms of gas and solute exchange
        - mechanism of heat exchange
        - source of peripheral resistance (no longer tested)
    - Composition of blood
        - plasma, chemicals, blood cells
        - erythrocyte production and destruction (spleen, bone marrow)
        - regulation of plasma volume
        - coagulation, clotting mechanisms, role of liver in production of clotting factors
    - Oxygen and carbon dioxide transport by blood
        - hemoglobin, hematocrit
        - oxygen content
        - oxygen affinity
    - Details of oxygen transport: biochemical characteristics of hemoglobin
        - modification of oxygen affinity
- Lymphatic System
    - Major functions
        - equalization of fluid distribution
        - transport of proteins and large glycerides
        - production of lymphocytes involved in immune reactions
        - return of materials to the blood
        - Composition of lymph (similarity to blood plasma; substances transported)
        - Source of lymph (diffusion from capillaries by differential pressure)
        - Lymph nodes (activation of lymphocytes)
- Immune system: Innate and Adaptive Systems
    - Cells and their basic functions
        - macrophages, neutrophils, mast cells, natural killer cells, dendritic cells
        - T-lymphocytes
        - B-lymphocytes, plasma cells
    - Tissues
        - bone marrow
        - spleen
        - thymus
        - lymph nodes
    - Basic aspects of innate immunity and inflammatory response
    - Concept of antigen and antibody
    - Structure of antibody molecule
    - Mechanism of stimulation by antigen; antigen presentation

Respiratory System – Page 119

- General structure and function

    - gas exchange, thermoregulation
    - protection against disease, particulate matter
- Breathing mechanisms
    - diaphragm, rib cage, differential pressure
    - resiliency and surface tension effects

Skin System – Page 121

- Functions in homeostasis and osmoregulation
- Functions in thermoregulation
    - hair, erectile musculature
    - fat layer for insulation
    - sweat glands, location in dermis
    - vasoconstriction and vasodilation in surface capillaries
- Physical protection
    - nails, calluses, hair
    - protection against abrasion, disease organisms
- Structure
    - layer differentiation, cell types, tissue types (epithelial, connective)
    - relative impermeability to water

Digestive and Excretory Systems

Digestive System – Page 125

- Ingestion
    - saliva as lubrication and source of enzymes
    - epiglottal action
    - pharynx (function in swallowing)
    - esophagus (transport function)
- Stomach
    - storage and churning of food
    - low pH, gastric juice, protection by mucus against self-destruction
    - production of digestive enzymes, site of digestion
    - structure (gross)
- Liver
    - production of bile
    - role in nutrient metabolism, vitamin storage
    - role in blood glucose regulation, detoxification
    - structure (gross)
- Bile
    - storage in gall bladder
    - function
- Pancreas
    - production of enzymes, bicarbonate
    - transport of enzymes to small intestine
    - structure (gross)
- Small intestine

    - Structural characteristics of skeletal, smooth, and cardiac muscle; striated vs nonstriated
    - Nervous control
        - motor neurons
        - neuromuscular junctions, motor end plates
        - voluntary and involuntary muscles
        - sympathetic and parasympathetic innervation
- Skeletal System
    - Functions
        - structural rigidity and support
        - calcium storage
        - physical protection
    - Skeletal structure
        - specialization of bone types, structures
        - joint structures
        - endoskeleton versus exoskeleton
    - Cartilage (structure and function)
    - Ligaments, tendons
    - Bone structure
        - calcium-protein matrix
        - bone growth (osteoblasts, osteoclasts)

Reproductive System and Development – Page 145

- Reproductive System
    - Male and female reproductive structures and their functions
        - gonads
        - genitalia
        - differences between male and female structures
    - Gametogenesis by meiosis
    - Ovum and sperm
        - differences in formation
        - differences in morphology
        - relative contribution to next generation
    - Reproductive sequence (fertilization, implantation, development, birth)
- Embryogenesis
    - Stages of early development (order and general features of each)
        - fertilization
        - cleavage
        - blastula formation
        - gastrulation
            - first cell movements
            - formation of primary germlayers (endoderm, mesoderm, ectoderm)
        - neurulation
    - Major structures arising out of primary germ layers
- Developmental Mechanisms

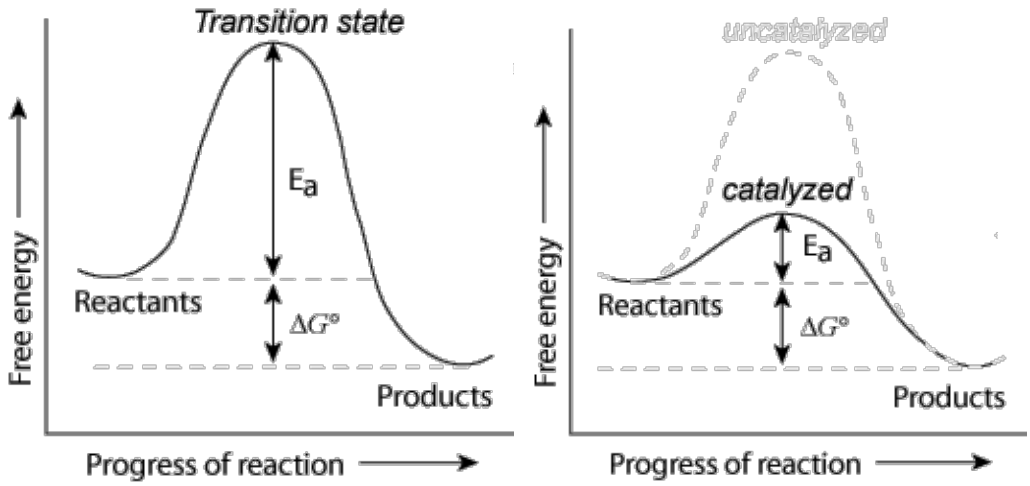
    - Cell specialization
        - determination
        - differentiation
        - tissue types
    - Cell communication in development
    - Gene regulation in development
    - Programmed cell death

Evolution – Page 157

- Evolution
    - Natural selection
        - fitness concept
        - selection by differential reproduction
        - concepts of natural and group selection
        - evolutionary success as increase in percent representation in the gene pool of the next generation
    - Speciation
        - definition of species
        - polymorphism
        - adaptation and specialization
        - concepts of ecological niche, competition
        - concept of population growth through competition
        - inbreeding
        - outbreeding
        - bottlenecks, genetic drift
        - divergent, parallel, and convergent evolution
        - Symbiotic relationships
            - Parasitism
            - Commensalism
            - Mutualism
    - Relationship between ontogeny and phylogeny (Ontogeny recapitulates phylogeny)
    - Evolutionary time as measured by gradual random changes in genome
    - Origin of life
- Comparative anatomy
    - Chordate features
        - notochord
        - pharyngeal pouches, branchial arches
        - dorsal nerve cord
    - Vertebrate phylogeny: vertebrate classes and relations to each other

Molecular Biology: Enzymes and Metabolism

Enzyme structure and function

- Function of enzymes in catalyzing biological reactions
    - Enzymes are catalysts, which are things that increase the rate of a reaction, but does not get used up during the reaction.
    - Structure determines function. A change in structure => a change in function.
    - Important biological reactions catalyzed by enzymes:
        - Metabolism
        - DNA synthesis
        - RNA synthesis
        - Protein synthesis
        - Digestion
- Reduction of activation energy
    - 

    - Enzymes decrease the activation energy (E_a) of a reaction by lowering the energy of the transition state.

- Enzymes increase the rate of a reaction by decreasing the activation energy.
- Enzymes will increase the rate constant, k, for the equation rate = k[A][B].
- Enzymes do NOT change the K_{eq} of a reaction.
- Enzymes do not change K_{eq} because it lowers the activation energy for BOTH forward and reverse reactions.
- Enzymes will make the reverse reaction go faster also.
- Enzymes do not change ΔG, the net change in free energy.
- Enzymes affect the kinetics of a reaction, but not the thermodynamics.

- Substrates and enzyme specificity
  - Enzyme-substrate interactions occur at the enzyme's active site.
  - Enzyme-substrate specificity derives from structural interactions.
  - Lock and key model: rigid active site. Substrate fits inside the rigid active site like a key.
  - Induced fit model: flexible active site. Substrate fits inside the flexible active site, which is then induced to "grasp" the substrate in a better fit.
  - Enzymes can be specific enough to distinguish between stereoisomers.
  - Enzymes can be protein or RNA.
    - Almost all enzymes in your body is made of protein.
    - The most important RNA enzyme in your body is the ribosome.
  - Enzyme structure derives from 4 levels.
    - Primary: this is the sequence of the protein or RNA chain.

        - Secondary: this is hydrogen bonding between the protein backbone. Examples include alpha helices and beta sheets (backbone H-bonding). For RNA, this is base pairing.
        - Tertiary: this is the 3-D structure of the enzyme. This involves -R group interactions and spatial arrangement of secondary structure.
        - Quaternary: when more than 1 chain is involved. When you hear about "dimers", "trimers", "tetramers", "oligomers", that's quaternary structure.
    - Heat and extreme pH denatures enzymes by altering their structure.

Control of enzyme activity

- Feedback inhibition
    - The product of a pathway inhibits the pathway.
    - For example, hexokinase, the first enzyme in glycolysis, is inhibited by its product glucose-6-phosphate.
- Competitive inhibition
    - An inhibitor competes with the substrate for binding to the active site.
    - Competitive inhibition increases the amount of substrate needed to achieve maximum rate of catalysis.
    - Competitive inhibition does NOT change the maximum possible rate of the enzyme's catalysis.
    - You can overcome competitive inhibition by providing more substrate.
- Non-competitive inhibition
    - An inhibitor binds to an allosteric site on the enzyme to deactivate it.
    - The substrate still have access the active site, but the enzyme is no longer able to catalyze the reaction as long as the inhibitor remains bound.

    - Non-competitive inhibition decreases the maximum possible rate of the enzyme's catalysis.
    - Non-competitive inhibition does NOT change the amount of substrate needed to achieve the maximum rate of catalysis.
    - You can't overcome non-competitive inhibition by adding more substrate.

Basic metabolism

- Metabolism consists of two parts: Catabolism and anabolism.
- Catabolism is breaking stuff down for energy. This is the part that the EXAM (and what we) focuses on.
- Anabolism is using energy to build stuff for storage.
- Unless otherwise stated, everything here on metabolism is about catabolism - breaking things down for energy.
- Another name for metabolism is cellular respiration.
- Steps of aerobic metabolism (needs oxygen)
    - Glycolysis
    - Oxidative decarboxylation
    - Krebs cycle
    - Electron transport chain.
- Steps of anaerobic metabolism (don't need oxygen)
    - Glycolysis
    - Alcohol or lactic acid fermentation
- Aerobic metabolism of glucose
    - Complete oxidation of metabolite (glucose) to carbon dioxide.
    - ~30 ATP produced per glucose.
    - $C_6H_{12}O_6 + 6O_2 => 6CO_2 + 6H_2O$

- $C_6H_{12}O_6$: this is glucose. You get it from your diet.
- $6O_2$: this is molecular oxygen that you breathe in.
- $6CO_2$: this is carbon dioxide produced by the Krebs cycle. Both the carbon and oxygen in this CO_2 comes from the metabolite (glucose).
- $6H_2O$: this is water produced in the electron transport chain. The oxygen comes completely from the molecular oxygen that you breathe in.
- If we were to follow the carbon in the metabolite (glucose), it will end up in carbon dioxide.
- If we were to follow the oxygen in the metabolite (glucose), it will end up in carbon dioxide.
- If we were to follow the oxygen you breathe in, it will end up in water.
- As for the hydrogens, they'll either be in water, exist as protons in solution, or be transferred to some other entity.
- As we can see, the total reaction involves complete oxidation of the metabolite (glucose) and complete reduction of molecular oxygen.
- When electrons pass from the metabolite (glucose) to molecular oxygen, energy is released.
- The electron transport chain harnesses this energy.

- Anaerobic metabolism of glucose
  - Partial oxidation of metabolite (glucose) to pyruvate.
  - 2 net ATP produced per glucose.
  - Pyruvate is then reduced to either alcohol or lactate.
  - Bacteria reduce pyruvate to alcohol in a process called alcohol fermentation.
  - Humans reduce pyruvate to lactate in a process called lactic acid fermentation.

- Glycolysis, anaerobic and aerobic, substrates and products
    - Glycolysis = convert glucose (6 carbons) to 2 molecules of pyruvate (3 carbons).
        - Location: cytosol.
        - 2 net ATP made for every glucose (2 input ATP, 4 output ATP).
        - 2 NADH made for every glucose.
        - Occurs under both aerobic and anaerobic conditions.
        - Glycolysis is inhibited by ATP.
    - Aerobic decarboxylation (mitochondrial matrix) = convert pyruvate (3 carbons) to an acetyl group (2 carbons).
        - 1 NADH made for every pyruvate.
        - Only occurs in the presence of oxygen.
        - Acetyl group attaches to Coenzyme A to make acetyl CoA.
    - Anaerobic fermentation (cytosol) = redox reaction: reduce pyruvate, oxidize NADH.
        - 1 NAD^+ made for every pyruvate.
        - Alcohol fermentation = pyruvate reduced to ethanol.
        - Lactic acid fermentation = pyruvate reduced to lactate.
        - The purpose of anaerobic fermentation is to regenerate NAD^+, which is needed for glycolysis.
- Krebs cycle, substrates and products, general features of the pathway
    - Location: matrix of mitochondria.
    - Acetyl CoA feeds into the cycle.
    - 3 NADH made per acetyl CoA.
    - 1 $FADH_2$ made per acetyl CoA.
    - 1 ATP (GTP) made per acetyl CoA.

- Coenzyme A is regenerated (during the first step of the cycle).
- Krebs cycle, TCA, Tricarboxylic acid cycle, citric acid cycle all mean the same thing.
- Krebs cycle is Inhibited by ATP and NADH.

- Electron transport chain and oxidative phosphorylation, substrates and products, general features of the pathway
  - Location: the cristae (inner membrane of mitochondria).
  - Input NADH
  - Proton gradient
  - The electron transport chain (ETC) is essentially a series of redox reactions, where NADH gets oxidized to NAD^+ and O_2 gets reduced to H_2O.
  - The series of redox reactions consists of electrons passing from NADH to FMN, to Coenzyme Q, iron-sulfur complexes, and cytochromes (cytochrome b, c and aa_3) before finally being used to reduce oxygen.
  - NADH is highest in energy, while O_2 is lowest in energy. When electrons are passed from NADH down a series of proteins and finally to O_2, energy is released.
  - $FADH_2$ is lower in energy than NADH, that's why it releases less energy when it gets oxidized.
  - $FADH_2$ skips FMN and passes its electrons to Coenzyme Q.
  - The energy released from these reactions generates a proton gradient, which drives ATP synthase to make ATP. This is called oxidative phosphorylation.
  - Proton gradient
    - The energy released from passing electrons down the ETC is used to pump protons into the intermembrane space of the mitochondria.
    - H^+ concentration is very high in the intermembrane space (higher than those in the matrix). Thus, this establishes an electrochemical gradient called the proton gradient.

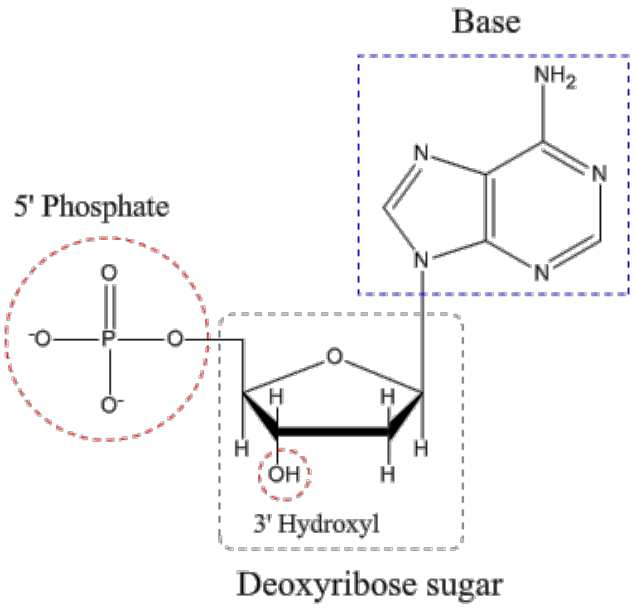
        - H^+ wants to migrate down the proton gradient (from the intermembrane space back into the matrix), but it can only do this by going through the ATP synthase.
        - Like a water mill, ATP synthase harnesses the energy of the falling protons to convert ADP into ATP.
    - The ETC is inhibited by certain antibiotics, by cyanide, azide, and carbon monoxide.
- Metabolism of fats and proteins
    - Fat metabolism
        - Location: beta-oxidation occurs in the matrix of the mitochondria. Ester hydrolysis occurs in the cytosol.
        - Fatty esters gets hydrolyzed into free fatty acids by lipases.
        - For example, triacylglycerol gets hydrolyzed into free fatty acids and glycerol.
        - With the help of ATP, the fatty acid is "activated" at the acid end by CoA (to be precise, it turns into a thioester).
        - A process called beta-oxidation breaks down the fatty-CoA, 2 carbons at a time, to make acetyl CoA.
        - β-oxidation produces acetyl CoA and also $FADH_2$ and NADH.
        - The acetyl CoA feeds into the Krebs cycle, and the $FADH_2$ and NADH feed into the ETC.
        - On a per gram basis, fats give more energy than any other food source.
    - Protein metabolism
        - Proteins are broken down into amino acids by peptidases.
        - The nitrogen in the amino acid is converted to urea (for desert animals, birds and reptiles, it is uric acid).

- The carbon in the amino acid is converted to pyruvate or acetyl-CoA, (or other metabolical intermediates such as oxaloacetate), depending on what amino acid it is.
- The carbon products from amino acid metabolism can either feed into the Krebs cycle, or be the starting material for gluconeogenesis.

Molecular Biology: DNA structure and function

Nucleic acid structure and function

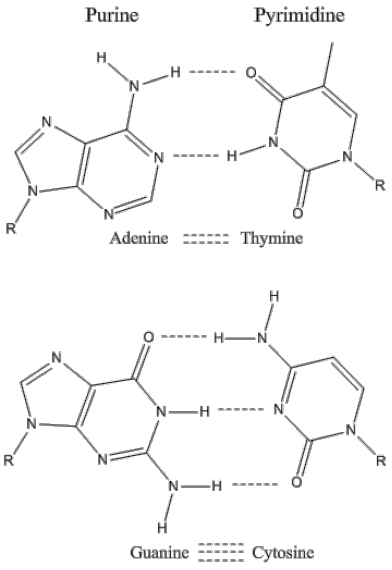
- Description
  - DNA = deoxy-ribo-nucleic acid
  - RNA = ribo-nucleic acid
  - deoxy = 2'-H (vs 2'-OH in RNA)
  - ribo = ribose sugar = pentose sugar
  - acid = phosphate group gives it acidity
- Nucleotides and nucleosides



  - Nucleotide = base (Adenine, Guanine, Thymine, Cytosine) + sugar + phosphate.
  - Nucleoside = base + sugar = Adenosine, Guanosine, Thymidine, Cytidine.
  - Sugar phosphate backbone = phosphodiester bonds linking the 5' phosphate to the 3' hydroxyl group of the pentose sugar

- Base can either be purines A and G (the big ones with 2 rings) or pyrimidines T and C (the small ones with 1 ring).
- Thymine is replaced with Uracil in RNA
- The phosphate group gives DNA its acidity.

- Deoxyribonucleic acid (DNA): double helix, Watson-Crick model of DNA structure
  - The "double" in the double helix means that DNA is found in a double-stranded form - 2 single-stranded chains of DNA stuck to each other via hydrogen bonding of the base pairs.
  - The 2 single-strands are anti-parallel to each other. Going from 5' to 3' of one strand means going from 3' to 5' of the other strand.
  - The "helix" in the double helix means that the entire thing is wound up in a spiral.
  - 

- Base pairing specificity: A with T, G with C
  - 

  - A forms 2 hydrogen bonds with T.
  - G forms 3 hydrogen bonds with C.
  - GC bonds are stronger. DNA with high GC content will be harder to break apart.

- Complementary strands of DNA hydrogen bond with each other.
- 5'-ATGC-3' will be complementary to 5'-GCAT-3' or 3'-TACG-5', but NOT 5'-TACG-3'. make sure you get the 5's and 3's right.

- Function in transmission of genetic information
  - Because of the complementary nature of base pairing, DNA can transmit genetic information through replication.

- DNA denaturation, reannealing, hybridization
  - denaturation = separation of 2 complementary strands = caused by high temperature
  - reannealing = coming together of the 2 complementary strands after they've been separated
  - hybridization = annealing = coming together of complementary strands
  - annealing is generally used in PCR reactions, where primer anneals to the template strand
  - hybridization is generally used in Southern blotting (probe anneals to target) and plasmid ligation (sticky ends anneal)

DNA replication

- Mechanism of replication: separation of strands, specific coupling of free nucleic acids

1. First, the double stranded DNA must separate, or unwind. To do this:
   - DNA gyrase (class II topoisomerase) is responsible for uncoiling the DNA ahead of the replication fork.
   - Helicase is responsible for unwinding the DNA at the replication fork.
   - Single-strand binding protein (SSB) is responsible for keeping the DNA unwound after the helicase. SSBs stabilize single-stranded DNA by binding to it.
2. Next, you start making DNA that is complementary to the newly unwound/separated DNA. Note, all biological DNA synthesis occurs from the 5' to the 3' end.

        - Primase gets this started by laying down a short RNA primer on the unwound DNA. The primer is made of RNA, but is complementary to the DNA sequence. Later, this RNA is replaced with DNA.

        - DNA polymerase then takes over and makes DNA that is complementary to the unwound DNA.

        - DNA synthesis occurs on both strands of the unwound DNA. The synthesis that proceeds in the direction of the replication fork is the leading strand. The synthesis that proceeds in the opposite direction to the replication fork is the lagging strand. The lagging strand contains Okazaki fragments.

    3. Finally, RNA primers are replaced with DNA by a special DNA polymerase. The Okazaki fragments in the lagging strands are then stitched together by DNA ligase.

    - DNA synthesis is bidirectional: 2 replication forks form and proceeds in opposite directions (like an expanding bubble).

    - Biological DNA synthesis always proceeds from the 5' end to the 3' end.

    - DNA polymerase has proof-reading activity, which means it corrects any mistakes (mutations) it makes.

    - Replication occurs once every cell generation, during the S phase. (Cell division may occur twice in meiosis, but replication still occurs once only)

- Semi-conservative nature of replication

    - Newly synthesized DNA contains one old strand and one new strand.

    - Meselson and Stahl proved this by experiment: Basically, they used heavy (^{15}N) DNA as the old (pre-replication) DNA, and used light (^{14}N) nucleotides for the synthesis of new DNA. They can tell the difference between heavy and light DNA by centrifugation. What they found was that when heavy DNA undergoes one round of replication in light nucleotides, the DNA made is of intermediate weight. After the second round of replication, the DNA is split between intermediate and light weight.

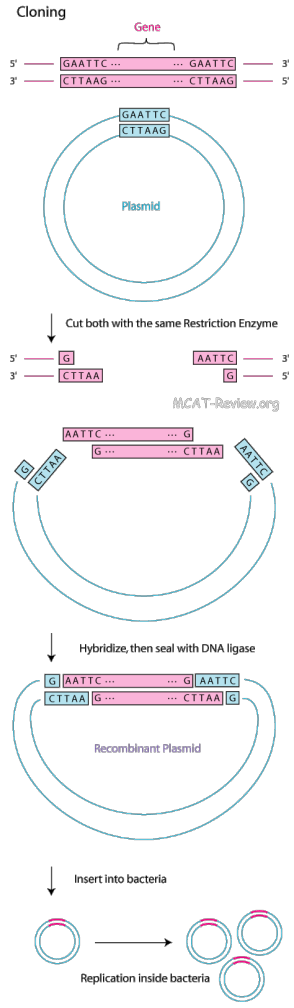
    - If DNA replication were completely conservative, only heavy and light DNA would be seen, and nothing in between. This was not the case.

    - If DNA replication were dispersive, everything would be of intermediate weight. Again, this was not the case because after the second round of replication, light DNA was seen.

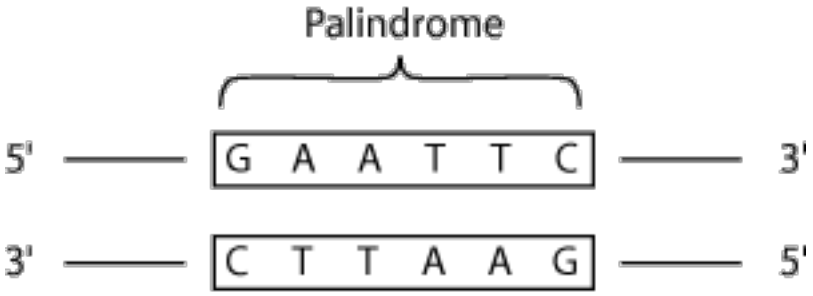
Repair of DNA

- Repair during replication
    - DNA polymerase has proof-reading activity (also called 3' → 5' exonuclease activity). If a wrong nucleotide gets incorporated, the polymerase will "back-up" and replace it with the correct one.
    - The special polymerase that replaces the RNA primers with DNA also have 5' → 3' activity. This allows the polymerase to clear away short stretches of incorrect nucleotides (RNA or incorrect DNA) and replace it with the right ones (DNA). This process is also called repair.
- Repair of mutations
    - Mismatch repair: enzymes recognize incorrectly paired base-pairs and cuts out the stretch of DNA containing the mismatch. Then polymerase re-adds the correct nucleotides in.
    - During mismatch repair, the repair enzyme must decide what strand of DNA to cut since DNA contains 2 strands. To do this, the enzyme cuts the DNA strand that do not have methylations. The original (old) DNA has methylations, but the newly synthesized DNA do not have them until shortly after replication. Thus, there is a window of time when mismatch repair enzymes can know what strand to cut if mismatch is encountered.
    - Base-excision repair: a damaged base gets cut out. Then the base's sugar phosphate backbone gets cut out. And then, several more nucleotides next to the base get cut out. Finally, polymerase remakes the cut out nucleotides.
    - Nucleotide-excision repair: damaged nucleotide(s) gets cut out and then polymerase replaces it. This is like mismatch-repair, but it's not for mismatch. It's for damages like thymine dimers, and other damages that changes normal nucleotides into abnormal nucleotides.
    - Nick translation: this is basically 5' → 3' exonuclease activity coupled to polymerase activity. The polymerase here chugs along, chews off the bad nucleotides and then replaces them with new nucleotides. This is what happens when RNA primers are replaced with DNA.
    - SOS response in E. Coli: during replication, when there's just too much DNA damage for normal repair to handle, the SOS repair system comes along. Instead of correcting any DNA damages during replication, the polymerase replicates over the damaged DNA as if it were normal. By using the damaged DNA as a template error rates are high, but it's still better than not replicating at all.

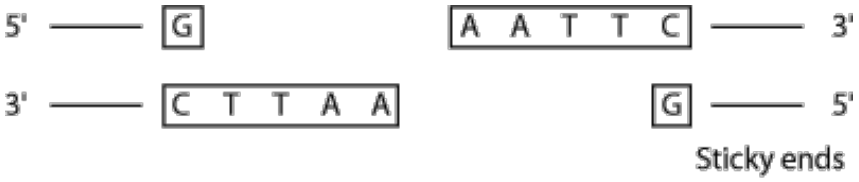
Recombinant DNA

- Gene cloning
  - 

    - The plasmid must have a restriction site because you need to open it up for the insertion of your gene.
    - The plasmid must have an origin of replication because you want to clone your gene, which is inside your plasmid.
    - The plasmid must have an antibiotic resistant gene because this lets you kill competing, useless bacteria that doesn't have your plasmid. When you add an antibiotic, only the bacteria with the antibiotic resistant plasmid will live.
    - Plasmids replicate independently of the genomic DNA of the bacteria.
- Restriction enzymes



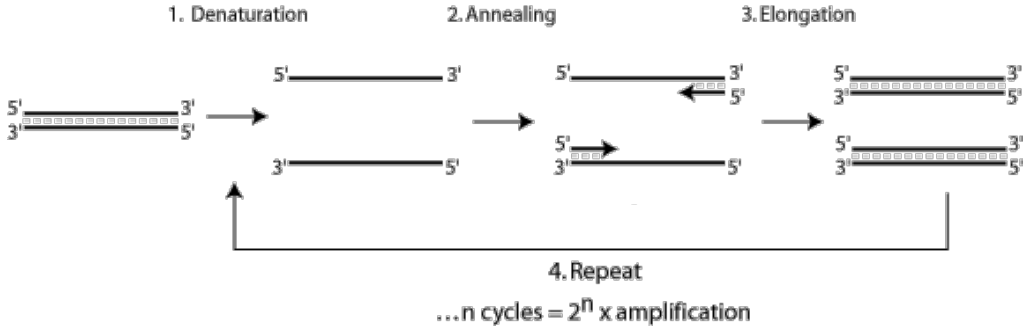
-
    - Restriction enzymes (also called restriction endonucleases) cut double stranded DNA at palindrome sequences. The resulting fragments are called restriction fragments.
    - If you read from 5' → 3' of one strand, then read from 5' → 3' of the other strand, and they are the same, then the section of the double stranded DNA that you just read is a palindrome sequence.



-
    - Some restriction enzymes cut to make sticky ends, which can hybridize.
    - Some restriction enzymes cut to make blunt ends, which cannot hybridize.

- DNA libraries = the result of cloning an organism's entire DNA (genomic or cDNA)
    - Genomic library = entire genomic DNA -> fragmented by restriction enzyme -> cloned
    - cDNA library = entire mRNA population -> reverse transcription into cDNA -> cloned
- Generation of cDNA: mRNA + reverse transcriptase = cDNA

- Hybridization
    - Hybridization, also called annealing, is where DNA strands base pair with each other.
    - In Southern blotting, DNA probes are used to hybridize onto DNA fragments containing a target sequence.
    - In gene cloning, hybridization refers to the process where sticky ends from a restriction fragment of a gene base pairs with the same sticky ends on a plasmid.
- Expressing cloned genes
    - Expression = Cloned gene -> mRNA -> protein
    - Expression needs a vector with the transcription and translation machinery
    - The cloned gene needs to be placed downstream of a strong promoter so that a lot of mRNA will be transcribed
- PCR



1. Denaturation: heat (90 °C) to separate double stranded DNA template.
2. Annealing: cool reaction in order for primers to anneal to the now single stranded DNA template.
    - Excess amount of primers, so they out complete re-annealing of the template strands.
3. Elongation: use heat stable polymerase to extend the primers.
4. Repeat steps 1 to 3 for n cycles. The resulting amplification of the original DNA template after n cycles is 2^n.

- Gel electrophoresis and Southern blotting
    - Gel electrophoresis = separates DNA fragments on a sheet of gel

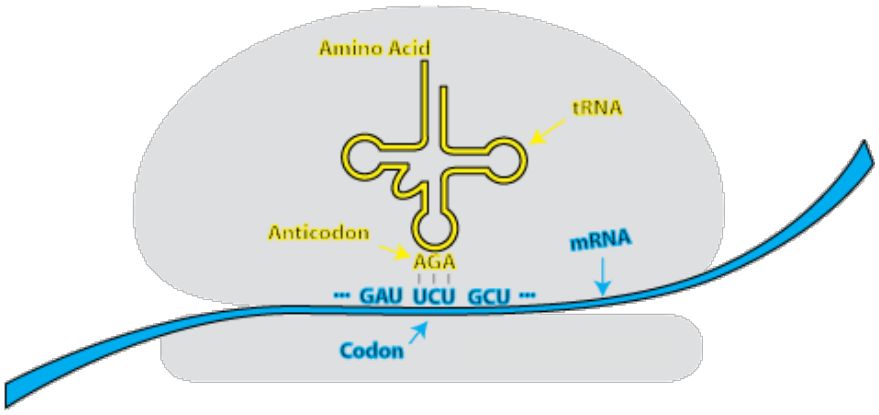
    - Southern blotting = probes make your DNA light up on that sheet of gel
    - Probe for southern blotting = DNA that is complementary to the target DNA
    - Other blots
        - Northern blot: RNA target, DNA/RNA probe
        - Western blot: protein target, antibody probe
- DNA sequencing
    - Sanger sequencing
        - basis: differential chain termination (using dideoxy-NTPs), then detected by capillary electrophoresis
        - pros: cheap
        - cons: can only sequence a short distance, can only detect mutations if it's at high levels
    - Nextgen sequencing = massive parallel sequencing
        - basis: addition of different nucleotide causes different color fluorescence, detected on a 2D chip containing many simultaneous reactions
        - pros: can sequence an entire genome, can detect mutations at very low levels
        - cons: expensive
- Analyzing gene expression
    - Gene expression correlates with mRNA levels, so measure RNA
    - What genes are expressed and at what levels (global picture)? Use gene expression profiling (microarray). Eg: what genes are overexpressed in certain cancer
    - How much is this gene expressed? Use reverse transcription then real time quantitative PCR. Eg: residual BCR-ABL in CML
- Stem cells
    - Stem cells = cells that have the potential to differentiate into many different cell types

    - Example: hematopoietic stem cells -> neutrophils, lymphocytes, red blood cells, platelets
    - Uses: hematopoietic stem cell (bone marrow) transplant as a cure for leukemia
- Practical applications of DNA technology
    - Medical applications: PCR coupled with DNA sequencing = detects mutations / variants = used for diagnosis, monitoring disease level, or predict whether a patient will respond to a certain treatment
    - Human gene therapy = using viruses to infect and introduce functional genes into human cells
    - Pharmaceuticals: uses cloning, expression, and protein purification to isolate proteins/enzymes to treat patients who are deficient in those
    - Forensic evidence: DNA fingerprinting = paternity test = identifies a criminal/person
    - Environmental cleanup: they are making genetically engineered bacteria that can breakdown oil spills or plastic polymers
    - Agriculture: genetically modified foods = introducing genes in crops to make them grow better and be resistant to pests
- Safety and ethics of DNA technology
    - Side effect of human gene therapy: the viruses make mistakes when introducing the genes, resulting in mutations that cause cancer
    - We are not absolutely certain about the long-term health effects of genetically modified foods
    - Sequencing someone's entire genome exposes all their underlying genetic diseases - potential basis for discrimination from insurance companies

Molecular Biology: Protein Synthesis

Genetic code

- Central Dogma: DNA -> RNA -> protein
    1. DNA: resides in the nucleus. It codes information in genes.
    2. Transcription: Inside the nucleus, the DNA genes get transcribed into RNA (messenger RNAs or mRNAs).
    3. RNA: The mRNAs get transported out of the nucleus into the cytoplasm. mRNAs are working copies of the gene.
    4. Translation: ribosomes read off the mRNAs to make proteins.
    5. Protein: synthesized by ribosomes. They are the end product of what's encoded in the genes and they perform all the functions in the cell.
- The triplet code
    - mRNA (nucleotides) must code for protein (amino acids)
    - To do this: 3 nucleotide = 1 codon = 1 amino acid
    - Codons are continuous, non-overlapping and degenerate
    - Continuous because one codon follows right after another. There're no nucleotides in between
    - Non-overlapping because the 3 nucleotides that consist of one codon never serve as part of another codon
    - Degenerate because more than one codon codes for a given amino acid
- Codon-anticodon relationship

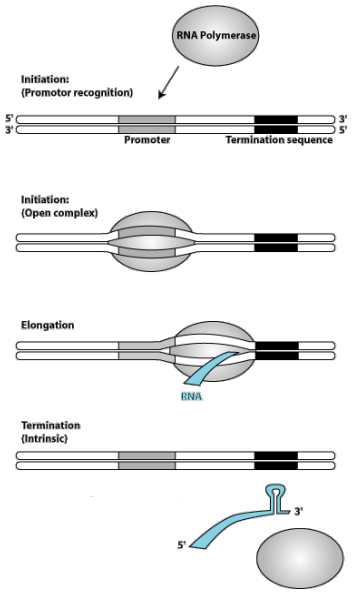
- 

    - Anticodon: the 3 bases on the "tip" of the tRNA. A single tRNA contains a single anticodon at the "tip" and the corresponding amino acid at the "tail". Anticodons are complementary to their corresponding codon.
    - The codon-anticodon relationship: During translation, codons pair with anticodons so that the correct amino acids can be linked to a given codon.
- Degenerate code, wobble pairing
    - Degenerate = more than one codon codes for a given amino acid
    - Wobble pairing = the last/3rd nucleotide of the codon doesn't have to match exactly with the anticodon, will still incoporate the same amino acid during translation
    - Wobble pairing is the mechanism that explains the degenerate nature of the triplet code
- Missense, nonsense codons
    - Missense codon: mutated codon that results in a different amino acid
    - Nonsense codon: mutated codon that results in something other than an amino acid. For example, a stop codon
- Initiation, termination codons (function, codon sequences)
    - Initiation codon (AUG): signals the start of translation. Lies just downstream of the Shine Dalgarno sequence (Kozak sequence for eukaryotes)

    - Termination codon (UAG,UGA,UAA): signals the end of translation. Unlike other codons, tRNA are not involved. Instead a protein called "release factor" comes along and terminates translation

- mRNA composition and structure (RNA nucleotides, 5' cap, poly-A tail)
    - mRNA stands for messenger RNA. It's the product of transcription and the template for translation.
    - The 5' cap is a modified nucleotide linked in a special way to the mRNA. This protects the 5' end from exonuclease degradation.
    - The poly-A tail protects the 3' end of the mRNA from exonuclease degradation.
    - Eukaryotic mRNA: 5' cap - nucleotides - 3' polyA.
    - Prokaryotic mRNAs don't have the 5' cap or polyA tail.
    - More mRNA = more level of expression = more protein made
    - Stronger promoter, less DNA/histone methylation = more mRNA made

Transcription



- tRNA, rRNA composition and structure (eg., RNA nucleotides)
    - Both tRNA (transfer RNA) and rRNA (ribosomal RNA) are products of transcription. However, they do not serve as the template of translation. tRNA is responsible for bringing in the correct amino acid during translation. rRNA makes up the ribosome, which is the enzyme responsible for translation.
    - tRNA is made of nucleotides, many of which is modified for structural and functional reasons. At the 3' end of the tRNA, the amino acid is attached to the 3'OH via an ester linkage.
    - tRNA structure: clover leaf structure with anticodon at the tip, and the amino acid at the 3' tail.
    - rRNA is made of nucleotides, many of which is modified for structural and functional reasons.
    - rRNA is highly structured because it contains the active site for catalysis. The rRNA of the large ribosomal subunit is responsible for catalyzing peptide bond formation, and can do this even without ribosomal proteins.
- Mechanism of transcription (RNA polymerase, promoters, primer not required)
    1. Chain Initiation: RNA polymerase binds to the promoter (TATA box) of the double stranded DNA (closed complex). The double stranded DNA template opens up (open complex).
    2. Chain elongation: nucleoside triphosphates (AUGCs) adds corresponding to the DNA template. No primer is required. RNA elongates as the RNA polymerase moves down the DNA template. RNA is made from the 5' to 3' direction.
    3. Chain termination: there are 2 ways that transcription can terminate.
        1. Intrinsic termination: specific sequences called a termination site creates a stem-loop structure on the RNA that causes the RNA to slip off the template.
        2. Rho (ρ) dependent termination: a protein called the ρ factor travels along the synthesized RNA and bumps off the polymerase.

- mRNA processing in eukaryotes, introns, exons
    - protect from degradation: 5' cap and 3' polyA added
    - RNA splicing: cut out introns, keep and stitch together the exons
    - Alternate splicing = different ways you can do RNA splicing to make different end products
- Ribozymes, spliceosomes, small nuclear ribonucleoproteins (snRNPs), small nuclear RNAs (snRNAs)
    - Ribozymes = RNA enzymes = can have protein parts, but it's actually the RNA part that's doing the catalysis. Best example is the ribosome.
    - Spliceosomes = machinery that does RNA splicing = composed of RNA and proteins = possibly a ribozyme
    - snRNPs = RNA + protein = subunits that assemble into the spliceosomes and other RNA modification machinery
    - snRNAs = the RNA portion of snRNPs
- Functional and evolutionary importance of introns
    - Function: RNA splicing, alternate splicing, gene regulation
    - Evolution: evolved from selfish/parasitic/mobile genetic elements

Translation

- Roles of mRNA, tRNA, rRNA
    - mRNA (messenger RNA): contains codons that code for the peptide sequence.
    - tRNA (transfer RNA): contains the anticodon on the "tip" and the corresponding amino acid on the "tail". Link the correct amino acid to its corresponding mRNA codon through codon-anticodon interaction.
    - rRNA (ribosomal RNA): forms the ribosome. Catalyzes the formation of the peptide bond.
- Role and structure of ribosomes

- Ribosome is the enzyme that catalyzes protein synthesis.
- Ribosome has 2 subunits - the large and the small.
- The large subunit is responsible for the peptidyl transfer reaction.
- The small subunit is responsible for the recognizing mRNA and binds to the Shine-Dalgarno sequence on the mRNA (Kozak sequence for eukaryotes).
- Both subunits are needed for translation to occur and they come together in a hamburger fashion that sandwiches the mRNA and tRNAs in between.

- Mechanism of translation: initiation, termination, co-factors

1. Chain Initiation: To begin translation, you need to form the initiation complex. The initiation complex is basically an assembly of everything needed to begin translation. This includes mRNA, initiator tRNA (fmet), and the ribosome (initiation factors, and GTP aids in the formation of the initiation complex). The initiation complex forms around the initiation codon (AUG), which is just down stream of the Shine-Dalgarno sequence. The Shine-Dalgarno sequence is the "promoter" equivalent of translation for prokaryotes (Kozak sequence for eukaryotes).
2. Chain Elongation: protein is made from the N terminus to the C terminus. mRNA codons are read from the 5' to the 3' end. Elongation consists of:
    1. Binding: new tRNA with its amino acid (tRNA+amino acid is called aminoacyl-tRNA) enters the A site. GTP and elongation factor required.
    2. Peptidyl transfer: attachment of the new amino acid to the existing chain in the P site. The mechanism is a little strange, what happens is that the already existing chain in the P site migrates and attaches to the aminoacyl-tRNA in the A site.
    3. Translocation: the lone tRNA in the P site gets kicked off (E site), and the tRNA in the A site, along with the peptide chain attached to it, moves into the P site. The mRNA gets dragged along also - the codon that was in the A site is

now in the P site after translocation. The A site is now empty and ready for the binding of a new aminoacyl-tRNA to a new codon. Elongation factor and GTP required.

3. Chain termination: When a stop codon is encountered, proteins called release factors, bound to GTP, come in and blocks the A site. The peptide chain gets cleaved from the tRNA in the P site. Peptide chain falls off, and then the whole translation complex falls apart.

- Amino acid activation: enzymes called aminoacyl-tRNA synthetases attach the correct amino acids to their corresponding tRNAs. ATP required.

- Post-translational modification of proteins

    - Add carbohydrate groups: localization tags, gives mucous texture to proteoglycans

    - Adding fatty groups: membrane anchored proteins

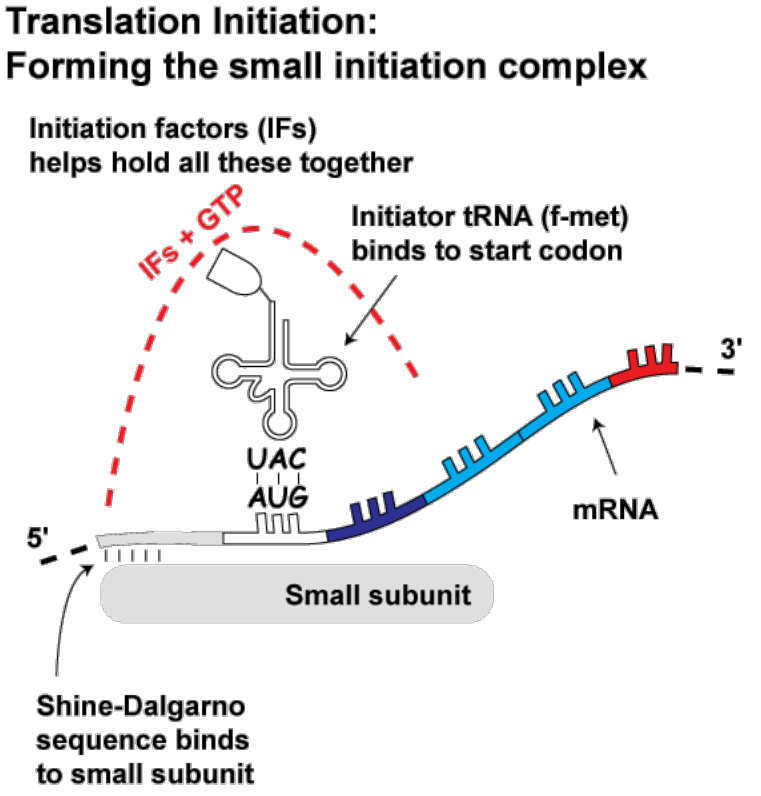
    - Acetylation: localization tags

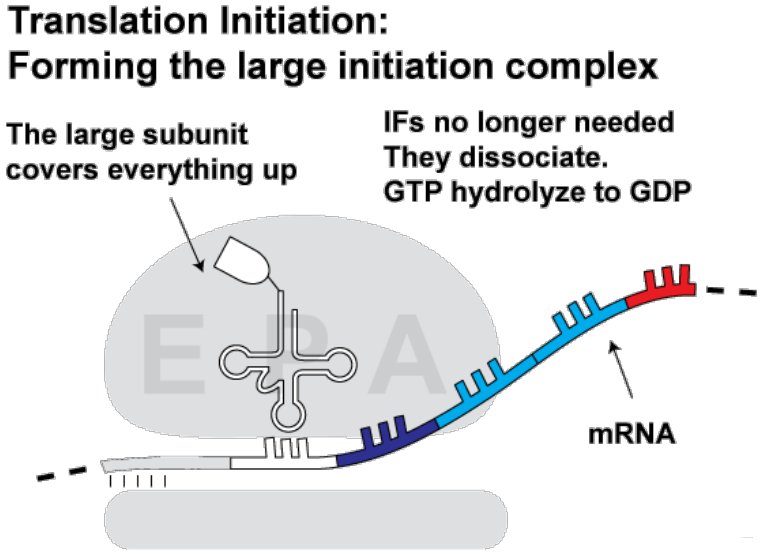
    - Disulfide bond formation: joins different subunits

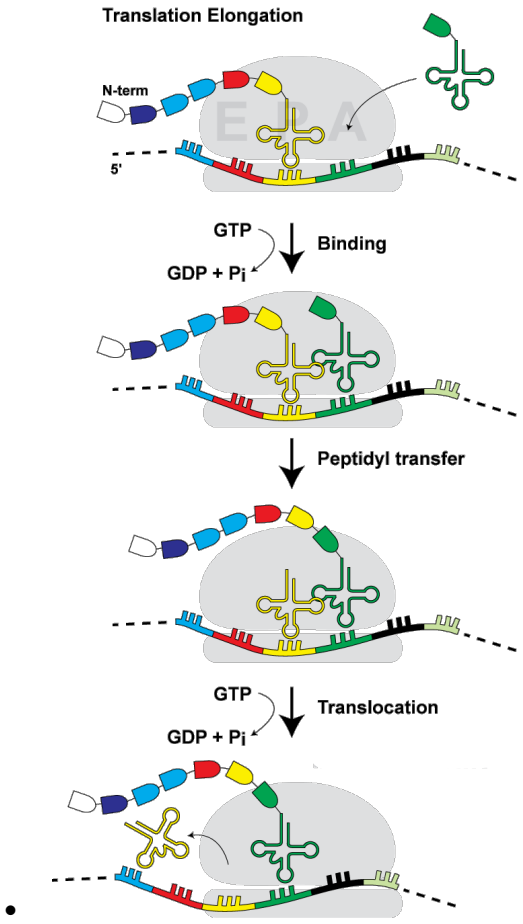
    - Phosphorylation: activating/inactivating an enzyme

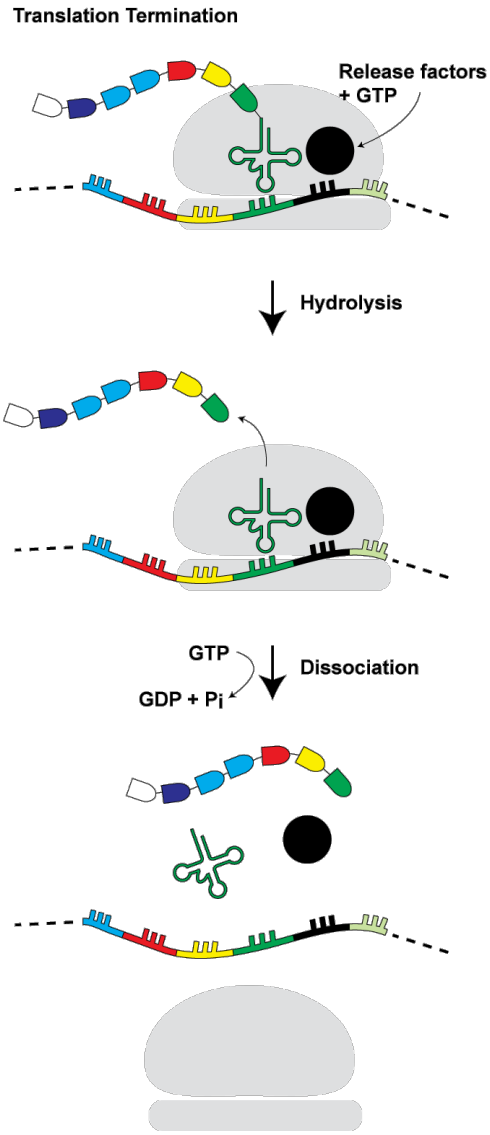
    - Ubiquination: tags protein for destruction

Diagram of translation - graphical overview of initiation, elongation and termination

- 

- 


Translation Elongation
N-term
5'
GTP
GDP + Pi
Binding
Peptidyl transfer
GTP
GDP + Pi
Translocation


Translation Termination
Release factors
+ GTP
Hydrolysis
GTP
GDP + Pi
Dissociation

Molecular Biology: Eukaryotes

Eukaryotic chromosome organization

- Chromosomal proteins
    1. Histones: responsible for the compact packing and winding of chromosomal DNA. DNA winds itself around histone octamers.
    2. nonhistone chromosomal proteins: all the other proteins are lumped together in this group. Responsible for various roles, such regulatory and enzymatic.
- Single copy vs repetitive DNA
    - Tandem repeats (repeats right next to each other, eg: CAGCAGCAG)
        - Trinucleotide repeats: too much can cause diseases. Eg: Huntington disease and fragile X syndrome
        - Satellites, minisatellites and microsatellites: unique pattern of repeats identifies an individual (paternity testing, forensics) or a particular transplant donor (bone marrow engraftment studies)
    - Interspersed repeats: mobile elements/transposons have repetitive DNA at both ends of the sequence
- Supercoiling: a coil on top of a coil, helps to compact very large amounts of genomic DNA to fit into a compact chromosome
- Telomeres, centromeres
    - Telomere: the 2 ends of the chromosome.
    - Centromere: a region on the chromosome, can be at the center or close to one of the ends. After replication, sister chromatids are attached at the centromere. During mitosis, spindle fibers are attached at the centromere and pulls the sister chromatids apart.
- A common question is what is the difference between chromatin and chromosome. The answer is chromatin is the "stuff" that chromosomes are made of. If the chromosome is a cotton shirt, then chromatin is cotton.

Control of gene expression in prokaryotes

- Transcription factors (proteins) binds to enhancers or silencers (DNA) to affect transcription. Enhancers increase transcription when bound by transcription factor, silencers decrease transcription when bound. Enhancers and silencers in prokaryotes are close to the core promoter, and is part of the extended promoter.

- Operons are groups of genes whose transcription can be regulated by binding of either repressors or inducers onto a stretch of DNA on the operon called the operator. Repressors reduce transcription, inducers increase transcriptions.

- Jacob-Monod model describes the lac operon: repressor binds operator (DNA near promoter), blocking transcription

- Sometimes you come across the term co-repressors and co-inducers. When a co-repressor binds to its target, the resulting complex becomes either an active repressor or an inactive inducer. When a co-inducer binds to its target, the resulting complex becomes either an active inducer or an inactive repressor.

- alpha factors: these are how phages control transcription inside their bacterial host. By making different α factors at different times, the phage can control the correct transcription sequence of early, middle, and late genes. For example, the α factor for late gene is not made until last.

- Transcription attenuation: works in the trp (tryptophan) operon. When tryptophan is scarce and needed, transcription occurs normally. However, if there's already a lot of tryptophan present, then transcription terminates prematurely.

- Negative control = repressor, anything that decreases transcription

- Positive control = inducer, enhancer, anything that increases transcription

Control of gene expression in eukaryotes

- Transcription regulation

    - Transcription factors (protein) bind to enhancers or silencers (DNA) to affect transcription. Enhancers increase transcription when bound, while silencers decrease it. The main difference in eukaryotes that sets them apart from prokaryotes is that enhancers/silencers can be very far away from the actual promoter, and can be upstream or downstream. The DNA must must loop back on itself so that the transcription factor bound to enhancer/silencer can actually make contact with the promoter. Intermediate proteins are involved in the process.

    - Eukaryotes lack the bacterial transcription regulation mechanisms such as the operon and attenuation.

- DNA binding proteins, transcription factors
    - DNA-binding proteins bind to DNA.
    - transcription factors bind to DNA, so they have a DNA-binding domain.
    - DNA-binding domains interact with the grooves in the double helix (major grooves and minor grooves).
    - Advanced: common DNA-binding domains include helix-turn-helix (HTH), zinc finger, basic-region leucine zipper (bZIP).
- Gene amplification and duplication
    - Gene duplication = 2x amplification
    - Mechanism: either a portion of DNA gets duplicated within a chromosome or the entire chromosome is duplicated
    - Certain genes are amplified in cancer such as MYC and RAS
    - Certain gene amplifications can be used as a target for treatment: Her2 amplification is treated with Herceptin in breast cancer
    - Certain gene amplifications affect the prognosis of a disease: intrachromosomal amplification of chromosome 21 = worse prognosis in acute lymphoblastic leukemia
    - Other gene amplifications have no effect at all other than to increase the size of the genome (eg. Selfish/parasitic DNA that serves no function but is amplified)
- Post-transcriptional control, basic concept of splicing (introns, exons)
    - tRNAs and rRNAs modifications: some normal nucleotides are modified to control the structure of these RNAs.
    - mRNAs modifications
        - RNA splicing: sequences called introns are cut out, sequences called exons are kept and spliced (joined) together.
        - Alternate splicing: different ways of cutting up and RNA and rejoining the exons pieces make different final RNA products.
        - 5' capping and 3' poly-A tail: these help to protect the RNA from degradation so they can last longer.

- After the correct modifications, RNA is transported out of the nucleus where they can function in translation.
- After some time, RNA is degraded. The rate and timing of RNA degradation can be controlled by the cell.

- Cancer as a failure of normal cellular controls, oncogenes
  - Failure of normal cellular controls:
    - Cancer cells continue to grow and divide in situations normal cells would not.
    - Cancer cells fail to respond to cellular controls and signals that would halt this growth in normal cells.
    - Cancer cells avoid apoptosis (self-destruction) that normal cells undergo when extensive DNA damage is present.
    - Cancer cells stimulate angiogenesis (cause new blood vessels to grow to nourish the cancer cell).
    - Cancer cells are immortal while normal cells die after a number of divisions.
    - Cancer cells can metastasize - break off and then grow in another location.
  - Oncogenes: genes that cause cancer when activated. The product of many oncogenes are involved in speeding up cell division. Before an oncogene is activated, it is a harmless proto-oncogene. Something occurs that changes the proto-oncogene to an oncogene. The classic example of oncogene is the src.
  - Tumor suppressors: if the oncogene is the "bad" gene, tumor suppressors are the "good" genes. The product of many tumor suppressors are involved in slowing down or controlling cell division. If something happens that cause the tumor suppressor to no longer function, then the cell becomes cancerous. The classic example of tumor suppressor is the p53.

- Regulation of chromatin structure
  - Chromatin = DNA wrapped around histones
  - Chromatin can be regulated by modifying DNA (methylation) or histone (methylation, acetylation)
  - Euchromatin: less compact chromatin, more exposed DNA, actively transcribed

    - Heterochromatin: more compact chromatin, less exposed DNA, not actively transcribed

- DNA methylation = CpG methylation (natural) or alkylating agent (chemotherapy) induced methylation
- CpG islands = GC-rich DNA sequence near promoters that is the target for methylation
- The methylation occurs on the cytosine nucleotide to make 5-methylcytosine
- The enzyme is DNA methyltransferase (DNMT)
- Methyltransferases can work in both ways (add or remove methyl groups), depending on the enzyme
- Methylating CpG islands silences a gene
- Clinical utility: MGMT promotor methylation status
    - Glioblastoma (brain cancer) is treated by an alkylating agent (chemotherapy) +/- radiation
    - MGMT = methyltransferase enzyme that removes alkyl/methyl groups from DNA = undo's the chemotherapy
    - Bad = active MGMT = unmethylated MGMT promotor = undo's chemotherapy
    - Good = Inactive MGMT = methylated MGMT promotor = effective chemotherapy
- Non-coding RNAs = not translated into protein = anything other than an mRNA
    - rRNA = makes up the ribosome
    - tRNA = brings amino acids to the ribosome
    - snRNA = makes up the RNA splicing machinery
    - snoRNA = guides RNA modification
        - RNA is heavily modified in RNAs where a structural purpose is needed (rRNA, tRNA, snRNA)
        - 2'O methylation (protects against hydrolysis/degradation)
        - Convert Uracil to pseudoUracil (plays a role in tRNA structure and integrity)

- miRNA = makes up the RNA silencing machinery (blocks mRNA translation or degrades mRNA)

Genetics

Mendelian concepts

- Phenotype and genotype
    - Phenotype: what is observed. For example, height, color, whether the organism exhibits a trait.
    - Genotype: the genetic make up. For example, homozygous dominant (TT), heterozygous (Tt), homozygous recessive (tt).
- Gene: a gene is a stretch of DNA that codes for a trait. In molecular biology, the gene codes for a protein, which acts to bring about a trait.
- Locus: location (of a gene) on a chromosome.
- Allele: single and multiple
    - An allele is a variant of a gene. A gene may have a number of alleles. All alleles of the same gene exist at the same locus.
    - A cell holds 2 alleles of each gene. One allele from mom, one allele from dad.
    - When a gene has only 2 alleles, then that's the simple case we're used to seeing. For example, the trait for height in peas is governed by T and t. TT and Tt gives tall plants, and tt gives short ones.
    - When a gene has more than 2 alleles, then that's called multiple alleles. For example, blood type is governed 3 alleles: I^A I^B and i. Because a cell can only hold 2 of these alleles, the different combinations an individual can have are:

Genotype	Blood type (phenotype)
I^AI^A or I^Ai	A
I^BI^B or I^Bi	B
I^AI^B	AB
ii	O

- Homo- and heterozygosity

    - Homozygous: when the two alleles that an individual carries are the same. For example, AA or aa.
    - Heterozygous: when the two alleles that an individual carry are different. For example, Aa.

- Wild type: the "normal" allele or phenotype for an organism. The wild-type is usually the most prevalent, although it doesn't necessarily have to be true.
- Recessiveness: the "weak" allele. The recessive allele is only expressed if both copies are present. Only a single copy is needed for the dominant allele. The recessive allele is usually denoted as the lower case letter, the dominant allele is usually denoted as the upper case letter. For example, blond hair is recessive. Both alleles for blond hair need to be present, otherwise the hair is dark.
- Complete dominance

Genotype	Phenotype
AA	Dominant
Aa	Dominant
aa	Recessive

- Co-dominance

Genotype	Phenotype
AA	A
AB	Both A and B
BB	B

- An example of co-dominance is the A and B blood type alleles. Type A cells have A antigens. Type B cells have B antigens. Type AB makes both antigens.
- Incomplete dominance, leakage, penetrance, expressivity
    - Incomplete dominance:

Genotype	Phenotype
AA	A

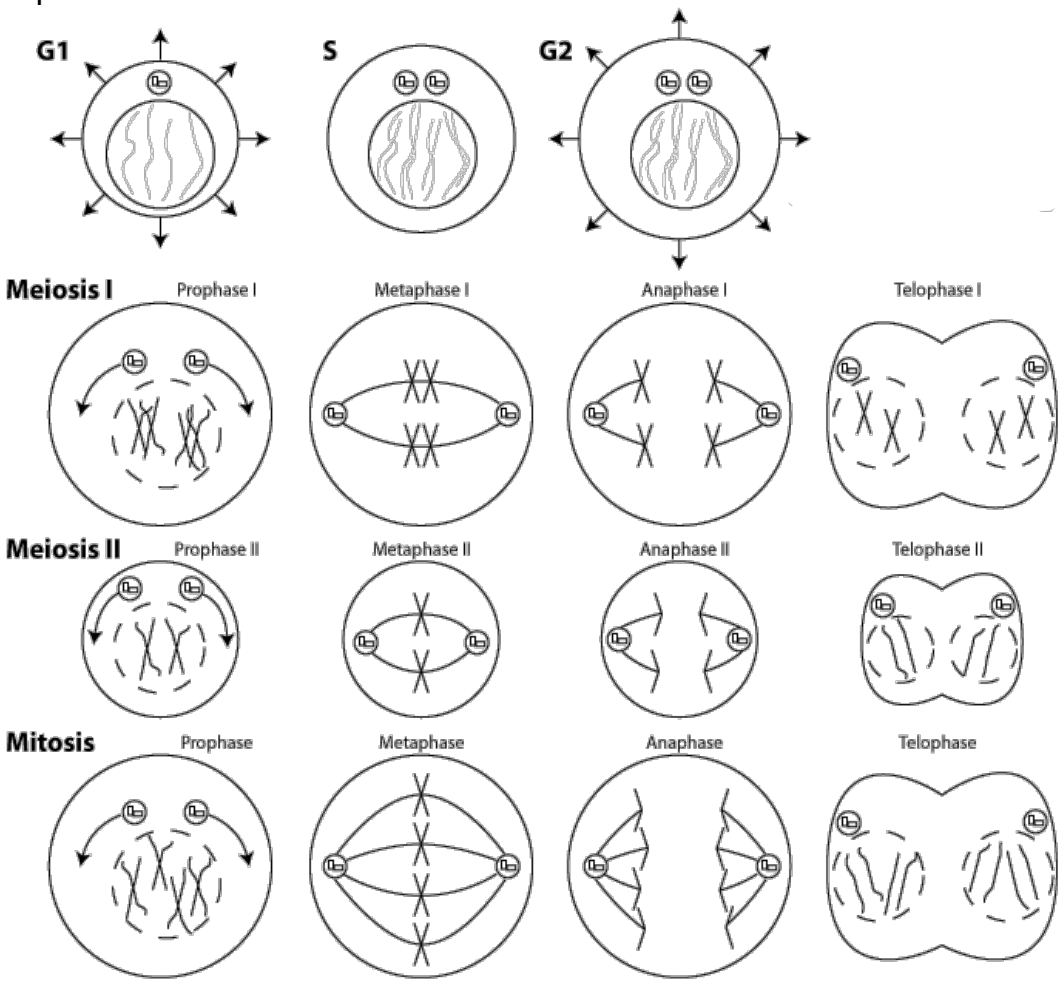
AB	In between A and B
BB	B

    - An example of incomplete dominance is the color of chickens. A cross between black chickens and white chickens give rise to bluish grey chickens.
    - leakage: gene flow from one species to another.
    - Penetrance is the frequency that a genotype will show up in the phenotype. 100% penetrance means that if you have the genes for being smart, then you'll definitely be smart! Less than 100% penetrance means that you may have the genes for being smart, but you may not actually be smart.
    - Expressivity is to what degree a penetrant gene is expressed. Constant expressivity means that if your genes for being smart manages to penetrate (show up as a trait), then you're IQ is 120. Variable expressivity means that your IQ doesn't have to be 120, it could be somewhat lower or somewhat higher.
- Hybridization: viability
    - Hybrid vigor = increased viability for offspring of parents who are genetically more different
    - Mechanism = less chance to receive 2 copies of the same detrimental recessive gene
- Gene pool: all of the alleles in a population.

Meiosis and genetic variability

- Significance of meiosis: meiosis introduces genetic variability by genetic recombination. Genetic recombination is the product of independent assortment and crossing-over, which introduces genetic variability.

- Important differences between meiosis and mitosis



mitosis	meiosis
no tetrad	tetrad formation (pairing of homologous chromosomes) and cross over
daughter cells identical to parent cell	daughter cells different from parent cell
diploid (2n) daughter cells	haploid (n) daughter cells
1 division involved	2 divisions involved
2 daughter cells	4 sperm cells or 1 egg (with polar bodies)

- Segregation of genes
    - Independent assortment
        - Independent assortment generates genetic variation.

        - A cell has 2 copies of each somatic chromosome- one from mom, one from dad (homologous chromosomes). Independent assortment shuffles these chromosomes, and then places only one copy of each into the gamete. This way, the gamete may have chromosome 1 from mom, chromosome 2 from dad, chromosome 3 from dad, ... etc.

        - The mechanism of independent assortment is the following: During metaphase I of meiosis, homologous chromosome pair up along the metaphase line in random orientation - sometimes the mom's chromosome is on the left, sometimes it's on the right. During anaphase I of meiosis, the homologous chromosomes are pulled apart. Those on the left will be put into one daughter cell, those on the right will be put into another.

    - Linkage

        - Because of independent assortment, genes on different chromosomes are randomized. However, genes on the same chromosome can not be randomized by this mechanism.

        - Genes on the same chromosome are linked to some extent.

        - Crossing over is a mechanism that reduces linkage. However, crossing over is only efficient when the genes are physically apart from each other on the chromosome.

        - When the genes are further apart on the chromosome, crossing over makes them less linked.

        - The physically closer the genes are on the chromosome, the more linked they are.

    - Recombination: also called genetic recombination, is the process that introduces genetic diversity into the gametes during meiosis. There are 2 processes that makeup recombination: independent assortment and crossing over.

        - Crossing over occurs during prophase I (the actual site of cross over is the chiasma. The chiasma is made possible because of pairing of homologous chromosomes called the tetrad, which is formed by a process called synapsis).

        - Single crossovers: results in genetic recombination. The chromatids involved in this single crossover exchange alleles at a given locus. Results in 2/4 recombinants.
        - Double crossovers:
            - Scenario 1: results in no genetic recombination. The chromatids involved in this double crossover exchange alleles at first, but then it exchanges them back, resulting in no net recombination. This is called the 2-strand double crossover. Results in 0/4 recombinants.
            - Scenario 2: results in genetic recombination. The chromatids exchange alleles during a crossover. Then, one of the crossover chromatid exchanges with a different chromatid. This is called the 3-strand double crossover. Results in 2/4 recombinants.
            - Scenario 3: results in genetic recombination. The chromatids exchange, then 2 totally different chromatids on the same chromosome exchange. This is called the 4-strand double crossover. Results in 4/4 recombinants.
        - Synaptnemal complex: the protein complex that glues the tetrad together
        - Tetrad: the paired homologous chromosome structure
    - Sex-linked characteristics = gene for the characteristic is on the X chromosome.
    - Very few genes on Y chromosome
        - The Y chromosome is very small and carries few genes of importance.
        - All the sex-linked alleles are carried on the X chromosome.
    - Sex determination: XX = female, XY = male
    - Cytoplasmic/extranuclear inheritance
        - Cytoplasmic inheritance = inheritance of things other than genomic DNA.

        - All cellular organelles, such as mitochondria, is inherited from the mother.

- Mutation
    - General concept of mutation-error in DNA sequence
        - Mutation = change in DNA sequence by means other than recombination.
    - Types of mutations: random, translation error, transcription error, base substitution, inversion, addition, deletion, translocation, mispairing
        - Random mutation = random changes in DNA sequence. Can be due to radiation, chemicals, replication error ...etc.
        - Translation error = even if the DNA for a gene is perfect, errors during translation can cause expression of a mutant phenotype.
        - Transcription error = even if the DNA of a gene is perfect, errors during transcription can cause expression of a mutant phenotype.
        - Base substitution = mutation involving a base (ATGC) changing to a different base.
        - Inversion = a stretch of DNA (a segment of a chromosome) breaks off, then reattaches in the opposite orientation.
        - Addition = also called insertion = an extra base is added/inserted into the DNA sequence.
        - Deletion = a base is taken out of the DNA sequence.
        - Addition/insertion and deletion mutations result in a frameshift mutation.
        - Translocation = a stretch of DNA (a segment of a chromosome) breaks off, then reattaches somewhere else.
        - Mispairing = A not pairing with T, or G not pairing with C.
    - Advantageous vs. deleterious mutation

        - Advantageous = results in a benefit to the fitness of the organism. For example, the mutation that causes flies to become wingless is advantageous in an environment that is very windy.
        - Deleterious = results in a harmful effect to the fitness of the organism. For example, a mutation that causes an organism to be sterile.
    - Inborn errors of metabolism = genetic diseases resulting in faulty metabolism. For example PKU (Phenylketonuria) is an inborn error of metabolism where people can't metabolize phenylalanine. There's no cure, but the treatment involves avoiding things containing the amino acid phenylalanine.
    - Relationship of mutagens to carcinogens
        - Mutagen = something that causes mutation.
        - Carcinogen = something that causes a mutation that causes cancer.
        - All carcinogens are mutagens.
        - Not all mutagens are carcinogens.
    - Genetic drift = random changes in allele frequency due to chance = not due to natural selection
    - Synapsis or crossing-over mechanism for increasing genetic diversity
        - Synapsis: homologous chromosomes come together and form tetrad
        - Crossing-over: exchange of genetic material between homologous chromosomes after the tetrad forms
        - Increases genetic diversity by introducing new allele combinations in the chromosome you're about to give to your offspring

Analytic methods

- Hardy-Weinberg Principle

- $p+q = 1$
- $(p+q)^2 = 1 \rightarrow p^2 + 2pq + q^2 = 1$
- Five Assumptions of Hardy-Weinberg
  - Infinitely large population (no genetic drift)
  - No mutation
  - No migration
  - Random mating (no sexual selection)
  - No natural selection

- Test cross: back cross, concepts of parental, F1 and F2 generations
  - Test cross: so you have something with dominant phenotype. It could either be Aa or AA. To find out, you cross it with the homozygous recessive aa. If Aa, half the offspring will express the recessive phenotype. If AA, no offspring will express the recessive phenotype.
  - Back cross = mating between the offspring and the parent = preserve parental genotype.
  - Parental generation = P = generation of the parent. On a pedigree, the is the row that represents the parents
  - F1 generation = Felial 1 = children. On a pedigree, this is the row below the parents, and represents the children of the parents.
  - F2 generation = Felial 2 = grandchildren. On a pedigree, this is the row below the F1, and represents the children of the F1 and grandchildren of the parents.
- Gene mapping: crossover frequencies
  - Gene mapping = physical location genes on the chromosome (eg. toward the end, closer to the middle, etc)
  - Further apart = higher crossover frequency
- Biometry: statistical methods

- Biometry = using statistics to analyze biological data
- null hypothesis = first assuming that you are wrong - there is no relationship in your data
- p value = calculated chance that the null hypothesis is right, that you are wrong
- p value < 0.05 means less than 5% chance the null hypothesis is right (basically the null hypothesis is wrong, you are right, there is a relationship in your data)
- t-test: compares 2 data sets
- ANOVA: compares 3+ data sets
- Fisher exact test: compares data in a 2x2 table
- Variance, standard deviation: evaluates the distribution of a single set of data. Higher value = data is more spread out
- Skew = asymmetry in the bell curve. Skewed left = longer "tail" of the bell curve on the left.

Microbiology

Cell Theory

- Theory:
    - Living things are made of cells
    - The cell is the most basic unit
    - Cells divide and self-replicate
- History: cells were first discovered by Robert Hooke using a microscope to examine cork (wood)
- Impact: promoted the study of cells and the field of microbiology and cell biology

Classification and Structure of Prokaryotic Cells

- Lack of nuclear membrane, mitotic apparatus: Bacteria do not have a membrane-enclosed nucleus. Their genetic material is located in an irregular region called the nucleoid. Bacteria do not have spindles and asters that make up the eukaryotic mitotic apparatus. Instead, the prokaryotic cytoskeleton helps pull the replicated DNA apart.
- Lack of typical eukaryotic organelles: Bacteria don't have Golgi, ER, mitochondria, chloroplasts.
- Prokaryotic domains
    - Eubacteria are the bacteria we encounter every day
    - Archaea are the prokaryotes that inhabit extreme environments (high salt, temperature, or chemicals).
- Major classifications of bacteria by shape
    - Bacilli (rod-shaped): Streptococcus causing pneumonia, strep throat
    - Spirilli (spiral shaped): Helicobacter pylori causing gastric ulcers

    - Cocci (spherical): Staphylococcus causing skin infections/cellulitis/MRSA

- Presence of cell wall in bacteria: bacterial cell wall is made of peptidoglycan, a polysaccharide-protein molecule. In contrast, plant cell wall is made of cellulose and fungi cell wall is made of chitin.

- Flagellar propulsion, mechanism

    - Bacterial flagella is made of flagellin. In contrast, eukaryotic flagella is made of microtubules.

    - The mechanism of the bacterial flagella is rotation. A rotor at the base of the flagella drives the rotation, powered by a proton or sodium gradient. (Compare this to eukaryotic flagella, which is powered directly by ATP)

Prokaryotic cell: growth and physiology

- Reproduction by fission

    - DNA replicates

    - Replicated DNAs separate by attaching to the cell membrane as the cell elongates (in contrast to mitosis, no spindle fibers needed).

    - Cytokinesis divides the parent cell into two daughter cells.

- High degree of genetic adaptability, acquisition of antibiotic resistance

    - Mutation

    - Transformation: bacteria take in plasmids and DNA fragments and integrates them into the genome.

    - Transduction: bacteriophages undergoing lysogenic life cycle incorporate the viral DNA into the bacterial genome.

    - Conjugation: Bacteria transfer DNA between one another through the sex pilus.

- Exponential growth: Bacterial growth starts off being exponential because of the nature of binary fission. Later, when food becomes short, and it gets crowded, growth slows and eventually plateaus.

- Existence of anaerobic and aerobic variants
    - Obligate aerobe = must have oxygen for growth.
    - Obligate anaerobe = dies when oxygen is present.
    - Facultative anaerobe = doesn't need oxygen for growth, but grows better with oxygen.
- Symbiotic relationships
    - Parasitic = bacteria benefits at the expense of the host. Disease causing bacteria are examples of parasitic relationships.
    - Mutualistic = both bacteria and host benefits. For example, the E. Coli in your gut; the natural flora on your skin.
    - Commensalistic = one benefits while the other has no effect.
- Chemotaxis: bacteria don't have eyes, so they sense chemicals for navigation (eg: moving toward places with higher concentrations of food, avoiding places with higher concentrations of toxins)

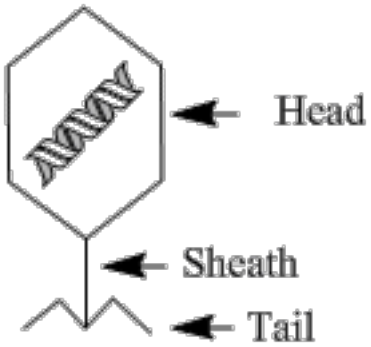
Prokaryotic cell: genetics

- Existence of plasmids, extragenomic DNA, transfer by conjugation
    - Plasmids are double stranded DNA.
    - A plasmid can exist and replicate independently of the genomic DNA, or be integrated into it.
    - Plasmids are inherited.
    - Plasmids are not essential for growth and reproduction in the wild.
    - Conjugation transfers genetic material between bacteria via a pillus.
        - A bacteria able to make the pillus (F+) has a plasmid that contains the pillus genes.
        - F+ bacteria can transfer the plasmid to an F- bacteria.
        - Conjugation can also transfer some genomic DNA (because F+ plasmid can integrate into the chromosome).

- Transformation: incorporation into bacterial genome of DNA fragments from external medium
    - When a bacteria dies, it lyses and spills many DNA fragments into the environment.
    - Another bacteria encounters these DNA fragments, takes them in, and integrates them into its own genome.
    - If the DNA fragments contained an antibiotic resistant gene, then the transformation just made the bacteria antibiotic resistant.
- Regulation of gene expression, coupling of transcription and translation
    - Regulation at the transcription level: some genes are actively transcribed, while others are not. Activators and inhibitors modulate the transcription of a gene.
    - Regulation at the translation level: Some mRNA gets translated more. In prokaryotes, mRNAs with better Shine-Dalgarno sequence are translated more. In eukaryotes, translation regulation can involve adding more polyAs to mRNA (longer mRNA life time), modulating the translation machinery (phosphorylation of initiation factors), or storing mRNAs to be translated at a later time (mRNA masking).
    - Prokaryotes regulate gene expression predominantly at the transcription level (eg. Operons, in which inducers increase transcription, and inhibitors decrease transcription). Eukaryotes have more regulation at other levels, and can also undergo RNA splicing, which can splice RNA in different ways to make different mRNAs.
    - Transcription-translation coupling: in prokaryotes, translation occurs as the mRNA is being transcribed (no RNA processing in prokaryotes).
    - In a coupled transcription-translation system, regulation by attenuation can occur for the Trp gene:
        - When cell is full of Trp, translation occurs fast because of abundant Trp amino acid. This fast ribosome movement across the transcribing mRNA causes the Trp mRNA transcription to terminate. Because Trp is not needed.

        - When cell is starved of Trp, translation occurs slower because Trp amino acid is lacking. This slower ribosome movement across the transcribing mRNA causes the Trp mRNA to be made to its completion.

Virus structure

- General structural characteristics (nucleic acid and protein, enveloped and nonenveloped)
    - Nucleic acid can be DNA or RNA, single stranded or double stranded.
    - Protein coat covers the nucleic acid.
    - Some viruses have an envelope derived from the host's cell membrane, while others lack it (nonenveloped).
        - Enveloped viruses bud off the host's membrane.
        - Nonenveloped viruses cause the host to burst to release viral particles.
    - Smaller than bacteria.
- Lack organelles, nucleus: Viruses don't have any organelles or a nucleus. The genetic material is simply packed inside a protein coat.
- Structural aspects of typical bacteriophage
    - 

    - Head stores genetic material.
    - Sheath provides a passage way for genetic material to be injected into the host bacteria.
    - Tail fibers attach to the host bacteria.

- Genomic content RNA or DNA: Viruses can contain either RNA or DNA as their genomic content. Out of the RNA viruses, those that convert their genome into DNA inside their host are called retroviruses.

- Size relative to bacteria and eukaryotic cells: Viruses are roughly 100 times smaller than bacteria, and 1000 times smaller than eukaryotic cells.

Viral life cycle

- Self-replicating biological units that must reproduce within specific host cell: Viruses can not replicate by themselves. They depend on the host's replication organelles to replicate. The host's ribosomes will make the necessary protein coats and polymerases that replicate the viral genetic material. Retroviruses contain their own reverse polymerase to convert RNA to DNA before the host's polymerases take over.

- Generalized phage and animal virus life cycles:

    - attachment to host, penetration of cell membrane or cell wall, and entry of viral genetic material

    - use of host synthetic mechanism to replicate viral components: Host's ribosomes synthesize the necessary enzymes. Host's ATP provides necessary energy. The host also provides the raw materials such as nucleotides and amino acids.

    - self-assembly and release of new viral particles: The coat proteins and viral genetic material will assemble into viral particles all by themselves.

- Retrovirus life cycle: integration into host DNA

    - First, retrovirus enters the host.

    - The viral reverse transcriptase then converts the viral RNA genome into double-stranded DNA.

    - A virally encoded enzyme called integrase adds in the viral DNA into the host's genome at a random place.

    - When the host replicates, the viral DNA gets replicated also.

- Transduction: transfer of genetic material by viruses

1. Virus infects cell: host DNA degraded into fragments, viral DNA takes over control.
2. Host DNA fragment gets packed into virus progeny by accident.
3. Virus progeny infects another cell, injects previous host's DNA fragment.
4. Fragment enters cell, find its homologous counterpart, and crossover.

Fungi

- General characteristics
    - Made of hyphae filaments.
    - Parasitic hyphae = haustoria
    - A mass of hyphae is called mycelium.
    - Have cell wall made of chitin.
    - All fungi are heterotrophs - they are either parasites or saprobes.
    - Lichens = fungi + algae. Algae provides food, fungi provides water and protection.
    - Mycorrhizae = fungi + plant roots. Plant provides food, fungi provides more absorption surface area.
    - Yeast, molds, mushrooms are all fungi.
- General aspects of life cycle
    - Can be sexual or asexual.
    - Reproduces via spores or mycelial fragmentation.
    - Most fungi have both a haploid and a diploid stage of life cycle.

Generalized Eukaryotic Cell

Plasma Membrane

- General function in cell containment
- Composition of membranes
    - Lipid components
        - Phospholipids (forms bilayer)
        - Steroids, cholesterol (provide more fluidity)
        - Waxes (provide more stability)
    - Protein components: receptors, channels, transport proteins
    - Fluid mosaic model: the fluid mosaic model basically describes the membrane as protein boats floating in a sea of lipids.
- Membrane dynamics
    - Invaginates to take things in: phagocytosis, pinocytosis, endocytosis
    - Buds off: exocytosis
    - Changes shape: chemotaxis with the aid of changes in cytoskeleton
    - Let's things through: small nonpolar molecules, others by the aid of channels or pumps
- Solute transport across membranes
    - Thermodynamic considerations
        - Mixing a charged ion with hydrophobilic lipid bilayer is thermodynamically unfavorable by entropy
        - Therefore, ions can't pass through the lipid bilayer without assistance from channels/pumps

    - Osmosis: water diffuses freely across the membrane, but not ions. So osmosis occurs readily
        - Colligative properties depend on the number of solute dissolved in solvent
        - Solvent will move as to dilute the component with more solute dissolved (given a semipermeable membrane that lets solvent pass but not the solutes)
        - Osmotic pressure = pressure exerted by solvent via osmosis = counter pressure needed to prevent osmosis
        - The bigger the difference in solute concentration, the bigger the osmotic pressure
        - Too much osmotic pressure, and the cell will lyse (eg: if you put animal cells in water)
    - Passive and active transport: things that can't readily diffuse across the membrane are transported across the membrane either without energy (passive) or with energy (active).
        - Passive transport = no ATP needed = channels, facilitated diffusion = direction of movement is down a concentration gradient
        - Active transport = ATP needed = sodium/ptassium pump = up/against a concentration gradient
        - Sodium-potassium pump: 3 sodium (NA^+) out, 2 potassium (K^+) in. Thus, the cell maintains a negative resting potential.
- Membrane channels: lets ions through the cell membrane
- Membrane potential: the resting potential of the cell membrane is negative because of the sodium-potassium pump.
- Membrane receptors, cell signaling pathways, second messengers
    - Many hormones can't cross the plasma membrane, so they bind to membrane receptors on the outside.
    - Receptor binding triggers the production of second messengers.

    - Second messengers cause a change inside the cell (through a protein kinase cascade).
    - Cell signaling pathways:
        - Contact signaling = physical contact triggers a change inside cell.
        - Chemical signaling = chemical binding to receptor triggers a change inside cell.
            - Nerves use neurotransmitters.
            - The endocrine system use hormones.
        - Electrical signaling = change in membrane potential triggers change in cell.
            - Action potential along neurons propagates and cause release of neurotransmitters into synapse..
            - Action potential along muscle cell membrane causes contraction.

- Exocytosis and endocytosis: exo = getting stuff out, endo = taking stuff in.
- Intercellular junctions
    - gap junctions: connects two cells, and allows stuff to flow through between the cells.
    - tight junctions: stitches/glues two cells together, and does not allow stuff to flow through between the cells. A series of cells with tight junctions also effectively forms an impermeable barrier.
    - desmosomes: connects two cells together by linking their cytoskeleton. They are organized for mechanical strength, not an impermeable barrier.

Membrane-Bound Organelles and Defining Characteristics of Eukaryotic Cells

- Defining characteristics (membrane bound nucleus, presence of organelles, mitotic division)
    - Defining characteristics = what sets eukaryotes apart from prokaryotes.
    - Eukaryotes have a true nucleus (membrane-bound), while prokaryotes don't.
    - Eukaryotes have membrane-bound organelles (ER, Golgi, lysosomes, mitochondria), prokaryotes don't.
    - Eukaryotes divide by mitosis (all them chromosomes line up and stuff), prokaryotes undergo binary fission (no chromosomes, just a circular ring of DNA, no need for complex mitosis)
- Nucleus (compartmentalization, storage of genetic information)
    - compartmentalization: nuclear membrane / nuclear envelope surrounds the nucleus.
    - genetic information is stored inside the nucleus as DNA.
- Nucleolus (location and function)
    - location is a region inside the nucleus.
    - function is to transcribe ribosomal RNA (rRNA).
- Nuclear envelope, nuclear pores
    - nuclear envelope is a double membrane system made of an outer and an inner membrane. Also called nuclear membrane.
    - nuclear pores are holes in the nuclear envelope where things can pass into and out of the nucleus. Transcription occurs in the nucleus, and those transcribed RNA need to pass out of the nucleus. Things like transcription factors need to pass into the nucleus where they can access the DNA to be transcribed.

Membrane-bound Organelles

- Mitochondria

- site of ATP production: an apparatus called the ATP synthase makes ATP from ADP by utilizing the proton gradient as the driving force. The proton gradient is where the proton H+ concentration is higher in the inter-membrane space than the matrix of the mitochondria.
- self-replication; have own DNA and ribosomes.
    - mitochondria replicate independently from the cell containing the mitochondria.
    - mitochondria does not share the same genome with its host.
    - mitochondria has their own ribosomes, which are different from the host's ribosomes in both sequence and structure.
    - All these serve to support the endosymbiosis theory.
- inner and outer membrane
    - Inner membrane surrounds the matrix.
    - The folds of the inner membrane make up the cristae.
    - Between the outer and inner membrane is the intermembrane space.
    - The intermembrane space is high in protons H+.
    - The outer membrane separates the mitochondria from the cytoplasm.

- Lysosomes (vesicle containing hydrolytic enzymes)
    - Digests things like food and viral/bacterial particles.
    - Things you want to digest gets into a vacuole by endocytosis or phagocytosis, and then the vacuole fuses with the lysosome. Anything inside gets digested by the hydrolytic enzymes.
- Endoplasmic reticulum:
    - rough (RER) and smooth (SER)
        - rough ER has ribosomes studded over it, smooth ERs don't.

        - RER deals with protein synthesis, folding, modification, and export.
        - SER deals with biosynthesis of lipids and steroids, and metabolism of carbohydrates and drugs.
        - In the muscles, the SER or SR stores and regulates calcium.
    - RER (site of ribosomes): the ribosomes attach to the outside of rough ER and synthesis protein into the lumen.
    - role in membrane biosynthesis: SER (lipids), RER (transmembrane proteins)
        - SER = makes lipids of the plasma membrane.
        - RER = makes transmembrane proteins, carries them on its membrane, RER membrane forms vesicles and bud off, fuses with the plasma membrane, transmembrane proteins now on the plasma membrane.
    - RER (role in biosynthesis of transmembrane and secreted proteins that cotranslationally targeted to RER by signal sequence)
        - Transmembrane proteins, or proteins that are to be secreted (need RER vesicle) have a signal sequence right at the beginning.
        - When ribosome starts making those proteins, they make the signal sequence first.
        - Signal sequence recruits a signal recognition particle that drags it to the RER.
        - ribosome now on the RER continues making the protein, but snakes it into the lumen.
        - Signal sequence is clipped off.
    - All ERs are connected to the nuclear membrane.
- Golgi apparatus (general structure; role in packaging, secretion, and modification of glycoprotein carbohydrates)
    - looks like stacks of pancakes.

    - modifies and/or secretes macromolecules for the cell.
    - RER make protein → modified in the Golgi → buds off golgi and secreted out of cell by exocytosis.
    - Glycoprotein = protein with attached saccharides.
    - Golgi can glycosylate proteins as well as modifying existing glycosylations.
    - Glycosylation affects protein's structure, function, and protect it from degradation.
- Peroxisomes: organelles that collect peroxides
    - Contain oxidative enzymes for intracellular digestion

Cytoskeleton

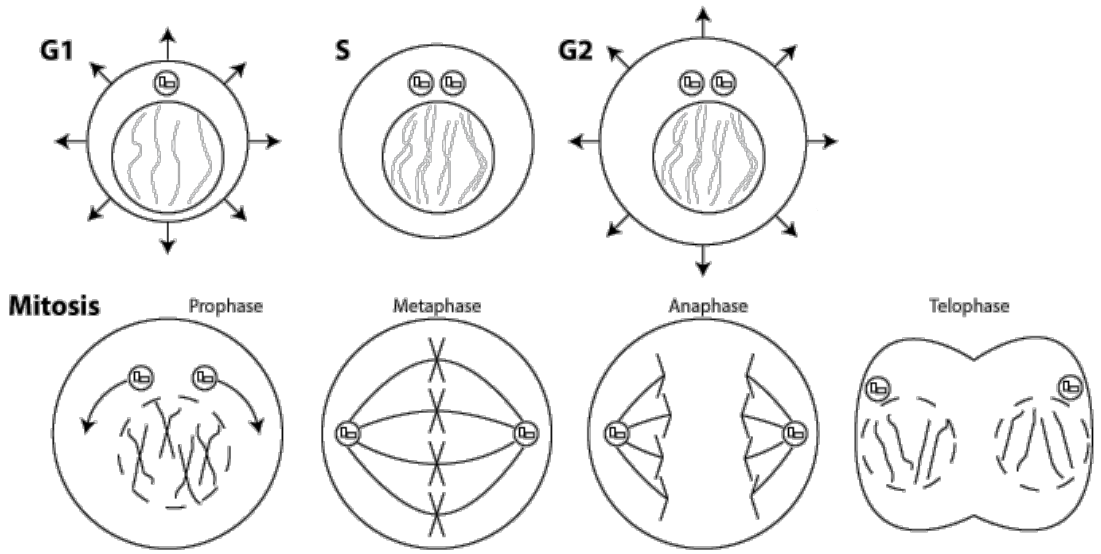
- General function in cell support and movement
- Microfilaments (composition; role in cleavage and contractility)
    - made of actin
    - responsible for cytokinesis. Supports cell shape by bearing tension.
- Microtubules (composition; role in support and transport)
    - made of tubulin
    - responsible for mitotic spindle, cilia/flagella, intracellular transport of organelles and vesicles. Supports cell shape by bearing compression.
- Intermediate filaments (role in support)
    - composition is varied.
    - supports cell shape by bearing tension.
- Composition and function of eukaryotic cilia and flagella
    - made of microtubules (eukaryotic)
    - cilia can be for locomotion, sensory, or for sweeping mucus.

    - flagella is used for locomotion.
- Centrioles, microtubule organizing centers. Microtubules radiate out of these barrel shaped structures, which are made of microtubules themselves.

Tissues Formed From Eukaryotic Cells

- Epithelial cells
    - Formed from the ectoderm and endoderm
    - Example: skin, intestinal epithelium
    - Cancer of epithelial cells is called carcinoma
- Connective tissue cells
    - Formed from the mesoderm
    - Example: muscle, fat
    - Cancer of connective tissue cells is called sarcoma

Cell Cycle and Mitosis



- Interphase and mitosis (prophase, metaphase, anaphase, telophase)
    - Interphase

        - G1 = Growth
        - S = Synthesis (replicate DNA)
        - G2 = Growth
    - Prophase = Prepare (condense chromatin into chromosomes, break down nuclear membrane, assemble mitotic spindle, centriole pairs move toward opposite poles of the cell)
    - Metaphase = Middle (Chromosomes line up in the middle)
    - Anaphase = Apart (Sister chromatids pulled apart to opposite sides of cell)
    - Telophase = Prophase in reverse = de-condense chromosomes, re-form nuclear membrane, break down mitotic spindle.
- Mitotic structures and processes
    - centrioles, asters, spindles: responsible for pulling apart the sister chromatids
    - chromatids, centromeres, kinetochores: sister chromatids are duplicated copies of the chromosome. chromatids are joined at the centromere. There's a protein at the centromere called the kinetochore, where spindle fibers attach to pull the chromatids apart.
    - nuclear membrane breakdown and reorganization: for most eukaryotes, the nuclear membrane breaks down at the beginning of mitosis, and reforms at the end of mitosis around each of the two newly formed nuclei.
    - mechanisms of chromosome movement: chromatids move apart during anaphase by the spindle fibers. Microtubules cause the chromosome movement.
- Phases of cell cycle: G0, G1, S, G2, M
    - G0 = no more DNA replication or cell division. Examples include nerves and muscles.
    - G1 = growth = make organelles, increase in cell size.
    - S = DNA replication. Centrioles also replicated.

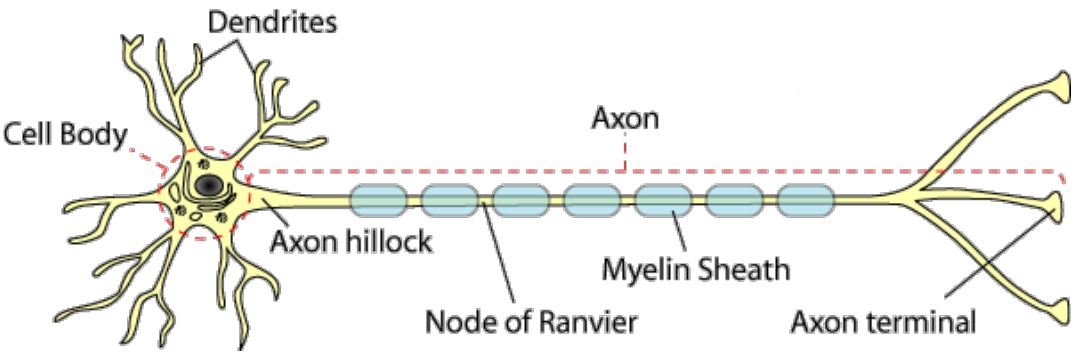
    - G2 = growth = make organelles, increase in cell size.
    - M = mitosis.
- Growth arrest: the cell cycle can be arrested for many reasons:
    - Too much genomic mutation/damage causes a cell to arrest in M phase.
    - Contact inhibition: normal epithelial cells stop growing when it gets crowded such that it's touching adjacent cells.
    - Lack of food can also cause growth arrest.
- Apoptosis (Programmed Cell Death)
    - Apoptosis = death that is clean and healthy.
    - Apoptosis = activation of caspases that digest the cell from within.
    - No spilling of cell contents.
    - Afterwards, the apoptosed cell releases chemicals that attract macrophages, and gets engulfed.
    - Apoptosis can be brought upon by development (eg tadpole losing tail) or by immune response (infected/cancerous cells killed by cytotoxic T cells/natural killer cells).

Biosignaling

- Oncogenes = genes that promote cell proliferation = causes cancer when out of control (eg: RAS, MYC)
- Tumor repressor genes = genes that checks proliferation, promotes apoptosis = causes cancer if dysfunctional (eg: p53, Rb)

Specialized Eukaryotic Cells and Tissues

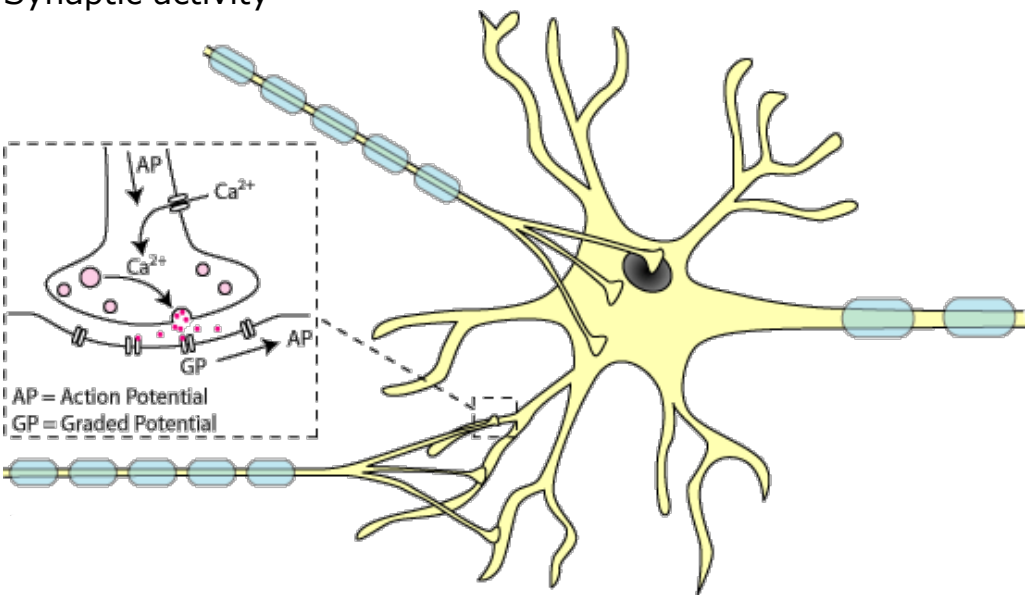
Nerve Cell/Neural



- Cell body (site of nucleus and organelles)
    - Contains nucleus and organelles just like any other cell.
    - Has well-developed RER and golgi (makes a lot of proteins).
- Axon (structure, function)
    - Axon = Conducting region of the nerve.
    - Axon terminals = secretory regions of nerve.
    - Other names for axon terminal = synaptic knob = bouton.
- Dendrites (structure, function)
    - Receptive region of the nerve = gets input.
    - The branching helps to increase the surface area for reception.
- Myelin sheath, Schwann cells, oligodendrocytes, insulation of axon
    - Myelin sheath = Covers the axon intermittently, with gaps called nodes of Ranvier.
    - The purpose of myelin sheath is to speed up conduction by insulating the nerve in intervals. This intermittent insulation causes action potential to jump from one node of Ranvier to the next.

    - Schwann cells = makes myelin sheath in the peripheral nervous system by wrapping around the axon.
    - Oligodendrocytes = the central nervous system analogue of Schwann cells, makes myelin sheath around CNS axons.
    - Insulation of axon = achieved by the myelin sheath. Insulation occurs in intervals, which causes action potential to jump from one node of Ranvier to the next.
    - Myelin sheath is a good insulator because it is fatty and does not contain any channels.
- Nodes of Ranvier (role in propagation of nerve impulse along axon)
    - Action potential jumps from one node of Ranvier to the next.
    - This jumping of action potential speeds up conduction in the axon.
- Synapse (site of impulse propagation between cells)
    - Synapse = conduction from one cell to another.
    - Axodendritic synapse = axon terminal of one neuron (presynaptic) → dendrite of another neuron (postsynaptic).
    - Axosomatic synpase = axon terminal of one neuron (presynaptic) → cell body of another neuron (postsynaptic).
    - Axoaxonic synapse (rare) = axon terminal of one neuron (presynaptic) → axon hillock of another (postsynaptic).

- Synaptic activity

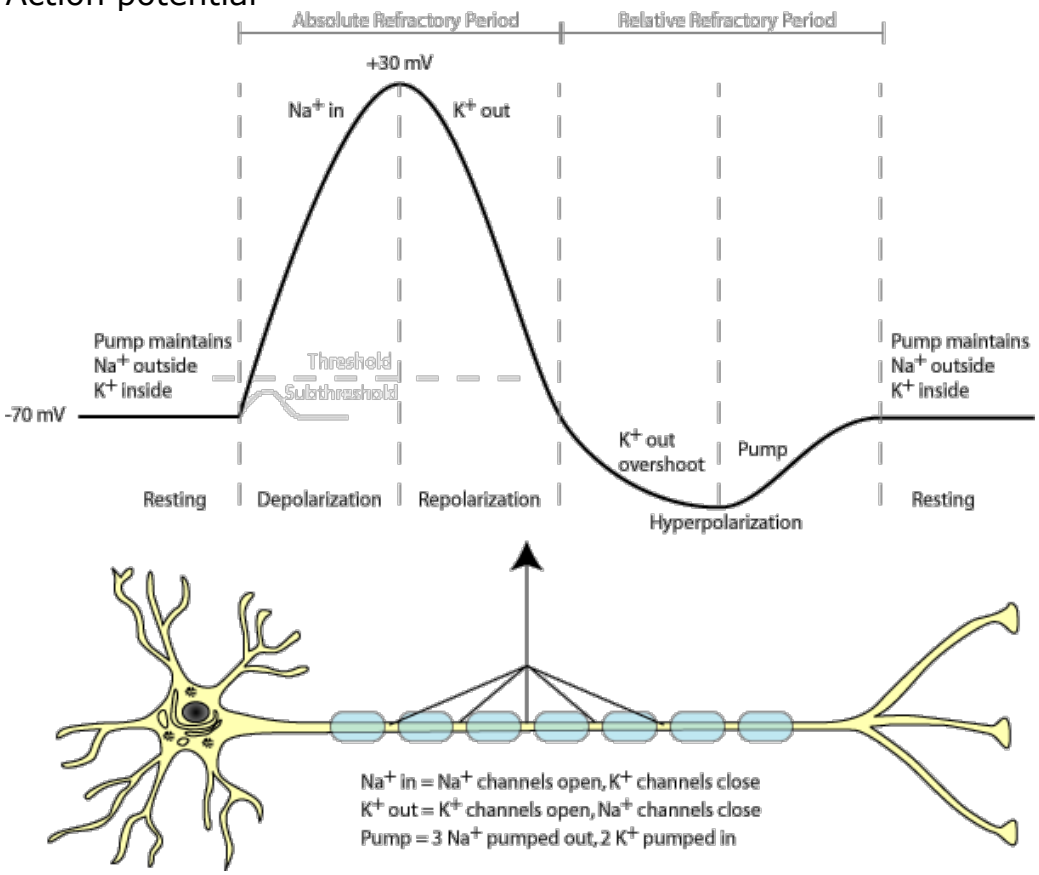


  - transmitter molecules
    - Transmitter molecules = neurotransmitters
    - Action potential → release of neurotransmitters by presynaptic axon terminal → picked up by receptor of postsynaptic neuron.
    - Release of neurotransmitter = exocytosis of vesicles containing neurotransmitters. Triggered by calcium influx when action potential reaches axon terminal.
    - Neurotransmitter reception = diffusion of neurotransmitter across the synaptic cleft, binds to receptor, opens up ion channels that causes a change in membrane potential of the postsynaptic neuron (graded potential). If this graded potential is large enough, it will trigger a full-fledged, all-or-nothing action potential in the postsynaptic neuron.
    - Neurotransmitters are quickly eliminated (destroyed by enzymes, reuptake by presynaptic terminal, or diffuse away) so that they don't persistently stimulate the postsynaptic neuron.
    - Neurotransmitter molecules:
      - Acetylcholine (ACh)
      - Norepinephrine (NE)

        - Dopamine
        - Serotonin
        - Histamine
        - ATP
    - synaptic knobs
        - Synaptic knob is another name for axon terminal.
        - Contains vesicles of neurotransmitters waiting to be exocytosed.
        - Action potential reaching the synaptic knob causes an influx of calcium, which signals the vesicles to fuse with cell membrane (exocytosis) to release the neurotransmitters into the synaptic cleft.
    - fatigue
        - Continuous synaptic activity → depletion of neurotransmitters → fatigue.
    - propagation between cells without resistance loss
        - Action potential is all-or-nothing.
        - As long as the neurotransmitters cause the postsynaptic cell to reach a certain threshold potential, the action potential induced is just as large as the presynaptic action potential.
        - In summary, propagation between cells involves no resistance loss because the postsynaptic action potential is just as large as the presynaptic potential - all action potentials are all-or-nothing.
- Resting potential (electrochemical gradient)
    - Na^+-K^+ pump = 3 Na^+ out, 2 K^+ in = net negative to the inside, net positive to the outside.
    - K^+ leakage = the resting cell membrane has channels that allow K^+ to leak out, but don't allow Na^+ to leak in = net negative to the inside, net positive to the outside.

- Resting potential is -70 mV because the cell is more negative on the inside, and more positive on the outside.
- Electrochemical gradient = combination of electrical and chemical gradient = both electrical potential and ion concentration gradient across membrane.

- Action potential



  - Stages of an action potential:

    1. Resting: cell at rest, sodium-potassium pump maintaining resting potential (-70 mV). Lots of sodium outside, lots of potassium inside. Ion channels closed so the established ion gradient won't leak.

    2. Depolarization: sodium channels open, positive sodium rushes inside, membrane potential shoots up to +30 mV. Lots of sodium inside, lots of potassium inside.

    3. Repolarization: potassium channels open, sodium channels close, positive potassium rushes outside, membrane

potential drops back down. Lots of sodium inside, lots of potassium outside (opposite of the resting state).

4. Hyperpolarization: potassium channels doesn't close fast enough, so the membrane potential actually drops below the resting potential for a bit.

5. Refractory period: the sodium-potassium pump works to re-establish the original resting state (more potassium inside, sodium outside). Until this is done, the neuron can't generate another action potential. Absolute refractory period = from depolarization to the cell having re-established the original resting state. Relative refractory period = After hyperpolarization till resting state re-established.

- threshold, all-or-none
  - When a stimulus (graded potential) depolarizes above a threshold value, an action potential will occur.
  - Action potentials are all-or-none, meaning that if it occurs, all action potential have the same magnitude.
  - One graded potential just barely makes the threshold value, another overshoots it a lot, but both will cause the same action potential.
- sodium-potassium pump
  - 3 sodium out.
  - 2 potassium in.
  - net positive out.
  - causes membrane to be more negative on the inside, hence negative membrane potential.

- Excitatory and inhibitory nerve fibers (summation, frequency of firing)
  - Excitatory = stimulates an action potential to occur
  - Excitatory synapse = receptor binding causes postsynaptic potential to be more positive (depolarization) = if it gets above threshold, action potential results.

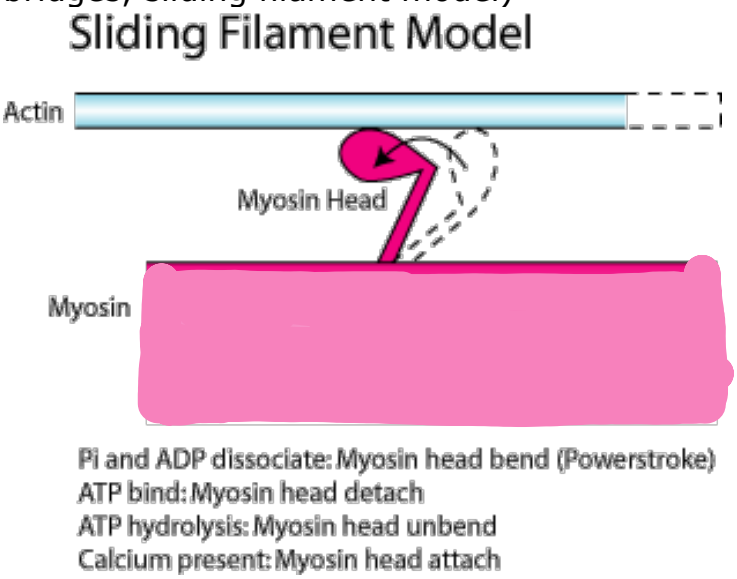
- Inhibitory = inhibits an action potential from occuring.
- Inhibitory synapse = receptor binding causes postsynaptic potential to be more negative (hyperpolarization) = makes it more difficult to reach threshold.
- Summation = two or more nerves firing at the same time.
    - Two subthreshold excitatory nerves firing at the same time can sum to reach the threshold.
    - A threshold excitatory nerve and an inhibitory nerve firing at the same time, and the resultant signal won't reach the threshold.
- Frequency = Firing, then quickly firing again.
    - If the first fire is subthreshold, fire again before the previous depolarization dies, and the new depolarization will be even higher than the first time.

Muscle Cell/Contractile

- Structural characteristics of striated, smooth, and cardiac muscle
    - Striated = skeletal muscles, voluntary, has stripes, multiple nuclei shared within the same muscle fiber. Strong, but tire easily = shaped like long fibers.
    - Smooth = visceral, involuntary muscles, no stripes, single nucleus per cell. Weak, but doesn't tire easily = shaped like almonds, tapered on both ends.
    - Cardiac = heart muscles, involuntary, has stripes, single nucleus per cell, strong and doesn't tire easily = highly branched, shaped like fibers cross-linked to one another.
- Abundant mitochondria in red muscle cells (ATP source)
    - Red muscle = high endurance, but slow.
        - Aerobic respiration predominant.
        - Many mitochondria because red muscles undergo aerobic respiration.

        - Equipped to receive abundant oxygen supply: many capillaries, many myoglobin.
        - High endurance, doesn't tire easily.
    - White muscle = fast, but fatigue easily.
        - Anaerobic respiration (glycolysis) predominant.
        - Few mitochondria because white muscles undergo mainly glycolysis.
        - Equipped for short bursts of glycolysis: stores high amounts of glycogen.
    - Pink muscle = intermediate between red and white muscle.

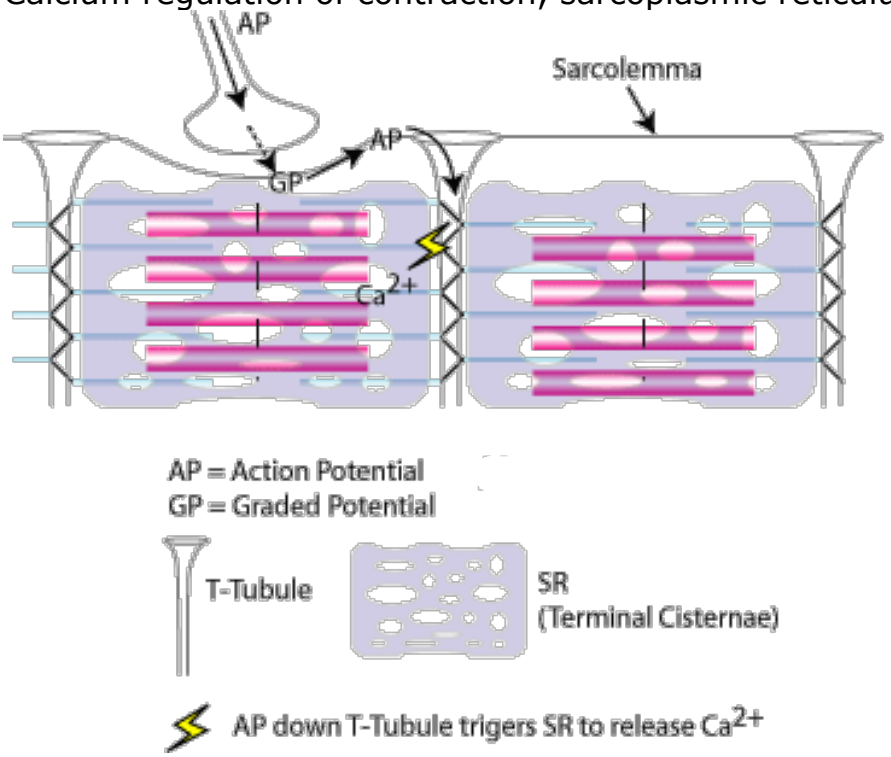
- Organization of contractile elements (actin and myosin filaments, cross bridges, sliding filament model)



    - Actin filament = thin filament = has troponin and tropomyosin on it.
    - Myosin filament = thick filament = has myosin heads on it.
    - Cross bridge = myosin head binds to actin.
    - Sliding filament model = Cross bridge forms, myosin head bends (power stroke), causes actin to move (slide) in the direction of the power stroke (toward the M line). When all the actin slide toward the M line like this, the muscle fiber contracts.

- Something counter-intuitive about the sliding filament model: ATP is not directly needed for the powerstroke. ATP binding is needed for detachment of myosin head to actin. ATP hydrolysis is needed for de-powerstroke (unbend myosin head).
- Rigor mortis = no ATP after a person dies, myosin heads can't detach after power stroke, muscle remain in contracted position.
- So what is troponin and tropomyosin there for? Ans: tropomyosin on actin blocks the myosin head from forming cross bridges. However, troponin moves tropomyosin out of the way at high Ca^{2+} levels (Ca^{2+} binds to troponin, and troponin moves tropomyosin).

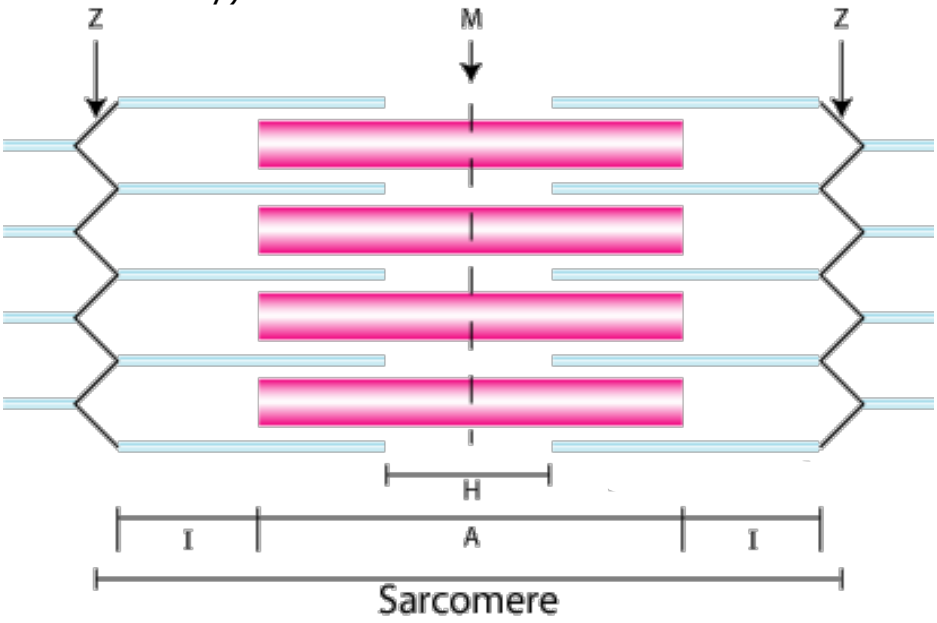
- Calcium regulation of contraction, sarcoplasmic reticulum



- Sarcoplasmic reticulum (SR) = smooth ER in muscle = stores calcium, releases them in response to AP.
- The SR is also called terminal cisternae where it meets T-tubules at the edges of the sarcomere.
- T-tubule = extension of the muscle cell membrane that runs deep into the cell, so that action potential can reach there.
- Muscle contraction:

1. Nerve stimulates muscle.
2. Action potential runs along muscle cell membrane.
3. Goes deep into the muscle cell via T-tubules.
4. Stimulates the SR (terminal cisternae) to release calcium.
5. Calcium causes muscle to contract via the sliding filament mechanism.

- Sarcomeres ("I" and "A" bands, "M" and "Z" lines, "H" zone - General structure only)



  - I band = thinnest = thin filaments only = sides of the sarcomere.
  - H zone = fattest = thick filaments only = center of the sarcomere, spans the M line.
  - A band = contains both thick and thin filaments, center of the sarcomere spans the H zone.
  - M line = line of **m**yosin in the **m**iddle of the sarcomere, linked by accessory proteins.
  - Z line = zigzag line on the sides of the sarcomere, connects the filaments of adjacent sarcomeres.
  - mnemonics

        - I = thin like the letter I.
        - H = fat like the letter H.
        - A = letter width in between I and H, so a mixture of thick and thin filaments.
        - M = middle line = myosin (linked by accessory proteins).
        - Z = zigzag line
        - Moving from middle to the side of sarcomere = M HAIZ, the Muscle says HAIZ.
- Presence of troponin and tropomyosin
    - Tropomyosin = long protein that spirals along actin, blocks myosin head from cross-linking.
    - Troponin = binds tropomyosin, moves it out of the way when calcium is around.

Other specialized cell types

- Epithelial cells (cell types, simple epithelium, stratified epithelium)
    - Squamous = flat.
    - Cuboidal = cube.
    - Columnar = column shaped.
    - Simple epithelium = single cell layer = good for absorption, secretion, filtration, diffusion.
        - Simple squamous: endothelium, capillary wall, alveolar wall.
        - Simple cuboidal: gland ducts, kidney tubules.
        - Simple columnar: stomach and gut.
    - Stratified epithelium = two or more cell layers = good for protection against abrasion.
        - Stratified squamous: skin.

        - Stratified cuboidal/columnar: not common.

- Endothelial cells
    - Endothelial cells = lines the inside of organs and blood vessels = simple squamous epithelium.
    - Thin, single layer cells facilitate diffusion.
- Connective tissue cells (major cell types, fiber types, loose vs. dense, cartilage, extracellular matrix)
    - Connective tissue structure = Cells + extracellular matrix.
        - Cells: secrete the extracellular matrix (ground substance and fibers).
        - Ground substance: glue that holds the matrix together.
        - Fibers: mostly collagen, gives the matrix strength.
    - Connective tissue cells and tissue types: bone, fat, tendons, ligaments, cartilage, blood.
        - Osteoblasts make bone.
        - Fibroblasts make connective tissue proper (fats, tendons, ligaments, beneath epithelia).
        - Chondroblasts make cartilage.
        - Hematopoietic stem cells make blood.
    - Nomenclature:
        - -blast = stem cell actively producing matrix.
        - -cyte = mature cell, doing housekeeping.
    - Fiber types:
        - Collagen = the most common fiber type. Very strong. Present in large amounts in dense connective tissue.
        - Elastic fibers = can stretch.

        - Reticular fibers = can branch and form nets. Found in loose connective tissue.

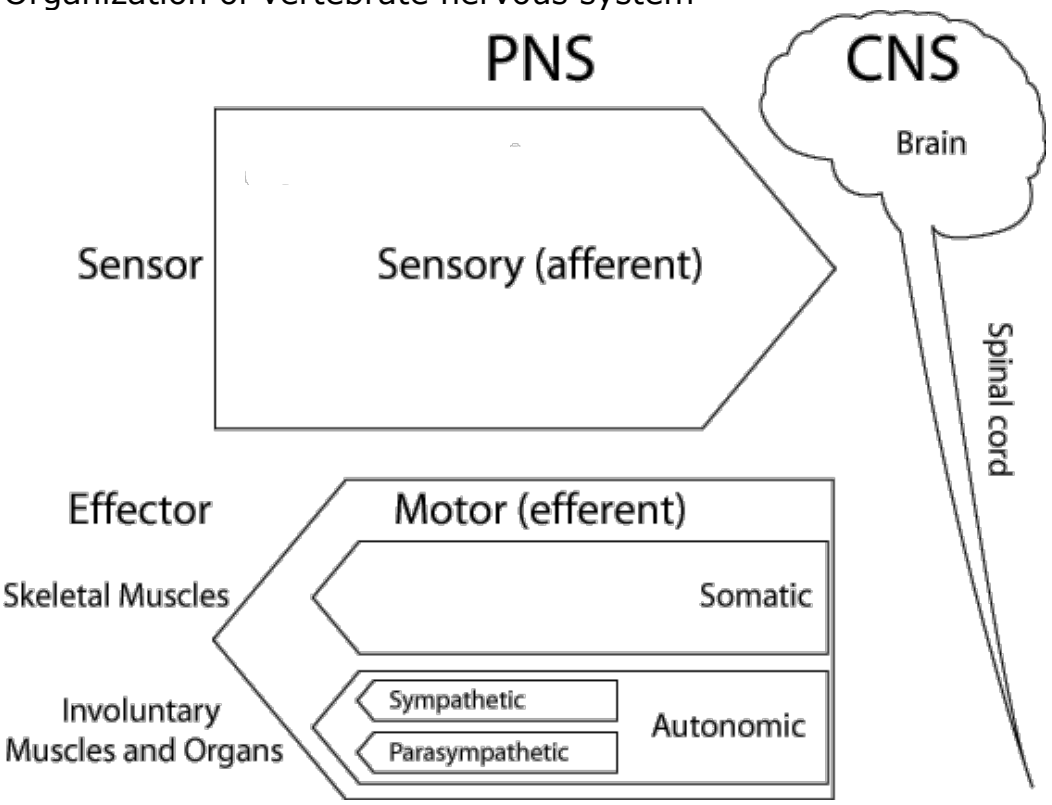
- loose vs. dense
    - Loose = loose fibers, lots of fluff (ground substance, cells) = anything that you don't associate with being fibrous = fat, paddings around organs.
    - Dense = dense fibers predominantly collagen = genuinely fibrous, little fluff (ground substance, cells) = tendon, ligament.
- Cartilage = chondrocytes + matrix = elastic, flexible, used as padding in spinal discs, ends of bones, ear.
- Extracellular matrix = secreted by cells = ground substance (glue) and fibers.

Nervous and Endocrine Systems

Nervous System: Structure and Function

- Major functions
    - high-level control and integration of body systems
    - response to external influences
    - sensory input
        - sensory = afferent
        - nerve impulses conveyed to the CNS.
    - motor output
        - motor = efferent
        - nerve impulses from the CNS to effector organs.
    - integrative and cognitive abilities

- Organization of vertebrate nervous system



  - CNS = Central Nervous System = Brain and spinal cord
    - Brain
    - Spinal Cord
  - PNS = Peripheral Nervous System = Everything else
    - Sensory = Afferent = Nerves carrying signal toward CNS.
    - Motor = Efferent = Nerves carry signal toward effector organs.
      - Somatic Nervous System = Voluntary = Controls skeletal muscles.
      - Autonomic Nervous System = Involuntary = Effects visceral organs.
        - Sympathetic division = fight or flight response.
        - Parasympathetic division = Rest.
- Sensor and effector neurons

    - Sensor = senses, carries sensory signals from the body to the CNS.
    - Effector = causes an effect = carries motor signals from the CNS to the body.
- Sympathetic and parasympathetic nervous systems (functions, antagonistic control)
    - Sympathetic = prepares body for activity = fight or flight response.
        - Increase heart rate, blood pressure
        - More blood flow to muscles, less to digestive system.
        - Pupil dilation.
        - Break down glycogen to release glucose into blood.
    - Parasympathetic = prepares body to rest
        - Decrease heart rate, blood pressure.
        - Less blood to muscles, more to digestive system.
        - Pupil constriction.
        - Synthesizes glycogen for storage from glucose.
- Reflexes
    - feedback loop, reflex arc, effects on flexor and extensor muscles
        - Feedback loop = positive feedback (reinforce initial event), negative feedback (counteracts initial event), or reflex arc (usually a type of negative feedback).
            - positive feedback = uterine contraction lead to oxytocin release, which causes more uterine contraction.
            - positive feedback = blood clotting platelets activated at wound site attract more platelet activation and clumping.

        - negative feedback = drop in blood pressure causes ADH release, which increases it. Conversely increase in blood pressure causes a drop in ADH.
        - Reflex arc = withdrawal from a painful stimulus = negative feedback.
        - Reflex arc = knee jerk = tapping the knee tendon causes sudden stretching of the muscle, which lead to contraction of that muscle that creates the knee jerk = negative feedback.
    - Reflex arc = receptor → sensory neuron → integration center → motor neuron → effector
        - receptor = site of stimulus
        - sensory neuron = carries impulse from receptor to integration center
        - integration center = connects sensory to motor neuron via synapse inside the CNS
            - monosynaptic = no interneuron, direct synapse of sensory to motor.
            - polysynaptic = interneuron(s) present.
        - motor neuron = carries impulse toward effector.
        - effector = site of response to the stimulus
    - Examples of reflexes: knee-jerk, withdrawal from pain
    - Effects on flexor and extensor muscles
        - During the knee-jerk, in addition to contracting the extensor, the reflex relaxes the flexor.
        - Golgi tendon reflex: sudden contraction of the quads (extensor), causes a negative feedback that relaxes the quads and contracts the hamstrings (flexor).
- role of spinal cord, brain
    - Spinal cord provides the synapse (or synapses if it's polysynaptic) for the reflex arc.

        - Even though the reflex arc bypasses the brain, the brain is still aware of it happening.
    - efferent control
        - Brain can override spinal reflexes (eg. you don't jerk away from getting a vaccine shot)

Nervous System: Sensory Reception and Processing

- Skin, proprioceptive, and somatic sensors
    - Skin: touch, heat and pain receptors close to the surface (dermis-epidermis boundary), pressure receptors deeper in the dermis.
    - proprioceptor: senses the position of a body part, located in muscle and connective tissue.
    - somatic sensors:
        - mechanoreceptors - touch, pressure
        - thermoreceptor - temperature change (a warm object will feel warm if your hand is cool, but won't feel warm if your hand is already warm)
        - photoreceptor - light
        - chemoreceptor - taste, smell
        - nocioreptors - pain (extreme heat, cold, pressure, chemicals)
- Olfaction, taste
    - Olfaction:
        1. Chemicals enter the nose via nostrils.
        2. Gets into the nasal cavity.
        3. Trapped in the mucus on top of the nasal cavity.
        4. Picked up by the membrane receptors on cilia (non-mobile, but they increase the surface area) of the olfactory receptor cell.

5. Causes cell depolarization, and subsequent transduction of signal to the brain.

- Taste:
    0. Chemicals dissolve in saliva.
    1. Carried inside taste bud
    2. Hair-like microvilli of taste cells inside taste bud picks up chemicals.
    3. Releases neurotransmitters to send signal to brain.

- Hearing
    - ear structure
        - Ear canal = auditory canal.
        - Tympanic membrane = eardrum.
        - Ear bones = malleus (hammer) → incus (anvil) → stapes (stirrup).
        - Vestibule = contacts the oval window (where stirrup vibrates), is continuous with semicircular canals and cochlea.
        - Cochlea = spiral = houses hair cells.
        - Semicircular canals = 3 of them perpendicular to one another = senses position and movement of the head, help you balance.
    - mechanism of hearing
        0. Sound enters ear.
        1. Hits ear drum (tympanic membrane)
        2. Malleus (hammer) → Incus (anvil) → Stapes (stirrup)
        3. Vibrates fluid in Cochlea.
        4. Transmits to fluid in Cochlea.

5. Cochlear hair cells excited by vibrations, and sends signal to brain.

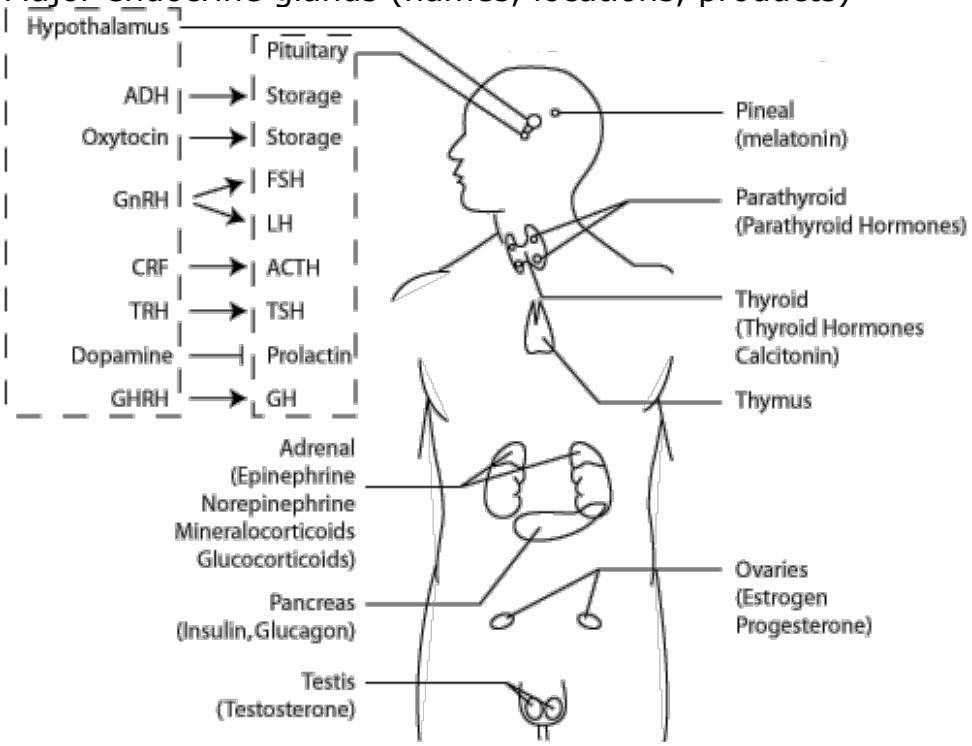
- Vision
    - light receptors
        - Photoreceptor cells located on the back of the retina.
        - Rods = senses light and dark (no color), more sensitive.
        - Cones = senses color, less sensitive.
        - Rhodopsin = chemical responsible for light reception = Retinal (chemical) + Opsin (transmembrane protein)
        - Light converts cis-retinal → trans-retinal.
        - trans-retinal then causes hyperpolarization of photoreceptor cell, which prompts the chain of events that sends signal to the brain.
        - Sends signal to brain via a bundle of nerves on the back of the retina (where the blind spot is)
    - eye structure
        0. Light first travels through the cornea
        1. Through the pupil (hole in the iris muscle)
        2. Lens = focuses light on retina.
        3. Vitreous humor = fluid.
        4. Retina = screen on the back of the eye = contains photoreceptors.
    - visual image processing
        - The lens of the eye, just like a convex lens in physics, forms a real image on the retina.
        - Real images are inverted.
        - The brain processes this inverted image to make it seem upright in your mind.

        - The brain combines the two images from each eye to make a 3D image, from which you can judge distance.
        - Another reason for combining the two images from both eyes is that it gets rid of the blind spot in each eye.

Endocrine system: Hormones

- Function of endocrine system (specific chemical control at cell, tissue, and organ level)
    - Endocrine system = make hormones = specific control of all target cells of that hormone.
- Definition of endocrine gland, hormone
    - endo = within, crine = to secrete
    - endocrine glands secreting hormones into surrounding tissue fluids.
    - endocrine vs. exocrine, autocrine, paracrine
        - endocrine: hormone, no duct, acts long distances
        - exocrine: non-hormone secretions into ducts.
        - autocrine: local chemicals, act short distances on themselves
        - paracrine: local chemicals, act short distances on other cells
    - hormone = chemicals that regulate metabolism and function of cells.

- Major endocrine glands (names, locations, products)



  - Hypothalamus: Releasing hormones for the pituitary, ADH and oxytocin.
    - Releasing hormones/factors stimulates pituitary to release its hormone.
    - GnRH = Gonadotropin Releasing Hormone = stimulates pituitary to release FSH and LH.
    - CRF = Corticotropin Releasing Factor.
    - TRH = Thyroid Releasing Hormone.
    - Dopamine = inhibits prolactin release.
    - GHRH = Growth Hormone Releasing Hormone.
    - ADH = Antidiuretic Hormone = Vasopressin = increase water reabsorption in kidney = conserve water, increase blood pressure.
    - Oxytocin = stimulates uterine contractions during labor, also milk secretion during suckling.
  - Pituitary: makes FLAT PEG, stores ADH and oxytocin.

        - **F**SH = Follicle Stimulating Hormone = Stimulate ovary follicles to mature, testis to produce sperm.
        - **L**H = Luteinizing Hormone = LH surge triggers ovulation, stimulates testis to produce testosterone.
        - **A**CTH = AdrenoCorticoTropic Hormone = Stimulates adrenal cortex to release glucocorticoids and mineralocorticoids.
        - **T**SH = Thyroid Stimulation Hormone = Stimulate thyroid to release thyroid hormones.
        - **P**RL = Prolactin = Stimulates breast to produce milk.
        - **E** = Endorphins.
        - **G**H = Growth Hormone = Stimulates growth of muscle, bone, burns fat.
    - Pineal: makes melatonin, which makes you sleepy at night.
    - Thyroid
        - Thyroid hormones: increase metabolism, requires iodine.
        - Calcitonin: turns blood Ca^{2+} into bone. Lowers blood Ca^{2+}.
    - Parathyroid: makes Parathyroid Hormone (PTH), which increases blood Ca^{2+} by bone resorption, dietary calcium absorption, and calcium reabsorption in kidneys.
    - Thymus: Thymus hormones (thymo-, thymic), stimulates T cells to develop.
    - Adrenal
        - Epinephrine and norepinephrine = fight or flight response
        - Mineralocorticoids = aldosterone = increase Na^{+} and water retention, raises blood pressure.
        - Glucocorticoids = cortisol = stress hormone = increase blood sugar.
        - Androgens = testosterone.

    - Pancreas
        - Glucagon = increases blood sugar (break down glycogen, stimulate gluconeogenesis).
        - Insulin = lower blood sugar (stimulates glucose uptake by cells).
    - Ovary: make estrogen (and a small amount of testosterone).
    - testis: make testosterone.
- Endocrine diseases
    - Diabetes
        - no insulin made, or no insulin receptors
        - glucose can't enter cells
        - high blood sugar
        - cell starved of sugar, leading to fatty acid metabolism, which leads to production of ketone bodies, which lead to ketoacidosis (more acidic blood).
        - sugar in urine, leading to more water in urine due to osmosis.
    - Hypothyroidism
        - Decreased thyroid hormone.
        - Low metabolism.
        - If cause of disease is lack of iodine in diet, then goiter develops from an accumulation of thyroid hormone precursor lacking iodine.
    - Hyperthyroidism
        - Too much thyroid hormone.
        - High metabolism.
    - Gigantism = too much Growth Hormone during growing age = well-proportioned giants.

    - Acromegaly = too much Growth Hormone later on in life = disproportioned growth of certain areas of the body (the parts that still respond to growth hormone).

- Major types of hormones
    - amino acid based = amino acid derivatives = most hormones are this type.
    - steroids = cholesterol derivatives = testosterone, estrogen, adrenocortical hormones.

Endocrine system: Mechanisms of hormone action

- Cellular mechanisms of hormone action
    - water soluble hormones
        - Can't cross the plasma membrane.
        - Bind to membrane receptors on the outside of cells.
        - Secondary messengers then relay the signal inside the cell.
    - lipid-soluble hormones
        - Able to cross the plasma membrane.
        - Directly activate genes.
    - cAMP pathway:
        1. Amino acid hormone binds membrane receptor.
        2. G protein activated.
        3. Adenylate cyclase activated.
        4. cAMP made.
        5. Protein kinase cascade.
    - Phospholipid pathway:
        0. Amino acid hormone binds membrane receptor.
        1. G protein activated.

2. Phospholipase C activated.
3. Membrane phospholipid split into DAG and IP3.
4. DAG triggers protein kinase cascade.
5. IP3 releases Ca^{2+} from the ER.

- Steroid pathway:
  0. Steroid hormone (and thyroid hormone even though it's amino acid based) goes inside the cell.
  1. Hormone binds receptor inside the cell (cytoplasm or nucleus).
  2. Hormone-receptor complex (transcription factor) turns certain genes on inside the nucleus.

- Transport of hormones (bloodstream): hormones travel long distances via blood and lymph.
- Specificity of hormones (target tissue)
  - Specificity depends on the target cells having the receptors for the hormone, and non-target cells lacking receptors for the hormone.
  - Cells can either upregulate or downregulate the receptors they express.
- Integration with nervous system (feedback control)
  - The nervous system can modulate and override normal control of hormones based on the status of the body. For example, the body's blood "normal" glucose level is set higher when you're under stress.
  - Hormones can modulate the nervous system. For example, low estrogen levels during menses give you a bad mood.
  - Normal control of hormones
    - Humoral: glands directly respond to chemical levels in the blood (parathyroid respond to low blood calcium).

- Neural: glands release hormones when stimulated by nerves (fight or flight response).
- Hormonal: glands release hormones when stimulated by other hormones (tropic hormones).

Circulatory, Lymphatic and Immune Systems

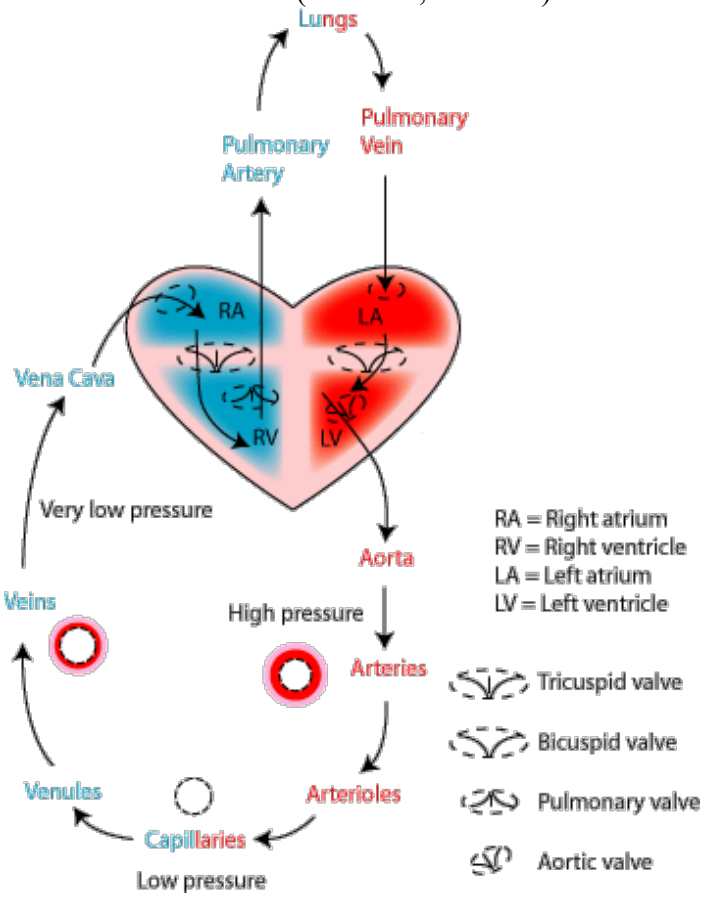
Circulatory System

- Functions (circulation of oxygen, nutrients, hormones, ions, and fluids; removal of metabolic waste)
    - Oxygen delivery to tissues
        1. diffuses into the blood in alveolar (lung) capillaries
        2. binds to hemoglobin in red blood cells
        3. gets transported to tissues
        4. used in cellular respiration
    - Carbon dioxide delivered out
        1. cellular respiration makes CO2: carbonic anhydrase converts it to bicarbonate.
        2. CO2 gets transported by blood: dissolved CO2, dissolved bicarbonate ion (major), bound to hemoglobin and plasma proteins
        3. diffuses out of the alveolar capillaries
        4. exhaled out
    - Nutrients
        - nutrients absorbed (either by diffusion or active transport) into blood stream in the small intestines.
        - nutrients can also be released into the blood stream by cells. For example, glucagon causes glucose to be released into the blood stream.
        - nutrients can be taken up by cells. For example, insulin causes cells to take in glucose from blood.
    - Hormones released by endocrine glands, circulate the blood in order to reach their target cells.

- Fluids and ions circulate the blood and are regulated by how much reabsorption of water and salt occurs in the kidney.
- Urea = metabolic waste, travels in the blood to the kidneys, where it is filtered out and passed in urine.

- Role in thermoregulation
  - Vasoconstriction conserves heat. When it's cold, vasoconstriction occurs in the arterioles that feed the skin. Less blood flows near the surface of the skin, less heat lost.
  - Vasodilation cools you down. When it's hot, vasodilation occurs in the arterioles that feed the skin. More skin blood flow, more heat lost to the surroundings.

- Four-chambered heart (structure, function)



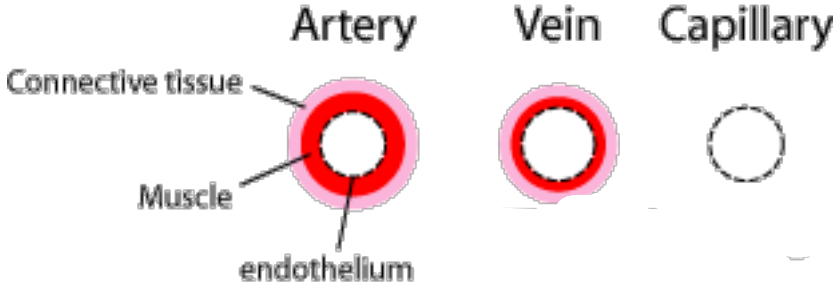
1. Deoxygenated blood returns to the heart: superior/inferior vena cava → right atrium
2. Deoxygenated blood gets pumped to the lungs: right atrium → right ventricle → pulmonary artery → lungs

3. Blood arrives at the lungs and gets oxygenated.
4. Oxygenated blood returns to the heart: lungs → pulmonary vein → left atrium
5. Oxygenated blood gets pumped to the body: left atrium → left ventricle → aorta

- Blood going through the heart including the valves
    0. Vena cava
    1. Right atrium
    2. Tricuspid valve
    3. Right ventricle
    4. Pulmonary valve
    5. Pulmonary artery
    6. Lung
    7. Pulmonary vein
    8. Left atrium
    9. Bicuspid (Mitral) valve
    10. Left ventricle
    11. Aortic valve
    12. Aorta
- Systolic and diastolic pressure
    - blood pressure = pressure blood exert on the walls of the blood vessel.
    - systolic pressure = blood pressure when blood is being pumped (the ventricles are contracting).
    - diastolic pressure = blood pressure when blood is not being pumped (the ventricles are relaxing).
- Pulmonary and systemic circulation
    - Pulmonary circulation = heart → lungs → back to heart = oxygenates blood

- Systemic circulation = heart → body → back to heart = delivers oxygenated blood to body
- Pulmonary circulation = shorter than systemic circulation = less resistance = less blood pressure.
- Systemic circulation: vasodilation when oxygen levels are low → more blood flow to oxygen-starved tissue.
- Pulmonary circulation: vasoconstriction when oxygen levels are low → less blood flow to low oxygen/blocked alveoli → more blood flow to good alveoli where gas exchange can occur.

- Arterial and venous systems (arteries, arterioles, venules, veins)



  - structural and functional differences
    - Blood flows from artery → arteriole → capillary → venule → vein.
    - Artery
      - Elastic artery
        - Aorta and its major branches.
        - Major function = provide elastic pipe for blood straight out of the heart.
        - Lots of elastic tissue.
        - Layers: endothelium, smooth muscle, connective tissue.
        - Not active in vasoconstriction.
      - Muscular (distributing) arteries
        - Major function = distribute blood to specific organs.
        - Lots of muscle.

        - Layers: endothelium, lots of smooth muscle, connective tissue.
        - Some activity in vasoconstriction.
- Arteriole
    - Ranges from being like a smaller version of the artery, to being a larger version of the capillary with smooth muscles spiralling around it.
    - Major function = controls blood flow to the capillaries.
    - Active in vasoconstriction. The arterioles allow the body to control which tissues gets more blood.
    - The arteriole is the most important site for vasoconstriction. Although other vessels are capable of vasoconstriction, you should always think of the arteriole when you see vasoconstriction.
- Capillary
    - Layer: single cell thick endothelium.
    - Major function: blood-tissue solute exchange.
    - Not active in vasoconstriction.
- Venule
    - Ranges from being like a large capillary to being like a small vein.
    - Major function: merge of capillaries to be conducted to veins.
    - No vasoconstriction.
- Vein
    - Layers: endothelium, smooth muscle, connective tissue.
    - Major function: returns blood back to the heart.
    - Has valves to prevent the back flow of blood.
    - Breathing, skeletal muscles, and smooth muscle adaptations help blood flow through the vein at low pressure.

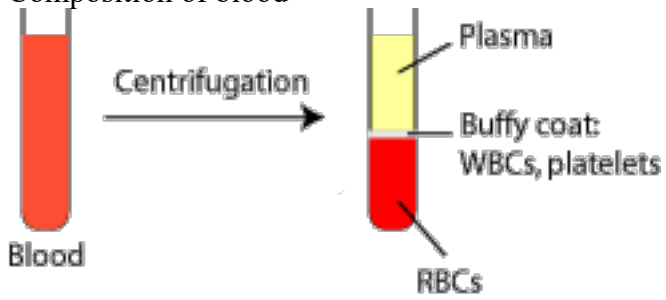
        - Vasoconstriction can occur in the vein.
    - You can argue that the aorta has a single aortic valve right where it connects to the heart. But for the purposes of the EXAM, arteries don't have valves, veins do.
    - Thickness: artery > vein > arteriole > venule > capillary
    - Differences between arteries and veins
        - arteries are thicker, more muscular than veins.
        - veins have valves, arteries don't.
        - arteries carry blood away from the heart (oxygenated except for pulmonary artery). Veins carry blood back into the heart (deoxygenated except for pulmonary vein).
    - Differences between artery and arteriole
        - arterioles are smaller.
        - vasoconstriction occurs predominantly at the arterioles.
- pressure and flow characteristics
    - Blood pressure of arteries > arterioles > capillaries > venules > veins
    - Blood pressure is highest in the arteries (specifically the aorta) because the heart pumps directly into the aorta.
    - Blood pressure is lowest in the veins (specifically the vena cava) because flow resistance brings the pressure down.
    - Blood pressure is also lower when you elevate a blood vessel (think physics, $P = \rho gh$, where h is the depth - raising your arm like taking it to shallower water)
    - Blood pressure can be regulated by vasoconstriction (increase bp), vasodilation (decrease bp), and hormones (ADH, aldosterone, renin, adrenaline all increases bp).
    - Blood flows from artery → arteriole → capillary → venule → vein.
    - Blood squirts from arteries, flows from veins, and oozes from capillaries.

        - The elasticity of arteries causes blood to flow even when the heart is resting between pumps (this is why your diastolic blood pressure is not zero)
        - Adaptations that help blood flow through the vein at low pressure:
            - Respiratory pump: when you inhale, your stomach squeezes on the veins, and your chest sucks on it.
            - Muscular pump: skeletal muscle squeezes on the veins when you exercise.
            - When you're scared, smooth muscles around veins constrict and squeezes blood.

- Capillary beds
    - mechanisms of gas and solute exchange
        - Diffusion is the major mechanism of gas and solute exchange, whether it is diffusion as a free molecule, or bound to carrier proteins.
        - Continuous capillary
            - No pores on endothelial cells. May have clefts at cell boundaries.
            - Exchange may occur through the clefts, or by vesicle trafficking through endothelial cells.
            - Found in skin and muscles.
            - Blood-brain barrier = sealing of clefts by tight junctions.
        - Fenestrated capillary
            - Small pores, large enough for molecules, but not blood cells to leak through.
            - Found in small intestines to facilitate nutrient absorption.
            - Found in endocrine organs to allow passage of hormones.
            - Found in kidneys to allow blood filtration.
        - Sinusoidal capillary
            - Large pores, large enough for blood cells to leak through.

        - Found in lymphoid tissues, liver, spleen, bone marrow.
        - Large pores facilitate lymphocyte travel to tissues.
        - Large pores also facilitate blood cell modifications.
    - mechanism of heat exchange
        - radiation - your body gives off IR signal.
        - conduction - you touch something cold, or take a hot bath.
        - evaporative cooling - you sweat, and it cools you as it evaporates.
    - source of peripheral resistance (no longer tested)
        - Blood viscosity: blood cells and plasma proteins give blood a higher resistance to flow compared to water. Diseases that increase the amount of blood cells increase resistance.
        - Total blood vessel length: more blood vessels you have, the more resistance to flow. Overweight = more blood vessels to service the fat cells = more resistance.
        - Blood vessel diameter: vasoconstriction increases resistance, vasodilation decreases it. Obstruction from plaques inside blood vessels also increases resistance.

- Composition of blood



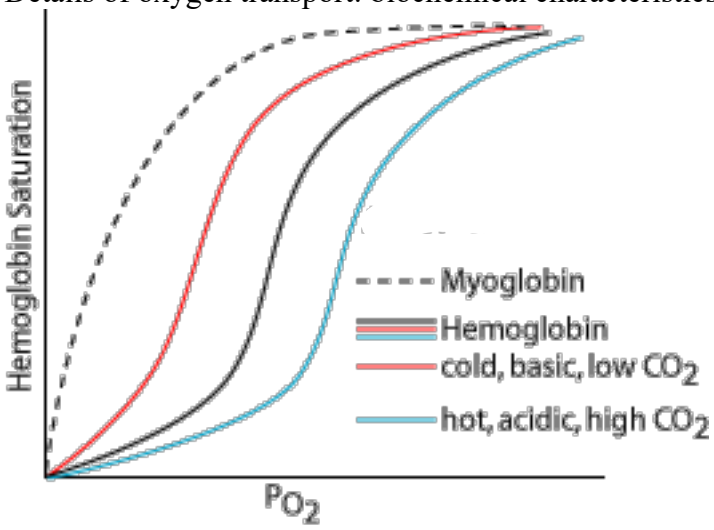
    - plasma, chemicals, blood cells
        - plasma = water and chemicals = mostly water, plasma proteins, electrolytes, gases, nutrients, wastes, hormones.
        - blood cells
            - red blood cells (RBCs or erythrocytes)

        - contain hemoglobin, transports O2 and CO2
        - no nucleus, which gives it a biconcave disk shape
        - most abundant cell in blood.
    - white blood cells (WBCs or leukocytes)
        - larger than RBCs
        - lobed or irregular shaped nuclei
        - fights off pathogens
    - platelets
        - technically not cells, but cell fragments
        - responsible for clotting blood
- erythrocyte production and destruction (spleen, bone marrow)
    - Bone marrow = makes RBCs from stem cells.
    - Spleen = destroys aged and damaged RBCs.
    - Other sites for RBC destruction include the liver and bone marrow.
    - Components of hemoglobin from destroyed RBC gets recycled
        - iron = recycled
        - heme → bilirubin → bile → excreted in feces
        - protein (globin) = broken down to amino acids
- regulation of plasma volume
    - Blood osmolarity
        - Higher blood osmolarity → water goes into blood → higher blood volume
        - Lower blood osmolarity → water goes into tissues → lower blood volume
    - ADH (vasopressin): ↑ water reabsorption in kidney.

        - Aldosterone: ↑ salt reabsorption, leads to ↑ water reabsorption in kidney.
    - coagulation, clotting mechanisms, role of liver in production of clotting factors
        - Platelets contain enzymes and chemicals needed involved in the clotting process.
        - Liver produces clotting factors (eg. fibrinogen), which circulates in blood plasma.
        - Coagulation = liquid blood → gel
        - Clotting mechanism:
            - Platelet plug formation: wound + platelets → platelets clump at wound, release chemicals, activates clotting factors.
            - Coagulation: series of clotting factor/enzyme activation that ends in fibrinogen → fibrin. Fibrin being the fiber mesh that seals the clot.
            - Retraction and repair: clot contracts, gets compact, but after the wounded blood vessel repairs itself, the clot dissolves.
- Oxygen and carbon dioxide transport by blood
    - hemoglobin, hematocrit
        - hemoglobin = (heme + globin) x 4
            - heme = chemical ligand binding iron
            - globin = protein that surrounds heme
            - 4 subunits of the heme-globin complex form a tetramer called hemoglobin.
            - hemoglobin can bind oxygen and carbon dioxide
        - hematocrit = % volume of blood that is red blood cells, usually ~ 45%
    - oxygen content
        - each iron atom in hemoglobin can bind one oxygen.
        - hemoglobin has 4 subunits containing 4 iron atoms.
        - each RBC has hundreds of millions of hemoglobin molecules.

- oxygen affinity
    - hemoglobin has a sigmoidal oxygen binding curve. This is because oxygen binding to one subunit "relaxes" the conformation of the other subunits, and makes it easier for additional oxygen to bind.
    - carbon monoxide binds hemoglobin tighter than oxygen.
    - fetal hemoglobin binds oxygen tighter than adult hemoglobin.
    - myoglobin binds oxygen tighter than hemoglobin.

- Details of oxygen transport: biochemical characteristics of hemoglobin



    - modification of oxygen affinity
        - Higher levels of carbon dioxide → lower oxygen affinity of hemoglobin.
        - Lower pH → lower oxygen affinity.
        - Higher temperature → lower oxygen affinity.
        - Working muscle = hot, acidic, high CO2, needs oxygen. So, hemoglobin must unload its oxygen, and it does this by lowering its oxygen affinity.

Lymphatic System

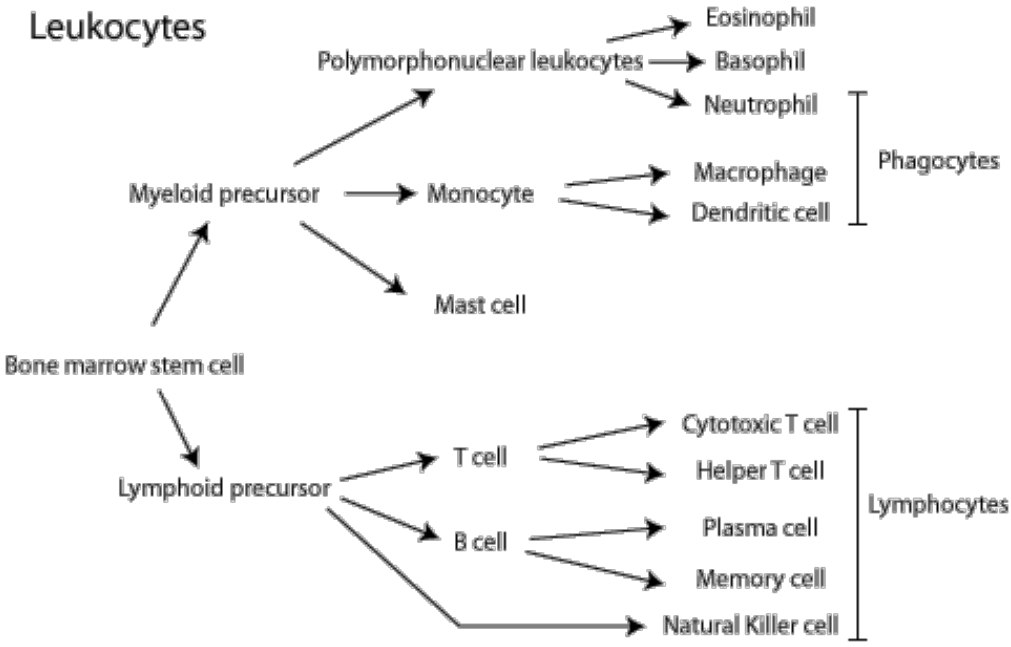
- Major functions
    - equalization of fluid distribution

        - Interstitial fluid pressure > lymphatic pressure → lymph vessel flaps open → interstitial fluid enters lymphatic capillaries → lymphatic circulation merges with veins → returns the fluid to blood
        - Interstitial fluid pressure < lymphatic pressure → lymph vessel flaps close → prevents lymph from leaking back out.
    - transport of proteins and large glycerides
        - fats get absorbed into the lacteals in the small intestine.
        - lacteal = lymphatic capillary in the small intestine.
        - plasma protein that leaked into interstitial fluids get returned to the blood via the lymphatic system.
    - production of lymphocytes involved in immune reactions
        - technically, lymphocytes are produced in the bone marrow from blood stem cells.
        - however, lymphoid tissues provide a place where lymphocytes can reside, proliferate, and differentiate.
        - lymphoid tissue is found in lymph nodes, thymus, and scattered throughout various organs.
        - lymph tissue contains many lymphocytes that cleans/filters lymph.
        - thymus is the place where T cells mature.
    - return of materials to the blood
        - cells and plasma proteins that leak out of the blood capillaries gets collected by the lymphatic capillaries and returned to the vein.
    - Composition of lymph (similarity to blood plasma; substances transported)
        - Lymph = stuff that leaks out of the capillaries = mostly water, plasma protein, chemicals, and white blood cells.
    - Source of lymph (diffusion from capillaries by differential pressure)
        - blood plasma from capillaries → interstitial fluid → lymph → returned to blood
    - Lymph nodes (activation of lymphocytes)

- Lymph nodes are concentrated with white blood cells.
- When pathogens or foreign antigens get inside a lymph node, lymphocytes that reside there get activated.
- Activation = lymphocytes start releasing chemicals that stimulate an immune response = proliferation, antibody production, release of cytokines.

Immune system: Innate and Adaptive Systems

- Cells and their basic functions



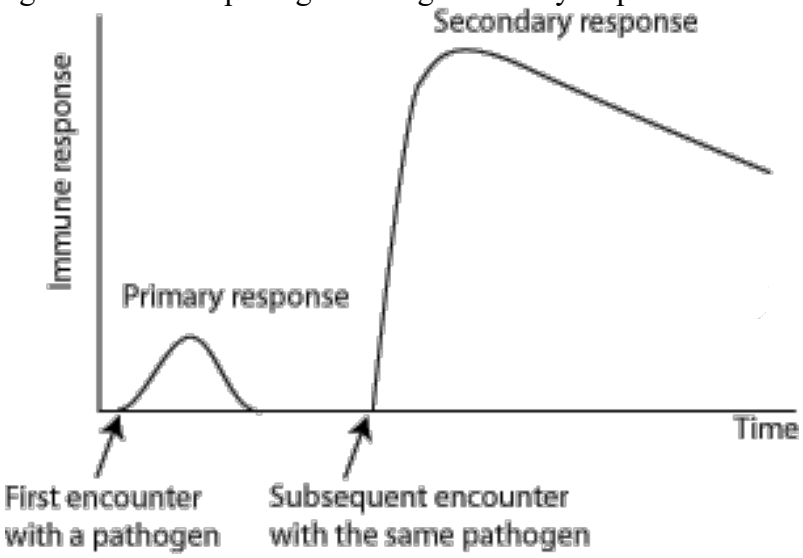
  - macrophages, neutrophils, mast cells, natural killer cells, dendritic cells
    - macrophages = phagocytose pathogen and then act as antigen presenting cell.
    - neutrophils = Polymorphonuclear leukocytes = PMNs = phagocytose pathogen and destroys it.
    - mast cells: release histamine during an allergic response, bring about inflammation.
    - natural killer cells: kills infected/abnormal cells.
    - dendritic cells: the best antigen presenting cells.
  - T-lymphocytes

        - Matures in the **T**hymus.
        - cytotoxic T cells recognize antigen on infected cells, and signal for apoptosis.
        - helper T cells recognize antigen on antigen-presenting cells, and signal for activation of B cells, T cells, and macrophages.
    - B-lymphocytes, plasma cells
        - Matures in **B**one marrow.
        - B cells form plasma cells and memory cells when exposed to antigen.
        - plasma cells = secrete antibody.
        - memory cells = stick around in case the same antigen attacks in the future.

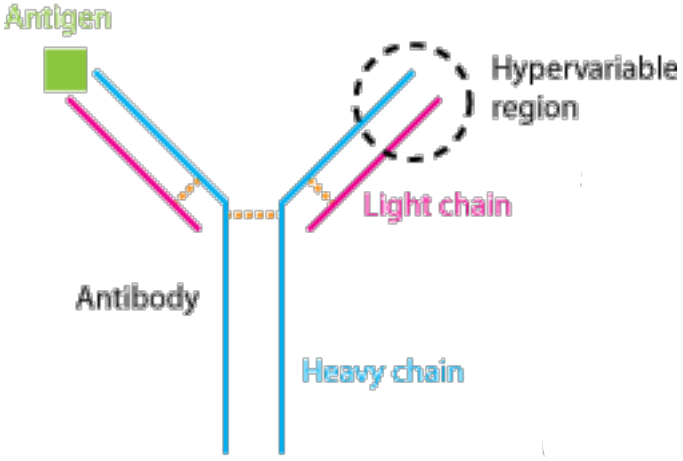
- Tissues
    - bone marrow
        - all blood cells arise from stem cells in the bone marrow.
        - B lymphocytes differentiate in the bone marrow.
    - spleen
        - Provides a site for WBCs to reside and proliferate.
        - Removes pathogens from blood.
        - Removes old RBCs and platelets.
    - thymus: T lymphocytes differentiate in the thymus.
    - lymph nodes
        - Provide a site for WBCs to reside and proliferate.
        - Removes pathogens from lymph.
        - Residing lymphocytes monitor lymph for foreign antigens, and initiate an immune response when exposed to foreign antigens.

- Basic aspects of innate immunity and inflammatory response: Innate = first line of defense = kills anything that doesn't look right = not specific to a particular pathogen / antigen
    - Skin: natural flora, layer of keratin.
    - Mucus membranes: traps pathogen in mucus, and cilia moves it out.
    - Phagocytes: engulf pathogen.
    - Natural killer cells: destroy infected cells.
    - Antimicrobial proteins: tears (lyse bacteria), interferons (interfere with virus replication), complement (punches holes in cell/pathogen membrane).
    - Fever/inflammation: WBCs are more active at higher temperature, and inflammation recruits WBCs to site of infection by sending out chemical signals and making capillaries more permeable.
- Adaptive immunity = highly specific for a particular pathogen / antigen.
    - antigen presenting cells present foreign antigen on their surface.
    - antigen is recognized by T and B cells.
    - cytotoxic T cells kill infected cells.
    - helper T cells activate macrophages, T and B cells.
    - B cells produce antibodies.
    - antibodies bind to antigens and bring about
        - neutralization: pathogen can't adhere to host cell
        - opsonization: makes it easier for phagocytosis
        - complement activation: kills infected cell by punching holes in cell membrane.
    - memory cells are made that are much more efficient (does not need T cell activation) in proliferating and making antibodies in case the same infection strikes in the future.

- memory cells allow the body to mount a greater, and more sustained response against the same pathogen during secondary response.



- Concept of antigen and antibody
  - Antibody = lock, Antigen = key. Each antibody is specific to the binding of an antigen.
  - Antibody is like a Y, the tips of the fork bind antigen.
  - The tips of the fork are called hypervariable regions because they are unique to each antigen-specific antibody.
  - The antibody consists of 2 light chains and 2 heavy chains linked together by disulfide bonds.
- Structure of antibody molecule



- Mechanism of stimulation by antigen; antigen presentation

    - pathogen enters antigen-presenting-cell (APC)
    - pieces of the pathogen gets displayed at the surface of APCs.
    - T cell receptors recognize the presented antigen, and activates various immune responses.

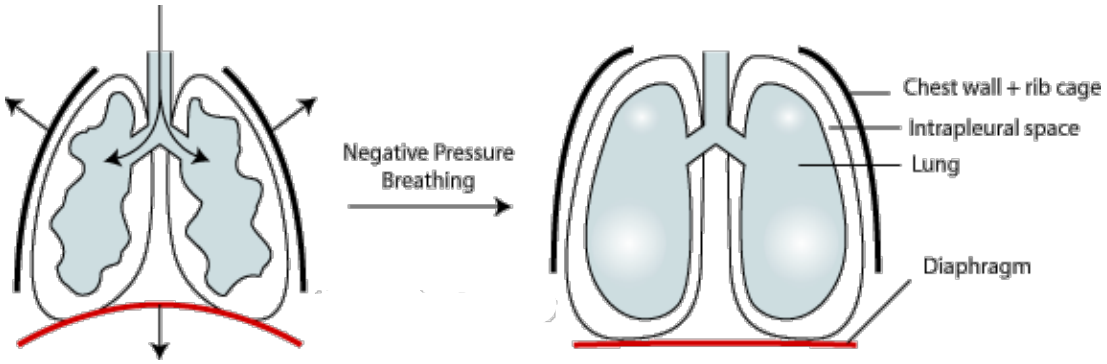
- scenario 1: extracellular pathogen
    1. macrophage engulfs pathogen.
    2. pieces of the pathogen becomes the antigen and gets presented at the macrophage's cell surface.
    3. helper T cells recognize the presented antigen, and activates macrophages to destroy pathogen. Helper T cells also activate B cells to produce antibodies against the pathogen.
- scenario 2: intracellular pathogen
    0. pathogen invades host cell.
    1. pieces of the pathogen gets presented on the host cell surface.
    2. cytotoxic T cells recognize the presented antigen, and signals the infected cell to self-destruct.

Respiratory System

General structure and function

- gas exchange, thermoregulation
    - In lungs: oxygen diffuses into blood. Carbon dioxide diffuses out of blood.
    - The mechanism of this gas exchange follows Henry's law, which basically says that there is an equilibrium concentration of oxygen that should be dissolved in blood.
    - When blood reaches the lungs, it has less than the equilibrium concentration of oxygen because the body used the oxygen up. Therefore, oxygen diffuses into blood.
    - The CO_2 in blood that reaches the lungs is higher than the equilibrium concentration because of the body releases them. Therefore, CO_2 diffuses out of blood.
    - Thermoregulation: breathing causes you to lose heat (you breathe out warm, moist air).
- protection against disease, particulate matter
    - Nostril hair filters out particles.
    - Mucus lining of respiratory tract traps pathogens and particles.
    - Cilia on mucus lining of respiratory tract sweeps pathogen and particles out, where you either spit it out or swallow it into stomach acid.
    - Macrophages reside in alveoli.

Breathing mechanisms



- diaphragm, rib cage, differential pressure
    - Diaphragm = muscle that pulls downward when contracting, which increases chest volume, decreases pressure, and sucks air into lungs.
    - Rib cage = expands outward during breath intake. Intercostal muscles help this expansion. At rest, the rib cage maintains lung volume, prevent lung from collapsing, forms a cage around lungs for protection.
    - Differential pressure = difference between intrapulmonary (inside lung) pressure and intrapleural (outside lung) pressure.
        - Intrapulmonary pressure = atmospheric pressure (lung is open to the outside, so has same pressure as outside).
        - Intrapleural pressure = less than atmospheric pressure = sucks on the lungs, prevent lung from collapsing. During breath intake, intrapleural pressure decreases even further, causing the lung to expand.
    - Negative pressure mechanism in breathing is just a fancy term for sucking. You breathe in by establishing negative pressure in the lung (sucking). However, when someone gives you mouth-to-mouth, that's positive pressure.
- resiliency and surface tension effects
    - Lung is elastic, it recoils as soon as you relax after breath intake. If not for the rib cage, the lung would collapse even further.
    - Surface tension causes the lung to collapse. Surfactants produced in the alveoli decreases surface tension, and helps alveoli to stay open.

Skin System

Functions in homeostasis and osmoregulation

- Heat homeostasis:
    - Too cold: hair stands up (goose bumps), vasoconstriction decreases blood supply at skin (less heat loss).
    - Too hot: sweat (evaporative cooling), vasodilation increases blood supply at skin (more heat loss).
- Water homeostasis: Insulates body against water loss.
- Osmoregulation: sweat excretes salts and nitrogenous wastes (urea, uric acid, ammonia)
- Some other functions of the skin:
    - protect against UV radiation by making melanin (absorbs UV)
    - make vitamin D upon exposure to sunlight.
    - Act as blood reservoir. Vasoconstriction in skin shunts blood to other organs.
    - Sense touch, pressure, pain, heat, cold.
    - Protection.

Functions in thermoregulation

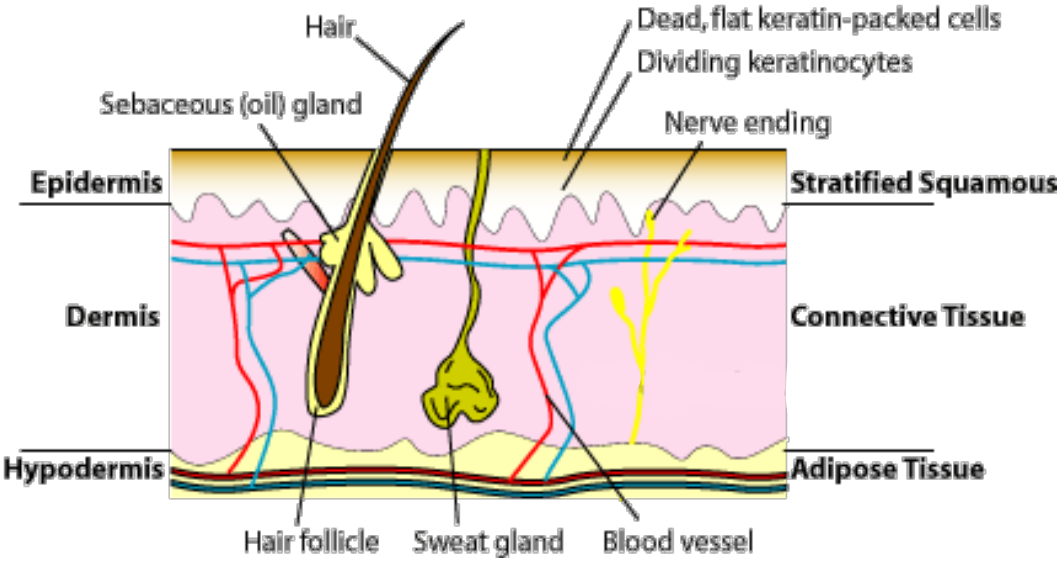
- hair, erectile musculature
    - hairs help insulate the body by trapping air in them.
    - Normally hair lies at an angle to the skin, with erectile muscle attaching to it.
    - When it's cold, erectile muscles contract, and the hair stands up. This erect position helps hair to trap more air, providing better insulation.
- fat layer for insulation: fat in hypodermis act as insulation.

- sweat glands, location in dermis: produce sweat, cools the body by evaporative cooling.
- vasoconstriction and vasodilation in surface capillaries
    - When it's cold: vasoconstriction of arterioles reduce blood supply to skin capillaries. Leads to less heat loss at skin surface.
    - When it's hot: vasodilation of arterioles increase blood supply to the skin capillaries. Leads to more heat loss at skin surface.

Physical protection

- nails, calluses, hair
    - nail = hard keratin = tougher than the soft keratin on skin.
    - calluses = extra thick layer of dead keratin-packed cells on the surface of skin.
    - hair = hard keratin.
- protection against abrasion, disease organisms
    - Keratin protect skin against abrasion.
    - The tight seal made from keratin-packed cells and glycolipids form a barrier against pathogens.
- Chemical protection: Sweat is acidic, contains antibodies, and antimicrobial agents. Sebum (skin oil) kills bacteria.
- Natural flora: good bacteria on the surface of skin don't cause harm to you, and they fight off bad bacteria that can harm you.

Structure



- layer differentiation, cell types, tissue types (epithelial, connective)
    - Epidermis = stratified squamous epithelial tissue = protection
        - Keratinocytes = cells that produce keratin = dominates the epidermis.
        - Keratinocytes start off like normal cells at the bottom of the epidermis, but gets flatter as you go up, and becomes dead, keratin plates at the surface of the skin.
        - Melanocytes = cells that make melanin, the skin pigment.
        - Dendritic cells (Langerhans cells) = phagocytes that eat pathogen and present foreign antigens to activate immune response.
    - Dermis = connective tissue = blood, nerve supply
        - Fibroblasts = make fiber and ground substance (glue) for the extracellular matrix that makes up connective tissue.
        - Hair follicles, sweat glands, and oil (sebum) glands.
        - Blood vessels and nerves.

    - Hypodermis = adipose tissue = absorbs shock and provides insulation.

- relative impermeability to water: due to layer of dead, keratin-packed cells sealed with glycolipids.
    - Keratin is water insoluble, and layers of dead, keratin-packed cells reside on the skin surface.
    - Glycolipids seal the space between the dead keratin-packed cells.
    - Sebum (skin oil) contribute some. But oil glands are not present everywhere (absent in palms and soles).

Digestive System

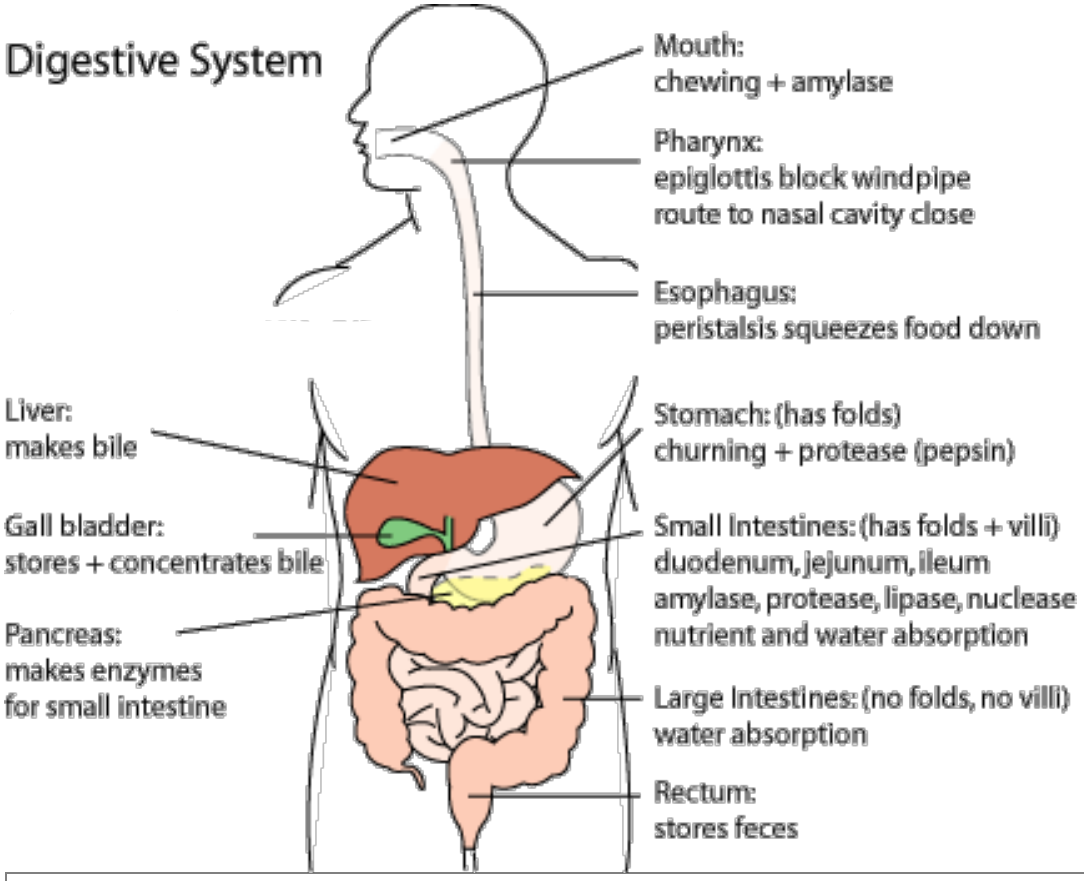


Table of digestive tract	
Organ	**Digestive Activities**
Mouth	Mechanical digestion: chewing Chemical digestion: saliva contains amylase and lipase
Stomach	Mechanical digestion: churning Chemical digestion: protease (pepsin)
Small intestine	Chemical digestion: amylase, protease, lipase (assisted by bile from liver/gall bladder), nuclease (all enzymes predominantly from the pancreas) Nutrient and water absorption
Large intestine	Water absorption

Table of enzymes	
Enzyme	**Where found**
Amylase	Mouth and small intestine
Protease	Stomach and small intestine
Lipase	Mouth and small intestine
Nuclease	Small intestine

Ingestion

- saliva as lubrication and source of enzymes
    - saliva dissolves food.
    - saliva contains mucin, a protein that lubricates the bolus (chewed up food ball).
    - saliva contains amylase, which breaks down polysaccharides (starch and glycogen).
    - saliva also contains antibodies and lysozyme that kill pathogens.
- epiglottal action
    - epiglottis = flap of cartilage that closes off airway when you're swallowing.
- pharynx (function in swallowing)
    - pharynx = throat = between mouth and esophagus.
    - muscular tube that squeezes and routes food to the esophagus when swallowing (closes off pathways to nasal cavity and airway).
- esophagus (transport function)
    - muscular tube that propels bolus (food) to the stomach by peristalsis.
    - peristalsis = squeezing stuff through a tube (esophagus/gut) by smooth muscle.

Stomach

- storage and churning of food
    - storage = the stomach is a muscular bag that is elastic and can stretch to store food.

    - churning = mechanical digestion = mixing food.

- low pH, gastric juice, protection by mucus against self-destruction
    - Parietal cells secrete HCl that causes the pH to be very acidic.
    - Gastric juice = HCl + pepsin + hormones = secreted by the stomach (parietal and chief cells, and enteroendocrine cells)
    - Pepsin = protease that works best in acidic environment.
    - Goblet cells secrete mucus lining that protect the stomach from the acid and self-digestion.
- production of digestive enzymes, site of digestion
    - Chemical digestion: Stomach produces pepsin, which digests proteins (secreted in an inactive form, gets activated in acidic environment)
    - Pepsin is special in that it works best at very acid pH.
    - Mechanical digestion: Stomach churns food.
- structure (gross)
    - banana shaped bag that can stretch.
    - inner membrane densely folded (rugae), so can accommodate stretching.
    - sealed off on the top by the cardiac (gastroesophageal) sphinctor.
    - sealed off on the bottom by the pyloric sphinctor.

Liver

- production of bile: liver makes bile from cholesterol, stores it in gall bladder.
- role in nutrient metabolism, vitamin storage
    - Makes and stores glycogen from glucose.
    - Gluconeogenesis from glycerol and amino acids (deamination).
    - Breaks down fats, makes cholesterol, makes lipoproteins used to transport fats.
    - Stores vitamins (A, D and B12) and iron.
    - Detox: metabolize alcohol, remove ammonia in blood.

- role in blood glucose regulation, detoxification
    - Blood glucose regulation by liver:
        - Blood sugar too low: gluconeogenesis.
        - Blood sugar too high: glycogeneis.
    - Detoxification: metabolize alcohol (alcohol dehydrogenase), remove blood ammonia, inactivate various other drugs/toxins.
- structure (gross): largest gland in body, spans both sides of the abdomen (though right side much larger). Ducts draining to duodenum and gall bladder.

Bile

- storage in gall bladder
    - Gall bladder stores excess, unused bile, and concentrates it. Secretes it when needed.
- function: bile is an emulsifying agent (not an enzyme). Bile breaks down large fat droplets into smaller microscopic droplets by forming micelles. This increases the total surface area of the fat for lipase action.

Pancreas

- production of enzymes, bicarbonate
    - Pancreas is the major source for all the digestive enzymes.
        - Amylase - digests starch.
        - Various proteases.
        - Lipase - digests fat.
        - Ribonuclease - digests nucleic acids.
    - Pancreas makes HCO_3^- to neutralize the HCl from the stomach.
- transport of enzymes to small intestine
    - Digestive enzymes of pancreas = exocrine = flows into small intestine via duct.
- structure (gross): tadpole-shaped gland with duct leading to duodenum.

Small intestine

- absorption of food molecules and water
    - Small intestine is the major place for digestion and absorption.
    - Folds, villi, and microvilli increases the surface area for absorption.
    - Absorbs digested food into circulation (fats into lacteals, all others into capillaries).
    - Active transport occurs to absorb against the concentration gradient.
        - Intestinal lumen (less glucose) -> enterocyte (more glucose): Secondary active transport by Na^+-K^+ pump + Na^+-Glucose symport.
    - Passive/facilitated diffusion occurs to absorb down the concentration gradient.
        - Enterocyte (more glucose) -> extracellular fluid (less glucose): Facilitated diffusion (then the glucose will go from the extracellular fluid to blood).
- function and structure of villi
    - Villi = finger-like protrusions inside small intestine.
    - Microvilli = same as villi but on the surface of a single absorptive cell.
- production of enzymes, site of digestion
    - The small intestine is the major place for digestion and absorption.
    - Pancreas is the major source for enzymes. However, the small intestine does make some of its own enzymes, including protease and amylase.
- neutralization of stomach acid
    - The pancreas makes bicarbonate ion to neutralize the HCl from the stomach.
    - This neutralization facilitates enzymes in the small intestine, which would be denatured by stomach pH.
- structure (anatomic subdivisions)
    1. Duodenum.
    2. Jejunum.

3. Ileum.

Large intestine

- anatomic subdivisions (old topic)
    1. Cecum: blind pocket containing appendix.
    2. Ascending colon
    3. Transverse colon
    4. Descending colon
    5. Sigmoid colon
    6. Rectum: stores feces.
- absorption of water: The large intestine absorbs any remaining water that is not absorbed by small intestine.
- bacterial flora
    - Ferment undigested nutrients, make gas.
    - Produce vitamin K (important for clotting).
- structure (gross): lobes/pockets along its length due to muscle tone. Unlike small intestine, the large intestine has no folds or villi.

Rectum (storage and elimination of waste, feces)

- Rectum stores feces.
- The anal sphincter ties the end of the rectum.
- During defecation, sphincter opens, feces are released through the anus.

Muscular control

- sphincter muscle
    - Cardiac sphincter (gastroesophageal sphincter): sphincter between esophagus and stomach. Prevents back flow of food.

    - Pyloric sphincter: between stomach and small intestine. Releases food into the small intestine a small amount at a time.
    - Anal sphincter: at the end of rectum. ties the end of the rectum.
- peristalsis: involuntary movement of smooth muscles, squeezes food along the digestive tract.

Excretory System

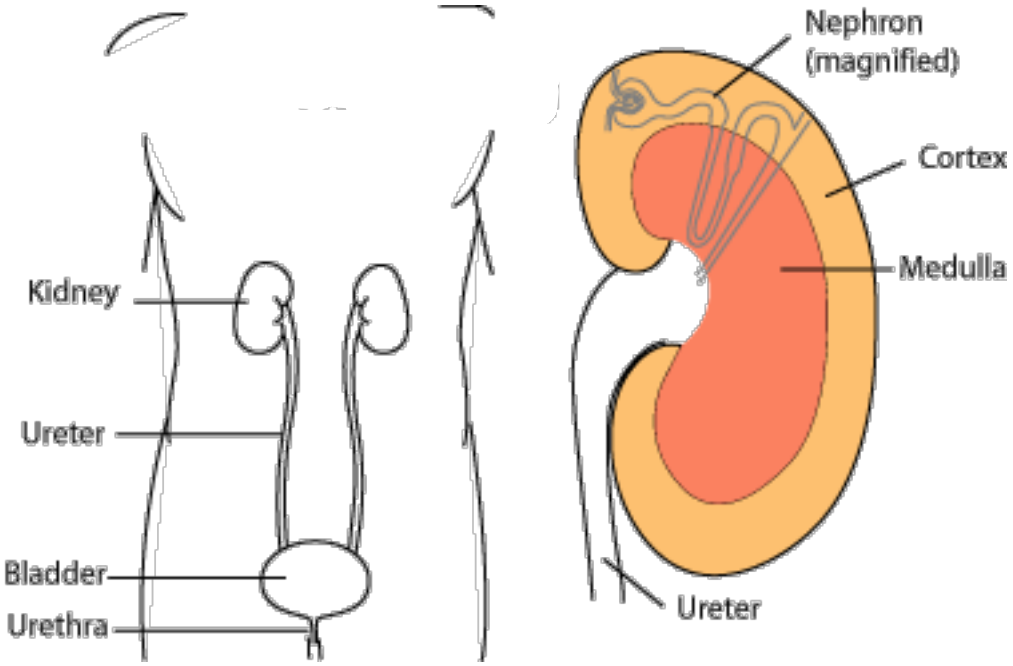
Roles in homeostasis

- blood pressure
    - If blood pressure too low:
        - Renin-angiotensin pathway: Kidney (JGA cells) release renin, triggers formation of angiotensin II, which stimulates aldosterone release, the end result is to raise blood pressure.
        - Aldosterone (aka mineralocorticoid): Adrenal glands release aldosterone, causes kidney (distal tubules) reabsorb more Na^+, which in turn causes more water reabsorption.
        - ADH (made in hypothalamus, stored in pituitary): causes more water reabsorption in the kidney tubules, raising blood pressure. High levels also cause vasoconstriction.
    - If blood pressure too high, all the above hormones stop releasing. Also, the heart can release ANP (Atrial natriuretic peptide), which antagonizes aldosterone and cause kidney to excrete both more Na^+ and more water. ANP can also cause vasodilation.
- osmoregulation
    - Blood plasma is mainly Na^+ and Cl^- (Inside cells is mainly K^+ and hydrogen phosphate ions).
    - Blood osmolarity is determined predominantly by Na^+ and Cl^-.
    - Blood osmolarity too low → aldosterone, reabsorb Na^+. Cl^- follows.
    - Kidney tubules' secretion and reabsorption regulates osmolarity.
    - Other ions
        - K^+ is regulated by aldosterone.
        - Aldosterone: reabsorb Na^+, pee out K^+
        - Calcium and phosphate regulated by PTH.

        - PTH = parathyroid hormone = more Ca^{2+} reabsorption in kidney tubules (also, bone break down to release calcium and phosphates, and small intestine to absorb more calcium).

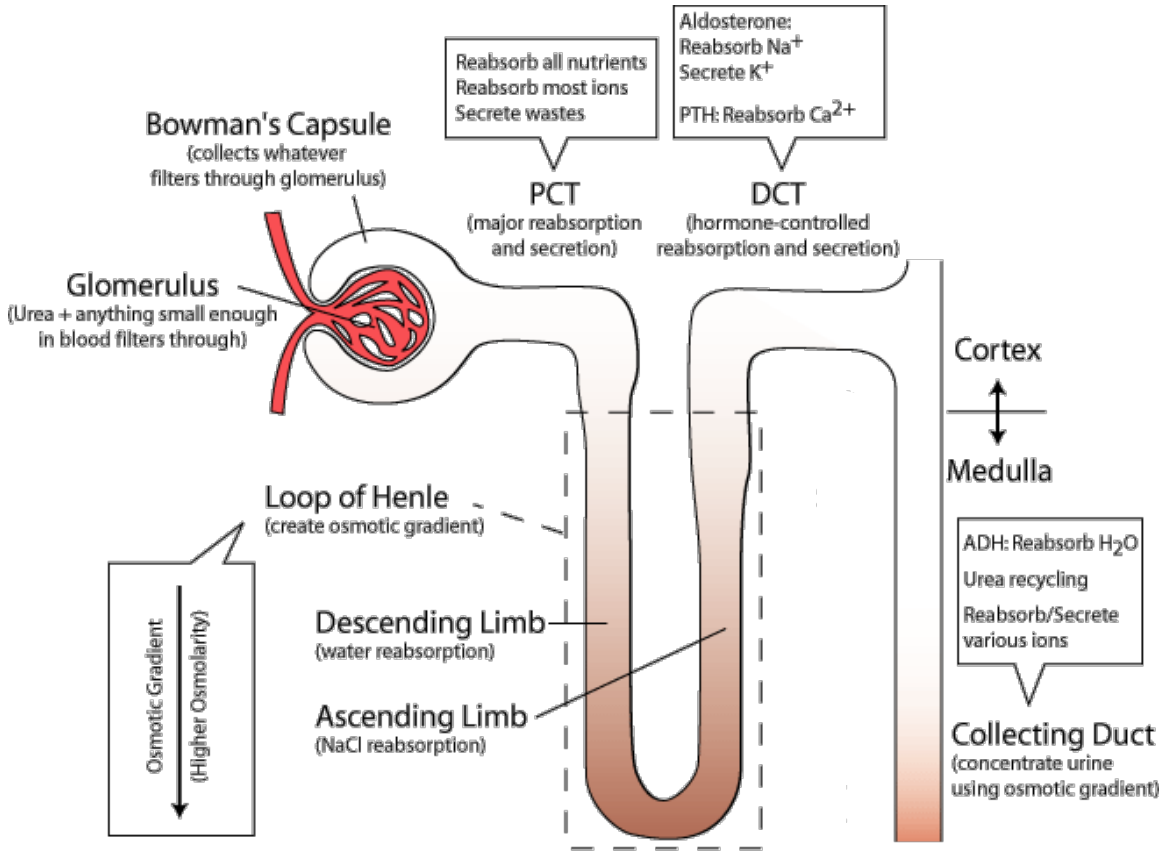
- acid-base balance: keep blood pH constant.
    - Buffer systems: Bicarbonate buffer system (blood and extracellular fluid), Phosphate Buffer System (inside cells)
    - $CO_2 + H_2O \leftrightarrow H_2CO_3 \leftrightarrow H^+ + HCO_3^-$
    - Breathing out CO_2 decreases the acidity in blood.
    - Kidney tubules:
        - Bicarbonate ion (HCO_3^-): peeing it out makes blood more acidic. Reabsorption makes blood more basic. (not the other way round, use Le Chatelier's principle, or simply note that bicarbs bind H^+, so they have the opposite effect on pH)
        - H^+ secretion gets rid of acidity.
- removal of soluble nitrogenous waste
    - Urine = concentrated urea in water, with some salt.
    - Urea = harmless form of toxic ammonia = nitrogenous waste.
    - Amino acids → Ammonia → Urea → peed out.

Kidney structure



- cortex = outer shell of kidney = contains the convoluted tubules.
- medulla = inner part of kidney = contains loop of Henle.

Nephron structure



Quick facts:	
PCT	proximal convoluted tubule
DCT	distal convoluted tubule
pH homeostasis	tubules secrete H+ if blood too acidic don't reabsorb (same effect as secrete) HCO_3^- if too basic
urea recycling	urea diffuse out of collecting duct back into loop of Henle help maintain osmotic gradient
Wastes secreted by PCT	NH_4^+, Creatinine, Organic Acids
Loop of Henle	The longer the loop of Henle, the more concentrated the urine can be produced
Countercurrent Mechanism	Powered by NaCl pumps in upper ascending limb. Results in osmotic gradient down loop of Henle

- Nephron = functional unit of kidney = glomerulus, Bowman's capsule, proximal tubule, loop of Henle, distal tubule, collecting duct (shared by many nephron).
- glomerulus = ball of fenestrated capillaries.
- Bowman's capsule = Cup/Capsule that surrounds the glomerulus.
- proximal tubule = convoluted tubule on the side of the Bowman's capsule = the major site for reabsorption (nutrient, salts and water) and secretion (except for K^+, the secretion of which is the job of distal convoluted tubule in response to aldosterone).

- loop of Henle = U shaped loop that dips into the renal medulla = countercurrent multiplier mechanism occurs here
    - Descending limb = water reabsorption by osmosis (permeable to water, but not to solute).
    - Bottom of U = most concentrated.
    - Ascending limb = salt reabsorption (permeable to salt, but not water).
- distal tubule = convoluted tubule on the side of the collecting duct = hormone-controlled (fine tunes the work done by the proximal tubule) reabsorption of salts and water. Aldosterone-controlled secretion of K^+
- collecting duct = the distal tubules of many nephrons drain here = ADH-controlled reabsorption of water, hormone-controlled reabsorption/secretion of salts.

Formation of urine

- glomerular filtration
    - Powered by hydrostatic pressure.
    - Both good stuff, bad stuff and ions are filtered out, as long as it's small enough.
    - Good stuff: nutrients
    - Bad stuff: urea (and creatinine and uric acid)
    - Good stuff reabsorbed, bad stuff peed out.
- secretion and reabsorption of solutes
    - Proximal convoluted tubules reabsorb all the good stuff (nutrients) and most of the ions. Bad stuff left in the filtrate (urea) to be peed out, also actively excreted (NH_4^+, creatinine, organic acids).
    - Loop of Henle reabsorbs water and salt using the countercurrent mechanism.
    - Distal convoluted tubules selectively reabsorb or secrete stuff based on hormonal control.
    - Collecting duct reabsorb water to concentrate urine if ADH present. (Also can secrete and reabsorb stuff based on hormonal control)
    - Regulation of blood pH: secrete H^+ when blood too acidic, pee out (don't reabsorb) HCO_3^- when blood too basic.

- concentration of urine
    - The distal convoluted tubule contains dilute solution of urea.
    - The collecting duct concentrates it by water reabsorption (facilitated diffusion) when ADH is present.
    - Water reabsorption in the collecting duct is possible because the loop of Henle has very high osmolarity (very concentrated) at the bottom.
- countercurrent multiplier mechanism (basic function)
    - What does the Countercurrent multiplier do? It creates an osmotic gradient down the loop of Henle, which is used by the collecting duct to concentrate urine.
    - What drives the creation of this gradient? NaCl pump on ascending limb.
    - What's countercurrent? Descending limb: water flow out of filtrate, impermeable to salt. Ascending limb: salt flow out of filtrate, impermeable to water.
    - What's multiplier? The gradient-producing power of each individual NaCl pump multiplies down the length of the loop of Henle. Longer the loop of Henle, greater the osmotic gradient, more concentrated urine can be produced.
    - What is urea recycling? Urea at the bottom of collecting duct leaks out into the interstitial fluid and back into the filtrate. Contributes to the high osmolarity at the bottom of the loop of Henle.

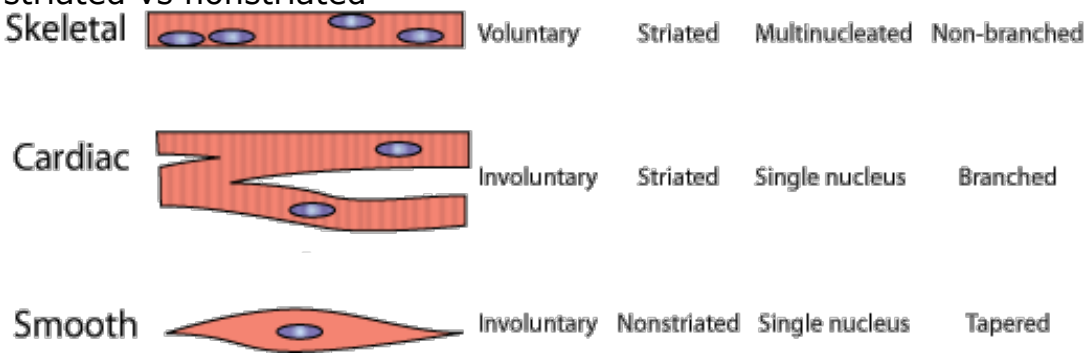
Storage and elimination (ureter, bladder, urethra)

- Collecting ducts drain into the ureter.
- Ureters drain into the bladder.
- Bladder stores urine: its special epithelium (transitional epithelium) can squish to accommodate storage of large amounts of urine.
- Urine gets peed out of the bladder through the urethra.

Muscle and Skeletal Systems

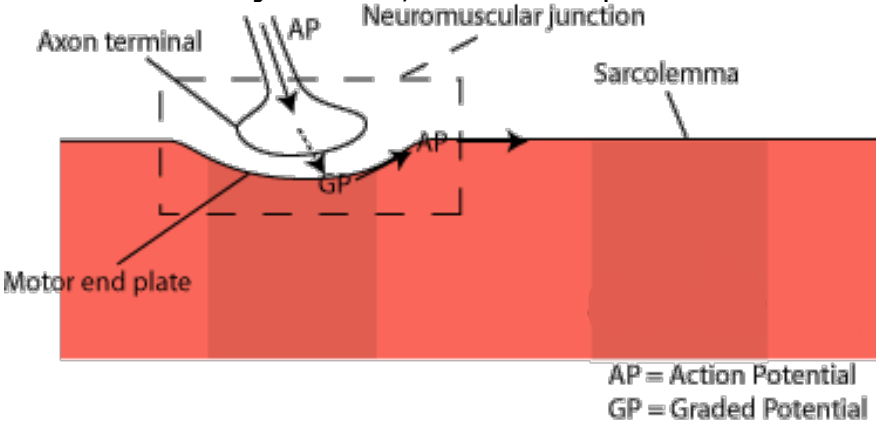
Muscle System

- Functions
    - support, mobility
        - Support = muscles maintain your posture when you sit/stand, muscles also stabilize joints, help prevent dislocations.
        - Mobility = you move because of skeletal muscles. Your guts move because of smooth muscles. Your blood flow because of pumping action of the heart.
    - peripheral circulatory assistance
        - Heart is a muscle that pumps blood.
        - Contraction of skeletal muscles around the deep veins help squeeze the blood through those veins.
        - Diaphragm contraction (breathing) sucks blood into the chest cavity, and also squeezes on abdominal veins.
    - thermoregulation (shivering reflex)
        - Muscles generate heat when you shiver in response to cold.
- Structural characteristics of skeletal, smooth, and cardiac muscle; striated vs nonstriated



- Skeletal muscle = striated, voluntary, shaped like long fibers, multinucleated.
- Smooth muscle = nonstriated, involuntary, shaped like almonds (tapered ends), one nucleus per cell.
- Cardiac muscle = striated, involuntary, branched, shaped like fibers cross-linked to one another, typically one nucleus per cell.
- Striated = due to sarcomere structure (A bands dark, I bands light). Skeletal and cardiac muscles have sarcomeres.
- Nonstriated = smooth muscles don't have sarcomeres so they're not striated. They still have myosin, actin, and use the sliding filament mechanism. They just are not organized into sarcomeres.
- Read more about sarcomeres here.

- Nervous control
  - motor neurons = efferent neurons = signals muscles/organs to do stuff = the opposite of sensory neurons.
    - Somatic motor neurons = controls skeletal muscles.
    - Autonomic motor neurons = sympathetic and parasympathetic divisions = controls involuntary (smooth, cardiac) muscles.
  - neuromuscular junctions, motor end plates



    - neuromuscular junction = nerve (axon terminal) meets muscle (motor end plate).

        - motor end plate = part of muscle cell membrane (sarcolemma) that synapse with the motor neuron, has receptors for the neurotransmitters.

        - what happens at the neuromuscular junction? Action potential of nerve reach axon terminal → release neurotransmitters into synapse → receptors on motor end plate (sarcolemma) picks this signal → graded potential created → if reaches threshold, then action potential created → action potential travels down the sarcolemma and cause muscle to contract.

    - voluntary and involuntary muscles

        - voluntary = you can control = skeletal muscles, eg. Biceps.

        - involuntary = you can't control = smooth (eg. gut) and cardiac (heart) muscles.

    - sympathetic and parasympathetic innervation

        - sympathetic = fight or flight = heart beat faster, pupil dilation, raise blood pressure, blood to muscles, less blood to digestive system.

        - parasympathetic = rest and digest = opposite of sympathetic = heart slower, pupil constriction, lower blood pressure, blood to digestive system.

        - Both sympathetic and parasympathetic are motor neurons that innervate involuntary muscles.

Skeletal System

- Functions

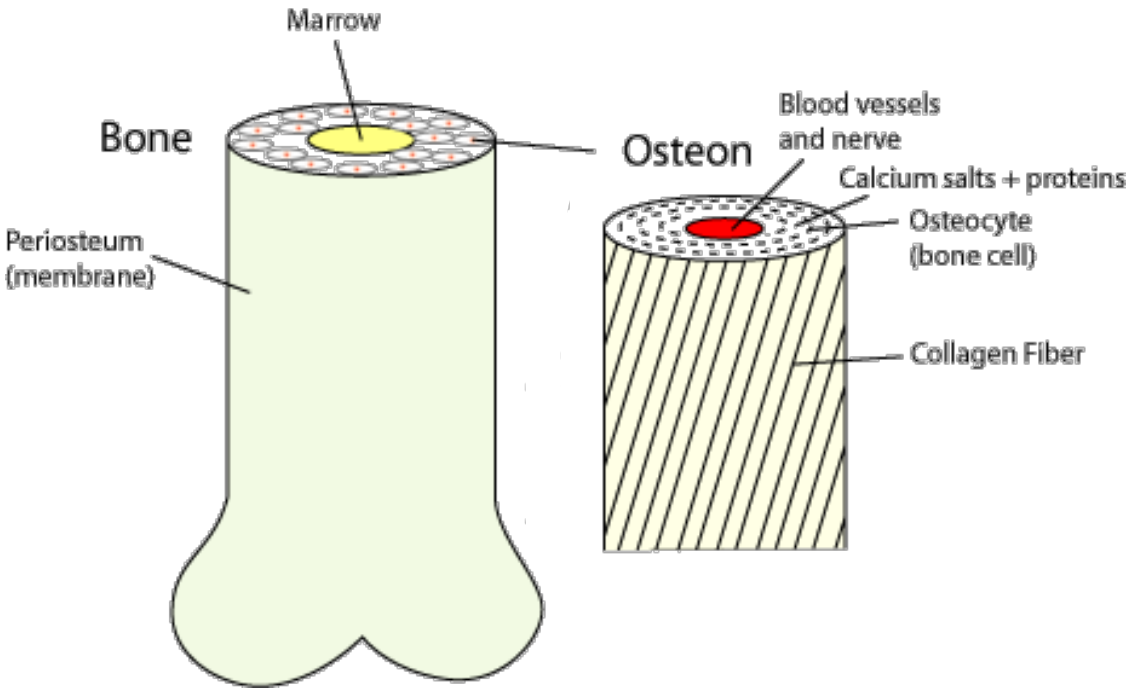
    - structural rigidity and support: bone forms the body's framework.

    - calcium storage: bone stores calcium. When blood calcium is low, parathyroid hormones signal bone tissue to break down and release calcium.

- physical protection: rib cage protects internal organs. Skull protects brain. Spine protects spinal cord. Many large bones also shelter bone marrow that contains stem cells that make blood.

- Skeletal structure
  - specialization of bone types, structures
    - Long bones: shaped like a rod. eg. arm, leg, finger bones.
    - Short bones: shaped like a cube. eg. wrist, ankle bones.
    - Flat bones: bones that are flat. eg. sternum, shoulder blades, ribs, skull.
    - Irregular bones: complicated shapes. eg. vertebrae, hip.
  - joint structures
    - Joint = where bone meets bone.
    - Joints can be mobile or non-mobile.
      - Mobile joints (synovial) have a fluid-containing cavity to lubricate movements of the bones.
      - Non-mobile joints connect bone to bone with cartilage or fiber.
    - Ball and socket joint: shoulder, hip.
    - Hinge joint: elbow.
    - Gliding joint: wrist.
    - Immobile joint: plates of the skull, rib-to-sternum.
    - The joint type that allows most freedom of movement = ball-and-socket.
  - endoskeleton versus exoskeleton
    - Endoskeleton = what we have, skeleton on the inside.
    - Exoskeleton = what insects have, skeleton (chitin) on the outside.

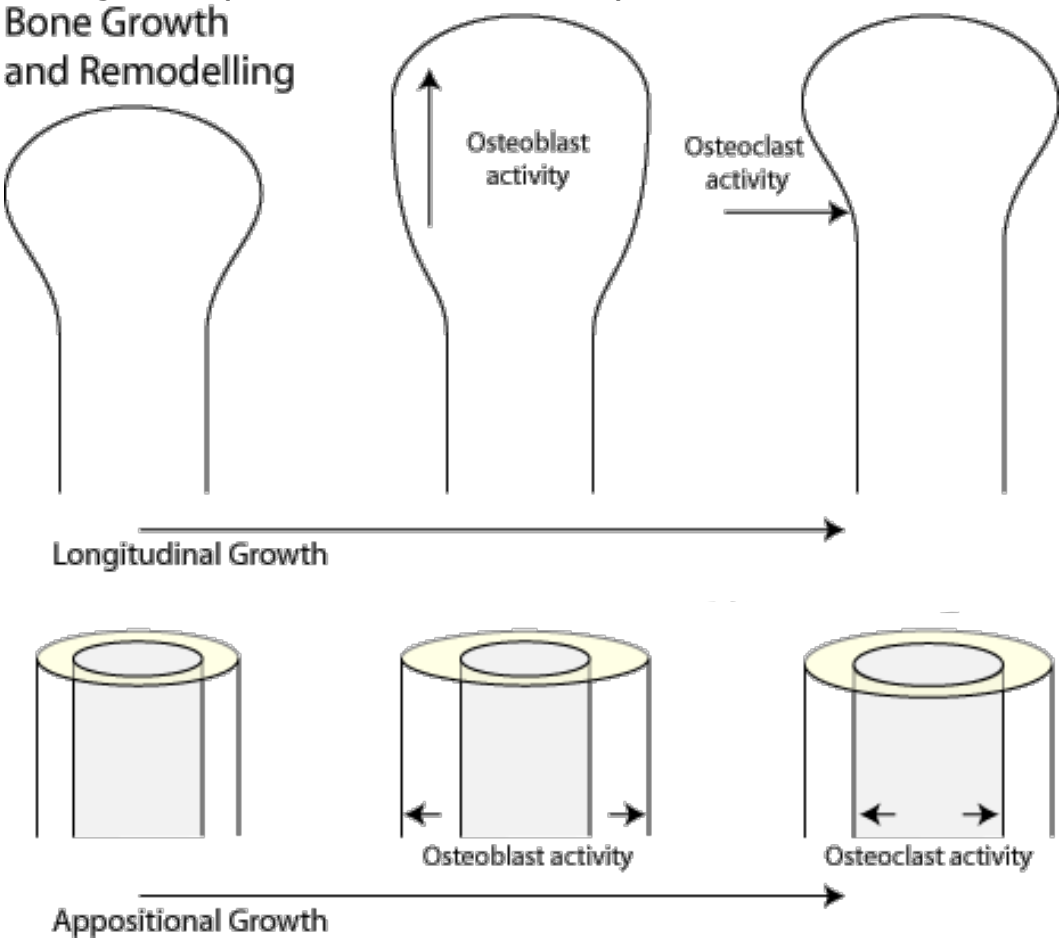
- Cartilage (structure and function)
    - Cartilage = cells + extracellular matrix.
    - Cartilage cells = chondrocytes.
    - Extracellular matrix = secreted by the cells, contains fiber meshworks that give the cartilage its characteristic properties (flexibility and resilience)
    - Functions
        - Flexibility: ear, nose, epiglottis, end of ribs
        - Resilience, compressibility: Ends of bones in joints, knee, between vertebrae.
- Ligaments, tendons
    - Ligament = connect bone to bone, stabilize joints.
    - Tendon = connect muscle to bone, anchors muscle.
- Bone structure



    - Macroscopically: bone = solid strucuture with canals inside where blood vessel runs, and holes where cells can reside, the

whole thing surrounded by membrane that contains stem cells (osteoblasts) and osteoclasts.

- Microscopically: bone = cell + extracellular matrix = arranged in cylinders called osteons, with blood vessel and nerve running through the middle of the cylinder.
- Cell = osteocytes (bone cells).
- calcium-protein matrix: the extracellular matrix of bone consists of calcium salts, collagen fibers, and ground substance (glue).
- bone growth (osteoblasts, osteoclasts)



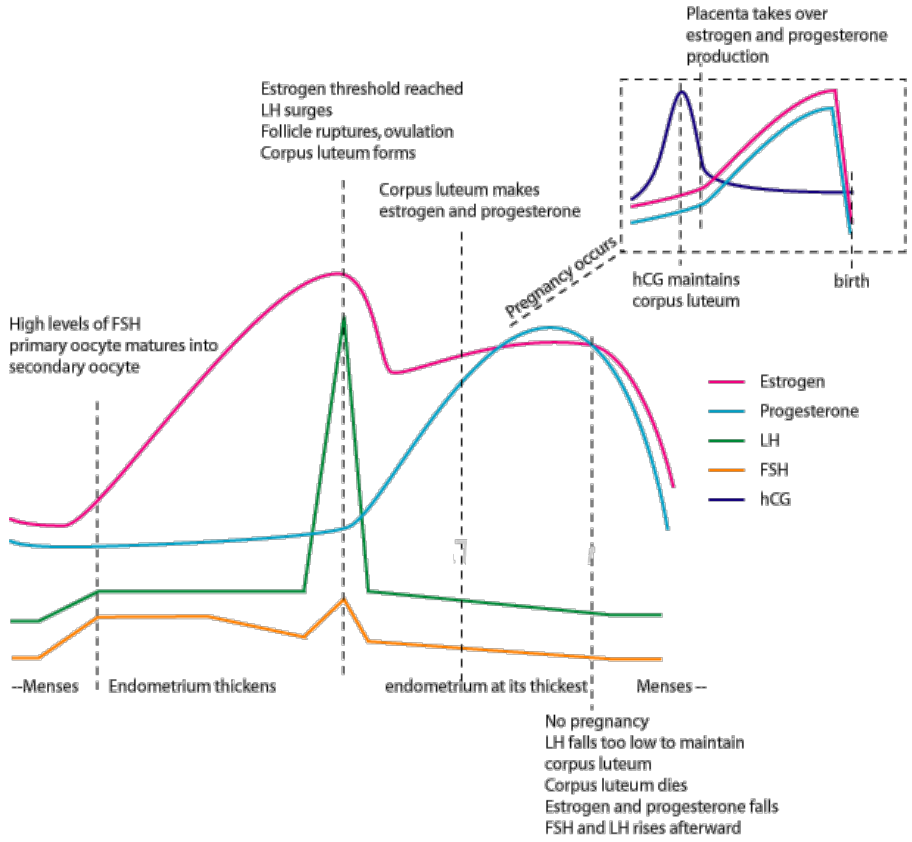
  - Growth in length:
    - Lengthwise bone growth occurs at the ends of long bones at the knobs.
    - Osteoblasts' role in lengthwise bone growth is to add bone tissue at the bone ends.

        - By itself, osteoblasts will lengthen the knobs at the ends of the bone.
        - Osteoclasts' role in bone growth is to remodel bone tissue by chipping away the knobs until it's the right size and shape.
    - Growth in diameter:
        - Osteoblasts' role in diameter growth of bones is to add bone tissue to the outside of the bone.
        - Osteoclasts' role in diameter growth of bones is to remove some bone tissue from the inside of the bone (bones are hollow).
        - Without osteoclasts, diameter growth will result in bones that are too thick and too heavy. Even with osteoclasts, bones still grow thicker, just not unwieldly thick.
- Osteoblasts vs osteoclasts vs osteocytes
    - Osteoblasts = stem cells that give rise to osteocytes = builds bone.
    - Osteocytes = mature bones cells = reside in bone for housekeeping.
    - Osteoclasts = large cells that break down bone.

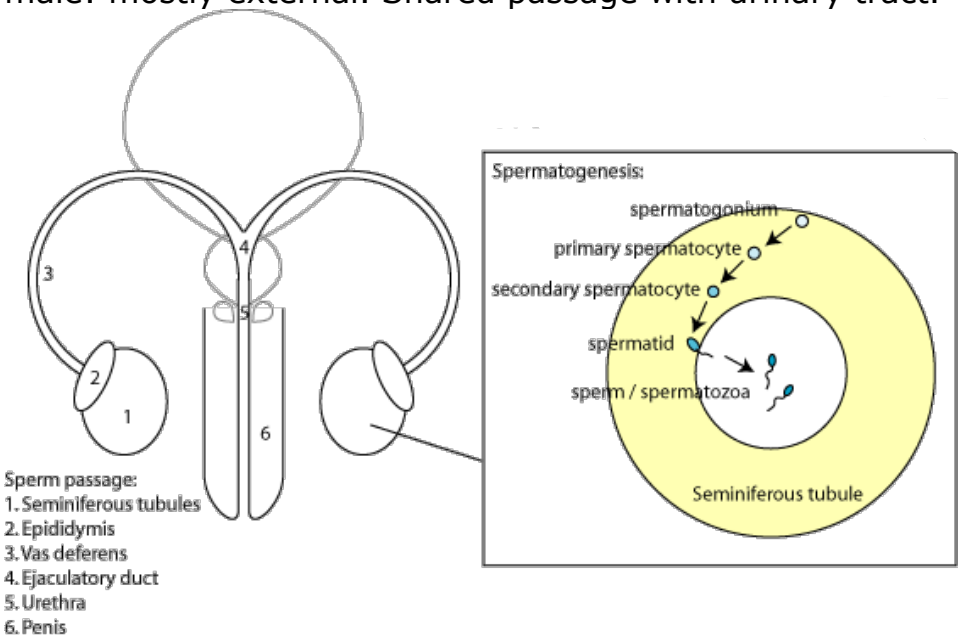
Reproductive System and Development

- Male and female reproductive structures and their functions
    - gonads
        - male: testes
            - makes sperm in the seminiferous tubules.
            - makes testosterone.
            - external.
        - female: ovaries
            - houses immature egg, which matures monthly after puberty.
            - makes estrogen.
            - internal.
    - genitalia
        - male: testes, penis, and various ducts and glands.
            - sperm made in the seminiferous tubules.
            - stored in the epididymis.
            - travels through vas deferens → ejaculatory duct → urethra → penis
            - mnemonic: seven up = **S**eminiferous tubules, **E**pididymis, **V**as deferens, **E**jaculatory duct, **n**othing, **U**rethra, **P**enis.
        - female: ovaries, fallopian tubes, uterus, vagina
            - Monthly cycle: primary oocyte matures into secondary oocyte every month. To prepare for it, the endometrium thickens. If fertilization doesn't occur, menses occur, and the cycle begins anew.
            - GnRH = stimulates release of FSH and LH.

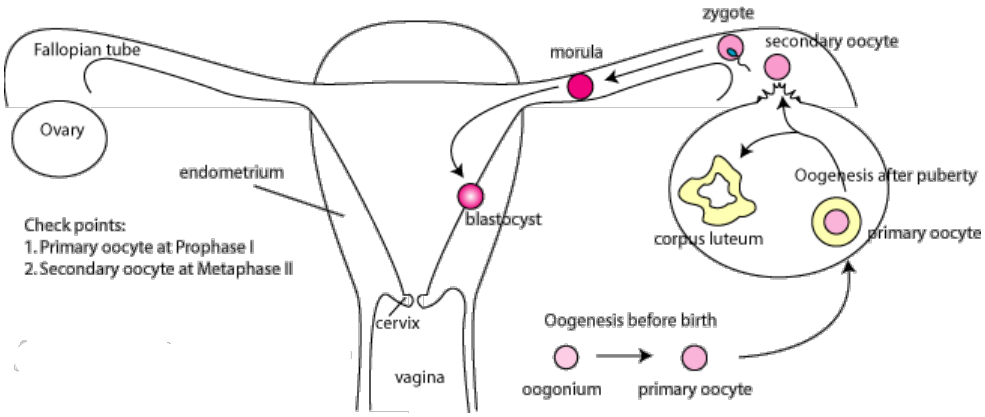
- FSH = folicle stimulating hormone = stimulates growth and maturation of follicle.
- Follicle = houses oocyte and produces estrogen.
- Estrogen = normally inhibits LH and FSH, but causes LH surge when it reaches a certain threshold.
- Estrogen reaches this threshold → surge of LH occurs.
- LH = leutinizing hormone = luteinizing hormone = stimulates the outer cells of the follicle = turns it into corpus luteum + maintains it.
- LH surge triggers primary oocyte → secondary oocyte → rupture of follicle.
- Corpus luteum = makes estrogen and progesterone = maintains endometrium.
- No fertilization → LH falls → corpus luteum dies → estrogen and progesterone fall → endometrium dies (menses) → cycle begins anew with FSH and LH re-rising.
- Fertilization occurs → implanted embryo releases hCG → hCG mimics LH to maintain corpus luteum → estrogen and progesterone maintained by corpus luteum → placenta takes over the responsibility of making estrogen and progesterone later on.



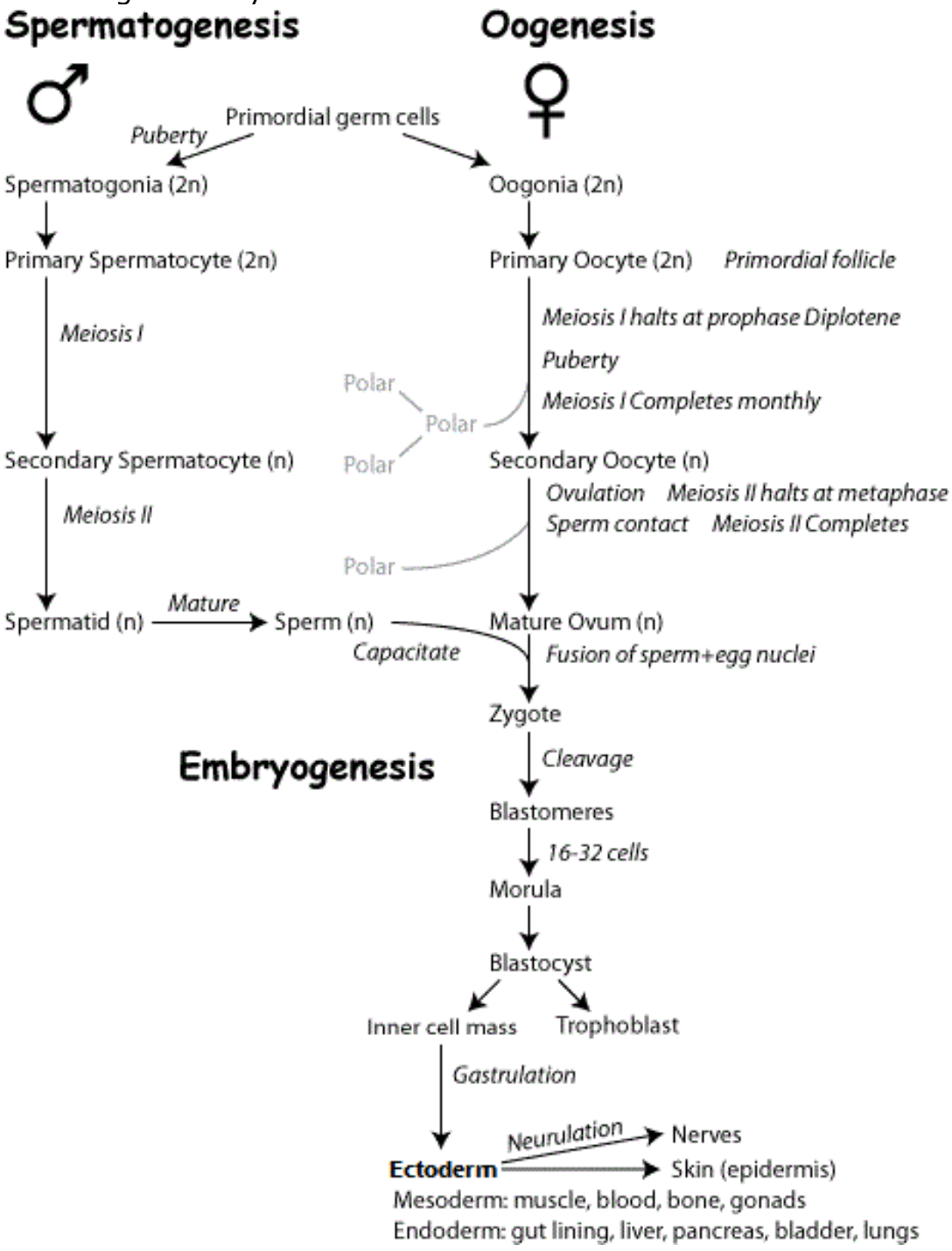
- differences between male and female structures
  - male: mostly external. Shared passage with urinary tract.



- female: mostly internal. Separate passage from urinary tract.



- Gametogenesis by meiosis



  - Male = spermatogenesis = occurs in the seminiferous tubules.

    1. Spermatogonium (2n) = stem cell. Mitosis of spermatogonium can either create more spermatogonium or create primary spermatocyte.

2. Spermatogonium (2n) → mitosis → primary spermatocyte (2n). Occurs after puberty.
3. Primary spermatocyte (2n) → meiosis I → Secondary spermatocyte (n).
4. Secondary spermatocyte (n) → meiosos II → spermatid (n).
5. Spermatid (n) → mature → sperm (n). The fancy name for sperm is spermatozoa.

- Female = oogenesis = occurs in the ovaries, then fallopian tubes.

0. Oogonium (2n) = stem cell.
1. Oogonium (2n) → mitosis → primary oocyte.
2. Primary oocyte (2n) arrests at prophase I (occurs before birth). One comes out of arrest every month (between puberty and menopause).
3. Primary oocyte (2n) → meiosis I → secondary oocyte (n). Ruptures from ovary follicle into the fallopian tube.
4. Secondary oocyte (n) arrests at metaphase II. Comes out of arrest if fertilization occurs.
5. Secondary oocyte (n) → meiosis II → ovum (n).

- Ovum and sperm
    - differences in formation

Male and female gametogenesis side by side		
Male	**Female**	**Difference**
Spermatogonium (2n)	Oogonium (2n)	Spermatogonium renews its population by mitosis throughout life. Oogonium stops renewing its population sometime before birth
Primary spermatocyte	Primary oocyte	Primary oocye arrests at prophase I
Secondary spermatocyte	Secondary oocyte	Secondary oocyte arrests at metaphase II
Sperm	Ovum	Between the secondary spermatocyte and the sperm, there's the spermatid

    - differences in morphology
        - Sperm = motile = flagella.
        - Egg = non-motile = round.
    - relative contribution to next generation
        - Sperm contributes DNA only (the egg actively destroys sperm mitochondria).
        - Egg contributes DNA + everything else (mitochondria, organelles, epigenetics).
- Reproductive sequence (fertilization, implantation, development, birth)
    1. fertilization: sperm + egg → zygote
    2. implantation:
        0. zygote
        1. morula (solid ball)
        2. blastula (sea urchins) or blastocyst (mammals)
        3. the blastocyst is the one that implants in the endometrium
    3. development:

0. zygote
1. blastocyst
2. implantation
3. gastrulation
4. organogenesis

4. Birth:
    - Switch from getting oxygen from mom's blood → breathing.
    - Switch from getting nutrients from mom's blood → suckling.
    - Fetal circulation (which bypasses lungs and liver) → normal circulation (by closing off ducts and openings).

Embryogenesis

- Stages of early development (order and general features of each)
    - fertilization
        1. Sperm meets egg
        2. Acrosomal reaction causes sperm to penetrate egg
        3. Cortical reaction causes egg to prevent additional sperm from penetrating
        4. Egg completes meiosis II
        5. Sperm and egg nuclei fuse
    - cleavage
        - Normal mitotic cell divisions: cell grows then divides, grows again, then divides.
        - Cleavage = mitotic divisions without cell growth.
    - blastula formation

0. fertilization produces zygote
1. cleavage produces a solid ball called the morula
2. morula hollows out into the blastula or blastocyst
    - blastula occurs in non-mammals
    - blastocyst occurs in mammals
3. blastocyst implants

- gastrulation
    - first cell movements
        - Cells from the surface migrate inwards.
        - gastrulation occurs slightly different for different animals. Some by invagination, some by migration, some by splitting.
        - In mammals, the cells start migrating inward at the primitive streak.
    - formation of primary germlayers (endoderm, mesoderm, ectoderm)
        - The cells that migrate inwards form the endoderm.
        - The cells that remain outside is the ectoderm.
        - The cells in the middle are the mesoderm.
- neurulation
    - ectoderm → brain and spinal cord
    - the ectoderm does so by folding into a tube

- Major structures arising out of primary germ layers
    - endoderm = innermost layer = guts, lungs, and digestive internal organs (liver, pancreas).
    - mesoderm = middle layer = muscle, blood and bone tissues, and interal organs (kidney and gonads).

- ectoderm = outermost layer = skin and nerves (including the brain).

Developmental Mechanisms

- Cell specialization = commitment followed by differentiation
  - commitment = specification followed by determination
  - specification = cell is just beginning to be commited to develope into a certain cell type. The commitment can be reversed at this stage.
  - determination = irreversible commitment to become a certain cell type.
  - differentiation = becoming a cell type and adopting its specialized functions.
    - epidermal cells produce keratin to protect skin against abrasion.
    - myocyte produce actin and myosin to make muscles contract.
    - neurons make neurotransmitters to transmit electrochemical impulses.
  - tissue types
    - Epithelial: skin, lining of organs
    - Connective: blood, bone, tendons, ligaments, cartilage
    - Nervous: brain, spinal cord, nerves
    - Muscle: skeletal, smooth, and cardiac muscle
- Cell communication in development
  - Induction: one group of cells changing the behavior of an adjacent group of cells.
  - inducer = the one that sends the signal for the other to change.
  - responder = the one that gets the signal and changes.

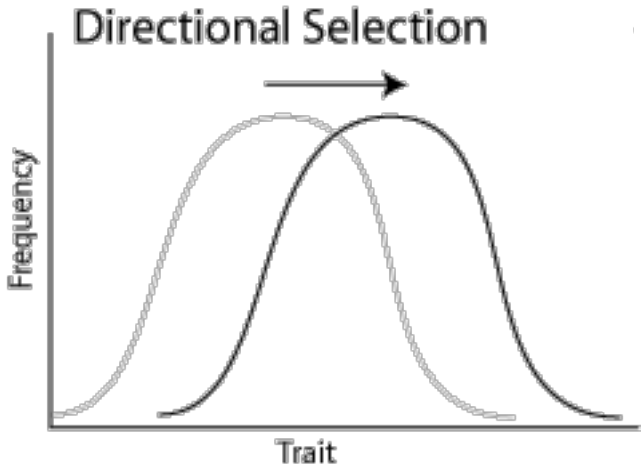
    - For example, the optic vesicle is able to induce the ectoderm to develope into lens.
    - Another example is the induction of wing feathers in the chick by the dermal mesenchyme.
    - Induction mechanisms: physical touching of cells (juxtracine) or by releasing chemicals (paracrine).
- Cell migration
    - Gastrulation, neural crest cell migration
    - Hirschprungs disease: defective neural crest cell migration
- Pluripotency: stem cells (able to differentiate into other cell types)
    - Stem cells in bone can differentiate into osteoblasts or osteocytes
    - Stem cells in bone marrow can differentiate into neutrophils, lymphocytes, red blood cells or platelets
- Gene regulation in development
    - Differential gene transcription:
        - modification of DNA (methylations) can shut off or turn on genes.
        - modification on histones (methylations, acetylations) that wrap the DNA can shut off or turn on genes.
        - to make or not to make transcription factors can regulate what genes get transcribed.
    - Differential RNA processing:
        - selecting what RNA make it outside the nucleus to be translated.
        - alternative splicing of RNA.
    - Translation regulation

        - some mRNA are made to last longer than others (more proteins translated off of it), and some are made to be rapidly degraded (less proteins translated off of it).
        - selective inhibition of translation of stored RNA in the oocyte. Get translated only when needed after fertilization.
    - Post-translational regulation
        - some proteins are inactive until modified by certain enzymes.
        - active proteins can be selectively marked for degradation by ubiquitin.
- Programmed cell death
    - apoptosis = programmed cell death.
    - During apoptosis, strong proteases are activated and they digest the cell from within. In mammals, the proteases are called caspases.
    - The spaces between our fingers are created by apoptosis.
    - The tail of a tadpole undergoes apoptosis when it morphs into a frog.
- Existence of regenerative capacity in various species
    - Newts can regenerate limbs
    - Cells in their limb stump can dedifferentiate and revert back to stem cells
- Senescence and aging
    - Every time a cell replicates, the telomere shortens. Eventually, they run out of telomeres
    - As a person age, their cells acquire irreversible DNA damage by radiation and chemicals. Not all can be repaired, and they accumulate

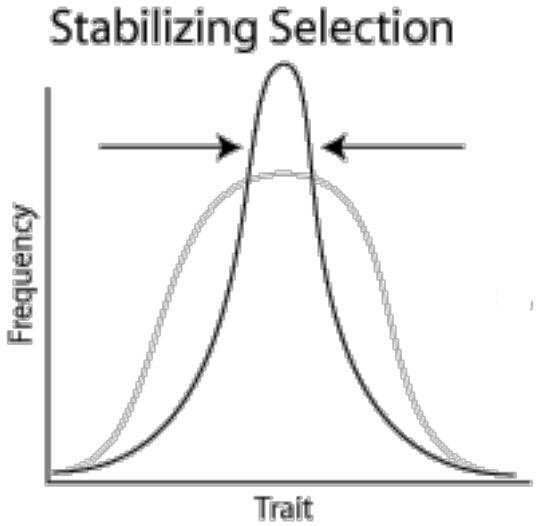
Evolution

Evolution

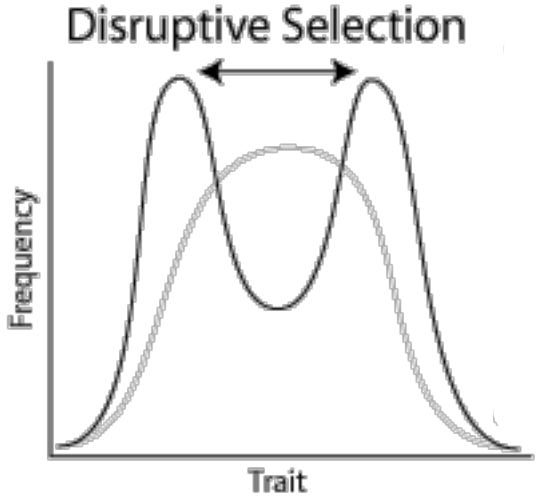
- Natural selection
    - Fitness concept
        - Fitness is defined as the ability to pass your genes on, or reproductive success.
        - The classical trick question gives you an individual who is strong, healthy, long-living, but does not reproduce. In this case, no matter how good the other traits are, if the individual does not reproduce, then it has a fitness of zero.
    - Selection by differential reproduction
        - Individuals who reproduce more viable offspring are selected *for*.
        - Individuals who reproduce less viable offspring are selected *against*.
    - Concepts of natural and group selection
        - Natural selection = survival and reproduction of the fittest.



        - Directional selection: selects for a trait on one extreme. For example, selection for height of canopy trees in a rainforest: trees compete for sunlight, so selection favors trees to become higher and higher.



- Stabilizing selection: selects for a trait that is moderate, and selects against the extremes. For example, birthweight: too low birthweight means that the baby is premature, too high birthweight means that the mom will have a hard time delivering, so there's a "just right" birthweight that is selected for.



- Disruptive selection: selects for the extremes. For example, birds occupying a habitat with 2 distinct niches (eating berries for a living and eating seeds for a living): small beaks are selected for eating berries, large beaks are selected for cracking seeds, medium beak is left out.

- Group selection = natural selection acting on the group, not the individual.
    - Explains why altruism exists.
    - Altruism sacrifice the fitness of the individual to benefit the group (family), which shares similar genes with the individual. When

the benefit outweighs the cost, the altruistic behavior is selected for.

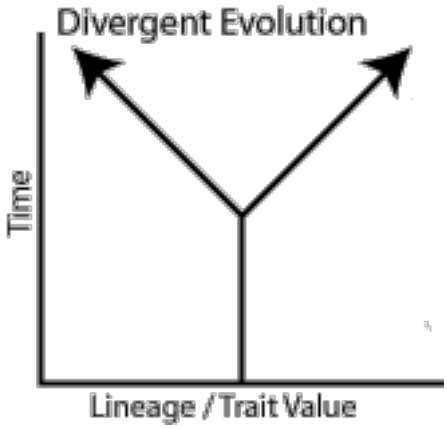
- Evolutionary success as increase in percent representation in the gene pool of the next generation
  - If the frequency of an allele increased, then that's evolutionary success for that allele.
  - If the frequency of alleles of an individual increased in a population, then that's evolutionary success for that individual.

- Speciation
  - Definition of species
    - Three conditions for biological species
      1. Be able to interbreed.
      2. Be able to produce fertile, viable offspring.
      3. Does this naturally.
    - A dog and a cat can't interbreed, so they don't belong to the same species.
    - A horse and a donkey can interbreed, but their offspring, the mule, is sterile. So horses and donkeys aren't the same species.
    - Some species of flowers can cross pollinate to produce fertile offspring. However, this never occurs in nature because one is bee-pollinated and the other is bird-pollinated. Thus, they are different species even though they can potentially produce fertile offspring.
    - Speciation is the formation of a new species. This can occur due to barriers to successful interbreeding within an initial species.
  - Polymorphism
    - Polymorphism is just a fancy word for different forms of alleles/traits.
  - Adaptation and specialization
    - Adaptation is the genetic change in a population caused by natural selection.
    - Adaptation is caused by Darwin's natural selection, not by Lamarck's ideas. A giraffe's neck is long because long necks increase the survival

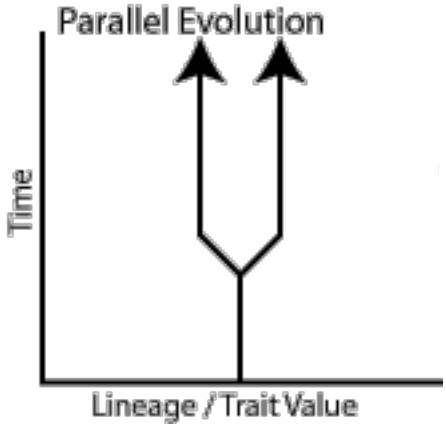
rate, so more long-necked giraffes survive to reproduce, and over many generations, the population evolved long necks. The wrong idea by Lamarck is that the giraffe had to reach for higher leaves on trees, so it stretched itself a longer neck.

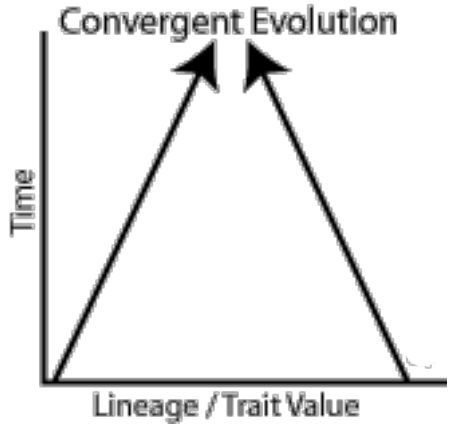
- Specialization = adaptation of traits to better fill a niche.

- Concepts of ecological niche, competition
  - A species' ecological niche is what resources the species uses to survive in its environment.
  - Two species can avoid competition, and better use the environment's resources by occupying different niches.
  - As long as two species occupy different niches, there's no competition because they use different resources.
  - When niches overlap, there's competition.
  - Specialization occurs to better occupy a particular niche.
- Concept of population growth through competition
  - Population growth is checked by competition.
  - When resources get scarce, competition increases, which slows down population growth.
  - Competition within a species can force members within the species to occupy different niches, which drives speciation.
- Inbreeding
  - Inbreeding is mating between relatives.
  - Inbreeding increases the frequency of homozygotes, decreases heterozygotes, and decreases genetic diversity.
  - Inbreeding depression occurs because of the increase in the frequency of homozygous recessive detrimental alleles.
  - Some species (naked mole rats) naturally inbreed because:
    - They stay in one small area and don't migrate much.
    - Detrimental homozygous recessive alleles are eliminated because of many generations of natural selection.

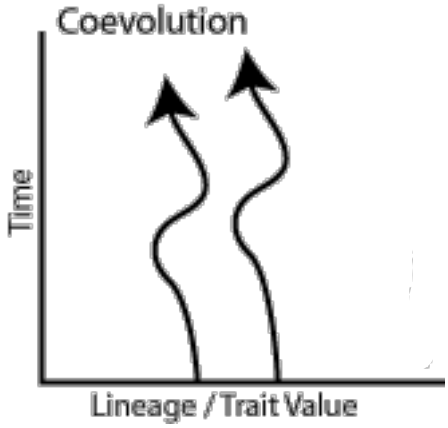
- Outbreeding
    - Outbreeding is mating with non-relatives, which is just the opposite of inbreeding.
    - Outbreeding increases heterozygosity.
- Bottlenecks, genetic drift
    - A bottleneck is a severe reduction in population size. This can be caused, for example, by a natural disaster that wipes out a majority of the population.
    - Genetic drift is the random changes in allele frequencies.
    - The effect of genetic drift increases as population size decreases.
    - Bottlenecks increase the effect of genetic drift.
- Divergent, parallel, and convergent evolution
    - 

    Divergent evolution
        - Same lineage, evolving apart to be more different.
        - For example, bats and horses. Both share the same lineage as mammals, but the limb of the bat became wings while the horse developed hooves.
        - Divergent evolution produces homologous structures (bat's wing and horse's hoof).

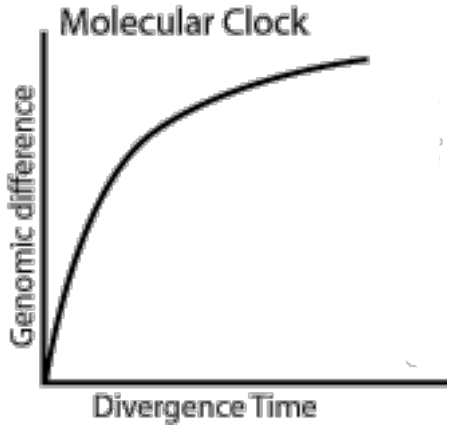
- 

Parallel evolution
    - Same lineage, evolving closer together to be similar, using similar mechanisms.
    - For example, the feeding structure in different species of crustaceans. The feeding structure came from mutation of pair of legs, turning them into mouth parts. This is a prime example of parallel evolution: same lineage, similar traits, evolved from similar mechanisms/mutations.
- 

Convergent evolution
    - Different lineage, evolving closer together to be similar, using different mechanisms.
    - For example, bats and butterflies. Both have wings, but they came from totally different lineages, evolved through different mechanisms/mutations. Convergent evolution produces analogous structures (bat's wing and butterfly's wing).



- Coevolution
    - Two species evolve in response to each other.
    - For example, predator/prey or host/parasite species.
    - Not yet an official exam topic, but many students confuse parallel evolution with coevolution.

- Evolutionary time as measured by gradual random changes in genome
    - Random genetic mutations (drift) that are not acted on by natural selection (neutral) occur at a constant rate.
    - By measuring the amount of these neutral mutations, you can find out how much time has passed.
    - You can compare genome differences between two species to find out how long ago they diverged.
    - Another name for this concept is the Molecular Clock.
    - 

Evolution

Evolution

- Symbiotic relationships (got moved into a different section)
    - Parasitism
        - Relationship where one benefits (parasite), and the other is harmed (host).
        - For example, worms living inside animal intestines.
    - Commensalism
        - Relationship where one benefits, and the other is not affected.
        - For example, some plant seeds disperse by sticking to animal fur.
    - Mutualism
        - Relationship where both species benefit.
        - For example, lichens are made from a mutualistic relationship between fungi and algae. The fungus provides anchor/absorption, and the alga provides photosynthesis.
- Relationship between ontogeny and phylogeny
    - Ontogeny = development through the life of an organism.
    - Phylogeny = development through evolutionary time of lineages/species.
    - In early development, vertebrate embryos share similar features, reminiscent of a common ancestor.
        - Gill slits
        - Notochord
        - Segmentation
        - Paddle-like limbs
    - Ontogeny recapitulates phylogeny is the idea that the development of an organism repeats the evolutionary history of its species; starting with the fish-

like common ancestor, which then changes to the modern form as development continues to adulthood.

- Origin of life

    1. Organic molecules created by atmospheric gases zapped by lightning, which falls into the ocean to make primordial soup (Oparin and Haldane). Urey-Miller's experiment proved this in a lab.

    2. RNA World hypothesis: the simple organic molecules formed RNA polymers that can self-replicate (Having enzymatic activity as well as serving as template).

    3. Protocells: aggregates of RNA, proteins inside lipid envelopes.

    4. Prokaryotes: first anaerobic heterotrophs because early atmosphere blocks the light required for photosynthesis, then anaerobic autotrophs that undergoes photosynthesis and makes oxygen, then aerobics that utilize oxygen.

    5. Eukaryotes: evolved by endosymbiosis, where a big cell engulfed a smaller cell and then developed a mutualistic relationship. Heterotrophs engulfed mitochondria. Autotrophs engulfed chloroplasts.

Comparative anatomy

- Chordate = one of the phylums in the kingdom Animalia.
- Chordate features
    - Notochord = the "backbone" of the embryo, except that it's not made of bone. In vertebrates, bones will replace the notochord to form the vertebrae.
    - Pharyngeal pouches, branchial arches (pharangeal pouches) = gill slits in the embryo. Later develop into various head and neck structures in human.
    - Dorsal nerve cord = forms the nervous system. In higher chordates, the nerve cord develops into the brain and spinal cord.
- Vertebrate = a group of chordates (subphylum).
- Vertebrate phylogeny: vertebrate classes and relations to each other
    - Fish: In the beginning, there was fish.

- Jawless (Agnatha): The very first fish were jawless, slimy, eel-like.
    - Cartilaginous (Condrichthyes/sharks/rays): Then some developed jaws and a skeleton. Condrichthyes has a skeleton made of cartilage.
    - Bony (Osteichthyes/food fish): Osteichthyes has a skeleton made of bone.
        - Amphibians: the Bony Fish came onto land because their bony skeleton is strong enough to support their weight.
        - Reptiles: Can penetrate further onto land because they don't dry out like amphibians do. Similar to amphibians, the reptiles lay eggs.
            - Mammals: First to branch off from the reptiles. Unlike the reptiles, mammals have milk glands, hair, and different tooth morphology (heterodontic).
            - Birds: next to branch off from the reptiles. Like the reptiles, birds lay eggs. (which came first, the chicken or the egg? Ans: the egg, because the chicken is a bird, and reptiles laid eggs before birds even existed.)