BIOLOGY

THE CELL

Cell Theory

Cell Theory

- All living things are composed of cells
- The cell is the basic functional unit of life
- Cells arise only from pre-existing cells
- Cells carry genetic information as DNA. DNA is passed from parent cells to daughter cells

Tools and Methods

Microscopy

- **Magnification –** Visual increase in apparent size of an object.
- **Resolution –** The ability to differentiate two closely placed objects.
- **Compound Light Microscope –** Most often used microscope, commonly for non living or dead specimens. Specimens are sliced into thin pieces, prepared using various chemicals, and coverslipped.
  - **Diaphragm –** Controls the amount of light passing through the specimen, which is important for image contrast.
  - **Coarse Adjustment Knob –** Roughly focuses the image by moving the stage.
  - **Fine Adjustment Knob –** Finely focuses the image by moving the stage.
- **Phase Contrast Microscope** – Less often used microscope, allows for the viewing of living organisms based on differences in refractive indices of different subcellular structures.
- **Electron Microscope –** The most powerful microscope, commonly for non living or dead specimens. Allows imaging to the atomic level, but requires impregnation with heavy metals to allow for appropriate contrast.

Autoradiography – An essential compound necessary for cellular function is replaced by a manufactured version of the compound containing radioactive elements. The cells are allowed to carry out biological functions and the radioactive elements are imaged to track the functions of interest.

Centrifugation – A sample is spun at high speeds. Various contents settle at different rates and into separate layers depending on particulate shape and density, measured as the sedimentation coefficient/rate. The apparent centrifugal force has more of an effect on particulate with higher mass/density.

Prokaryotes versus Eukaryotes

Prokaryotes – Unicellular organisms. Includes mostly bacteria.

- **Genome –** Contains a single circular strand of DNA in a region called the

nucleoid. Also contains smaller circular strands of DNA, called Plasmids, which may provide traits such as antibiotic resistance. Plasmids replicate independently of the nuclear genome and copies of plasmids can be transferred from one bacteria to another.

- **Structure** – All bacteria have a cell membrane and cytoplasm but do not contain membrane bound organelles.
- **Shape –** Spherical shaped bacteria are called Cocci, rod shaped are called Bacilli.
- **Motility –** Some bacteria have flagella for movement.

Eukaryotes – Unicellular or multicellular organisms. Includes animals, plants, fungi, and protists.

- **Genome –** Contains linear DNA known as chromosomes, found in the nucleus.
- **Structure –** All eukaryotes have a cell membrane enclosing cytosol, in which organelles are suspended. Cell wall present in plants, fungi, and some protists.
- **Motility –** Some eukaryotes have flagella for movement.

<u>Eukaryotic Organelles</u>

Cell Membrane – Phospholipid bilayer impregnated with proteins, lipid rafts, and other molecules that control movement of solutes in and out of the cell. Such molecules move freely throughout the membrane. Nonpolar, or sufficiently small or uncharged, particles readily pass through the membrane. For instance, nonpolar steroid hormones pass through the membrane to bind to receptors within the cell while polar/partially polar protein molecules must bind to receptors within the membrane, who then transfer the message to second messengers such as cAMP.

- **Transport Proteins –** Gates, channels, or pumps that allow or force specific molecules into or out of the cell.
- **Cholesterol –** Molecule that helps with membrane fluidity as well as the production of all steroid hormones.
- **Cell Adhesion Molecules (CAMs) –** Proteins that allow cells to recognize each other and contribute to proper differentiation and development.

Cell Wall – A wall that surrounds plant, fungi, and and protist cells and serves as defense and structural support. Plant cell walls are composed of cellulose, fungi have walls made of chitin, and protist cell walls are usually made of calcium carbonate.

Nucleus – The cells genetic material is within the nucleus. A double membrane encloses the nucleus to maintain the nucleic environment separate from the cytoplasm, however the membrane does have nuclear pores for transport of molecules across the membrane.

- **DNA –** Consists of coding regions known as genes. Linear DNA is wrapped around organizing proteins known as histones and further wound into linear strands called chromosomes/chromatids.
- **rRNA –** Ribosomal RNA is synthesized within the nucleolus, a subsection within the nucleus.

Ribosomes – Responsible for protein synthesis. Free ribosomes produce proteins for use

within the cell and ribosomes attached to the endoplasmic reticulum synthesize proteins for export.

Endoplasmic Reticulum – A network (reticulum) of interconnected organelles. Smooth ER is ribosome free and serves lipid synthesis and detoxification functions. Rough ER includes ribosomes and serves in protein production for export. The ER, smooth or rough, also acts as part of the export system of the cell.

Golgi Apparatus – A network of membrane bound sacs that function in repackaging and sorting in the shipping process. It receives materials from the ER, repackages them, then sends them towards the cell surface for exocytosis, usually via secretory vesicles.

Vesicles and Vacuoles – Vesicles are membrane bound bubbles that pinch off of other membranes and are used to transport or store materials that are ingested, secreted, processed, or digested by the cell. Vacuoles are larger and more likely to be found in plant cells.

Lysosomes – Specialized vesicles that use hydrolytic acidic enzymes to chemically break down materials ingested by the cell. Lysosomes do not directly ingest the material from outside, it is brought to them by endosomes, transport vesicles. Lysosomes generally keep their hydrolytic enzymes separate from the rest of the cell to prevent undesired damage. However, if necessary lysosomes can break down damaged cellular components that need to be replaced or cause death of the cell as a whole through autolysis. The damage of key organelles or their components, such as the DNA of the nucleus, may lead to apoptosis and autolysis.

Mitochondria – Powerhouse of the animal cell. Composed of an outer membrane that lets in nutrients necessary for respiration as well as an inner membrane that contains the molecules and enzymes necessary for the electron transport chain. The inner contains numerous folds known as cristae, which increase the surface area for reactions. Between the two membranes is the intermembrane space. Within the inner membrane is the matrix, which contains many other enzymes important to cellular respiration. Mitochondria are semiautonomous, they contain their own DNA and replicate independently of the nucleus via binary fission.

Chloroplasts – Powerhouse of plants and algae. They are plastids which contain pigments such as chlorophyll to absorb light energy and convert it to chemical energy using water, carbon dioxide, and sunlight. Like mitochondria, they contain their own DNA and may have evolved via symbiosis.

Microbodies – Specialized organelles that catalyze specific reactions by use of the proper enzymes and substrates.

- **Peroxisomes –** Peroxisomes are responsible for the creation of hydrogen peroxide and are used to break fats down into usable molecules as well as to catalyze detoxification reactions in the liver.
- **Glyoxysomes –** Glyoxysomes serve a role in germinating plants. They break lipids into carbohydrates usable for energy until the plant can sustain itself by photosynthesis.

Centriole – A cylindrical structure made of bundles of microtubules. They serve in the formation and organizing of the spindle apparatus on which chromosomes move during mitosis. Animals contain a pair of centrioles, oriented at 90 degrees to each other. Most plants and fungi do not have centrioles.

Cytoskeleton – Acts as the highway system of the cell and provides structural strength. Composed of microfilaments, microtubules, and intermediate filaments.

- **Microfilaments –** Solid polymerized rods of actin protein, they are the smallest roads for transport. They interact with myosin in muscle cells for contraction and are involved in intracellular transport of materials as well as ameboid movement.
- **Microtubules –** Hollow polymerized rods of tubulin protein, they are the largest roads for transport as well as structural support. They are involved in chromosomal separation during cell division. They are also the structural basis for cilia and flagella, which are structures involved in a variety of processes, from the trapping of foreign matter to the motility of some cells.
- **Intermediate Filaments –** A collection of fibers that help maintain the overall integrity of the cytoskeleton.

<u>Movement Across the Cell Membrane</u>

Simple Diffusion – Most basic type of diffusion, requires no energy input. Substrates move down their chemical gradient. The simple diffusion of water is called osmosis, which is when water moves from an area of high water concentration to an area of low water concentration, or an area of low solute concentration to high solute concentration. Areas of high solute concentration are hypertonic to areas of low solute concentration, which are hypotonic. If both areas have identical concentrations, they are isotonic. Isotonicity does not prevent movement, only net movement.

Facilitated Diffusion (Passive Transport) – Simple diffusion for molecules that need a little extra help, does not require energy. Substrates still move down their chemical gradient. Integrated membrane proteins serve as channels or gates for the diffusion of substrates.

Active Transport – The movement of substrates against their concentration gradient, always requires energy. Integrated membrane protein pumps push substrates in or out against their gradients. This is useful for purposely creating higher gradients, such as charge gradients to achieve action potentials.

Endocytosis and Exocytosis – Allow the cell to compartmentalize certain functions, creating specific environments favorable to certain reactions, such as digestion.

- **Endocytosis –** The cellular membrane invaginates and engulfs material into the cell. The invagination pinches off and becomes a vesicle, transporting or storing the engulfed material. Endocytosis of fluids and dissolved particles is pinocytosis. Endocytosis of large solids, such as bacteria, is phagocytosis.
- **Exocytosis –** The reverse of endocytosis. A vesicle containing a material bonds with the cellular wall, releasing the material into the environment.

Tissues

Epithelial Tissue – Line any surface of the body or any body cavity. Function in protection, absorption, secretion, and sensation.

Connective Tissue – Supports the body and provides a framework for higher level interactions. Bone, cartilage, tendons, ligaments, adipose tissue, and blood are all connective tissues.

Nervous Tissue – Neurons are the primary nerve cell. They use electrochemical gradients and action potentials for cellular signaling and the coordinated control of multiple tissues, organs, and organ systems.

Muscle Tissue – There are three types of muscle tissue: skeletal, smooth, and cardiac. They all exhibit contractile ability and strength.

Viruses

Virus – An acellular structure comprised of genomic material (circular/linear, single strand/double strand, RNA/DNA) and a protein coat called a capsid. Since they cannot reproduce independently, they are known as obligate intracellular parasites.They must express and replicate their genetic information by hijacking a cell's machinery because they do not have the necessary machinery to do it themselves. The new copies of a virus reproduced in this process are called virions. Bacteriophages specifically target bacteria by attaching to the bacterial membrane, releasing the genetic material from the protein coat and injecting it into the cell.

ENZYMES

Thermodynamics and Kinetics

Endothermic – A reaction with net energy absorption.

Exothermic – A reaction with net energy release.

Enzymes – Proteins that catalyze a reaction by lowering the necessary activation energy, similar to traveling through a tunnel in a hill rather than climbing over the hill—catalysts allow use of this tunnel. Enzymes are unchanged by the reaction, so less enzymes are needed than substrate. Catalyzed reactions reach equilibrium quicker, but the equilibrium state is unchanged. That is, the difference between initial energy and final energy is the same in both catalyzed and uncatalyzed reactions, those in catalyzed reactions just get there first.

- **Key Features of Enzymes**
  1. Lower reaction activation energy
  2. Increase reaction rate
  3. Do not alter equilibrium constant
  4. Are not changed or consumed by a reaction

5. Are pH and temperature sensitive, each with optimal function at a specific pH and temperature
6. Do not affect overall change in free energy of a reaction
7. Are specific for a particular reaction or class of reactions

- **NOTE:** Most enzymes end in the suffix -ase

Enzyme Specificity

Enzyme Specificity – Each enzyme catalyzes only a single reaction or class of reactions.

Substrate – The molecule/molecules upon which an enzyme acts.

Enzyme-Substrate Complex – The complex between the enzyme and substrate.

Active Site – Location within the enzyme where the substrate is held during the chemical reaction.

Lock and Key Theory – The less accepted theory that the enzyme's active site (lock) is already in the appropriate conformation for the substrate (key) to bind. Thus, no alteration of the tertiary or quaternary structure is necessary upon binding.

Induced Fit Theory – The more accepted theory that the enzyme's active site is not already conformed to fit the substrate and that upon interaction, both the substrate and the enzyme find that a change in conformation is more comfortable for both of them. Thus, the shape of the active site is only truly complementary upon binding to the substrate.

Cofactors

Cofactors – Nonprotein molecules required by most enzymes to be effective, since amino acids and proteins cannot directly undergo the redox reactions or group transfers necessary for some reactions. Bound to enzymes in a variety of ways ranging from weak to strong covalent bonds.

- **Small Metallic Ions –** Small metallic ions that act as cofactors, such as iron serving as the oxygen binding site for hemoglobin.
- **Coenzymes –** Small organic molecules that act as cofactors, usually vitamins.
  - **Soluble Vitamins –** Readily dissolve in water. Excess is urinated out, making overdose difficult. Includes B and C vitamins.
  - **Insoluble Vitamins –** Readily dissolve in fats. Stored in the liver or adipose tissue. Includes A, D, E, and K vitamins.

Apoenzymes – Enzymes without their cofactors.

Holoenzymes – Enzymes with their cofactors.

Prosthetic Groups – Cofactors tightly bound to their enzymes.

Enzyme Kinetics

Effects of Concentrations – As concentrations of substrate increases, the reaction rate increases, up to the point of saturation, at which an increase in concentration will no longer increase the rate. This point is the maximum velocity, or V_{max}, of a

reaction.

- **Michaelis-Menten Equation –** States that when $K=V_{max}$, $K_m=S$, where K is reaction rate and S is substrate. That is to say that up until the point that half of all enzyme active sites are full, an increase in substrate concentration will greatly affect the reaction rate. After all enzyme active sites are half full, increases in substrate levels have less of an impact and the reaction rate asymptotically approaches V_{max} as substrate levels are further increased.

Effects of Temperature – Enzyme catalyzed reaction rates double in velocity for every 10 degrees celsius increase, until the ideal 37 degree body temperature is reached, after which point enzyme activity falls off sharply as enzymes are denatured or otherwise made less effective.

Effects of pH – Most human enzymes work best around a pH of 7.4, below which is acidosis and above which is alkalosis, although there are some exceptions, such as enzymes in the acidic environment of the stomach or others in the basic environment of the small intestine.

<u>Regulation of Enzymatic Activity</u>

Allosteric Regulation – Regulation by use of an enzymes allosteric sites.

- **Allosteric Sites –** Allosteric enzymes have multiple binding sites. The active site as well as at least one allosteric site, which can regulate the availability of the active site.
- **Allosteric Enzymes –** Alternate between an active and inactive form depending on allosteric site binding, where the inactive form is available to be activated by a substrate and carry out a reaction.
- **Allosteric Activators –** Binding of an activator molecule will result in a conformational change that makes the active site more available to substrate.
- **Allosteric Inhibitors –** Binding of an inhibitor molecule will result in a conformational change that makes the active site less available to substrate.

Inhibition Regulation – Regulation by a the products of an enzymatic reaction or by other molecules that can bind to an enzyme.

- **Feedback Inhibition –** Products of an enzymatic reaction pathway may bind to enzymes earlier in the pathway, effectively preventing more substrate from binding to that enzyme's active site and reducing the reaction rate. This process is constantly ongoing. Once high amounts of product have been produced, then high amounts of feedback inhibition occurs, drastically slowing or even stopping further reactions until the current products are used up and the active sites are once again free to react. This process prevents overproduction of end products.
- **Reversible Inhibition**
    - **Competitive Inhibition –** An inhibitor binds to the active site to block substrates from binding. However, if the amount of substrate is higher than the amount of inhibitor, the enzyme is more likely to bind to the substrate, assuming equal affinity for both.

    - **Noncompetitive Inhibition –** An inhibitor binds to an allosteric site, inducing a change in conformation. Since the inhibitor and substrate are not both competing for the same binding site, this inhibition is noncompetitive and cannot be overcome by higher substrate concentrations.
    - **Uncompetitive Inhibition –** An inhibitor binds directly to the enzyme-substrate complex and so is uncompetitive with the substrate since it actually requires binding of the substrate to the enzyme before it can bind.
- **Irreversible Inhibition –** The enzyme active site is made permanently unavailable or the enzyme is otherwise permanently altered to prevent further reactions. For instance, aspirin irreversibly blocks COX active sites, permanently preventing the reactions which produce prostaglandins. More COX enzymes must be produced before more prostaglandin can be produced.

Inactive Enzymes

Zymogens – Some enzymes would be potentially harmful or otherwise problematic if they were not strictly controlled. Such enzymes are produced in the inactive form as zymogens and have a regulatory domain which must be removed or otherwise altered before binding can occur. Zymogens end in the -ogen suffix. Such as fibrinogen for fibrin, the clotting protein.

CELLULAR METABOLISM

Transfer of Energy

Autotrophs – Organisms that can convert light energy (usually from the sun) into organic molecules which can later be burned for chemical energy.

- **Photosynthesis –** Anabolic process by which plants, algae, and fungi absorb light energy and convert it into chemical energy.

Heterotrophs – Organisms that cannot absorb and convert light energy into usable energy. They must consume organic molecules formed by autotrophs, then break these organic molecules down to harvest chemical energy.

Energy Carriers – Serve as high energy electron transporters between the cytoplasm and the mitochondria.

Adenosine Triphosphate (ATP) – Primary source of immediate energy use within the cell. Rapid formation and/or degradation make ATP a very useful molecule. ATP is generated during glucose catabolism. Composed of the nitrogenous base adenine, a ribose sugar, and three phosphate groups. The energy comes from the phosphate bonds between phosphate groups. Breaking bonds will result in ADP or AMP and each bond break results in 7kcal/mol of energy. Glucose catabolism provides sufficient energy to reverse this reaction and rebind the phosphate groups, reforming ATP.

Electron Transport Chain – Some coenzymes are capable of accepting high energy

electrons during glucose oxidation in the form of H^-. Such coenzymes include NAD^+ and FAD, which become NADH and $FADH_2$ once reduced.

1. Coenzyme is reduced, resulting in NADH
2. Coenzyme transports hydrogen to the membrane site of transport chain
3. NADH transfers 2 electrons and 1 proton (H^+) to the initial intermembrane transport protein. NADH becomes NAD^+.and exits the cycle, ready to accept more hydrogen and begin again.
4. Protons are pushed to the outside of the membrane while electrons are transported through a series of transport proteins within the membrane. This creates a proton gradient with higher concentrations outside of the membrane.
5. Terminal protein transfers electrons to awaiting oxygen and protons (H^+)to form water, which then exits the cycle.
6. The ATP synthase enzyme, located within the membrane, allows protons to reenter the cell, utilizing the proton gradient and flow of protons like a watermill. This flow of protons produces enough energy for ATP synthase to phosphorylate ADP to produce ATP. The protons may then join with awaiting oxygen and electrons to form water, which then exits the cycle.

<u>Glucose Catabolism</u>

Glycolysis – Anaerobic series of reactions that can be carried out by all organisms, outside of the mitochondria in eukaryotes, that results in pyruvate and energy used to form ATP from ADP and NADH from NAD^+. Pyruvate proceeds to Krebs Cycle, NADH proceeds to ETC.

Glucose + 2 ADP+ 2 P_i + 2NAD^+→ 2 Pyruvate +2 ATP +2 NADH +2 H^++2 H_2O

- *INPUTS: 1 Glucose*
- *OUTPUTS: 2 Pyruvate, 2 ATP, 2 NADH, 2 H_2O*

- **Glucose –** 6 carbon saccharide
- **Dihydroxyacetone Phosphate**
- **Glyceraldehyde 3-Phosphate (PGAL)**
- **Pyruvate –** 3 carbon pyruvic acid molecule
- **Substrate-Level Phosphorylation –** The direct generation of ATP from ADP and $P_{inorganic}$.

Fermentation – The anaerobic reduction of pyruvic acid in the cytoplasm into either ethanol or lactic acid coupled with the oxidation of NADH back into NAD^+. Must be reformed for glycolysis to continue. When oxygen supply is insufficient, fermentation is the only way. Occurs in anaerobic organisms or in aerobic organisms when oxygen is in short supply.

- **Alcohol Fermentation –** Occurs in yeast and some bacteria.
  1. Pyruvate (3C) → Acetaldehyde (2C) + CO_2
  2. Acetaldehyde (2C) + NADH + H^+ → Ethanol (2C) + NAD^+
  - *INPUTS: 1 Pyruvate*

- *OUTPUTS:1 Ethanol, 1 NAD^+, 1 CO_2*

- **Lactic Acid Fermentation –** Occurs in some fungi and bacteria and in mammals when oxygen needs exceed supply.
  1. Pyruvate (3C) + NADH + H^+ → Lactic Acid + NAD^+
  - *Inputs: 1 Pyruvate*
  - *Outputs: 1 Lactic Acid, 1 NAD^+*
  - **Cori Cycle –** Once sufficient oxygen is present, lactic acid may be converted back into pyruvate through the Cori Cycle, for use in cellular respiration.
  - **Oxygen Debt –** The amount of oxygen required to convert lactic acid back into pyruvate in the Cori Cycle.

Cellular Respiration – Aerobic process that employs an electron transport chain, with oxygen being the final electron receptor.

$C_6H_{12}O_6 + 6O_2 \rightarrow 6CO_2 + 6H_2O + 36\text{-}38ATP$

1. **Pyruvate Decarboxylation –** Pyruvate (3C) from glycolysis enters the mitochondrial matrix and is decarboxylated—a CO_2 molecule is removed. The remaining 2C molecule is bound ot coenzyme A and converted to acetyl-CoA. One NAD^+ is reduced to NADH per pyruvate, or 2 per glucose.
   - *2 Pyruvate (3C) +2 CoA +2 NAD^+ → 2 Acetyl CoA (2C) + 2 CO_2 + 2NADH*
   - *INPUTS: 2 pyruvate (3C), 2 Coenzyme A, 2 NAD^+*
   - *OUTPUTS: 2 Acetyl CoA, 2 CO_2, 2 NADH*
2. **Citric Acid Cycle/Krebs Cycle/Tricarboxylic Acid Cycle –** Cycle within the mitochondrial matrix that produces a small amount of net energy as well as coenzyme electron carriers for the ETC. Requires water input. Produces CO_2 output, which we exhale. Produces 2 ATP per glucose directly, as well as the coenzyme electron carriers necessary to produce 22 more via the ETC.
   - *INPUTS: 2 Acetyl CoA, 6 NAD^+, 2FAD, 2GDP, 2P_i, 4H_2O*
   - *OUTPUTS: 4CO_2, 6 NADH, 2 FADH, 2 ATP, 4 H^+, 2Coenzyme A*
3. **Electron Transport Chain –** ATP producing process that occurs across the inner mitochondrial membrane. Some coenzymes are capable of accepting high energy electrons during glucose oxidation in the form of H^-. Such coenzymes include NAD^+ and FAD, which become NADH and $FADH_2$ once reduced.
   - Each NADH molecule generates 3 ATP, each $FADH_2$ molecule generates 2 ATP. This is because the electrons from NADH travel a greater distance through the ETC and so more energy may be harvested in that time.
   1. Coenzymes are reduced, resulting in NADH and $FADH_2$
   2. NADH transports hydrogen to Complex I, $FADH_2$ directly to Complex II
   3. NADH transfers 2 electrons and 1 proton (H^+) to the initial intermembrane transport protein. NADH becomes NAD^+.and exits the cycle, ready to accept more hydrogen and begin again. $FADH_2$ performs a similar task, beginning at Complex II.
   4. Carrier Q transfers electrons from Complex I directly to Complex III and from

Complex II to Complex III. Electrons do not transfer from Complex I to Complex II.

5. Protons are pushed to the outside of the membrane at each major protein complex while electrons are transported through a series of transport proteins within the membrane. This creates a proton gradient with higher concentrations in the intermembrane space. This is called the *proton motive force*.
6. Complex III transfers electrons to Complex IV.
7. Complex IV donates electrons to awaiting oxygen and protons (H^+) to form water, which then exits the cycle.
8. The ATP synthase enzyme, located within the membrane, allows protons to reenter the cell, utilizing the proton gradient and flow of protons like a watermill. This flow of protons produces enough energy for ATP synthase to phosphorylate ADP to produce ATP in a process called *oxidative phosphorylation*. The protons may then join with awaiting oxygen and electrons to form water, which then exits the cycle.

- **Cyanide –** A toxin which blocks the final transfer of electrons to O_2
- **Dinitrophenol –** A toxin which blocks the ability of the mitochondria to form a proton gradient

Review of Glucose Catabolism – ATP produced Total: 36. Note, in prokaryotes, the 2 NADH from glycolysis don't have a mitochondrial membrane to traverse, so they can get in earlier in the cycle, each producing 1 extra ATP. Thus, prokaryotes are capable of producing 38 ATP per glucose.

- **Substrate-Level Phosphorylation –** Degradation of one molecule of glucose produces a net of 4 ATP. 2 from Glycolysis and 2 from 2 turns of Krebs Cycle.
  - ATP from SLP: 4 Total
- **Oxidative Phosphorylation –** ETC ATP production from NADH is 4 from Glycolysis (these NADH cannot traverse the membrane and donate directly to Carrier Q, so they produce only 2 ATP each), 6 from pyruvate decarboxylation, and 18 from the Krebs Cycle. There are 2 $FADH_2$ molecules, which each generates 2 ATP for a total of 4.
  - ATP from NADH: 28 Total
  - ATP from $FADH_2$: 4 Total

Alternative Energy Sources

- **Carbohydrates –** Carbohydrates can be broken down in the liver and then stored as glycogen, for later use. Glycogen will be converted to glucose-6-phosphate when needed.
- **Lipids –** Lipids are stored in adipose tissue as triglycerides. Three long-chain fatty acids are attached to a glycerol (3C) molecule for long term storage. When needed, these triglycerides are transported to the mitochondrial matrix to undergo *beta-oxidation*. Each round of beta-oxidation results in one NADH and one

$FADH_2$. Triglycerides have 3 fatty acids (16C each) bound to glycerol, or 48C total. Beta oxidation removes 2 at a time, so the cycle may be performed 24 times, resulting in 24 NADH and 24 $FADH_2$. Thus, triglycerides are a very efficient method of energy storage.

- **Proteins –** Used as energy sources only when carbohydrates are insufficient. The removal of amine moiety by *transaminases* results in a-keto acids. These acids can usually be converted into acetyl CoA for the Krebs Cycle.

REPRODUCTION

Cell Division

Cell Division – Cell reproduction process. Most somatic cells undergo division, this allows for growth, healing, etc. Some cells never undergo division (muscle and nerve). *Cancerous cells* enter a state of unregulated cell division.

Apoptosis – Programmed cell death, which regulates cell division. Each somatic cell divides only 20-50 times before it can no longer divide without making errors, it then undergoes apoptosis and is not replaced.

Binary Fission – The process of division/reproduction for prokaryotes.

Haploid (n) – Germ cells, each containing 23 chromosomes.

Diploid (2n) – Autosomal cells, each containing 46 chromosomes.

Chromosome – May refer to a *chromatid* or pair of *sister chromatids*.

- **Chromatid –** One complete double stranded DNA molecule.
- **Sister Chromatids –** Two chromatids that are identical copies of each other.

Centrioles – Paired, cylindrical, microtubule bundles responsible for the organization and division of genetic material during division. Located in the *centrosome*.

Centromere – Center of a chromatid

Telomere – Region of genetic material at the end of the chromosome to protect it from deterioration or fusion with other chromosomes.

Kinetochore – Spindle apparatus attachment point on the chromatid, at centromere.

Aster – Point on mitotic fibers with which they attach to chromosomes during mitosis.

Autosome – Somatic chromosome

Allosome – Sex chromosome

The Cell Cycle

Interphase – The three stages leading up to and following mitosis. Interphase is the longest part of the cell cycle. Dividing cells spend 90% of their time in interphase. Cells that do not divide (muscle cells, nerve cells) are permanently in an offshoot of G1 called G0. Genetic material is in a less condensed and invisible form known as *chromatin* so that genetic information may be easily accessed for transcription and replication.

- **G1 (Presynthetic Gap) Stage –** Energy and protein producing organelles

(mitochondria, ribosomes, ER) are produced and the cell doubles in size. These criteria must be met before the Synthesis Stage, further progress is governed by a *restriction point*.

- **S (Synthesis) Stage –** Enough genetic material is synthesized for each daughter cell. After synthesis/replication, each chromosome consists of 2 identical *chromatids* bound together at the center by a centromere. Cells entering G2 have twice as many chromatids (92) as cells in G1 have chromosomes (46).
- **G2 (Postsynthetic Gap) Stage –** The quality control stage before cell division. The cell must have the proper amount of organelles and cytoplasm.

Mitosis – The actual process of cell division.

- **M (Mitosis) Stage**
  - **Prophase –** Chromosomes condense, *kinetochores* and *kinetochore fibers* appear at *centromeres*, nuclear membrane dissolves, centrosomes migrate to opposite ends and microtubule spindle fibers begin to form.
  - **Metaphase –** Centrosomes are at opposite ends, kinetochore fibers attach to spindle fibers and chromosomes align at *metaphase plate*.
  - **Anaphase –** Sister chromatids separate, unzipping from centromeres down to *telomeres* as they are pulled towards their respective centrosomes.
  - **Telophase –** Spindle apparatus disappears, new nuclear membranes form, chromosomes uncoil and retake interphase form.
- **Cytokinesis –** Splitting of the cytoplasm and organelles into 2 daughter cells, each with necessary amount of organelles and cytoplasm.

<u>Asexual Reproduction</u>

Asexual Reproduction – Reproduction of offspring from the genetic material of a single parent. Daughters are genetically identical to parent (except for random mutations that may arise).

- **Binary Fission –** Occurs in prokaryotes, usually bacteria, and some simple eukaryotic cells. Circular chromosome attaches to cell wall and replicates. Cell grows and invaginates along the midline, eventually pinching off to form two cells of equal size.
- **Budding –** Occurs in some eukaryotes, hydra and yeast. Equal replication followed by unequal cytokinesis. Each cell receives same amount of genetic material, but the daughter cell receives far less cytoplasm and so is far smaller than the parent cell. Budded cell may stay attached as it grows to full size or pinch off immediately.
- **Regeneration –** Occurs in lower organisms, such as lizards or worms. An entire body segment may be regenerated to full size and function from only a small functional piece of it. This process is hampered in humans, usually due to nervous damage (as nerves do not divide), but still occurs amongst liver tissue.
- **Parthenogenesis –** Occurs among many social insects, such as bees and ants,

although it has been artificially induced in rabbits. Adult organisms develop from unfertilized eggs, but will be haploid (n) in nature as they only received half of the potential genetic material.

Sexual Reproduction

Meiosis – Production of gametes (sex cells). One round of replication followed by two rounds of division. Each round of meiosis results in 4 haploid (n) daughter cells.

- **Meiosis I (Reductional Division)**
  - **Prophase I –** Chromosomes condense, the spindle apparatus forms, the nuclear envelope disappears. Homologous chromosomes, produced during meiotic interphase, intertwine in a process called *synapsis*. The point of synapsis is called the chiasma. Each chromosome of the homologous pair consists of its own pair of sister chromatids. Overall, this appears as four connected chromatids known as a *tetrad*.
    - **Homologous Chromosomes –** One from each parent. Each codes for the same gene.
    - **Crossing Over –** Homologous chromosomes may attach and break off at the chiasma, effectively swapping some genes and resulting in *recombinant chromosomes*. Swapping occurs between homologous chromosomes, resulting in the sister chromatids within each homolog now being different. Crossing over increases genetic diversity.
  - **Metaphase I –** Tetrads align at the equatorial plate and attach to spindle fibers by their kinetochores.
  - **Anaphase I –** Tetrads are pulled from each end and homologous pairs are separated in a process called *disjunction*. Each chromosome of paternal origin is now separated and from it's homologue and either chromosome from either parent can end up in either daughter cell. The sorting of chromosomes in this way is random and each daughter cell will thus acquire a unique pool of alleles from a random mix of paternal and maternal origin.
  - **Telophase I –** New nuclear membranes form, chromosomes still consist of sister chromatids attached at the centromere. The cell proceeds with division, resulting in 2 haploid (n) daughter cells, each with 23 sister chromatids.
- **Meiosis II (Equational Division)**
  - **Prophase II –** Centrioles migrate to opposite poles and spindle apparatus begins to form.
  - **Metaphase II –** Chromosomes align at the metaphase plate. Centromeres divide, separating the chromosomes into pairs of sister chromatids.
  - **Anaphase II –** Sister chromatids are split and pulled to opposite poles by spindle fibers.
  - **Telophase II –** A nuclear membrane forms around each haploid (n) nucleus. Cytokinesis follows and 2 daughter cells are formed.

Gonads – Structure which produces sex cells, sperm or ovum.

- **Sperm –** Haploid (n) male sex cell.
- **Ovum –** Haploid (n) female sex cell.

Fertilization – Sperm and ovum fuse to form a diploid (2n) *zygote* in the *fallopian tubes*.

Male Reproductive Anatomy

- **Testes –** Male gonads, composed of two functional components, the *seminiferous tubules* and the *interstitial cells*.
  - **Seminiferous Tubules –** Highly coiled tubules that are the site of meiosis, sperm cell production.
    - **Sertoli Cells –** Nurse cells located within the seminiferous tubules that provide nourishment to sperm cells.
  - **Interstitial Cells –** These cells secrete testosterone and other male sex hormones (androgens).
- **Scrotum –** External pouch containing the testes that maintains a temperature 2-4 degrees celsius lower than body temperature. This temperature differential is essential to proper sperm production.
- **Penis –** External organ that bears the distal end of the urethra and functions in semen and urine discharge.
- **Epididymis –** Mature sperm are passed to the epididymis where they form flagellum to gain motility and are then stored until ejaculation.
- **Ejaculation –** During ejaculation, sperm travel through the *ejaculatory duct* and then the *urethra*, exiting through the *penis*.
- **Semen –** A mixture of sperm cells and *seminal fluid*.
  - **Seminal Fluid –** A fluid produced through joint effort by the *seminal vesicles*, *prostate gland*, and *bulbourethral gland*.
    - **Seminal Vesicles –** Contribute fructose to nourish the sperm.
    - **Prostate Gland –** Contribute alkaline properties to the fluid, to aid in sperm survival within the relatively acidic female reproductive tract.
    - **Bulbourethral Gland –** Produces pre-ejaculate to lubricate the urethra for upcoming sperm as well as neutralize traces of acidic urine and flush out any remaining urine.

Spermatogenesis – Production of sperm within the seminiferous tubules. Produces four functional sperm for every one spermatogonium. Males have an unending supply of spermatogonia.

- **Spermatogonia –** Diploid stem cells which will lead to sperm formation.
  - **Primary Spermatocytes –** Diploid (2n) cells following stem cell differentiation. Primary spermatocytes undergo meiosis I.
  - **Secondary Spermatocytes –** Haploid (n) cells produced by meiosis I. Secondary spermatocytes undergo meiosis II.
  - **Spermatids –** Haploid (n) cells produced by meiosis II. Spermatids undergo

maturation to become *spermatozoa*.

- **Spermatozoa**
  - **Head –** *Acrosome* (cap), necessary to penetrate the ovum, containing genetic material.
  - **Midpiece –** Metabolic area to produce energy from fructose.
  - **Tail (flagellum) –** Allows for motility.

Female Reproductive Anatomy

- **Ovaries –** Female gonads, each composed of thousands of *follicles*. Produce estrogen and progesterone.
  - **Follicles –** Multilayered sacs that contain, nourish, and protect immature ova.
- **Menstruation –** Between menarche and menopause, once per month an egg is released into the peritoneal sac, which lines the abdominal cavity. It then moves through the *fallopian tube (oviduct)*, which is lined with cilia to move the egg along. The egg awaits fertilization in the fallopian tubes. The fallopian tubes exit into the *uterus*, the site of fetal development. The cervix is at the lower end of the uterus, which exits into the *vaginal canal*.
- **Vulva –** The external female anatomy, collectively.

Oogenesis – The production of female gametes. All oogonia a woman will ever have are formed during fetal development. Each primary oocyte results in only one functional ovum.

- **Primary Oocytes –** Diploid (2n) cells, predifferentiated at birth, unlike the gametic stem cells in males which differentiate later in life. Undergoes meiosis I, producing a secondary oocyte and a polar body by uneven cytokinesis.
  - **Polar Body –** Receives almost no cytoplasm and never produces functional gametes.
  - **Secondary Oocyte –** Haploid (n) cell following meiosis I. Secondary oocytes are arrested in metaphase II and do not complete meiosis II until fertilized, at which point it splits into an ovum and another polar body.
    - **Zona Pellucida and Corona Radiata –** Two cell layers surrounding the oocyte. Meiosis II proceeds once the sperm penetrates these layers.

Fertilization – Secondary oocytes are capable of being fertilized within 24 hours of ovulation. Sperm can survive for up to 2 days within the acidic environment of the female reproductive tract. The fusion of spermatozoa and oocytes usually occurs within the fallopian tube and results in a single diploid cell called a *zygote*.

- **Penetration –** Sperm cells release acrosomal enzymes to digest the *corona radiata* and then penetrate the *zona pellucida*. The first sperm to contact the oocyte cell membrane forms a tubelike *acrosomal apparatus*, which extends to and penetrates the membrane. Its nucleus (genetic material) then enters the ovum (no longer an oocyte).
- **Cortical Reaction –** Following penetration, calcium ions are released into the ovum cytoplasm, leading to the formation of the *fertilization membrane*. The

fertilization membrane is impenetrable to other sperm to prevent multiple fertilizations.

Multiple Births

- **Monozygotic (Identical) Twins –** A single fertilized egg (zygote) splits into two, each zygote containing the same DNA. Each new cell matures normally. If division is incomplete, conjoined twins may develop. Identical twins are genetically identical.
- **Dizygotic (Fraternal) Twins –** Two eggs are accidentally released in one cycle and each is fertilized. Each zygote implants in the uterine wall independently and develop separate placenta, chorion, and amnion. Fraternal twins are no more genetically identical than any other pair of siblings.

EMBRYOLOGY

Early Developmental Stages

Cleavage – Process of rapid mitotic cell division following fertilization. The first cleavage ends the unicellular stage of existence, turning the zygote into an *embryo*. Throughout the cleavage process, the embryo does not grow in overall size, only in number of cells. Therefore each daughter cell is half the size of the parent cell. The time between divisions is not sufficient for cell growth and there is not room in the pellucid zone to expand anyway. Because of this, the cleavage process results in an increase in nucleus to cytoplasm ratio per cell as well as surface area to volume ratio per cell, increasing nutrient/gas diffusion rates.

- **Indeterminate Cleavage –** The first 4 cleavage events, up to 16 cells, resulting in cells that may still develop into full organisms. If one such cell separates from the rest, it may develop into an identical twin.
  - **Stem Cell –** Primordial cells with the pluripotent ability to form any cell type, or an entire organism.
- **Determinate Cleavage –** Cleavage events following the first 4, more than 16 cells, resulting in cells whose fates are "determined", whom may only develop as a part of a larger organism, and whom are now committed to differentiation.
  - **Morula –** A solid mass of about 32 or more cells, resembling a mulberry. The morula is still the original size of the zygote. At this point, the embryo is still being moved through the fallopian tube and towards the uterus.
  - **Blastula (Blastocyst) –** A hollow mass of cells following further development of the morula in a process called *blastulation*. The inner cavity is known as the *blastocoel*. There is an outer cell mass wall and an inner cell mass attached to one portion of the wall. At this point, the embryo is prepared for implantation into the uterine wall.
    - **Outer Cell Mass (Trophoblast) –** Outer wall of the blastocyst. The trophoblast will develop into the *chorion* and the *placenta*.

- **Inner Cell Mass (Embryoblast) –** Mass attached to the inner surface of the trophoblast and protruding into the blastocoel. The inner cell mass will eventually develop into the organism itself.

Implantation – During blastulation, about 1 week post fertilization, the *endometrium* (mucosal membrane) of the uterine wall has been promoted by the steroid hormone *progesterone* to receive the embryo. The blastula secretes enzymes which also help with the implantation process. Implantation in the uterine wall will be a key step in the embryo connecting to maternal circulation for nutrient/gas exchange. As the embryo further develops, a *placenta* forms, an organ specifically tasked with nutrient/gas exchange across the endometrium.

Gastrulation – The generation of three distinct cell layers. A portion of the outer layer of cells begins to push into the blastocoel. Soon, the blastocoel is gone and the overall cell has taken a pacman sort of shape. The embryo is now known as a *gastrula*. The outer cell layer is known as the *ectoderm* and the "mouth of the pacman" is known as the *endoderm*. The cavity created by the endoderm is the *arhenteron*, which later develops into the gut. The opening of the archenteron is known as the *blastopore*. Eventually, the area between the ectoderm and endoderm will be distinguishable as the *mesoderm*.

- **Primary Germ Layers**
  - **Ectoderm (Outer Layer)–** Skin, neurons, pituitary gland, eyes, ears
  - **Mesoderm (Middle Layer) –** Muscles, vessels, kidney tubules
  - **Endoderm (Inner Layer) –** Pancreas, liver, thyroid, lung, bladder, urethra
- **Deuterostomes –** Higher level organisms, such as humans, in which the blastopore develops into the anus.
- **Protostomes –** Lower level organisms, in which the blastopore develops into the mouth.

Neurulation – Development of the nervous system. The nervous system is derived from the ectoderm. Nervous cells are *induced* by *inducer chemicals* to migrate inwards, innervating the inner organism.

- **Notochord –** A rod of mesodermal cells that forms along the axis of the organism. The notochord induces ectodermal cells to slide inward and form *neural folds*, which surround a *neural groove*.
- **Neural Folds –** Two folds of ectodermal cells with a neural groove in between, like two mountains around a valley. The two folds migrate towards each other, eventually combining and turning the neural groove into a *neural tube*. Near the tip of each neural fold is a *neural crest cell*.
- **Neural Tube –** Tube of ectodermal cells which will develop into the central nervous system.
- **Neural Crest Cells –** Ectodermal cells which will migrate outwards to develop into the peripheral nervous system, including ganglia, the adrenal medulla, and Schwann cells.

Fetal Respiration

Placenta – Organ primarily formed from an extra-embryonic membrane called the *chorion*, which itself develops from trophoblast cells. Primary organ for nutrient/gas exchange across the endometrium. The placenta allows for just enough proximity of the maternal/fetal blood to allow gas/nutrient exchange through diffusion without actually allowing the different blood to mix. The placenta also functions in immunity for the fetus, since there is no functional fetal immune system. Bacteria and and many foreign particles are too large to diffuse across the placenta, however viruses and toxins such as alcohol and other drugs may readily diffuse across the membrane.

Umbillical Cord – Provides attachment to the chorion to allow fetal nutrient/gas exchange.

Embryonic Membranes

- **Allantois –** Thin, tough embryonic membrane filled with amniotic fluid that serves as a shock absorber during pregnancy and labor.
- **Amnion –** Embryonic membrane surrounding the allantois.
- **Yolk Sac –** Embryonic membrane surrounding the amnion. Site of early blood vessel development.
- **Chorion –** Outermost embryonic membrane, adding yet another layer of protection. *Chorionic villi* eventually grow into the placenta to support gas exchange.

Nutrient Flow – Nutrients/gases flow down their concentration gradient. For this to happen, a system must be in place to ensure that the concentration gradient moves fresh nutrients/gas towards the placenta and waste products out of the placenta.

- **Fetal Hemoglobin (Hb-F) –** The fetal oxygen transport protein exhibits a higher affinity for oxygen than does maternal protein. This is a vital part of the fetal/maternal gas gradient.

Fetal Circulation

Fetal Lungs – In adult circulation, blood is oxygenated by the lungs. The fetal lungs are not yet functional and anyway are surrounded by amniotic fluid, so oxygen is provided via diffusion across the placenta.

Fetal Heart – In the fetus, blood is routed away from the lungs via two shunts.

- **Foramen Ovale –** A shunt located between the right atrium and left atrium to bypass the right ventricle and thus pulmonary circulation. This shunt is sealed after birth for proper adult heart function.
- **Ductus Arteriosus –** While the foramen ovale is meant to bypass the right ventricle, the valve between the right atrium and ventricle is still functional, so some blood does make it into the right ventricle still. At this point, there is the ductus arteriosus shunt which connects the pulmonary artery to the aorta.

Fetal Liver – The fetal liver is underdeveloped and not able to fully function. However,

it will still try to function, using up any of the valuable blood that flows past it. Because of this, the *ductus venosus* reroutes oxygenated blood past the liver and to the inferior vena cava, The liver has its own predesignated blood supply directly from the heart

Gestation

Gestation – Human pregnancy lasts around 266 days total. Generally, the larger the animal the longer the gestation period and the fewer the offspring.

- **First Trimester –** Major organs begin to develop and some begin to function. By the end of the second month, most organs have formed and the embryo is now referred to as a fetus. At the end of the third month, the fetus is about 9cm long.
- **Second Trimester –** The fetus undergoes a tremendous amount of growth, it begins to move, and its appearance is more human. By the end of the sixth month, the fetus is 30-36cm long.
- **Third Trimester –** During the seventh and eighth months there is continued rapid growth and brain development. During the final month, antibodies are transported from the mother to the fetus for protection once outside the womb. Towards the end of the third trimester the growth rate slows and the fetus becomes less active as it has less room to move around.

Birth

Vaginal Childbirth – Accomplished by rhythmic contractions of uterine smooth muscle, coordinated by prostaglandins and peptide hormone oxytocin.

1. The cervix thins out and the amniotic sac ruptures (water breaking).
2. Strong uterine contractions result in birth of the fetus.
3. The placenta and umbilical cord are expelled (afterbirth).

THE MUSCULOSKELETAL SYSTEM

Skeletal System

Skeletal System

- **Exoskeletons –** A skeletal system which encases the entire organism, common amongst arthropods. Exoskeletons provide maximum protection to the organism, but must be shed regularly for growth.
- **Endoskeletons –** A skeletal system within the body. Less protective than an exoskeleton, but does not need to be shed for growth.

Human Skeletal System – Endoskeletal system derived from the endoderm.

- **Axial Skeleton –** Consists of the skull, rib cage, and vertebral column, providing a central framework for the body.
- **Appendicular Skeleton –** Consists of the arms, legs, and pelvic and pectoral

girdles, attached to the axial skeleton for stability.

Cartilage

Cartilage – Connective tissue that is softer and more flexible than bone, relatively avascular, and not innervated. Consists of *chondrin* matrix. Much of the fetal skeleton is composed of cartilage. Cartilage is more useful than bone in locations where flexibility, shock absorption, or reduced sheer is necessary.

- **Chondrin –** A firm, but elastic, matrix secreted by chondrocytes.

Bone

Macroscopic Bone Structure

- **Compact Bone –** Compact and strong portion of bone that provides strength.
- **Cancellous (Spongy) Bone –** Honey comb portion of bone consisting of bony points known as *trabeculae*. These cavities are filled with bone marrow.
  - **Red Bone Marrow –** Liquid tissue filled with hematopoetic stem cells, actively involved in the generation of all types of blood cells.
  - **Yellow Bone Marrow –** Liquid tissue composed primarily of fat and relatively inactive.
- **Long Bones –** Typically of the appendicular skeleton, comprised of cylindrical shafts called *diaphyses* and dilated ends called *epiphyses*.
  - **Diaphysis –** Shaft of a long bone with a compact bone outer shell and a hollow canal within to contain marrow.
  - **Epiphysis –** End of a long bone with a compact bone outer shell and spongy bone interior for increased shock dispersion.
  - **Epiphyseal Plate (Growth Plate) –** Cartilaginous structure dividing the diaphysis and epiphysis that is the site of longitudinal growth. The growth plate is sealed over time by the effects of estrogen or testosterone (released beginning in puberty). It takes until about the age of 25 to completely seal.
- **Periosteum –** Fibrous connective tissue sheath covering the entire long bone and serving as insertion for tendons and ligaments.

Microscopic Bone Structure

- **Bone Matrix –** The matrix which provides the strength in compact bone.
  - **Organic Components –** Collagen fibers, glycoproteins, and other peptides.
  - **Inorganic Components –** Calcium, phosphate, and hydroxide ions harden together to form hydroxyapatite crystals. Minerals such as sodium, magnesium, and potassium are also stored in bone.
- **Haversian Systems (Osteons) –** Structural units of the bone matrix. Each Haversian system consists of a central microscopic channel called the *Haversian canal*, encircled by concentric circles of bony matrix called *lamellae*. Between each lamellae ring are *lacunae*.
  - **Haversian Canal –** Central canal of the Haversian system, providing blood vessels, nerve fibers, and lymph flow to the bone.

    - **Lacunae –** The site of mature bone cells, known as osteocytes, which are responsible for bone maintenance. Each lacunae is connected to a system of *canaliculi*, smaller canals which connect the lacunae to each other and to the Haversian canals for nutrient and waste exchange.

Bone Formation (Ossification)

- **Endochondral Ossification –** The process of creating bone through the hardening of cartilage, responsible for the formation of most long bones of the body.
- **Intramembranous Ossification –** The process of creating bone through the transformation of undifferentiated embryonic connective tissue (mesenchymal tissue).

Bone Remodeling

- **Osteoblasts –** Cells responsible for the constant formation of bone. Osteoblast build bone using both organic and inorganic materials.
- **Osteoclasts –** Cells responsible for the constant destruction of bone. Osteoclasts release enzymes that dissolve bone, releasing calcium into the bloodstream.
- **Bone Maintenance –** The process of bone maintenance through constant bone construction and deconstruction. Bone maintenance is affected by hormones as well as by exercise and use.
    - **Bone Reformation –** Essential ingredients such as calcium and phosphate are obtained from the bloodstream.
    - **Bone Resorption** - Ions are broken down and released back into the bloodstream.

<u>Joints</u>

Movable Joints – Joints that allow for the motion of bones relative to each other, strengthened by *ligaments* and surrounded by *synovial capsules*. The articular surfaces of the bones are covered in *articular cartilage*.

- **Ligaments –** Fibrous connective tissue connecting bone to bone.
- **Synovial Capsules –** A capsule of connective tissue surrounding the *articular cavity* and filled with *synovial fluid*.
    - **Synovial Fluid –** Fluid that acts as a liquid between the solid joint structures moving against each other.
- **Articular Cartilage –** Hyaline cartilage that covers the articular surface to absorb shock, reduce shear, and reduce wear directly to the bone.

Immovable Joints – Joints, such as within the skull, that require little or no motion.

<u>Skeletal Muscle</u>

Myocyte – Multinucleate muscle cell. What we refer to as a muscle is simply a parallel arrangement of many myocytes.

Innervation – Skeletal muscle is innervated by the *somatic nervous system*, and is thus voluntary. Any voluntary muscle contractions are of skeletal muscle.

Structure

- **Sarcomere –** The basic contractile unit of the muscle.
- **Myofibrils –** A bundle of sarcomeres, surrounded by a covering called the

sarcoplasmic reticulum.
    - **Sarcoplasmic Reticulum –** A network organelle similar to the endoplasmic reticulum, but containing high volumes of calcium cations.
- **Sarcoplasm (Muscle Cell Cytoplasm) –** Modified cytoplasm surrounding the myofibrils and sarcoplasmic reticulum.
- **Sarcolemma (Muscle Cell Membrane) –** The cell membrane of a muscle cell, encompasing the sarcoplasm and many bundles of myofibrils. The sarcolemma is capable of propagating an action potential.
    - **Transverse Tubules (T Tubules) –** A system of tubules connected to the inner surface of the sarcolemma and perpendicular to the myofibrils, allowing for ion flow.

Muscle Fiber Types

- **Red (Slow Twitch) Fibers –** Muscle fibers with a high *myoglobin* content, which primarily derive their energy aerobically. Red fibers contract slower, and are more difficult to fatigue.
    - **Myoglobin –** Protein similar to hemoglobin, but able to bind to oxygen more tightly than hemoglobin.
- **White (Fast Twitch) Fibers –** Muscle fibers with low *myoglobin* content, which primarily derive their energy anaerobically. White fibers can contract quicker, but are easier to fatigue.

<u>The Sarcomere</u>

Structure – Sarcomeres are the basic functional unit of muscle cells. They are made up of *thin filaments* and *thick filaments*.

- **Thin Filaments –** Filaments composed of *actin*, along with *troponin* and *tropomyosin*.
- **Thick Filaments –** Filaments composed of organized bundles of *myosin*.
- **Z Lines –** Define the boundaries of each sarcomere and are responsible for the striated (striped) appearance of muscle. During contraction, the distance between adjacent Z lines decreases.
- **M Lines –** A line defining the center of each sarcomere, exactly between two Z lines.
- **I Band –** Zone containing only thin filaments. During contraction, the I band becomes smaller as the thin/thick filaments overlap. *The letter I is thinner than the letter H and is associated with thin filaments*
- **H Zone –** Zone containing only thick filaments. During contraction, the H zone becomes smaller. *The letter H is thicker than the letter I and is associated with thick filaments*
- **A Band –** The A band contains the thick filaments in their entirety, including any overlap with thin filaments.

Contraction – A series of coordinated steps, repeated for continuous shortening.

- **Initiation –** An action potential travels down a motor neuron until it reaches the

nerve terminal. Neurotransmitters are then released into the synapse where they bind to receptors on the muscle. This junction is called the *neuromuscular junction*.

- **Shortening of the Sarcomere –** The neurotransmitter begins an action potential along the sarcolemma and t-tubules and into the muscle fiber itself. The sarcoplasmic reticulum is responsive to depolarization and stores large amounts of calcium ions. As the action potential reaches the sarcoplasmic reticulum, calcium ions are released. The released calcium binds to troponin, causing tropomyosin to shift and reveal the *myosin-binding sites* on actin. Myosin can now bind to the exposed sites on actin, forming actin-myosin cross bridges, and pull on actin to shorten the sarcomere. 1 ATP provides the energy for the power stroke after which the products of ATP hydrolysis detach, leaving room for a new ATP. Once another ATP binds to myosin, it detaches from actin and it is ready for reattachment to another actin and another power stroke.
- **Relaxation –** Once the sarcoplasmic reticulum is no longer stimulated, calcium levels will fall, preventing further binding of actin and myosin. If ATP is not present to release the myosin from actin, as in death, the rigid structure of rigor mortis is formed.

Stimulus and Muscle Response

- **Stimulus Intensity –** Muscle cells exhibit an all-or-none response. A stimulus must reach a *threshold value*, or there will be no response.
  - **Tonus –** A constant state of low level contraction, necessary for some muscles.
- **Simple Twitch –** The response of a single muscle fiber to a brief stimulus at or above threshold.
  - **Latent Period –** The time between when threshold is reached and the onset of contraction. The action potential spreads across the muscle and calcium ions are released.
  - **Contraction Period –** The contraction of a muscle.
  - **Relaxation Period –** The relaxation of a muscle.
  - **Refractory Period –** A period following contraction in which the muscle is less responsive or unresponsive to stimuli.
    - **Absolute Refractory Period –** A period during which no amount of stimuli will generate a response as the muscle resting potential is being restored.
    - **Relative Refractory Period –** A period in which the muscle can be stimulated, but only at a higher threshold than normal.

<u>Smooth Muscle</u>

Smooth Muscle – The muscle type responsible for involuntary actions. It can contract by autonomic nervous system stimulation or by myogenic activity. It consists of actin and myosin mechanisms, but the fibers are disorganized and so are not striated like skeletal muscle.

- **Autonomic Nervous System –** The part of the nervous system responsible for involuntary contractions.
- **Myogenic Activity –** The action by which smooth muscle can contract without nervous system input.

Cardiac Muscle

Cardiac Muscle – Cardiac muscle exhibits characteristics of both skeletal and smooth muscle. Cardiac muscle is involuntary, striated, and may exhibit myogenic activity.

Energy Reserves

ATP Generation Muscles can generate ATP from fatty acids, glucose, glycogen, or creatine phosphate.

- **Creatine Phosphate –** In times of plenty, phosphate is transferred from ATP to creatine as a means of storing the phosphate. In times of high energy need, the phosphate may be transferred back from creatine to ADP to create ATP. This provides a quick source of ATP rather than having to produce it from glycolysis or the TCA cycle.

Myoglobin – A protein complex similar to hemoglobin, but found in the muscle. Like hemoglobin, it also binds to oxygen. When oxygen supply is insufficient, we can tap into the myoglobin stores to keep aerobic respiration going.

Connective Tissue

Connective Tissue Fibers – Protein fibers that are a major component of connective tissues.

- **Collagen Fibers –** Fibers with high tensile strength.
- **Elastic Fibers –** Fibers with high elasticity.
- **Reticular Fibers –** Fibers which connect connective tissues to adjacent tissues.

Connective Tissue Cells -

- **Fibroblasts –** Cells that secrete connective tissue fibers.
- **Macrophages –** White blood cells that engulf bacteria and dead cells.

Dense Connective Tissue – Connective tissue with a high proportion of collagenous fibers. Fibers are woven and parallel, like steel cables.

- **Tendons**
- **Ligaments**

Muscle-Bone Interactions

Origin – The end of the muscle attached to stationary bone, usually the proximal end.

Insertion – The end of the muscle attached to moving bone, usually the distal end.

Antagonism – Muscles don't have an elongation mechanism, they require an opposing muscle for elongation or movement in the opposite direction.

Synergism – Accessory muscles assist the principal muscles during movement.

DIGESTION

Anatomical Considerations

Intracellular Digestion – Digestion of nutrients within cells, such as glycolysis.

Extracellular Digestion – Digestion of nutrients outside of cells.

Alimentary Canal – Mammalian digestion occurs within the lumen of the alimentary canal, which is not within cell borders and is technically outside of the body. The entrance is the mouth and the exit is the anus. In between is one continuous tube sectioned off by sphincters.

- **Upper Esophageal Sphincter**
- **Lower Esophageal Sphincter**
- **Pyloric Sphincter**
- **Ileocecal Valve**
- **Internal Anal Sphincter**
- **External Anal Sphincter**
- **Urethral Sphincter**

Digestion – The breakdown of food into its constituent organic molecules. Lipids are broken into fatty acids. Carbohydrates and starches are broken into monosaccharides. Proteins are broken into amino acids

- **Mechanical Digestion –** The breakdown of intermolecular bonds between molecules of nutrients.
- **Chemical Digestion –** The breakdown of intramolecular bonds within molecules of nutrients.
  - **Carbohydrates**
    - **Mouth –** Salivary amylase
    - **Small intestine –** Pancreatic amylase, intestinal disaccharidases
  - **Lipids**
    - **Mouth –** Salivary lipase
    - **Small Intestine –** Pancreatic lipase, liver bile
  - **Proteins**
    - **Stomach –** Gastric pepsin
    - **Small Intestine –** Pancreatic peptidases, intestinal peptidases

Absorption – The transport of the products of digestion from the digestive tract into the circulatory system for distribution throughout the body.

Primary Digestive Organs

- **Oral Cavity**

- **Pharynx**
- **Esophagus**
- **Stomach**
- **Small Intestine**
- **Large Intestine**

Accessory Digestive Organs

- **Salivary Glands**
- **Pancreas**
- **Liver**
- **Gall Bladder**

Epithelium

Epithelium – Continuous sheets of epithelium cover every inner and outer surface of the body. These cells are tightly joined and together and have immune, secretory, and absorptive roles.

- **Layer Classification**
  - **Simple –** A sheet of epithelium one layer thick.
  - **Stratified –** A sheet of epithelium multiple layers thick.
  - **Pseudostratified –** A sheet of epithelium that appears to consist of multiple layers, but really consists of only one layer of cells of varying sizes.
- **Shape Classification**
  - **Cuboidal –** Cube shaped epithelial cells.
  - **Columnar –** Column/rectangular prism shaped cells.
  - **Squamous –** Flat, scale-like epithelial cells.

Mucous Membranes – Epithelial linings that prevent fluid loss and allow for selective absorption.

Basement Membrane – A connective tissue layer which connects epithelium to other tissue types.

Oral Cavity

Mechanical Digestion – Mechanical digestion begins in the mouth with mastication, also known as chewing. This breaks intermolecular bonds to increase surface area of nutrients exposed to chemical digestion. The tongue shapes the food into a bolus, which can then be easily swallowed.

Chemical Digestion – The breaking of intramolecular bonds of nutrients. The amount of chemical digestion that actually occurs in the mouth is limited by the amount of time the food stays in the mouth.

- **Salivary Amylase –** Enzyme secreted by the salivary glands that aids in carbohydrate digestion by hydrolysis.
- **Salivary Lipase –** Enzyme secreted by the salivary glands that aids in lipid digestion by hydrolysis.

Pharynx

Pharynx – The cavity between the mouth/nose and the esophagus. The pharynx is also connected to the larynx, a part of the respiratory tract.

Epiglottis – A structure that folds down to cover the trachea during swallowing. This prevents food from entering the respiratory tract. Improper function of the epiglottis can lead to choking.

Esophagus

Esophagus – The section of digestive tract between the pharynx and the stomach. The esophagus is a muscular tube, striated proximally but transitions to smooth muscle by the time it reaches the thorax. This is because the upper $1/3^{rd}$ of the esophagus is voluntary while the remainder of the esophagus and digestive tract in general is involuntary.

Peristalsis – An involuntary series of contractions along a tube-like muscular structure, usually with the intent of transporting some substance within the tube.

Lower Esophageal Sphincter – The sphincter between the esophagus and stomach. Weakness of this sphincter allows for reflux of food and acid into the relatively unprotected lower esophagus, causing a painful burning sensation, heartburn.

Stomach

Stomach – Digestive organ capable of mechanical and chemical digestion, as well as about 2 liters worth of food storage. Stored food is slowly released into the small intestine for further digestion and eventual absorption. The stomach is primarily for digestion, very little absorption can happen through the stomach mucosa.

Stomach Mucosa – A thick layer of epithelium which contains glands for enzyme secretion.

- **Gastric Glands –** Glands that respond to signals from the brain, stimulated by the sight, smell, and taste of food.
  - **Mucous Cells –** Cells which produce mucous to prevent autodigestion.
  - **Chief Cells –** Cells chiefly in charge of stomach digestion. Chief cells secrete pepsinogen, the inactive form of pepsin, an enzyme that cleaves peptide bonds.
  - **Parietal Cells –** Cells that secrete HCl (pH 2), which serves many purposes. HCl activates pepsinogen, kills most harmful bacteria, and helps in mechanical digestion.
- **Pyloric Glands –** Glands that secrete the hormone *gastrin*.
  - **Gastrin** – A hormone which increases HCl production in the stomach.

Stomach Secretions

- **H^+ (HCl)** - Kills microbes, denatures proteins, converts pepsinogen into protein
- **Pepsinogen/Pepsin –** Partially digests proteins.
- **Mucous –** Protects the mucosa.
- **Bicarbonate –** Protects the mucosa.

- **Water –** Dissolves and dilutes ingested materials.
- **Intrinsic Factor –** Required for normal absorption of vitamin B12.

Gastric Juice – The combination of secretions from chief and parietal cells.
Chyme – The semifluid mixture of food and gastric juice.

Small Intestine

Small Intestine – 6 meter long tubelike structure between the stomach and large intestine. Most chemical digestion and absorption occurs in the small intestine.

- **Duodenum –** Most digestion occurs in the duodenum. As chyme enters the duodenum, it triggers secretions from the accessory organs as well as from the small intestine itself.
- **Jejunum** -Most absorption occurs across the brush borders of the jejunum or ileum.
- **Ileum** -Most absorption occurs across the brush borders of the jejunum or ileum.

Pyloric Sphincter – Sphincter between the stomach and the small intestine.
Villi – Small hairlike projections on the inner wall of the small intestine that increase overall absorptive surface area.
Microvilli – Even smaller villi that cover each villi, further increasing the overall absorptive surface area.
Intestinal Bacteria – Over 400 species of bacteria reside within the gut, aiding in digestive and absorptive functions.
Intestinal Secretions – Chyme in the duodenum stimulates the secretion of several compounds and enzymes.

- **Disaccharidases –** Enzymes capable of breaking disaccharides into monosaccharides. Maltase, lactase, and sucrase.
- **Peptidases –** Enzymes that break down proteins.
- **Enterokinase –** Enzyme which activates the pancreatic peptidases.
- **Secretin –** A hormone that stimulates the release of pancreatic juice.
- **Cholecystokinin (CCK) –** A hormone released by the duodenum which stimulates the gallbladder to release bile and the pancreas to release pancreatic juice.
- **Enterogastrone –** A hormone that may be released by the duodenum if necessary to slow the movement of fats through the duodenum to increase digestion and absorption time. Especially useful after a vary fatty meal.

Pancreatic Juice – A mixture of several enzymes in a bicarbonate (basic) solution. This basic solution neutralizes acidic chyme to provide for the more neutral pH necessary for the digestive enzymes at this stage. Pancreatic juice contains enzymes capable of hydrolyzing carbohydrates, lipids, and proteins.

- **Pancreatic Amylase –** Enzyme capable of breaking down carbohydrates.
- **Pancreatic Lipase –** Enzyme capable of breaking down lipids.
- **Pancreatic Peptidases –** Enzymes capable of breaking down proteins.

    - **Trypsinogen**
    - **Chymotrypsinogen**
    - **Elastinogen**
    - **Carboxypeptidase**
- **Intestinal Enterokinase –** Enzyme produced by the small intestine which activates trypsinogen, which in turn activates the other pancreatic peptidases.

Bile – Alkaline fluid produced by the liver and composed of bile salts, bile pigments, and cholesterol. Bile is stored in the gallbladder, which releases it as needed into the duodenum through the bile duct. The release of bile through the bile duct is initiated by the hormone cholecystokinin (CCK). CCK is secreted by the small intestine in response to the entrance of chyme. Like pancreatic juice, bile also helps to neutralize acidic chyme.

- **Bile Salts –** Amphipathic molecules that serve as a bridge between aqueous and lipid environments, helping to emulsify fats within the small intestine. Fats normally cluster together as a result of being in an aqueous environment, which decreases surface area contact with water. By emulsifying the fats, chemical digestion is more effective.
    - **Micelle –** After digestion, monoglycerides and fatty acids associate with bile salts and phospholipids to form micelles. Micelles are necessary to transport the poorly soluble lipids to the enterocyte surface, where they can be absorbed.

Absorption

- **Simple Carbohydrates –** Absorbed by active transport and facilitated diffusion into the epithelial lining in the gut. They then diffuse into the intestinal capillaries on the other side of the epithelial lining. The carbohydrates make their way to the *hepatic portal circulation* where they are then absorbed by the liver before final release into the circulation.
- **Amino Acids –** Absorbed by active transport and facilitated diffusion into the epithelial lining in the gut. They then diffuse into the intestinal capillaries on the other side of the epithelial lining. The amino acids make their way to the *hepatic portal circulation* where they are then absorbed by the liver before final release into the circulation.
- **Fats –** Diffuse passively into the epithelial lining and then into the intestinal capillaries. Since fats are nonpolar, they can easily traverse cellular membranes with no need for active or facilitated transport. Fats bypass the *hepatic portal circulation* and so fat blood levels are not regulated by the liver. Once in the bloodstream the monoglycerides reform into larger fats which are then packaged into insoluble *chylomicrons*, then they enter the lymphatic system through *lacteals*, small vessels that form the beginning of the lymphatic system. The lacteals converge and enter the venous circulation through the lymphatic duct in the neck region.
    - **High Density Lipoproteins –** Chylomicrons are processed in the blood into

HDLs, the healthy version of lipoproteins.
    - **Low Density Lipoproteins –** Chylomicrons are processed into the blood into LDLs, the less healthy version of lipoproteins.
- **Vitamins**
    - **Water Soluble Vitamins (B and C) –** Absorbed into the body within or alongside other water soluble nutrients, such as carbohydrates, amino acids, and water.
    - **Fat Soluble Vitamins (A, D, E, and K) –** Absorbed into the body within or alongside fats.

Large Intestine

Large Intestine – Section of the digestive tract primarily tasked with water absorption, although overall water balance in the body is controlled by the kidneys. The large intestine is wider, but shorter than the small intestine.

- **Cecum –** A pocket that connects the small and large intestines and attaches to the appendix.
    - **Appendix –** Accessory structure that may have some function in preventing infection by harmful bacteria and storing some amount of beneficial bacteria.
- **Colon –** Responsible for absorbing water and salts in undigested foodstuff. Too little or too much water absorption can cause diarrhea or constipation respectively.
- **Rectum –** Storage site for feces, the mixture of indigestible material, water, bacteria, and other secretions that aren't reabsorbed.
    - **Anus –** Opening through which feces is excreted. Consists of two sphincters.
        - **Internal Sphincter –** Involuntary sphincter.
        - **External Sphincter –** Voluntary sphincter.

RESPIRATION

Anatomy

Lungs – Organ responsible for gas exchange.

Cilia – Hairs or hairlike structures responsible for filtering particulate matter from breathed air. Located in the nasal cavity, the trachea, and the bronchi.

Respiratory Tract

- **Mouth/Nares**
    - **External Nares –** Openings in the nose through which air enters. The nares then connect to the nasal cavity.
- **Larynx –** As the pharynx is a pathway from mouth to esophagus, the larynx is the passageway from the mouth to the trachea.
- **Trachea**

    - **Epiglottis –** Structure which prevents food and liquid from entering the glottis (opening to the trachea) during swallowing.
- **Left/Right Bronchi**
- **Bronchioles –** The branching into bronchioles and eventually into alveoli greatly increase surface area.
- **Alveoli –** Tiny structures at which gas exchange occurs. A network of capillaries surround each alveoli to transport oxygen and carbon dioxide. Alveoli are the functional units of the lung.
    - **Surfactant –** A detergent that coats the alveoli, lowering the surface tension and preventing the alveoli from collapsing inward.

<u>Ventilation</u>

Thoracic Cavity – Cavity which contains the lungs and heart.

Diaphragm – A muscle at the base of the thoracic cavity which separates the heart and lungs from the organs of digestion.

Inspiration – The act of breathing, induced by movement of the diaphragm.

Pleurae – Membranous sacs made of two layers that surround each lung.

- **Visceral –** The pleural layer adjacent to the lungs.
- **Parietal –** The pleural layer not adjacent to the lungs.
- **Intrapleural Space –** The thin, fluid filled, space in between the visceral and parietal pleural layers. The pressure differential between the intrapleural space and the lungs helps to drive air into the lungs.

Stages of Ventilation

- **Inhalation –** Active process by which the diaphragm and external intercostal muscles expand the thoracic cavity. As intrapleural volume increases, pressure decreases. The intrapleural pressure is now lower than the atmospheric pressure in the lungs. The lungs will expand into the intrapleural space and more air will be drawn in from the atmosphere. This mechanism is referred to as *negative pressure breathing*.
- **Exhalation –** Passive process by which relaxation of the diaphragm and external intercostal muscles decreases volume of the thoracic cavity and intrapleural space. This increases intrapleural pressure to a point higher than atmospheric pressure in the lungs and gases are exhaled as a result. Remember that surfactants prevent the collapse of alveoli during exhalation.

Control of Ventilation

- **Ventilation Centers –** Neurons located in the medulla oblongata fire rhythmically to cause regular contraction of respiratory muscles. The ventilatory response is primarily driven by abundance of carbon dioxide rather than lack of oxygen.
- **Respiratory Rate –** Ventilation center neurons are particularly sensitive to carbon dioxide concentrations. As carbon dioxide concentrations increase, so does respiratory rate.

- **Chemoreceptors –** Chemoreceptors on ventilation neuron surfaces measure blood pH, which is directly tied to blood carbon dioxide levels.

Lung Capacities and Volumes

Spirometer – A device for measuring lung capacity and ventilation rate.

Total Lung Capacity (TLC) – The maximum amount of air a healthy human's lungs can hold, about 6-7 Liters.

Vital Capacity (VC) – The capacity of air that we can actually force in or out at any given time. The TLC minus the RV. Also, the VC=TV+ERV+IRV

Residual Volume (RV) – The residual amount of air than cannot be forcefully moved out of the lungs. The TLC minus the VC.

Tidal Volume (TV) – The normal breath size, about one liter.

Expiratory Reserve Volume (ERV) – The excess air leftover after exhaling a tidal volume.

Inspiratory Reserve Volume (IRV) – The amount of excess air that can be inhaled after inhaling a tidal volume.

Gas Exchange

Pulmonary Arteries – Carry deoxygenated blood from the heart to the alveoli. Gas exchange is driven by concentration gradients of each gas.

Pulmonary Veins – Carry oxygenated blood from the alveoli to the heart.

THE CARDIOVASCULAR SYSTEM

Anatomy

Heart – Four chambered organ with 2 reservoirs prior to the 2 pumps.

- **Left Atrium –** Reservoir leading into the left ventricle. Receives oxygenated blood from the pulmonary circulation.
- **Left Ventricle –** Pumps oxygenated blood into the systemic circulation.
- **Right Atrium –** Reservoir leading into the right ventricle. Receives deoxygenated blood from the systemic circulation.
- **Right Ventricle –** Pumps deoxygenated blood into the pulmonary circulation.

Blood Flow

1. **Left Atrium**
2. **Left Ventricle**
3. **Aorta**
4. **Arteries**
5. **Arterioles**
6. **Capillaries**
7. **Venules**

8. **Veins**
9. **Vena Cavae**
    - **Superior Vena Cava –** Drains the head and arms
    - **Inferior Vena Cava –** Drains the torso and legs
10. **Right Atrium**
11. **Right Ventricle**
12. **Pulmonary Arteries**
13. **Left Atrium**

Portal System – A series of two or more capillary beds connected to each other by venules. Such sysems each have a special purpose.

- **Hepatic Portal System –** Connects the vasculatures of the digestive tract and liver.
- **Hypophyseal Portal System –** Connects the vasculatures of the hypothalmus and pituitary gland.

<u>The Heart</u>

Cardiac Muscle Tissue – A muscle tissue with traits of both skeletal and smooth muscle. Cardiac muscle tissue is ONLY found in the heart and is also the ONLY type of muscle tissue found in the heart.

Note: The heart is behind and to the left of the sternum, at a tilt so that the exterior of the right atrium form the base of the heart. Also not that the heart wall varies in thickness by location. As the left ventricle needs to produce the highest force it also has the most muscle as well as the thickest walls, at about 1/2" thick.

Valves – Different hearts in the blood and veins ensure that the blood flows only in one direction.

- **Heart Valves**
    - **Atrioventricular (AV) Valves –** Prevent backflow into the atria.
        - **Tricuspid Valve –** The right AV valve, composed of 3 leaflets.
        - **Bicuspid (Mitral) Valve –** The left AV valve, composed of 2 leaflets
    - **Semilunar Valves –** Prevent backflow into the ventricles.
        - **Pulmonic Valve –** Right semilunar valve, composed of 3 leaflets.
        - **Aortic Valve –** Left semilunar valve, composed of 3 leaflets.

Contraction -

- **Phases –** There are two phases of contraction, systole and diastole.
    - **Systole –** Ventricular contraction.
    - **Diastole –** Ventricular relaxation.
    - **Heart Sounds –** Lub Dub
        - **S1 (Lub) –** The closing of the atrioventricular valves prior to systole
        - **S2 (Dub) –** The closing of the two semilunar valves after systole
    - **Cardiac Output –** The total blood volume pumped by the heart in one minute, usually about 5 Liters per minute, which is about the average human volume of

blood Cardiac Output = (Heart Rate) X (Stroke Volume)
    - **Heart Rate –** Heart contractions per minute.
    - **Stroke Volume –** Volume of blood pumped per heart contraction.
- **Mechanism and Control –** The cardiac muscle is controlled by the autonomic nervous system, and is involuntary. However, cardiac muscle also demonstrates *myogenic activity*, and can to some extent beat independently of any nervous impulse. Therefore, the autonomic nerves can tell the heart to speed up or slow down, but the heart will continue to pump on its own regardless.
    - **Signal Pathway**
        - **Sinoatrial (SA) Node –** The SA node is a small bundle of cells in the wall of the right atrium. Impulse begins at the SA node and occurs at the rate of 60-100 times per minute regardless of neural input. The depolarization travels across the two atria, resulting in atrial contraction, before reaching the AV node.
        - **Atrioventricular (AV) Node –** The AV node is located between the right atrium and ventricle. The AV node delays the depolarization just long enough for the ventricles to fill with blood, and then releases the wave of depolarization.
        - **Atrioventricular Bundle (Bundle of His) –** The bundle of his is directly connected to the AV node and runs through the interventricular wall.
        - **Purkinje Fibers –** The Purkinje fibers branch out from the bundle of his at the base of the interventricular wall. They then split left and right to carry the depolarization along the wall of each ventricle.
    - **Sympathetic –** Increases the heart rate.
    - **Parasympathetic Input –** Slows the heart rate via the *vagus nerve*.

<u>Blood Vessels</u>

Blood Vessels – There are three main types of blood vessels. Arteries are made of all the same cell types, just in different proportions. One major difference is that arteries have much more smooth muscle.

- **Arteries –** Arteries are strong, elastic, thick walled vessels that always carry blood away from the heart. Only pulmonary arteries and fetal arteries carry deoxygenated blood. All other arteries carry oxygenated blood. The elasticity of arteries compresses the blood within, providing the diastolic blood pressure. Without this elasticity, blood pressure in diastole would drop to zero and we would die-astole.
- **Veins –** Veins are inelastic, thin walled vessels that always carry blood to the heart. Only pulmonary and fetal veins are oxygenated. All other veins are deoxygenated. Approximately ¾ of our blood volume is in the veins at any given moment.
    - **Venous Valves –** With little or no smooth muscle to move blood back towards

the heart, veins rely on one way valves to prevent backflow. If a valve fails, blood will pool in the area and the vein will distend, this is a varicose vein.
    - **Skeletal Muscle Pumps –** With little or no smooth muscle to move blood towards the heart, veins rely on nearby skeletal muscles to compress the vein and force the blood towards the heart. This is why inactivity of the skeletal muscles (especially of the lower extremities) during something like a long flight can allow the blood to pool, coagulate, and increase the risk of an embolism.
- **Capillaries –** Vessels composed only of a single endothelial cell layer, with slit pores in between the cells that allow for nutrient and gas exchange.

Blood Pressure – The pressure of the blood. Pressure is generally very high in the arteries and very low in the veins, with the largest reduction in pressure occurring between the arterioles, capillaries, and venules. This pressure drop is necessary, because the capillaries, venules, and veins could not withstand the pressures present in the arteries.

- **Sphygmomanometer –** A device used for measuring blood pressure. It will measure the gauge pressure of the systemic circulation, that is the pressure above atmospheric pressure (760mmHg).

<u>Blood</u>

Composition – Blood is 55% plasma and 45% cells.

- **Plasma –** The liquid portion of blood, an aqueous mixture of nutrients, salts, gases, hormones, and proteins.
- **Cells –** There are three major categories of blood cells. All blood cells are formed from the same hematopoetic stem cells in blood marrow.
    - **Erythrocytes (Red Blood Cells) –** Cells that specialize in the transport of oxygen. By the time an erythrocyte is mature, it has lost it's nuclei and organelles to make room for a maximum amount of hemoglobin. Each erythrocyte contains approximately 250,000 hemoglobin proteins, each of which can carry 4 oxygen molecules. That's 1,000,000 oxygen molecules per erythrocyte. Molecular oxygen is nonpolar and so has low solubility in water. Because of this we need a specialized transporter to supply us with sufficient oxygen. Note that the biconcave shape of an erythrocyte helps them squeeze through capillaries and increases to surface area for gas exchange.
    - **Leukocytes (White Blood Cells) –** Cells that specialize in immunity and comprise about 1% of total blood volume.
        - **Granulocytes –** Leukocytes that appear granular under microscope
            - **Neutrophil**
            - **Basophil**
            - **Eosinophil**
        - **Agranulocytes –** Leukocytes without visible granules under microscope

        - **Lymphocytes**
        - **Monocytes/Macrophages**
    - **Platelets –** Cell fragments derived from the breakup of *megakaryocytes*. Platelets are crucial to blood clotting.

Blood Antigens – There are 2 major types of antigens found on red blood cells.

- **ABO Antigens –** Blood types refer to the proteins present on the surface of blood cells. Blood type alleles are codominant, which allows for the possibility of type AB blood.
    - **Type A Blood –** Expresses A antigen. The body produces B antibodies.
    - **Type B Blood –** Expresses B antigen. The body produces A antibodies.
    - **Type AB Blood –** Expresses A and B antigens. The body will not make A or B antibodies. (Universal Recipient)
    - **Type O Blood –** Expresses no antigens. The body will produce A and B antibodies. This body may only receive type O blood. However, their blood may be donated to anybody as it will not trigger A or B antibodies. (Universal Donor)
- **Rh Factor –** Another type of surface protein expressed on red blood cells, first discovered in Rhesus monkeys (Rhesus-Rh). We are generally only concerned with the predominant Rh protein and classify blood cells as positive (Rh+) or negative (Rh-) for that protein. Rh factor can be a problem during pregnancy in an Rh- woman who is bearing an Rh+ child. As long as the two blood types don't mix there is not a problem. If they do mix, the mother's antibodies will attack the child in a condition called *erythroblastosis fetalis*.

<u>Functions of the Cardiovascular System</u>

Transport of Gases – The two major gases transported in the blood are oxygen and carbon dioxide.

- **Oxygen Transport –** Oxygen is primarily transported by *hemoglobin* in erythrocytes, as molecular oxygen is nonpolar and has low solubility in water.
    - **Hemoglobin –** Protein composed of four subunits, each of with carries an iron atom which is capable of binding or unbinding oxygen via a redox reaction.
        - **Conformational Shift –** After the first oxygen binds, the hemoglobin changes conformation which alters its oxygen affinity, making it easier for the next three oxygen to bind. After the first oxygen is released, there is another change in conformation which alters its oxygen affinity, making it easier for the next three oxygen to unbind. Furthermore factors such as increased CO2 partial pressure, increased temperature, and decreased pH, are all signs of a potentially increased metabolic rate and therefore signal a shift to decrease oxygen affinity, releasing more into the cells that need it.
- **Carbon Dioxide Transport –** Carbon dioxide is the primary waste product of cellular respiration. However, like oxygen it is nonpolar and not very soluble in

the plasma. Carbon dioxide can be transported by hemoglobin, but hemoglobin has a much higher affinity for oxygen, which often knocks off carbon dioxide. For this reason, carbon dioxide is mainly transported in the form of bicarbonate.

- **Bicarbonate Ion (HCO_3^-) -** Carbon dioxide enters the red blood cell and encounters the enzyme carbonic anhydrase, which combines CO2 and H2O to form carbonic acid, H_2CO_3. Carbonic acid then dissociates into HCO_3^- and a proton, both of which are soluble in water. This also accounts for increased carbon dioxide output lowering the nearby pH. Once the HCO_3^- and proton reach the lungs, carbonic anhydrase reverses the reaction to produce CO2 and water and the CO2 is released across the alveoli into the atmosphere.
- **Bohr Effect –** The increase in carbonic acid decreases plasma pH, which shifts hemoglobin oxygen affinity.

Transport of Nutrients and Wastes

- **Nutrients –** Nutrients are absorbed into the body, mostly via the small intestine, and are then transported to the cells.
  - **Carbohydrates and Amino Acids –** Carbohydrates and amino acids are absorbed across the small intestine, enter the intestinal capillaries, then pass through the hepatic portal system for processing before being released into systemic circulation.
  - **Fats –** Fats are absorbed into lacteals in the small intestine, bypassing the hepatic portal system via the lymph system. Once in the bloodstream, fats are processed into lipoproteins.
- **Wastes –** Wastes, such as carbon dioxide, urea, and ammonia enter the bloodstream and travel down their concentration gradients. They will eventually enter the excretory organs where they will be secreted for removal.
- **Pressure Gradients –** The Starling forces (hydrostatic and osmotic pressures) are in a constant tug of war. Generally, there is an overall higher hydrostatic pressure in the arteries and higher osmotic pressure in the veins. This provides for the one way flow of plasma. However, there is a net pressure difference, where not all fluid that leaves the arteries enters the veins. This excess fluid enters the lymphatic system.
  - **Hydrostatic Pressure –** The force per unit area exerted by the blood. High hydrostatic pressures force blood out of capillaries.
  - **Colloid Osmotic Pressure –** The osmotic pressure generated by the concentration of particles, mostly protein, in the plasma. High osmotic pressures pull blood into capillaries.

Clotting – Platelets protect the vascular system in the event of damage to a vessel by forming a clot, which prevents excess blood loss.Note that connective tissue underlies most other tissues. When platelets encounter exposed collagen, they take this as a sign of injury and begin the process of clotting. The platelets first release *thromboplastin* which converts *prothrombin* into *thrombin*. *Thrombin* then converts *fibrinogen* into *fibrin*. Fibrin is a fiber like protein that aggregates into a

net-like structure over the area of damage. This fibrin net catches cells and other nutrients, forming a clot. A surface clot is called a scab.

THE IMMUNE SYSTEM

Anatomy

Lymph Nodes – Filter lymph fluid.
- **Spleen –** A large lymph node that stores and filters blood.

None Marrow – White blood cell production.

Thymus – Secretes thymosin, which stimulates T Cell maturation

Leukocytes – White blood cells that may contribute to either innate or adaptive immunity.
- **Granulocytes**
  - **Neutrophils**
  - **Basophils**
  - **Eosinophils**
- **Agranulocytes**
  - **Lymphocyte**
    - **B Cells –** Adaptive immunity
    - **T Cells –** Adaptive immunity
  - **Monocytes/Macrophages –** Nonspecific Immunity.

Nonspecific (Innate) Immune Response – The immune response carried out that does not require learning and does not target a specific antigen.

Specific (Adaptive) Immune Response – The immune response that is developed as immune cells learn to recognize and respond to specific antigens.
- **Humoral Immunity**- Blood immunity, driven by B Cells and antibodies.
- **Cell Mediated Immunity –** Driven by T Cells.

Hypersensitivity Reactions
- **Autoimmunity –** When immune cells cannot differentiate between "self" and "not self" and begin attacking their own body.
- **Allergies –** When immune cells are hypersensitive to antigens that are not inherently threatening.

Nonspecific Defense Mechanisms

Skin (Integument) – The skin is the first line of immune defense. It provides a physical barrier to pathogens, as well as secretion of antibacterial enzymes as a component of sweat. Within the respiratory tract, cilia trap particulate which may be carriers for pathogens. Some mucous membranes, such as those around the eye and oral cavity, secrete a nonspecific bactericidal enzyme (lysozyme) in tears and saliva.

Inflammation – Nonspecific immune reaction. Vasodilation allows macrophages to exit

the bloodstream and chemotaxis summons them to the site of injury or disease. Neutrophils, basophils, and eosinophils may be summoned in a similar fashion.
- **Macrophages –** A phagocytic cell that participates in nonspecific immunity.
- **Mast Cells –** These cells are scattered throughout connective tissue. If damaged, they release histamine and other chemicals that stimulate inflammation.
- **Natural Killer Cells –** Cells that destroy the body's own cells that have been infected, or cancer cells.

Interferon – A protein that prevents viral replication and dispersion, it may be released by immune cells or cells that are infected by a virus.

<u>Humoral Immunity</u>

Humoral Immunity – Immunity that involves the production of antibodies.

- **Antibodies (Immunoglobulins) (Ig) –** Large Y shaped proteins produced by B Cells in response to specific antigens. Once an antibody binds to its antigen, it may attract leukocytes to immediately phagocytize the antigens and their cells or first lump together with other antibodies on the target cell to form a large insoluble complex to make phagocytosis easier.
  - **Composition** – Each antibody is Y shaped, with antigen binding regions at the two tips of the Y. Antibodies are Y shaped, being composed of 2 heavy chains and 2 light chains. The other end of the Y is called the *constant region*, which acts to recruit macrophages.
    - **Heavy Chains**
    - **Light Chains**
- **B Cells –** B Cells are lymphocytes that mature in the spleen and other lymph nodes. New antigens stimulate them to divide and produce 2 types of daughter cells in a process known as *primary response*. If a known antigen is encountered, there is a similar, but much more rapid, reaction known as *secondary response*. The development of memory cells is the basis for the efficacy of vaccinations.
  - **Plasma Cells –** Plasma cells are released into the blood, producing large amounts of antibodies that neutralize invaders or tag them for killing. These cells will die off relatively quickly.
  - **B Memory Cells –** Memory cells stay in the lymph nodes for quicker activation in case of future exposure to the same antigen. These cells may last the lifetime of the human.

<u>Cell-Mediated Immunity</u>

T Cells – Lymphocytes which mature in the thymus.

- **Helper T Cells –** Coordinate the immune response by secreting *lymphokines*. HIV destroys Helper T Cells, so a coordinated immune response is not possible.
  - **Lymphokines –** Molecules capable of recruiting other immune cells.
- **Suppressor T Cells –** Suppress the immune response once the infection has been

adequately contained.
- **Killer (Cytotoxic) T Cells –** Cells that are capable of directly killing virally infected cells by secreting toxic chemicals.
- **T Memory Cells** - Memory cells stay in the lymph nodes for quicker activation in case of future exposure to the same antigen. These cells may last the lifetime of the human.

Immunosuppressants – Drugs that can prevent activation of the immune response. Useful for making a body accept a transplanted organ or in cases of autoimmunity.

Immunization

Active Immunization – The body is stimulated to produce antibodies against a certain pathogen.
- **Natural Exposure –** Antibodies are generated by B Cells once the body is infected.
- **Artificial Exposure (Vaccination) –** Antibodies are generated by B Cells in response to pathogenic proteins, but the pathogen is either not present, dead, or weakened and so the host is never truly infected.

Passive Immunization – The transfer of antibodies from one human to another, such as during pregnancy and breastfeeding.

Lymphatic System

Lymphatic System – A circulatory system which carries lymph fluid toward the heart.
- **Lacteals –** The smallest lymphatic vessels, which collect fats from the villi in the small intestine, allowing them to bypass the liver.
- **Lymph Nodes –** Lymphatic structures in the pathway of the lymphatic circulation which contain B cells.

HOMEOSTASIS

Homeostasis

Homeostasis – An systemic equilibrium. Internal conditions in humans must be maintained within a very narrow margin to continue normal function. The kidneys, liver, large intestine, and skin play major roles in maintaining homeostasis.

The Kidneys

Structure
- **Cortex –** The outermost layer of the kidney.
- **Medulla –** The layer beneath the cortex.
- **Renal Hilum –** Deep opening on the medial aspect of the kidney, through which

the renal artery, renal vein, and ureter run.
    - **Renal Artery –** Enters the kidney through the hilum, then branches out through the medulla and into the cortex as *afferent arterioles*.
        - **Afferent Arterioles –** Smaller arteries formed from the renal artery.
            - **Glomeruli –** The capillaries derived from the ends of afferent arterioles.
        - **Efferent Arterioles –** After passing through the glomeruli, blood enters a second set of arterioles rather than venous structures.
            - **Vasa Recta –** The capillaries derived from the ends of the efferent arterioles.
    - **Renal Vein**
    - **Ureter**
- **Nephron –** The functional unit of the kidney, of which each kidney has about 1 million.
    - **Bowman's Capsule –** A cuplike structure surrounding the glomeruli, which then leads to the proximal convoluted tubule.
    - **Proximal Convoluted Tubule**
    - **Loop of Henle**
        - **Descending Limb**
        - **Ascending Limb**
    - **Distal Convoluted Tubule**
    - **Collecting Duct**
- **Portal System –** Two sets of capillaries through which blood must travel before returning to the heart

Osmoregulation

- **Filtration –** 20% of the blood that passes through the glomerulus is filtered into Bowman's Space. The filtrate is similar to blood, except that cells and proteins were too large to cross the glomeruli. The filtrate is isotonic to the blood at this point.
- **Secretion –** The nephron can secrete salts, acids, bases, and urea directly into the tubule by active or passive transport. This allows the kidneys to expel anything that is in excess within the blood or too large to cross the glomerular pores.
- **Reabsorption –** Certain substances that are filtered and/or secreted may be reabsorbed. Some substances, like glucose and amino acids, are always reabsorbed. Reabsorption occurs in the proximal and distal tubules, the Loop of Henle, and the collecting duct.

Nephron Function

- **Selective Permeability**
    - **Proximal/Distal Tubules –** Permeable to most substances, including water.
    - **Descending Limb of Loop of Henle –** Permeable to water, but not salt.
    - **Ascending Limb of Loop of Henle –** Permeable to salt, but not water.
    - **Collecting Duct –** May be permeable to salt and water, depending on state of

hydration.

- **Osmolarity Gradient –** The kidney can actively alter the concentration of various solutes within the kidney interstitium (inner medulla, outer medulla, and cortex) to affect osmotic gradients. The kidneys *actively* pump ions to create concentration gradients to *passively* move water.
  - **Countercurrent Multiplier System**
    - **Cortex –** About the same osmolarity as the tubule.
    - **Medulla –** Can range from isotonic with blood when trying to excrete water up to four times more concentrated when trying to conserve water.
- **Flow of Filtrate**
  - **Proximal Convoluted Tubule (Cortex) –** Glucose, amino acids, water soluble vitamins, and salts are reabsorbed with water.
  - **Descending Limb of Loop of Henle (Medulla) –** Only permeable to water. As the loop descends, medulla becomes hypertonic to pull water out of the tubule. *Passive* water loss drives the intratubule osmolarity to about the same as the medulla.
  - **Ascending Limb of Loop of Henle (Medulla) –** Only permeable to salt. As the filtrate ascends, the medulla becomes less concentrated and the salt is *actively* transported out of the tubule. This keeps the filtrate isotonic to the interstitium.
  - **Distal Convoluted Tubule –** The distal convoluted tubule reabsorbs water and salt as necessary to maintain isotonicity with surrounding cortex.
  - **Collecting Duct –** Final urine concentration depends on the permeability of the collecting duct. Since the collecting duct moves through the hypertonic medulla on the way out of the kidney, the more permeable, the more water is lost to the kidney interstitium, and the more concentrated the urine.

Hormonal Regulation – The permeability of the collecting duct can be controlled by hormones.

- **Aldosterone –** A steroid hormone secreted by the adrenal cortex in response to angiotensin which itself is released in response to decreased blood volume and pressure. Aldosterone prevents the collecting duct from absorbing sodium, since water follows solute the water does not enter the collecting duct and instead remains in the body, increasing blood volume and pressure.
  - **Aldosterone Blockers –** For hypertension, drugs that block aldosterone may be taken which lead to sodium and water loss into the collecting duct which results in blood volume and pressure loss.
- **Antidiuretic Hormone / Vasopressin (ADH) –** Vasopressin is a peptide hormone that causes the cell junctions of the collecting duct to increase permeability, since the medulla is hypertonic water is lost from the collecting duct. Vasopressin is made in the hypothalamus, stored in the posterior pituitary, and secreted when blood osmolarity is high.

    - **Vasopressin Blockers –** Some chemicals, like alcohol and caffeine inhibit vasopressin and lead to frequent excretion of dilute urine.

Excretion – Anything that doesn't leave the tubule within the kidney will be excreted. From the tubule, fluid (urea, uric acid, and ions) collects in the renal pelvis and then travels down the ureters to be stored in the urinary bladder until voided. Urine is voided through the urethra.

- **Unhealthy Urine Constituents –** Blood, protein, and glucose should never be present in urine. Their presence indicates kidney pathology. Erythrocytes should be too large to cross into the renal vessels, their presence indicates a problem at the glomeruli. Protein and glucose freely cross the membrane, but should be fully reabsorbed by the system before leaving the kidneys.

<u>The Liver</u>

Role in Homeostasis – To maintain blood glucose levels and to eliminate nitrogenous waste through urea.

Hepatic Portal Vein – The portal system which delivers nutrients to the liver for processing immediately after absorption.

Glycogen – Complex sugar formed from linking glucose molecules together. When blood sugar levels are high, the liver stores excess glucose in the form of glycogen.

- **Gluconeogenesis –** The formation of glucose from non-sugar precursors.

Nitrogenous Wastes – Amino acids contain amino groups, and when sugar is in short supply proteins can be burned by the mitochondria for fuel. This produces nitrogenous waste.

- **Deamination –** Removal of the amino group from an amino acid. The remainder of the acid may be used for fuel. The amino groups begin to form toxic ammonia. To prevent ammonia build up the liver combines ammonia with carbon dioxide to create urea, which is then expelled in urine.

Other Functions of the Liver

- Break down of toxins
- Break down of old erythrocytes
- Storage of vitamins and cofactors
- Synthesis of bile
- Synthesis of blood proteins

<u>The Large Intestine</u>

Role in Homeostasis – The large intestine is capable of reabsorbing water and excreting certain salts.

<u>The Skin</u>

Structure – The skin (integument) is the largest organ of the body.

- **Epidermis –** Outer layer.
  - **Stratum Corneum –** Outer most layer, dead cells which have lost their nuclei and resemble scales (squames).
  - **Stratum Lucidum**
  - **Stratum Granulosum**
  - **Stratum Spinosum**
  - **Stratum Basalis –** Inner most layer, responsible for production of new skin cells.
- **Dermis –** Middle layer.
  - **Papillary Layer –** More superficial layer, loose connective tissue.
  - **Reticular Layer –** Deeper layer, denser connective tissue.
- **Hypodermis –** Inner (subcutaneous) layer.

Function – The skin protects us from the outside environment, transfers sensory information from the outside environment, and helps to regulate our temperature.

- **Melanocytes –** Epidermal cells that secrete the pigment *melanin* which helps protect us from UV light.
- **Thermoregulation –** Vasodilation, vasoconstriction, and sweating all help regulate body temperature. In sweating, our body temperature serves as the heat of vaporization. Subcutaneous fat may serve as temperature insulation.
  - **Endotherms (Homeotherms) –** Animals which must maintain a constant internal temperature.
  - **Ectotherms –** Animals whose internal temperature is dependent upon the temperature of the external environment.
  - **Torpor –** A decreased state of arousal entered into during excessively hot or cold seasons. Metabolic rate, heart rate, and respiration all decrease significantly. Torpor allows the animal to utilize minimal energy while in inhospitable environments.
    - **Estivation –** Torpor during hot seasons.
    - **Hibernation –** Torpor during cold seasons.

THE ENDOCRINE SYSTEM

<u>Anatomy</u>

Endocrine System – A system of organs which act at a distance, generally through the bloodstream, and whose focus is duration of stimulation rather than velocity of stimulation.

Signaling Types – Signaling types depend upon distance.

- **Autocrine –** A cell secretes a hormone which attaches to its own receptors to elicit a response.

- **Paracrine –** A cell secretes a hormone which attaches to receptors of a nearby cell to elicit a response. (Ex: neural junction)
- **Endocrine –** A cell secretes a hormone which attaches to receptors of a far away cell to elicit a response, action at a distance.

<u>Endocrine Glands</u>

Hormone Types

- **Peptide Hormone**
- **Steroid Hormone**

Organ Types – Hormone activity is dependent upon the secretion of hormones, as well as the presence of hormone receptors.

- **Brain**
  - **Hypothalamus –** Located in the forebrain above the pituitary and below the thalamus. Elicits organism wide effects by controlling the pituitary via a paracrine mechanism. The hypothalamus itself is stimulated by neural activity and regulated by neural feedback.
    - **Interaction with Anterior Pituitary –** The hypothalamus releases hormones into the *hypophyseal portal system*, which then travel into the anterior pituitary to bind to receptors causing the release of other hormones.
      - **Gonadotropin-Releasing Hormone (GnRH) releases:**
        - **Follicle Stimulating Hormone (FSH)**
        - **Luteinizing Hormone (LH)**
      - **Growth Hormone-Releasing Hormone (GHRH) releases:**
        - **Growth Hormone (GH)**
      - **Prolactin Inhibitory Factor (PIF) limits the release of:**
        - **Prolactin**
      - **Thyroid-Releasing Hormone (TRH) releases:**
        - **Thyroid-Stimulating Hormone (TSH)**
      - **Corticotropin-Releasing Factor (CRF) releases:**
        - **Adrenocorticotropic Hormone (ACTH)**
    - **Interaction with Posterior Pituitary –** Neurons from the hypothalamus extend into the posterior pituitary, where the terminal ends release hormones.
      - **Hypothalamic Neurons Release:**
        - **Oxytocin**
        - **Antidiuretic Hormone (ADH)/Vasopressin**
  - **Pituitary Gland –** Gland located beneath the hypothalamus, composed of 2 lobes which are functionally distinct.
    - **Anterior Pituitary Component**
      - **Direct Hormones –** Bind to target organ receptors to elicit a direct

effect.
        - **Growth Hormone (GH) –** Regulates growth. In childhood, an excess results in *gigantism* while a deficit results in *dwarfism*. In adulthood, GH affects the short bones more, resulting in *acromegaly*.
        - **Prolactin –** Stimulates milk production in the *mammary glands*.
        - **Endorphins –** Decrease the perception of pain.
    - **Tropic (Intermediate) Hormones –** Bind to target organ receptors to elicit that organ to release more hormones. This next set of hormones may elicit the final effect.
        - **ACTH –** Elicits the adrenal cortex to release glucocorticoids.
        - **TSH –** Elicits the thyroid to absorb iodine and to release *thyroid hormone*.
        - **LH & FSH –** Released in response to high *GnRH* levels.
  - **Posterior Pituitary Component –** Receives and stores hormones released by the hypothalamus.
    - **Oxytocin –** Secreted during childbirth, allows for coordinated uterine contractions as well as milk production.
    - **ADH/Vasopressin –** Secreted in response to high blood osmolarity or low blood volume/pressure. Affects the permeability of the collecting duct to water.
- **Pineal Gland/Body –** Secretes melatonin, which may involve *circadian rhythms*.

- **Throat**
  - **Thyroid Gland –** The thyroid sets basal metabolic rate and calcium homeostasis. Controlled by TSH (pituitary) and TRH (hypothalamus).
    - **Thyroxine (T4) and Triiodothyronine (T3) (Thyroid Hormones) –** Increase cellular respiration and the efficiency of cellular respiration to increase the basal metabolic rate. A lack of the thyroid hormones decreases the basal metabolic rate.
      - **Hypothyroidism –** Insufficient iodine intake results in a decrease in thyroid hormone production and subsequently leads to lethargy, low body temp, slow heart rate, and weight gain.
        - **Cretinism –** Hypothyroidism at birth and infancy may cause mental retardation and developmental delays.
      - **Hyperthyroidism –** A nearby tumor or overstimulation of the thyroid may cause overproduction of the thyroid hormones and subsequently lead to increased activity, high body temp, high heart rate, and weight loss.
    - **Calcitonin –** Decreases blood calcium levels by increasing excretion from the kidneys, decreasing absorption from the gut, and increasing storage in the bone.

- **Parathyroid Glands –** 4 small pea shaped structures attached to the posterior of the thyroid gland.
  - **Parathyroid Hormone (PTH) –** Antagonistic to *calcitonin*. Increases blood calcium levels by decreasing excretion through the kidneys, increasing calcium absorption in the gut, and increasing bone resorption.

- **Thoracic**
  - **Heart**
    - **Atrial Natriuretic Peptide –** Helps regulate salt and water balance.
  - **Thymus –** Gland behind the breastbone, which atrophies by adulthood.
    - **Thymosin –** Important for proper T Cell development and differentiation.
- **Abdominal**
  - **Pancreas**
    - **Islets of Langerhans –** Small group of endocrine cells within the pancreas.
      - **Alpha Cels**
        - **Glucagon –** Secreted in times of famine, elicits combustion of fats and proteins, glycogenolysis, and gluconeogenesis.
      - **Beta Cells**
        - **Insulin –** Secreted in times of high blood sugar, elicits muscle and liver cells to store excess glucose as glycogen.
          - **Hypoglycemia –** Low blood glucose, high insulin levels.
          - **Hyperglycemia –** High blood glucose, low insulin levels.
            - **Diabetes Mellitus** - High blood glucose, low insulin levels or resistivity to insulin.
              - **Polyuria –** Increased or frequent urination.
              - **Polydipsia –** Increased or frequent thirst.
      - **Delta Cells**
        - **Somatostatin –** Stimulated by high blood glucose and amino acid concentrations, inhibits both glucagon and insulin.
  - **Kidneys**
    - **Erythropoietin –** Stimulates bone marrow to increase erythrocyte production. Secreted in response to low blood oxygen levels.
  - **Adrenal Glands –** Glands which sit atop the kidneys and which are composed of 2 anatomically and functionally distinct regions.
    - **Adrenal Cortex**
      - **Corticosteroids (Cholesterol Derivatives)**
        - **Glucocorticoids (Sugar) –** Regulate glucose levels, affect protein metabolism, and limit the inflammatory response.
          - **Cortisol –** Naturally released in response to stress.
          - **Cortisone**
        - **Mineralocorticoids (Salt) –** Regulate salt and mineral balance in cooperation with the kidneys.

        - **Aldosterone –** Causes increased renal reabsorption of salt and therefore water.
            - **Renin-Angiotensin-Aldosterone System –** Decreased blood volume causes the kidneys to secrete renin, which activates angiotensin I, which converts to angiotensin II, which stimulates the adrenal cortex to secrete aldosterone.
    - **Cortical Sex Hormones (Sex) –** Secretes male sex hormones, similar to the testes, but in much lower amounts. If overstimulated in women, could result in masculinizing effects.
        - **Androgens**
- **Adrenal Medulla –** A derivative of the nervous system, nestled within the adrenal cortex.
    - **Sympathetic Hormones**
        - **Catecholamines**
            - **Epinephrine –** Increases cardiac and skeletal muscle activity.
            - **Norepinephrine –** Decreases smooth muscle (digestive) activity.
- **Gastrointestinal Glands –** Stimulated by presence of food, releases intestinal peptides.
    - **Secretin**
    - **Gastrin**
    - **Cholecystokinin**

- **Gonads**
    - **Testes**
        - **Testosterone –** Release stimulated by LH. Testosterone is important for spermatogenesis, male embryonic differentiation, and male puberty development. Has negative feedback effect on FSH, LH, and GnRH.
            - **Androgen Insensitivity Syndrome –** Testosterone receptors in a male are absent, resulting in secondary female characteristics.
    - **Ovaries**
        - **Hormones**
            - **Estrogen –** Secreted by the *corpus luteum* in response to elevated FSH and LH, responsible for secondary female characteristics. Also lead to thickening of *endometrium* each month in preparation for zygote implantation.
            - **Progesterone –** Secreted by the *corpus luteum* in response to LH stimulation. Responsible for the development and maintenance of the endometrium. By the end of the first trimester, the placenta secretes progesterone rather than the *corpus luteum*.
        - **The Menstrual Cycle –** The cyclic growth and shedding of the endometrial lining.
            - **Follicular Phase –** Begins with menstrual flow, shedding the uterine

lining of the previous cycle. Estrogen begins to regrow the endometrial lining, stimulating vascularization and glandularization of the *decidua*.

- **Ovulation –** Increasing levels of estrogen eventual stimulate the release of an ovum from the ovary, which then travels to the abdominal cavity.
- **Luteal Phase –** LH causes the ruptured follicle to form the corpus luteum, which then secretes progesterone. High levels of estrogen and progesterone provide negatively feedback to GnRH, LH, and FSH to prevent double ovulation in one cycle.
- **Menstruation –** If implantation does not occur, *human chorionic gonadotropin (hCG)* will not be formed, progesterone levels will fall, and the uterine lining is sloughed off. The loss of estrogen and progesterone removes the block from GnRH, allowing the next cycle to begin.

- **Pregnancy –** In cases of fertilization, the corpus luteum is maintained by the presence of hCG, which is secreted by the blastocyst and placenta. HCG levels fall, but estrogen and progesterone levels continue to rise as the placenta secretes them.
  - **Home pregnancy tests –** Check for hCG in the urine.
- **Menopause –** Between the ages of 45 and 55, decreased responsiveness of the ovaries to FSH and LH results in fewer follicles developing each month as well as decreased estrogen and progesterone levels. FSH and LH lose their negative feedback mechanism and their levels increase, resulting in flushing, hot flashes, bloating, headaches, and irritability.

<u>Mechanisms of Hormone Action</u>

Peptide Hormones – Composed of amino acids. Large precursor polypeptides are cleaved into individual peptides which are activated and packaged by the Golgi and released via exocytosis. Peptide hormones are charged and so cannot generally cross the phospholipid bilayers of cells. Peptide hormones must bind to receptors on cell surfaces, acting as *first messengers.* Upon binding, they stimulate *second messengers*, such as cAMP, an interaction catalyzed by *adenylate cyclase*. CAMP may then bind to intracellular targets. Peptide hormone effects may be turned on and off quickly due to the nature of the signaling cascade, but their effects usually do not last long without constant stimulation.

- **Signaling Cascade –** A messenger system in which the original message may be exponentially amplified. The actions of cAMP, and therefore the cascade, may be halted by *phosphodiesterase*.

Steroid Hormones – All steroid hormones are derived from cholesterol, a nonpolar molecule, and are therefore nonpolar themselves. Steroids can easily cross phospholipid bilayers and their receptors are usually intracellular or intranuclear. Upon binding to a receptor, they dimerize (pair up with another hormone-receptor complex). Such a dimer may attach directly to DNA to affect transcription,

altering the amounts of certain mRNA and protein in the cell to achieve their desired effects. Since transcription is not an immediate process, the effects of steroids take longer to see and take longer to wear off.

Amino Acid Derived Hormones – The least common, but very important, type of hormone. Includes epinephrine, norepinephrine, and thyroxine. They are derived from one or two amino acids, usually with a few modifications. For example, thyroxine is tyrosine plus four iodine atoms. Depending on the polarity of the molecule, they may act through a second messenger system or by entering the target cells directly.

THE NERVOUS SYSTEM

Neurons

Structure – While there are a variety of types of neurons, most have many similarities.

- **Soma –** The neuronal cell body, which contains the nucleus, ER, ribosomes, etc.
- **Dendrites –** Generally shorter processes which extend from the cell body, dendrites receive signals, send them to the cell body for processing, then another signal is sent out through the axon.
- **Axon –** A long process extending from the cell body, composed of specialized nerve fiber made to carry an electrical message,
  - **Axon Hillock –** The enlarged transition between the cell body and axon.
  - **Myelin Sheath –** Axonal covering which insulates the electrical signal and increases the velocity of the signal.
    - **Oligodendrocytes –** Myelin in the CNS.
    - **Schwann Cells –** Myelin in the PNS.
  - **Nodes of Ranvier –** Exposed areas of the axon in between individual Schwann Cells or Oligodendrocytes.
  - **Axon Terminal (Synaptic Bouton) –** The enlarged and flattened end of an axon at which the electrical signal is converted to a chemical signal and released into the synaptic cleft.
    - **Synaptic Cleft (Synapse) –** Small space between the terminal of one neuron and either the dendrites of the next neuron or a target organ. Neurotransmitter is released into this area to elicit a response in the neighboring cells.

Function

- **Action Potential –** All or none messaging system.
  - **Resting Potential**
    - **Resting Membrane Potential –** The potential voltage difference between

the inside and outside of the neuron, usually about -70mV.

- **Neuronal Selective Permeability –** Selectively permeable to sodium and potassium ions, as well as Na/Kase. The membrane is more passively permeable to sodium. The sodium/potassium pump sends sodium out of the cell and potassium into the cell, then potassium slowly leaks back out and down its concentration gradient, leaving a net negative charge within the cell. At around -70mV, the chemical gradients and electrical gradients are equal and opposite and the leak of potassium equals the influx of potassium.
  - **Na/Kase (Sodium/Potassium Pump) –** Actively pumps 2 potassium ions into a cell and 3 potassium ions out of the cell at a cost of 1 ATP. This pump never stops running.

- **Action Potential Initiation and Propagation**
  - **Depolarization –** Excitory inputs cause changes which make the cell less negative.
    - **Threshold Value –** If the *axon hillock* is depolarized to the threshold value (-55mV - -40mV), an action potential is triggered.
    - **Voltage Gated Ion Channels –** Membrane channels which respond to changes in electricity (depolarization) to initiate and propagate the wave of depolarization.
      - **Sodium Voltage Gated Channels –** Sodium voltage gated channels respond first, allowing sodium ions to rush into the cell down their electrical and chemical gradient. Sodium channels will not close until the membrane potential reaches +35mV.
      - **Potassium Gated Channels –** Potassium voltage gated channels open once the membrane potential is positive. Now the inside of the cell is overly positive and still high in potassium concentration, so potassium ions rush out and down their electrochemical gradient. This process is known as *repolarization*.
  - **Hyperpolarization –** Inhibitory inputs cause changes which make the cell more negative and less likely to depolarize. If the efflux of potassium during repolarization overshoots the resting potential (exceeding -70mV), then the cell is less likely to depolarize for a brief period until back in the range of the resting potential.
    - **Hyperpolarized Refractory Period**
      - **Absolute Refractory Period –** No amount of stimulation will cause another action potential to occur.
      - **Relative Refractory Period –** A greater than average stimulation is required to cause another action potential to occur.

<u>Synapse</u>

Synapse – The space between two neurons.

- **Presynaptic Terminal –** The neuron before the synapse.
- **Postsynaptic Terminal –** The neuron after the synapse.
- **Effector Cell –** If at the synapse a message is transferred from a neuron to a gland or muscle, that cell is termed an *effector cell*.

Neurotransmitters – Small molecules that are stored in vesicles at the axon terminal. Once the depolarization wave reaches the axon terminal, the vesicles fuse with the presynaptic membrane and release the neurotransmitters into the synapse via exocytosis. These molecules diffuse across the synaptic cleft and bind to receptors on the postsynaptic membrane. The message carried by neurotransmitters may be excitory or inhibitory.

- **Removal of Neurotransmitters –** To prevent the effects of neurotransmitters continuing indefinitely, some are broken down by enzymes in the synaptic cleft, some are recycled into the presynaptic cleft, and some simply diffuse out of the immediate area.

<u>Organization of the Vertebrate Nervous System</u>

Afferent Neurons – Carry information from periphery to the CNS.

Efferent Neurons – Carry information from the CNS to the periphery or effector cell.

Interneurons – Neurons involved only in local circuits.

Nerve – A bundle of many axons.

- Sensory Nerves
- Motor Nerves
- Mixed Nerves

Ganglia – Cluster of neuronal cell bodies in the PNS.

Nuclei – Cluster of neuronal cell bodies in the CNS.

Central Nervous System (CNS) – The brain and spinal cord. The farther up the CNS and towards the front of the brain, the more complex the function.

- **Brain –** Composed of white matter (axon bundles) and grey matter (soma clusters).
  - **Forebrain –** The most recently evolutionarily developed part of the brain.
    - **Telencephalon**
      - **Cerebral Cortex –** Convoluted grey outer layer of the brain, composed of four lobes. Responsible for highest level functioning in nervous system, including creativity and future planning.
        - Frontal Lobe
        - Parietal Lobe
        - Occipital Lobe
        - Temporal Lobe
      - **Corpus Collosum –** A structure above the thalamus, which connects the left and right hemispheres of the brain.

        - **Diencephalon** – The thalamus and hypothalamus, located directly at the center of the brain. All ascending sensory information passes through the thalamus before reaching the cerebral cortex.
    - **Midbrain –** Located inferior to the thalamus and posterior to the hypothalamus, serves as a relay point between the forebrain and other structures. Incoming information and outgoing information all pass through the midbrain.
    - **Hindbrain (Brainstem) –** Responsible for many involuntary functions, such as respiration. Located beneath the forebrain and midbrain.
        - **Cerebellum –** Checks that motor signals and sensory signals are in agreement. For instance, if you take a step and begin to fall, the cerebellum helps to adjust and react to this situation. Alcohol has profound effects on the cerebellum.
        - **Pons –** A bundle of nuclei (white matter) responsible transmitting signals in either direction, especially those to do with respiration, swallowing, hearing, equilibrium, taste, etc.
        - **Medulla Oblongata –** Modulates heart rate, breathing rate, and gastrointestinal tone.
- **Spinal Cord –** Nervous tissue running through the vertebral column, with nerves entering and exiting at each vertebra. Grey matter is deep, white matter is superficial. Sensory signals enter dorsally, while motor signals exit ventrally. The cell bodies of the sensory spinal cord neurons are clustered as *dorsal root ganglia*.
    - Cervical Section
    - Thoracic Section
    - Lumbar Section
    - Sacral Section

Peripheral Nervous System

- **Somatic Nervous System (SNS) –** Responsible for voluntary movement and reflexes. Controls primarily skeletal muscle. The SNS is a one neuron system, in which a motor neuron goes directly to a muscle without synapsing.
    - **Monosynaptic Reflex Arc –** A single synapse is between the sensory neuron that receives the sensation and the motor neuron that responds. One example is the *knee-jerk reflex* at the patellar tendon.
    - **Polysynaptic Reflex Arc –** There is at least one interneuron between the sensory neuron and motor neuron. The interneuron allows multiple effectors to be stimulated in reaction to a single stimuli. The *withdrawal reflex* is one such reflex, which usually involves withdrawing a body part while also maintaining balance or moving away from the stimulus with other body parts.
- **Autonomic Nervous System (ANS) –** Responsible for involuntary movement. Controls primarily smooth and cardiac muscle. The ANS is a two neuron system, in which two neurons work in series to transmit a message.

- **Preganglionic Neuron –** Soma is in the CNS and the axon travels to a ganglion on the PNS where it synapses with the soma of a postganglionic neuron which the affects the target tissue.
- **Postganglionic Neuron**
- **Sympathetic Nervous System –** Fight or flight, increases skeletal muscle activity, increases breathing and heart rate. *Preganglionic neurons* use acetylcholine, *postganglionic neurons* use epinephrine.
- **Parasympathetic Nervous System –** Rest and recovery, increases digestive function, decreases breathing and heart rate. Both p*reganglionic and postganglionic neurons* use acetylcholine.
  - **Vagus Nerve –** A major parasympathetic nerve, rooted as a cranial nerve and serving the thorax. It slows heart rate and breathing rate.

<u>Special Senses</u>

Sensory Neurons

- **Interoceptors –** Monitor internal environment parameters, such as blood volume, pH, and partial pressure of CO2.
- **Proprioceptors –** Monitor body positioning.
- **Exteroceptors –** Responsible for monitoring the external environment, such as light, sound, touch, taste, and temperature.
- **Nociceptors –** Sense pain.

The Eye

- **Sclera –** The white covering of the eye, covers the entire outer surface except at the cornea.
- **Choroid –** A layer directly beneath the sclera which provides nutrients and oxygen to the eye.
- **Retina –** Inner layer of the eye, containing photoreceptors which convert light into a nervous signal. The outer eye linings enclose posterior chamber and the inner fluid of the eye, the *vitreous humor*.
  - **Rods –** Transmit black and white images and respond to low light situations. More useful at night.
    - **Rhodopsin –** The only pigment found in rods.
  - **Cones –** Transmit color images, but are less sensitive to light in general. Only useful during the day.
    - **Red Cones –** Absorb red light.
    - **Green Cones –** Absorb green light.
    - **Blue Cones –** Absorb blue light.
- **Cornea –** A transparent outer structure which bends and focuses light. The cornea encloses the anterior chamber of the eye and the *aqueous humor*.
- **Pupil –** The opening through which light passes.
  - **Iris –** The pigmented muscular structure which alters the diameter of the pupil

to adjust the amount of light entering the eye.
- **Lens –** The structure behind the pupil which does the final focusing of light.
  - **Ciliary Muscles –** Adjust the thickness of the lens.
  - **Suspensory Ligament –** Suspends the lens and attaches it to the ciliary body.
- **Bipolar Cells –** Photoreceptors send signals to bipolar cells, which relay that information to the *retinal ganglion cells*.
- **Optic Nerve –** The axons of the retinal ganglion cells bundle to form the optic nerve, which exits at the back of the eye.
  - **Blind Spot –** Near the optic nerve is a blind spot caused by the displacement of photoreceptors by the optic nerve.

The Ear – The ear transduces sound waves into electrical signals and contains nerves that aid in coordination and balance.

- **Outer Ear**
  - **Auricle (Pinna) –** Outer ear structure, funnels sound towards the auditory canal.
  - **Auditory Canal –** Funnels sound towards the ear drum.
- **Middle Ear**
  - **Tympanic Membrane (Eardrum) –** Sound causes the eardrum to vibrate which then causes the ossicles to vibrate.
  - **Ossicles (Middle Ear Bones) –** Transmits vibration through the *oval window* and into the fluid filled inner ear.
    - **Malleus**
    - **Incus**
    - **Stapes**
- **Inner Ear –** Ossicle vibration at the oval window causes fluid waves within the inner ear that depolarize the *hair cells* of the cochlea. Action potentials from the hair cells travel via the *auditory nerve* to the brain.
  - **Semicircular Canals –** There are 3 semicircular canals in each ear, one oriented in each plane. The canals are filled with *endolymph*, whose movement through the canals puts pressure on the hair cells inside. The brain interprets the fluid movement in each canal and processes that to determine acceleration/deceleration and balance.

The Chemical Senses

- **Gustatation (Taste) –** Taste receptors are located on the tongue, soft palate, and epiglottis. Each one is composed of about 40 epithelial cells, with microvilli protrusions which have the actual taste receptors. Nerve fibers weave around the taste buds. There are four taste sensations: sweet, sour, salty, and bitter.
- **Olfaction (Smell) –** Olfactory receptors are found in the olfactory membrane, in the upper part of the nostrils. The receptors are specialized neurons from which cilia project. Odorous substances bind to receptors on the cilia, depolarizing the olfactory receptors. Axons from the olfactory receptors bundle into the *olfactory*

nerves, which project directly into the *olfactory bulbs* in the base of the brain.

GENETICS

Introduction

Chromosomes – A structure of DNA. A section of chromosome that codes fro a specific trait is a *gene*.

- **Genes –** The heritable traits that can be passed on from one generation to the next.
  - **Alleles –** Different forms of a gene, such as different blood types or different hair color.

Genotype – The allelic distribution of genes in an organism.

Phenotype – The outward appearance of an organism, based on genotype.

Mendelian Genetics

True Breeding – Breeding in which the offspring only ever have the same traits as in the parents.

Mendel's Firs Law (Law of Segregation)

- **Tenets of the Law of Segregation**
  1. Genes exist in alternative forms (alleles).
  2. An organism has two alleles for each gene, one from each parent.
  3. The two alleles segregate during meiosis, resulting in gametes that carry only one allele for each trait.
  4. If the two alleles are different, only the *dominant allele* will be fully expressed. If both alleles are the same, that individual is *homozygous*. Otherwise, they are *heterozygous*.
- **Monohybrid Cross –** A cross in which only one trait is studied.
  - **P Generation (Parent) –** The individuals being crossed.
  - **F Generation (Filial) –** The offspring.
    - **Self Cross –** The crossing of a particular F generation with itself.
- **Punnett Square –** A diagram which predicts the relative genotypic and phenotypic frequencies resulting from crossing two individuals.
- **Test Cross / Back Cross –** The crossing of an unknown (AA or Aa) plant with a plant of recessive (aa) phenotype/genotype to determine the genotype of the unknown plant. If the offspring genotypes are known, we can work backwards in a *back cross*.

Mendel's Second Law (Law of Independent Assortment) – Each gene's inheritance (assortment) is independent of (unrelated to) the inheritance of any other genes.

- **Dihybrid Cross –** A cross in which two traits are studied.

- **Unlinked Genes –** Genes that operate according to Mendel's Second Law.
- **Linked Genes –** Genes that are inherited together, and to which Mendel's Second Law does not apply.
- **Statistical Analyses**
  - 1:1 – Heterozygous Dominant X Homozygous Recessive
  - 3:1 – Heterozygous Dominant X Heterozygous Dominant

<u>The Chromosomal Theory of Inheritance</u>

Segregation and Independent Assortment

- **Diploid Species –** Those with homologous chromosomes. Each homolog carries a different allele.
- **Reductional Division (Meiosis I) –** Cells are reduced from diploid to haploid, homologous pairs separate, but sister chromatids remain attached until Meiosis II. Since this is when alleles split, independent assortment occurs during Meiosis I.

Nonindependent Assortment and Genetic Linkage

- **Genetic Linkage –** Two genes that are located close to each other on the chromosome are likely to be inherited together. During Meiosis I, homologs separate into different cells. If two genes are on the same chromosome, they tend to segregate together.

Recombination Frequencies: Genetic Mapping

- **Recombination (Crossing Over) –** The process by which two DNA molecules exchange genetic information, resulting in a new combination of alleles. This happens when homologs pair up into *tetrads* in Prophase I.
- **Recombination Frequencies**
  - **Completely Linked Genes –** 0% chance of recombination.
  - **Completely Unlinked Genes –** 50% chance of recombination.
- **Genetic Map –** A diagram showing the relative distance between the genes on a chromosome.
  - **Map Unit –** By convention, one map unit corresponds to a 1% chance of recombination occurring.

<u>Variations on Mendelian Genetics</u>

Incomplete Dominance – Cases in which neither allele is dominant, resulting in a phenotype which is a mixture of the two parental phenotypes. This mixture is expressed as a spectrum. For instance, a red and white flower produce a pink flower.

Codominance – Cases in which both alleles are dominant, resulting in a phenotype which is a mixture of the two parental phenotypes. For instance, a red and white flower produce a red and white spotted flower. Another example is blood type.

Penetrance – The number of individuals in a population carrying the alleles who actually express the phenotype.

- **High Penetrance –** Most or all of the individuals with the dominant gene express it, such as in Huntington's Disease. However, it is not *fully penetrant*, as 5% of individuals with the affected allele do not express the traits of Huntington's.

Expressivity – The varying expression of disease symptoms despite identical genotypes.

Inherited Disorders

- **Recessive Disorders –** For a recessive disease to present, the individual must be homozygous recessive. This usually results from the mating of two carriers or one carrier and one recessive homozygote.
  - **Carriers –** Heterozygotes are carriers for such disease, as they may pass it to their offspring but will not express the disorder themselves.
  - **Early Acting Lethal Disorders –** Disorders which cause death before the individual may reproduce, either during fetal development or early childhood.
- **Dominant Disorders –** Only one copy of the allele is required for the disorder to be expressed.
  - **Late Acting Lethal Disorder –** Disorders which cause death later in life, well after the individual would have had a chance to reproduce.

Sex Determination

- **Autosomes (Somatic Chromosomes) –** The first 22 chromosomes.
- **Allosomes (Sex Chromosomes) –** The 23rd chromosome, which determines sex.
  - **Female Allosomes** - XX
  - **Male Allosomes** - XY

Sex Linkage – Females have 2 X chromosomes, so may be homozygous or heterozygous for genetic conditions on those chromosomes. Males have only one X chromosome, so if that chromosome is affected, the male will express that condition.

- **Hemizygous –** A male with a genetic condition on his only X chromosome. Because they do not have another X chromosome to mask the condition on that chromosome, X-linked recessive diseases are much more common in males.

<u>Pedigree Analysis</u>

Pedigree – A diagram shoeing the genetic distribution of traits for multiple generations of an organism.

<u>Chromosomal Aberrations</u>

Numerical Abnormalities

- **Normal Diploid –** 46 Chromosomes (23 Pairs of Chromosomes).
- **Aneuploidy (Abnormal Diploid) –** An abnormal number of chromosomes, commonly caused by nondisjunction in which homologs or sister chromatids fail to separate. Other than Trisomy 21, most aberrations result in spontaneous abortion before birth (unless they are on the sex chromosome, which is more resilient).
  - **Monosomy –** A single chromosome.

    - **Trisomy –** A grouping of 3 chromosomes.
    - **Sex Aberrations**
        - **XO –** Females with a single X chromosome.
        - **XXX –** Females with 3 X chromosomes, metafemales.
        - **XXY –** A male with breasts and undescended testes, usually sterile.
        - **XYY –** A taller than average male.

Chromosomal Breakage – Chromosomes may be damaged spontaneously or by environmental factors.

- **Deletion Mutation –** The loss of chromosomal material.
    - **Duplication –** When the deleted fragment joins a homologous chromosome.
    - **Translocation –** When the deleted fragment joins another chromosome.
- **Inversion Mutation –** A piece of genetic material is removed, then inverted and reattached in the same place it was originally, only upside down now.

MOLECULAR GENETICS

DNA

Deoxyribonucleic Acid (DNA) – Polynucleotide organic molecule which carries genetic information. In eukaryotes, generally in a double stranded helix shape. The nature of DNA only allows for transcription and translation to work in a 5' → 3' direction.

- **Nucleotide –** The basic unit of DNA. (No Spoon)
    - **Deoxyribose Sugar –** The backbone, to which Nitrogenous bases and Phosphate groups are attached.
    - **Nitrogenous Base –** Hydrogen bonds hold complementary nitrogenous bases together. C always bonds to G and A always bonds to T (or U).
        - **Pyrimidines –** Single ringed nitrogenous bases.
            - **Cytosine (C)**
            - **Thymine (T)/Uracil (U)**
        - **Purines –** Double ringed nitrogenous bases.
            - **Adenine (A)**
            - **Guanine (G)**
    - **Phosphate Group**

Antiparallelity – One strand of DNA has a 5' → 3' polarity, while the complementary strand has a 3' → 5' polarity. Enzymes can only move along DNA in a 5' → 3' direction. At the 5' end, an OH group is at the number 5 carbon, at the 3' end, an OH group is at the number 3 carbon.

- **Watson Crick DNA Model –** The double stranded helical antiparallel model.

Eukaryotic DNA Replication – DNA undergoes a *semiconservative* replication mechanism, in which 1 original strand and 1 new strand compose each new double stranded molecule.

- **Origin of Replication –** An area at which DNA is unwound so that replication y begin.
  - **Replication Forks –** The splitting shape of DNA where it is being unwound and split for replication. The replication forks begin at the *origin of replication* and move in opposite directions.
- **Unwinding and Initiation –** Unwinding occurs in both directions, simultaneously
  - **DNA Helicase –** The enzyme responsible for unwinding the helix to generate two single strands from one double strand.
  - **Single-Strand Binding Proteins (SSB) –** Proteins which attach to each single strand after they are split to keep them from rewinding and reassociating.
  - **Topoisomerase/DNA Gyrase –** Moves ahead of DNA Helicase to prevent *supercoiling*, which is overwinding of the helical structure.
  - **DNA Polymerase –** The enzyme responsible for adding the individual nucleotides to the growing strand. However, Polymerase requires an *RNA primer* to know where to start.
  - **RNA Polymerase/Primase –** Enzyme which generates the *RNA primer* on a single strand of DNA so that Polymerase will know where to begin.
- **Synthesis**
  - **Leading Strand –** The 5' → 3' strand, which the *DNA Polymerases* can continuously form.
  - **Lagging Strand –** The 3' → 5' strand, which the *DNA Polymerase* must work on backwards (5' → 3'), away from the formation of the replication fork. DNA polymerase molecules work on small sections of about 1000 base pairs at a time, these sections are known as *Okazaki Fragments*.
    - **DNA Ligase –** Enzyme which works to connect all of the discontinuous *Okazaki Fragments*.

<u>RNA</u>

Ribonucleic Acid (RNA) – Similar to DNA, except the deoxyribose sugar is replaced with ribose sugar, it is usually single stranded rather than double stranded, and the pyrimidine base Uracil (U) replaces Thymine (T).

- **Messenger RNA (mRNA) –** During transcription, mRNA carries the genetic message from the nucleus to the ribosomes in the cytoplasm, since DNA cannot leave the nucleus. The genetic information is caried in codon units.
  - **Monocistronic –** In eukaryotes, each mRNA message will only be translated into one peptide product.
  - **Polycistronic –** In prokaryotes, each mRNA message may be translated into

multiple different peptide products, depending on where on the mRNA ribosomes begin reading the message.

- **Transfer RNA (tRNA) –** Once the genetic message reaches a ribosome, amino acids must be linked to the nascent polypeptide chain. There are about 20 amino acids and there is a specific tRNA for each amino acid. The tRNA with an anticodon which matches the mRNA codon will provide its amino acid to the ribosome.
- **Ribosomal RNA (rRNA) –** Ribosomal RNA, along with specialized proteins, compose ribosomal subunits, and overall a ribosome. Ribosomal RNA is necessary for proper function of the Ribosome.
- **Heterogeneous Nuclear RNA (hnRNA) –** The precursor to mRNA. HnRNA is much larger and also includes riboproteins in its structure.

<u>Protein Synthesis (Eukaryotic)</u>

Transcription – The encoding of RNA with the genetic information, so that it may transfer it from the nucleus to the cytoplasm. The DNA itself could not make the trip, as it would be quickly degraded outside of the nucleus. Note that Transcription produces hnRNA (pre-mRNA), which will later be converted to mRNA.

- **Antisense Strand –** DNA is unwound in a process similar to replication, but only one strand is used to transfer the information to mRNA, this strand is called the *antisense strand*.
- **RNA Polymerase –** The enzyme which catalyzes the production of the RNA strand.
- **Promoters –** Specific sequences of DNA which signal to the enzymes where to begin transcription.
- **Termination Sequences –** Specific sequences of DNA which signal to the enzymes to detach and end transcription.

Post-Transcriptional Processing -Before hnRNA can leave the nucleus, it must undergo processing which will allow it to properly interact with the ribosomes. Once processing is complete, the RNA molecule is considered mRNA.

1. A 5' cap must be added to stabilize and protect the starting end of the transcript.
2. A 3' tail must be added to stabilize and protect the ending end of the transcript.
3. Noncoding regions (introns) are removed, so that only coding regions (exons) remain.

The Genetic Code

- **Codon –** A 3 letter nucleotide sequence which codes for a specific amino acid.
- **Degeneracy/Redundancy –** With 4 nitrogenous bases (A,C,G, and T/U) and 3 nitrogenous bases per codon, a total of 64 codons can be made (4^3). However, there are only 20 amino acids for which these codons can code for. This gross excess of codons is the redundancy of the genetic code. The more codons code for a single amino acid, the more “redundant” or “degenerate” that amino acid is.

More commonly used amino acids are generally more redundant. Thanks to redundancy, a change in the genetic code does not always result in an altered protein.

Translation – The process of translating the nitrogenous base sequence into an amino acid sequence to produce peptides or polypeptides/proteins.

- **tRNA –** On one end tRNA has nucleotides complementary to the mRNA, this is the *anticodon*. On the other end tRNA is bound to the amino acid that corresponds to the codon in question.
  - **tRNA Synthetase –** An enzyme that helps bind the appropriate amino acid to the tRNA molecule. The "charged" or "loaded" tRNA then detaches.
  - **Aminoacyl-tRNA Complex –** A "charged" tRNA-amino acid complex
- **Ribosomes –** An organelle composed of 2 subunits, one large and one small, each made of ribosomal proteins and rRNA.
  1. **A Site –** Attachment site which holds the Aminoacyl-tRNA Complex.
  2. **P Site –** Polypeptide site at which the polypeptide chain is actually composed.
  3. **E Site –** Exit site for the polypeptide.
- **Polypeptide Synthesis**
  - **Initiation –** mRNA binds to a small ribosomal subunit in the presence of *initiation factors*. The ribosome slides down the mRNA until it reaches a start codon.The initiation Aminoacyl-tRNA Complex, *Methionine tRNA*, pairs with the start codon. At this point the large ribosomal subunit joins. At this point, the tRNA is at the *P Site* as it is the beginning of the polypeptide chain.
  - **Elongation –** Once the complex has been formed, the ribosome can slide along the mRNA, adding amino acids as it goes. The *A Site* is filled with the mRNA codon and tRNA anticodon, which hydrogen bond together. *Peptidyl Transferase* uses the energy stored in the Aminoacyl-tRNA complex at the P site to form a peptide bond between the amino acid in the A site and the Methionine in the P site. *Translocation* is necessary to add the next amino residue. *Translocation* is the sliding of the ribosomal complex down the mRNA, expelling the uncharged tRNA and moving the tRNA complex from the A site to the P site, the A site is now empty and waiting for the next tRNA.
  - **Termination –** Once a *termination codon* enters the A site, instead of a new tRNA complex binding to the A site, a protein called *release factor* binds to the termination codon, allowing the end of the peptide chain to be expelled from the P site.
- **Polyribosome –** The act of multiple ribosomes simultaneously translating a single strip of mRNA.

Post-Translational Modifications – Polypeptides may be modified following transcription. These modifications include:

- Cleavage
- Addition of sugars

- Addition of phosphate groups (phosphorylation)
- Addition of carboxyl groups (carboxylation)
- Addition of methyl groups (methylation)

Mutations

- **Base Pair Mutations/Point Mutation –** A mutation occuring at only a single nucleotide residue. Depending on where it is in the residue, and genetic redundancy, it may or may not have an effect on the final polypeptide.
  - **Silent Mutation –** A point mutation, usually in the third codon position, which causes an amino acid change in the final polypeptide product thanks to redundancy.
  - **Missense Mutation –** A point mutation, usually in the first or second codon position, which causes an amino acid change in the final polypeptide product.
  - **Nonsense Mutation –** A point mutation which changes the its codon to a stop codon, resulting in premature termination of the polypeptide chain. The effect this has on the final polypeptide product depends on where in the genetic chain it occurs. If early, it could be disastrous, if late it may just slightly reduce polypeptide function.
- **Frame Shift Mutation**
  - **Base Pair Insertion –** The addition of one or more nucleotides, resulting in a shift of the reading frame (unless three are added together). May result in a change to the remainder of the polypeptide and may also result in a nonsense mutation.
  - **Base Pair Deletion –** The removal of one or more nucleotides, resulting in a shift of the reading frame (unless 3 are removed together). May result in a change to the remainder of the polypeptide and may also result in a nonsense mutation.

Mutagenesis

- DNA polymerase may make mistakes during DNA replication.
- Ionizing radiation may damage DNA.
- Elements known as *transposons* may insert/remove themselves into the genome.

<u>Viral Genetics</u>

Viral Structure – Viruses may only contain a few genes or may contain a few hundred genes. Their genetic material may be single stranded or double stranded RNA or DNA. Viruses also have a protein coat surrounding the genetic material, called a capsid. Viruses are specific to certain hosts and may even be specific to only certain cell types within that host.

Infection of Host Cell – Viruses cannot reproduce on their own and so must invade a host cell and hijack its machinery. Viruses can only affect cells which recognize and interact with the viral *capsid*, otherwise the cell is essentially invisible to the virus. Some viruses may only insert some genetic material into the host cell,

leaving the capsid attached to the outside. Some viruses may insert their genetic material and capsid into the host cell.

Genome Replication and Transcription

- **DNA Containing Viruses**
  - **DNA Viruses that Enter the Nucleus –** Since these viruses are DNA based, they may enter the nucleus and hijack the human enzymes directly without needing to bring any enzymes of their own.
  - **DNA Viruses that do not Enter the Nucleus –** These viruses are DNA based, but since they never enter the nucleus (they operate within the cytoplasm) which is where our DNA replicating enzymes are located they must bring along enzymes of their own.
- **RNA Containing Viruses –** RNA viruses operate in the cytoplasm only. Since we do not have RNA replicating enzymes, they may either bring along such enzymes as *RNA replicase* or they may substitute their RNA for our mRNA and allow our enzymes to produce peptides on their behalf.
  - **Retroviruses –** A subclass of RNA viruses which create DNA from RNA using an enzyme called *reverse transcriptase*. These viruses then integrate the newly synthesized DNA into the host genome, where it will eventually be replicated, transcribed, and translated into peptides. A well known retrovirus is HIV.

Translation and Progeny Assembly – The viral genome is translated into proteins using the ribosomes, tRNA, amino acids, and enzymes of the host cell. These proteins are usually structural and serve as components for new viral particles, called *virions*. A single virus may create hundreds or thousands of virions.

Progeny Release – There are two main options for progeny release.

- **Cellular Lysis –** The cell may burst (lyse) due to the number of viruses within or the viral infection may initiate apoptosis of the host cell. The disadvantage to this is that the virus can no longer use this cell to continue its life cycle.
- **Extrusion –** The virus leaves the host cell by fusing with the plasma membrane and budding/pinching off of the outside. The advantage of extrusion is that it keeps the host cell alive, which may then continue viral production.

Bacteriophages – Viruses that specifically target bacteria. Bacteriophages insert their genetic material into a bacterium, leaving their protein coat attached to the outer surface of the cell membrane. Depending on the specific phage, the virus may enter a *lytic* or *lysogenic* cycle.

- **Lytic Cycle –** The virus produces virions to the extent that the cell swells and eventually bursts (lyses). These viruses are termed *virulent*.
- **Lysogenic Cycle –** The virus incorporates its genetic material into the host genetic material. As the host reproduces, it also reproduces the viral genome. Eventually, due to the environment, chemicals, radiation, etc., lysogenic viruses will enter the lytic cycle.
  - **Superinfection –** Infection by one strain of phage generally makes the bacteria

less susceptible to infection by other phages.

Bacterial Genetics

Bacterial Genome – Bacteria are prokaryotes, single celled organisms with circular DNA and no membrane bound organelles. However, the genome does localize to an area within the cell known as the *nucleoid*. Bacterial transcription and translation occur in the same area at almost the same time, since there are no membranes separating the process and no pretranslational processing to be done. Note that, unlike eukaryotic mRNA, bacterial mRNA is polycistronic, meaning that one strand of mRNA can code for multiple proteins depending on where on that strand the enzymes begin translation.

- **Plasmids –** Extrachromosomal rings of self replicating DNA which often code for antibiotic properties.
  - **Episomes –** A subset of plasmids which are capable of integrating into the bacterial genome.

Replication – There is only ever one *origin of replication* on a bacterial chromosome, since it is circular and contains relatively few genes.

Genetic Variance

- **For Favorable/Stable Environments (Maintains current attributes)**
  - **Binary Fission –** A method of asexual reproduction implemented in stable and favorable environmental conditions to rapidly produce offspring that are exact copies of the parent cell.
- **For Unfavorable/Unstable Environments (Increases genetic diversity)**
  - **Transformation –** The integration of foreign genetic material (plasmid) into the host genome. The result is a bacterium genetically unique from the original bacterium or other bacteria from the same generation.
  - **Conjugation –** Similar to sexual reproduction, it involves two bacteria forming a *cytoplasmic bridge*, which allows for the transfer of genetic material. The transfer is from the male (F+) to the female (F-). The male may donate a portion of the F+ genome so that both bacteria will be male or may donate the entire F+ genome so that the male becomes female and the female becomes male. If the plasmid genome has been integrated into the male DNA (transformation) the bacteria may attempt to donate its entire genome, although the bridge usually collapses before the transfer is complete. Bacteria which have undergone this change are referred to as *Hfr*, high frequency recombination.
    - **Sex Pilus –** The male appendage which forms the *cytoplasmic bridge*.
    - **Sex Factors –** Specialized plasmids that serve as the sex factor. The most well studied is the F factor.
  - **Transduction –** A transfer of genetic material from one bacterium to another via a bacteriophage. If the phage genome incorporates into the bacterial

genome and then excises it may take bacterial DNA with it. Once the virus infects a new cell this DNA incorporates into the new bacterium's genome.

Gene Regulation – Prokaryotic genetic regulation is primarily at the transcriptional level. Transcription is based on RNA Polymerase's access to the genome, which is directed by *operons*.

- **Operon –** A genetic unit which marks the starting point for transcription, comprised of *structural genes*, an *operator gene*, a *promoter gene*, and a *regulator gene*..
  1. **Regulator Gene –** Codes for a protein known as the *repressor*, which binds to the operator and acts as a negative feedback to prevent polymerase from moving from the promoter gene to the structural genes.
     - **Inducible System –** Repressor proteins are constantly produced. Transcription requires the presence of a molecule known as an *inducer* which binds to the *inducer* to prevent it from blocking transcription.
     - **Repressible System –** Repressor proteins are constantly produced, but cannot bind to the operator without the assistance of a *corepressor* molecule. The corepressor is often an end product of transcription.
  2. **Promoter Gene –** Provides a binding site and starting point for RNA polymerase.
  3. **Operator Gene –** Nontranscribable region of DNA capable of binding a *repressor gene*.
  4. **Structural Genes –** Genes which code for the protein of interest.

EVOLUTION

Theories of Evolution

Lamarck's Theory of Evolution – An early, and now disproven, theory that *use* and *disuse* of certain organs and tissues would either lead them to develop or atrophy. Over time, the development or atrophy of these tissues/organs would lead to new species. NOTE: The main reason Lamarck was wrong is the fact that traits are inherited, not acquired or developed.

- **Acquired Characteristics –** Characteristics of an organism developed through *use/disuse*.

Darwin's Theory of Evolution – Darwin's original theory, proposed in *On the Origin of Species*. Darwin's theory would be proven mostly correct, and with some refinements led to *Neo-Darwinism*, which is the modern and most widely accepted evolutionary theory.

1. Organisms produce offspring, some of which survive until maturity to produce more offspring.

2. Chance variations within a population may be *inheritable*. Such variations that increase the chances of surviving until maturity to produce more offspring are termed *favorable*.
3. More individuals with greater preponderance of *favorable* traits will on average survive until maturity to produce more offspring, and so such desirable traits will on average be passed on more so than undesirable traits. This process is called *natural selection*. Over long periods of time, aggregations of traits result in speciation. *Fitness* is the reproductive success of an organism.

Neo-Darwinism (The Modern Synthesis) – The same as Darwin's Theory, but with the addition of *differential reproduction*.

- **Differential Reproduction –** Genes ultimately change due to mutation or recombination. When such a genetic change is favorable it is more likely to be passed on, the opposite is also true. The genes passed on more often become more pervasive in the *gene pool*, which is the sum total of all genes from all individuals within a population at a given time. NOTE: The gene pool, and therefore the population is what changes over time. An individual/species does not evolve, a population does.

Punctuated Equilibrium Theory – The observation of the fossil record showing that certain populations experience bursts of rapid evolution over short periods of time rather than experiencing very gradual evolution over long periods of time.

<u>Evidence of Evolution</u>

Evidence in Paleontology – Evidence gathered by relating the ages of different fossils to their anatomies and relative abundances, as determined by radiographic dating, to determine the chronological succession of species in the fossil record.

Evidence in Biogeography – Evidence suggestive of *divergence*, in which organisms of the same species that become separated may evolve in different ways. Ex: The various flora and fauna that Darwin studied in the Galapagos Islands.

Evidence in Comparative Anatomy – Evidence of the degree of similarity of similar structures in different species.

- **Homologous Structures –** Similar in structure and sharing a common evolutionary origin. (Ex: bat wings, human arms, whale flippers)
- **Analogous Structures –** Serve a common purpose, but evolved separately in each species. (Ex: bird wings, insect wings)
- **Vestigial Structures –** Remnants of organs which have lost their ancestral function. (Ex: human coccyx, human appendix)

Evidence in Comparative Embryology – Evidence found by analyzing similarities between the embryos of different species. (Ex: gills which exist at some point in development of all chordates (including humans))

Evidence in Molecular Biology – Evidence found by analyzing similarities in the DNA of different species to determine their degree of similarity. (Ex: chimpanzees are 95% similar to humans, mice are 85% similar to humans.

Genetic Basis of Evolution

Hardy Weinberg Equilibrium – How often an allele appears in the gene pool is called the *gene frequency*. Evolution is a result of changes in gene frequencies in the gene pool over time. When the gene frequencies do not change, the gene pool is in equilibrium and evolution does not occur. There are 5 criteria for equilibrium:

1. A large population.
2. No mutations within the population.
3. Mating within the population is random.
4. No migration of individuals into or out of the population.
5. Genes in the population are all equally successful at reproducing.

If all criteria have been met, the population is in *Hardy-Weinberg Equilibrium*.

- **p** = frequency of the dominant allele (A).
- **q** = frequency of the recessive allele. (a)
- **p + q = 1**, for frequencies of alleles in a population
- $\mathbf{(p + q)^2 = 1^2}$ or $\mathbf{p^2 + 2pq + q^2 = 1}$, for frequencies of phenotypes in a population
  - where p^2 = frequency of AA (Dominant Homozygotes)
  - where 2pq = frequency of Aa (Heterozygotes)
  - where q^2 = frequency of aa (Recessive Homozygotes)

Microevolution – Microevolutionary mechanisms often disturb the Hardy Weinberg Equilibrium. Microevolution within a population generally occurs over relatively short periods of time, tens to hundreds of years.

- **Natural Selection –** Genotypes with favorable variations are selected through natural selection and the frequencies of those genotypes increase naturally in the gene pool.
- **Mutation –** Gene mutations change allele frequencies in a population, shifting gene equilibria.
- **Assortive Mating –** If mates are not random, but instead determined by phenotype or proximity, the relative genotype ratios will be affected.
- **Genetic Drift –** Changes in the composition of the gene pool due to chance. The *founder effect* is an example of genetic drift, in which an isolated population also has an isolated gene pool.
- **Gene Flow –** Migration of individuals between populations result in a loss or gain of portions of the gene pool.

Modes of Natural Selection

Natural Selection – Evolutionary method capable of generating change over long periods of time, thousands to millions of years.

- **Stabilizing Selection –** Stabilizing selection maintains phenotypes within a certain range by eliminating extremes. For instance, birth weight. Fetuses that weigh too little may not be healthy enough too survive, fetuses that weigh too

much may be injured during birth.

- **Directional Selection –** The emergence and dominance of an extreme phenotype in response to pressures to adapt. For instance bacteria with antibiotic resistance, or insects with insecticide resistance.
- **Disruptive Selection –** Extreme phenotypes to both sides of the norm are expressed more as the norm is suppressed. For instance, the Galapagos finches that Darwin studied either had large beaks or small beaks, unlike their medium beaked ancestors. This is because the seeds on the island were all very large or very small, selecting for large and small beaks and suppressing medium beaks.

Altruistic Behavior

Altruistic Behavior – When social organisms sacrifice advantageous traits for the benefit of others. For instance, worker insects which are sterile and only exist to support the reproducing insects.

- **Kin Selection –** Organisms may behave altruistically if they are closely related to successfully reproductive organisms.
- **Inclusive Fitness –** The number of alleles an individual passes on to the next generation, even if only indirectly through altruistic behavior.

Speciation

Speciation – The emergence of new species, commonly due to extended periods of isolation. Once the point of *reproductive isolation* has been reached, the two species may be considered distinct.

- **Prezygotic Isolating Mechanisms**
  - **Temporal Isolation –** Isolation caused by each group breeding at different times of the day or during different seasons.
  - **Ecological Isolation –** Isolation caused by two groups living in the same territory, but in different habitats. They rarely meet and so rarely mate.
  - **Behavioral Isolation –** Isolation caused by lack of interest in each other, perhaps due to pheromones, courtship displays, etc.
  - **Reproductive Isolation –** Isolation caused by the incompatibility of genitalia.
  - **Gametic Isolation –** Isolation caused when intercourse may occur, but fertilization may not.
- **Postzygotic Isolating Mechanisms**
  - **Hybrid Inviability –** Genetic incompatibilities result in abortion of the hybrid zygote, even if intercourse and fertilization are successful.
  - **Hybrid Sterility –** Hybrid offspring are sterile and incapable of further reproducing.
  - **Hybrid Breakdown –** First generation hybrids are viable and fertile, but second generation hybrids are not.

Adaptive Radiation

Adaptive Radiation – When a single ancestral species gives rise to a number of different species. Each new species occupies a unique ecological *niche*. For example, Darwin's ancestral finch led to the development of 13 new finch species. Such rapid evolution to fill niches decreases competition for limited resources.

Patterns of Evolution

Convergent Evolution – The independent development of similar characteristics in two or more lineages not sharing a recent common ancestor. Such characteristics are usually in response to similar environmental pressures.

Divergent Evolution – The independent development of dissimilar characteristics in two or more lineages sharing a recent common ancestor. Such characteristics are usually in response to isolation, separation, and different environmental pressures.

Parallel Evolution – The development of similar characteristics in related species in response to analogous environmental selection pressures.

Origin of Life

Formation of Organic Molecules (Monomers & Polymers)

- **Early Atmosphere –** High mounts of Carbon, Hydrogen, and Nitrogen, along with lesser amounts of Oxygen. Suggested by Oparin and Haldane.
  - **Primordial Soup –** The early mixture of Carbon, Hydrogen, and Nitrogen and sea water.
- **Miller –** Carried out an experiment in which he mixed gases of the early atmosphere and exposed them to an electrical discharge to produce organic molecules and even self replicating RNA.

Formation of Protobionts – Abiotically produced organic polymers in aqueous solution have been shown to assemble spontaneously into protocells called *microspheres*. Microspheres exhibit many characteristics of life, but not all.

Formation of Genetic Material – Protobionts could theoretically grow and divide but did not have an adequate way of passing genetic material onto the next generation. Eventually, nucleotides self assembled into RNA, which was capable of self replicating. In time, evolutionary trends pushed towards the more stable DNA molecules over RNA.