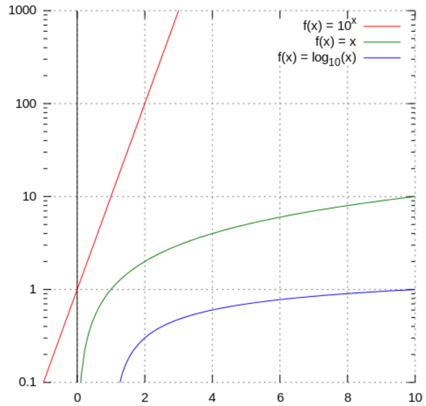
AAMC Content Outline

General Math

- Recognize and interpret linear, semilog, and log-log scales and calculate slopes from data found in figures, graphs, and tables



Semi-log graph or semi-log plot is a way of visualizing data that are related according to an exponential relationship. One axis is plotted on a logarithmic scale.

This kind of plotting method is useful when one of the variables being plotted covers a large range of values and the other has only a restricted range

- Demonstrate a general understanding of significant digits and the use of reasonable numerical estimates in performing measurements and calculations
- Use metric units, including converting units within the metric system and between metric and English units (conversion factors will be provided when needed), and dimensional analysis (using units to balance equations)

Engineering Notation	
Name/Symbol	Multiplier
pico (p)	10^{-12}
nano (n)	10^{-9}
micro (μ)	10^{-6}
milli (m)	10^{-3}
1	10^{0}
Kilo (K)	10^{3}
Mega (M)	10^{6}
Giga (G)	10^{9}
Tera (T)	10^{12}

- Perform arithmetic calculations involving the following: probability, proportion, ratio, percentage, and square-root estimations
- Demonstrate a general understanding (Algebra II−level) of exponentials and logarithms (natural and base 10), scientific notation, and solving simultaneous equations
- Demonstrate a general understanding of the following trigonometric concepts: definitions of basic (sine, cosine, tangent) and inverse (sin–1, cos–1, tan–1) functions; sin and cos values of 0°, 90°, and 180°; relationships between the lengths of sides of right triangles containing angles of 30°, 45°, and 60°
- Demonstrate a general understanding of vector addition and subtraction and the right-hand rule (knowledge of dot and cross products is not required)

Scientific Inquiry and Reasoning Skills

1) Knowledge of Scientific Concepts and Principles
- Demonstrating understanding of scientific concepts and principles
- Identifying the relationships between closely-related concepts

2) Scientific Reasoning and Problem Solving
- Reasoning about scientific principles, theories, and models
- Analyzing and evaluating scientific explanations and predictions

3) Reasoning about the Design and Execution of Research
- Demonstrating understanding of important components of scientific research

- Reasoning about ethical issues in research

4) Data-Based and Statistical Reasoning

- Interpreting patterns in data presented in tables, figures, and graphs
- Reasoning about data and drawing conclusions from them

Biological and Biochemical Foundations of Living Systems

"*This section tests processes that are unique to living organisms, such as growing and reproducing, maintaining a constant internal environment, acquiring materials and energy, sensing and responding to environmental changes, and adapting. It also tests how cells and organ systems within an organism act independently and in concert to accomplish these processes, and it asks you to reason about these processes at various levels of biological organization within a living system*"

Foundational Concept 1: Biomolecules have unique properties that determine how they contribute to the structure and function of cells and how they participate in the processes necessary to maintain life.

1A. Structure and function of proteins and their constituent amino acids

Amino Acids (BC, OC)

Description

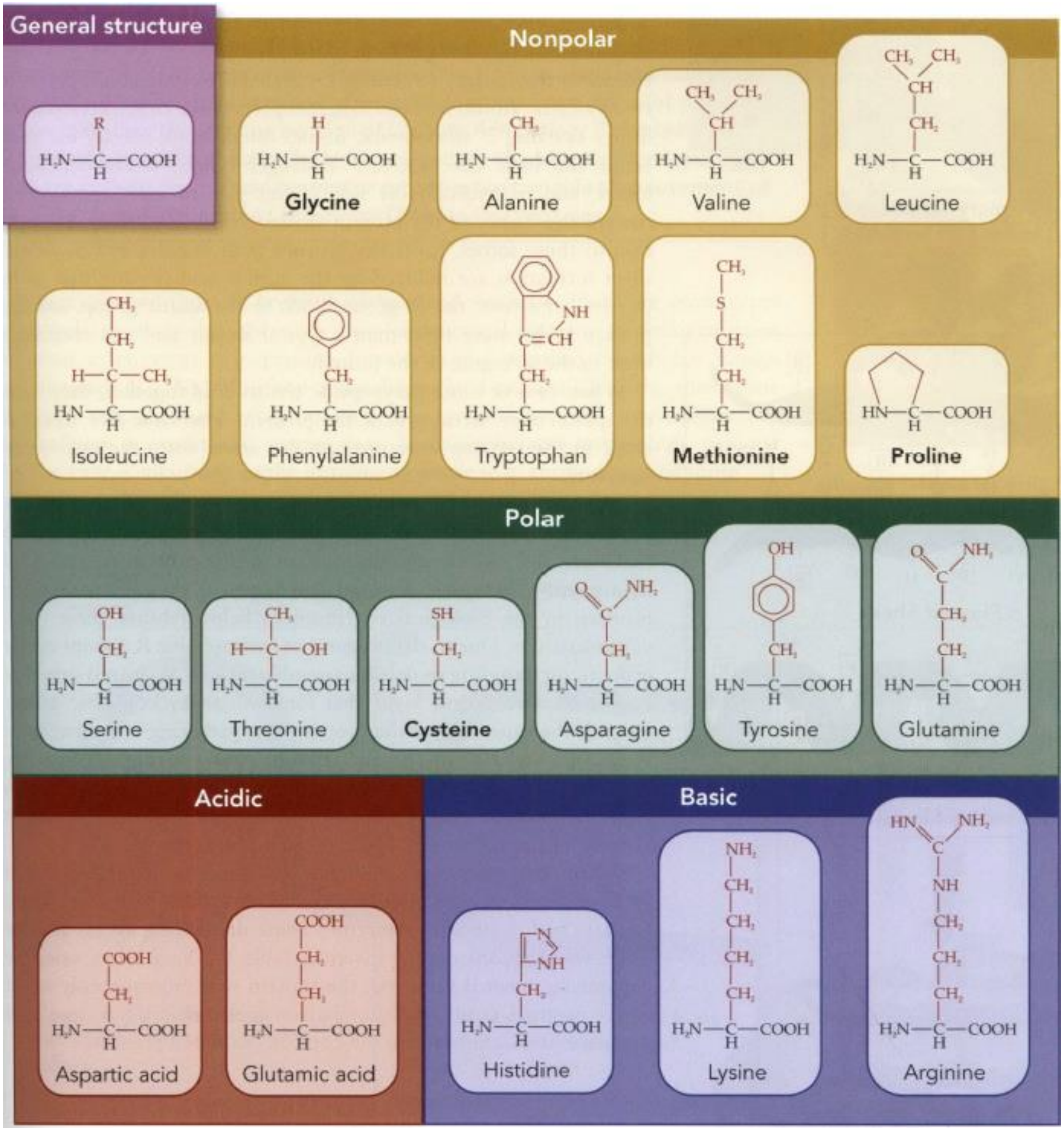


Table 2.2 Abbreviations for amino acids

Amino acid	Three-letter abbreviation	One-letter abbreviation	Amino acid	Three-letter abbreviation	One-letter abbreviation
Alanine	Ala	A	Methionine	Met	M
Arginine	Arg	R	Phenylalanine	Phe	F
Asparagine	Asn	N	Proline	Pro	P
Aspartic acid	Asp	D	Serine	Ser	S
Cysteine	Cys	C	Threonine	Thr	T
Glutamine	Gln	Q	Tryptophan	Trp	W
Glutamic acid	Glu	E	Tyrosine	Tyr	Y
Glycine	Gly	G	Valine	Val	V
Histidine	His	H	Asparagine or aspartic acid	Asx	B
Isoleucine	Ile	I	Glutamine or glutamic acid	Glx	Z
Leucine	Leu	L			
Lysine	Lys	K			

Table 2.2
***Biochemistry*, Seventh Edition**

Absolute configuration at the α position

- **Amino acids are all L and have the absolute configuration of S**. Cysteine is an exception: it is still L, but its absolute configuration is R.

Amino acids as dipolar ions

- Amino acid in physiological pH exists as a zwitterion
- Start off positive, become more negative (as pH becomes greater and they lose H^+ ions
- Isoelectronic point calculation (average of surrounding pKa's)

Classifications

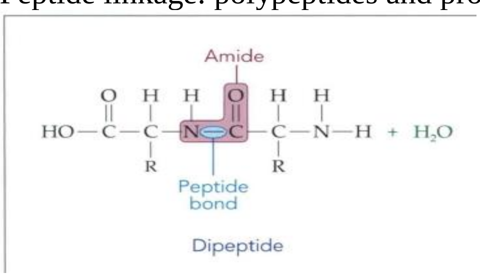
- Acidic or basic
  - Acidic: Aspartic and Glutamic
  - Basic: Histidine, Lysine, and Arginine
    - Note: At pH of 7, Histidine is neutral (it's pKa is 6)
    - Arginine and lysine have side chains with pH of roughly 10
    - Arginine has a "guanidine" group
- Hydrophobic or hydrophilic
  - Hydrophobic: GAVLIM PPT

<u>Reactions</u>

Sulfur linkage for cysteine and cystine

- Disulfide links are effectively oxidations

Peptide linkage: polypeptides and proteins



Peptide bond has slight double bond character – prevents bond from rotating freely, affects secondary structure and tertiary structure to some extent

Hydrolysis

- Most macromolecules of living cells are broken apart by **hydrolysis**
  - Ex: ATP hydrolysis, digestion
- **Dehydration** – two molecules combine to form a larger molecule and water is formed as a byproduct

Protein Structure (BIO, BC, OC)

Structure (1^o to 4^o)

- Primary structure – sequence of amino acids
- secondary structure - α-helix or β-sheets
  - β-sheets – can be parallel or antiparallel
  - reinforced by h-bonds **between carbonyl oxygen of one amino acid and the hydrogen on the amino group** of another
  - single protein usually contains both structures at various location throughout
- Tertiary structure-3D shape formed by curls and folds of the peptide chain
  - Five forces:
  - 1. Covalent disulfide bonds between cysteines to form the dimer cysteine
  - 2. electrostatic interactions (between acidic and basic)
  - 3. hydrogen bonds
  - 4. van der Waals
  - 5. hydrophobic forces
  - Proline also plays a part – kink
  - Note: Salt bridges contain both electrostatic interactions and hydrogen bonding (both have to be charged)
- Quaternary structure
  - two or more polypeptide chains
  - same five forces as tertiary

Conformational Stability (Denaturing and folding, hydrophobic interactions, solvation layer)

- Many different conformations available for any one protein, but it will generally exist in one of few possible conformations that have the highest stability
- The solvation layer (or shell) describes the structured organization of a solvent (e.g. water) around a solute (e.g. a polypeptide or protein). In the case of a protein which displays hydrophobic residues on its surface, the surrounding water will orient into a highly structured organization to optimize hydrogen bonding among water molecules (as hydrogen bonding with the presented hydrophobic side chains is not an option). This highly ordered rearrangement has a much lower entropy and is less favorable than if polar side chains were present on the surface of the protein. Thus, a conformation that buries its hydrophobic residues inside the protein leads to less disruption of water's hydrogen bonding, allowing for less structure and higher entropy, which increases the protein's conformational stability.
  - results in **less entropic penalty**
- Two types of proteins – globular and structural
  - globular – more diverse, function as enzymes, hormones, membrane pumps, receptors, transport and storage, immune response, etc
  - Structural – made from long polymers, maintain and add strength to cellular and matrix structure
    - collagen – most abundant type of protein in the body, adding great strength to skin, tendons, ligaments, and bone

Denaturing Agents	Forces Disrupted
Urea	Hydrogen bonds
Salt or change in pH	Electrostatic bonds
Mercaptoethanol	Disulfide bonds
Organic solvents	Hydrophobic forces
Heat	All forces

Separation techniques

Isoelectric point

- The isoelectric point is influenced by the anionic or cationic character of the protein's amino acid side chains at a certain pH. Separation can be performed by the movement of proteins over a pH gradient in a gel electrophoresis. Proteins at their isoelectric point also have lower solubility and may precipitate out of solution.
  - The cathode (negative) is at the high pH end, while the anode (positive) is at the low pH end
  - Proteins moving from left to right get their protons stripped off and become more negative.

        - Negatively charged acidic proteins would be found towards the left, closer to lower pH's (they have lower isoelectric points)
        - Positively charged basic protons will be found towards the right, closer to higher pH's (they have higher isoelectric points.
- Note: the Cathode is always negative in biochemistry, and the anode is always positive (**an**ions flow to the **an**ode)

Electrophoresis

- Electrophoresis focuses on separating proteins mainly by size or charge in the course of moving across an electric field, usually with a support medium (e.g. a gel). At the end of the migration, the proteins can be stained to show the location of various protein samples, and conclusions can be drawn about the characteristics of the protein. For example, a small protein will travel farther than a larger protein, and a positively charge protein will be pulled towards the cathode (-) while a negatively charged protein will be pulled towards the anode (+)

SDS-PAGE - used to analyse proteins. As a separation medium (also referred to as matrix) a polyacrylamide-based discontinuous gel is implemented in this type of electrophoresis. In addition, SDS (sodium dodecyl sulfate) is used. This anionic surfactant (detergent) covers the intrinsic charges of proteins. About 1.4 grams of SDS bind to a gram of protein,[3][4][5] corresponding to one SDS molecule per two amino acids, so that the proteins have a constant negative charge distribution. Thus, the proteins will be separated out by size only.

Reducing SDS Page – cleaves disulfide bonds, destroys quaternary and tertiary structure

Non-reducing SDS page – does not cleave disulfide bonds, destroys quaternary and tertiary structure

Native Page – keeps quaternary structure

Non-Enzymatic Protein Function (BIO, BC)

Binding

- A special feature of some proteins is the capability to bind other molecules with non-covalent interactions. Protein binding can be characterized by its affinity and specificity for the binding target. Affinity describes how readily the protein binds its target, and specificity refers to the preferential binding of the target over other entities. A change in the protein's conformation can alter affinity and specificity as seen in the control of voltage-gated ion channels in cell membranes

Immune System

- The high degree of protein variability allows for a key feature of the adaptive (or acquired) immune system, the production of antibodies. An antibody is a type of protein that has a unique and very specific binding site that will readily bind its target, called an antigen, such that its target is inactivated or tagged for immune response.

Motors

- A motor protein can perform mechanical work by coupling exergonic (energy releasing) ATP hydrolysis to a conformational change that allows for interaction with the protein's target substrate. Muscle contraction, for example, is achieved through a process of the motor **protein myosin** binding and releasing its microfilament (**actin**) substrate. Myosin also acts on microfilaments of the cytoskeleton to generate cellular movement.
- Two other types of motor proteins, kinesins and dyneins, act on **microtubules** and play a role in transport within the cell. Kinesin walks microtubule "tracks" to deliver cellular cargo (e.g. chromosomes during mitosis, vesicles), generally in an **antegrade direction** (center to periphery). Dynein is used in **retrograde** cargo transport in the axons of neurons, and is capable of sliding microtubules in relation to one another, generating the movement of cilia and flagella.

Enzyme Structure and Function (BIO, BC)

Function of enzymes in catalyzing biological reactions

- An enzyme is a biological catalyst, in that it accelerates chemical reactions in a biological system. An enzyme accomplishes this acceleration by interacting with the reactants (the enzyme's substrates) in a manner which stabilizes their transition state (‡), which in turn lowers the activation energy (Ea) of the reaction, and a lower activation energy allows for the reaction to proceed faster.
- Although an enzyme interacts with its substrates, it is not consumed in the reaction like a reactant. Once a reaction completes, the enzyme is again available to process new substrate. In a biological context, the reusable nature of enzymes to catalyze a particular reaction (the enzyme's specificity) offers a mechanism of controlling reactions by directing which enzymes are present and active, and in what quantities.

Enzyme classification by reaction type

- Because of their specificity, a particular enzyme will only catalyze a singular or narrow set of similar reactions, allowing for classification by reaction type. Names for classes of enzymes are generally descriptive of the type of reaction they catalyze and usually end in the suffix -ase .

    - **Major Class** **Description of reaction activity**
    - Oxidoreductases oxidation of a hydrogen (or electron) donor (loses) and reduction of the acceptor (gains)
    - Transferases move a functional group from a donor molecule to an acceptor molecule
        - Ex: protein kinases

- Hydrolases — couple breaking a bond with hydrolytic cleavage (breaking water)
  - Ex: proteases
- Lyases — breaking a bond with elimination to form a double bond (or ring) or adding to a double bond
- Isomerases — alter the geometry or structure of the reactant molecule (rearrangements)
- Ligases — couple forming a bond (joining two molecules) with ATP hydrolysis

Reduction of activation energy

- Over the duration of a reaction, the reactants must move through a high energy transition state before becoming products. The difference between the free energy of the reactant(s) and the free energy of the transition state is called activation energy. When the activation energy required to arrive at the transition state is lower, the reaction will proceed faster. Thus, in stabilizing the transition state, an enzyme reduces activation energy and increases reaction rate.

Substrates and enzyme specificity

- Enzyme specificity describes the highly selective nature of an enzyme for a particular reaction or set of reactions. The reactants for a specific enzyme then are narrowly defined and called its substrates.

Active Site Model

- The active site model describes the location on the enzyme where it interacts with its substrate. The shape and local chemical characteristics (functional groups) of an active site are responsible for the specificity of the enzyme. In their interactive state, the enzyme and its substrate, bound at the active site, are called the enzyme-substrate complex.

Induced-fit Model

- The induced-fit model describes how the interaction of an enzyme and its substrate is often reliant on effects the substrate has on the enzyme as well as effects the enzyme has on the substrate. The binding of an enzyme to its substrate results in a release of free energy called binding energy, with which suitable substrate in close proximity to an enzyme may cause a small change in the shape of the enzyme that is enough to boost the enzyme's affinity for the substrate, a more complementary conformation, thus "inducing" a better fit for the enzyme and its substrate.

Mechanism of catalysis

- A mechanism of catalysis is the way in which the chemical reaction is assisted in moving forward.

Mechanism	**Description**
Approximation	simply brings reactants together in proximity and proper orientation
Covalent catalysis	a reactive group on the enzyme is temporarily covalently bonded to the substrate
Acid-base catalysis	a reactive group on the enzyme acts as a proton donor or acceptor
Metal ion catalysis	assists in electrophilic or nucleophilic interactions or binds to substrate (increasing binding energy)

- Cofactors
  - Cofactors are inorganic ions that assist an enzyme in its catalytic activity. Examples include Fe2+ and Mg2+. (The term cofactors is sometimes used to describe the superset of **non-protein helper compounds with inorganic ions** in one subset and **organic molecules called coenzymes** in another. In this usage, cofactors, inclusive of coenzymes, may **be closely or covalently bound to the enzyme as a holoenzyme**. Without the required cofactor, an enzyme is in an inactive state, or an **apoenzyme**.)
- Coenzymes
  - **Coenzymes** are small, **organic** molecules that assist an enzyme in its catalytic activity. Examples include *heme*, *NAD^+*, and *coenzyme A*. Many coenzymes are derived from vitamins.
- Water-soluble vitamins
  - Water-soluble vitamins include the series of B-vitamins and Vitamin C and are a dietary requirement **as precursors to coenzymes** (or as the coenzyme itself in the case of Vitamin C). (ADEK are fat soluble)

Effects of local conditions on enzyme activity

- Enzyme activity can be dramatically affected by changes in temperature and pH. Low temperatures slow reaction rates, and high temperatures may increase reaction rates but also cause denaturing in protein enzymes. Fluctuations in pH can also denature a protein enzyme by disrupting the non-covalent interactions that stabilize its 2°, 3°, and 4° structures.
- Ideal temperatures of many enzymes is

Control of Enzyme Activity (BIO, BC)

Kinetics

- General (catalysis)
  - Catalysis is the process of accelerating a chemical reaction. As biological catalysts, enzymes speed up the rate of reaction but do not affect the equilibrium (Keq) or the (thermodynamically) favorable direction of the reaction.
  - A favorable (spontaneous) reaction is one in which the free energy of the products is lower than the free energy of the reactants ($\Delta G < 0$). However, a thermodynamically favorable reaction may not proceed (at a perceptible rate) on account of a kinetic barrier, e.g., activation energy, which is where enzymes come in.
- Michaelis–Menten

- **In general, reaction rate is directly proportional to the frequency of effective collisions** between reactant molecules (collision theory). Higher reactant concentrations have a higher probability of collision. Similarly, in an enzyme-catalyzed reaction, an increase in the relative concentration of substrate will increase the reaction rate up to a maximum rate (with enzyme concentration held constant).
- At the point where an enzyme is catalyzing reactions as fast as it can (**maximum turnover**), adding more substrate will not make any difference and the reaction rate is at its maximum, Vmax. Adding more enzyme at this point will allow reaction rate to continue to increase and define a new Vmax. (**That is, Vmax is defined for a specific enzyme concentration**.)
- The Michaelis-Menten equation calculates the rate of reaction (v) using Vmax, the substrate concentration ([S]), and the Michaelis constant (Km). Km equals the substrate concentration required for the reaction rate to reach ½Vmax. **As a constant, Km does not fluctuate with changes in enzyme concentration and is indicative of enzyme-substrate affinity**. Enzyme-catalyzed reactions with high enzyme-substrate affinity will reach the ½Vmax benchmark at a lower substrate concentration (have a lower Km), whereas lower enzyme-substrate affinities will result in needing a higher substrate concentration to reach ½Vmax (have a higher Km).

$$V_0 = \frac{V_{\max}[S]}{(K_M + [S])} \quad \frac{1}{V_o} = \frac{1}{V_{max}} + \frac{K_m}{V_{max}}\frac{1}{[S]}$$

- Catalytic Efficiency: $k_{cat} = V_{max} / [E_t]$
- catalytic efficiency is Kcat / Km (Makes intuitive sense

- Cooperativity
  - An exception to the Michaelis-Menten equation are enzymes with multiple binding sites (often over multiple subunits) that undergo **cooperativity**, a case in which the binding of one ligand will increase the affinity for binding another ligand at a different site. Binding sites that are not substrate active sites are called **allosteric sites**, and enzymes that undergo a change in catalytic activity on account of a molecule binding at an allosteric site are referred to as **allosteric enzymes**.
  - If the Hill coefficient is greater than 1, enzymes express cooperativity
  - Sigmoidal curves (the steeper, the more cooperative)

Feedback regulation

- **Feedback regulation** of an enzyme occurs when a product of the reaction binds to an **allosteric** site on the enzyme, affecting its catalytic activity. This effect can be *positive*, producing a change that increases enzyme-substrate affinity, or *inhibitory*, reducing the activity at the active site or inactivating it completely. Binding molecules in feedback regulation may also extend to other reactants and products in an enzyme's metabolic pathway, producing upstream or downstream effects.

Inhibition – types

- Competitive
  - A **competitive inhibitor** is a molecule that is similar enough to an enzyme's substrate that it can compete for the space occupying the active site. While a competitive inhibitor is bound to the active site, substrate cannot be processed.
- Non-competitive
  - A non-competitive inhibitor is a molecule that binds to an allosteric site on the enzyme, causing a conformational change that decreases catalytic activity at the active site ***regardless*** of whether a substrate is already bound.
- Mixed (BC)
  - A mixed inhibitor is a molecule that binds to an allosteric site on the enzyme, causing a conformational change that decreases catalytic activity at the active site. Mixed inhibitors generally have a preference towards binding either the enzyme-substrate complex or the enzyme alone
- Uncompetitive (BC)
  - An **uncompetitive inhibitor** is a molecule that **binds only to the enzyme-substrate complex**, rendering it catalytically inactive.
  - It is important to note that this does not change the slope of the lineweaver-Burke plot: the ratio of K_M / V_{max} is the same

Inhibition type	Binding state	Binding site	Blocks substrate	Effect on K_m	Effect on V_{max}	Overcome by ↑[S]
Competitive	E	active site	yes	increases	no effect	yes

Inhibition type	Binding state	Binding site	Blocks substrate	Effect on K_m	Effect on V_{max}	Overcome by ↑[S]
Noncompetitive	E or ES	allosteric site	no	**no effect**	decrease	no
Mixed	E or ES	allosteric site	no	increases or decreases	decrease	**partially**
Uncompetitive	ES	allosteric site	no	decreases	decrease	no

Regulatory enzymes

Enzymes often work in concert, forming biochemical pathways that use sequences of enzyme-catalyzed reactions to achieve an overall goal (e.g. glycolysis). Enzymes along a pathway that are specifically targeted for regulation of the pathway are referred to as regulatory enzymes.

- Allosteric enzymes
  - The catalytic activity of an allosteric enzyme is regulated by an effector molecule (acting as an activator or inhibitor) that **binds an allosteric site**, resulting in a conformational change to the enzyme that either activates or inhibits the active site on the enzyme. **In homotropic allosteric regulation** the effector molecule is also the enzyme's substrate, while the effector in **heterotropic allosteric regulation** is not a substrate of the enzyme.
- Covalently-modified enzymes
  - Covalent modification can either activate or deactivate an enzyme through the addition or removal of a modifier using a reversible covalent bond (e.g. phosphorylation).
- Zymogen
  - A zymogen (or proenzyme; generally indicated by the suffix -ogen) is an inactive precursor that will undergo **irreversible conversion** to the final active form of an enzyme. Activation triggers include proteolytic cleavage of an **activation segment,** change in environmental pH, or cofactors.

Content Category 1B: Transmission of genetic information from the gene to the protein

Nucleic Acid Structure and Function (BIO, BC)

Description

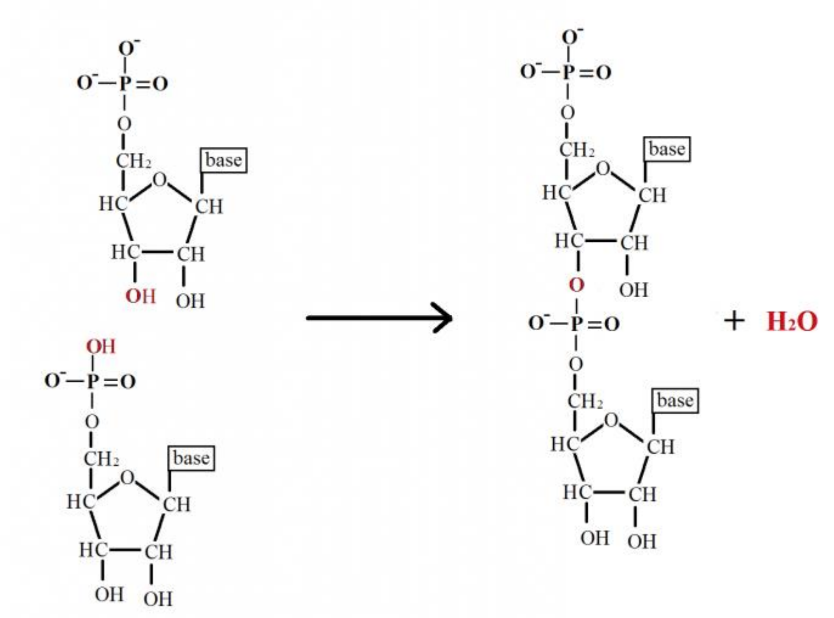
- Nucleic acids are organic macromolecules composed of a limited variety of monomers (nucleotides) linked together into polymer strands (DNA, RNA) with characteristic stability (**DNA more stable**; RNA less stable).

Nucleotides and nucleosides

- The monomeric unit of nucleic acid is a **nucleotide**, which in turn is composed of three parts: a sugar ring, a heterocyclic base, and a phosphate group. A corresponding **nucleoside** is structurally similar with a sugar ring and heterocyclic base but lacks a phosphate group.
- The sugar ring can be either a ribose (found in RNA) or 2′-deoxyribose (found in DNA).

Sugar phosphate backbone

- In the structure of a nucleotide, the sugar subunit is situated as a hub, linked on one side to the phosphate group and, on another side, to the base. This arrangement lends itself to the polymer construction of nucleic acids by the formation of **phosphodiester bonds** that **connect the sugar of one nucleotide to the phosphate group of the next nucleotide in the strand**. Following these sugar-phosphate linkages down the length of the nucleic acid polymer gives the impression of a backbone with a variety of bases, each extending from its sugar link.



Pyrimidine, purine residues

- The five common nucleotides found in DNA and RNA are divided in to purines (double ring structure) and pyrimidines (single ring structure).

Base	Ring structure	Found in DNA	Found in RNA
Adenine	purine	Yes	Yes
Guanine	purine	Yes	Yes
Cytosine	pyrimidine	Yes	Yes
Thymine	pyrimidine	Yes	No
Uracil	pyrimidine	No	Yes

Deoxyribonucleic acid (DNA): double helix, Watson–Crick model of DNA structure

- The Watson-Crick model of the structure of DNA elucidated a **double stranded** composition with the two strands wound into a **double helix**. In addition to the helical formation, each strand runs **antiparallel** (its nucleotides oriented in the opposite direction of its partner strand), with the sugar-phosphate backbone running along the outside and bases projected into the center of the helix where they hold the formation by **hydrogen bonding** to the bases projected inward from the other strand.

Base pairing specificity: A with T, G with C

- The hydrogen bonding between bases on each strand of a double stranded molecule of DNA is arranged with specificity between certain base pairs with each pair composed of a purine and a pyrimidine.

Purine	Pyrimidine	Number of hydrogen bonds
Adenine	Thymine	2
Guanine	Cytosine	3

Function in transmission of genetic information (BIO)

- The structure of nucleic acids as polymers with unique sequences of bases (by way of their nucleotide residues) gives way to a high fidelity means of transmitting genetic information by reading and replicating the base sequence for a strand of DNA. This process is performed in DNA replication, whereby each strand of the double-stranded DNA molecule is introduced to a new partner strand by matching new nucleotides with the correct base pairing, and in transcription, where a new molecule of RNA is created by linking nucleotides that pair with the sequence of bases on a template strand of DNA.

DNA denaturation, reannealing, hybridization

- The double helix of double-stranded DNA is stabilized by the hydrogen bonding between base pairs along the length of the molecule. Disruption of the hydrogen bonds, such as in the case of high temperature, can cause the unwinding of the two strands (**denaturation**), which can then also be brought back together when proper conditions return (**reannealing**).
- A single strand of DNA will readily bind to another single strand of DNA in the process of **hybridization** where there is a **significant amount of base pair matching** between their sequences (in conditions conducive to its hydrogen bonds).

DNA Replication (BIO)

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

- Replicating a molecule of double-stranded DNA involves unwinding its helical structure, separating its two strands, and filling in new partner strands from free nucleic acids (nucleotides). **Specific coupling** assures that nucleotides are incorporated with correct base-pairing along the length of each of the separated strands (A with T, G with C).

- Each of the separated strands is read and matched with appropriate nucleotides to create a newly synthesized partner strand. Nucleotides are added by attaching the phosphate group of the nucleotide (found on its 5′ carbon) to the open 3′ carbon on the end of the elongating strand. Thus replication proceeds by reading the original strand 3′ → 5′ and elongating the new strand **5′ → 3′**.

- Because the strands of double-stranded DNA run antiparallel, replication is performed in opposite directions, with one side extending its newly synthesized strand towards the replication fork and one side away. Only short portions (**Okazaki fragments**) can be synthesized in the direction away from the fork as it unzips, making this side the **lagging strand**. Replication on the **leading strand**, by contrast, is continuous into the direction of the replication fork as it unzips.

Semi-conservative nature of replication

- DNA replication is **semi-conservative** on account of its two resulting molecules of double-stranded DNA each having retained a strand from the original molecule in addition to the newly synthesized strand.

Specific enzymes involved in replication

Enzyme	**Role**
DNA helicase	works at the replication fork to unwind the helix (unzips DNA)
Topoisomerases, including DNA gyrase	relax super-coiling that results from unwinding the helix
Single-stranded binding proteins (SSBPs)	bind to the separated strands of DNA to keep them from reannealing
Primase	creates short RNA primer that is temporarily attached for DNA polymerase to extend from
DNA polymerase	follows the replication fork, working to add new nucleotides in 5′ → 3′ direction; proofreads and removes incorrect nucleotides
DNA ligase	helps to anneal strands; joins Okazaki fragments
Telomerase	lengthens telomeres of linear eukaryotic DNA

Note: **DNA polymerase 3** is essential for the replication of the leading and the lagging strands whereas **DNA polymerase 1** is essential for removing of the RNA primers from the fragments and replacing it with the required nucleotides.

Origins of replication, multiple origins in eukaryotes

- The process of DNA replication begins at an **origin of replication**, where the molecule's two strands are separated, producing a replication bubble with two replication forks unzipping the DNA bidirectionally away from the origin. Prokaryotes usually have a single origin of replication for **their single, circular DNA**. Eukaryotes, however, have multiple origins of replication across their numerous linear chromosomes.

Replicating the ends of DNA molecules

- Linear chromosomes will arrive at an issue with replication at the ends of their **lagging strands** by which a portion of the strand at the very end (located in the **telomere**, a region of repetitive sequences at the end of the chromosome) is unable to be synthesized due to the lack of a 3′ end of a nucleotide to extend from. This issue results in the **progressive shortening** of the telomeres in linear chromosomes after numerous rounds of replication. The issue is resolved in presence of **telomerase** which acts to lengthen the telomeres with repetitive sequences, thereby protecting them from loss during replication.

Repair of DNA (BIO)

Repair during replication

- In replicating the DNA, there is the possibility of introducing mutations through errors in base-pairing. To limit this possibility, mismatched bases can be detected and repaired during replication.
- In **prokaryotes**, **DNA Polymerase III**, which is responsible for the 5′ → 3′ elongation of the newly synthesized strand, can exercise **3′ → 5′ exonuclease activity**. That is, DNA Pol III can proofread **upstream** (3′ → 5′; the opposite direction of elongation) the last nucleotide added and, if an error is found, excise and correct it. **DNA Polymerase I**, which is also responsible **for removal and replacement** of the RNA primer, provides 5′ → 3′ exonuclease activity to **repair mismatches in the direction of elongation.**

Repair of mutations

- Errors that escape correction during replication can still be identified and repaired later by a **mismatch repair mechanism**, a concert of **mismatch repair proteins** that identify mismatched bases by way of **characteristic distortion of the sugar-phosphate backbone**. Once mismatches are found, the incorrect match is excised (via exonuclease), replaced (via polymerase) with the correct nucleotide, and joined (via ligase) to its adjacent nucleotides in the strand.
- More complex but similar processes of DNA repair during and after replication take place in eukaryotes.

Genetic Code (BIO)

Central Dogma: DNA → RNA → protein

The triplet code

- allows for 64 different combination
- unambiguous – any single series of 3 nucleotides codes for only one amino acid
- nearly universal

Codon–anticodon relationship

Degenerate code, wobble pairing

- mRNA – template
- tRNA – plays a vital role in actually rendering the triplet code of the mRNA into a specific amino acid sequence
- has two ends:
- one end: anticodon – will bind to complementary codon sequence on mRNA
- other end: carries the amino acid that corresponds to that codon
- the first two base pairs in codon and anticodon must be complementary
- however, there is some flexibility in bonding at the third base pair position
- wobble pairing – helps explain why multiple codons can code for the same amino acid

Missense, nonsense codons

- A base substitution may have three different effects on an organism's protein. It can cause a missense mutation, which switches one amino acid in the chain for another. It can cause a nonsense mutation, which results in a shorter chain because of an early stop codon.

Initiation, termination codons

- Start Codon – AUG - Methionine
    - (school starts in august)
    - Stop codons: UAA, UAG, UGA

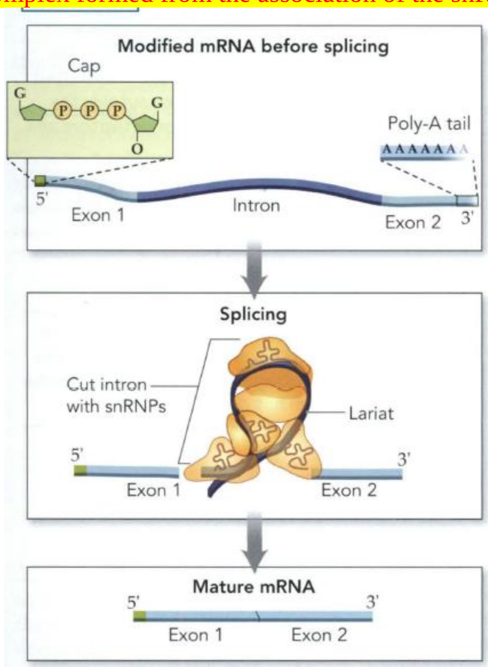
Messenger RNA (mRNA)

Transcription (BIO)

- 1) Initiation
    - group of DNA binding proteins called transcription (nuclear) factors identify a promoter on the DNA strand
        - **promoter** – sequence of DNA nucleotides that designates a beginning point for transcription
        - at the promoter, the **transcription factors (nuclear factors)** assemble into a transcription initiation complex, which includes the major enzyme RNA polymerase
        - **consensus sequence** – most commonly found promoter nucleotide sequence recognized by a given species of RNA polymerase
            - variation from the consensus sequence causes RNA polymerase to bond less tightly and less often to a given promoter, which leads to the associated genes being transcribed less frequently
    - **RNA polymerase** *unzips* DNA double helix, creating the transcription bubble
- 2) Elongation – RNA polymerase transcribes only one strand of the DNA sequence into complementary strand
    - **transcribed strand** = template strand, or antisense (-) strand
    - **Coding strand** = (+) sense strand
    - RNA polymerase moves in the 3'→ 5' direction, building new RNA strand in the 5'→3' direction
    - there is no proof-reading mechanism that corrects for errors in the transcription process
        - errors in RNA are just not transmitted to progeny
- 3) Termination – occurs when termination sequence is reached
    - can also involve special proteins, known as **Rho proteins**, that help to dissociate RNA polymerase from the DNA template
- Transcription is the main level of activation or deactivation of genes
    - **activators** and **repressors** (proteins) bind to DNA close to promoter and either activate or repress the activity of RNA polymerase
        - often allosterically regulated by small molecules such as cAMP
    - **Enhancers** – short, non-coding regions of DNA found in eukaryotes, function similarly to activators but act at a much greater distance from the promoter

Transfer RNA (tRNA); ribosomal RNA (rRNA)
Mechanism of transcription
mRNA processing in eukaryotes, introns, exons

- Modification of RNA
  - post-transcriptional processing occurs both in eukaryotes and prokaryotes
  - In Eukaryotes
    - primary transcript must under modifications that include: helping the molecules that initiate translation recognize the mRNA, protect the mRNA from degradation, eliminate extraneous sequences of nucleotides, and provide a mechanism for **variability in protein products from a single transcript**
    - **5' cap** – serves as an attachment site in protein synthesis during translation and as a protection against degradation by enzymes that cleave nucleotides, called **exonucleases**
    - poly A tail – added at 3' end to protect form exonucleases
  - Splicing – removes introns, exons remain
    - joins the ends of exons together
    - involves **snRNPs**, which contain assortment of proteins and snRNA
      - snRNA acts as a **ribozyme**—an RNA molecule capable of catalyzing chemical reactions
      - snRNPs recognize nucleotide sequences at the ends of introns, pulls the ends together (forming an intron loop of **lariat**), then excises the introns and joins the ends of exons
    - **spliceosome** – complex formed from the association of the snRNPs and additional associate proteins



  - alternative splicing – allows cell to incorporate different coding sequences into mature mRNA
    - introns may play an important function in gene expression
    - alternative splicing, together with other eukaryotic techniques such as the use of alternative promoter sites or terminating transcription at different sites, allows the cell to create vast diversity of proteins
  - Takes place in nucleus of eukaryotes
    - in contrast, prokaryotes can carry out transcription and translation concurrently, and they do not modify RNA transcripts prior to the start of translation

Ribozymes, spliceosomes, small nuclear ribonucleoproteins (snRNPs), small nuclear RNAs (snRNAs)
Functional and evolutionary importance of introns

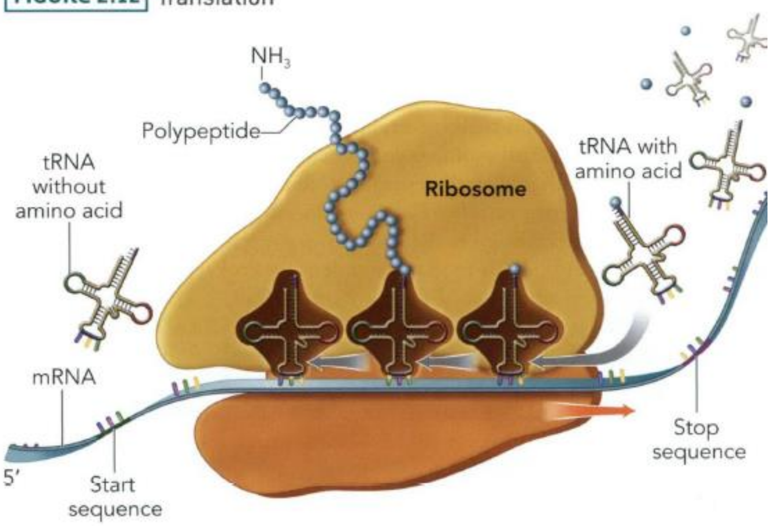
- While introns do not encode protein products, they are integral to gene expression regulation. Some introns themselves encode functional RNAs through further processing after splicing to generate noncoding RNA molecules (RNA that is not translated into a protein)
- Alternative splicing is widely used to generate multiple proteins from a single gene. Furthermore, some introns play essential roles in a wide range of gene expression regulatory functions such as non-sense mediated decay[19] and mRNA export

Translation (BIO)
Roles of mRNA, tRNA, rRNA

Role and structure of ribosomes
Initiation, termination co-factors
Post-translational modification of proteins

- takes place on ribosome (Note: the chemical composition of ribosomes on eukarya and Bacteria are slightly different)
  - small subunit and large subunit, made from rRNA and many separate proteins
  - Prokaryotic ribosomes – 30S and 50S, combined sedimentary coefficient of 70S
  - Eukaryotic ribosomes – 40S and 60S, combined sedimentary coefficient of 80S
  - assembled in the nucleolus
    - small and large subunits exported separately to the cytosol
- Same steps as transcription – initiation, elongation, and termination
  - initiation
    - **initiation factors** help attach 5' end to small subunit of ribosome
    - a tRNA containing the 5'-CAU-3' anticodon sequesters methionine and settles into the P site
      - **signal for the large subunit to join and form the initiation complex**
  - Elongation
    - ribosome slides down mRNA one codon at a time in the 5'→3' direction, matching each codon to a complementary tRNA anticodon
    - the corresponding amino acids attached to these tRNAs are bound together into a growing polypeptide
    - requires the input of energy
    - C-terminus of methionine attaches to the N-terminus of the amino acid at the A site in a dehydration reaction, forming a peptide bond
      - takes place through peptidyl transferase activity, which is catalyzed by rRNA in the ribosome
        - another example of ribozyme function
      - the tRNA that carried methionine moves to the E site (for exit)
    - E- exit, P – Peptide bond, A – accept
  - Termination
    - stop codon is reached
    - proteins known as **release factors** bind to A site
    - allows water molecule to add to the end of the polypeptide chain
    - polypeptide is freed, ribosome breaks up
- Even as the polypeptide is being translated, it begins folding

FIGURE 2.12 Translation



- After translation
  - post-translational modifications – affect which products of translation ultimately become functional proteins
    - sugars, lipids, or phosphates can be added to amino acids to influence functionality
    - cleavage can occur
    - formation of quaternary structure
  - Final destination
    - proteins translated by free-floating ribosomes function in the cytosol
    - proteins synthesized by ribosomes that attach to the rough ER during translation are injected to the ER lumen
      - can become membrane-bound proteins of nuclear envelope, ER, golgi, lysosomes, plasma membrane, or can be secreted from the cell

        - the growing polypeptide itself may or may not cause the ribosome to attach to the ER, depending upon the polypeptide
            - a 20 aa sequence called a signal peptide near the front of the polypeptide is recognized by protein-RNA signal-recognition particle (SRP) that carries the entire ribosome complex to a receptor protein on the ER
            - signal peptide is usually removed by an enzyme
            - signal peptide can also target to mitochondria, nucleus, or other organelles

Eukaryotic Chromosome Organization (BIO)
Chromosomal proteins
Single copy vs. repetitive DNA - The vast majority of the genome consists of non-coding DNA sequences, much of which is repetitive
Supercoiling
Heterochromatin vs. euchromatin
Telomeres, centromeres

    - sister chromatids joined together at centromeres
        - kinetochore – structure of protein and DNA located at the centromere of joined chromatids of each chromosome

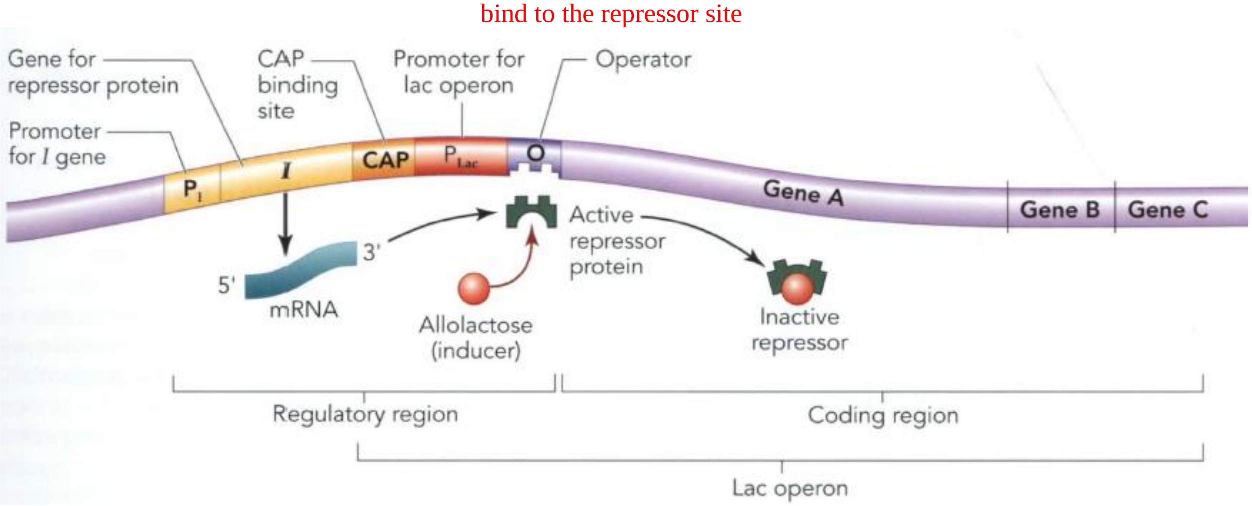
- Chromosomes
    - consists of compactly wrapped DNA and protein in a hierarchy of organizational levels
    - proteins – histones
        - have **basic** functional groups, which give net positive charge that attracts the negatively charged DNA strands
        - 8 histones – **nucleosome**
        - nucleosomes wrap into coils, which wrap into supercoils
        - cannot be transcribed
- Chromatin – entire DNA/protein complex, and a small amount of RNA
    - Tightly condensed = heterochromatin
        - constitutive heterochromatin – permanently coiled
    - Euchromatin – uncoiled, able to be transcripted ("YOU"-Chromatin)
        - is only coiled during nuclear divisions
    - Nucleotide sequences that code for protein products often contain single copy DNA
        - as opposed to repetitive DNA, which makes up non-coding regions
- DNA methylation
    - involves the addition of an extra methyl group to particular **cytosine** nucleotides
    - causes DNA to be wound more tightly—methylated sections are thus inaccessible to transcription machinery
    - If methylation is in the repressor region of a gene, it can increase activation of that gene
- Chromosomal Vocabulary
    - inside human somatic cell,
        - 46 double-stranded DNA molecules
        - chromatin associated with each one is wound into chromosome
        - in human cells, each chromosome possess a partner that codes for the same traits—homologues
    - Diploid – contains homologous pairs
    - Haploid – does not contain homologues
    - There are 46 chromosomes before replication, and 46 chromosomes after replication
        - the replicated and un-replicated versions of a chromosome are each considered to be a single chromosomes
        - the duplicates can be referred to separately as sister chromatids

Control of Gene Expression in Prokaryotes (BIO)
Operon Concept, Jacob–Monod Model

- The model proposed by Jacob and Monod predicted that a specific DNA sequence near the transcription start site of the lac operon is a binding site for lac repressor.

Gene repression in bacteria
Positive control in bacteria

- In Prokaryotes
  - primary function of gene regulation is to respond to changes in the environment
    - in contrast, the maintenance of homeostasis is the hallmark of multicellular organisms
  - Prokaryotic mRNA typically include several genes in a single transcript (**polycistronic**), whereas eukaryotic mRNA includes only one gene per transcript (**monocistronic**)
  - Operon – genetic unit consisting of operator, promoter, and genes that contribute to a single prokaryotic mRNA
    - Lac Operon in E. Coli
      - E coli generally prefers to use glucose when it is present
      - lac operon codes for enzymes that allow E. coli to import and metabolize lactose when glucose is not present in sufficient qualities
        - the lac operon is thus only activated if two conditions are met: if glucose is scarce and lactose is present
        - low glucose → high cAMP levels
        - cAMP binds to and activates Cap, which binds to a CAP site located adjacent and upstream to promoter on lac operon
        - CAP activates promoter, allowing transcription
      - second regulatory site –operator, located adjacent and downstream to the promoter
        - when lactose is not present in the cell, repressor protein binds to the operator site and prevents transcription of lac genes, thereby preventing gene expression
        - when lactose is present, it binds to lac repressor protein, making that protein unable to bind to the repressor site



    - No glucose → activation, lactose → lack of repression
      - presence of lactose can induce the transcription of lac operon only when glucose is not present

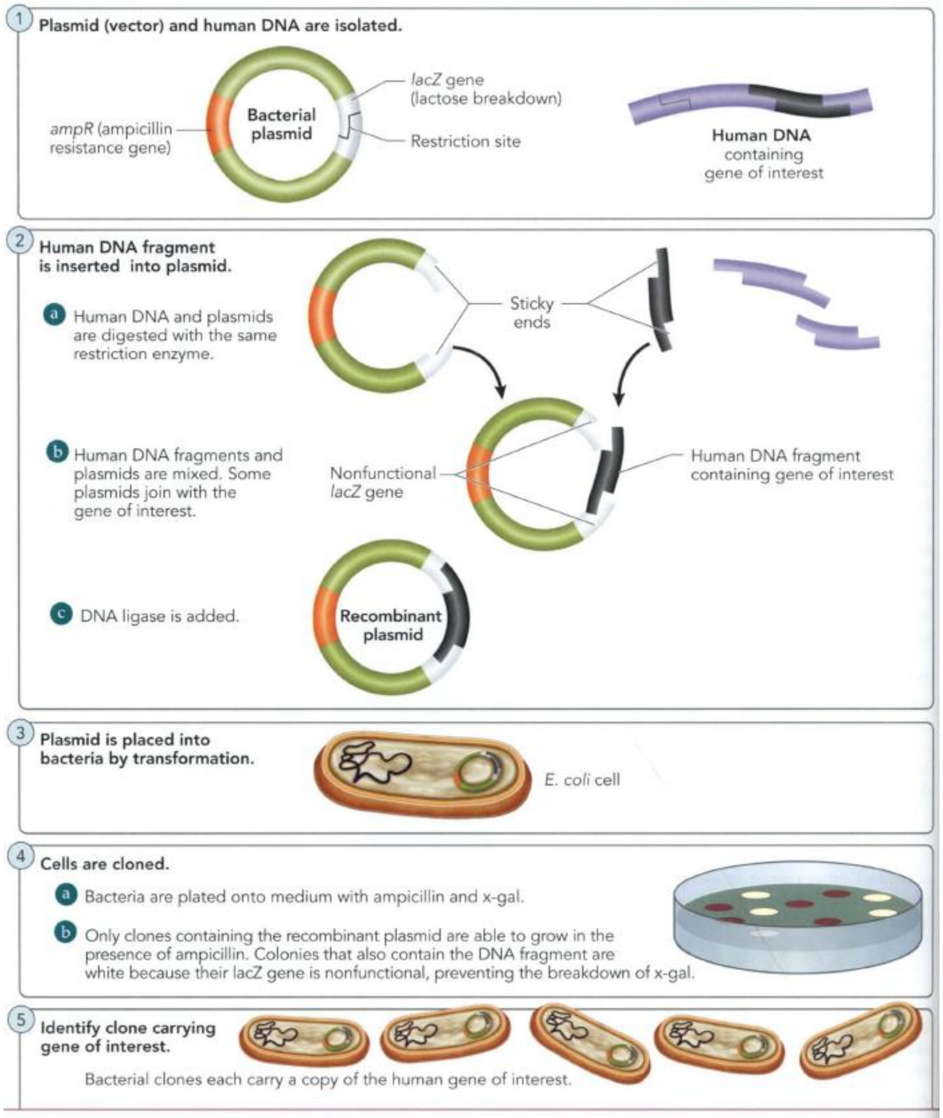
Control of Gene Expression in Eukaryotes (BIO)
Transcriptional regulation
DNA binding proteins, transcription factors
Gene amplification and duplication
Post-transcriptional control, basic concept of splicing (introns, exons)
Cancer as a failure of normal cellular controls, oncogenes, tumor suppressor genes
Regulation of chromatin structure
DNA methylation
Role of non-coding RNAs

- Epigenetics – the changes made around the genome that <u>do not alter actual nucleotide sequence</u>
  - these changes instruct the cellular machinery how to read the genome, thereby altering gene expression
  - include changes such as the <u>attachment of chemical markers to the genome</u>, histone protein modification, and use of non-coding RNAs to influence gene expression
  - Epigenetic markers and histone modifications can be passed down from one generation to the next
- Histone acetylation typically promotes transcription by modifying chromatin structure, decreasing its condensation.
- Cancer
  - proto-oncogenes can be converted to oncogenes, genes that cause cancer, by mutagens such as UV radiation or chemicals, or simply by random mutations
  - carcinogens – mutations that cause cancer
  - mutagens may also inactivate tumor suppressor genes

Recombinant DNA and Biotechnology (BIO)

Gene cloning

- Cloning
  - Recombinant DNA placed within a bacterial genome using a vector (typically a plasmid)
  - bacteria then grown in large quantities
    - not all bacteria take up the vector
      - include a gene in original vector that lends resistance to a certain antibiotic
        - screens for bacteria that does not take up the vector
      - include lacZ gene in original vector—an endonuclease with a recognition site that cleaves the lacZ gene can then be used to place the DNA fragment into the vector
        - we can thus screen out the vectors that don't have our GOI, as they will still have the lacZ gene and will turn blue in the presence of X-gal
- Eukaryotic DNA contains introns, and since bacteria have no mechanism for removing introns, it is useful to clone DNA with no introns
  - mRNA produced by DNA is reverse transcribed with reverse transcriptase, forming cDNA
  - adding DNA polymerase to cDNA produces a double strand of desired DNA fragment



Restriction enzymes

- Restriction Enzymes – cut only at specific sequences – restriction site
  - palindromic sequence 4-6 nucleotides long
    - Ex: GGATCC
  - most restriction endonucleases cleave DNA strand unevenly, leaving complementary single-stranded ends
    - can reconnect through hybridization and are termed sticky ends
    - phosphodiester bonds of fragments can be joined by **DNA ligase**
- we take advantage of the fact that two DNA fragments cleaved by the same endonuclease can be joined together
  - recombinant DNA
  - can be used to generate a DNA library for the purpose of DNA cloning

DNA libraries

- A DNA library is a collection of DNA fragments that have been cloned into vectors so that researchers can identify and isolate the DNA fragments that interest them for further study. There are basically two kinds of libraries: genomic DNA and cDNA libraries. Genomic DNA libraries contain large fragments of DNA in either bacteriophages or bacterial or P1-derived artificial chromosomes (BACs and. PACs). cDNA libraries are made with cloned, reverse-transcribed mRNA, and therefore lack DNA sequences corresponding to genomic regions that are not expressed, such as introns and 5′ and 3′ noncoding regions. cDNA libraries generally contain much smaller fragments than genomic DNA libraries, and are usually cloned into plasmid vectors.

Generation of cDNA

Hybridization

- hybridization – can be used as a technique to find a particular gene in a library
  - fluorescently or radioactively labeled complementary sequence of the desired DNA fragment (probe) is used to search the library

Expressing cloned genes

- Gene A → isolate mRNA → reverse transcriptase → cDNA → amplify by transforming into a plasmid (containing Antibiotic resistant genes for marker → incorporate into bacteria → bacteria replicate

Polymerase chain reaction

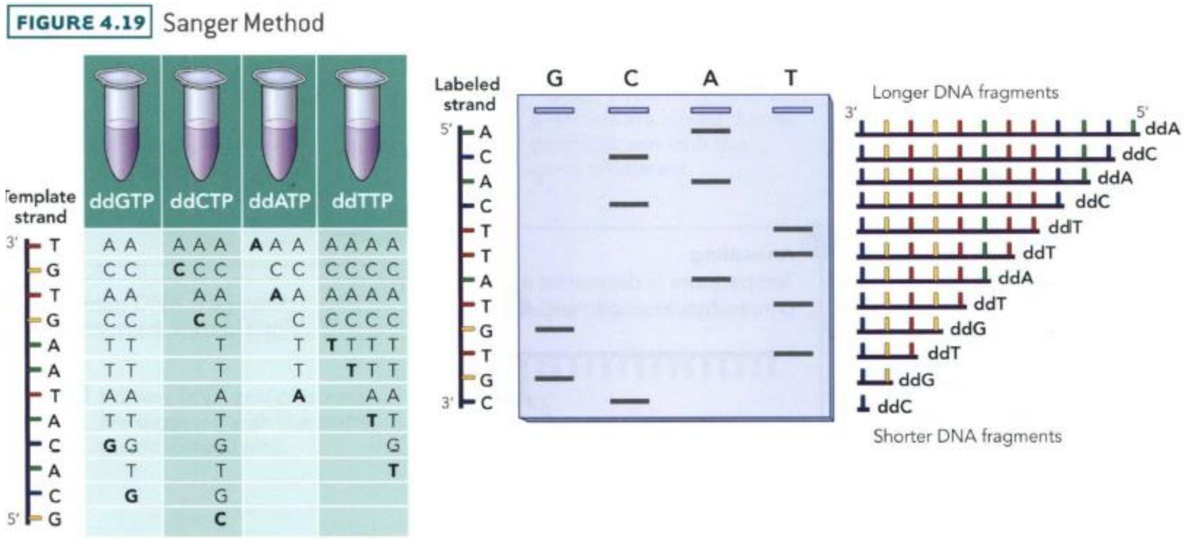
- Polymerase Chain Reaction
    - much faster way of cloning
    - developed using a specialized polymerase enzyme found in a species of bacterium adapted to life in nearly boiling waters
    - the double strand of DNA to be cloned is placed in a mixture with many copies of two DNA primers, one for each strand
        - heating to 95 – denature
        - cool to 60 – primers anneal
        - 72 – heat resistance polymerase added with supply of nucleotides
    - 2^n copies
    - quantitative PCR – used to quantify the amount of DNA in each cycle

Gel electrophoresis and Southern blotting

- gel electrophoresis
    - nucleic acids are negatively charged, migrate through gel
    - larger particles move more slowly
    - Proteins are separated by a different type of gel
        - usually denatured in the presence of a detergent before they are placed in the gel
        - detergent coats each protein with negative charge proportional to its length
        - proteins can also be separated based on isoelectric points
    - Ladder – mixture of DNA, RNA , or polypeptide fragments of known sizes or quantities
        - used for comparison
- Blotting – after gel electrophoresis, for visualization purposes
    - molecules transferred from gel onto membrane, allowing for easier manipulation or visualization
    - Southern Blotting – target fragments of known DNA sequence in a large population of DNA
        - gel placed in basic solution to denature DNA fragments (double to single strand)
        - nitrocellulose placed on top or below gel, transferred to this membrane
        - labeled probe with complementary nucleotide sequence is added
        - visualize
    - Northern Blot – identifies RNA fragments
    - Western blot – detect a particular protein in a mixture of proteins
        - visualization usually occurs through antibodies
            - primary antibody specific to protein in question used first
            - secondary antibody-enzyme conjugate added
                - recognizes and binds the primary antibody and marks it with an enzyme for visualization
                - reaction catalyzed by enzyme attached to the secondary antibody produces color or something

DNA sequencing

- Sanger Sequencing
- ddNTPs incorporated, results in termination of replication
- For example: one tube contains both adenine and ddATP
    - there would be some DNA strands that terminated at every adenine
- use Gel electrophorsesis to compare the relative lengths of these strands



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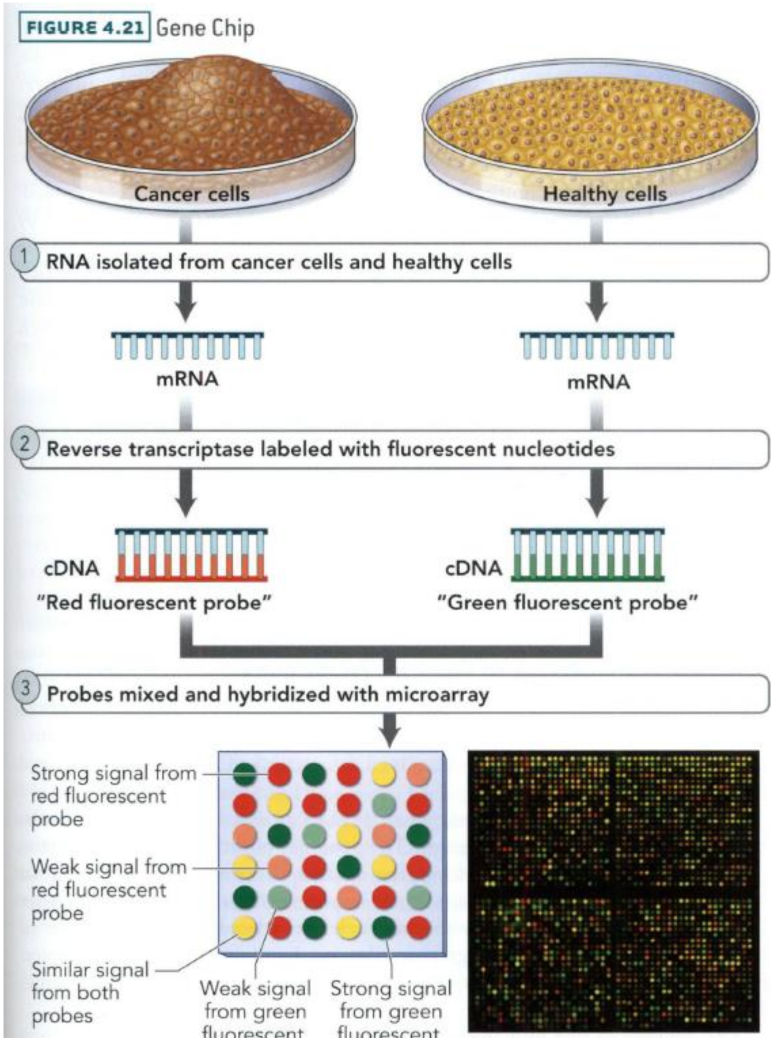
Analyzing gene expression

- gene chip – microarray
- two different conditions (often the same cell type before and after a stimulus, or cancer cell)
- mRNA from first situation labeled in red, while mRNA from second is labeled in green
  - genes that are downregulated from situation 1 to 2 appear as red dots in the appropriate area of the gene chip
  - genes that are upregulated appear green
  - if gene's expression levels are unchanged, there will be an equal amount of green and red mRNA, creating a yellow spot
- Wells are labelled with complementary strands of RNA



Microarrays, or gene chips, show which genes are active in the cells being tested.

Determining gene function

- usually through knockouts
  - to make a knockout animal, it is necessary to knock out the genes from gametes or from embryonic stem cells and to grow the animal from a zygote
- alternatively, gene expression can be reduced by the use of RNA interference – prevents translation of mRNA
  - does not result in as complete of a knockout as stem cells

Stem cells

Stem cells are undifferentiated biological cells that can differentiate into specialized cells and can divide (through mitosis) to produce more stem cells. They are found in multicellular organisms. In mammals, there are two broad types of stem cells: embryonic stem cells, which are isolated from the inner cell mass of blastocysts, and adult stem cells, which are found in various tissues. In adult organisms, stem cells and progenitor cells act as a repair system for the body, replenishing adult tissues. In a developing embryo, stem cells can differentiate into all the specialized cells—ectoderm, endoderm and mesoderm (see induced pluripotent stem cells)—but also maintain the normal turnover of regenerative organs, such as blood, skin, or intestinal tissues.

Practical applications of DNA technology: medical applications, human gene therapy, pharmaceuticals, forensic evidence, environmental cleanup, agriculture

- Identification
  - Restriction fragment length polymorphism (RFLP) identifies individuals
    - genomes of different individuals possess different restriction sites and varying distances between them
    - produces unique band pattern after fragmenting the DNA sample with endonucleases
  - Single nucleotide polymorphisms
    - the genome of one human differs from the genome of another at about one nucleotide in every 1000
- human gene therapy
  - genetic manipulation of an affected individual's DNA, in which the defective allele of the gene is replaced by the correctly functioning one
  - theoretically can be accomplished through viral vector or altering the genome of stem cell and letting it replicate

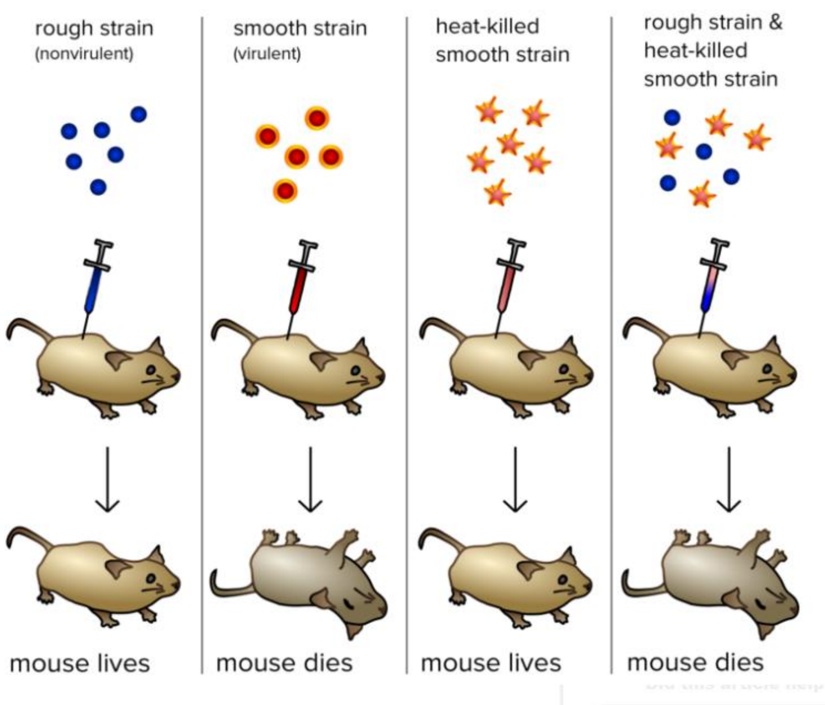
Safety and ethics of DNA technology

Content Category 1C: Transmission of heritable information from generation to generation and the processes that increase genetic diversity

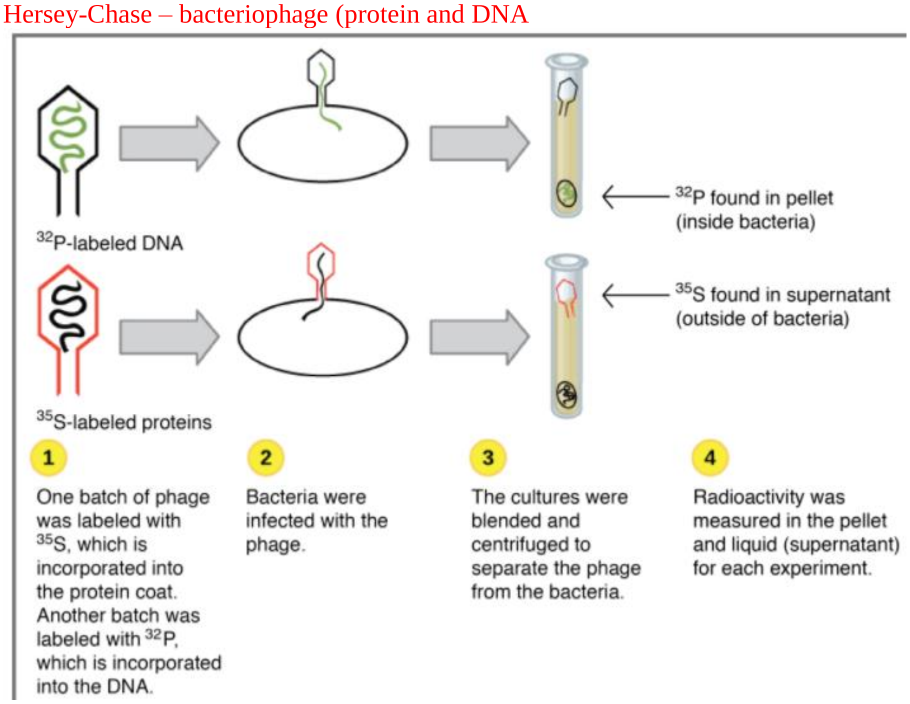
Evidence that DNA is Genetic Material (BIO)

Griffith Experiment – injecting mice with heat-killed S (did not cause disease)

Harmless R bacteria combined with harmless heat-killed S bacteria injected – killed mouse, found living S bacteria



Hersey-Chase – bacteriophage (protein and DNA



Mendelian Concepts (BIO)

Phenotype and genotype

Gene

Locus
Allele: single and multiple
Homozygosity and heterozygosity
Wild-type
Recessiveness
Complete dominance
Co-dominance

Codominance is a form of dominance wherein the alleles of a gene pair in a heterozygote are fully expressed. This results in offspring with a phenotype that is neither dominant nor recessive. A typical example showing codominance is the ABO blood group system.

Incomplete dominance, leakage, penetrance, expressivity

- Incomplete dominance is a form of intermediate inheritance in which one allele for a specific trait is not completely expressed over its paired allele. This results in a third phenotype in which the expressed physical trait is a combination of the phenotypes of both alleles.
- Leakage – gene flow from one species to another
- Penetrance – frequency that a genotype will result in the phenotype (even if you have the genotype, you might not have the phenotype – percent of people that have the phenotype with the genotype
- Expressivity is to what degree a penetrant gene is expressed. Constant expressivity means that if your genes for being smart manages to penetrate (show up as a trait), then your IQ is 120. Variable expressivity means that your IQ doesn't have to be 120, it could be somewhat lower or somewhat higher

Hybridization: viability

- **Genetic hybridization** is the process of interbreeding individuals from genetically distinct populations to produce a hybrid. A **genetic** hybrid would therefore carry two different alleles of the same gene.
- The process of two complementary, single-stranded DNA or RNA combining together, producing a double-stranded molecule through base pairing. This technique is used for interbreeding between individuals of genetically distinct populations.
- In summary, a postzygotic reproductive barrier is a mechanism that reduces the **viability** or reproductive capacity of **hybrid** offspring. **Hybrid** zygote abnormality is a type of postzygotic barrier in which **hybrid** zygotes fail to mature normally.

Gene pool

- The **gene pool** is the set of all genes, or genetic information, in any population, usually of a particular species.
  - In biology, a **population** is all the organisms of the same group or species, which live in a particular geographical area, and have the capability of interbreeding.[

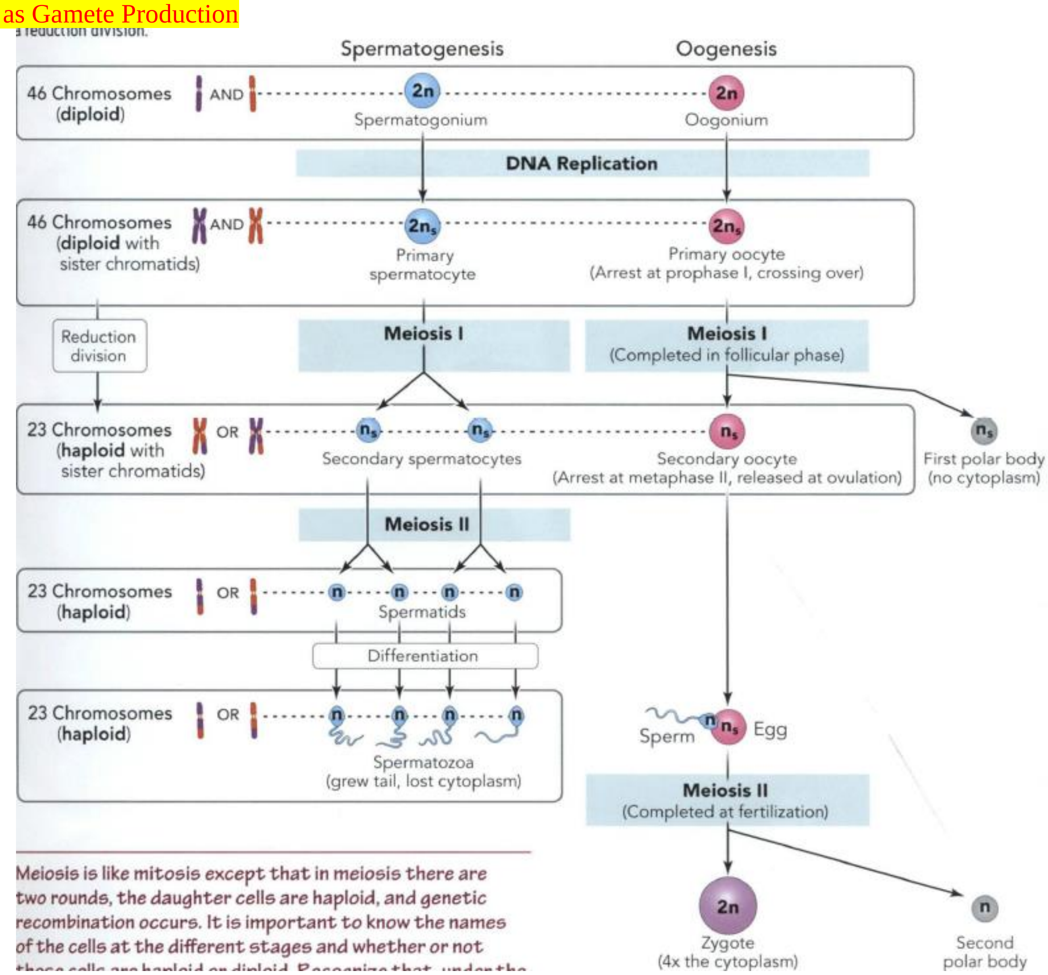
Meiosis and Other Factors Affecting Genetic Variability (BIO)

Significance of meiosis

Meiosis

- only in spermatogonium and oogonium
- Meiosis I – reductional division to make two haploid cells
  - Prophase I
    - homologous chromosomes line up alongside each other
      - crossing over – at synaptonemal complex
        - creates X shape – Chiasma
        - genes on same chromosomes closer together are more likely to cross over together, and are said to be linked
          - gene mapping
        - single and double crossovers possible
      - appears as tetrads – total of four chromatids
  - Metaphase I
    - the two homologues remain attached, move to metaphase plate
    - 23 tetrads lined up (as opposed to 46 chromosomes lined up in mitosis)
  - Anaphase I
    - homologous chromosomes separate (as opposed to mitosis, where sister chromatids separate
  - Telophase I
    - nuclear membrane may or may not reform, and cytokinesis may or may not occur
    - When cytokinesis occurs, the new cells are haploid with 23 replicated chromosomes
    - are called secondary spermatocytes or secondary oocytes
- Meiosis II – proceeds through prophase II, metaphase II, anaphase II, and telophase II, appearing much like mitosis
- Nondisjunction
  - primary nondisjunction (anaphase I)

- one of the cells will have two extra chromatids (which make up a complete chromosome), and the other will be missing a chromosome
  - Secondary nondisjunction
    - one cell has an extra chromatid, another lacks a chromatid
- Meiosis as Gamete Production



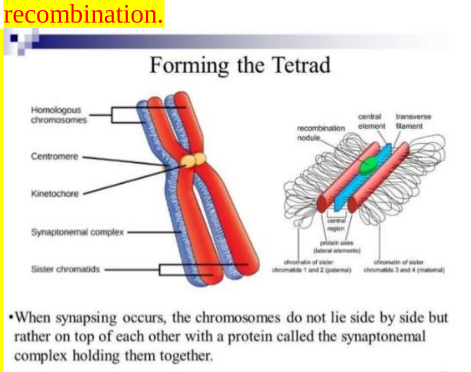
Stages in Males	Stages in Females	Chromosomes	Stage is Reached
Spermatogonium	Oogonium	Diploid	Progenitor cell present at birth
Primary spermatocyte	Primary oocyte	Diploid	After mitosis
Secondary spermatocyte	Secondary oocyte	Haploid	After meiosis I
Spermatid	Ootid*	Haploid	After meiosis II
Sperm (or spermatozoa)	Ovum*	Haploid	After maturation process

TABLE 2.4 > Summary of Chromosomes and Sister Chromatids

Process	Start	Finish
Replication	Diploid (46 chromosomes)	Diploid with sisters (46 chromosomes, 92 chromatids)
Mitosis	Diploid with sisters (46 chromosomes, 92 chromatids)	Diploid (46 chromosomes)
Meiosis I	Diploid with sisters (46 chromosomes, 92 chromatids)	Haploid with sisters (23 chromosomes, 46 chromatids)
Meiosis II	Haploid with sisters (23 chromosomes, 46 chromatids)	Haploid (23 chromosomes)

Important differences between meiosis and mitosis

- Segregation of genes
  - When an organism makes gametes, each gamete receives just **one gene copy**, which is selected randomly. This is known as the **law of segregation**

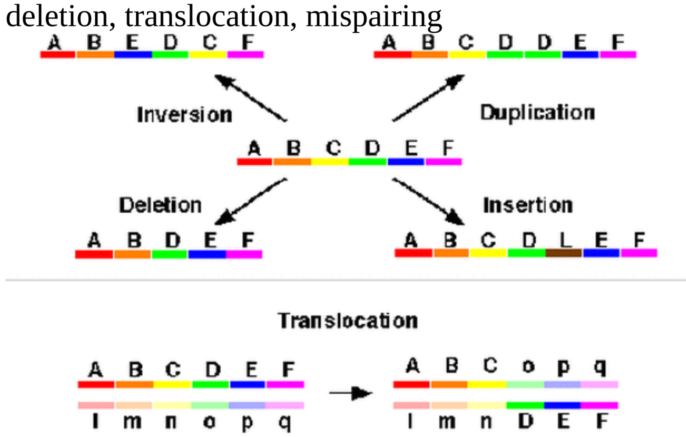
        - results from **alleles splitting in Meiosis II**
- Independent assortment
    - The Principle of **Independent Assortment** describes how different genes **independently** separate from one another when reproductive cells develop
- Linkage
    - **Genetic linkage** is the tendency of DNA sequences that are close together on a chromosome to be inherited together during the meiosis phase of sexual reproduction.
- Recombination
    - Single crossovers
    - Double crossovers
        - Say you have DNA strand C and DNA strand D
        - CCCCCCCCCCCCCCCCCCCCCCCCC
        - DDDDDDDDDDDDDDDDDDDDDDDDD
        - single crossover yields
        - CCCCCCCCCCCCCCCCCDDDDDDDD
        - DDDDDDDDDDDDDDDDDCCCCCCCC
        - double crossover yields
        - CCCCCCCCDDDDDDDCCCCCCCCCC
        - DDDDDDDDCCCCCCCDDDDDDDDDD
    - Synaptonemal complex
        - homologous chromosomes line up alongside each other
            - crossing over – at synaptonemal complex
                - creates X shape – Chiasma
                - genes on same chromosomes closer together are more likely to cross over together, and are said to be linked
                    - gene mapping
                - single and double crossovers possible
            - appears as tetrads – total of four chromatids
        - The **synaptonemal complex** (SC) is a protein structure that forms between homologous chromosomes (two pairs of sister chromatids) during meiosis and is thought to mediate chromosome pairing, synapsis, and recombination.
        - 

    - Tetrad
- Sex-linked characteristics
- Very few genes on Y chromosome
- Sex determination
    - A baby's **sex** is **determined** at the time of conception. When the baby is conceived, a chromosome from the sperm cell, either X or Y, fuses with the X chromosome in the egg cell, **determining** whether the baby will be female (XX) or male (XY).
- Cytoplasmic/extranuclear inheritance

- Extranuclear inheritance or cytoplasmic inheritance is the transmission of genes that occur outside the nucleus. It is found in most eukaryotes and is commonly known to occur in cytoplasmic organelles such as mitochondria and chloroplasts or from cellular parasites like viruses or bacteria.
- The extranuclear genomes of mitochondria and chloroplasts however replicate independently of cell division. They replicate in response to a cell's increasing energy needs which adjust during that cell's lifespan. Since they replicate independently, **genomic recombination of these genomes is rarely found** in offspring contrary to nuclear genomes, in which recombination is common.
- Mitochondrial disease are received from the mother, fathers don't as sperm do not contribute

Mutation

- General concept of mutation — error in DNA sequence
- Types of mutations: random, translation error, transcription error, base substitution, inversion, addition, deletion, translocation, mispairing



- Advantageous vs. deleterious mutation
- Inborn errors of metabolism
    - **Inborn errors of metabolism** are rare genetic (inherited) disorders in which the body cannot properly turn food into energy. The disorders are usually caused by defects in specific proteins (enzymes) that help break down (metabolize) parts of food
- Relationship of mutagens to carcinogens
- The **Ames test** is a widely employed method that uses bacteria to test whether a given chemical can cause mutations in the DNA of the test organism. More formally, it is a biological assay to assess the mutagenic potential of chemical compounds.[1] A positive test indicates that the chemical is mutagenic and therefore may act as a carcinogen, because cancer is often linked to mutation. The test serves as a quick and convenient assay to estimate the carcinogenic potential of a compound because standard carcinogen assays on mice and rats are time-consuming (taking two to three years to complete) and expensive. However, false-positives and false-negatives are known.
- **carcinogen is an agent that induces neoplasia, i.e. cancer.**
    - What's an agent? Chemicals, radiation, and viruses are among the agents implicated in causing cancer.
- A mutagen is a chemical that can cause changes (mutations) to the genetic material of a cell (DNA).
    - **A mutagen is one possible pathway to carcinogenesis.**
    - When mutations occur in germ cells (i.e. sperm or ova) it is possible for the mutation to be transmitted to offspring.
- A mutagen may be a carcinogen, but the link is not absolute. That is, **not all chemicals shown to be mutagens are necessarily carcinogens**.
    - Conversely, not all carcinogens are mutagens.
    - There are nongenotoxic carcinogens—chemicals that cause cancer by several mechanisms including by inducing sustained cell injury.

Genetic drift

- **Genetic drift** is a mechanism of evolution in which allele frequencies of a population change over generations due to chance (sampling error).
- Genetic drift occurs in all populations of non-infinite size, but its effects are strongest in small populations.

Genetic drift can have major effects when a population is sharply reduced in size by a natural disaster (**bottleneck effect**) or when a small group splits off from the main population to found a colony (**founder effect**).

Synapsis or crossing-over mechanism for increasing genetic diversity

Analytic Methods (BIO)

Hardy–Weinberg Principle

- Hardy-Weinberg Principle
  - gene pool – total collection of all alleles in a pool
    - any change in the **gene pool** constitutes evolution (not phenotype)
      - Can be defined on the individual level when a change occurs in genes that can be passed down to subsequent generations, or at the level of the population where a change in the total gene pool (allelic frequencies) constitutes evolution. During speciation, new species evolve from older species, which illustrates the process of evolution on a macro scale. Things that deal with phenotypic shift, or change in the frequencies of phenotypes, without changing the overall allelic frequencies of that population, do not count.
  - 5 conditions
    - no selection for the fittest organism
    - Random mating
    - Large population
    - Immigration/emigration must not change the gene pool
    - Mutational equilibrium
  - If population approximates Hardy-Weinberg equilibrium, the following equation can be used to predict the frequencies of genotypes and phenotypes from allelic frequencies within a population
    - $p^2 + 2pq + q^2$
    - p^2 = homozygous dominant, $2pq$ = heterozygous, q^2 = homozygous recessive
    - $p+q = 1$

Testcross (Backcross; concepts of parental, F1, and F2 generations)

- To identify whether an organism exhibiting a dominant trait is homozygous or heterozygous for a specific allele, a scientist can perform a **test cross**. The organism in question is crossed with an organism that is **homozygous for the recessive trait**, and the offspring of the **test cross** are examined.

Gene mapping: crossover frequencies

Biometry: statistical methods

- Biometric identifiers are often categorized as physiological versus behavioral characteristics.[4] Physiological characteristics are related to the shape of the body. Examples include, but are not limited to fingerprint, palm veins, face recognition, DNA, palm print, hand geometry, iris recognition, retina and odour/scent. Behavioral characteristics are related to the pattern of behavior of a person, including but not limited to typing rhythm, gait,[5] and voice.[note 2] Some researchers have coined the term behaviometrics to describe the latter class of biometrics.[6]
- **Biometrics** is the technical term for body measurements and calculations. It refers to metrics related to human characteristics. Biometrics authentication (or realistic authentication)[note 1] is used in computer science as a form of identification and access control.[1][2] It is also used to identify individuals in groups that are under surveillance.

Evolution (BIO)

Natural selection

- Fitness concept Reproductive success, contribution to the gene pool
- Selection by differential reproduction
- Concepts of natural and group selection
  - **Group selection** is a proposed mechanism of evolution in which natural selection acts at the level of the group, instead of at the more conventional level of the individual
  - The behavior of animals could affect their survival and reproduction as groups, speaking for instance of actions for the good of the species.
- Evolutionary success as increase in percent representation in the gene pool of the next generation

Speciation

- Polymorphism
  - Polymorphism is common in nature; it is related to biodiversity, genetic variation, and adaptation; it usually functions to retain variety of form in a population living in a varied environment.[4]:126 The most common example is sexual dimorphism, which occurs in many organisms. Other examples are mimetic forms of butterflies (see mimicry), and human hemoglobin and blood types.
- Adaptation and specialization
- Inbreeding
  - **Inbreeding** is the production of offspring from the mating or breeding of individuals or organisms that are closely related genetically.[

- **Inbreeding results in homozygosity,** which can increase the chances of offspring being affected by recessive or deleterious traits.[3] This generally leads to a decreased biological fitness of a population[4][5] (called inbreeding depression), which is its ability to survive and reproduce

- Outbreeding
    - Breed from parents not closely related
- Bottlenecks

Evolutionary time as measured by gradual random changes in genome

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

Content Category 1D: Principles of bioenergetics and fuel molecule metabolism

Principles of Bioenergetics (BC, GC)

Bioenergetics/thermodynamics

- Free energy/Keq
    - Equilibrium constant
    - Relationship of the equilibrium constant and ΔG°
- Spontaneity of a reaction under specific conditions can be predicted using the relationship between the equilibrium constant K and ΔG
- The difference between ΔGº and ΔG

$$\Delta G^{\circ} = -RT \ln(K)$$

    - ΔGº – under specific case of standard state conditions
    - ΔG – far less specific, represents the energy change for any given reactions under any attainable conditions

$$\Delta G = \Delta G^{\circ} + RT \ln(Q)$$

- Relationship between K and ΔG:
    - if K = 1, then ΔGº = 0
    - if K > 1, then ΔGº < 0
    - if K < 1, then ΔGº > 0
        - This does not mean that a reaction is always spontaneous if it has an equilibrium constant greater than one
            - **spontaneity of a reaction depends on starting concentrations of products and reactants**
        - The relationship between K and ΔGº does say that if a reaction has an equilibrium constant greater than one, the reaction is spontaneous at the temperature used to derive that particular equilibrium constant and standard state
- Concentration
    - Le Châtelier's Principle

Le Chatelier's Principle

- When a system at equilibrium is stressed, the system will shift in a direction that will reduce that stress
    - Three stresses
        - addition or removal or product or reactant
        - changing the pressure or volume of the system
        - heating or cooling the system
    - The Haber Process: $N_{2(g)} + 3H_{2(g)} \rightarrow 2NH_{3(g)}$ + Heat
        - If we add N_2, the reaction is pushed to the right
        - If we add heat (analogous to adding more product), then the reaction is pushed to the left
        - If pressure is increased, equilibrium shifts to the right
            - there are four gas molecules on the left side and two on the right
            - A similar effect is found when a solution in equilibrium is concentrated or diluted
    - equilibrium shifts to the side with fewer moles when the solution is concentrated
- Endothermic/exothermic reactions
- Endothermic – reaction with positive enthalpy change
    - produces heat flow to the system
    - Anabolic reactions (building a large molecule from several smaller ones) are usually endothermic
        - **photosynthesis – uses energy to build glucose**

- Exothermic – reaction with negative enthalpy change
    - produces heat flow to the surroundings
    - Catabolic reactions (breaking down a large molecule into several smaller molecules)) are usually exothermic
        - **cellular respiration – breaks down glucose to release energy**
- Free energy: G
- Spontaneous reactions and ΔG°
- G = ΔH - TΔS
    - all three state functions refer to the system, but the equation also provides information about the surroundings
        - Heat transferred into the surroundings (exothermic) increases entropy of surroundings
        - Heat transferred into system (endothermic) increases entropy of system
            - thus, accounts for entropy change of both system and surroundings
    - Algebraic manipulation to ΔG = -TΔS
        - S must be positive for G to be negative – both required for spontaneous reaction
        - Both S and G must be 0 at equilibrium
- Extensive property and a state function
- Not conserved – can change for an isolated system
- **represents maximum non-PV work available for a reaction**
    - contracting muscles, transmitting work, batteries
-

Phosphoryl group transfers and ATP

- ATP hydrolysis ΔG << 0
- ATP group transfers
- High energy phosphoanhydride bonds are broken to release energy

Biological oxidation-reduction

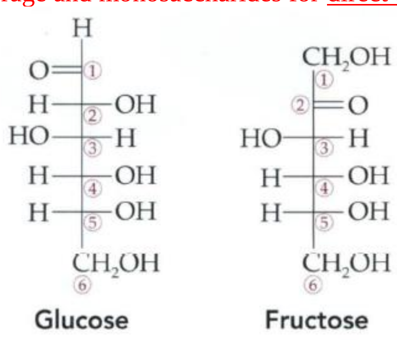
- Half-reactions
- Soluble electron carriers
    - water-soluble ones are free-floating in the cytosol (e.g. NADH, FADH2 etc)
      lipid-soluble ones are embedded in the membrane (e.g. CoQ, FMN etc)
- Flavoproteins
    - **Flavoproteins** are proteins that contain a nucleic acid derivative of riboflavin: the flavin adenine dinucleotide(FAD) or flavin mononucleotide (FMN).

Carbohydrates (BC, OC)

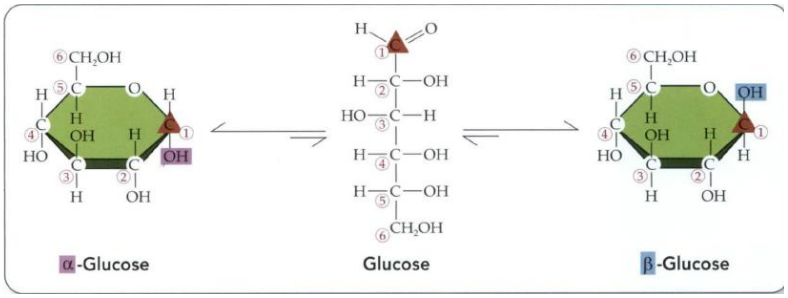
Description

Carbohydrates

- useful in energy storage and providing easily accessible energy to the body
    - high concentrations of C-H bonds (not as high as lipids)
    - Polysaccharides for energy storage and monosaccharides for direct use of energy by cells

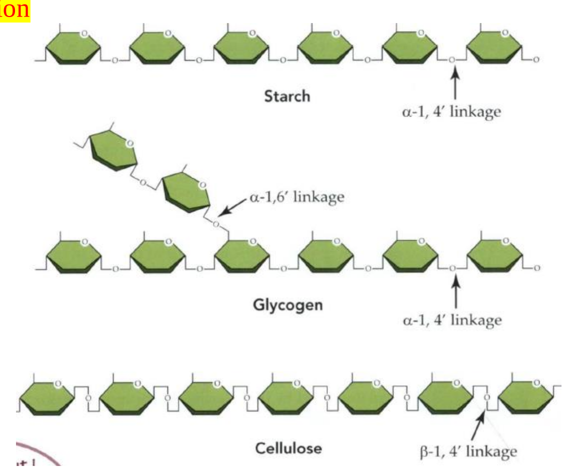


- Glucose normally accounts for 80% of the carbohydrates absorbed by humans
    - almost all digested carbohydrates reaching body cells have been converted to glucose by the liver or enterocytes (intestinal cells)
    - the cell can oxidize glucose to transfer its chemical energy to a more readily usable form, ATP



- **Alpha is axial**
- if cell has sufficient ATP, then glucose is polymerized to the polysaccharide form, **glycogen**, or converted to fat
- glycogen is a branched glucose polymer with **alpha linkages**
  - glycogen is more branched than amylopectin
- found in <u>large amounts in muscle and liver cells</u>
  - liver cells are one of the few cell types capable of reforming glucose from glycogen and releasing it back into the bloodstream when needed

- Absorption of glucose
  - only certain epithelial cells in digestive tract and proximal tubule of kidney are capable of absorbing glucose against a concentration gradient—through secondary active transport
  - <u>All other cells absorb glucose through facilitated diffusion</u>
    - insulin increases rate of facilitated diffusion
- **Starch** – plant glycogen
  - amylose – may be branched or unbranched, has same alpha linkages as glucose
  - amylopectin – resembles glycogen, has different branching structure
- **Cellulose** – <u>structural, has Beta linkages</u>
  - humans have enzymes to digest alpha but not beta linkages
  - Both alpha and Beta linkages are hydrolyzed using water



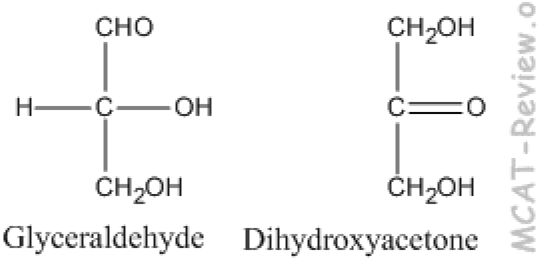
- Nomenclature and classification, common names
- Absolute configuration
- Cyclic structure and conformations of hexoses
- Epimers and anomers

Hydrolysis of the glycoside linkage
Monosaccharides
Disaccharides
Polysaccharides

- nomenclature
- Carbohydrate = Sugars, monosaccharides, disaccharides, polysaccharides
- Prefix:
- Deoxy = it has an -H in place of an -OH at a certain position.
- D/L = absolute configuration = assigned based on the chirality of the carbon atom furthest from the carbonyl group.
- α/β = anomeric configuration.
- Suffix: all sugars end in -ose.
- classification
- aldose = sugars with an aldehyde group.
- ketose = sugars with a ketone group.
- pyranose = sugars in a 6 membered ring structure = hexagon shaped. For example, glucopyranose = glucose in a 6 membered ring.
- furanose = sugars in a 5 membered ring structure = pentagon shaped. For example, fructofuranose = fructose in a 5 membered ring.
- #ose = sugar with # carbon atoms. For example, hexose = sugar with 6 carbons. Another example: aldopentose = a five-carbon sugar with an aldehyde group.
- In order to be classified as a carbohydrate, a molecule must have:
- at least a 3 carbon backbone.
- an aldehyde or ketone group.

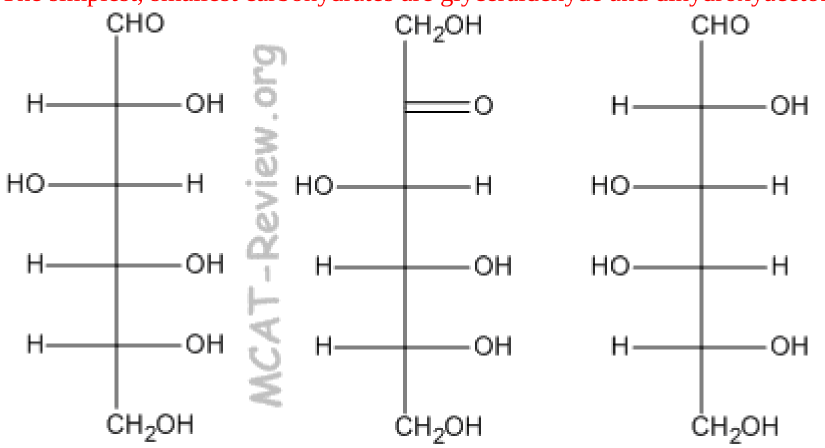
- at least 2 hydroxyl groups.
- common names

Smallest Carbohydrates



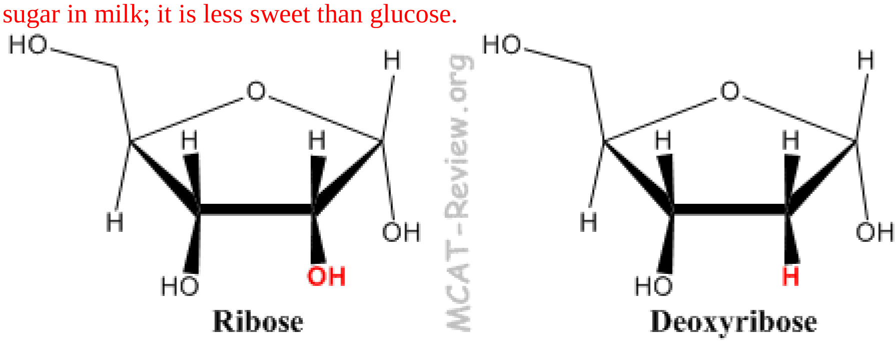
Glyceraldehyde Dihydroxyacetone

- The simplest, smallest carbohydrates are glyceraldehyde and dihydroxyacetone.



Glucose Fructose Galactose

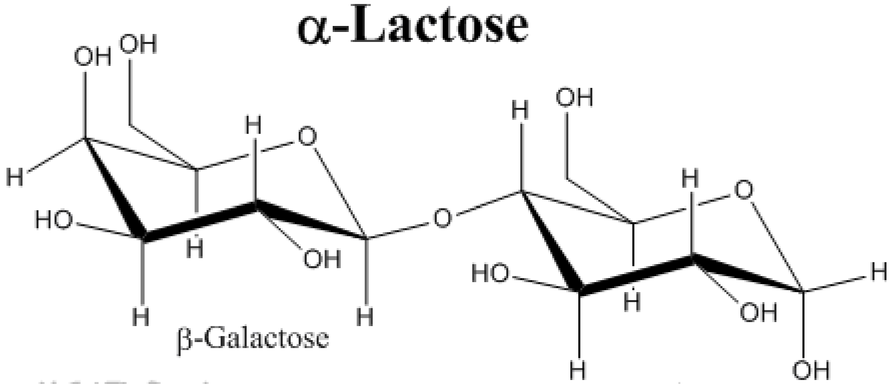
- The 3 common monosaccharides are glucose, fructose, and galactose. Glucose is our blood sugar and the product of photosynthesis. Fructose is the sugar in fruits, and it is sweeter than glucose. Galactose is one of the monomers that make up lactose, which is the sugar in milk; it is less sweet than glucose.



Ribose **Deoxyribose**

- The sugar that make up RNA is ribose, and for DNA it is deoxyribose (More precisely it's 2'-deoxyribose because the difference is at the 2 carbon).
- Sucrose is a disaccharide made from **α-glucose and β-fructose** joined at the hydroxyl groups on the anomeric carbons (making acetals). Sucrose is table sugar, the sugar we buy in stores.

α-Lactose



β-Galactose α-Glucose

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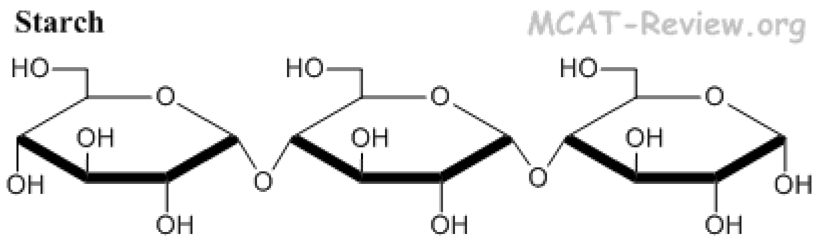
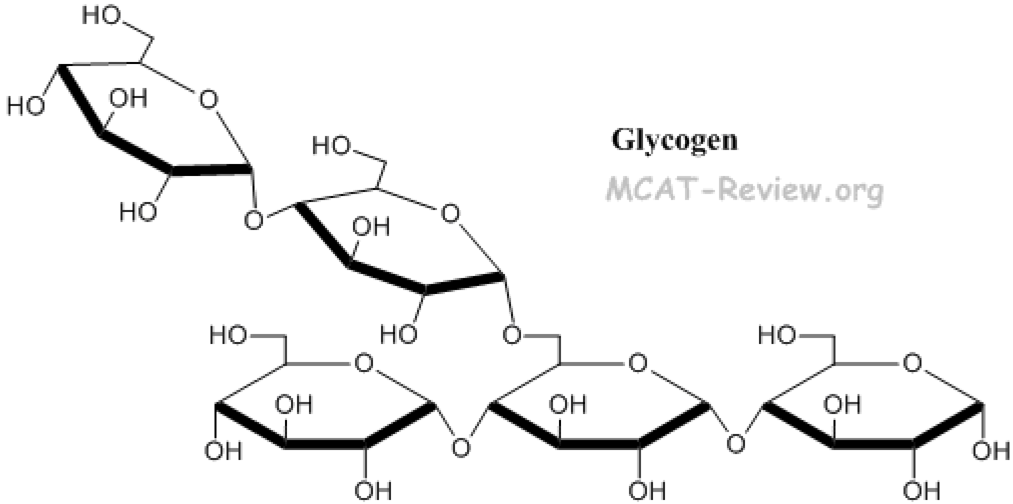
- Lactose is a disaccharide made from **β-galactose** and α/β-glucose joined by a 1-4 linkage.

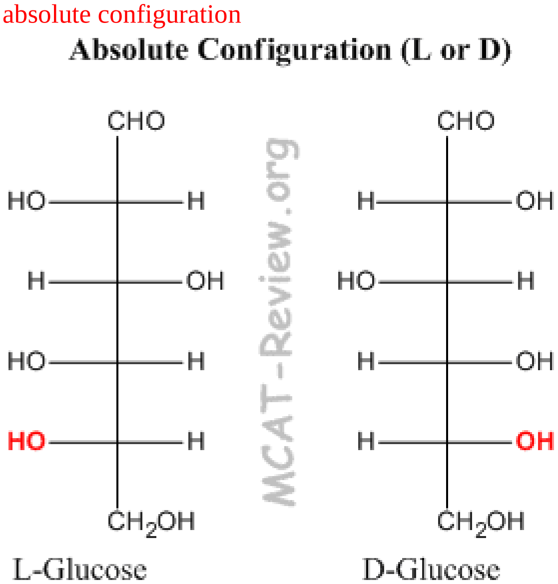


- Starch = glucose molecules joined by α1-4 linkage.



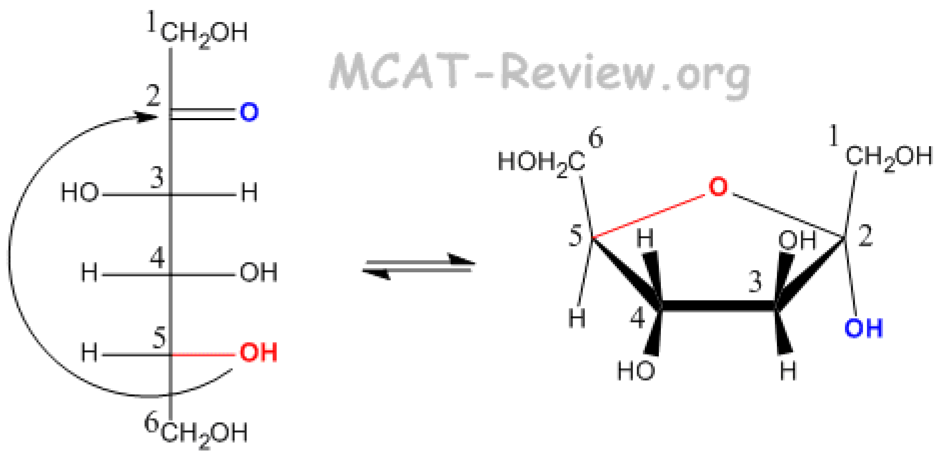
- Glycogen = same as starch, but with additional α1-6 linkages for branching.

- absolute configuration



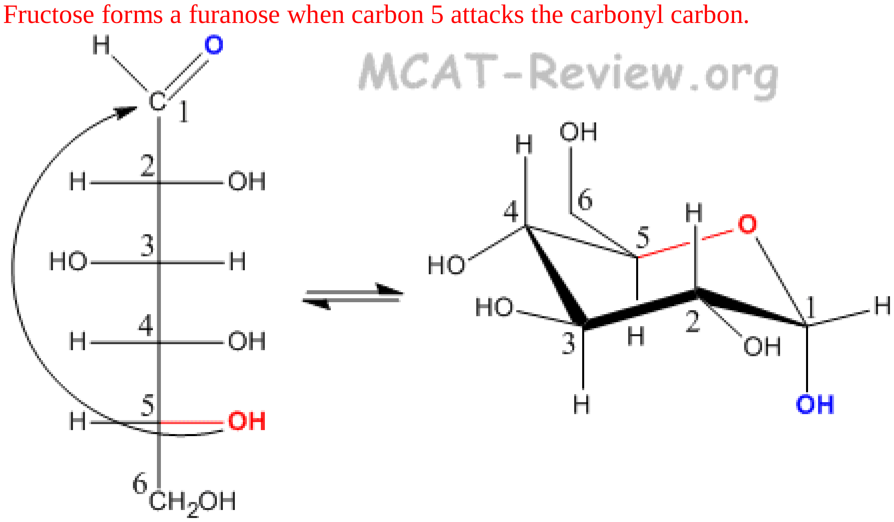
  - The chiral carbon furthest from the carbonyl group determines the absolute configuration L or D of the sugar.
  - If in the fischer projection, the OH group on the chiral carbon furthest from the carbonyl is **pointing left, then it's L. If it's pointing right, then it's D.**
  - Note: L and D are enantiomers, not epimers. So, every chiral carbon center inverts. It's just that you assign L and D based on the chiral carbon furthest from the carbonyl.

- cyclic structure and conformations of hexoses



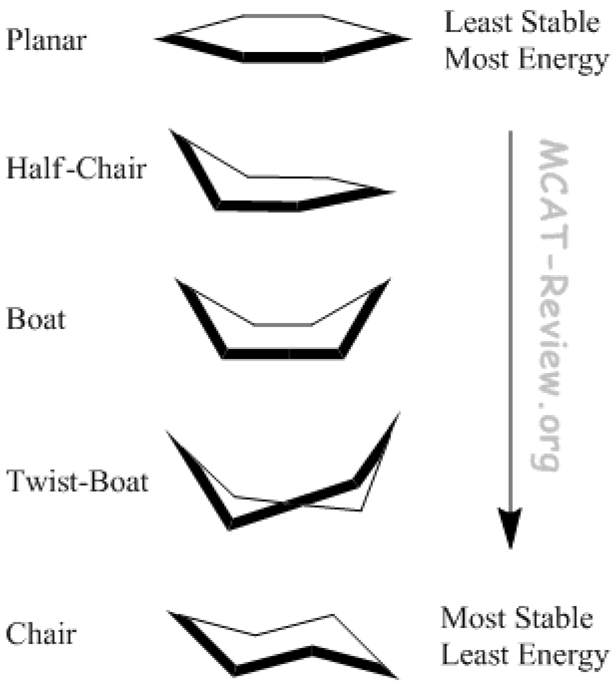
D-Fructose α-D-Fructose

- Fructose forms a furanose when carbon 5 attacks the carbonyl carbon.



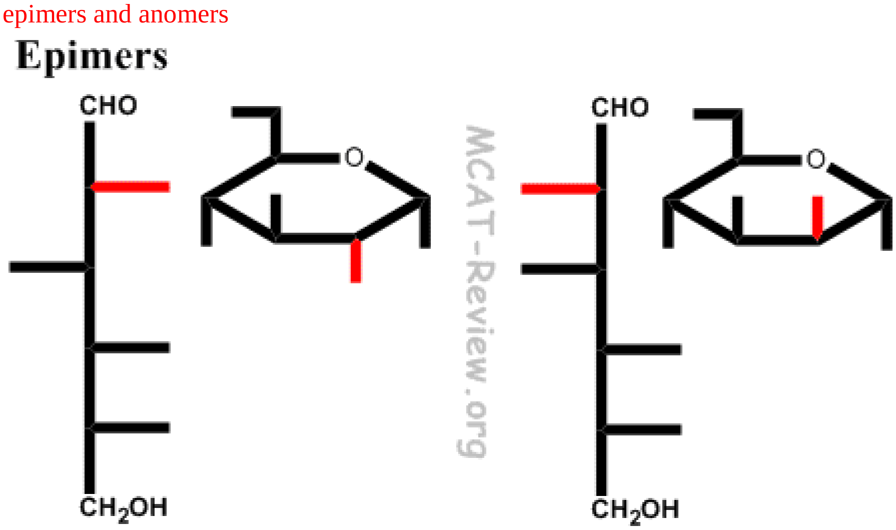
D-Glucose α-D-Glucose

- Glucose forms a pyranose when carbon 5 attacks the carbonyl carbon.
- Convert a Fischer projection to Haworth (cyclic) form
  - -OH groups that are pointing Left on the Fischer becomes Up on the Haworth.
  - -OH groups that are pointing Right on the Fischer becomes Down on the Haworth.
  - The -OH group on the anomeric carbon (the Fischer carbonyl) can be either up (beta) or down (alpha).
  - The CH_2OH group on the absolute configuration carbon (carbon 5) points up for D, and down for L.

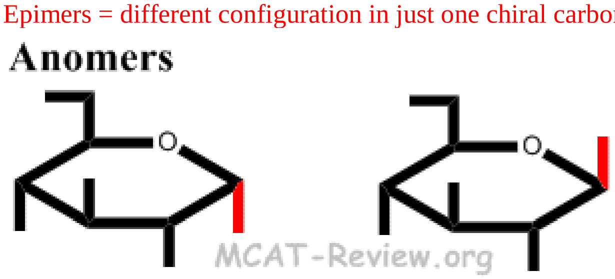


- In the planar conformation, everything is eclipsed.
- In the chair conformation, everything is staggered.
- All the conformations in between are partially eclipsed.
- The Boat conformation has Flagpole interactions because axial groups attached to the head and tail of the boat clash.
- The Twist-boat conformation lessens these Flagpole interactions in addition to reducing the number of eclipsed interactions.

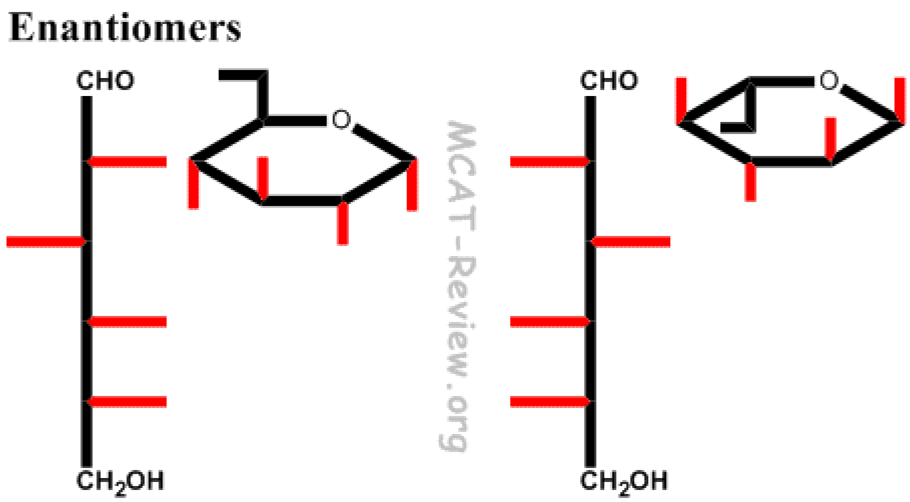
- epimers and anomers



- Epimers = different configuration in just one chiral carbon.

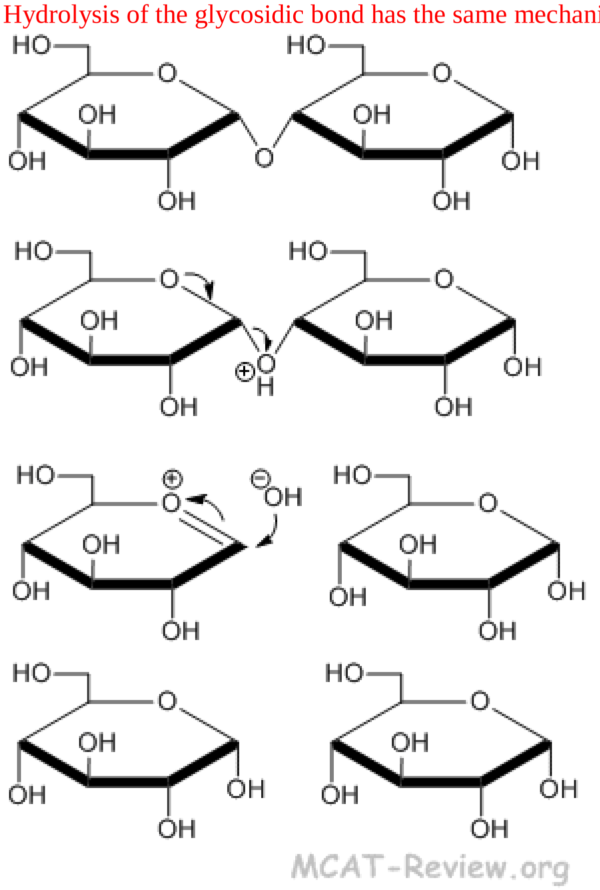


- Anomers = different configuration in the chiral, anomeric carbon when the molecule is in the cyclic form.
- Anomers are simply special types of epimers.
- Epimers are simply special types of diastereomers.
- Don't confuse with enantiomers (D/L configuration), in which everything changes configuration.



- Hydrolysis of the glycoside linkage

- Glycoside linkage = acetal linkage = linkage involving the hydroxyl group of the anomeric carbon.
- Glycoside linkage can also mean the linkage between the sugar and the base in nucleotides.
- Examples of glycosidic linkages = starch, glycogen, nucleotide.
- Hydrolysis of the glycosidic bond has the same mechanism as hydrolysis of the acetal bond.



- glycoside + H_2O + catalyst → hydrolysis.
- Catalysts include: Amylase for starch and glycosylase for nucleotides

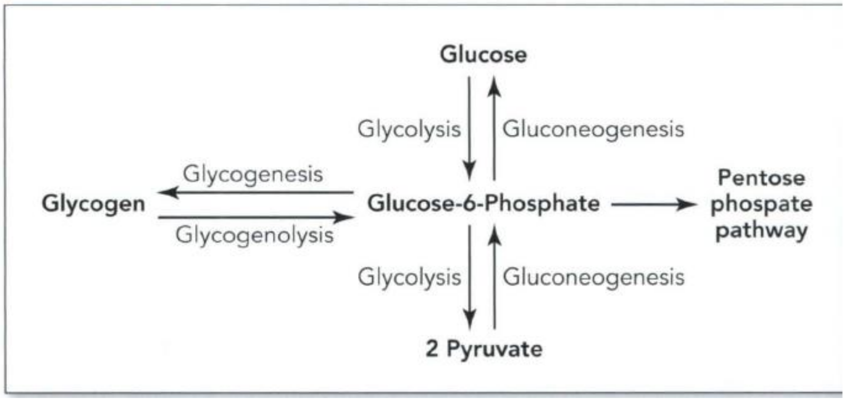
Glycolysis, Gluconeogenesis, and the Pentose Phosphate Pathway (BIO, BC)

Glycolysis (aerobic), substrates and products

- Feeder pathways: glycogen, starch metabolism
  - occurs in cytosol
  - ten steps
    - first half: two phosphates from two different ATP molecules added to glucose
      - trap glucose inside the cell and prime it to be split into two 3-carbon molecules
      - Energy input phase

- 2^{nd} half:
  - two newly created 3-carbon molecules are each converted to pyruvate
  - two ATP produced per 3-carbon molecule (4 total)
  - one NADH generated from NAD^+ per molecule (two NADH total)
  - energy output phase
- Production of ATP - substrate-level phosphorylation
- other monosaccharides such as fructose and galactose can feed into glycolysis
  - most fructose or galactose is converted into glucose by the liver anyway
  - however, they can still enter as an intermediate of the six-carbon phase
  - Glycerol can also feed in (at glucose 6-phosphate)
  - However, fats and proteins can only enter through the TCA

FIGURE 3.5 Central Role of Glucose 6-Phosphate



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- Glycogen and Starch Are Degraded by Phosphorolysis
- The glucose units of the outer branches of glycogen and starch gain entrance into the glycolytic pathway through the sequential action of two enzymes: glycogen phosphorylase (or the similar starch phosphorylase in plants) and phosphoglucomutase.
-

GLYCOLYSIS REACTIONS

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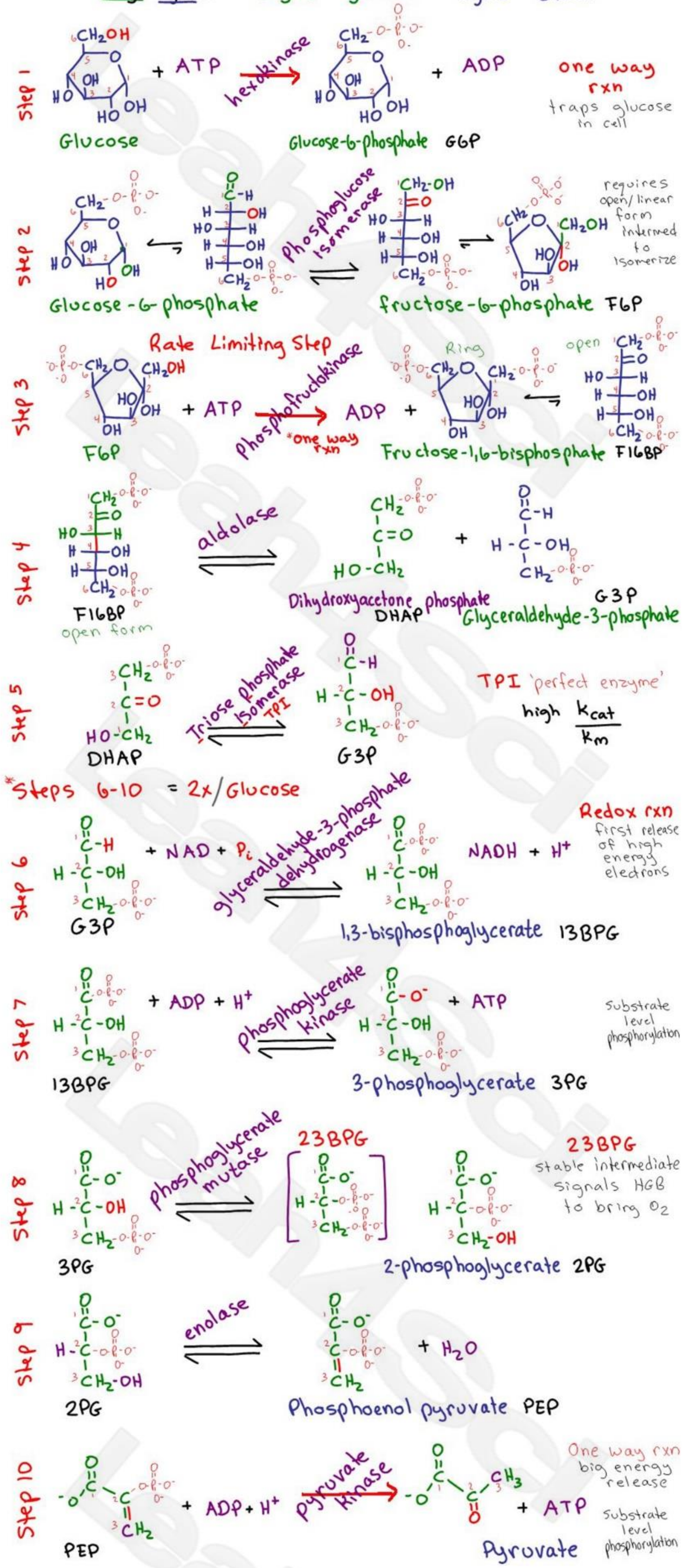
Glycolysis: Glyco = glucose Lysis = break



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Fermentation (anaerobic glycolysis)

- Fermentation – metabolism in the absence of oxygen
  - includes glycolysis and reduction of pyruvate to ethanol or lactic acid and the oxidation of NADH back to NAD^+
  - lactic acid or ethanol is expelled from the cell as waste product, along with CO_2
  - produces only 2 ATP per glucose
- Cori cycle = metabolic pathway in which lactate produced by anaerobic glycolysis in the muslces moves to the liver and is converted to glucose, which then returns to the muscles and is metabolized back to lactate

Gluconeogenesis (BC)

- synthesis of glucose – occurs in the liver and in the cortex of the kidneys, to a lesser extent
  - in fasting state, soon after glycogen breakdown begins, liver begins gluconeogenesis
  - in conjunction with glycogenesis, helps maintain the blood glucose level many hours after meal has been eaten
  - Almost identical to the reversed pathway of glycolysis
    - remember that enzymes catalyze both forward and backward reactions
    - a few reactions with particularly large G values have distinct enzymes (different pathways)
      - pyruvate kinase, phosphofructose kinase, hexokinase
      - large G values usually involve ATP or NADH
      - the steps in glycolysis with no large G have their reactants and products in a relatively constant proportion
  - to be a substrate for gluconeogenesis, the molecule must have a 3-carbon backbone
    - triglyceride backbone, some amino acids, lactic acid
  - Oxaloacetate apparently is a substrate for glucose
- Substrates ("glucogenic")
  - glycerol, lactate, alanine, glutamine, all citric acid cycle intermediates (through conversion to oxaloacetate)
  - *not acetyl CoA*
- glycolysis and gluconeogenesis, like glycogenesis and glycogenolysis, are competing processes that are regulated by competing hormones
  - Ex: insulin and glucagon
    - insulin promotes glycolysis and glycogenesis (decreasing glucose)
    - glucagon promotes gluconeogenesis and glycogenolysis (increasing glucose)

Pentose phosphate pathway (BC)

- Pentose Phosphate Pathway
  - alternative pathway to glycolysis
  - diverges from glycolysis and eventually merges back with glycolysis at glyceraldehyde-3-phosphate
  - purpose is to create **NADPH and some five carbon sugars**, including ribose
  - First half
    - oxidative branch – generates NADPH
      - NADPH – used for various synthetic functions of the body, such as making cholesterol
  - Second half
    - non-oxidative branch – creates important five-carbon sugars, like ribose
  - pathway is always active (constitutively active)
    occurs most commonly in tissues involved in lipid synthesis, such as in liver and adipocytes
  - regulated not by external hormones but by NADPH, which inhibits the first step
- **Glucose 6-phosphate dehydrogenase** catalyzes the production of 6-phosphogluconolactone

Net molecular and energetic results of respiration processes

- Glycolysis
  - Molecular: two molecules of pyruvic acid
  - two ATP
  - two NADH
- TCA
  - 2 ATP
  - 6 NADH
  - 2 $FADH_2$
  - 2 CO_2
    - In this stage, oxidation of glucose to CO_2 is completed
- ETC
  - Net yield of 34 ATP
  - 6 H_2O are formed when electrons unite with O_2

Principles of Metabolic Regulation (BC)

Regulation of metabolic pathways (BIO, BC)

- Maintenance of a dynamic steady state

Regulation of glycolysis and gluconeogenesis

- Glycolysis – reactions catalyzed by hexokinase, phosphofructokinase, and pyruvate kinase are virtually irreversible, and each of them serves as a control site
    - Phosphofructokinase is the key enzyme
        - high levels of ATP allosterically inhibit
        - AMP reverses the inhibitory action of ATP
        - Fall in pH also inhibits (from lactic acid)
        - Fructose 2,6-bisphosphate is a potent activator
- Pyurvate Dehydrogenase complex
    - formation from acetyl CoA from pyruvate is an irreversible step
        - pyruvate dehydrogenase complex
            - NADH and acetyl CoA inhibits
            - phosphorylation inhibits
                - increasing NADH/NAD+, acetyl CoA/CoA, or ATP/ADP ratio promotes **phosphorylation** and deactivation
- TCA
    - isocitrate dehydrogenase – allosterically stimulated by ADP, NAD+, **Mg^{2+}**
        - NADH inhibits, ATP inhibits
    - alpha-ketoglutarate dehydrogenase
        - inhibited by succinyl CoA and NADH, its product

Metabolism of glycogen

- **Glycogen phosphorylase** catalyzes the rate-limiting step in glycogenolysis

Regulation of glycogen synthesis and breakdown

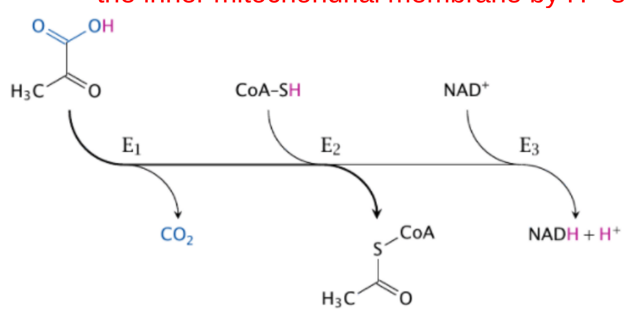
- Allosteric and hormonal control
- Glycogen breakdown and synthesis are regulated by cAMP cascade regulated through protein kinase A
    - phosphorylation of glycogen synthase decreases enzymatic activity
    - Protein phosphatase 1 reverses this effect
- Hormonal
    - Insulin stimulates glycogen synthesis by activating protein phosphatase 1

Analysis of metabolic control

Citric Acid Cycle (BIO, BC)

Acetyl-CoA production (BC)

- **Pyruvate dehydrogenase complex** (**PDC**) is a complex of three enzymes that converts pyruvate into acetyl-CoA by a process called pyruvate decarboxylation.
- Occurs in the mitochondrial matrix
    - pyruvate is produced in the cytosol—it easily crosses the outer mitochondrial membrane, and gets in the inner mitochondrial membrane by H+ symport



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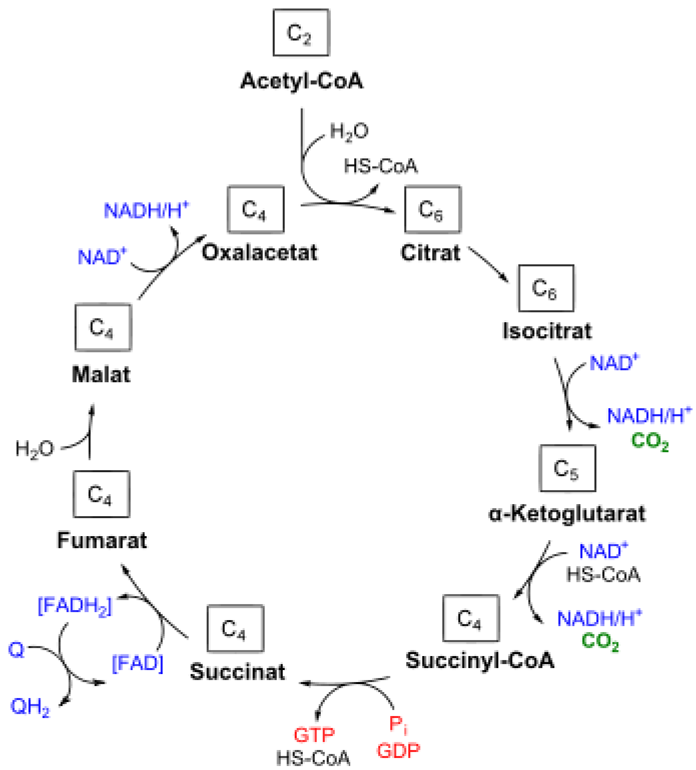
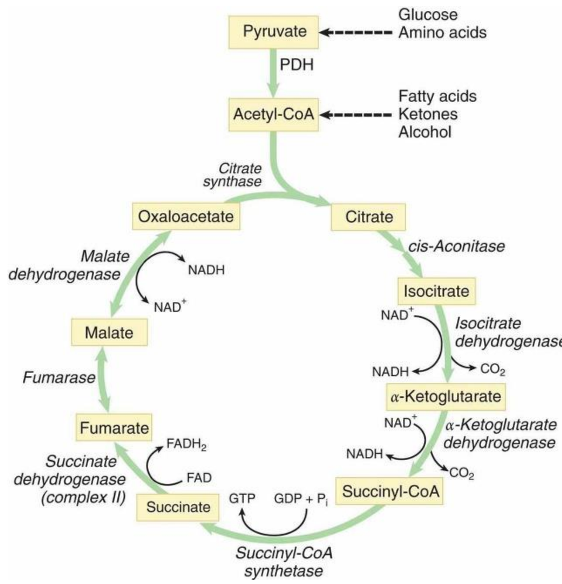
Reactions of the cycle, substrates and products



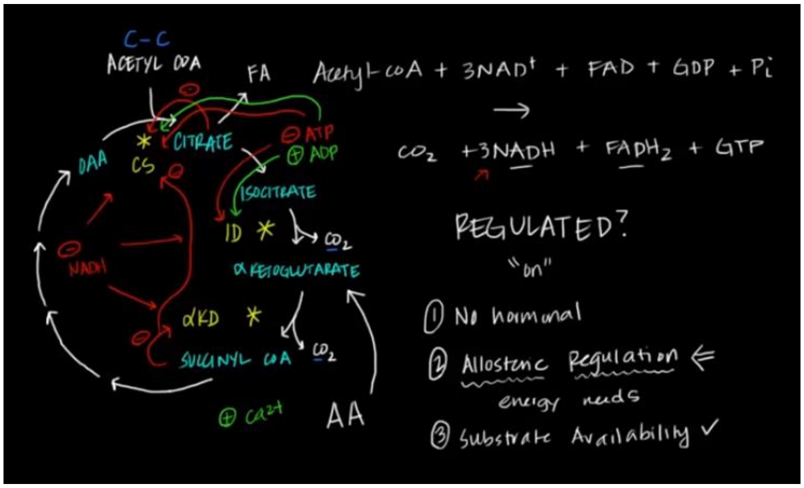


- Some pointers about this process:
  - The enzymes are named for the previous substrate
  - CIKSSFMO
    - Isocitrate → Alpha – ketoglutarate
      - CO2, NADH
    - Alpha ketoglutarate → Succinyl-CoA
      - CO2, NADH
    - Succinyl-CoA → Succinate
      - ATP
    - Succinate → Fumarate
      - FADH2
    - Malate → oxaloacetate
      - NADH
  - Succinate dehydrogenase is complex II in the ETC

Regulation of the cycle

Citric Acid Regulation

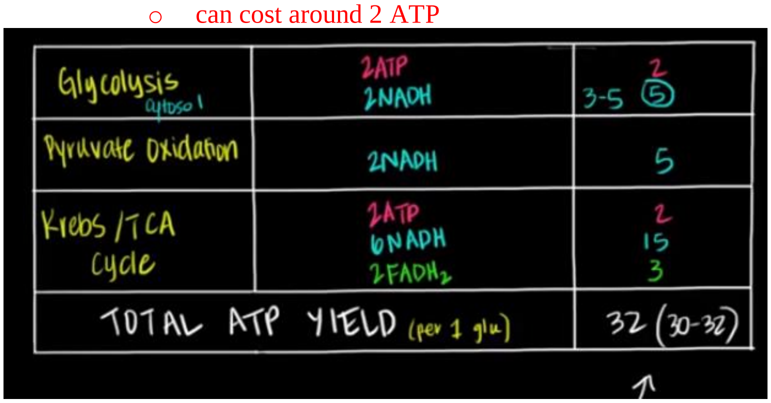
- Acetyl CoA + 3 NAD^+ + FAD^+ +GDP + Pi
  - produces Co2, 3NADH, FADH2, GTP
- No hormonal regulation
- Allosteric regulation
  - inhibitors
    - NADH inhibits CS, ID, and alpha KD
    - ATP – CS and ID
    - Citrate – CS
    - Succinyl CoA – CS
  - Activators
    - ADP: CS and ID
    - Ca2+: ID, alpha KD
- Substrate availability
  - Amino acids convert into alpha ketoglutarate
    - Amino acids usually speed the cycle up



Net molecular and energetic results of respiration processes

Calculating ATP produced in cellular respiraton

- 30-38 ATP
- NADH: 2-3 ATP
- FADH – 1-2 ATP
- Protein complex 1 and 3 pumps 4 H+, Complex 4 pumps 2 H+
    - NADH donates into Complex 1: total of 10 H+
    - FADH2 donates into complex 2: Total of 6 H+
- 4 protons per molecule of ATP
- NADH is shuttled from glycolysis to inner mitochondrial space
    - can cost around 2 ATP



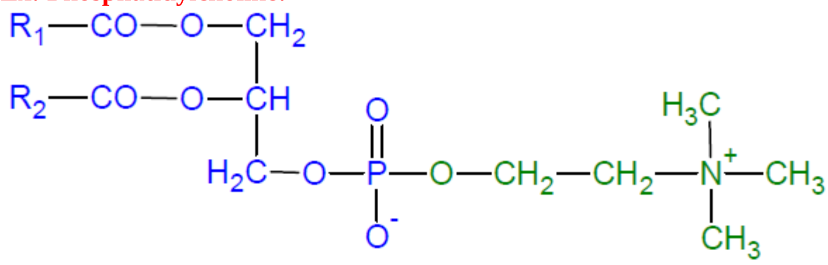
Glycolysis (cytosol)	2ATP 2NADH	2 3-5 ⑤
Pyruvate Oxidation	2NADH	5
Krebs /TCA cycle	2ATP 6NADH 2FADH2	2 15 3
TOTAL ATP YIELD (per 1 glu)		32 (30-32)

Metabolism of Fatty Acids and Proteins (BIO, BC)

Description of fatty acids (BC)

- **Fatty acids**
    - building blocks for most complex lipids
    - composed of long chains of carbons truncated at one end by a carboxylic acid
    - usually contain even number of carbons
    - Saturated – only single bonds
    - Unsaturated – one or more double bonds
    - Oxidation of fatty acids liberates large amounts of chemical energy for a cell
    - can be used for long-term energy storage
        - high concentration of carbon-hydrogen bonds allows them to store more energy per gram than any other macromolecule in the body
    - Most fats reach the cell in the *form of free fatty acids*, meaning fatty acids chains not attached to a backbone, than as triacylglycerols
- **Triacylglycerols**
    - three carbon backbone called **glycerol** attached to three fatty acid chains
    - can provide thermal insulation and padding to an organism
    - **Adipocytes** (fat cells) – specialized cells whose cytoplasm contains almost nothing but triglycerides
- Phospholipids – lipids with a phosphate group attached
    - most important: phosphoglycerides
        - built from a glycerol backbone, but a polar phosphate group replaces one of the fatty acids

- the phosphate group lies on the opposite side of the glycerol from the fatty acids, making the phospholipid polar at the phosphate end and nonpolar at the fatty acid end
    - **amphipathic**
- **Ex: Phosphatidylcholine:**

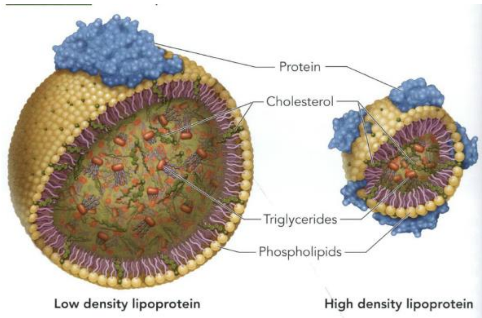


Phosphatidylcholine

- **Glycolipids** – similar to phospholipids, except that they have one or more carbohydrates attached to the three-carbon glycerol backbone instead of the phosphate group
    - also amphipathic
    - found in abundance in the membranes of myelinated cells in the human nervous system

Digestion, mobilization, and transport of fats

- hydrophobic, unlike proteins and carbs
- not easily transported in the aqueous environments of the digestive lumen and the intracellular space, but can easily pass thru membranes
- Most dietary fat consists of triglycerides, which are broken down to monoglycerides and fatty acids in the digestive process
    - these components then shuttled to brush border by bile micelles
- Once inside the enterocytes, the fats must be altered such that they can travel through the aqueous environment of the cell
    - monoglycerides and fatty acids are converted back into triglycerides at the smooth endoplasmic reticulum
        - amphipathic molecules—orient themselves with their charged ends pointing outward
        - form globules, move to the Golgi and are released via exocytosis
        - move into the lacteals of the lymph system
            - vs carbs and proteins, which are absorbed into the bloodstream
            - Most ingested fat that is absorbed moves through lymph system and enters the veins of the neck at the thoracic duct
    - The most significant absorption of fat occurs in the liver and adipose tissue
        - chylomicrons stick to the side of capillary walls, where lipoprotein lipase hydrolyzes the triglycerides
            - chylomicrons are lipoprotein particles that consist of triglycerides, phospholipids, cholesterol, and proteins
            - the products immediately diffuse into fat and liver cells
            - thus, the first stop for most of digested fat is the liver
- From adipose tissue, most fatty acids are transported in the form of free fatty acid, which combines with the protein albumin in the blood
- between meals, 95% of lipids in the plasma are in the form of lipoproteins
    - very low-density lipoproteins
    - intermediate-density lipoproteins
    - low-density lipoproteins
    - high-density lipoproteins
        - all made from triglycerides, cholesterol, phospholipids, and protein
        - As the density increases, first the relative amount of triglycerides decreases, and then the relative amount of cholesterol and phospholipids decreases



Oxidation of fatty acids

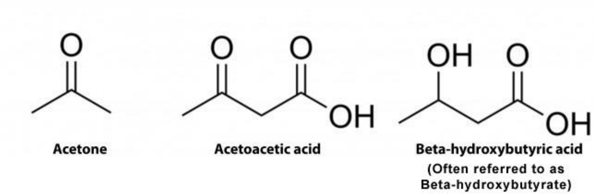
- Beta oxidation
- In biochemistry and metabolism, beta-oxidation is the catabolic process by which fatty acid molecules are broken down in the cytosol in prokaryotes and in the mitochondria in eukaryotes to generate acetyl-CoA, which enters the citric acid cycle, and NADH and FADH2, which are co-enzymes used in the electron transport chain
- **Beta-oxidation** of one 18 carbon **fatty acid** would **produce** 9 acetyl-CoA , 9 FADH, and 9 **NADH**

Saturated fats

Unsaturated fats

Ketone bodies (BC)

- Ketone bodies are three water-soluble molecules (acetoacetate, beta-hydroxybutyrate, and their spontaneous breakdown product, acetone) that are produced by the liver from fatty acids[1] during periods of low food intake (fasting), carbohydrate restrictive diets, starvation, prolonged intense exercise,[2] alcoholism or in untreated (or inadequately treated) type 1 diabetes mellitus. These ketone bodies are readily picked up by the extra-hepatic tissues, and converted into acetyl-CoA which then enters the citric acid cycle and is oxidized in the mitochondria for energy.[3] In the brain, ketone bodies are also used to make acetyl-CoA into long-chain fatty acids.



Anabolism of fats (BIO)

- Glucose can be converted to fatty acids by liver, which packages into VLDLs and releases into bloodstream
- **Acetyl coA** is a precursor for fatty acids
  - All the necessary enzymes are in the cytoplasm
- NADPH helps with this

Non-template synthesis: biosynthesis of lipids and polysaccharides (BIO)

Metabolism of proteins (BIO)

Protein Metabolism

- Anabolism – protein formation – occurs during fed state
  - associated with glycolysis, glycogenesis, and lipid storage
- Catabolism – protein breakdown – fasting state
  - associated with gluconeogenesis, glycogenolysis, and beta-oxidation and ketogenesis
- Remember, however, that translation has regulatory control with many levels
- Breakdown begins with hydrolysis of amino acid chains in the small intestines
  - enzymes such as trypsin, chymotrypsin, and carboxypetidase cleave protein
  - the small final amino acid chains are cleaved by enzymes of the brush border
  - they are then absorbed and released into circulation by intestinal epithelial cells
  - amino acid breakdown begins with removal of nitrogen group, producing ammonia and carbon chain
    - ammonia is fed into the urea cycle to become urea, which is excreted in the urine
    - carbon chain can then serve as a substrate **for various stage of the citric acid cycle**
- amino acids can be used to synthesize a number of biological substances besides proteins

Oxidative Phosphorylation (BIO, BC)

Electron transport chain and oxidative phosphorylation, substrates and products, general features of the pathway

Electron transfer in mitochondria

ATP and the Electron Transport Chain

- series of proteins that carries electrons from NADH to O2
    - include ubiquinone and cytochromes, which are intermediate electron carriers in the ETC
- As electrons passed along, protons are pumped into the intermembrane space, establishing proton-motive force
    - As protons diffuse back into mitochondrial matrix, they travel through ATP synthase, causing ATP to be generated
        - the horizontal flow of protons causes ATP synthase to turn
            - as it turn, it combines a phosphate group with an ADP to generate ATP
                - chemiosmotic coupling
- net coupling of 2 to 3 ATP manufactured for each NADH, depending on whether an ATP was spent to transport NADH into the mitochondrial matrix
- FADH2 – only 1-2 ATP produced
- Fundamentally a redox reaction
    - NADH is oxidized to become NAD+
    - O2 reduced to form water

- NADH, NADPH
- Flavoproteins
- Cytochromes
- Complex I (NADH coenzyme Q reductase; labeled I) accepts electrons from the Krebs cycle electron carrier nicotinamide adenine dinucleotide (NADH), and passes them to coenzyme Q (ubiquinone; labeled Q), which also receives electrons from complex II (succinate dehydrogenase; labeled II). Q passes electrons to complex III (cytochrome bc_1 complex; labeled III), which passes them to cytochrome *c* (cyt *c*). Cyt *c* passes electrons to Complex IV (cytochrome *c*oxidase; labeled IV)
- NADH donates to complex I (4 H+), FADH2 donates to complex II (no protons)
    - complex 3 pumps 4H+, complex 4 pumps 2
    - 4H+ = 1 ATP, NADH thus = 2.5 ATP, FADH2 = 1.5 ATP
- Cytochrome C is a one electron carrier, Coenzyme Q (ubiquinone) is a two electron carrier

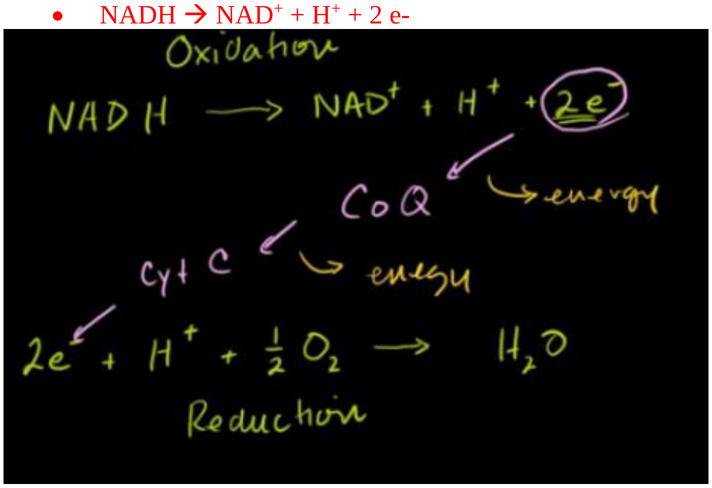
ATP synthase, chemiosmotic coupling
- ATP is pumped out through ATP/ADP translocase from the mitochondrial membrane

Proton motive force

Net molecular and energetic results of respiration processes

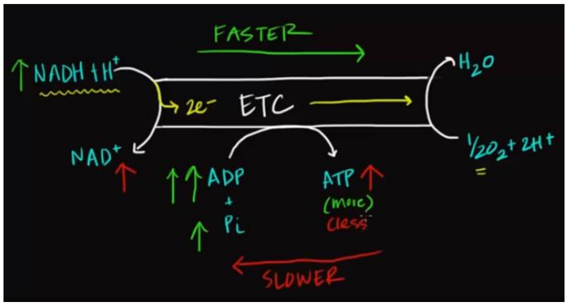
Regulation of oxidative phosphorylation

Electron Transport Chain
- 10 NADH, 2 FADH2 at this point
- NADH → $NAD^+ + H^+ + 2e^-$



- ATP synthase – as the axle turns, the ADP and P are squeezed together to form ATP
    - F0 in the membrane
    - F1 is what spins around
- oxidative phosphorylation vs substrate
    - oxidative is only in chemiosmotic
    - Substrate – in enzyme

Regulation of Oxidative phosphorylation
- Energy needs
    - ADP: ATP
- No major hormonal or allosteric regulation
    - it is downstream of many pathways



- Le'Chatelier's principle-based

Mitochondria, apoptosis, oxidative stress (BC)

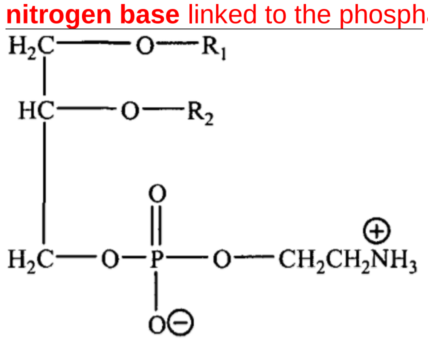
- Reactive oxygen species (ROS) – formed from faulty ETC
    - unstable number of electrons (like hydrogen peroxide)
    - improperly reduced oxygen
    - if repair mechanisms can't work, apoptosis
        - mitochondrial membrane permeability become more permeable (from BCL proteins)
        - allows cytochrome C to enter into cytoplasm
        - activate Caspases - type of protease after the aspartate residue
            - controlled cascade of actions
            - eventual result is a whole scale degredation

Hormonal Regulation and Integration of Metabolism (BC)
Higher level integration of hormone structure and function
Tissue specific metabolism
Hormonal regulation of fuel metabolism
Obesity and regulation of body mass

FOUNDATIONAL CONCEPT 2

Category 2A: Assemblies of molecules, cells, and groups of cells within single cellular and multicellular organisms

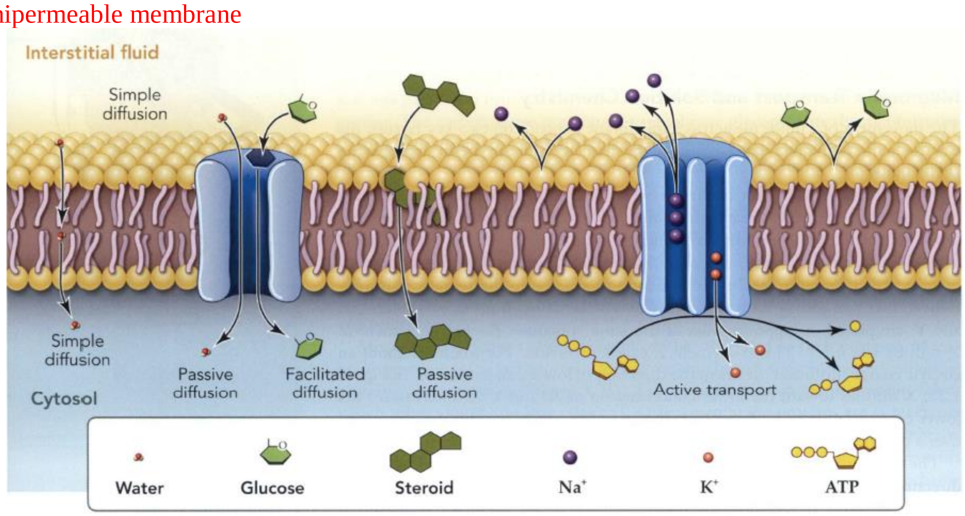
Plasma Membrane (BIO, BC)
General function in cell containment Composition of membranes

- Lipid components (BIO, BC, OC)
    - Phospholipids (and phosphatides)
        - Phosphatides = any of a class of compounds that are fatty acid esters of glycerol phosphate with a **nitrogen base** linked to the phosphate group.
        - 
    - Steroids
    - Waxes Fatty acid esters
- Protein components
- Fluid mosaic model

Membrane dynamics
Solute transport across membranes

- Thermodynamic considerations

- Osmosis
    - Colligative properties; osmotic pressure (GC)
- Passive transport
- Active transport
    - Sodium/potassium pump
- Membrane Transport
    - phospholipid – glycerol backbone with phosphate group and two fatty acids
        - amphipathic
        - when placed in aqueous solution, amphipathic molecules spontaneously aggregate, forming micelles
            - micelles form spontaneously, phospholipid bilayer has to be assembled
        - If enough phospholipids are present in a solution that is subjected to ultrasonic vibrations, liposomes may form
            - liposome is a vesicle surrounded by and filled with aqueous solution, has a lipid bilayer
    - Inner and outer layers of a membrane are called leaflets
        - lipid types arranged asymmetrically between the leaflets
        - glycolipids found in outer leaflets only
    - plasma membrane has other lipids in addition to phospholipids, such as glycolipids
    - Eukaryotic membranes, unlike prokaryotic plasma membranes, contain steroids such as cholesterol
    - Proteins are also embedded within the plasma membrane
        - integral/intrinsic proteins – amphipathic proteins that can cross the membrane from the inside of the cell to the outside
        - Peripheral/extrinsic proteins – located on the surfaces of membrane, generally hydrophilic
            - ionically bonded to integral proteins or the polar group of a lipid
        - both peripheral and integral proteins may contain carbohydrate chains, making them glycoproteins
            - carbohydrate portion always protrudes toward the outside of the cell
        - neither proteins nor lipids flip easily from one leaflet to the other
        - membrane proteins can act as transporters, receptors, attachment sites, identifiers, adhesive proteins, and enzymes
    - Fluid mosaic model
- Membrane transport and solution chemistry
    - Brownian motion—leads to diffusion – occurs in the direction of decreasing free energy
    - Electrochemical gradient – points in the direction that particle X will tend to move
    - Semipermeable membrane



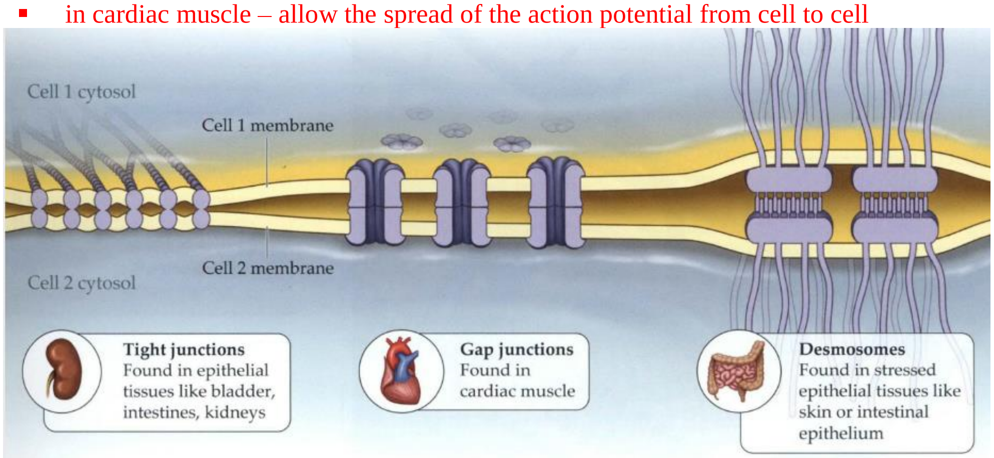
There are some important concepts here that require understanding and memorization. The membrane stuff is worth a second read through. For any molecule or ion, first determine whether it is moving against a gradient or with a gradient. If it is moving against a gradient, it requires active transport, regardless of size and charge. If it is moving with a chemical gradient, consider its chemical properties. Anything that is lipid soluble (nonpolar enough to slide right through the phospholipid bilayer) and small enough to fit around the cracks in the integral proteins can pass through the membrane without the aid of a protein. If it meets these criteria, the molecule or ion crosses the membrane by passive diffusion. Otherwise it requires a protein to cross the plasma membrane. This type of transport is called facilitated diffusion.

        - natural membrane generally impermeable to polar molecules that have a molecular weight greater than 100 g/mol without some type of assistance
        - the greater the polarity, the less permeable the membrane is to that substance
        - very large lipid soluble molecules, such as steroid hormones, can easily diffuse through the membrane

Membrane channels
Membrane potential
Membrane receptors
Exocytosis and endocytosis
Intercellular junctions (BIO)

- Gap junctions
- Tight junctions
- Desmosomes

- Connections Between Cells—Intercellular junctions
  - Tight junctions – form a watertight seal from cell to cell that can block water, ions, and other molecules from moving around and past cells
    - tissue held together by tight junctions can act as a complete fluid barrier
    - Epithelial tissue cells in organs like the bladder, intestines, and kidney are held together by tight junctions in order to prevent waste materials from seeping around the cells and into the body
  - Desmosomes – join two cells at a single point
    - attach directly to the cytoskeleton of each cell
    - strongest connection
    - Do not prevent fluid from circulating around the sides of a cell
    - found in tissues that normally experience a lot of stress due to sliding, like skin
    - Often accompany tight junctions
  - Gap junctions – small tunnels that connect cells, facilitating the movement of small molecules and ions between the cells
    - in cardiac muscle – allow the spread of the action potential from cell to cell



Membrane-Bound Organelles and Defining Characteristics of Eukaryotic Cells (BIO)
Defining characteristics of eukaryotic cells: membrane bound nucleus, presence of organelles, mitotic division
Eukaryotes

Prokaryotes	Eukaryotes
No membrane bound nucleus	True membrane bound nucleus
No membrane bound organelles	Membrane bound organelles
"Naked" DNA, without histone proteins	DNA is coiled with histone proteins
mRNA does not undergo post-translational modifications	mRNA undergoes splicing, addition of Poly-A tail, and addition of 5′ cap
Ribosomes are smaller	Ribosomes are larger
Cell walls are composed of peptidoglycan	Cell walls, if present, are composed of chitin (fungi) or cellulose (plants)
Flagella are made of flagellin	Flagella are made of microtubules
Division by binary fission	Division by mitosis

Nucleus

- Compartmentalization, storage of genetic information
- Nucleolus: location and function
- Nuclear envelope, nuclear pores
- Nucleus
    - the brain of the cell
    - wrapped in double phospholipid layer called the nuclear envelope
        - perforated with large holes called nuclear pores
            - RNA can exit, but DNA cannot
    - nucleolus – synthesis of rRNA

Mitochondria

- Site of ATP production
- Inner and outer membrane structure (BIO, BC)
- Self-replication
- Mitochondria and Energy
    - Endosymbiotic theory—mitochondria may have evolved from a symbiotic relationship between ancient prokaryotes and eukaryotes
    - contain circular DNA that replicates independently from nuclear DNA
        - contains no histones or nucleosomes
        - codes for mitochondrial RNA that is distinct from the RNA in the rest of the cell
            - Have their own ribosomes
            - some of the codons in mitochondria differ from the codons in the rest of the cell, an exception to the universal genetic code
        - mitochondrial DNA is passed to offspring from the mother even in organism in which male gametes contribute to the cytoplasm of the egg
    - surrounded by two phospholipid bilayers (like gram negative bacteria)
        - inner membrane invaginates to form cristae
            - holds the electron transport chain of aerobic respiration
        - Intermembrane space – between inner and outer membrane
    - High concentrations seen in the cell whenever energy needs are high (muscle cells)

Lysosomes: membrane-bound vesicles containing hydrolytic enzymes

- Lysosome – type of vesicle that contain hydrolytic enzymes
    - catalyzes the breakdown of macromolecules by hydrolysis
    - usually have interior pH of 5
    - fuse with endocytotic vesicles and digest their contents
    - Any material not degraded by the lysosome is ejected from the cell through exocytosis
    - Lysosomes also take up and degrade cytosolic proteins in an endocytotic process
    - under certain conditions lysosomes rupture and release their contents in the cytosol, killing the cell
    - *exist in large concentrations in cells about to undergo apoptosis*

Endoplasmic reticulum

Rough and smooth components

- Rough endoplasmic reticulum site of ribosomes

- Double membrane structure
- Role in membrane biosynthesis
- Role in biosynthesis of secreted proteins
    - Smooth ER
        - tubular, in contrast to rough ER, which tends to resemble flattened sacs
        - has a number of functions that differ according to the type of cell
            - In liver and kidney, smooth ER contains **glucose 6-phosphatase**, the enzyme used in the liver, intestinal epithelial cells, and renal tubule epithelial cells to hydrolyze glucose 6-phosphate to glucose, and important step in the breakdown of glycogen to produce glucose
            - In muscle cells, smooth ER is known as the sarcoplasmic reticulum, and it sequesters Calcium away from actin and myosin
        - plays a role in lipid metabolism
            - in liver, triglycerides are produced here
            - adipocytes store lipids inside of smooth ER
                - contribute to energy storage and body temperature regulation
        - oxidizes foreign substances—detoxifies drugs, pesticides, toxins, and pollutants
- Proteins and Vesicles
    - protein synthesis begins on ribosome
    - feeds protein into cytosol or endoplasmic reticulum
        - proteins that are translated in the cytosol remain there
        - Proteins that will be exported from the cell or sequestered in vesicles are translated on the ER
    - In some places the ER is contiguous with the outer layer of the nuclear envelope
        - As mRNA is translated, a particular sequence of amino acids, known as a signal sequence, directs the protein to the ER membrane for completion of translation
        - proteins that are translated on the rough ER are propelled into the ER lumen as they are created

Golgi apparatus: general structure and role in packaging and secretion

- The newly synthesized proteins are moved through the lumen toward the Golgi apparatus
    - main function is packaging and secreting proteins
    - small transport vesicles bud off from ER and carry proteins across cytosol to Golgi
    - Golgi then organizes and concentrates the proteins as they are shuttled by transport vesicles progressively outward from one compartment to the next
    - proteins are distinguished by their signal sequences and carbohydrate chains
    - golgi may alter proteins chemically by glycosylation or by removing amino acids
    - The vesicles may be expelled from the cell as secretory vesicles, released from the Golgi to mature into lysosomes, or transported to other parts of the cell such as mitochondria or even back to the ER
        - secretory vesicles release their contents through exocytosis, add to cell membrane
        - endocytotic vesicles made at the cell membrane are shuttled back to the Golgi for recycling of the cell membrane

Peroxisomes: organelles that collect peroxides

- Peroxisomes – vesicles in cytosol that are involved in lipid and protein storage
    - self replicate, rather than budding off membranes (like lysosomes from the Golgi)
    - involved in the production and breakdown of hydrogen peroxide
    - inactivate toxic substances such as alcohol, regulate oxygen concentrations, play a role in the synthesis and breakdown of lipids, and are involved in the metabolism of nitrogenous bases and carbohydrates

Cytoskeleton (BIO)

General function in cell support and movement

Microfilaments: composition and role in cleavage and contractility

- interact with myosin to cause muscle contraction
- also responsible for the pinching of the cytoplasm during cytokinesis (cleavage)
- both of these actions reshape the cell membrane

Microtubules: composition and role in support and transport

- Microtubules
    - platform for transport
    - mitotic spindle
    - support the shape of the cell
    - hollow tubes made from protein tubulin—globular protein that polymerizes into long straight filaments under certain conditions

- Thirteen of these filaments lie alongside each other to form the tube

Intermediate filaments, role in support

- Intermediate Filaments
  - maintain the cell's shape
  - primarily serve to impart structural rigidity to the cell
  - Keratin—type of intermediate filament found in epithelial cells, associated with hair and skin

Composition and function of cilia and flagella

- Eukaryotic flagella are made from 9+2 microtubule configuration
  - vs prokaryotic flagellum: thin strand of single protein called **flagellin**
  - Further, eukaryotic flagella undergo a whip-like action, while prokaryotic flagella rotate
  - Cross bridges made from the protein dynein connect each outer pair of microtubules to its neighbor
  - cilia have same structure, but move the fluid around the cell

Centrioles, microtubule organizing centers

- have a + and – end
  - - end attaches to a microtubule-organizing center (MTOC)
  - microtubule grows away from an MTOC at its + end
  - major MTOC in animal cells is the centrosome—composed of a pair of centrioles, which function in the production of flagella and cilia but are not necessary for microtubule production

Tissues Formed From Eukaryotic Cells (BIO)

Epithelial cells

Connective tissue cells

- There are four basic types of tissue in animals: epithelial tissue, muscle tissue, connective tissue, and nervous tissue
  - epithelium includes endothelium, which lines the vessels of the body, including the heart
  - Connective tissue is characterized by an extensive matrix (blood, lymph, bone, cartilage, tendons, ligaments)

Cell Theory (BIO)

History and development

Impact on biology

In biology, **cell theory** is the historic scientific theory, now universally accepted, that living organisms are made up of cells. Cells are the basic unit of structure in all organisms and also the basic unit of reproduction. With continual improvements made to microscopes over time, magnification technology advanced enough to discover cells in the 17th century. This discovery is largely attributed to Robert Hooke, and began the scientific study of cells, also known as cell biology. Over a century later, many debates about cells began amongst scientists. Most of these debates involved the nature of cellular regeneration, and the idea of cells as a fundamental unit of life. Cell theory was eventually formulated in 1839. This is usually credited to Matthias Schleiden and Theodor Schwann. However, many other scientists like Rudolf Virchow contributed to the theory.

The three tenets to the cell theory are as described below:

1. **All living organisms** are composed of one or more cells.
2. The cell is the **basic unit** of structure and organization in organisms.
3. Cells arise from pre-existing cells.

Classification and Structure of Prokaryotic Cells (BIO)

Prokaryotic domains

- Archaea
- Bacteria
- Prokaryotes do not have membrane bound organelles including a nucleus, while eukaryotes do
  - have nucleoid instead, also ribosomes, plasmids, proteins
  - single circular double-stranded DNA, twisted into supercoils and associated with **histones in Archaea** and with **proteins distinct from histones** in Bacteria
  - complex of DNA, RNA, and proteins in prokaryotes forms the nucleoid
- Archaea – extremophiles, have histones

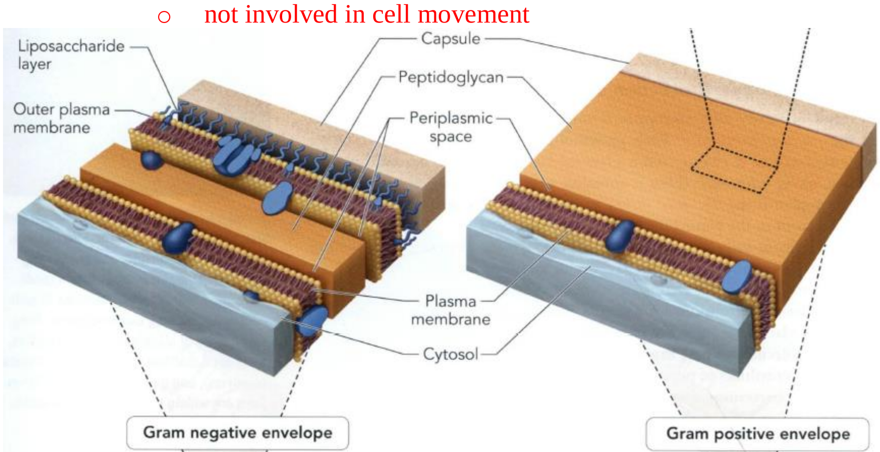
Major classifications of bacteria by shape

- Bacilli (rod-shaped)
- Spirilli (spiral-shaped)

- Cocci (spherical)

Lack of nuclear membrane and mitotic apparatus
Lack of typical eukaryotic organelles
Presence of cell wall in bacteria

- Bacterial envelopes
  - plasma membrane + everything it contains = protoplast
  - surrounding the protoplast is the bacterial envelope
  - component of the envelope adjacent to the plasma membrane is the cell wall
    - made of *peptidoglycan*
      - consists of a series of disaccharide polymer chains with amino acids
    - *cell wall is porous, allows large molecules to pass through*
  - Gram staining – technique used to prepare bacteria for viewing under microscope
    - gram positive – thick peptidoglycan cell wall, prevents gram stain from leaking out
      - purple
      - cell wall located just outside plasma membrane
        - space between membrane and wall = **periplasmic space**
          - contains many proteins that help nutrition
    - gram negative
      - appear pink when gram stained
      - think peptidoglycan wall
      - small cell wall located in between two plasma membranes
        - outer membrane more permeable than inner
          - allows molecules the size of glucose to pass through easily
          - possess lipopolysaccharides
            - can serve as a protective barrier from antibodies
      - also possess fimbriae, or pili
        - short tentacles that can attach a bacterium to a solid surface
        - not involved in cell movement



Flagellar propulsion, mechanism

- Bacterial flagella
  - long, hollow, rigid, helical cylinders made from a globular protein called flagellin
  - rotate counterclockwise to propel bacterium in a single direction
    - when they rotate clockwise, the bacterium tumbles, changing its orientation and allowing it to move in a new direction
  - Flagellum is propelled using the energy from a proton gradient rather than ATP
  - Chemotaxis – directed movement toward substances that will promote the survival and growth of bacterium

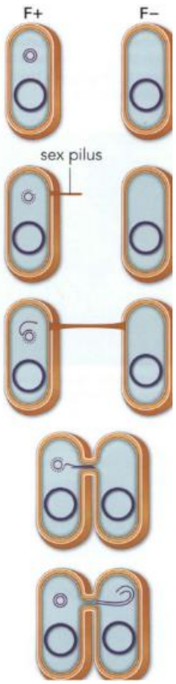
Growth and Physiology of Prokaryotic Cells (BIO)

Reproduction by fission

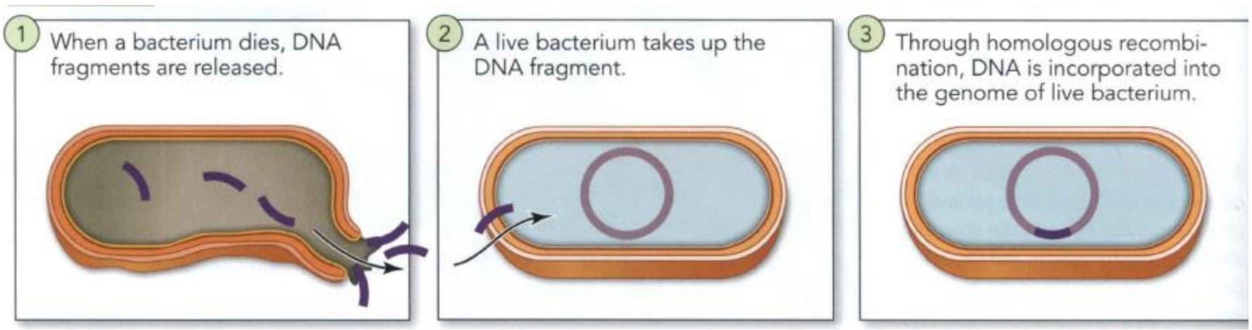
- Reproduction and Genetic Recombination
  - Bacteria do not undergo meiosis or mitosis. Instead, they undergo cell division via binary fission, a type of asexual reproduction
    - circular DNA is replicated

- two DNA polymerases begin at the same point on the circle (origin of replication) and move in opposite directions, making complementary single strands that combine with their template strands to form two complete DNA double stranded circles

- the cell then divides, leaving one circular chromosome in each daughter cell—genetically identical
- increase by exponential growth, until essential nutrients of the environment are exhausted



- Three alternative forms of genetic recombination allow bacteria to trade DNA: conjugation, transformation, and transduction
  - Conjugation – involves transfer of plasmid
    - if plasmid can integrate into the chromosome, it is also called an **episome**
    - not essential to the survival of the bacteria that carry them
    - Bacterium must contain a conjugative plasmid to initiate conjugation
      - conjugative plasmid posses the gene for the sex pilus
        - sex pilus – hollow protein tube that connects two bacteria to allow the passage of the plasmid from one to the other
      - passage of DNA is always from the cell that contains the conjugative plasmid to the cell that does not
    - two types of plasmids
      - F plasmid – fertility factor
        - bacterium with this factor is F+
        - can be in the form of an episome
          - if pilus is made while F factor is integrated into the chromosome, some or all of the test of the chromosome may be replicated and transferred
      - R plasmid – donates resistance to certain antibiotics
        - also a conjugative plasmid
  - Transformation
    - process by which bacteria incorporate DNA from the external environment into their genomes
      - this external DNA may be added to the external environment in the lab, or it may be released by lyses of other bacteria
      - can be demonstrated by mixing heat-killed virulent bacteria with harmless living bacteria
        - the living bacteria can receive the genes of the heat-killed bacteria through transformation and thus become virulent



        - Transduction
            - involves the transfer of genetic material by a virus
            - can occur when the capsid of a bacteriophage mistakenly encapsulates a DNA fragment of the host cell
            - when this virion infects a new bacterium, it injects harmless bacterial DNA fragments instead of virulent viral DNA fragments
            - virus that mediates transduction is called a vector

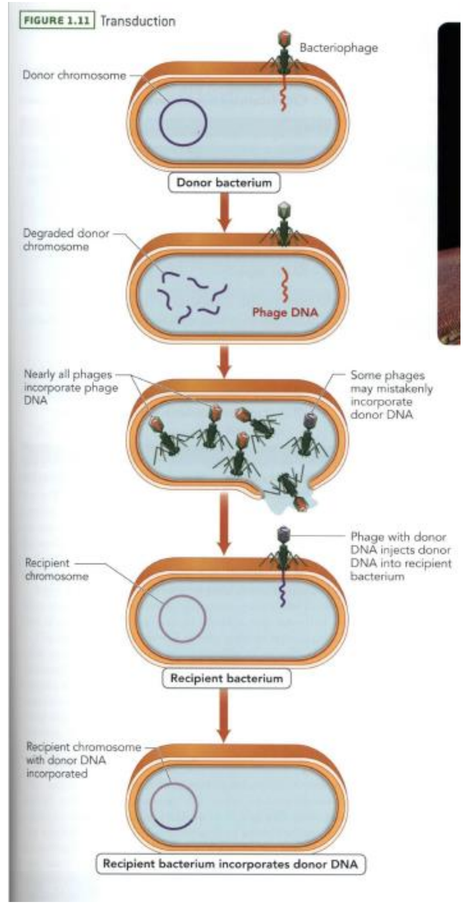


FIGURE 1.11 Transduction

High degree of genetic adaptability, acquisition of antibiotic resistance
Exponential growth
Existence of anaerobic and aerobic variants
Parasitic and symbiotic
Chemotaxis

Genetics of Prokaryotic Cells (BIO)
Existence of plasmids, extragenomic DNA
Transformation: incorporation into bacterial genome of DNA fragments from external medium
Conjugation
Transposons (also present in eukaryotic cells)
A **transposable element** (**TE** or **transposon**) is a DNA sequence that can change its position within a genome, sometimes creating or reversing mutations and altering the cell's genetic identity and genome size. Transposition often results in duplication of the same genetic material. Barbara McClintock's discovery of these **jumping genes**
Surrounded by inverted repeats

Virus Structure (BIO)
General structural characteristics (nucleic acid and protein, enveloped and nonenveloped)
Lack organelles and nucleus
Structural aspects of typical bacteriophage
Genomic content — RNA or DNA
Size relative to bacteria and eukaryotic cells

Viruses
- consists of protein coat – **capsid** – and genes in the form of DNA or RNA
- no organelles or nuclei
- surround themselves with a lipid rich envelope borrowed from the membrane of their host cell
    - typically contains some virus-specific proteins
- a mature virus outside the host cell is called a viral particle or **virion**
- not living, analogous to eukaryotic nucleus
- when inside a cell, a virus will remove its capsid and envelope to expose its genetic material in the cytosol
- Viral infection begins when virus binds to specific chemical receptor site on the host cell
    - usually a specific glycoprotein on the host cell membrane
    - next, the nucleic acid of the virus penetrates into the cell
        - a bacteriophage typically injects nucleic acids into the host cell through its tail after viral enzymes have digested a hole in the cell wall
        - most animal viruses do not leave the capsids outside the cell, but rather enter the cell through **receptor-mediated endocytosis**
- Some viruses have viral envelope, formed as they undergo exocytosis
    - can protect detection by the immune system
    - the receptors on the envelope allows it to bind to a new host cell
    - the original cell usually dies a little afterwards due to degradation of its membrane and usable cellular machinery
    - nonenveloped viruses typically do lyse a cell and cause death immediately
- Almost all RNA viruses replicate via an **RNA-dependent RNA polymerase (RdRP)**

- some RNA strands (+RNA) code for proteins
- However, when RdRP makes a copy of this strand, it will create a complimentary strand that cannot code for protein products (-RNA)
  - must undergo another replication with RdRP
- All cells carry either +RNA or –RNA
  - if a virus carries –RNA, it must undergo one replication by RdRP to form +RNA in order to code for proteins and then another one to be packaged into its progeny

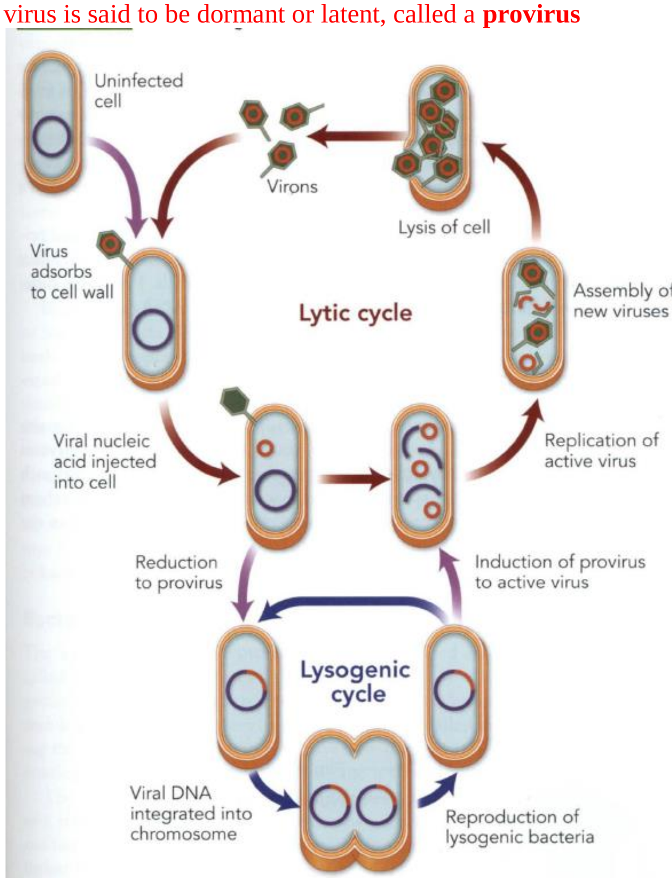
- other genome types unique to viruses include ssDNA and dsDNA
  - when virus inserts ssDNA into a cell, it is transported to nucleus, where DNA polymerase transcribes a complimentary strand, forming dsDNA
- some RNA viruses, called retroviruses, are able to **transcribe their RNA into double stranded DNA**
  - carried out by reverse transcriptase, which is carried by the retrovirus itself
  - the DNA produced can be potentially integrated into host DNA
    - Ex: HIV
    - exceedingly difficult to eradicate

Viral Life Cycle (BIO)

Self-replicating biological units that must reproduce within specific host cell

Generalized phage and animal virus life cycles

- Once inside the cell, there are two possible paths: lytic or lysogenic
  - **lytic**
    - virus commandeers the cell's synthetic machinery (ribosomes)
    - the translated proteins assemble to form a new virus
    - cell may fill with new viruses until it lyses, or it may release new viruses one at a time in a reverse endocytotic process
    - latent period – period from infection to lysis
    - a virus following a lytic cycle is a **virulent virus**, one capable of causing disease
  - **lysogenic**
    - viral DNA incorporated into host genome
    - is replicated along with the host DNA
    - temperate virus – may show no symptoms of infection
    - virus is said to be dormant or latent, called a **provirus**



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

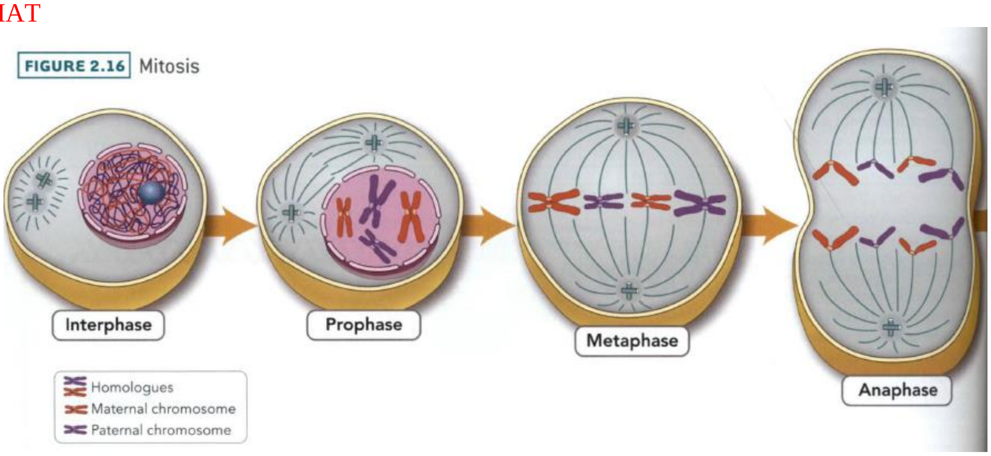
Use of host synthetic mechanism to replicate viral components
Self-assembly and release of new viral particles
Transduction: transfer of genetic material by viruses
Retrovirus life cycle: integration into host DNA, reverse transcriptase, HIV
Prions and viroids: subviral particles

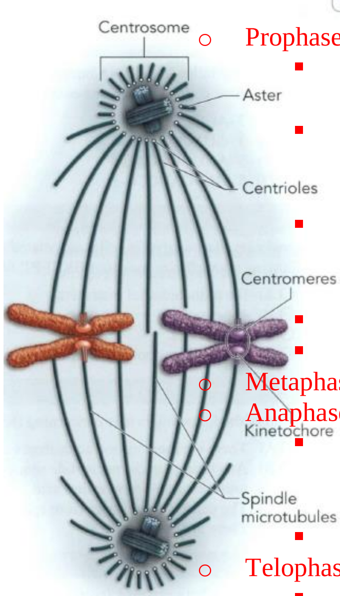
- Subviral particles – infectious agents related to viruses
  - **Viroids** – **small rings of naked RNA** without capsids, only infect plants
  - **prions** – naked proteins that cause infections in animals
    - can reproduce themselves, without DNA or RNA

Content Category 2C: Processes of cell division, differentiation, specialization

Mitosis (BIO)
Mitotic process: prophase, metaphase, anaphase, telophase, interphase

- Mitosis -PMAT

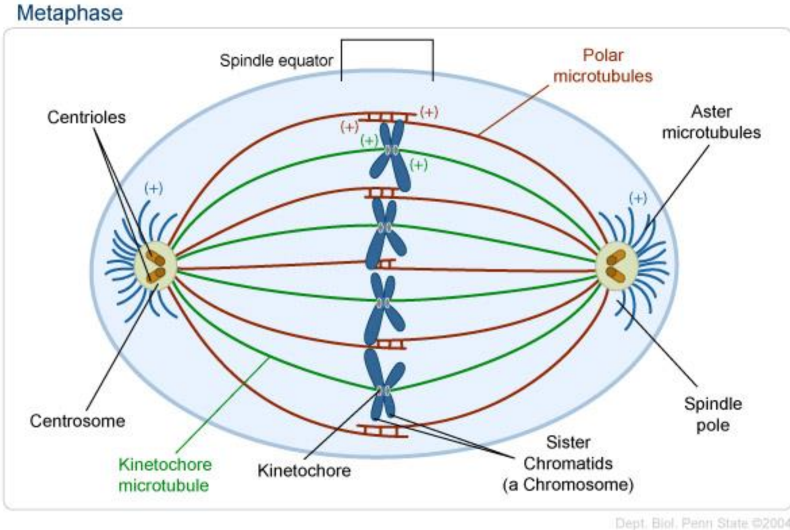




  - Prophase
    - condensation of chromatin into chromosomes
      - downregulates gene expression during mitosis
    - sister chromatids joined together at **centromeres**
      - kinetochore – structure of protein and DNA located at the centromere of joined chromatids of each chromosome
    - **centrosomes**, migrate to opposite poles
      - kinetochore microtubules – connect to centrosome
      - spindle microtubules – connect the two centrioles
    - First the nucleolus and then the defined nucleus disappear as the nuclear envelope breaks down
    - spindle apparatus begins to form
  - Metaphase – chromosomes align along equator
  - Anaphase
    - sister chromatids split at their attaching centromeres and segregate to opposite sides of cell ("Chromosomal migration")
      - shortening of kinetochore microtubules – disjunction
    - Cytokinesis – separation of cellular cytoplasm due to constriction of microfilaments around center of cell
  - Telophase
    - nuclear membrane reforms, followed by reformation of the nucleus
    - chromosomes decondense
    - cytokinesis continues

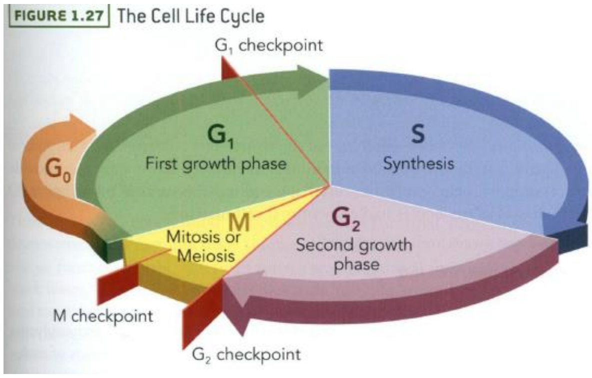
Mitotic structures
Centrioles, asters, spindles

Metaphase



Chromatids, centromeres, kinetochores
Nuclear membrane breakdown and reorganization
Mechanisms of chromosome movement
Phases of cell cycle: G0, G1, S, G2, M
Growth arrest
Control of cell cycle
Loss of cell cycle controls in cancer cells

- Cell cycle



  - G1, G2, and S = interphase, M = mitosis
  - G1
    - cell has just divided, begins to grow in size, producing new organelles and proteins
    - RNA and protein synthesis are highly active
    - must reach a certain size to continue to the next stage
    - cell growth assessed at the **G1 checkpoint** near the end of G1
      - if conditions are favorable for division, the cell enters S phase
      - otherwise, the cell enters G0
        - main factor is cell size, based on ratio of cytoplasm to DNA
  - G0 – non growing state
    - variable – in humans, enterocytes of intestine divide more than twice per day, while liver cells spend a great deal of time in G0. Mature muscle and neuron cell remain in G0 permanently
  - S – cell devotes most of its energy to DNA replication
    - Organelles and proteins produced more slowly than in G1
    - exact duplicate of each chromosome is created
  - G2 – cell prepares to divide
    - cellular organelles continue to duplicate
    - RNA and proteins (especially tubulin for microtubules) are actively produced)
    - **G2 checkpoint** – checks for **mitosis promoting factor (MPF**)
      - when level of MPF is sufficiently high, mitosis is triggered
  - M –mitosis
    - **M checkpoint** towards the end ensures that chromosomes are aligned correctly before the cell divides
  - Sometimes a cell acquires a mutation that allows the cell to bypass these checkpoints, can develop into cancer

- tumor repressor – deactivation of a checkpoint protein
- oncogene – activation of a gene that causes the proliferation of the cell

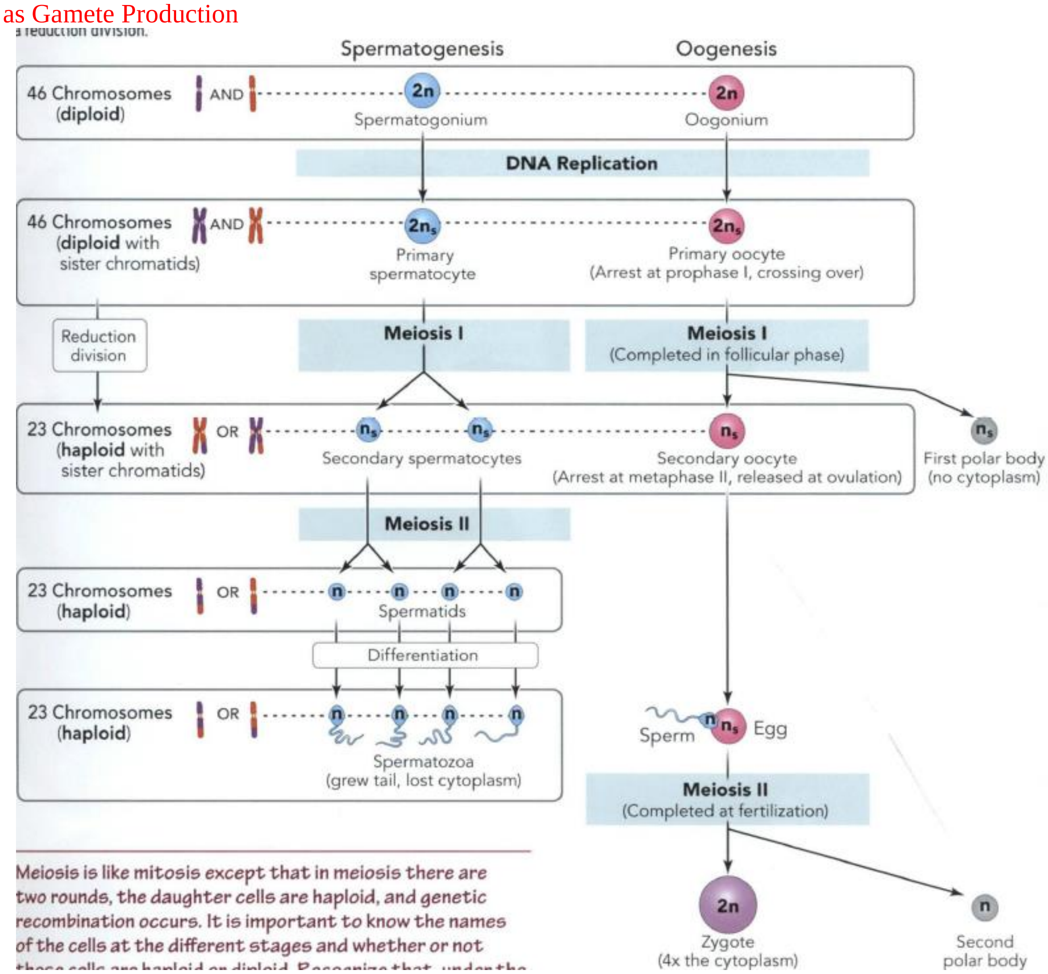
Biosignalling (BC)
Oncogenes, apoptosis

Reproductive System (BIO)
Gametogenesis by meiosis
Ovum and sperm

- Differences in formation
- Differences in morphology
- Relative contribution to next generation

Reproductive sequence: fertilization; implantation; development; birth

- Meiosis as Gamete Production



Stages in Males	Stages in Females	Chromosomes	Stage is Reached
Spermatogonium	Oogonium	Diploid	Progenitor cell present at birth
Primary spermatocyte	Primary oocyte	Diploid	After mitosis
Secondary spermatocyte	Secondary oocyte	Haploid	After meiosis I
Spermatid	Ootid*	Haploid	After meiosis II
Sperm (or spermatozoa)	Ovum*	Haploid	After maturation process

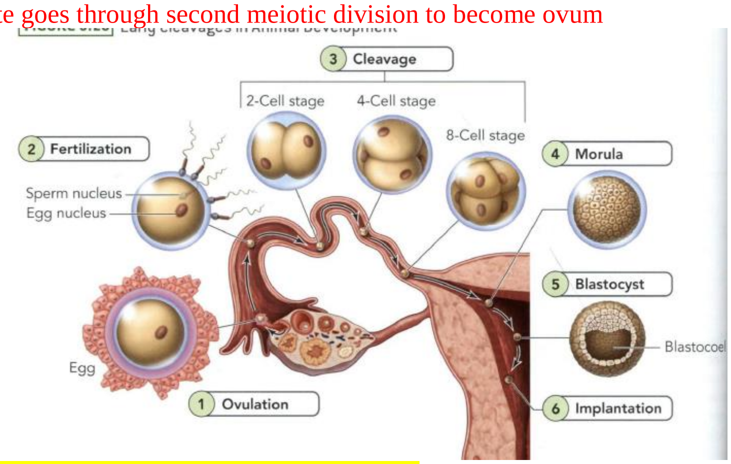
Embryogenesis (BIO)
Stages of early development (order and general features of each)

- Fertilization
- Cleavage

- Blastula formation
- Gastrulation
    - First cell movements
    - Formation of primary germ layers (endoderm, mesoderm, ectoderm)
- Neurulation

Major structures arising out of primary germ layers
Neural crest
Environment–gene interaction in development

- Preganacy and Embryology
    - Egg is swept toward uterus by cilia once in the Fallopian tube
    - Fertilization usually occurs in fallopian tubes
        - Oocyte goes through second meiotic division to become ovum



    - Cleavage begins while zygote is still in Fallopian tube
        - zygote goes through many cycles of mitosis
            - at 16 or more cells, is called a morula
        - the first eight cells are totipotent, meaning that they have the potential to express any of their genes
    - Cells of morula continue to divide, forming a blastocyst
        - mostly hollow ball filled with fluid and small cell mass on one side
    - Blastocyst lodges in uterus – implantation
        - 7th day after fertilization
        - outer cells of blastocyst fuse with uterine tissue to form the placenta
        - small mass of cells on inside become the embryo
            - inner cell mass made up of stem cells
                - pluripotent
                    - has the ability to develop into most of the types of cells in the human body
    - Placenta begins secreting the peptide hormone HCG
        - prevents degeneration of the corpus luteum and maintains its secretion of estrogen and progesterone
            - HCG in blood and urine of the mother is the first outward sign of pregnancy
        - Placenta reaches full development by end of first trimester and begins secreting its own estrogen and progesterone while lowering its secretion of HCG
    - Determination – cell becomes committed to specialized developmental path
    - Differentiation – the specialization that occurs at the end of development
    - skin, liver, and blood cells all have multipotent stem cells that can regenerate these systems as needed – "multipotent"
    - Formation of gastrula in the third week after fertilization
        - primitive streak forms in mammals
        - three germ layers
            - Ectoderm – epidermis of skin, nervous system, sense organs. The lining of the mouth is derived from invagination of the ectoderm
            - Mesoderm – skeleton, muscles, blood vessels, heart, blood, gonads, kidneys, dermis of skin
            - Lining of digestive and respiratory tracts, liver, pancreas, thymus, thyroid. The lining of most epithelial tissues inside the body are derived from endoderm.
    - Formation of Neurula in process called neuralation
        - through induction, the **notochord** (made from mesoderm) causes overlying ectoderm to thicken and form into **neural plate**
            - notochord eventually degenerates

        - **neural tube** forms from neural plate to become spinal cord, brain, and most of the nervous system
        - the cells of the ectoderm that are close to the neural tube are known as the **neural crest**
            - cells of neural crest mostly form as accessory cells to nervous system (like Schwann cells)
    - Apoptosis and Senescence (process by which cells stop proliferating in response to environmental stressors and are ultimately cleared away by immune cells) also play role in development
    - After ninth week of pregnancy, major organs develop
        - fetus
    - After birth, motor development is from head to toe
        - progress starts with head, moves down to trunk, and moves down and out as limb movement is mastered
    - Puberty – biological changes that ultimately lead to sexual maturity
    - Adolescent development – psychosocial processes that accompany puberty

Mechanisms of Development (BIO)

Cell specialization

- Determination
- Differentiation
- Tissue types

Cell–cell communication in development

Cell migration

Pluripotency: stem cells

Cells that have not yet differentiated, or which give rise to other cells that will differentiate, are known as stem cells. Stem cells exist in embryonic tissues as well as adult tissues. The tissues a particular stem cell can differentiate into are determined by its potency. Cells with the greatest potency are called totipotent and include embryonic stem cells; totipotent cells can ultimately differentiate into any cell type, either in the fetus or in the placental structures. After the 16-cell stage, the cells of the morula begin to differentiate into two groups: the inner cell mass and the trophoblast cells. After a few more cycles of cell division, these totipotent cells start to differentiate into the three germ cell layers. At this stage, the cells are said to be pluripotent; these cells can differentiate into any cell type except for those found in the placental structures. Finally, as the cells continue to become more specialized, they are said to be multipotent. Multipotent stem cells can differentiate into multiple types of cells within a particular group. For example, hematopoietic stem cells are cells that are capable of differentiating into all of the cells found in blood, including the various types of white blood cells, red blood cells, and platelets—but not into skin cells, neurons, or muscle cells.

Gene regulation in development

Programmed cell death

Existence of regenerative capacity in various species

Senescence and aging

FOUNDATIONAL CONCEPT 3 – HUMAN PHYSIOLOGY

Content Category 3A: Structure and functions of the nervous and endocrine systems and ways in which these systems coordinate the organ systems

Nervous System: Structure and Function (BIO)

Major Functions

- High level control and integration of body systems
- Adaptive capability to external influences

Functions and Features of the Nervous System

- Includes brain, spinal cord, nerves, and neural support cells, as well as sense organs such as the eye and the ear
    - Brain and spinal cord make up CNS
    - transmits info to the rest of the body by way of PNS

Organization of vertebrate nervous system

Sensor and effector neurons

Structures of the Nervous System

- Sensory (Afferent) neurons receive signals from a receptor cell that interacts with the environment
    - brain filters for the most important information and discards 99% of sensory input
    - located dorsally (toward the back)
- Interneurons transfer signals from neuron to neuron

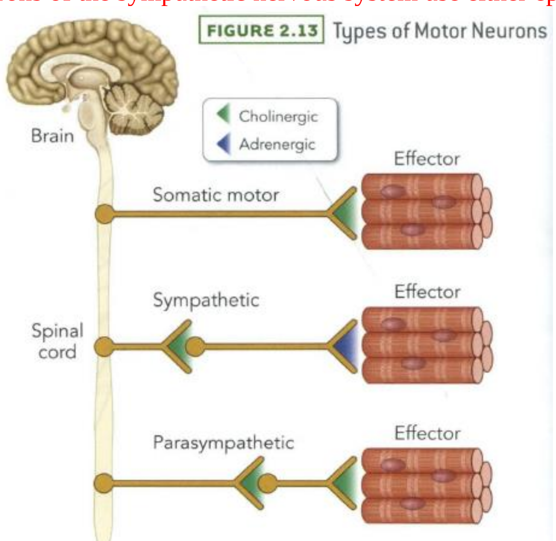
- 90% of neurons in the human body are interneurons

- Motor (efferent) neurons – carry signals to a muscle or gland called the effector
  - located ventrally (toward the front)
- Neuron processes (axons and dendrites) are typically bundled together to form nerves (called tracts in CNS)
- CNS – integrates nervous signals between sensory and motor neurons
- PNS – handles the sensory and motor functions of the nervous system
  - divided into somatic nervous system and autonomic nervous system
    - somatic –responds to external environment, voluntary
    - autonomic – involuntary response to the viscera (organs inside ventral body cavity)
  - sensory neuron cell bodies located in dorsal root ganglion
  - cell bodies of somatic motor neurons are located in the ventral horns of spinal cord
    - these neurons synapse directly on their effectors, release acetylcholine

Sympathetic and parasympathetic nervous systems: antagonistic control

- ANS
  - Sympathetic – fight or flight
    - increase heart rate and stroke volume
    - constriction of blood vessels around digestive and excretory organs to divert more blood flow to skeletal muscles
  - Parasympathetic – rest and digest
    - slows heart rate, increases digestive and excretory activity
  - These two systems have opposing influences on the same organs and thus exert antagonistic control
  - Sympathetic signals originate in neurons whose cell bodies are found in the spinal cord, while parasympathetic signals originate in neurons whose cell bodies can be found in both the brain and spinal cord
    - a group of cell bodies located in the CNS is called a **nucleus**; if located outside the CNS, it is called a **ganglion**
    - These neurons extend out from the spinal cord to synapse with neurons whose cell bodies are located outside the CNS
      - former neurons are called preganglionic neurons, and the latter are called postganglionic neurons
      - cell bodies of **sympathetic** postganglionic neurons lie **far** from their effectors, generally within the paravertebral ganglion, which runs parallel to the spinal cord
        - gathering of signals in large ganglia far from the effectors allows for a strong, coordinated signal, important for the sympathetic nervous system's "fight or flight" function
      - The **parasympathetic** nervous system's "rest and digest" functions do not require the careful coordination of signaling found in the SNS; thus the cell bodies of the parasympathetic postganglionic neurons lie in ganglia inside or **near** their effectors
  - The neurotransmitter used by all preganglionic neurons in the ANS and by postganglionic neurons in the parasympathetic branch is acetylcholine
  - The postganglionic neurons of the sympathetic nervous system use either epinephrine or norepinephrine

FIGURE 2.13 Types of Motor Neurons



  - Receptors for acetylcholine are called cholinergic receptors
    - Nicotinic – found on postsynaptic cells of the synapses between ANS preganglionic and postganglionic neurons and on skeletal muscle membranes at the neuromuscular junction

        - Muscarinic – found on the effectors of the parasympathetic nervous system
    - Receptors for epinephrine and norepinephrine are called adrenergic receptors

Reflexes

- Feedback loop, reflex arc
- Role of spinal cord and supraspinal circuits
- Reflex arc – quick response to a stimulus that occurs without direction from the CNS
    - information about the stimulus is still sent to the CNS, as the reflex is generated, allowing the perception of the stimulus and coordination of a more complex response
    - CNS can also send signals that dampen or enhance reflex responses according to the needs of the organism
        - Ex: inhibitory input from the supraspinal circuits descending from the CNS can decrease sensitivity and speed of the reflex so that it proceeds smoothly and only when needed
-

Integration with endocrine system: feedback control

Communication within the body

- Accomplished chemically via three types of molecules: neurotransmitters, local mediators, and hormones
    - governed by the nervous system, paracrine system, and endocrine system, respectively
- Signal can be fast or slow, specific or generalized, and fleeting or sustained in its effects
    - usually signal that is fast is fleeting, where a signal that is slow is usually sustained
    - Nervous system – fast and fleeting, specific
    - Endocrine system – slow and sustained, generalized
    - Paracrine – somewhat in between these extremes
- Neurotransmitters travel over very short intercellular gaps, local mediators function in the immediate area around the cell from which they were released, and hormones travel throughout the entire organism via the bloodstream
- Autonomic nervous system is more slow, sustained, and generalized than somatic system

Nerve Cell (BIO)

Cell body: site of nucleus, organelles
Dendrites: branched extensions of cell body
Axon: structure and function
Myelin sheath, Schwann cells, insulation of axon
Nodes of Ranvier: propagation of nerve impulse along axon
Synapse: site of impulse propagation between cells
Synaptic activity: transmitter molecules
Resting potential: electrochemical gradient
Action potential
Threshold, all-or-none
Sodium/potassium pump
Excitatory and inhibitory nerve fibers: summation, frequency of firing
Glial cells, neuroglia

Electrochemistry and the Neuron

- Neuron – so highly specialized that it has lost the ability to divide
    - depends almost entirely upon glucose for its chemical energy
    - uses facilitate transport to move glucose into it, but is not dependent on insulin for this, unlike most other cells
        - photoreceptors also do not depend on insulin
    - depends heavily on efficiency of aerobic respiration
    - unable to store significant amounts of glycogen and oxygen—relies heavily on blood for this
- Dendrites, cell body, and usually one axon with many small branches
- Summation – provides way for neuron to screen for the most important stimuli
    - spatial – multiple dendrites receive signals at same time
    - temporal – adds up the effects of signals that re received by a single dendrite in quick succession
- *Intensity* of stimulus can be coded by the *frequency of firing* of the sensory neuron or the *number and type of receptors* that respond
- Axon hillock generates an action potential in all directions
- Receptors and Ion channels
    - receptors bind ligands such as neurotransmitters and hormones, and respond by triggering processes within the cell

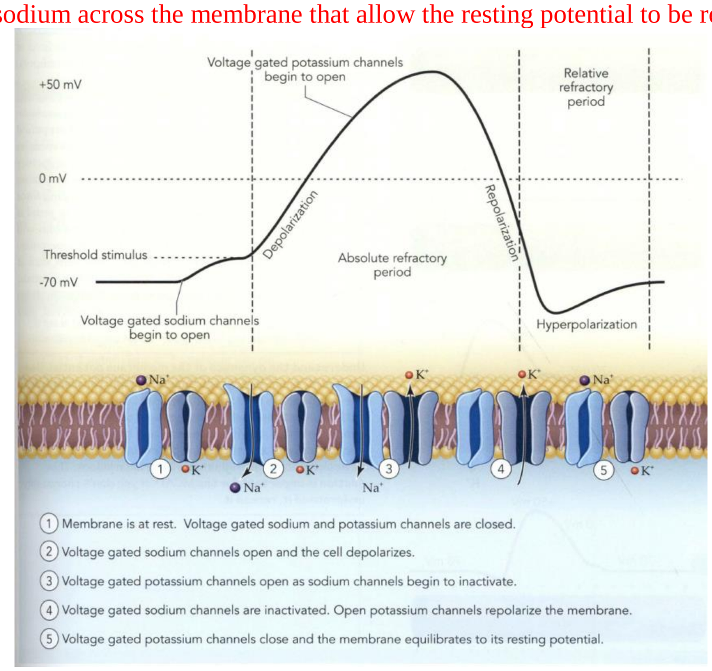
        - some receptors are themselves ion channels and open in response to the binding of a ligand
- Two most important ions: Na+ and K+
    - high EC concentration of Na, high IC concentration of K
    - Resting membrane voltage: -70 mV
    - buildup of negative charge just inside the cell membrane, and a buildup of positive charge just outside the membrane
    - In the neuron at rest, the membrane is highly permeable to K+ but almost completely impermeable to Na+
    - K+ ions in solution associate themselves with the negatively charged R groups of proteins within the cell
        - thus, as they start to move towards the membrane, they drag along the protein, which gets left behind
        - the positive charge building up along the outside of the membrane as K+ ions flow out of the cell attracts the negatively charged proteins, causing them to stay in their position near the membrane
    - NA/K pump functions to maintain or reestablish the chemical gradient that is lost by diffusion
        - 3 sodium out, 2 potassium in
        - prevents equilibrium, replenishes the concentration gradients of these ions
        - as a result, resting potential stays constant when the neuron is at rest
- Nernst equation:

$$E = E^{\circ} - \frac{RT}{nF}\ln(Q)$$

    - n = charge of ion
    - E° = standard cell potential – the voltage that exists when ion concentrations are equal in both parts of the cell – so zero
    - Q – ratio of EC to IC

$$E_{K^+} = -\frac{RT}{nF}\ln\left(\frac{[K^+]_{intracellular}}{[K^+]_{extracellular}}\right)$$

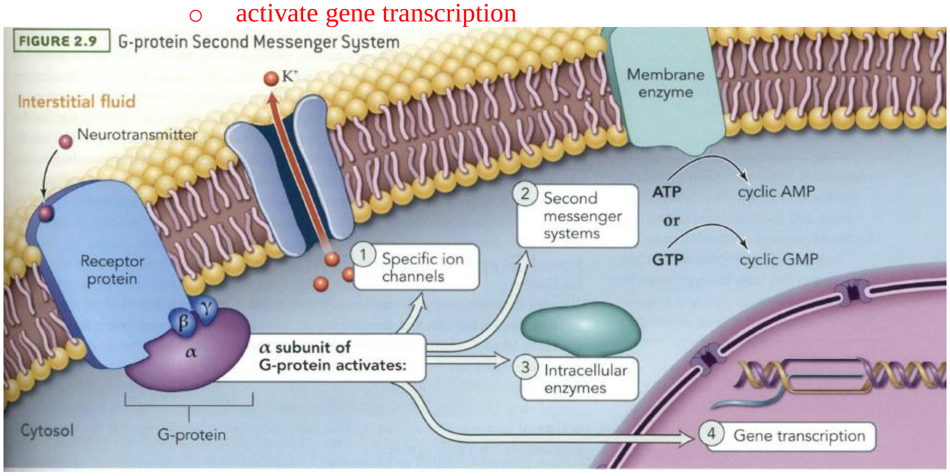
        - results in a negative potential
- Action Potential
    - can be conceptualized as a flip between permeability to potassium and permeability to sodium
    - Potassium voltage channels are less sensitive to voltage change than sodium channels, so they take longer to open
        - by the time they begin to open, most of the sodium channels are closing, diminishing the membrane's permeability to sodium
    - Throughout the action potential, the Na+/K+ pump keeps working, helping maintain the unequal concentrations of potassium and sodium across the membrane that allow the resting potential to be reset



    - **Accommodation** – threshold stimulus is reached, but is reached very slowly, so an action potential may not occur

Communication between Neurons: The Synapse
- Electrical synapses – uncommon
    - composed of gap junctions between cells

- cardiac muscle, visceral smooth muscle, and a very few neurons in CNS
    - do not involve diffusion of chemicals, transmit signals much more quickly than chemical synapses
    - signal can propagate bidirectionally, meaning that both cells involved in the synapse can send and receive signals
- Chemical Synapses
    - consist of a space between two neurons that is crossed by neurotransmitters
    - do not actually touch each other, unlike electrical synapses
    - unidirectional
    - membrane of presynaptic neuron near the synapse contains a large number of Ca^{2+} voltage gated channels
        - when an action potential arrives at a synapse, these channels are activated, allowing Ca^{2+} to flow into the cell
        - influx of calcium ions causes some of the neurotransmitter vesicles to be released from the synaptic cleft through exocytosis
    - postsynaptic membrane contains neurotransmitter receptor proteins
        - when neurotransmitter attaches to the receptor proteins, the postsynaptic membrane becomes more permeable to ions—ions move across ion channels
    - *If a presynaptic cell is fired too often it will not be able to replenish its supply of neurotransmitter vesicles, resulting in fatigue*
    - neurotransmitters in the synaptic cleft may be destroyed by an enzyme in the matrix of the synaptic cleft and its parts recycled by the presynaptic cell; it may be directly absorbed by the presynaptic cell via active transport; or may diffuse out of the synaptic cleft
    - Single neuron usually secretes only one type of neurotransmitter
        - However, a neuron may be able to respond to multiple types of neurotransmitters if its dendrites have the corresponding receptors
    - Any given synapse is designed either to inhibit or to excite, but not both
        - on the other hand, some neurotransmitters can produce an inhibitory or excitatory effect depending on the receptor in the postsynaptic membrane
            - Ex: Acetylcholine has an inhibitory effect on the heart, but an excitatory effect on the visceral smooth muscle of the intestines
    - Receptors my be ion channels themselves, which open when their receptive neurotransmitters attach, or they may act via a second messenger system, meaning that they activate another molecule inside the cell to make changes
        - Secondary messenger systems are preferred for prolonged changes, such as those involved in memory formation
        - G proteins commonly initiate second messenger systems
            - attached to the receptor protein along the inside of the postsynaptic membrane
            - when a receptor is stimulated, the α-subunit (component of G protein) breaks free, and can:
                - activate separate specific ion channels
                - activate a second messenger (cyclic AMP or GMP)
                - activate intracellular enzymes
                - activate gene transcription



    - Formation of an action potential in a single neuron is influenced by information from many synapses
        - most synapses contact dendrites, but some may directly contact other cell bodies, axons, or even other synapses
        - Firing of one or more of these synapses creates a change in neuron cell potential
            - EPSP or IPSP
            - typically, 40-80 synapses must fire simultaneously on the same neuron in order for an EPSP to create an action potential

Supporting Cells: Glia

- support cells, do not convey electrical signals
- capable of cell division
  - in case of traumatic injury to brain, it is the neuroglia that multiply to fill any space created in the central nervous system
- Six types: microglia, ependymal cells, satellite cells, astrocytes, oligodendrocytes, and Schwann cells
  - **m**icroglia – **m**acrophages of the CNS
  - **Ep**endymal cells – **ep**ithelial cells that line the space containing the cerebrospinal fluid
    - use cilia to circulate the cerebrospinal fluid
  - **s**atellite cells – **s**upport ganglia, which are groups of cell bodies in the PNS
  - **a**strocytes – **s**tar-shaped neuroglia in CNS that give physical support to neurons and help maintain the mineral and nutrient balance in the interstitial space**, blood brain barrier**
  - Oligodendrocytes – form myelin in CNS
  - Schwann ells – for myelin in PNS
    - Myelinated cells appear white, while neuronal cell bodies appear gray
      - white matter – myelinated axons
      - gray matter – bundles of cell bodies of neurons
    - Myelin acts as an insulator, increasing resistance to passage of ions thru membrane
    - action potential jumps from one node of Ranvier to the next—saltatory conduction

Electrochemistry (GC)

: direction of electron flow, Nernst equation

$$E_{K^+} = -\frac{RT}{nF}\ln\left(\frac{[K^+]_{intracellular}}{[K^+]_{extracellular}}\right)$$

Note: Positive if it's Extracellular / intracellular

Biosignalling (BC)

Gated ion channels

- Voltage gated
- Ligand gated

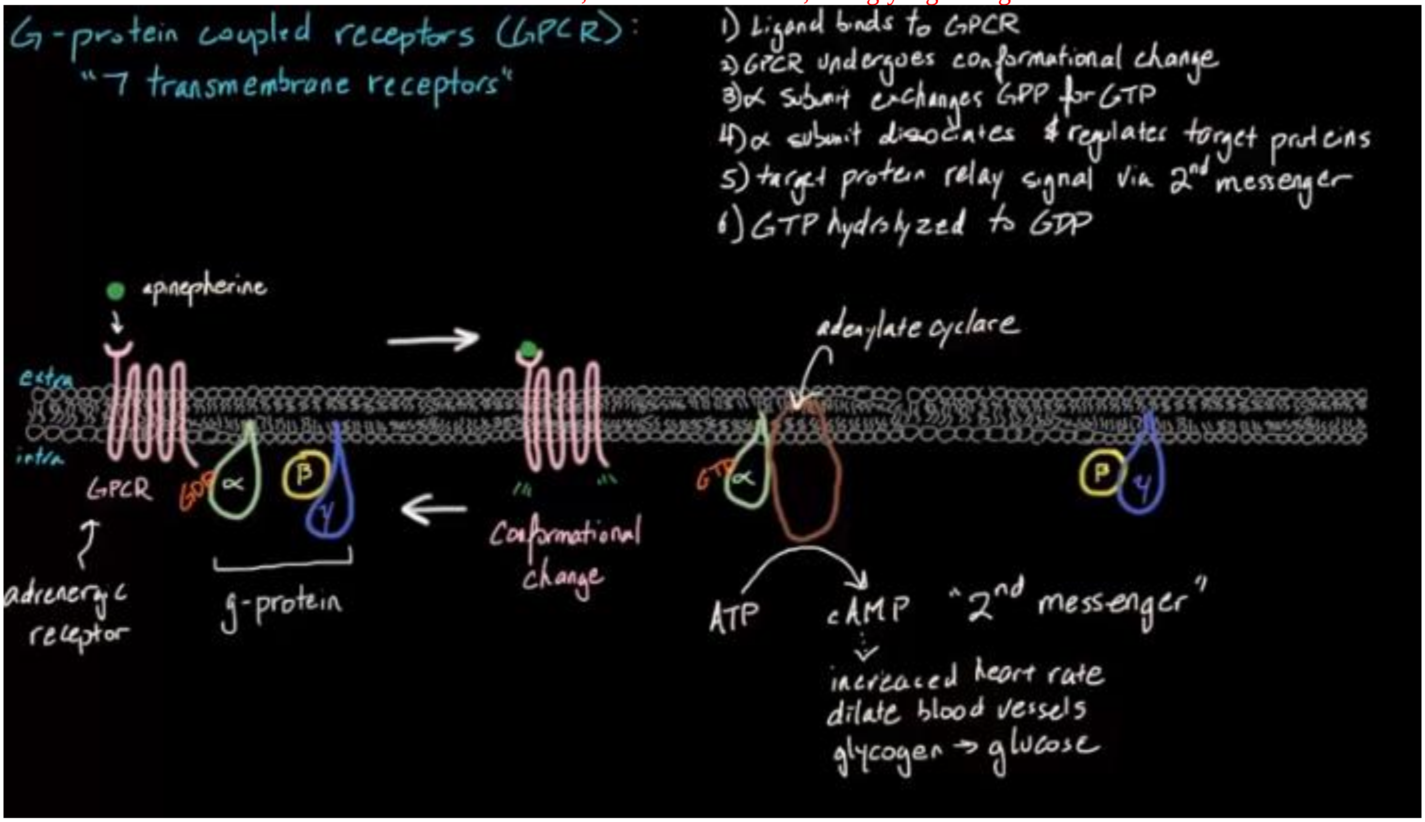
Receptor enzymes

G protein-coupled receptors

G-protein coupled Receptors

- GPCRs
- Only found in eukaryotes
- Largest class of receptors
- 7 transmembrane alpha helices
  - "7 transmembrane receptors"
- All proteins that are linked to this receptors have three subunits
  - Alpha, beta, an dgamma
  - These G proteins bind GTP or GDP
    - Inactive: GDP
    - Active: GTP
- Binding of ligand
  - Conformational change
  - Alpha subunit exchanges GDP for GTP
  - Cause Alpha subunit to dissociate
    - Alpha subunit and beta-gamma dimer
  - Alpha subunits regulates target proteins
    - Beta-gamma subunits can regulate as well, but alpha is more common
  - Target protein relays a signal
  - GTP is hydrolyzed to GDP – everything goes back to normal
- Example: Adrenaline
  - GPCR is adrenergic receptor
  - Conformational change, exchange GDP for GTP
  - Alpha subunit seeks out **adenylate cyclase**
    - Takes ATP to produce cAMP

- cAMP is a second messenger
  - increase heart rate, dilate blood vessels, turn glycogen to glucose



"Enzyme Linked Receptors"

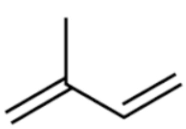
- Receptors that function as receptors
- "Catalytic Receptors"
- Ligand binding domain (Extracellular), enzyme function domain (intracellular)
- Receptor Tyrosine Kinases (RTKs)
  - Tyrosine is in the intracellular portion
  - Transfer phosphate molecules
  - Occur in pairs
  - Once they bind, the pair moves together, forms a cross-linked dimer
    - Phosphorylates tyrosine on other unit (cross phosphorylation)
    - Serve as docking sites for other proteins
      - These proteins need SH2 proteins to bind to phosphorylated tyrosine
      - Signal transduction follows, ultimately regulates gene transcription
  - Growth factors
    - Many cancers are involved in faulty RTKs

Lipids (BC, OC)

Description; structure

- Steroids
- Terpenes and terpenoids

Terpenes (/ˈtɜːrpiːn/) are a large and diverse class of organic compounds, produced by a variety of plants, particularly conifers,[1] and by some insects such as termites or swallowtail butterflies, which emit terpenes from their osmeteria. They often have a strong odor and may protect the plants that produce them by deterring herbivores and by attracting predators and parasites of herbivores.[2][3] The difference between terpenes and terpenoids is that terpenes are hydrocarbons, whereas terpenoids contain additional functional groups.



- Terpene hydrocarbons are classified according to the number of isoprene units: Monoterpenes: 2 isoprene units, 10 carbon atoms. Sesquiterpenes: 3 isoprene units, 15 carbon atoms. Diterpenes: 4 isoprene units, 20 carbon atoms

Endocrine System: Hormones and Their Sources (BIO)

As a general note on Hormone feedback loops:

- Hormones do not cause irregularities, they respond to them
    - **high effect leads to high regulatory hormones to fix it**, not from low amounts of regulatory hormones that caused it

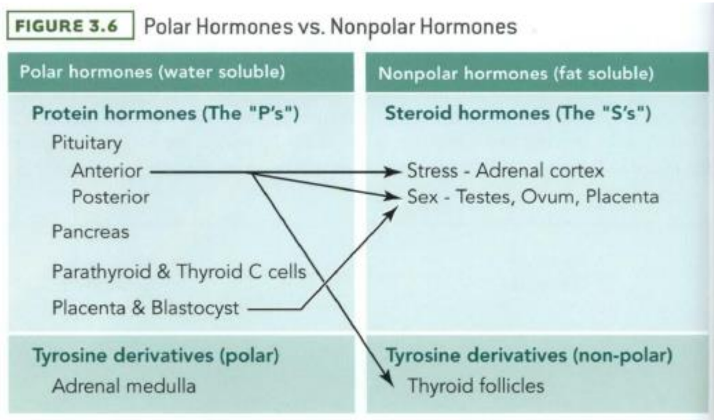
Function of endocrine system: specific chemical control at cell, tissue, and organ level
Definitions of endocrine gland, hormone
Major endocrine glands: names, locations, products
Major types of hormones
Neuroendrocrinology — relation between neurons and hormonal systems

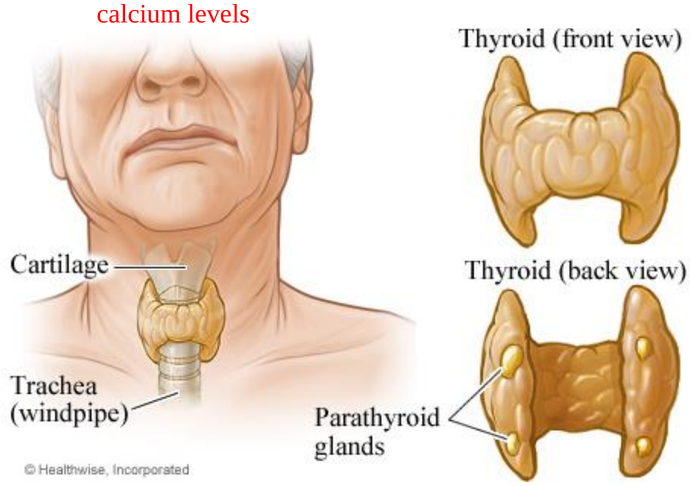
Endocrine System: Mechanisms of Hormone Action (BIO)

Cellular mechanisms of hormone action
Transport of hormones: blood supply
Specificity of hormones: target tissue
Integration with nervous system: feedback control
Regulation by second messengers

The Endocrine System

- Exocrine – releases hormones outside the body through ducts
- Endocrine – releases hormones directly into the bloodstream
- Hormones do not move directly to their target tissue, but are released through the bloodstream
    - all bind to protein receptors
    - *very low concentrations of hormones in the blood can have significant effects on the body*
- Types of Hormones
    - Peptide
        - water soluble
        - Attach through a membrane-bound receptor
        - Most commonly act through activating an enzyme or a second-messenger system
        - manufactured in rough ER as preprohormones (larger than active hormones)
            - Preprohormones are cleaved in ER lumen to become prohormone
            - Golgi – cleaves and modified prohormone (adds carbs)
    - Steroid
        - **made in smooth ER and mitochondria**
        - require protein transport molecule
        - diffuse through the cell membrane of their effectors
        - combine with receptor in the cytosol or nucleus, act at the level of transcription
        - glucocorticoids and mineral corticoids of adrenal cortex: cortisol and aldosterone (stress)
        - Gonadal hormones: Estrogen, progesterone, testosterone (sex)
    - Tyrosine derivatives
        - thyroid hormones: T_3 and T_4 and catecholamines in adrenal medulla epinephrine and norepinephrine
        - thyroid hormones are lipid soluble
            - increase transcription of large numbers of genes in nearly all cells of the body
        - Epinephrine and norepinephrine are water soluble
            - act thru cAMP
- Hydrophilic hormones are fast and fleeting, hydrophobic hormones are slower and more sustained
- Glands secrete only hydrophilic or only hydrophobic hormones



- Every hydrophobic hormone has a corresponding regulatory hydrophilic hormone
- The Peptide-secreting glands
    - Pituitary
        - posterior pituitary – continuation of the nervous system
            - bundle of axons in of neurons whose cell bodies lie in the hypothalamus
            - *storage site for hormones that are synthesized by the hypothalamus*
            - ADH and oxytocin
                - ADH – stimulates receptors on cells of kidney's collecting ducts to facilitate reabsorption of water
                - Oxytocin – stimulation of labor and milk ejection for nursing
        - Anterior pituitary – higher regulatory gland of the endocrine system
            - Location: beneath hypothalamus
            - releases hormones that release other hormones
            - *group of endocrine cells rather than extension of the nervous system*
            - hypothalamus communicates by releasing hormones into shared blood vessels
            - HALF PiT
                - HGH – stimulates growth in almost all cells of the body
                    - increases mitosis, cell size, rate of protein synthesis, mobilizing fat stores, increasing use of fatty acids for energy, decreasing use of glucose
                - ACTH – stimulates the adrenal cortex to release glucocorticoids via the second messenger system using cAMP
                - TSH – stimulates thyroid to release T3 and T4 using cAMP
                    - T3 and T4 have negative feedback effect on TSH release
                - Prolactin – promotes lactation by the breasts
                    - hypothalamus mainly inhibits the release of prolactin
                        - suckling stimulates the hypothalamus to simulate anterior pituitary to release prolactin
    - parathyroid glands
        - release PTH in response to low levels of calcium
        - receptors present on osteoblasts, which increase osteoclast activity and increase bone breakdown, releasing calcium
            - however, remember that osteoblasts function to build and repair bone, lowering levels of blood calcium levels
        - 

- Thyroid C cells – release Calcitonin
    - decreases calcium levels in blood
    - inhibitory effect on osteoclast
      - breakdown of bone decreases while the rate of bone formation is unchanged – level of blood calcium thus increases
- Basically:
    - parathyroid: PTH (raises blood calcium)
    - Thyroid C: Calcitonin (lowers blood calcium)
    - Thyroid: T3 and T4 (basal metabolic rate, acts on all cells)
- Pancreas – insulin and glucagon
    - insulin – acts on most cells in the body to take up glucose
      - made by Beta cells of the pancreas
      - lowers blood glucose levels
      - net anabolism (conservation of fat, glycogenesis)
    - glucagon – acts on liver to stimulate release of glucose into bloodstream
      - made by alpha cells
      - acts through cAMP
- Placenta – only exists during pregnancy
    - secrete HCG after implantation
      - travels to ovaries, signal the continuing synthesis of steroid hormones progesterone and estrogen
        - suppress menstruation, allows the buildup of the uterine wall in prep for implantation
    - secretes Progesterone and estrogen later
    - The only organ that secretes both polar and nonpolar hormones (besides thyroid gland and adrenal gland)
- Adrenal gland – located on top of the kidneys
    - medulla (inside)
      - stress response
      - secretes polar tyrosines epinephrine and norepinephrine
        - vasoconstrictors of most internal organs and skin, but are vasodilators of skeletal muscle
      - secreted into bloodstream
    - Cortex (outside)
      - blood pressure regulation and stress response
        - glucocorticoids and mineralcorticoids (cortisol and aldosterone)
        - Glucocorticoids are cortisol because they raise the blood glucose level
        - Mineralcorticoids are minerals because they allow the reabsorption of salt
        - cortisol – for chronic stress, stimulates **gluconeogenesis in the liver** to increase blood glucose levels
          - raises blood glucose thru other ways as well
        - aldosterone – salt reabsorption
- Thyroid gland – basal metabolic rate
    - nonpolar tyrosines T3 and T4
    - regulated by TSH form anterior pituitary
    - widespread effect due to the presence of receptors on cells in almost all parts of the body
    - increased transcription (like nonpolar steroid hormones)
- Gonads
    - Testes – testosterone – male puberty and spermatogenesis
    - Ovaries – estrogen and progesterone – female pubertal development and progression of menstruation and pregnancy
      - affected by HCG

- Tropic Hormones – hormones that have other endocrine glands as their targets
  - TSH, ACTH, LH, and FSH (FLAT) – all released from anterior pituitary
- Blood Chemistry Hormones – control concentrations of sodium, glucose, and calcium in the bloodstream
  - peptide hormones released from the posterior pituitary, pancreas, parathyroid, and thyroid
- Osmolarity: ADH vs Aldosterone
  - primary stimulus for ADH is high plasma osmolarity
  - Primary stimulus for Aldosterone is low blood volume
- Blood Glucose
  - insulin and glucagon from pancreas
    - other hormones can increase blood glucose, such as HGH, cortisol, and epinephrine
    - Stress leads to increased blood levels
- Calcium regulation

- in low concentrations in absence of phosphorus, it is soluble and generally associated with the movement of intracellular proteins
- In higher concentrations in the presence of phosphorus, will cause calcium phosphate to precipitate from solution
  - hydroxyapatite, the principle mineral of bone
- Regulated by parathyroid hormone and calcitonin

- Stress Hormones
  - Epinephrine, Cortisol
- Determinants of Metabolic Rate
  - T3 and T4
- Reproduction and Development
  - anterior pituitary, posterior pituitary, gonads, and placenta

TABLE 3.2 > Major Hormones of the Endocrine System

Gland	Hormone	Solubility	Effect
Anterior pituitary	HGH	Water soluble	Growth of nearly all cells
	ACTH	Water soluble	Stimulates adrenal cortex
	FSH	Water soluble	Growth of follicles in female; Sperm production in male
	LH	Water soluble	Causes ovulation; stimulates estrogen and testosterone secretion
	TSH	Water soluble	Stimulates release of T_3 and T_4 in the thyroid
	Prolactin	Water soluble	Promotes milk production
Posterior pituitary	Oxytocin	Water soluble	Milk ejection and uterine contraction
	ADH	Water soluble	Water absorption by the kidney; increases blood pressure
Adrenal cortex	Aldosterone	Lipid soluble	Reduces Na^+ excretion; increases K^+ excretion; raises blood pressure
	Cortisol	Lipid soluble	Increases blood levels of carbohydrates, proteins, and fats
Adrenal medulla	Epinephrine	Water soluble	Stimulates sympathetic actions
	Norepinephrine	Water soluble	Stimulates sympathetic actions
Thyroid	T_3, T_4	Lipid soluble	Increase basal metabolic rate
	Calcitonin	Water soluble	Lowers blood calcium
Parathyroid	PH	Water soluble	Raises blood calcium
Pancreas	Insulin	Water soluble	Promotes glucose entry into cells, decreasing blood glucose levels
	Glucagon	Water soluble	Increases gluconeogenesis, increasing blood glucose levels
Ovaries	Estrogen	Lipid soluble	Growth of female sex organs; causes LH surge
	Progesterone	Lipid soluble	Prepares and maintains uterus for pregnancy
Testes	Testosterone	Lipid soluble	Secondary sex characteristics; closing of epiphyseal plate
Placenta	HCG	Water soluble	Stimulates corpus luteum to grow and release estrogen and progesterone
	Estrogen	Lipid soluble	Enlargement of mother's sex organs; stimulates prolactin secretion
	Progesterone	Lipid soluble	Maintains uterus for pregnancy

Category 3B: Structure and integrative functions of the main organ systems

Respiratory System (BIO)

General function

- Gas exchange, thermoregulation
- Protection against disease: particulate matter

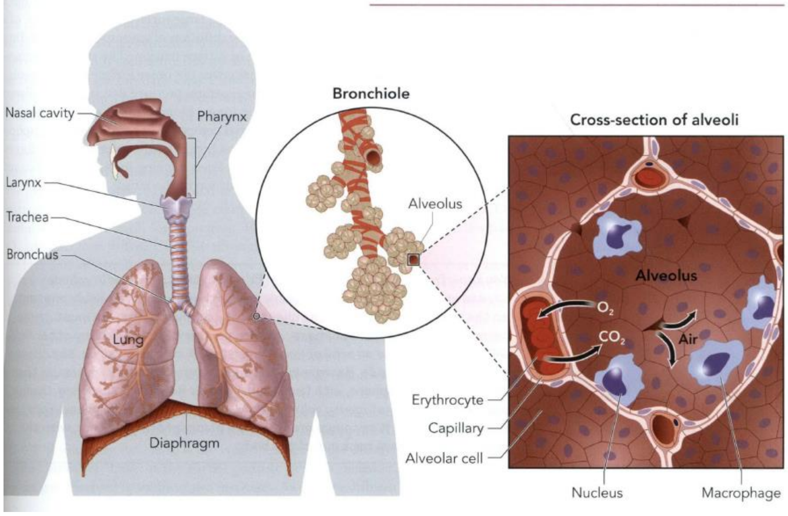
- Bring in O_2, get rid of CO_2
- Protection against disease by trapping harmful incoming particulate matter and ushering it back out of the body
- thermoregulation
  - panting, evaporation
  - nasal and tracheal capillary beds

Structure of lungs and alveoli

- Air enters through the nose and then moves through the pharynx, larynx, trachea, bronchi, bronchioles, alveoli
  - pharynx – throat, functions as a passage way for food and air
  - larynx – contains vocal cords, sits behind the epiglottis
  - trachea – lies in front of esophagus
    - mucus and cilia collect particulate matter and usher it back out
  - Oxygen diffuses from each alveolus into an adjacent capillary, where it is picked up by red blood cells
  - red blood cells release carbon dioxide, which diffuses into the alveolus and is expelled upon exhalation

FIGURE 4.1 Respiratory System

amount of surface area for gas exchange. The cardiovascular system branches into capillaries for similar reasons.



Breathing mechanisms

- Diaphragm, rib cage, differential pressure
- Resiliency and surface tension effects
- Mechanics of respiration
  - Differential pressures
    - when airway and alveoli are at negative gauge pressure (less than atmospheric pressure), air flows inward
    - when airway and alveolar pressure become greater than atmospheric pressure, air flows back out to the environment
  - Inspiration occurs when **medulla oblongata** of the midbrain signals diaphragm to contract
    - diaphragm – thin sheet of skeletal muscle that is innervated by the **phrenic nerve**
      - flattens upon contraction, expanding the chest cavity
    - intercostal muscles (rib muscles) also help to expand chest cavity
      - expansion causes negative pressure
  - Inhalation – contracted diaphragm, Exhalation – relaxed diaphragm
  - During inspiration, the ability of the lungs to expand in response to changing pressure is **counteracted** by surface tension in the alveoli
    - thin layer of water that cover inner surface of alveolus
    - also contain a type of cell that produces surfactant, a material composed of amphipathic phosopholipids
      - coats the alveolar surface and breaks up the intermolecular forces between water molecules, reducing surface tension
      - surfactant thus makes it easier to breathe
-

Thermoregulation: nasal and tracheal capillary beds; evaporation, panting

Particulate filtration: nasal hairs, mucus/cilia system in lungs

Alveolar gas exchange

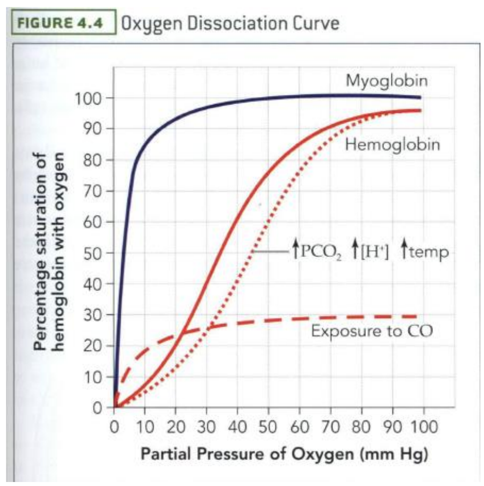
- Diffusion, differential partial pressure
- Henry's Law (GC)

- Chemistry of gas exchange
  - inside lungs, the pO_2 = 110 mmHg, pCO_2 = 40 mmHg
  - Deoxygenated blood in pulmonary capillaries, pO_2 = 40 mmHg, pCO_2 = 46 mmHg
  - **Fick's Law**
    - rate of diffusion is directly proportional to the surface area and differential partial pressure across the membrane, inversely proportional to the thickness of the membrane across which diffusion occurs
  - **Henry's law** – describes the amount of gas that can be dissolved into blood
    - amount of gas that can be dissolved in solution is directly proportional to the partial pressure of the gas in equilibrium with the liquid
      - thus, as the partial pressure of a gas increases, the concentration of the gas dissolved in solution also increases
    - As oxygen diffuses into the capillaries from the alveoli, the pO_2 of the blood rises until it reaches the high partial pressure of O_2 found in the alveoli
    - The "bends" – dissolved gases quickly released from blood when you quickly elevate your position
-

pH control

Regulation by nervous control

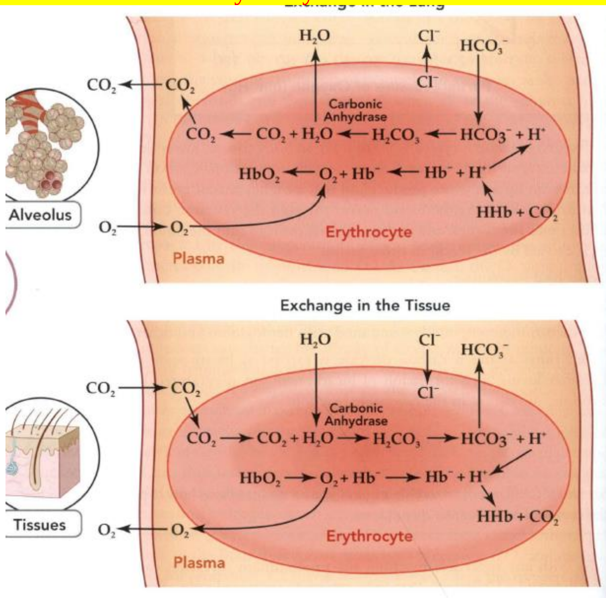
- CO2 sensitivity
- Hemoglobin
  - four polypeptide subunits, each with single heme cofactor
    - heme cofactor is an organic molecule with an atom of iron at its center
  - when one of the iron atoms binds with O2, the oxygenation of the other heme groups is accelerated
    - cooperativity



  - Rightward shift of the oxygen dissociation curve
    - in response to increase in carbon dioxide pressure, hydrogen ion concentration, or **temperature**
      - all reflect the body's increased need for oxygen
    - reflects hemoglobin's lowered affinity for oxygen
    - In response to Hydrogen ions: Bohr effect
      - increasing CO2 concentrations in bloodstream causes lowered pH
    - CO2 and Hydrogen ions affect the oxygen dissociation curve through allosteric effects
      - bind to deoxygenated hemoglobin and cause a change in shape that then discourages the binding of oxygen
      - 2,3-DPG also does this
        - *increases in response to low-oxygen environments to ensure that tissues still receive oxygen*
    - Carbon monoxide
      - **competitive inhibitor**, prevents binding of oxygen
      - however, **shifts the curve left**, reflecting the remaining sites' heightened affinity for oxygen while the maximum saturation percentage of hemoglobin is reduced
      - Thus, overall ability of oxygen to be carried bound to hemoglobin is decreased, while the oxygen that is able to bind does not unload at tissues as it should
        - why CO poisoning is dangerous
- Carbon dioxide is carried by the blood in three forms
  - dissolved in solution
  - **as a bicarbonate ion (the most by far)**

- in **carbamino compounds** (combined with hemoglobin and other proteins)

- $CO_2 + H_2O \leftrightarrow HCO_3^- + H^+$
    - enzyme: **carbonic anhydrase**
    - At tissues, where there is high concentration of CO2, forward reaction dominates
    - At lungs, where there is low CO2 pressure, the reverse direction is favored, allowing the conversion of the bicarbonate ion to CO2 for expiration
- Carbonic anhydrase is **present inside the red blood cells but not in the plasma**
    - bicarbonate builds up in the red blood cells
    - bicarbonate diffuses out of the euthrocytes and into the plasma
        - to prevent buildup of negative charge, chloride ions move into red blood cell in exchange for bicarbonate ions
            - this is called **chloride shift**
            - occurs in lungs as well, but in opposite direction
    - At lungs, bicarbonate diffuses back into erythrocytes and is converted back into CO2



- **Haldane effect**
    - the oxygenation of hemoglobin lowers its affinity for carbon dioxide
    - facilitates the transfer of carbon dioxide from the blood to the lungs, and from tissues to blood
- Respiratory centers in medulla regulate breathing rate and can respond to changes in the chemical composition of blood, particularly to CO2
    - central chemoreceptors in **medulla**, peripheral chemoreceptors in the **carotid arteries and aorta**
        - increase breathing rate when CO2 is too high and pH is too low
    - Oxygen mainly monitored by peripheral chemoreceptors, CO2 monitored by central
    - Both peripheral and central responds to pH
        - low pH – increase breathing rate, expel CO2, raise pH
- Carboxyhemoglobin = hemoglobin + CO
- Carbamino hemoglobin = hemoglobin + CO2

Circulatory System (BIO)

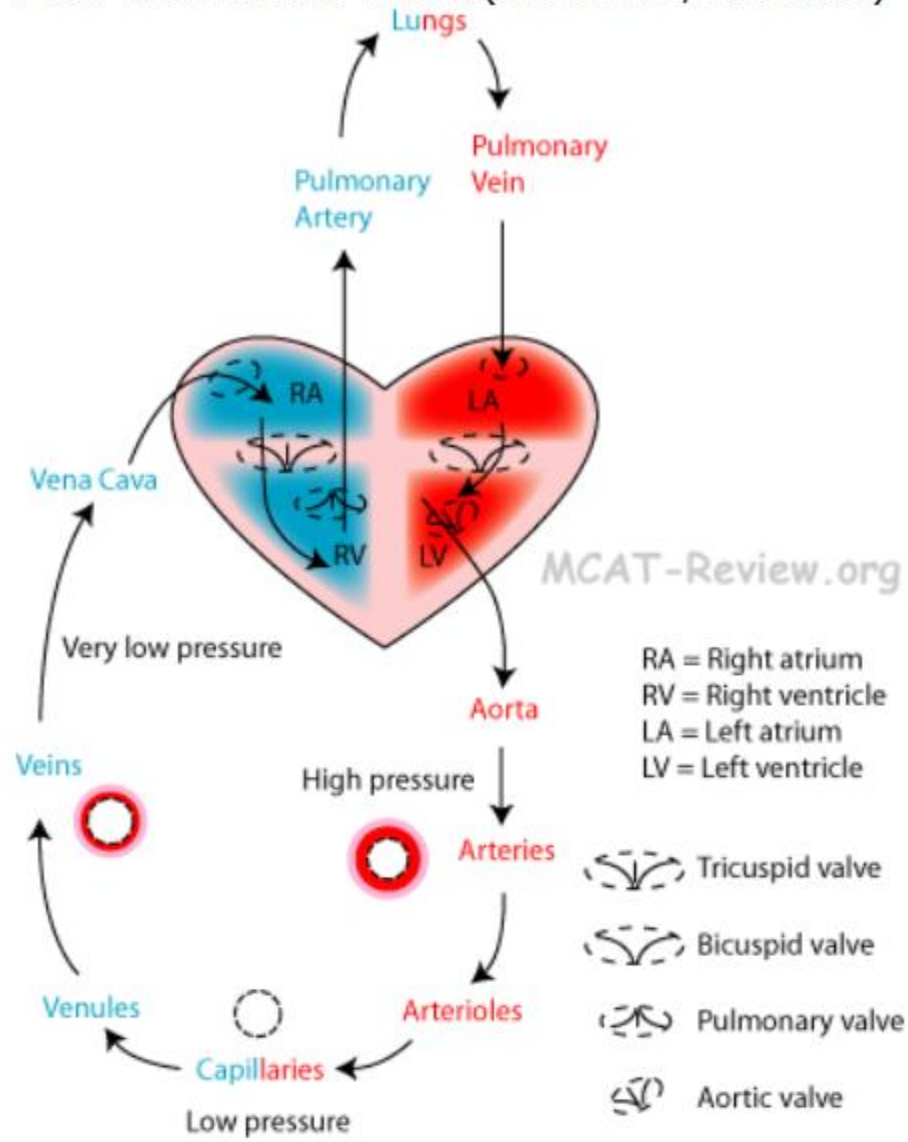
Functions: circulation of oxygen, nutrients, hormones, ions and fluids, removal of metabolic waste

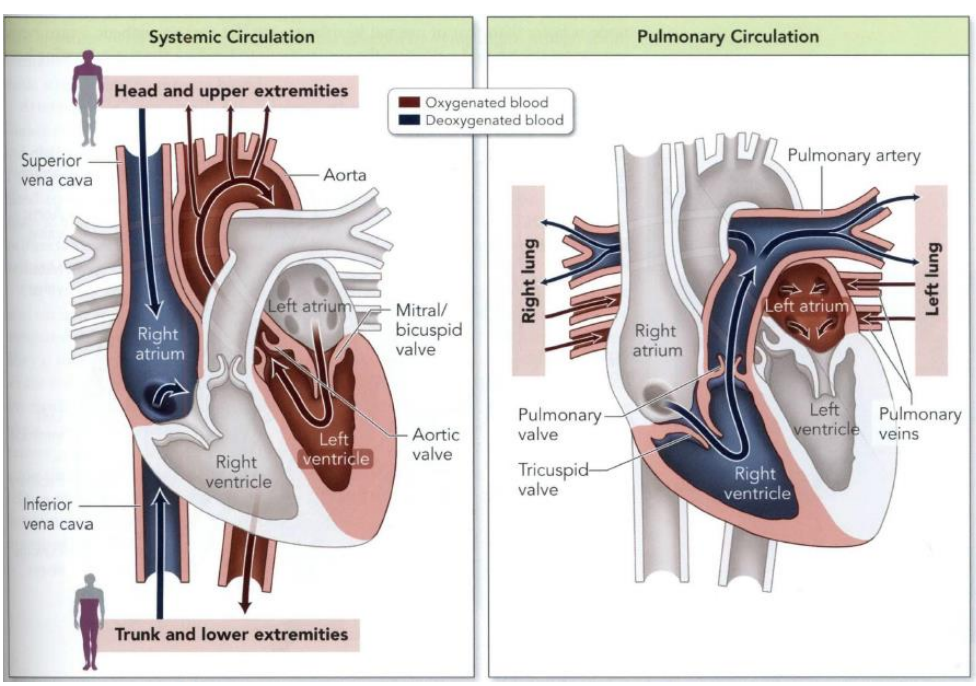
Role in thermoregulation

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

Four-chambered heart: structure and function

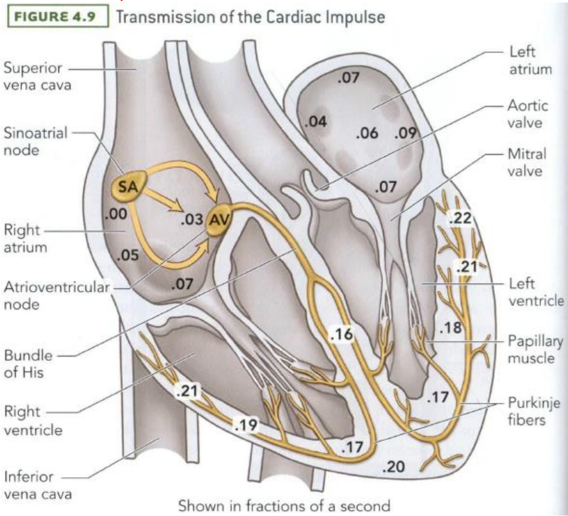
- Four-chambered heart (structure, function)





- Left ventricle is thicker and stronger than right ventricle

- The Cardiac Impulse
  - systole = contraction of ventricles, diastole = relaxation of the entire heart and then contraction of the atria



  - pace of SA node is faster than that of normal heartbeats, but the parasympathetic vagus nerve innervates the SA node, slowing the contractions to produce the typical resting heart rate
  - Delay before AV node, allows atria to finish their contraction and squeeze their contents into the ventricles before ventricles begin to contract

Endothelial cells

- Atrioventricular valves
  - Tricuspid (right), and mitral (left)
  - Tethered to the walls by papillary muscles
    - Chordae tendinae – keeps ventricles from shooting blood back up these valves
- Interventricular Septum – walls between vesicles
  - Membranous
  - Muscular
  - Ventricular Septal Defect – hole in membranous portion
- 3 layers to heart muscle
  - Endocardium – on inside, very similar to lining of blood vessels, thin—few cell layers thick
  - Myocardium – thicker, in the middle, all of the contractile vessel is present, needs energy
  - Pericardium – thin layer on outside, consists of inner and outer layer, with gap in between
    - Balloon that embryonic heart grows into
    - Inner – visceral (organs) pericardium
    - Outer – parietal pericardium

Systolic and diastolic pressure

- Blood Pressure and Flow
  - Systolic pressure – highest, measured in the arteries
  - Diastolic pressure – during relaxation of ventricles, lowest pressure
  - $Q = \Delta P/R$
    - total flow through system is constant

Pulmonary and systemic circulation

- Systemic circulation – directs oxygenated blood to tissues and then returns deoxygenated blood to heart
  - left ventricle – aorta – arteries – arterioles – capillaries – venules – veins – superior and inferior venae cavae – right atrium
- Pulmonary system - transports blood to the lungs for oxygenation
  - Right atrium – right ventricle – pulmonary arteries – arterioles – capillaries of lungs – venules – veins – pulmonary veins – left atrium

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

- Structural and functional differences
- Pressure and flow characteristics
  - Arteries
    - pressure store

            - thick elastic walls that stretch as they fill with blood during systole
            - when ventricles finish their contraction, the stretched arteries recoil, keeping the blood moving smoothly
            - innervated by sympathetic nervous system
                - epinephrine is a powerful vasoconstrictor, causes arteries to narrow
                - Larger arteries have less smooth muscle per volume and are less affected by sympathetic innervation
            - Arterioles
                - participate in thermoregulation by controlling flow of warm blood to capillaries in the skin
        - Veins – volume storage, hold about 64% of blood in a body at rest, acting as a reservoir
- Cross Sectional area on blood flow
    - Capillaries > veins > arteries (in total CSA)
    - blood velocity is inversely proportional to CSA because flow is constant
    - movement of blood slowest in capillaries – more time for exchange
    - Poiseuille's Law – demonstrates the impact of radius
    -
- Pressure changes
    - highest in aorta, decreases to reach lowest level in veins
    - to compensate for their lower pressure, veins have a valve system that prevents back flow of blood
    - contraction of skeletal muscle helps blood move through veins
        - still, the major propulsive force is the pumping of the heart
-

Capillary beds

- Mechanisms of gas and solute exchange
- Mechanism of heat exchange
- Source of peripheral resistance
    - Capillaries
        - exchange of materials with the tissues
        - huge total surface area
        - walls composed of endothelial cells only 1 cell thick
            - thin walls well suited for transport
        - when substances travel across the capillary wall, they enter the interstitium
        - Four methods by which materials cross capillary walls
            - pinocytosis
                - proteins
            - diffusion through capillary cell membranes
                - lipid-soluble
            - movement through pores in cells called fenestrations
                - proteins
            - movement through the spaces between the cells
                - water-soluble
- The arterioles, **capillaries**, and venules have very low Graetz numbers, $Gz < 0.4$, and act as perfect **heat exchangers** in which the blood quickly reaches the tissue temperature

Composition of blood

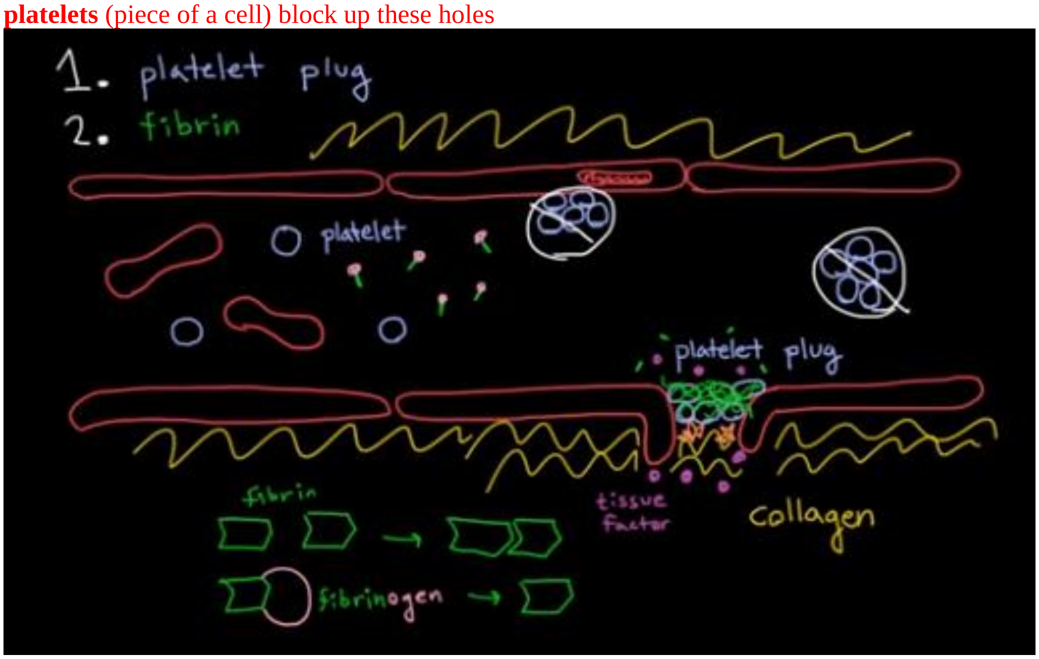
- Plasma, chemicals, blood cells
- connective tissue – contains cells and a matrix
- plasma, red blood cells, white blood cells
- Plasma – contains matrix of blood, includes water, ions, urea, ammonia, proteins, and other organic and inorganic compounds
    - body regulates overall volume of blood by altering amount of water in plasma
    - important proteins: Albumins – transport fatty acids and steroids, help regulate osmotic pressure
        - Immunoglobulins (antibodies) are a major component of the immune system
        - clotting factors
        - Plasma proteins act as a source of amino acids for tissue protein replacement
- Erythrocyte production and destruction; spleen, bone marrow
- Erythrocytes – essentially bags of hemoglobin
    - no organelles, not even nuclei, no mitosis
    - hemocrit – percentage by volume of red blood cells
        - usually 35-50%

- Erythropoiesis (from Greek 'erythro' meaning "red" and 'poiesis' meaning "to make") is the process which produces red blood cells (erythrocytes). It is stimulated by decreased O2 in circulation, which is detected by the kidneys, which then secrete the hormone erythropoietin.[2] This hormone stimulates proliferation and differentiation of red cell precursors, which activates increased erythropoiesis in the hemopoietic tissues, ultimately producing red blood cells (erythrocytes).
- The bone marrow of essentially all the bones produces red blood cells until a person is around five years old.
- As **red blood cells** wear out in the bloodstream, they are taken in by the spleen, an organ on the left side of the abdomen below the stomach, and **destroyed**.
- Regulation of plasma volume

Coagulation, clotting mechanisms

- Platelets – important function in coagulation
  - polymerization of the plasma protein fibrinogen to form fibrin threads that attach to the platelets and form a tight plug

How do we make blood clots?

- What is blood vessels get damaged? we will lose blood
  - **platelets** (piece of a cell) block up these holes
  - 

- **Collagen** is outside the blood vessel, not inside
  - chemically interacts with the platelets, causes them to stick together
- **Fibrin** – protein – forms a mesh, naturally sticks together
  - **fibrinogens** circulate blood, don't stick together
    - fibrin turns to fibrinogen only in site of damage
      - **Tissue factors** are outside blood vessels, signal fibrinogen to turn to fibrin

Oxygen transport by blood

- Hemoglobin, hematocrit
- Oxygen content
- Oxygen affinity

Carbon dioxide transport and level in blood

Nervous and endocrine control

- Blood Pressure must be regulated at around 100 mm Hg
  - **baroreceptor reflex** – quick nervous system reflex
    - located within arteries
    - alters both cardiac output and blood vessel resistance to flow
    - signals centers in brainstem to alter sympathetic and parasympathetic output to heart and blood vessels
      - PNS – slows heart's rate of contraction, decreases blood pressure
      - SNS – increases heart's rate of contraction, causes blood vessels to constrict, increases blood pressure
  - **renin-angiotensin-aldosterone system** – slower hormonal control
    - regulation of plasma volume
    - mechanoreceptors in arteries leading to kidneys detect decrease in blood pressure

        - cascade of enzymatic effects triggered by the secretion of renin leads to increased intake and retention of water, which increases volume and pressure
            - ADH and aldosterone are involved
    - *both involve detection of changes by mechanoreceptors*
    - changes total peripheral resistance through constriction or dilation of smooth muscle surrounding arterioles, which are the blood vessels that contribute the most to peripheral resistance
            - smaller = more resistance
            - capillaries have less resistance than arterioles because they are arranged in parallel

Lymphatic System (BIO)

Structure of lymphatic system

Major functions

- Equalization of fluid distribution
- Transport of proteins and large glycerides
- Production of lymphocytes involved in immune reactions
- Return of materials to the blood

Lymphatic System as a Drainage

- Lymphatic system collects excess interstitial fluid that results from fluid exchange in the capillary beds and return it to the blood
- also removes proteins and other particles too large to be taken up by capillaries
- pathway back to blood takes the excess fluid through lymph nodes, which are well prepared to elicit an immune response if necessary
- is an open system – fluid enters at one end and leaves at the other
- To enter lymph system, interstitial fluid flows between overlapping endothelial cells
    - cells overlap so that once inside, large particles cannot push their way out
- Typically, interstitial fluid has slightly negative gauge pressure
    - as the pressure rises above zero, lymph flow increases
        - facts include blood pressure, osmotic pressure, permeability of capillaries
- Lymph vessels contain intermittent valves, which allow fluid to flow in only one direction
- Lymph empries into large veins at thoracic duct and right lymphatic duct
- Throughout lymphatic system there are many lymph nodes, containing large quantities of lymphocytes
    - lymph nodes filter and trap particles
        - where lymphocytes are stimulated to respond to pathogens
- Note: Lymphocytes - T cells and B cells. White blood cells called lymphocytes originate in the bone marrow **but migrate to parts of the lymphatic system such as the lymph nodes, spleen, and thymus**. There are two main types of lymphatic cells, T cells and B cells.

Immune System (BIO)

Innate (non-specific) vs. adaptive (specific) immunity

The innate immune system consists of the primary defense, including barriers like skin or digestive enzymes. If the pathogen makes it past this, macrophages are first on the scene. Next, neutrophils emerge from their storage in the bone marrow, in response to the presence of the pathogen. They die after engulfing the pathogen and form pus. Eosinophils are activated only in response to pathogens, and basophils release many of the chemicals responsible for inflammation.

Inflammation is also an important contributor to the innate immune system. It serves to “wall off” the infected area, and is in response to chemicals such as prostaglandins, lymphokines, and histamines. The dilation of blood vessels in the area allows more macrophages to arrive.

First line – keep things out

- skin
- mucous membranes
- stomach acid (on the outside of our real bodies)

Second line

- inflammatory response
    - brining stuff to the fight
- phagocytes

Phagocytes – non specific

- contains lysozymes that digest the foreign particle

- Many phagocytes are called antigen-presenting cells

Major Histocompatibility Complex Type II

- Present on surface

Neutrophils – fast and abundants

Macrophages

Dendritic Cells – nothing nervous, best activators of specific immune system

Phagocytes are leukocytes (White blood cells)

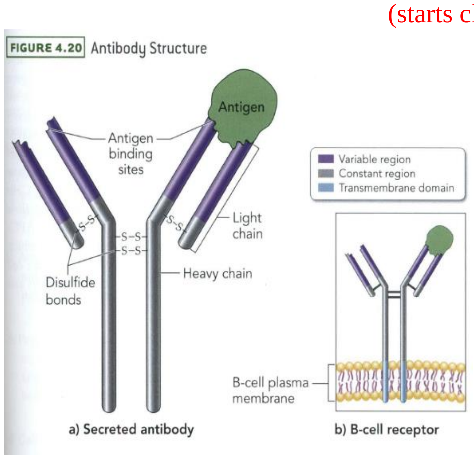
Adaptive immune system cells

Lymphocytes – type of leukocytes (white blood cells)

- B and T lymphocytes
- B lymphocytes are produced in bone marrow
- T lymphocytes also start off in the bone marrow, but mature in the thymus
- T-lymphocytes
- T-cell immunity
    - cell-mediated immunity – effective against cells that have already been infected because it is not restricted to free-floating substances
    - involves T-lymphocytes, which mature in the thymus
        - has an antibody-like protein at its surface that recognizes antigens
            - T-cell receptor (TCR)
            - However, T-lymphocytes never make free antibodies
- Helper T cells bind to MHC II, Cytotoxic T Cell bind to MHC I
    - Cytotoxic – binds to MHC I, becomes activated
        - helper and effector
            - effector – release perforins, kill cells that have gone awry
    - Primary Response
        - TCR recognizes appropriate antigen under right conditions
        - T-lymphocytes differentiate into:
            - Helper T-cells assist in activating B-lymphocytes and other T-lymphocytes
                - are the cells attacked by HIV
            - Memory T-cells are like memory B-cells
                - Memory cells are pretty much just copies of the original cells, makes this entire process happen more quickly during the next infection
            - Suppressor T-cells play a negative feedback and regulatory role
            - Killer T-cells bind to the antigen-carrying cell and release perforin, a protein that punctures the antigen-carrying cell
                - they themselves are not destroyed when they kill invading pathogens, *unlike macrophages and neutrophils*
                - They are also called CD8+ cells
    - A little more on helper T cells
        - activated by dendritic cells the best
        - proliferates
            - effector helper T cells, memory helper t cells
            - effector T cells – release cytokines, raise the alarm
        - A helper T cell that is also activated by the exact same virus as the B cell
            - helps activate the MHCII B cell to differentiate
            - helps guard against B cells that attack self – it has to also be activated by a helper T cell activated by the same disease
- B-lymphocytes – humoral response
- The B-cell immunity is in response to invading substances that have not yet made their way into the cell. It consists of B-lymphocytes synthesizing antibodies (immunoglobulins) that are specific for a particular antigen (the invading substance). It requires around 20 days to reach its full potential. With the help of helper T-cells, the B-lymphocytes differentiate into plasma cells (which secrete lots of antibodies) and memory B-cells, which proliferate and remain in the body. That way, when the same pathogen attacks again, a new antibody does not have to be synthesized—we can immediately begin a specific, concentrated attack.
- It has MHCII complexes – it binds an antigen, absorbs it, and presents it to a helper T cell
    - this helper T cell helps activate the B cells into plasma cells (effector B cells) and memory B cells

- Remember that new types of antibodies aren't synthesized. The body to begin with has a shit ton of different types of antibodies that can recognize virtually any disease. However, there are only singular copies of these antibodies to begin with, nd the secondary response serves to increase the number of these antibodies in circulation – "Memory"

- In the secondary response, B-lymphocytes differentiate into plasma cells and memory-B cells. Plasma cells begin synthesizing free antibodies and release them into the blood.
  - B Cell immunity
    - Humoral or antibody-mediated immunity is effective against bacteria, fungi, parasitic protozoans, viruses, and blood toxins
    - however, it cannot act against invading substances that have already made their way into cells
    - **Each B-lymphocyte makes a single type of antibody or immunoglobulin**, which can recognize and bind to a particular potentially harmful foreign particle (an antigen)
      - Have different variable portions
      - has a fixed portion and a variable portion – there are 10^{10} combinations of variable proteins (self responding combinations are weeded out)
        - same DNA, but in their hematopoiesis, there is a lot of shuffling of DNA
    - initially, a B-lymphocyte displays this antibody on its membrane, and the antibody is called a B-cell receptor (BCR)
      - antibody binds to the **epitope** portion of the antigen
    - Later, many antibodies are produced as secreted proteins
      - process by which an antibody (BCR) recognizes a foreign particle is called antigen-antibody recognition
      - The portion of the antibody that binds to an antigen is highly specific and is called an antigenic determinant
    - Primary response – immune response that results form the first exposure to an antigen
      - requires 20 days to reach its full potential
      - BCR recognizes the appropriate antigen
      - B-lymphocyte, assisted by a helper T-cell, differentiates into plasma cells and memory B-cells (starts cloning rapidly)



- Plasma cells – begin synthesizing free antibodies and releasing them into the blood (effector cells)
  - opsonization – tag molecules for pickup from phagocytes
  - glues together viruses
- Memory B-cells proliferate and remain in the body
  - both long-lived
  - secondary response

- A Final Summary:
  - B cell – has membrane bound antibodies with one distinct variable portion
    - Activation requires:
      - binding of antigen to antibody
      - stimulation by helper T cell (stimulated by the same MHC II complex
    - After activation, becomes
      - effector cells (plasma cells) – antibody factory
      - Memory cells – for a faster response next time
  - T Cells – CD4 proteins or CD8 proteins
    - CD4 – binds to MHCII, are **helper t cells**
      - binds to dendritic cells a lot of the time, becomes activated
        - memory – for faster future response
        - effector – release cytokines, activate B cells
    - CD8 – **cytotoxic T cells** – binds to MHC I complex
      - kills infected or cancerous cells
        - memory – for faster future response

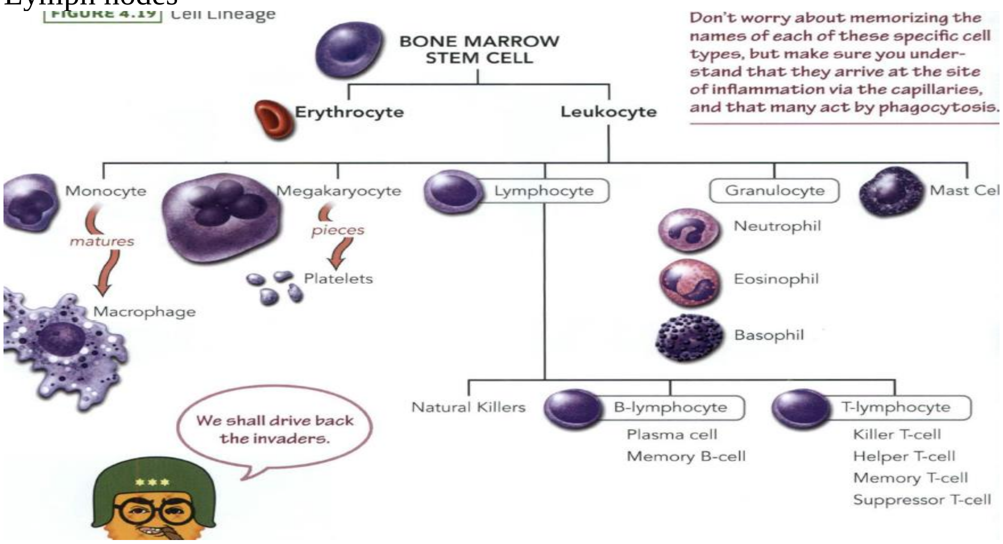
- effector – kills cells

Innate immune system cells

- Macrophages
- Phagocytes

Tissues

- Bone marrow
- Spleen
- Thymus
- Lymph nodes



Concept of antigen and antibody

There are several things that the antibodies can do. One of them is to signal natural killer cells and macrophages to engulf them. Another is to attract complement proteins that enhance their solublility or perforate holes. Another is to cause antigens to agglutinate. A fourth possibility is the base of the antibody to bind to mast cells, which release histamine.

Antigen presentation

All nucleated cells display MHC molecules, which display antigens on the surface of the cell. MHC I molecules display microbial antigens present within the cell—this is known as the endogenous pathway. This is usually for viruses and cancer and stuff. Therefore, the protein content will be the cell's own. All nucleated cells possess MHC I molecules. MHC II molecules are only for phagocytic cells—they display antigens brought from outside the cell—this is known as the exogenous pathway.

Clonal selection

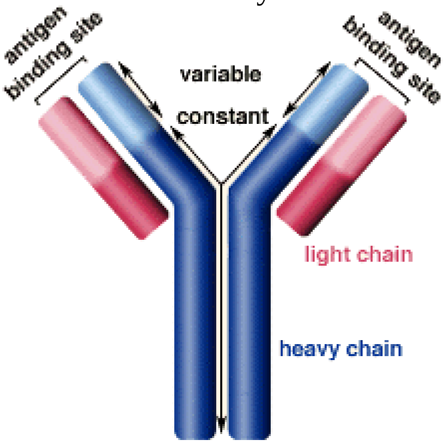
The danger of an unregulated immune system is that it might become hyperactive and attack the body. To prevent this, positive and negative clonal selection is done. In positive selection, cells that cannot recognize a specific antigen undergo apoptosis. In negative selection, cells that attack a host cell, not in response to an infection, undergo apoptosis. **T-cells undergo clonal selection in the thymus** while **B-cells undergo selection in the bone marrow**. After surviving selection, they reside in the lymphoid tissue or circulate in the blood and lymph fluid. Once these remaining surviving cells recognize the antigen, they differentiate and proliferate, completing the process of clonal selection.

The clonal selection theory can be summarized with the following four tenets:

- Each lymphocyte bears a single type of receptor with a unique specificity (by V(D)J recombination).
- Receptor occupation is required for cell activation.
- The differentiated effector cells derived from an activated lymphocyte will bear receptors of identical specificity as the parental cell.
- Those lymphocytes bearing receptors for self molecules will be Clonal deleted at an early stage.

Antigen-antibody recognition

Structure of antibody molecule



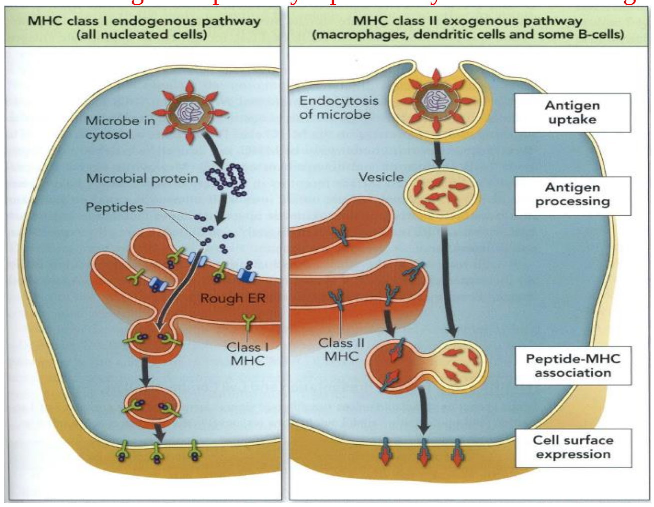
Recognition of self vs. non-self, autoimmune diseases

- Regulation of Immune System
  - autoimmune diseases—hyperactive immune system attacks body's own tissues
  - Each lymphocyte expresses BCRs or TCRs of a single specificity
    - total population of B and T cells can express millions of different BCRs and TCRs
  - Positive selection – cells must show that they are capable of recognizing antigens in the context of host MHC molecules, and those cannot will undergo apoptosis
  - Negative selection – cells must show they are not inappropriately activated by host cells in absence of invasion
  - T cells undergo clonal selection in thymus, while B-cells undergo selection in bone marrow
    - cells that survive the selection process are released to lodge in lymphoid tissue or to circulate between blood and lymph fluid
    - Once these surviving cells recognize the appropriate foreign antigen, they undergo differentiation and proliferation, thus completing the process of clonal selection

Major histocompatibility complex

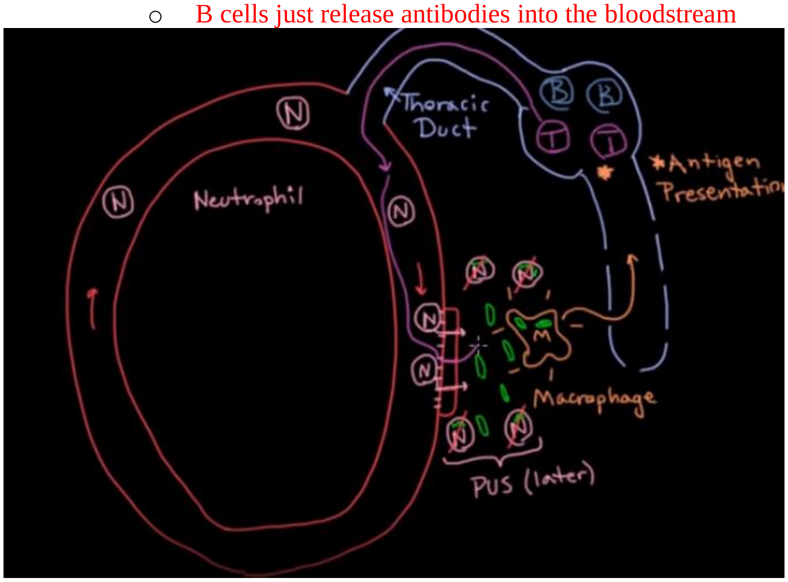
- Antigen Recognition
  - All human cells with nuclei express MHC molecules on surface
    - function is to display antigens for recognition
    - 2 major types:
      - MHC class I – display antigens derived from intracellular pathogens such as viruses and some bacteria
        - all nucleated cells have MHC class I
        - Endogenous pathway – process by which intracellular antigens are processed and displayed on the cell surface
      - MHC class II – display antigens derived from extracellular pathogens

- must be displayed by phagocytic cells
    - macrophages, some B-cells
- Exogenous pathway – process by which these antigens are processed and displayed



Location and movement of these immune cells

- Neutrophils circulate in the blood
    - eat up bacteria and die, become pus
    - squeeze out between endothelial cells
- Macrophages and stuff can't go back into the blood, but they can go to the lymphatic system
    - *that's how they present viruses to B and T cells, antigen presentation*
    - the activated T cells go through the lymphatic system, go through the thoracic duct
    - B cells just release antibodies into the bloodstream



Blood cells review

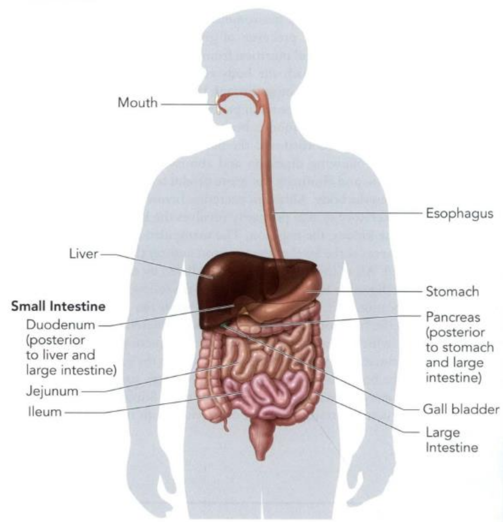
- All come from bone marrow (which are perfused with blood vessels themselves)
- Pluripotent hematopoietic cell
- Myeloid and Lymphoid lineage
    - lymphoid – NK cell, B cell, and T Cell
    - Myeloid – RBC, Megakaryocyte (makes platelets), neutrophil, basophil, eaosinophil, monocyte (becomes macrophage), mast cells
- What about the dendritic cell? – It comes from both lineages

Digestive System (BIO)

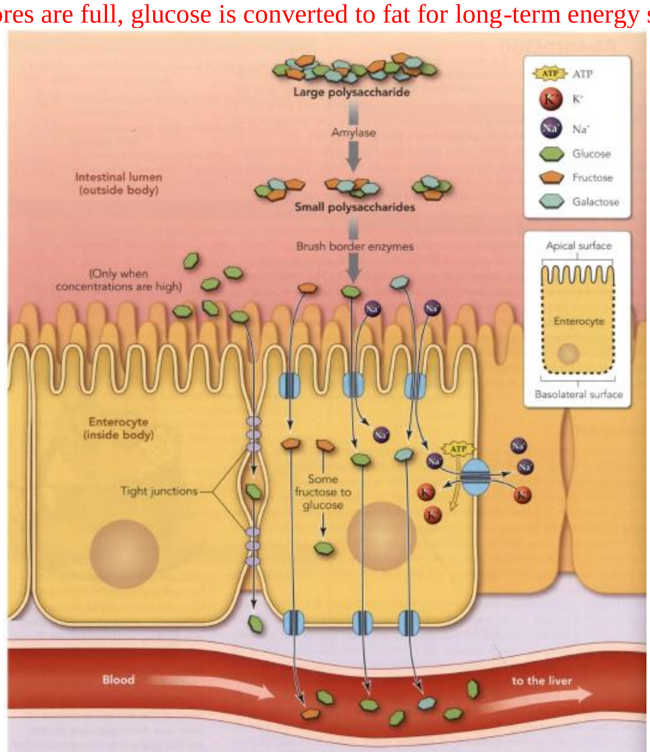
Digestive System

- Mouth, esophagus, stomach, small intestine, large intestine, anus
- considered outside the body

FIGURE 5.1 Anatomy of the Digestive System



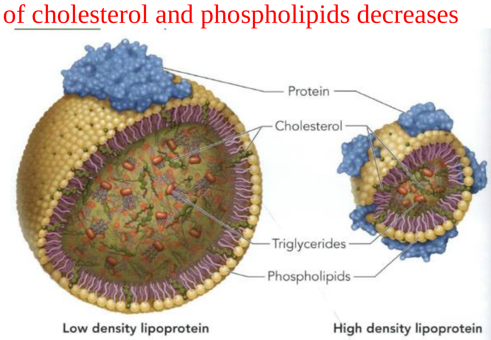
- Carbohydrates
  - Most of the end product of carbohydrate digestion is glucose
  - When glycogen stores are full, glucose is converted to fat for long-term energy storage



  - *Much of fructose and galactose is converted to glucose inside the enterocyte*
  - All Carbs absorbed into the bloodstream and carried by the portal vein to the liver
  - liver absorbs the carbohydrates and converts nearly all the galactose and fructose into glucose
  - In all cells except for enterocytes and cells of the renal tubule, glucose is transported from high concentration to low concentration through facilitated diffusion
  - Nearly all cells are capable of producing and storing some glycogen, but only muscle cells and liver cells store large amounts
- Proteins
  - like carbs, are hydrophilic and cannot easily pass through the membrane
  - Protein digestion results in amino acids, dipeptides, and tripeptides
    - absorption of many of these products occurs via a co-transport mechanism down the concentration gradient of sodium
  - Nearly all polypeptides that are absorbed into an enterocyte are hydrolyzed to their amino acid constituents by enzymes
  - from the enterocytes, amino acids are absorbed directly into the blood and then are taken up by all cells of the body, especially the liver
    - transport may be facilitated or active, but is never passive, since amino acids are too large and polar

- cells immediately create proteins from the amino acids so that the intracellular amino acid concentration remains low and the concentration is preserved
- When cells reach their upper limit for protein storage, amino acids can be burned for energy or converted into fat for storage
- Ammonia is a byproduct of gluconeogenesis from proteins. Nearly all ammonia is converted to urea by the liver and excreted in urine

- Fats
  - hydrophobic, unlike proteins and carbs
  - not easily transported in the aqueous environments of the digestive lumen and the intracellular space, but can easily pass thru membranes
  - Most dietary fat consists of triglycerides, which are broken down to monoglycerides and fatty acids in the digestive process
    - these components then shuttled to brush border by bile micelles
  - Once inside the enterocytes, the fats must be altered such that they can travel through the aqueous environment of the cell
    - monoglycerides and fatty acids are converted back into triglycerides **at the smooth endoplasmic reticulum**
      - amphipathic molecules—orient themselves with their charged ends pointing outward
      - form globules, move to the Golgi and are released via exocytosis
      - move into the lacteals of the lymph system
        - vs carbs and proteins, which are absorbed into the bloodstream
        - Most ingested fat that is absorbed moves through lymph system and enters the veins of the neck at the thoracic duct
    - The most significant absorption of fat occurs in the liver and adipose tissue
      - chylomicrons stick to the side of capillary walls, where lipoprotein lipase hydrolyzes the triglycerides
        - chylomicrons are lipoprotein particles that consist of triglycerides, phospholipids, cholesterol, and proteins
        - the products immediately diffuse into fat and liver cells
        - thus, the first stop for most of digested fat is the liver
  - From adipose tissue, most fatty acids are transported in the form of free fatty acid, which combines with the protein albumin in the blood
  - However, between meals, 95% of lipids in the plasma are in the form of lipoproteins
    - very low-density lipoproteins
    - intermediate-density lipoproteins
    - low-density lipoproteins
    - high-density lipoproteins
      - all made from triglycerides, cholesterol, phospholipids, and protein
      - As the density increases, first the relative amount of triglycerides decreases, and then the relative amount of cholesterol and phospholipids decreases



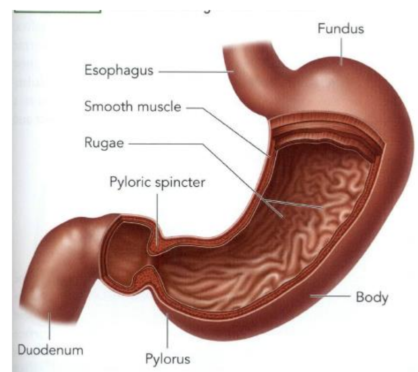
Ingestion

- Saliva as lubrication and source of enzymes
- Ingestion; esophagus, transport function
- Mouth and Esophagus
  - Ingestion – process of taking in food through the mouth
  - Two kinds of digestion – physical and chemical
    - physical – chewing food into a **bolus**, which is pushed through the esophagus
    - Chemical - **α-amylase in saliva**

                - breaks down long chains of starch into **polysaccharides**
    - Peristalsis – contraction of the smooth muscle in digestive tract, creates a wave motion that pushes along the partially digested food
    - no digestion occurs in esophagus

Stomach

- Storage and churning of food
- Low pH, gastric juice, mucal protection against self-destruction
- Production of digestive enzymes, site of digestion
- Structure (gross)
- The Stomach
    - Fundus, Body, pylorus
    - bolus moves into stomach through lower esophageal sphincter
    - pepsin – catalyzes breakdown of proteins in the stomach
    - lining of stomach is called the mucosa
    - physical digestion also occurs – churning of smooth muscle
        - food turns to chime, leaves stomach through pyloric sphincter
    - Inside of stomach is highly acidic
        - gastric juice, pH of 2
    - contains exocrine glands called gastric pits, use ducts to deliver their sections to specific locations in external environment
    - Four major types of cells
        - mucous cells – secrete mucous, lubrication and protection from acidic environment, secrete small amount of pepsinogen
        - Chief cells – secrete pepsinogen, the zymogen precursor to pepsin
        - parietal cells – secrete HCl through active transport
            - carbon dioxide involved in the process
            - lot of mitochondria
            - hydrogen from carbonic acid expelled to lumen side, bicarbonate ion expelled to interstitial fluid side
                - pH of blood raised, pH of stomach lowered
            - also secrete **intrinsic factor** that helps ileum absorb vitamin B12
        - G cells – secrete gastrin, a large peptide hormone that stimulates parietal cells to secrete HCl
    - Cells like Parietal cells have a lot of mitochondria for HCl release. Cells specializing in secretion, such as mucous cells, chief cells, and G cells, contain larger amounts of rough endoplasmic reticulum and Golgi bodies



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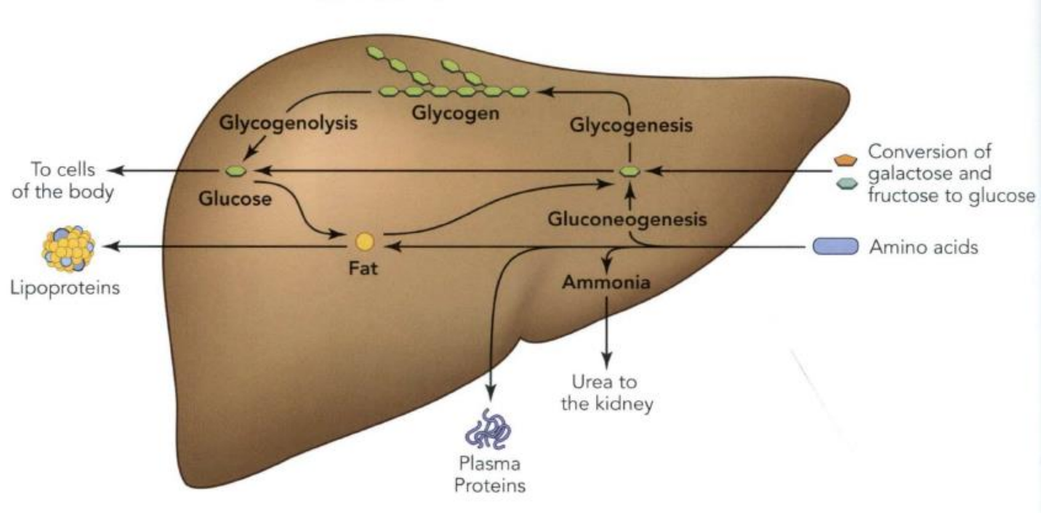
Liver

- Structural relationship of liver within gastrointestinal system
- Production of bile
- Role in blood glucose regulation, detoxification
- The liver – storage, distribution, and detox
    - located primarily in the upper right-hand quadrant of the abdomen adjacent to the organs of the digestive tract
    - Blood from the capillary beds of the intestines, stomach, spleen, and pancreas feeds into the large hepatic portal vein
        - carries all of the blood from the digestive system to the liver so that the liver can process the blood before it is re-circulated through the rest of the body
            - removes many ingested toxins from the bloodstream so that they do not enter wider circulation
            - All blood received by the liver collects in the hepatic vein, which leads to the vena cava
    - Metabolic functions
        - Carbohydrate metabolism – liver maintains normal blood glucose level through gluconeogenesis, glycogenesis, and the release of glucose stores according to the needs of the body
        - Fat metabolism – liver synthesizes bile from cholesterol and **converts carbs and proteins into fat**
            - oxidizes the fatty acids for energy, and forms most lipoproteins
            - *produces ketone bodies* when using fats for energy
            - **when the liver mobilizes fats or proteins for energy, the acidity of the blood increases**
        - Protein metabolism – **liver deaminates amino acids**, forms **urea from ammonia in the blood**, synthesizes plasma proteins like fibrinogen
        - Detoxification – detoxified chemicals are secreted by the liver as a part of bile or modified so that they can be excreted by the kidney
    - Storage functions

- Blood storage
- Glycogen storage – as a reserve to regulate blood glucose levels
- vitamin storage – liver stores vitamins A, D, and B12

- Immune Functions
  - Blood filtration – Kupffer cells phagocytize bacteria picked up from intestines
  - Erythrocyte destruction – Kupffer cells also destroy irregular erythrocytes, although most irregular erythrocytes are destroyed by the spleen



Bile

- Storage in gall bladder
- Function
  - Lipase—degrades fat, specifically triglycerides
    - however, since intestinal fluid is an aqueous solution, the fat clumps together, reducing the surface area upon which lipase can act
    - problem is solved by the addition of bile
      - produced in the liver and stored in the gall bladder
      - gall bladder releases bile through the cystic duct, which empties into the common bile duct shared with the liver
      - Bile emulsifies the fat**, breaking it up** into small particles without changing it chemically

Pancreas

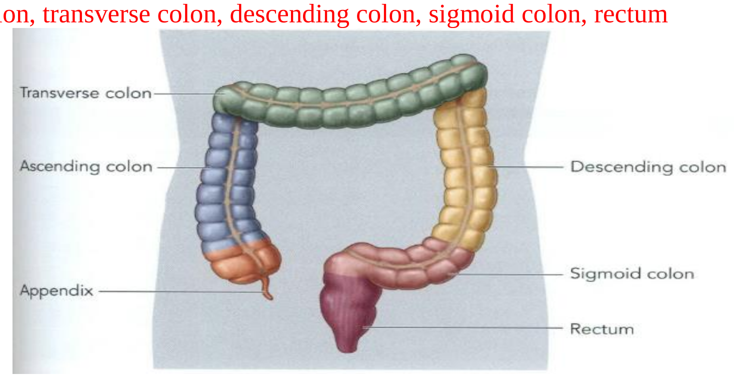
- Production of enzymes
- Transport of enzymes to small intestine
- Pancreas
  - aids the digestive process
  - neutralizes (the duodenum) the acid from stomach with bicarbonate ion secreted by the pancreas
  - endocrine gland that secretes insulin and glucagon
  - also acts as an exocrine gland, creating enzymes to the duodenum
    - trypsin, chymotrypsin, pancreatic amylase, lipase, ribonuclease, and deoxyribonuclease
    - released as zymogens
    - **trypsin is activated by the enzyme enterokinase located in the brush border**
    - **activated trypsin then activates the other enzymes**
  - Trypsin and chymotrypsin degrade proteins into small polypeptides
  - Most proteins reach the brush border as small polypeptides, where they are then reduced to amino acids, dipeptides, and tripeptides
  - pancreatic amylase—hydrolyzes polysaccharides to disaccharides and trisaccharides; much more powerful than salivary amylase
  - Lipase—degrades fat, specifically triglycerides
    - however, since intestinal fluid is an aqueous solution, the fat clumps together, reducing the surface area upon which lipase can act
    - problem is solved by the addition of bile

Small Intestine

- Absorption of food molecules and water
- Function and structure of villi
- Production of enzymes, site of digestion
- Neutralization of stomach acid
    - neutralizes (the duodenum) the acid from stomach with bicarbonate ion secreted by the pancreas
- Structure (anatomic subdivisions)
- Small Intestine
    - Duodenum, jejunum, ileum
    - Most digestion occurs in the duodenum, most absorption occurs in the jejunum and ileum
    - Wall of the small intestine is similar to wall of stomach except that the outermost layer contains finger-like projections called villi
        - within each villus are a capillary network and lymph vessel—called a lacteal
            - nutrients absorbed through the wall of the small intestine pas into the capillary or the lacteal, depending on the type of macromolecule
        - apical (lumen) side of each villus are microvilli
            - appear as fuzzy covering-brush border
                - Brush border enzymes: carbohydrate digesting enzymes and protein-digesting enzymes, and some nucleotide-digesting enzymes
        - goblet cells – secrete mucus to lubricate the intestine and help protect brush border
    - performs digestion on both a small and large scale
    - located deep between the villi are intestinal exocrine glands, called the crypts of Lieberkuhn
        - secrete lysozyme—contributes to regulation of bacteria within the intestine
-

Large Intestine

- Absorption of water
- Bacterial flora
- Structure (gross)
- Large Intestine
    - 5 parts
    - ascending colon, transverse colon, descending colon, sigmoid colon, rectum



    - Associate this with water absorption
        - Profuse water loss in the form of diarrhea often results when there is a problem with the large intestine
-

Rectum: storage and elimination of waste, feces

Muscular control

- Peristalsis

Endocrine control

- Hormones
- Target tissues
- Gastrointestinal Hormones
    - Brain stimulates the stomach to begin digestive process, stomach signals the small intestine, small intestine releases hormones that act on the pancreas
    - Enteric nervous system
        - *large network of neurons* surrounding the digestive organs, helping to regulate processes such as smooth muscle contraction, fluid exchange, blood flow to the digestive organs, and hormone release

Site	Hormone	Stimulus	Target	Effects
Stomach	Gastrin	ACh release from vagus nerve	Stomach	Stimulates production of HCl
Duodenum	Secretin	Arrival of HCl in chyme	Pancreas	Stimulates secretion of sodium bicarbonate and enzymes
	Gastric inhibitory peptide	Arrival of fat and protein digestates in chyme	Pancreas	Stimulates enzyme secretion
			Stomach	Decreases motor activity
	Cholecystokinin (CCK)	Arrival of fat digestates in chyme	Pancreas	Stimulates enzyme secretion
			Stomach	Decreases motor activity

- Secretin, gastric inhibitory peptide, and CCK increase blood glucose
- the decreased motility of the stomach resulting from the action of these hormones causes the stomach to release chime into the duodenum at a slowed pace, giving the pancreatic enzymes in the duodenum more time to emulsify fats

Source/Enzyme	Action
Salivary Glands	
Salivary amylase	Starch → Maltose
Stomach	
Pepsin	Proteins → Peptides; autocatalysis
Pancreas	
Pancreatic amylase	Starch → Maltose
Lipase	Fats → Fatty acid and glycerol
Nuclease	Nucleic acids → Nucleotides
Trypsin	Proteins → Peptides; Zymogen activation
Chymotrypsin	Proteins → Peptides
Carboxypeptidase	Peptides → Shorter peptides and amino acids
Small intestine	
Aminopeptidase	Peptides → Shorter peptides and amino acids
Dipeptidase	Dipeptides → Amino acids
Enterokinase	Trypsinogen → Trypsin
Nuclease	Nucleic acids → Nucleotides
Maltase	Maltose → Glucose
Lactase	Lactose → Galactose and glucose
Sucrase	Sucrose → Fructose and glucose

-

Nervous control: the enteric nervous system

Excretory System (BIO)

Roles in homeostasis

- Blood pressure
- Osmoregulation
  - maintaining homeostasis of body fluid volume and regulating blood pressure
- Acid–base balance
  - maintaining homeostasis of plasma solute composition and helping control plasma pH
- Removal of soluble nitrogenous waste
  - Excreting waste products, such *as urea, uric acid, ammonia, and phosphate*
-

Kidney structure

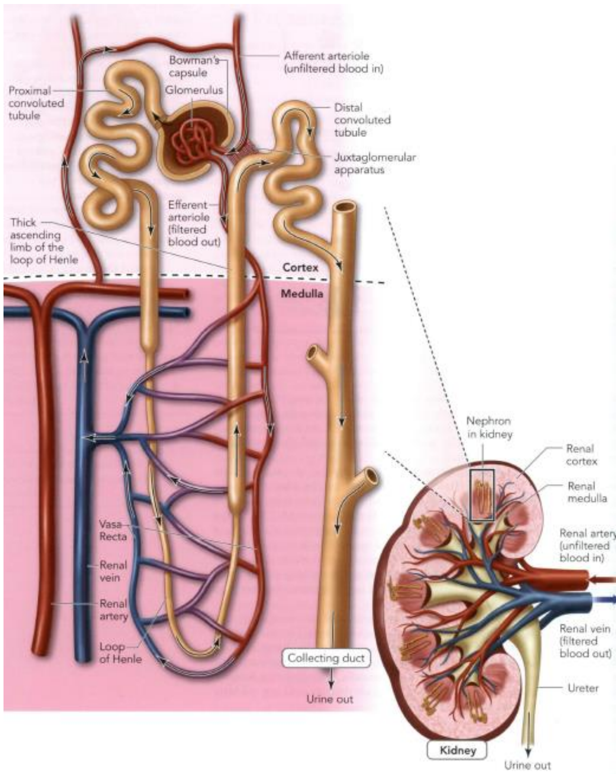
- Cortex
- Medulla
- Outer Cortex and inner medulla
- Urine is emptied into the renal pelvis, which is emptied by the ureter, which carries urine to the bladder

Nephron structure

- Glomerulus
- Bowman's capsule
  - Blood entering a nephron first flows into a capillary bed called the glomerulus
  - Together, the Bowman's capsule and the glomerulus make up the **renal corpuscle**

    - Hydrostatic pressure forces some plasma through the fenestrations of the glomerular endothelium and into Bowman's capsule
        - the fluid that enters Bowman's capsule is called filtrate or primary urine

- Proximal tubule
    - Filtrate moves from Bowman's capsule to the proximal tubule
        - *where most of secretion and reabsorption takes place*
        - hydrogen ions are secreted by the proximal tubule through an antiport system driven by the sodium concentration gradient
        - Reabsorption in the proximal tubule allows the kidney to retain valuable nutrients that were inadvertently filtered out and to return these substances to the rest of the body through capillary circulation
            - can occur through passive or active transport
                - these transport proteins can become saturated
                - once a solute has reached its transport maximum, any more solute is washed into the urine—transport maximum
            - water is reabsorbed into the renal interstitium of the proximal tubules across relatively permeable tight junctions by osmosis
        - Net result of proximal tubule: the amount of filtrate in the nephron is reduced and the solute composition is altered while the overall *concentration* of solutes is unchanged
-
- Loop of Henle
    - Filtrate then flows into the loop of Henle, which dips into the medulla
        - functions to increase the solute concentration, and thus the osmotic pressure, of the medulla
        - at the same time, the solute concentration of the filtrate leaving the loop of Henle is decreased
            - the initial descending and final ascending segments of the loop differ in their permeability to solutes and water
                - the descending loop has low permeability to salt and *high permeability to water*, so as filtrate descends into the medulla, water passively diffuses out into the medulla
                    - filtrate osmolarity increases
                - Ascending loop—solutes pass out, first by passive diffusion and then through active pumps
                    - thick ascending loop is nearly impermeable to water
                    - basically increases the solute concentration in the medulla while reducing it in the filtrate
                    - capillary bed called the vasa recta surround the loop of Henle and helps maintain the concentration of the medulla

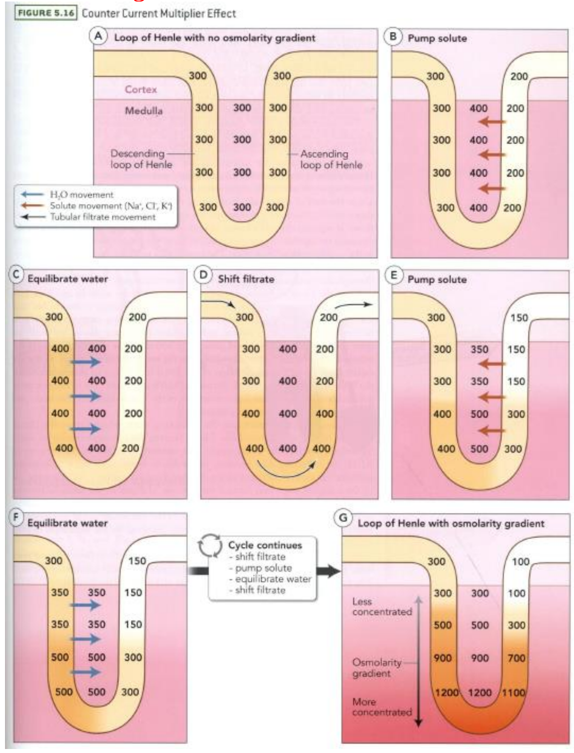


-
- Distal tubule
- Distal tubule
    - reabsorbs Na and Ca, while secreting K, H, and HCO3
    - aldosterone acts on distal tubule to increase number of sodium and potassium transport proteins in their membranes, causing blood pressure to increase
    - net effect of distal tubule is to lower the filtrate osmolarity
    - at the end of the distal tubule, in an area called the collecting tubule, ADH causes cells to become more permeable to water, causing filtrate to become more concentrated
- Collecting duct
- Collecting duct – *fluid at the top of the collecting duct has a concentration of salts about equal to that at the beginning of the nephron loop*
    - impermeable to water by default unless acted on by ADH, which then allows passive diffusion of water
    - concentrated medulla allows for concentrated urine
- If water conservation is necessary, ADH stimulates the opening of water channels in the collecting duct, allowing H2O to diffuse out and form concentrated urine

- If water conservation is not necessary, ADH is not secreted and the duct remains impermeable to H2O. The result is dilute urine

Formation of urine
- Glomerular filtration
- Secretion and reabsorption of solutes
- Concentration of urine
- Counter-current multiplier mechanism
- The Osmolarity gradient of the medulla is Critical
    - *The filtrate entering the loop of Henle is more concentrated than filtrate exiting loop*
    - loop of Henle has a countercurrent flow with the vasa recta and in between the descending and ascending loops
    - Single effect – process by which active transport of the solute by pumps in the wall of the thick ascending loop creates a concentration gradient
        - net result is to dilute the filtrate in the ascending limb while concentrating the medulla, and to concentrate filtrate in the descending limb
    - Counter-current multiplier mechanism
        - applies the single effect, which creates a static gradient, to a dynamic system where fluid is continually moving through the loop
        - Three steps (all happening at the same time, over and over again)
            - pump salt from filtrate to medulla
            - equilibrate water throughout the system
            - shift filtrate along the tube

FIGURE 5.16 Counter Current Multiplier Effect



- Like all other body tissues, the medulla requires a steady supply of oxygen and nutrients as well as a removal of waste products via capillary blood flow
    - countercurrent exchanger, which involves **vasa recta**, involves the need of the medulla to be met while avoiding disruption of the balance of solutes
    - The organization of the capillaries prevents the concentration gradient from disruption (random organization would mean that since the free flow of water and solutes is allowed in capillaries, the gradient would be destroyed)
        - hairpin loop structure, combined with slow blood flow
        - more concentrated at the bottom, less concentrated at the top

Storage and elimination: ureter, bladder, urethra

Osmoregulation: capillary reabsorption of **H2O, amino acids, glucose, ions**
- Juxtaglomerular apparatus monitors filtrate pressure in the distal tubule. *Cells secrete renin when pressure is too low*. Renin initiates a regulatory cascade that produces angiotensin I, II, and III, stimulating the adrenal cortex to secrete aldosterone.

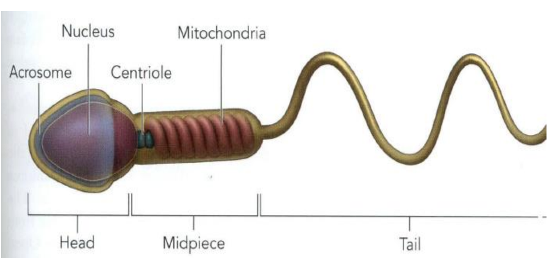
Muscular control: sphincter muscle

Reproductive System (BIO)
Male and female reproductive structures and their functions
Gonads
Genitalia
Differences between male and female structures
Hormonal control of reproduction

- Male and female sexual development
- Female reproductive cycle
- Pregnancy, **parturition** (childbirth), lactation
- Integration with nervous control

Reproduction and Development

- Male reproductive system
  - gonads (involved in the production of gametes) – testes
  - **Seminiferous tubules** – production of sperm
    - set of long, twisted tubes in the testes that are lined by **Sertoli cells** and **spermatogonia**
    - **Spermatogonia** in seminiferous tubules arise from epithelial tissue to become spermatocytes, spermatids, and then spermatozoa
    - **Sertoli cells**, stimulated by FSH, surround and nurture the spermatocyte and spermatids
    - **Leydig cells,** located in the interstitium between the tubules, release testosterone when stimulated by LH
      - **Testosterone is the primary androgen and stimulates germ cells to differentiate into sperm**
        - also responsible for the development of secondary sex characteristics
    - Sertoli cells also secrete inhibin, a peptide protein that acts on the pituitary gland to inhibit FSH



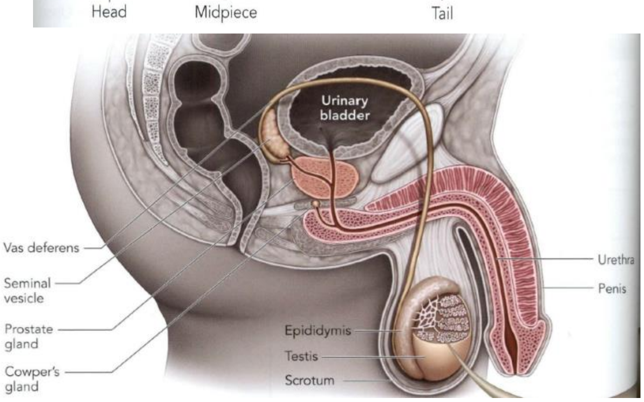
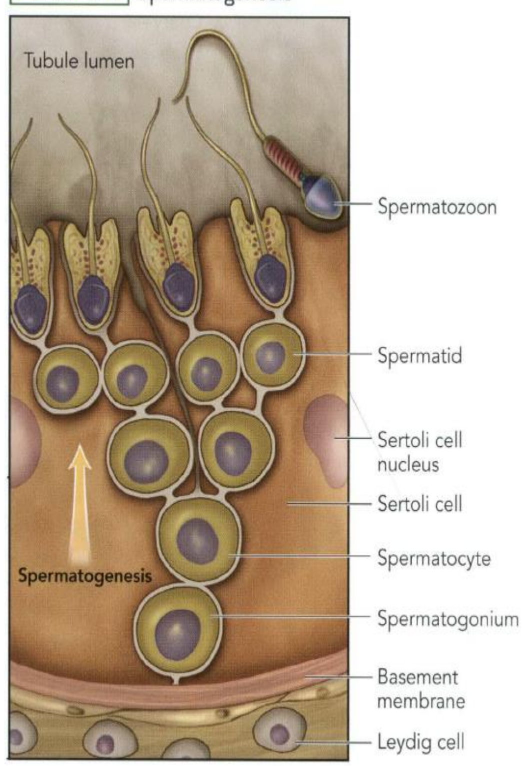
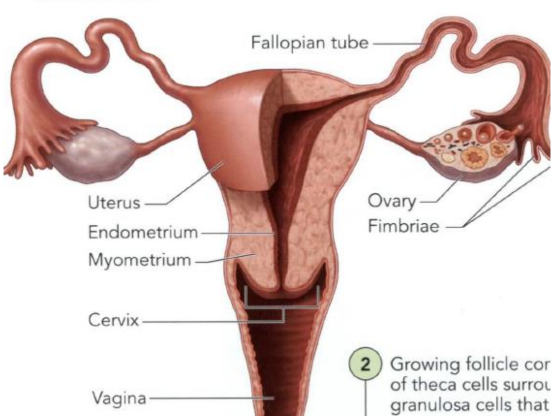


FIGURE 3.17 Spermatogenesis



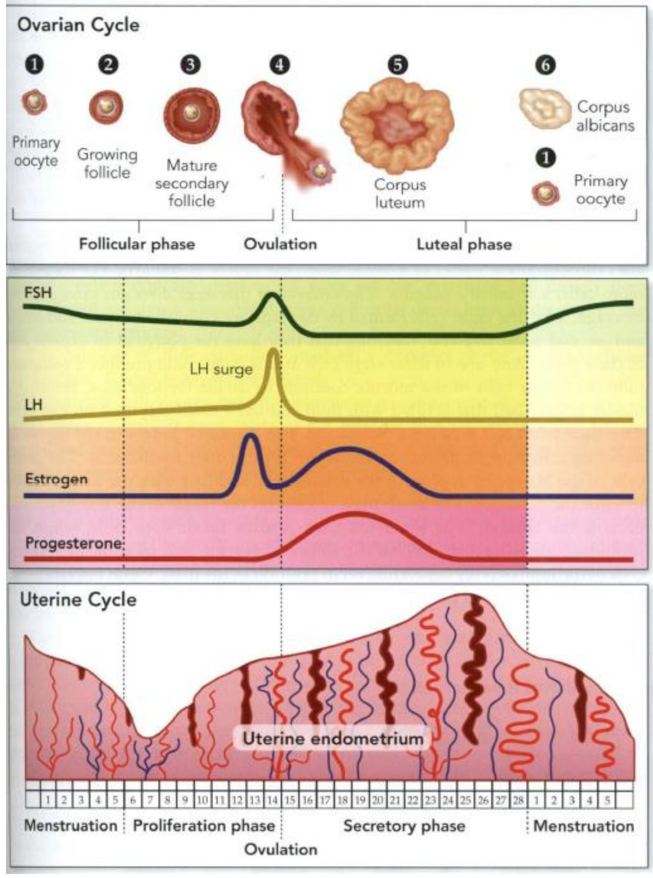
  - Spermatagonium – sperm stem cell before meiosis
  - Spermatocyte – once cell enters meiosis
  - Spermatid – After meiosis
  - Spermatozoon – mature sperm
    - acrosome contains *lysosome-like enzymes* for penetrating the egg during fertilization
    - midpiece contains many mitochondria to provide energy for tail
  - Path of spermatozoon

- *epididymis to mature and become motile*
    - upon ejaculation
        - spermatozoa are propelled through vas deferens into urethra and out of penis
  - Semen = complete mixture of spermatozoa and fluid that leaves penis
    - fluid from seminal vesicles, prostate, and bulbourethral glands
- Female Reproductive System



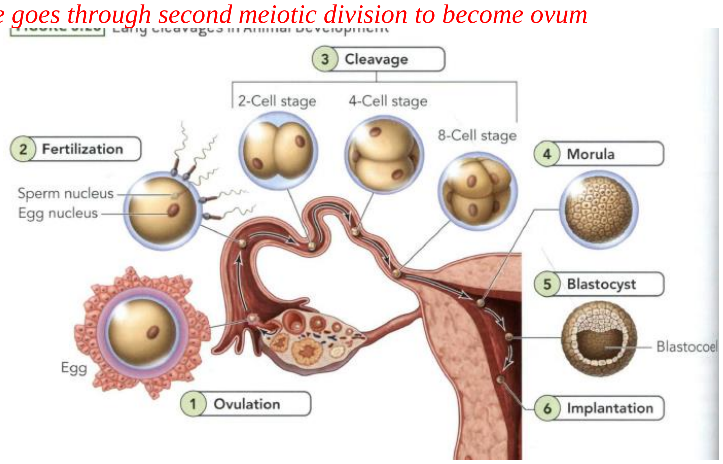
  - Cyclical
    - two cycles: one in ovaries and one in uterus
  - All of eggs of female are arrested as *primary oocytes, in prophase I of meiosis,* at birth
  - At puberty, ovarian cycle begins
    - FSH stimulates growth of granulosa cells around primary oocyte
      - granulosa cells secrete viscous substance around the egg called the **zona pellucida**
        - At this stage, it is called the **primary follicle**
      - Theca cells differentiate from interstitial tissue and grow around the follicle
        - **secondary follicle**
        - after stimulation by LH, theca cells secrete androgen, which is converted to **estradiol** (type of estrogen)
    - typically, estradiol inhibits LH secretion, but a dramatic rise in estradiol causes surge in LH
      - luteal surge – causes ovulation
        - release of secondary oocyte and corona radiata
          - corona radiata = zona pellucida and granulosa cells
        - Essentially, primary follicel
      - Egg swept into Fallopian tube
      - remaining portion of follicle = corpus luteum

FIGURE 3.19 The Menstrual Cycle



- As follicle matures and begins to release more estradiol, menstruation stops
- uterine wall enters the proliferation phase
  - building phase, lasts until ovulation
- After ovulation, the corpus luteum begins to secrete progesterone, which acts as a maintanence hormone for the uterus
- As the corpus luteum degrades into the **corpus albicans**, it is no longer able to secrete progesterone to maintain the uterine all
- uterine wall sloughs off and produces menstruation, starting new cycle

- Pregnancy and Embryology
  - Egg is swept toward uterus by cilia once in the Fallopian tube
  - Fertilization usually occurs in fallopian tubes
    - *Oocyte goes through second meiotic division to become ovum*



  - Cleavage begins while zygote is still in Fallopian tube
    - zygote goes through many cycles of mitosis
      - at 16 or more cells, is called a morula
    - the first eight cells are totipotent, meaning that they have the potential to express any of their genes
  - Cells of morula continue to divide, forming a blastocyst
    - mostly hollow ball filled with fluid and small cell mass on one side

- Blastocyst lodges in uterus – implantation
    - 7th day after fertilization
    - outer cells of blastocyst fuse with uterine tissue to form the placenta
    - small mass of cells on inside become the embryo
        - inner cell mass made up of stem cells
            - pluripotent
                - has the ability to develop into most of the types of cells in the human body
- Placenta begins secreting the peptide hormone HCG
    - prevents degeneration of the corpus luteum and maintains its secretion of estrogen and progesterone
        - HCG in blood and urine of the mother is the first outward sign of pregnancy
    - Placenta reaches full development by end of first trimester and begins secreting its own estrogen and progesterone while lowering its secretion of HCG
- Determination – cell becomes committed to specialized developmental path
- Differentiation – the specialization that occurs at the end of development
- skin, liver, and blood cells all have multipotent stem cells that can regenerate these systems as needed – "multipotent"
- Formation of gastrula in the third week after fertilization
    - primitive streak forms in mammals
    - three germ layers
        - ectoderm – epidermis of skin, nervous system, sense organs
        - Mesoderm – skeleton, muscles, blood vessels, heart, blood, gonads, kidneys, dermis of skin
        - Lining of digestive and respiratory tracts, liver, pancreas, thymus, thyroid
- Formation of Neurula in process called neurulation
    - through induction, the **notochord** (made from mesoderm) causes overlying ectoderm to thicken and form into **neural plate**
        - notochord eventually degenerates
    - **neural tube** forms from neural plate to become spinal cord, brain, and most of the nervous system
    - the cells of the ectoderm that are *close* to the neural tube are known as the **neural crest**
        - *cells of neural crest mostly form as accessory cells to nervous system (like Schwann cells)*
- Apoptosis and Senescence (process by which cells stop proliferating in response to environmental stressors and are ultimately cleared away by immune cells) also play role in development
- After ninth week of pregnancy, major organs develop
    - fetus
- After birth, motor development is from head to toe
    - progress starts with head, moves down to trunk, and moves down and out as limb movement is mastered
- Puberty – biological changes that ultimately lead to sexual maturity
- Adolescent development – psychosocial processes that accompany puberty

Muscle System (BIO)

Important functions

- Support: mobility
- Peripheral circulatory assistance
- Thermoregulation (shivering reflex)

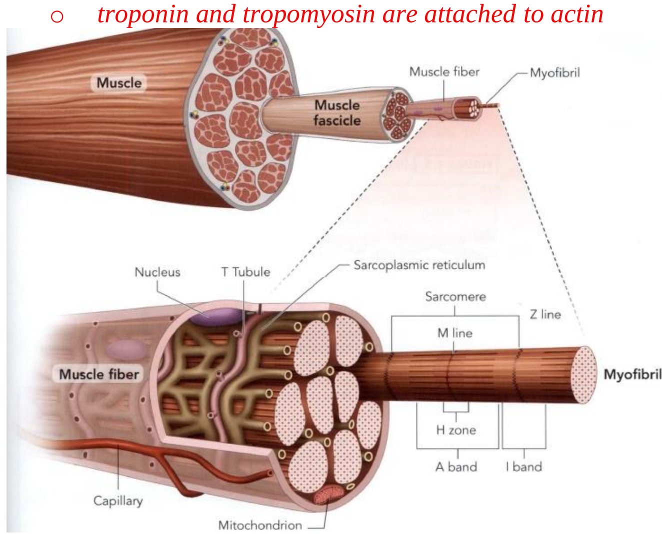
Muscle

- Three types: Skeletal, Cardiac, and Smooth
- Four functions: body movement, stabilization of body position, movement of substances through the body, and generating heat to maintain body temperature

Skeletal Muscle

- voluntary, innervated by somatic nervous system
- along with general movement, also involved in thermoregulation and the movement of fluids in the cardiovascular and lymphatic systems
- Muscle is attached to bone by tendon
    - connective tissue connecting bone to bone is called a ligament
- A muscle stretches across a joint in order to create movement at that joint when the muscle contracts
- origin of muscle is usually its attachment on the larger bone closer to the midpoint of the body
- Attachment at the other end of the muscle, known as its insertion, is on the smaller bone farther from the midpoint
- Muscles often work in groups
    - agonist – muscle whose contraction is primarily responsible for the movement

    - antagonist – stretches in response to the agonist's contraction and opposes the movement so that the motion is smooth and controlled
    - synergistic – assists the agonist by stabilizing the origin bone or by positioning the insertion bone during the movement
- another function: peripheral circulatory assistance – help squeeze blood and lymph through their respective vessels
- Thermoregulation – shivering reflex
- stores large amounts of glycogen
- Lever system
    - use more force to perform than if there were no lever at all
    - increases range and control of movement
- Muscle contraction
    - functional unit: Sarcomere
        - composed of many strands of two protein filaments
            - thick filaments made of myosin
            - thin filaments made of the globular protein actin
                - *troponin and tropomyosin are attached to actin*



Structure of three basic muscle types: striated, smooth, cardiac

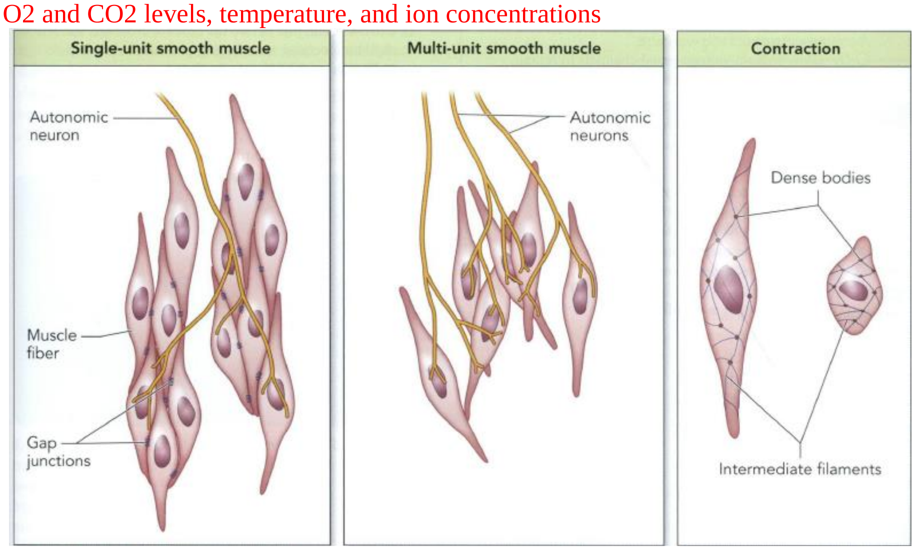
Cardiac muscle

- specialized, electrically-excitable tissue, permits the propagation of electrical signals that cause the heart to beat normally
- striated—composed of sarcomeres
- *contains only one nucleus*
- cells separated from each other by intercalated discs
    - contain gap junctions that allow an action potential to spread from one cardiac cell to the next via electrical synapses
- have large and numerous mitochondria to provide constant supply of ATP
- not connected to bone—forms a net that contracts in upon itself like a squeezing fist
- involuntary muscle
- sympathetic—increases heart rate, parasympathetic—decreases heart rate
- Action potential of cardiac muscle exhibits a plateau after depolarization
    - slow voltage-gated calcium channels—without this, the heart would beat way too fast
    - lengthens the time of contraction
    - repolarization is slower and more frequent than that of skeletal muscle
    - prevents sustained contraction---tetanus
- When left alone, the SA node has a frequency of self-excitation that is faster than a normal heartbeat
    - it is innervated by the vagus nerve, which decreases the heart rate

Smooth Muscle

- composes the muscular layer of internal organs and blood vessels
- contain only one nucleus, involuntary
- thick and thin filaments present, but are not organized into sarcomeres
- **contain intermediate filaments**, which are attached to dense bodies spread throughout the cell
    - thick and thin filaments attached to the intermediate filaments, and when they contract, they cause the intermediate filaments to pull the dense bodies together
- contraction—muscle cell shrinks length-wise

- Two types
  - single-unit
    - most common
    - connected by gap junctions that spread the action potential from a single neuron through a large group of cells, allowing the cells to contract as a single unit
    - electrical synapses via gap junctions in visceral muscle allow for faster signal transmission than would be possible with chemical synapses
    - found in small arteries, veins, stomach, intestine, uretus, and urinary bladder
  - multi-unit
    - each fiber is attached directly to a neuron
    - found in arteries, bronchioles, hair follicles, iris
- In addition to responding to neural signals, smooth muscle contracts or relaxes in the presence of hormones, or in response to changes in pH, O2 and CO2 levels, temperature, and ion concentrations



Muscle structure and control of contraction

- T-tubule system
- Contractile apparatus
- Sarcoplasmic reticulum
- Fiber type
- Contractile velocity of different muscle types
- Types of skeletal muscle:
  - type I: slow twitch
    - appear red because they contain large amounts of myoglobin
    - have large numbers of mitochondria
    - relatively slow contractile velocity, produce low amount of force
    - slow to fatigue and can be employed for long periods of time
    - aerobic
    - Will maybe have influx of lactate to use as a substrate for pyruvate
  - type II: Fast twitch
    - A: Fast oxidative
      - appear red
      - fast contractile velocity
      - resistance to fatigue, but not as resistant as Type I
      - long-term anaerobic
    - B: Fast glycolytic
      - have low myoglobin content and appear white
      - contract rapidly and are capable of generating great force, but they fatigue quickly
      - **contain large amounts of glycogen**
      - short-term anaerobic
  - most muscles in the body have a mixture of fiber types
  - the relative amounts of fiber types may influence a person’s natural aptitude for athletic activities

- Large amounts of type I in postural muscles, large amounts of type II A in upper legs, large amount of type II B in upper arms
- Adult human skeletal muscles do not usually undergo mitosis to create new muscle cells
  - number changes over time to meet the need for increased strength when the muscles are exposed to forceful, repetitive contractions
    - these changes include increased diameter of muscle fibers, *increased numbers of sarcomeres and mitochondria*, and lengthened sarcomeres
    - not more muscle fibers
-

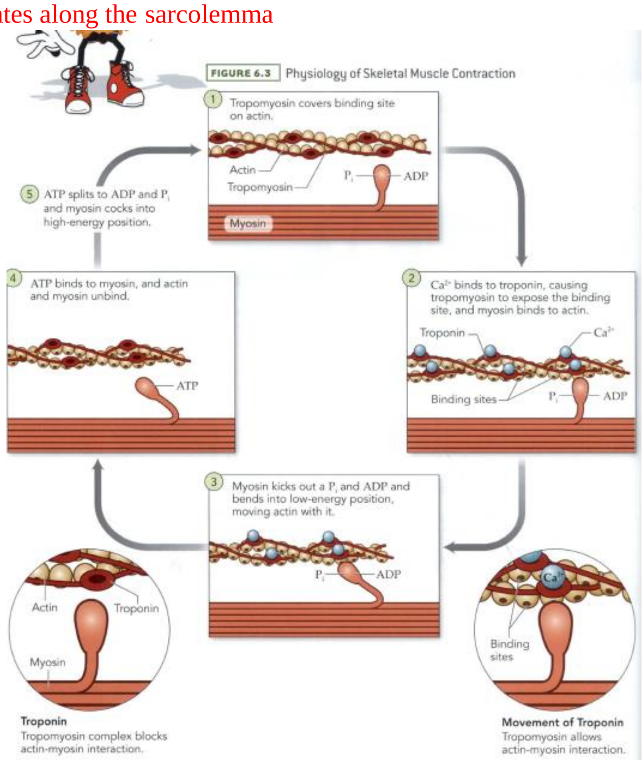
Regulation of cardiac muscle contraction

Oxygen debt: fatigue

- Limitations of Skeletal muscle
  - Fatigue—can result from nervous or metabolic causes
    - nervous—nerve can be temporarily unable to supply signals
    - metabolic fatigue—depletion of energy stores within the muscle
  - During strenuous exercise, the oxygen demands of metabolism exceed the body's supply of oxygen
    - under these conditions, muscles can switch from citric acid cycle and oxidative phosphorylation to anaerobic glycolysis to produce the necessary ATP
      - excess of lactic acid
    - Oxygen debt—the need for increased oxygen after exercise **in order to metabolize the excess lactic acid produced**

Nervous control

- Motor neurons
- Neuromuscular junction, motor end plates
- Sympathetic and parasympathetic innervation
- Voluntary and involuntary muscles
- Each myofibril is surrounded by sarcoplasmic reticulum
  - filled with calcium ions
- muscle cell contain many nuclei
- Contraction
  - motor neuron attaches to muscle cell at motor end plate
    - forms a neuromuscular junction
  - action potential releases **acetylcholine** into synaptic cleft
    - *activates ion channels in the sarcolemma* of muscle cell
      - creates an action potential that propagates along the sarcolemma
      - action potential moves deep into the muscle cell via *small infoldings of the sarcolemma called T-tubules*
    - action potentials transferred to the sarcoplasmic reticulum, causing voltage gated channels to open
    - releases Ca ions in sarcomere, allows myosin and actin fibers of the sarcomere to slide across each other



- Basically,
  - ADP + Pi: causes 90^o position
  - Ca^{2+} binds to troponin, which allows myosin to bind to actin
  - release of ADP and Pi: 45^o power stroke
  - ATP: release of actin
- Motor Units
  - muscle fibers do not contract all at once
  - between 2 and 2000 fibers are innervated by a single neuron---motor unit
  - Force depends on number and size of active motor units, as well as the frequency of action potentials in each neuron of the motor unit

    - Smaller motor units recruited first, larger ones recruited next
        - smooth increase in force

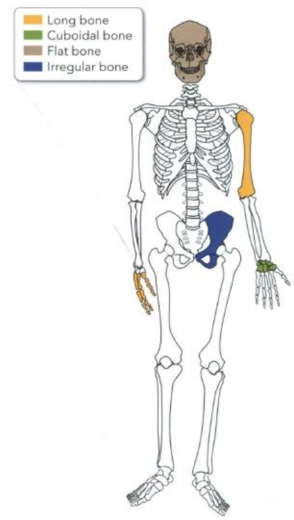
Skeletal System (BIO)

Functions

- Structural rigidity and support
- Calcium storage
- Physical protection

Skeletal structure

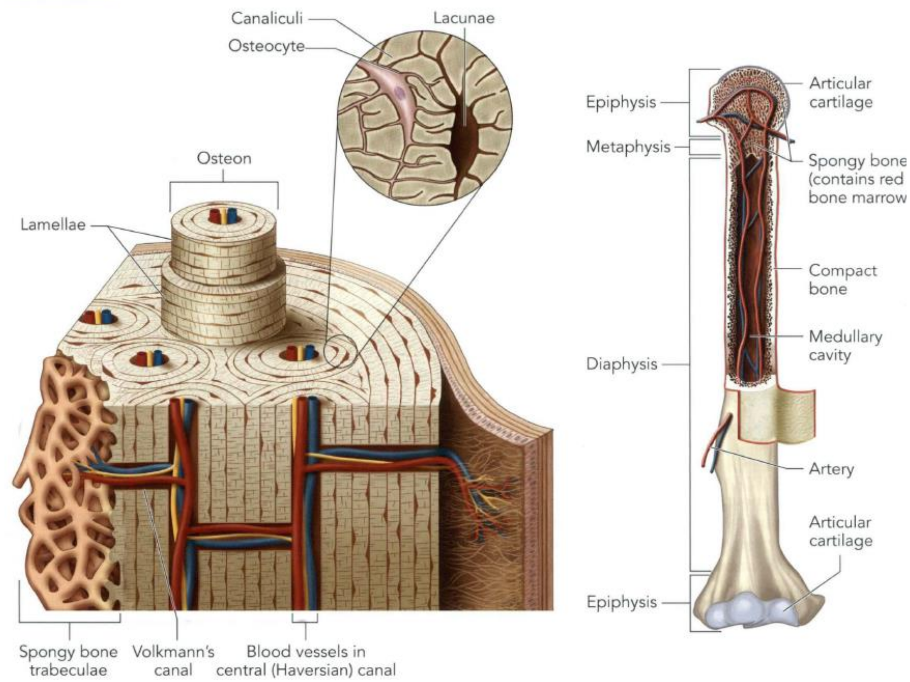
- Specialization of bone types, structures
- Bone Types and Structures



    - Long Bones – have shaft that is curved for strength
        - composed of compact and spongy bones
    - Short bones – cuboidal in shape
    - Flat bones – provide organ protection
    - Irregular bone – irregular shape
- Joint structures
- Joints
    - **fibrous**: occur between two bones held closely and tightly together by fibrous connective tissue, permitting extremely minimal movement
        - Ex: skull
    - **Cartilaginous joints** – also allow little movement, occur between two bones tightly connected by cartilage, such as ribs and sternum
    - **synovial joints** – most familiar as joints
        - not bound directly by cartilage, so wide movement is possible
        - separated by a capsule filled with **synovial fluid**
            - provides lubrication and nourishment, along with phagocytotic cells that remove microbes and particles
-
- Endoskeleton vs. exoskeleton

Bone structure

- **Calcium/protein** matrix
- Cellular composition of bone
- living tissue, one of the major types of connective tissue
- functions: support of soft tissue, protection of internal organs, assistance in body movement, mineral (calcium) storage, blood cell production, and energy storage in the form of adipose cells in bone marrow
- Bone tissue contains four types of cells surrounded by an extensive *calcium/protein* matrix composed of inorganic materials (most notably calcium) and proteins
    - **Osteoprogenitor** cells differentiate into osteoblasts
    - **Osteoblasts** secrete collagen and organic compounds upon which bone is formed
        - incapable of mitosis
        - as they release matrix materials around themselves, they become enveloped by the matrix and differentiate into osteocytes
    - **Osteocytes**, also incapable of mitosis, exchange nutrients and waste materials with the blood
    - **Osteoclasts** resorb bone matrix, releasing minerals back into the blood



- **Epiphyseal plate**—*sheet of cartilage between epiphysis and metaphysis,* where long bones grow in length when stimulated by growth hormone (GH) during childhood and adolescence
- Each bone contains two main types of bone structure: spongy bone and compact bone
  - typically consist of spongy bone on inside surrounded by a shell of compact bone
  - **spongy bone** (trabecular or cancellous bone) contains **red bone marrow**, the site of red blood cell development
  - **compact bone** (cortical bone) surrounds a hollow area inside the diaphysis known as the **medullary cavity**, which holds yellow bone marrow
    - yellow bone marrow contains adipose cells for fat storage
    - old parcels of bone continually replaced by new bone—remodeling
      - osteoclasts are followed by osteoblasts
      - lay down new bone matrix onto the tunnel walls
        - concentric rings called **lamellae**
        - leave open spaces in the center of the lamellae known as **Haversian canals**
        - allows for communication and nutrient exchange
      - **Haversian system** = lamellae and Haversian canals
        - contain blood and lymph vessels, and are connected by crossing canals called **Volkmann's canals**
        - Osteocytes trapped between lamellae exchange nutrients via spaces called **canaliculi**

Cartilage: structure and function

- Cartilage
  - flexible, resilient connective tissue
  - *composed of **collagen*** and has great tensile strength
  - Ex: ears
  - provides cushion, connection, and elasticity to the joints of the body
  - Three types: Hyaline, fibrocartilage, and elastic
    - hyaline – reduces friction and absorbs shock in joints, most common

Ligaments, tendons

- Ligament – fibrous connective tissue that attaches bone to bone
- Tendon – bone to muscle

Endocrine control

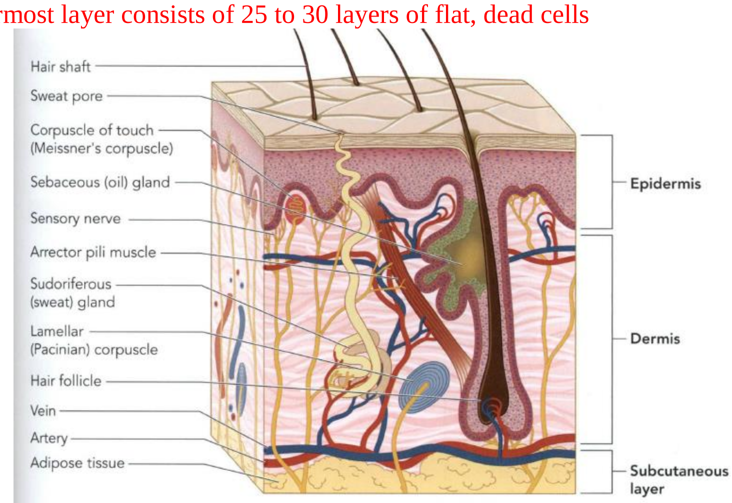
  - Remodeling of bone is subject to endocrine control
    - high levels of PTH signal osteoclasts to begin breaking down bone so that calcium can be released in the blood
- Bone's function in Mineral Homeostasis
  - Osteoblasts use calcium from the blood to form new osteon
  - osteoclasts break down bone and release calcium into bloodstream

- calcium salts are mostly insoluble
  - calcium in blood is mainly bound to proteins, and to a much lesser extent, by phosphates and other anions
- Too much Ca^{2+} causes membranes to become hyper-excitable, leading to fatigue and memory loss
- too little results in cramps and convulsions
- Most of Ca^{2+} is stored in the bone matrix as the mineral **hydroxyapatite**, which contributes to the strength of bones
- Collagen fibers give bone great **tensile** strength
- hydroxyapatite crystals lie alongside collagen fibers, giving bone great compressive strength
- Some Ca^{2+}

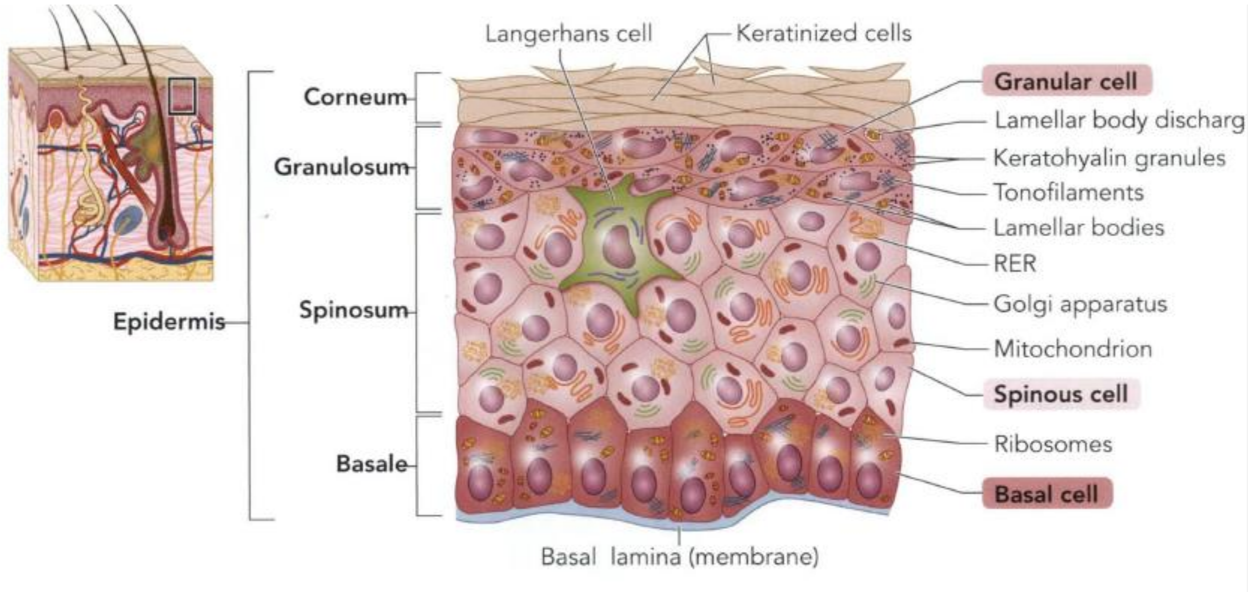
Skin System (BIO)

Structure

- Layer differentiation, cell types
- Skin has two principal parts – superficial epidermis, and the deeper dermis
  - beneath both of these layers is a subcutaneous tissue called the superficial fascia or hypodermis
    - this subcutaneous fat layer is an important heat insulator for the body
  - epidermis is avascular (no blood vessels) epithelial tissue, which primarily serves the purpose of protection from the environment
  - Four major cell types:
    - keratinocytes – compose 90% of the epidermis
      - produce keratin, which helps waterproof the skin
    - melanocytes transfer melatin (skin pigment) to keratinocytes
    - Langerhans cells interact with the helper T-cells of the immune system
    - **Merkel cells** attach to sensory neurons and function in the sensation of touch
  - deepest layer of epidermis contains Merkel cells and stem cells
    - stem cells continually divide to give rise to keratinocytes and other new replacement skin cells
    - as they rise, they accumulate keratin and die, losing their cytoplasm, nucleus, and other organelles
    - when they reach the outermost layer of skin, they shed off
    - outermost layer consists of 25 to 30 layers of flat, dead cells



  - Dermis is a connective tissue derived from mesodermal cells
    - serves a variety of functions and is embedded with *blood vessels, nerves, glands, and hair follicles*
    - collagen and elastic fibers in the dermis provide skin with strength, extensibility, and elasticity
    - the receptors that transmit the sensation of touch, including separate receptors for the sensations of pressure, pain, and temperature, are located here
    - hair follicles also present
      - **hair is a column of keratinized cells held tightly together**
    - also contains a wide variety of glands
      - sebaceous (oil) glands
      - when contracted, smooth muscle erectile musculature associated with each hair stands the hair up
      - two types of sweat glands are found in the skin separate from hair follicles
        - eccrine sweat glands – found over the entire surface of the skin and produce sweat in response to heat
        - apocrine sweat glands are congregated in certain regions of the dermis and produce acrid-smelling sweat in response to sweat



- CGSB
- cornea is the outside layer of the eye as well
- Relative impermeability to water
  - osmoregulation – skin is relatively impermeable to water, protecting against dehydration
    - water can be lost through sweating and excretion

Functions in homeostasis and osmoregulation
Functions in thermoregulation

- Functions:
  - Thermoregulation – skin helps to regulate body temperature
    - blood conducts heat from core of the body to skin
    - most of this heat is dissipated by radiation
      - only effective if the body temperature is higher than room temperature
      - more blood can be directed to surface capillaries through vasodilation to allow for greater heat loss, or blood can be shunted away from capillaries through vasoconstriction to reduce heat loss
    - sweating

- Hair, erectile musculature
- Fat layer for insulation
- **Sweat glands, location in dermis**
- Vasoconstriction and vasodilation in surface capillaries

Physical protection

- Nails, calluses, hair
- Protection against abrasion, disease

Hormonal control: sweating, vasodilation, and vasoconstriction

CHEMICAL AND PHYSICAL FOUNDATIONS OF BIOLOGICAL SYSTEMS
Foundational Concept 4
Content Category 4A: Translational motion, forces, work, energy, and equilibrium in living systems

Translational Motion (PHY)
Units and dimensions
Vectors, components
Remember that displacement magnitude vector may be the same, but displacement is not the same if they point in different directions
Vector addition

Speed, velocity (average and instantaneous)
Acceleration

The Kinematic Equations

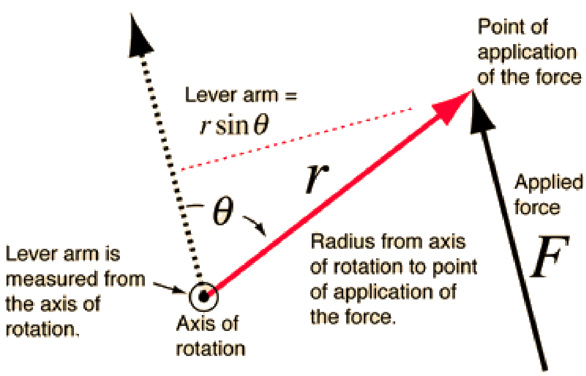
$$d = v_i{*}t + \frac{1}{2}{*}a{*}t^2 \qquad v_f^2 = v_i^2 + 2{*}a{*}d$$

$$v_f = v_i + a{*}t \qquad d = \frac{v_i + v_f}{2}{*}t$$

Force (PHY)
Newton’s First Law, inertia
Newton’s Second Law (F = ma)
Newton’s Third Law, forces equal and opposite
Friction, static and kinetic
Center of mass (Weighted Avg, dividing by mass)

Equilibrium (PHY
A system in equilibrium = net translational force and net torque is zero
Vector analysis of forces acting on a point object
Torques, lever arms

$$\text{torque} = \tau = rF\sin\theta$$



Work (PHY)
Work done by a constant force: W = Fd cosθ
Mechanical advantage
MA = Output force / input force = input arm distance / output arm distance
For pulleys, count the number of ropes (not including the rope you’re pulling on)
- It does not matter what direction you pull that rope you’re pulling on, it’s going to be the same force.

Work Kinetic Energy Theorem
- Relation bewteen KE and W: The work done on an object by a net force equals the change in kinetic energy of the object: W = KEf - KEi. This relationship is called the work-energy theorem.

Conservative forces
- A **conservative force** is a **force** with the property that the total work done in moving a particle between two points is independent of the taken path. ... When an object moves from one location to another, the **force** changes the potential energy of the object by an amount that does not depend on the path taken.

Energy of Point Object Systems (PHY)
Kinetic Energy: KE = ½ mv2 ; units
Potential Energy
- PE = mgh (gravitational, local)
- PE = ½ kx2 (spring)

Conservation of energy

- In physics, the law of **conservation** of energy states that the total energy of an isolated system remains **constant** — it is said to be conserved over time. In other words, this law means that energy can neither be created nor destroyed; rather, it can**only** be transformed from one form to another.

Power, units

$$\text{Power} = \frac{\text{Work}}{\text{Time}} = \frac{\text{Force} \cdot \text{Displacement}}{\text{Time}}$$

$$\text{Power} = \text{Force} \cdot \frac{\text{Displacement}}{\text{Time}}$$

$$\boxed{\text{Power} = \text{Force} \cdot \text{Velocity}}$$

-

Periodic Motion (PHY)

Amplitude, frequency, phase

- The total energy for oscillation on a spring is:
  - $E = ½ mv^2 + ½ kx^2$
  - Total energy is also equal to $½ kA^2 = ½ mv^2$
  - Thus, we have a way to relate amplitude with velocity (granted that we know the spring constant and mass of the object
    - $V_{max} = (k/m)^{1/2}A = 2\pi Af$
- Period does not depend on Amplitude
  - $T = 2\pi (m/k)^{1/2}$
  - $f = 1/2\pi (k/m)^{1/2}$
- The simple Pendulum
  - $k = mg/l$
  - $T = 2\pi (m/k)^{1/2} = 2\pi (l/g)^{1/2}$

Transverse and longitudinal waves: wavelength and propagation speed

- Transverse waves – medium is displaced perpendicular to direction of wave propagation
  - Light waves – alternating electric and magnetic waves – do not require medium
- Longitudinal waves – medium is displaced parallel to direction of wave propagation
  - Sound waves – transfer of energy as oscillations between high and low pressure
- Note the frequency does not change from medium to medium
  - the velocity (and wavelength) is determined by the medium
  - Assuming temperature is constant, two characteristics determine the velocity of a wave:
    - Elasticity – resistance to shape
    - Inertia – resistance to change in motion
    - $V = (B / p)^{1/2}$
      - B = bulk modulus (elasticity)
      - p = density (measure of inertia
        - elasticity increases as intermolecular forces increase
        - Inertia increases as mass and density increase
    - $V_{solid} > V_{liquid} > V_{gas}$

Content Category 4B: Importance of fluids for circulation of blood, gas movement, and gas exchange

Fluids (PHY)

Density, specific gravity

- $p = m / v$
- Specific gravity = $P_{substance} / P_{water}$

Buoyancy, Archimedes' Principle

- $F_b = pVg$
  - It's difference in force, which is equal to pressure x area
  - $P = pgh$
    - $pgh \times A = pghA = pVg$
- Archimedes principle: $F_b = m_{fluid}g$

- Fraction **submerged**
    - $\rho_{object} / \rho_{fluid} = v_{fluid} / v_{object}$
- Apparent weight:
    - F_N (weight) = $F_g - F_{buoyant}$
    - Apparent weight loss shortcut:
        - P_{fluid} / P_{object} x 100 (percent lost)
- Brick on Styrofoam
- Archimedes' principle also states that the ratio of the density of an object to the density of the fluid it's submerged in is equal to the ratio of

Hydrostatic pressure

- Pascal's Law
- $F_1 / A_1 = F_2 / A_2$
    - The greater the force, the greater the area, and the less the distance
- Hydrostatic pressure; $P = \rho g h$ (pressure vs. depth)

Viscosity: Poiseuille Flow

Q	Flow rate
P	Pressure
r	Radius
η	Fluid viscosity
l	Length of tubing

- $$Q = \frac{\pi P r^4}{8 \eta l}$$

Continuity equation (A·v = constant)

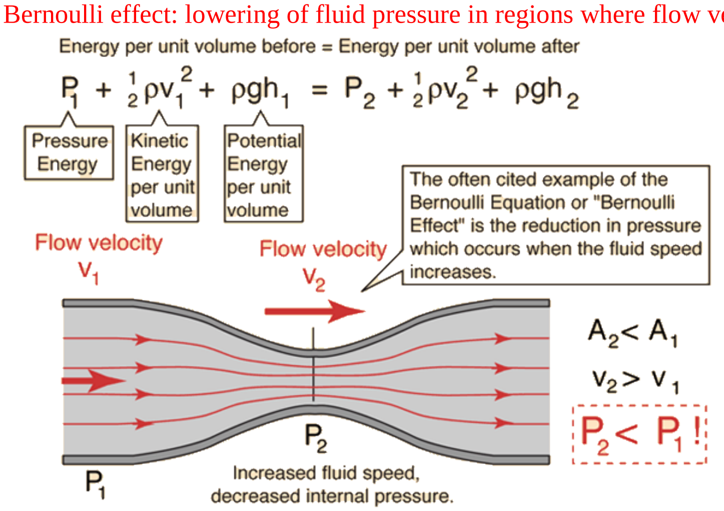
- Mass flow rate I = pQ
    - conserved in flow through a tube
- Volume flow rate Q is always constant for an ideal fluid (in space, not time)
    - pQ = pAv
    - since density p usually doesn't change,
    - $A_1 v_1 = A_2 v_2$

Concept of turbulence at high velocities

Surface tension

Bernoulli's equation

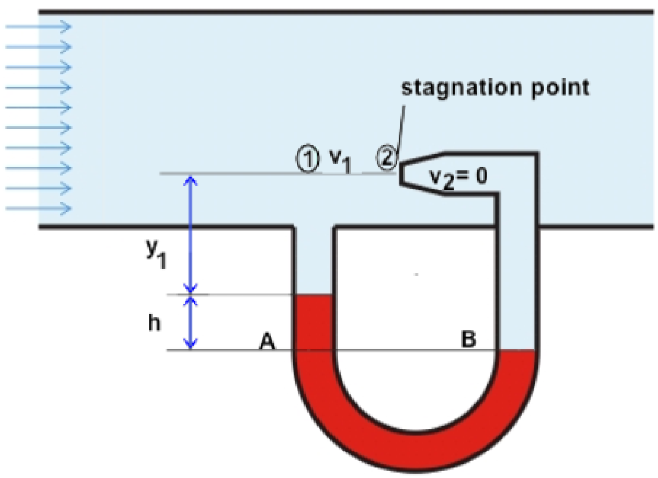
- Conservation of energy in fluids
- Bernoulli effect: lowering of fluid pressure in regions where flow velocity is increased



- Bernoulli's = a decrease in velocity must be accompanied by an increase in pressure, since a lower velocity fluid has less uniform translational motion and more random translational motion, which contributes to pressure

Venturi effect, pitot tube

- The **Venturi effect** is the reduction in fluid pressure that results when a fluid flows through a constricted section (or choke) of a pipe. The **Venturi effect** is named after Giovanni Battista **Venturi** (1746–1822), an Italian physicist.
- Pitot Tube
  - p' – density of manometer fluid
  - used to measure v (first used to measure velocity of Seine River)



$$P_1 + \frac{1}{2}\rho v_1^2 = P_2$$
$$\text{now } P_A = P_1 + \rho g y_1 + \rho' g h$$
$$P_B = P_2 + \rho g(y_1 + h)$$
$$\text{but } P_A = P_B, \text{ so}$$
$$P_2 - P_1 = \rho' g h - \rho g h$$
$$v_1 = \sqrt{2gh\left(\frac{\rho'}{\rho} - 1\right)}$$
$$\approx \sqrt{2gh\left(\frac{\rho'}{\rho}\right)}$$

-

Circulatory System (BIO)

Arterial and venous systems; pressure and flow characteristics

https://courses.lumenlearning.com/ap2/chapter/blood-flow-blood-pressure-and-resistance-no-content/

Gas Phase (GC, PHY)

Absolute temperature, (K) Kelvin Scale

Pressure, simple mercury barometer

- Mercury barometer
  - $P_{atm} = \rho gh$
    - P = atmospheric pressure
    - ρ = density of mercury in kg/m^3
    - g = 9.8 m/s/s/
    - h = height of the column
  - atm = 760 mmHg

Molar volume at 0°C and 1 atm = 22.4 L/mol

Ideal gas

- Definition

Kinetic Molecular Theory

- model if ideal gas
  - Gas molecules have no size
  - Gas molecules do not exert forces on one another
  - Gas molecules have completely elastic collisions
  - Average kinetic energy of gas molecules is directly proportional to the temperature of the gas
- Obeys ideal gas law:
  - PV = nRT
    - R = universal gas constant (0.08206 L atm K^{-1} mol^{-1})
      - or 8.314 J K^{-1} mol^{-1}
- Ideal Gas Law: PV = nRT
- Boyle's Law: PV = constant

If an MCAT® question told you to assume that a gas was in a balloon at an external pressure of 1 atm, it might seem like an unfounded assumption to say that the gas would also be at 1 atm inside the balloon. But, since the internal pressure of a flexible container must be equal to the external pressure, it is a valid assumption to make. For a rigid

- Charles' Law: V/T = constant
- Avogadro's Law: V/n = constant

Kinetic Molecular Theory of Gases

- Heat capacity at constant volume and at constant pressure (PHY)
- Heat Capacity
    - Added energy required to increase temperature of a given substance by 1 K
    - differs per substance
    - $C = q / \Delta T$
- Two heat capacities for any substance
    - C_v – constant volume heat capacity
        - no work, all energy change must be in the form of heat
        - none of the energy going into the system can escape as work done by the system
    - C_p – constant pressure heat capacity
        - some of the energy can leave the system as PV work done by the surroundings as the volume changes
- Thus, at constant pressure, a substance can absorb energy with less change in temperature by expelling some of the energy to the surroundings as work
    - $C_p > C_v$
    - However, this difference is only significant for molecules in the gas phase
        - liquids and solids are fairly resistant to changes in volume
- Large molecules tend to have higher heat capacities than those of smaller molecules
    - not all of the energy goes into increasing temperature of compound
        - can go into bond stretching
- Water has a higher heat capacity because of its strong intermolecular bonds
    - hydrogen bonds must first be broken for kinetic energy (and therefore temperature) to increase
- Heat capacity will always be positive
- 1 cal = 4.184 J
    - approximately equal to the amount of energy needed to raise one gram of water by one degree Celsius
    - 1 Cal = 4184 J
- Specific heat capacity – intrinsic proprety that represent the heat capacity per unit mass
    - $q = mc\Delta T$
- Boltzmann's Constant (PHY)

Temperature

- Represents the amount of molecular movement in a substance
    - translational, rotational, and vibrational energies
        - sum of these energies = thermal energy
            - increase in thermal energy increases temperature
            - temperature = thermal energy per mole o molecules
- $KE_{\text{zvg per mole of molecules}} = (3/2)\ RT$ (For an ideal gas, only temperature determines kinetic energy0
    - $KE_{\text{avg per molecule}} = 3/2\ kt$
        - k = Boltzmann's constant (1.38×10^{-23} J/K)
            - $R = N_A k$ (where N_A = avogadro's number)
- For an ideal gas, the volume vs temperature graph is exactly linear for any given pressure
- Kelvin is absolute, but Celsius is relative
-

Deviation of real gas behavior from Ideal Gas Law

- Qualitative
- Quantitative (Van der Waals' Equation)

Real Gases

- Deviate from ideal behavior when their molecules are close together, which occurs at high pressures and low temperatures
- Deviation from ideal behavior can be expressed quantitatively by Van der Waals' equation:

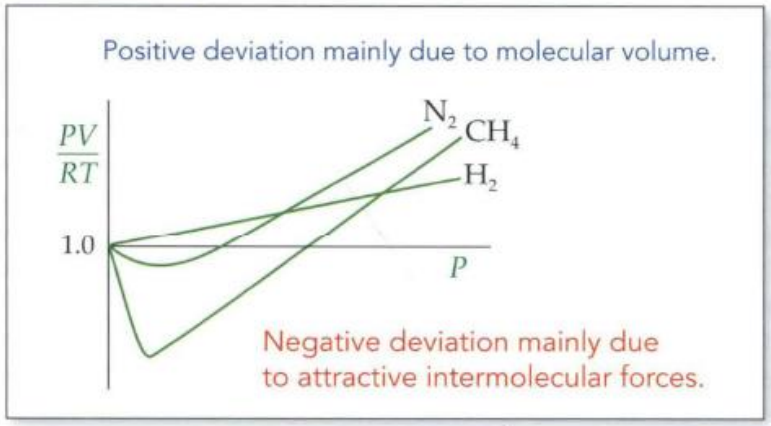
$$\left[P + \left(\frac{n^2 a}{V^2}\right)\right](V - nb) = nRT$$

- approximates real pressure and real volume of a gas
    - a and b are constants for specific gases
        - b accounts for actual volume occupied by a mole of gas
        - a reflects the strength of intermolecular attractions
    - a and b generally increase with the molecular mass and complexity of a gas

- In summary, $V_{real} > V_{ideal}$ and $P_{real} < P_{ideal}$
    - Therefore, accounting for the size of the molecule tends to increase the overall volume of the container
    - Accounting for intermolecular forces will tend to decrease the overall pressure

From PV = nRT, we expect PV/RT to equal one for one mole of an ideal gas at any temperature and pressure. Since volume deviates positively from ideal behavior and pressure deviates negatively, if PV/RT is greater than one for one mole of a real gas, the deviation due to molecular volume must be greater than the deviation due to the intermolecular forces. If PV/RT is less than one for one mole of a real gas, then the deviation due to intermolecular forces must be greater than the deviation due to molecular volume.

FIGURE 5.9 Deviations from Ideal Gas Law



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Partial pressure, mole fraction

Dalton's Law relating partial pressure to composition

- Partial Pressure – total pressure of gaseous mixture multiplied by mole fraction of the particular gas
    - $P_a = x_a P_{total}$
- Dalton's Law: total pressure exerted by a gaseous mixture is the sum of the partial pressures of each of its gases
    - $P_{total} = P_1 + P_2 + P_3$ ….

Partial Pressure Equilibrium Constant

- For reactions involving gases, the equilibrium constant can be written in terms of partial pressures instead of concentrations
- For aA + bB → cC + dD

$$K_p = \frac{P_C^c P_D^d}{P_A^a P_B^b} = \frac{products^{coefficients}}{reactants^{coefficients}}$$

- Concentration equilibrium constant (K_c) and partial pressure equilibrium constant (K_p) of same reaction are related by:

$$K_p = K_c(RT)^{\Delta n}$$

    - Δn = sum of the coefficients of the products minus the sum of the coefficients of the reactants

Content Catory 4C: Electrochemistry and electrical circuits and their elements

Electrostatics (PHY)

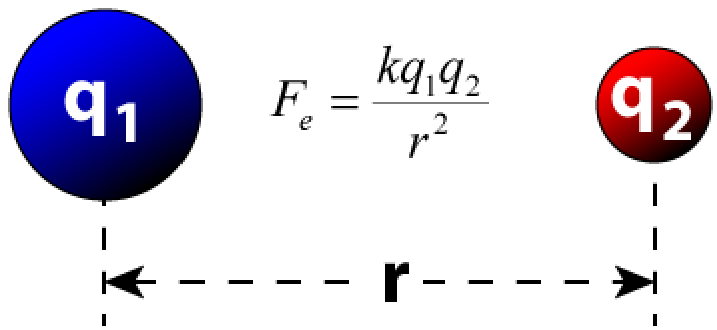
Charge, conductors, charge conservation

In physics, **charge conservation** is the principle that electric charge can neither be created nor destroyed. The net quantity of electric charge, the amount of positive charge minus the amount of negative charge in the universe, is always *conserved*.

Insulators

In a **conductor**, electric current can flow freely, in an**insulator** it cannot. Metals such as copper typify**conductors**, while most non-metallic solids are said to be good **insulators**, having extremely high resistance to the flow of charge through them.

Coulomb's Law



$$F_e = \frac{kq_1q_2}{r^2}$$

Electric field E

F=qE

- Field lines
- Field due to charge distribution

Electrostatic energy, electric potential at a point in space

- Electric Potential Energy
  - $U = qEd = kq_1q_2 / r$
- Electric potential: $V = Ed = kq_1 / r$
  - units: Volts (J/C)
- Electric field is a general way to talk about force (force per unit charge)
- Voltage is a general way to talk about Energy – energy per unit charge

Circuit Elements (PHY)

Current $I = \Delta Q/\Delta t$, sign conventions, units

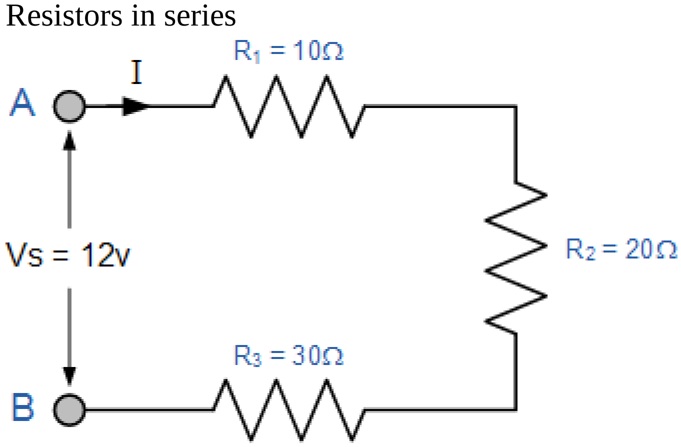
- $I = V / R$
- Units: Amps: Coulomb / sec
- direction of positive flow
- $P = IV = V^2 / R$ – the less resistance, the more current and the more power

Electromotive force, voltage

- electromotive force – difference in potential that tends to give rise to an electric current

Resistance

- Ohm's Law: I = V/R
- Resistors in series



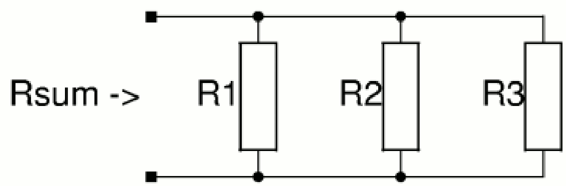
$$R_{total} = R_1 + R_2 + R_3$$

$$R_{total} = 3\ k\Omega + 10\ k\Omega + 5\ k\Omega$$

$$R_{total} = 18\ k\Omega$$

- Resistors in parallel

Parallel resistors



$$\frac{1}{Rsum} = \frac{1}{R1} + \frac{1}{R2} + \frac{1}{R3}$$

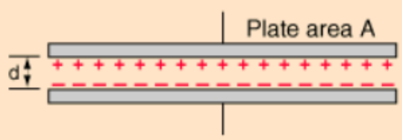
-
- Resistivity: ρ = R•L / A
  - Units: Ohm

Capacitance

- Capacitance – ability of a body to store an electric charge
  - A material with a large self-capacitance holds more electric charge at a given voltage
- Capacitance is a function only of the geometry of the design and the permittivity of the dielectric material between the plates of the capacitor
- SI unit is the farad (C/V)
- C = Q / V

Parallel plate capacitor

Parallel Plate Capacitor



$$C = \frac{\varepsilon A}{d} = \frac{k\varepsilon_0 A}{d}$$ Show

The capacitance of flat, parallel metallic plates of area **A** and separation **d** is given by the expression above where:

$\varepsilon_0 = 8.854 \ x \ 10^{-12} \ F/m$ = permittivity of space and

k = relative permittivity of the dielectric material between the plates.

k=1 for free space, k>1 for all media, approximately =1 for air.

Energy of charged capacitor

- Energy stored by a capacitor
- U = ½ QV = ½ CV^2 = ½ Q^2 / C
- Once a capacitor is fully charged, it is like a break in the circuit
- Some other notes:
  - electric field inside a capacitor is constant
  - increasing voltage across a capacitance increases amount of charge on a capacitor, but not its capacitance

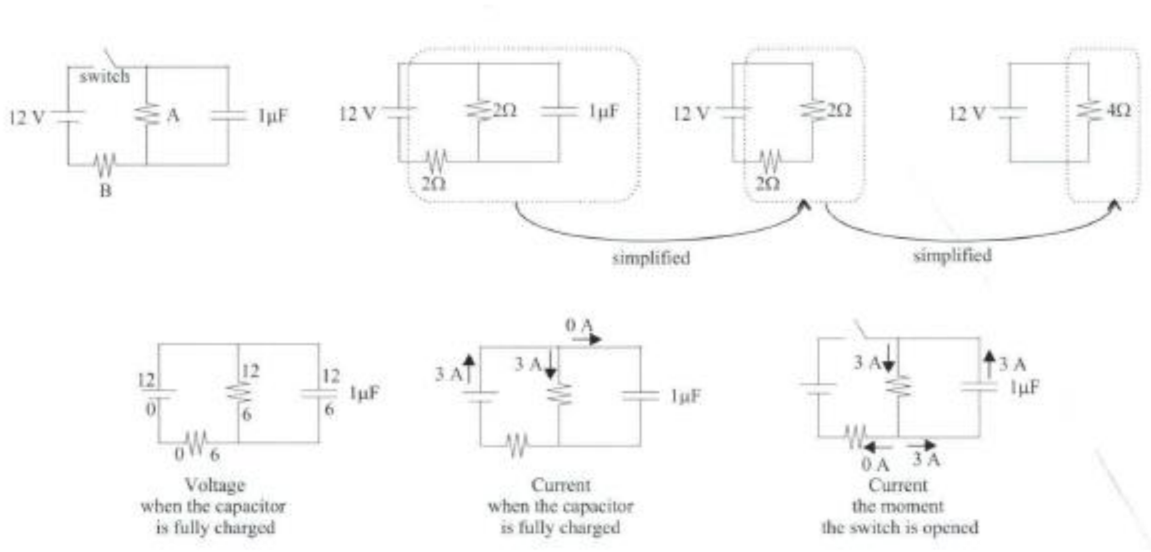
Capacitors in series

Series Capacitances

$$C_{total} = \frac{1}{\frac{1}{C_1} + \frac{1}{C_2} + \ldots \frac{1}{C_n}}$$

Capacitors in parallel

$$C_{Total} = C_1 + C_2 + C_3$$



Another detail on capacitors. The voltage drop is the same concept as dropping over a resistance. When using C = Q / V, for V, use the voltage drop over the capacitance (which can be different from battery voltage if there are resistors in series)

Dielectrics

quantity measuring the ability of a substance to store electrical energy in an electric field (k)

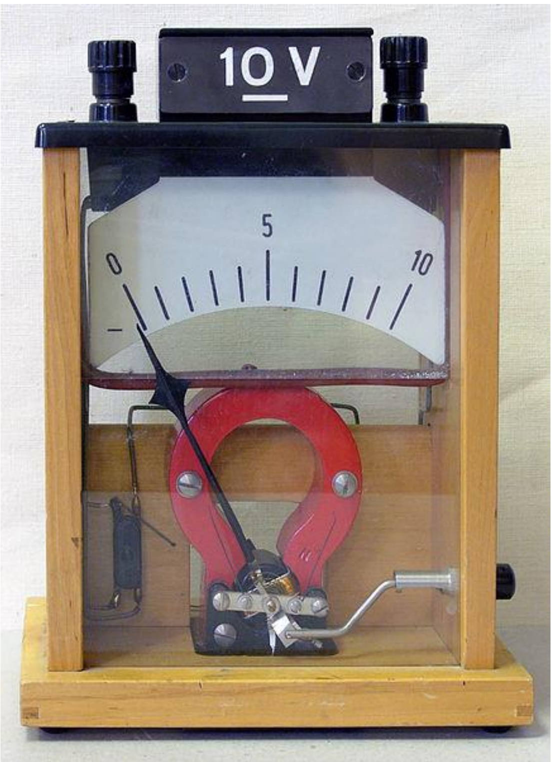
Conductivity

Metallic Electrolytic

Meters

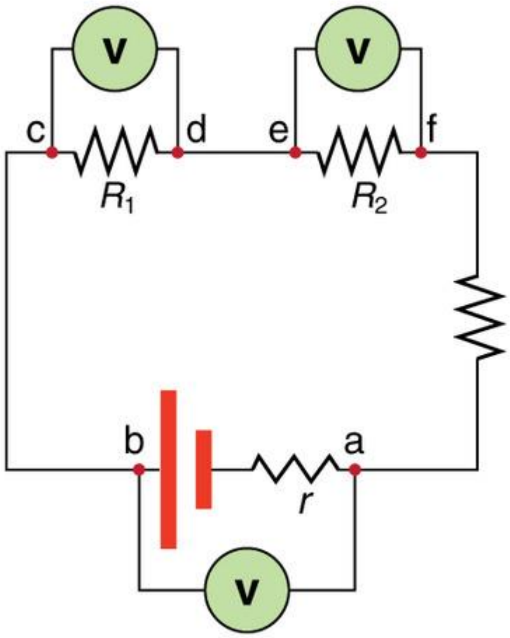
Voltmeters

A voltmeter is an instrument that measures the difference in electrical potential between two points in an electric circuit. An analog voltmeter moves a pointer across a scale in proportion to the circuit's voltage; a digital voltmeter provides a numerical display. Any measurement that can be converted to voltage can be displayed on a meter that is properly calibrated; such measurements include pressure, temperature, and flow.



Voltmeter: Demonstration voltmeter from a physics class

In order for a voltmeter to measure a device's voltage, it must be connected in parallel to that device. This is necessary because objects in parallel experience the same potential difference.



(a)

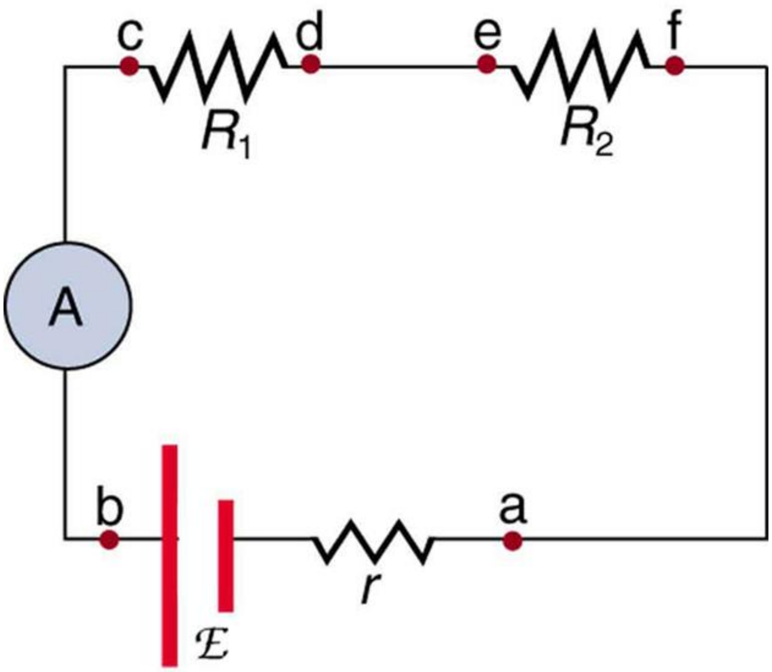
(b)

Voltmeter in Parallel: (a) To measure the potential difference in this series circuit, the voltmeter (V) is placed in parallel with the voltage source or either of the resistors. Note that terminal voltage is measured between points a and b. It is not possible to connect the voltmeter directly across the EMF without including its internal resistance, r. (b) A digital voltmeter in use

Ammeters

An ammeter measures the electric current in a circuit. The name is derived from the name for the SI unit for electric current, amperes (A).

In order for an ammeter to measure a device's current, it must be connected in series to that device. This is necessary because objects in series experience the same current. They must not be connected to a voltage source — ammeters are designed to work under a minimal burden, (which refers to the voltage drop across the ammeter, typically a small fraction of a volt).



Ammeter in Series: An ammeter (A) is placed in series to measure current. All of the current in this circuit flows through the meter. The ammeter would have the same reading if located between points d and e or between points f and a, as it does in the position shown. (Note that the script capital E stands for EMF, and r stands for the internal resistance of the source of potential difference.)

Some notes on Electric Circuits:

- Kirchoff's Rules
  - Loop rule: Voltage sum in a loop is zero
  - Junction Rule – current entering a loop = current leaving a loop
    - implications:
      - Series: same current, different voltage, increased resistance, large resistors drain more power
        - $P = I^2R$
      - Parallel: Same voltage, different current, increased capacitance, smaller resistors drain more power
        - $P = V^2 / R$
- Voltage always remains constant – voltage is not affected by changes in the current
  - only current and resistance changes

Magnetism (PHY)

Definition of magnetic field B

Motion of charged particles in magnetic fields; Lorentz force

Electrochemistry (GC)

Electrolytic cell

- Electrolysis
- Anode, cathode
- Electrolyte

electrolyte

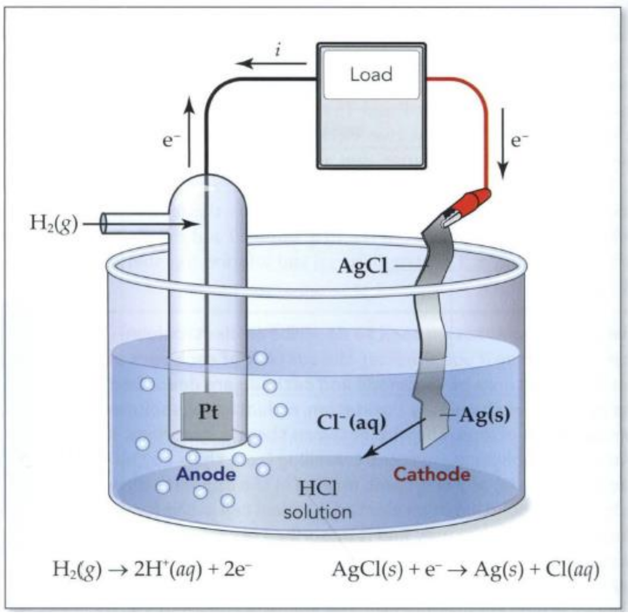
- Ions = electrolyte.
- Electrolytes conduct electricity by the motion of ions.
- Without electrolytes, there won't be a circuit because electricity won't be able to travel.
- Faraday's Law relating amount of elements deposited (or gas liberated) at an electrode to current
- Faraday's constant = coulombs of charge per mol of electron = total charge over total mols of electrons. $F = {}^{q}/_{n}$.
  - 96485 C / mol e-

- $It = nF$
- Current x time = mols of e⁻ x Faraday's constant.
- Electron flow; oxidation, and reduction at the electrodes

Electrochemical Cells

- Galvanic Cells
  - Two electrodes: anode and cathode
    - the **anode is marked with a negative sign** and the cathode is marked with a positive sign
    - oxidation takes place at anode, reduction takes place at cathode
      - ANOX, RED CAT
  - Cell potential (electromotive force) – potential difference between the terminals when they are not connected
    - connecting the terminals reduces the potential difference due to internal resistance within the galvanic cell
  - Electrons flow from the anode to the cathode
    - reduction occurs at the cathode
  - Current flow is opposite to electron flow
    - current flows from cathode to anode
- Standard state cell potential = sum of standard state potentials of the corresponding half reactions
  - cell potential for a galvanic cell is always positive; has chemical energy that can be converted to work

FIGURE 6.9 Galvanic Cell with Standard Hydrogen Electrode (SHE)



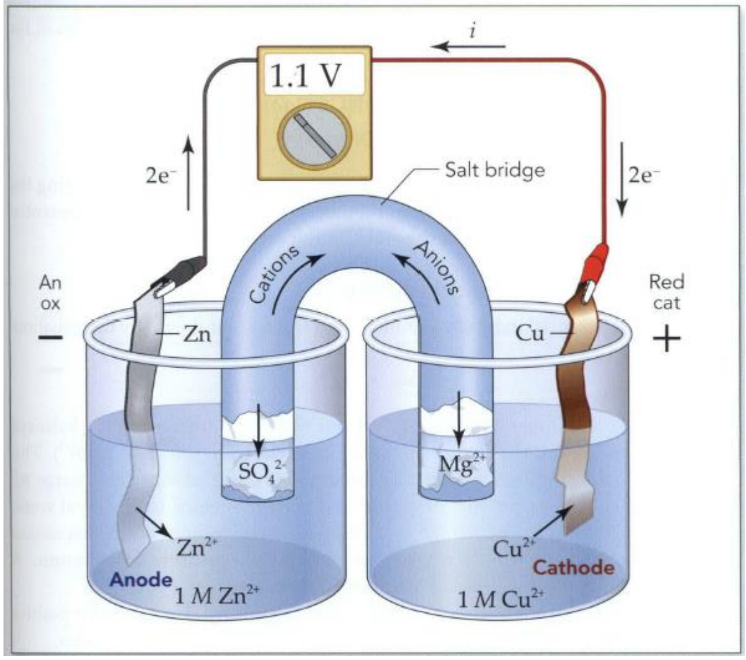
- When a cell contains two different solutions, a liquid junction is required to separate the solutions
  - a salt bridge is a type of liquid junction that minimizes the small potential difference inevitably created by the liquid junction
  - allows movement of ions between solutions without creating a strong extra potential within the galvanic cell
    - K^+ ions move toward the cathode about the same rate as Cl^- ions move toward the anode
  - without the salt bridge, the solutions in the cell would mix, providing a low resistance path for electrons to move from Zn(s) to Cu^{2+} (aq)
    - this would effectively short circuit the cell, leaving it with a cell potential of zero

$$Cu^{2+}(aq) + 2e^- \rightarrow Cu(s) \qquad E^\circ = 0.34\ V$$

$$Zn^{2+}(aq) + 2e^- \rightarrow Zn(s) \qquad -[E^\circ = -0.76\ V]$$

$$emf = 1.1\ V$$

FIGURE 6.10 Galvanic Cell



Here is exactly what's going on in the galvanic cell diagram in Figure 6.10. The solid zinc atoms would like to get rid of their electrons, but they need a place to put them. The Cu^{2+} ions in solution are happy to take them. This creates a potential difference. The question is how to transfer electrons without building up a charge difference, because separating charges is energy expensive. The copper wire gives the electrons a path with low resistance to flow, but the electrons won't flow if they are building up a charge difference. The salt bridge allows ions to move (negative ions toward the anode and positive ions toward the cathode) and carry away any charge buildup. As electrons leave the solid zinc strip, Zn^{2+} ions are formed and dissolve into solution. At the cathode, Cu^{2+} ions gain the electrons coming through the wire and form solid Cu.

IUPAC Conventions – Cell Diagrams

- Each phase is listed from left to right, beginning with the terminal attached to the anode and ending with the terminal attached to the cathode
  - often left out because they are always the same material and do not take part in the reaction
- A vertical line is placed between phases, and a double vertical line indicates a salt bridge
- a dotted vertical line indicates a boundary between two miscible liquids, and species in the same phase are separated by a comma

$$Pt'(s)|Zn(s)|Zn^{2+}(aq)\|Cu^{2+}(aq)|Cu(s)|Pt(s)$$

Cell Diagram

Free Energy and Chemical Energy

- A positive cell potential indicates a spontaneous reaction: $\Delta G = -nFE_{max}$
  - n = number of moles of electrons that are transferred in the balanced redox reaction
  - F = charge on one mole of electrons (96486 C mol^{-1})
  - E = voltage
- Product of charge and voltage is equal to electrical work, a type of nonPV work
- change in Gibbs free energy represents the maximum nonPV work available from a reaction at constant temperature and pressure
  - the negative sign indicates that the work is being done by the system
- E_{max} must be positive for G to be negative

Nernst Equation

- Expresses the relationship between chemical concentrations and potential difference

$$E = E^\circ - \frac{RT}{nF}\log(Q)$$

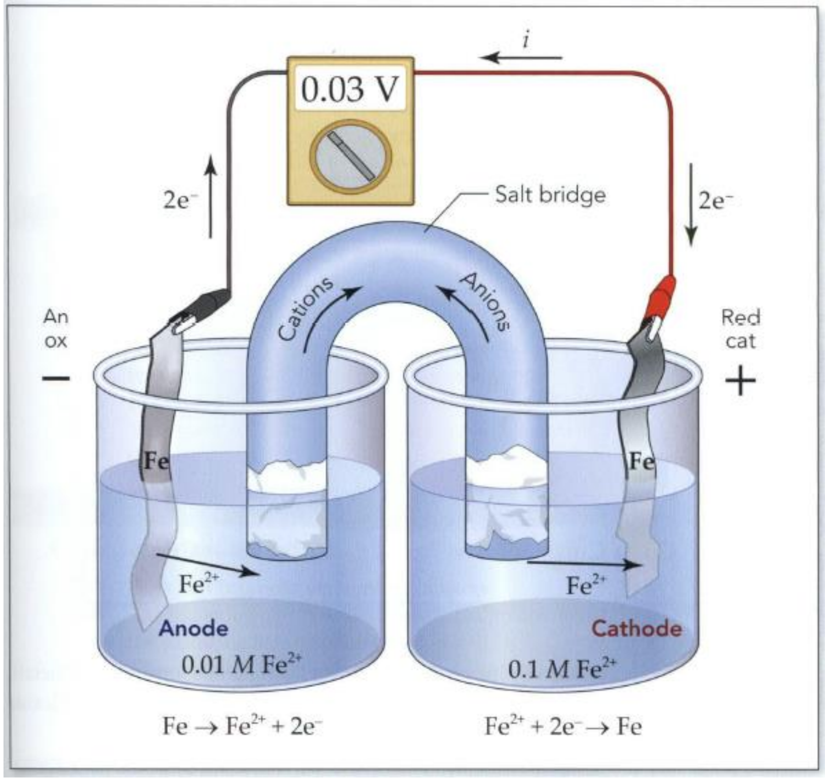
- The Nernst equation allows us to plug in nonstandard concentrations to create Q and find the cell potential

Concentration Cells and Electrolytic Cells

- Concentration cell is a limited form of a galvanic cell in which a reduction half reaction takes place in one half cell while the exact reverse of that half reaction is taking place in the other cell

- The cells differ in their ion concentrations

FIGURE 6.11 Concentration Cell



- When we add the two half reactions we get E = 0
  - if the concentrations were equal on both sides, then the concentration cell potential would be zero
- Electrons will flow in the direction that allows the concentrations in the half cells to become equal; **they will flow toward the side that has a greater concentration of positive ions**
  - The Anode solution will gain positive ions (products in solution) and the cathode side will lose positive ions (reactants in solution)
- For the cell above, we can use the Nernst equation to find the potential (at 25ºC)

$$E = E^\circ - \frac{0.06}{2}\ln\left(\frac{0.01}{0.1}\right)$$

- The electrolytic cell
  - created by hooking up a power source across the resistance of a galvanic cell and forcing the reactions to run in reverse
  - will have a negative emf
  - Reduction still takes place at the cathode and oxidation at the anode
  - Electrolytic cells are used in industry for metal plating and purifying metals
    - for instance, pure sodium can be collected through the electrolysis of sodium chloride solution

$$Na^+ + e^- \rightarrow Na \qquad E^\circ = -2.71\text{ V}$$

$$2Cl^- \rightarrow 2e^- + Cl_2 \qquad E^\circ = -1.36\text{ V}$$

  - Electrons still flow from the anode to the cathode
  - The assignment of positive and negative to electrodes in galvanic and electrolytic cells is based on perspective
    - Galvanic cells are used to provide energy to an external load, so the electrodes are labeled so that negative electrons are flowing toward the positive electrode
      - Electrons flow from the load to the cathode, so the **cathode is labeled positive in the galvanic cell**
    - The focus of electrolytic cells is within the cell itself. For instance, electrophoresis uses and electrolytic cell. Negatively charged amino acids within the electrolytic cell flow towards the positive electrode, so the **anode is labeled positive in the electrolytic cell (like in electrophoresis)**
- Final note: electrochemical cell can mean either galvanic or electrolytic
- For any and all cells: RedCat, AnOx
  - it's just the assignment of positive and negative that changes

-

Galvanic or Voltaic cells
- Half-reactions
- Reduction potentials; cell potential
- Direction of electron flow

Concentration cell
Batteries
- Electromotive force, Voltage
- Lead-storage batteries !!!
- Nickel-cadmium batteries!!!

Specialized Cell - Nerve Cell (BIO)
Myelin sheath, Schwann cells, insulation of axon
Nodes of Ranvier: propagation of nerve impulse along axon

Content Category 4D: How light and sound interact with matter

Sound (PHY)
Production of sound
- Sound is produced when something vibrates. The vibrating body causes the medium (air, water, etc) around it to vibrate. Vibrations in air are called traveling longitudinal waves, which we can hear. Sound waves consist of areas of high and low pressure called compressions and rarefactions, respectively.

Relative speed of sound in solids, liquids, and gases
- Solid>liquid>Gas
- Sound actually travels faster when it's humid, because

Intensity of sound, decibel units, log scale
- Intensity = power

Sound intensity level

$$\beta = 10\log\frac{I}{I_0} \quad \text{with } I_0 = 10^{-12}\ \text{W/m}^2$$

Units: decibels

Threshold of human hearing: 10^{-12} W/m² $\rightarrow \beta = 0$

Normal conversation: 10^{-6} W/m² $\rightarrow \beta = 65$ decibels

Threshold of pain: 1 W/m² $\rightarrow \beta = 120$ decibels

Twice the decibels does NOT feel twice as loud!

Attenuation (Damping)

Damping is dissipation of energy due to a force that is proportional to velocity.

Attenuation is a reduction of amplitude.

Attenuation could be accomplished by turning the volume knob on a radio, for example. It does not necessarily imply any damping is going on. Sometimes attenuation is accomplished by using damping.

Due to reflection, spreading, or absorption

Amplitude and velocity decreases, but not frequency

Doppler Effect: moving sound source or observer, reflection of sound from a moving object

$$f' = \frac{(v + v_0)}{(v - v_s)} f$$

f = actual frequency of the sound waves

f' = observed frequency

v = speed of the sound waves

v_0 = velocity of the observer

v_s = velocity of the source

Pitch correlates with frequency

- Note that the below expression is for standing waves on a string, not for sounds traveling in air

D is correct. Pitch correlates with frequency; $v = \lambda f$. We can set this equation equal to the one in the passage:

$$v = \sqrt{\frac{T}{\mu}} = \lambda f$$

to see that decreasing the tension decreases frequency, so choices A and B can be eliminated in favor of the lower tension in choices C and D. The speaking length of the wire is proportional to the wavelength (see question 128). Thus, increasing the length will increase the wavelength and decrease the frequency.

Resonance in pipes and strings

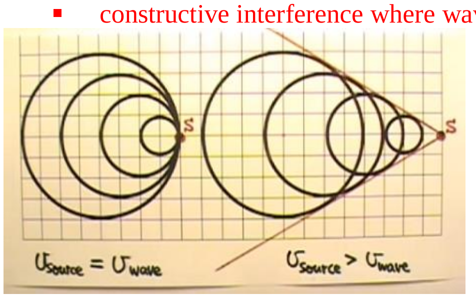
- When a wave reflects off a medium that is less dense, it is reflected upright. If it is more dense, it is inverted
- Standing waves cause the string to resonate or vibrate at its natural frequency
- open end of a pipe = unfixed end of a string
  - fixed – node
  - unfixed = antinode

Ultrasound

- time it takes for reflected waves to return to the probe
- Intensity of reflected waves – relative density
- Greater difference in density = **greater intensity** of reflected sound
- Intensity varies with the square of amplitude

Shock waves

- Conical wave front produced when $V_{sound} > c$
- constructive interference where wave crests meet, form a shock wave cone



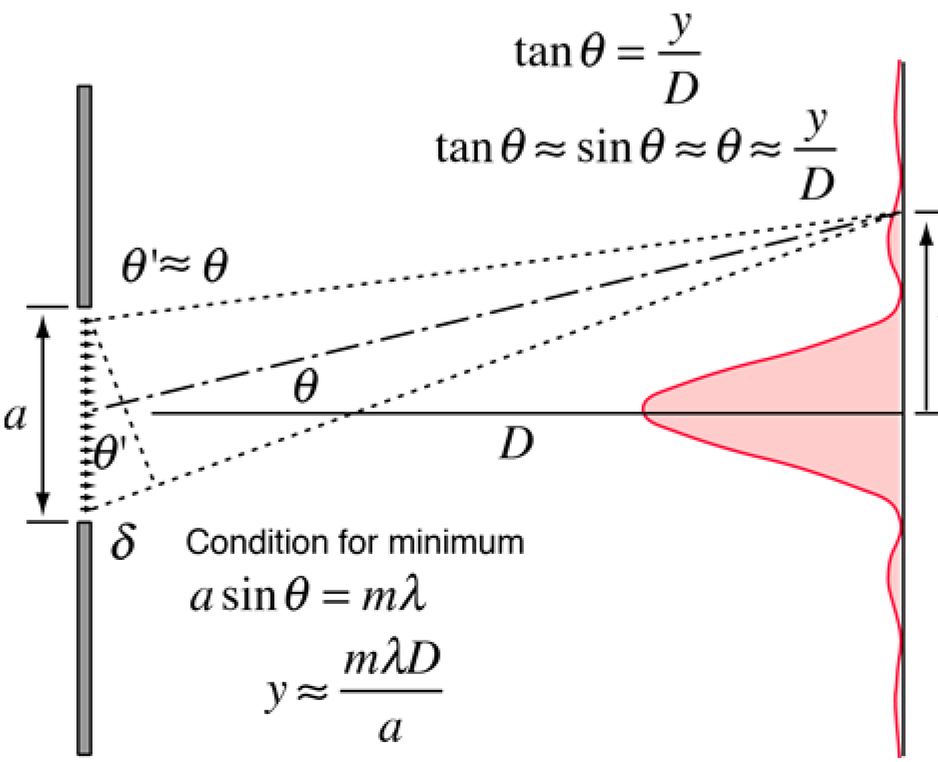
Light, Electromagnetic Radiation (PHY)

Concept of Interference; Young Double-slit Experiment

- When two **light** waves superpose with each other in such away that the crest of one wave falls on the crest of the second wave, and trough of one wave falls on the trough of the second wave, then the resultant wave has larger amplitude and it is called constructive **interference**
- Young's double-slit experiment (using coherent light
  - constructive: path length differs by λ
  - destructive: path length differs by $\lambda / 2$

Thin films, diffraction grating, single-slit diffraction

- Thin film interference
  - reflection changes phase (off material that is more dense), refraction does not
  - Destructive interference: thickness of film = half the wavelength (for material that is more dense)
  - Constructive interference: thickness of film = quarter of the wavelength
  - $2L = (m + ½) \lambda / n_2$
- Diffraction – significant if the size of an object or opening is small relative to the wavelength of a wave
  - diffraction grating – many small slits
  - maxima are spread out (each individual maxima)
  - fewer maxima, of more intensity
- Single-slit diffraction- every point on a wave is diffracting – Huygen's principle
  - usually, they just add up so you don't even notice
  - single-slit diffraction produces these points
  - What do we see?
    - Big bright spot in the middle, and then relatively weak patterns

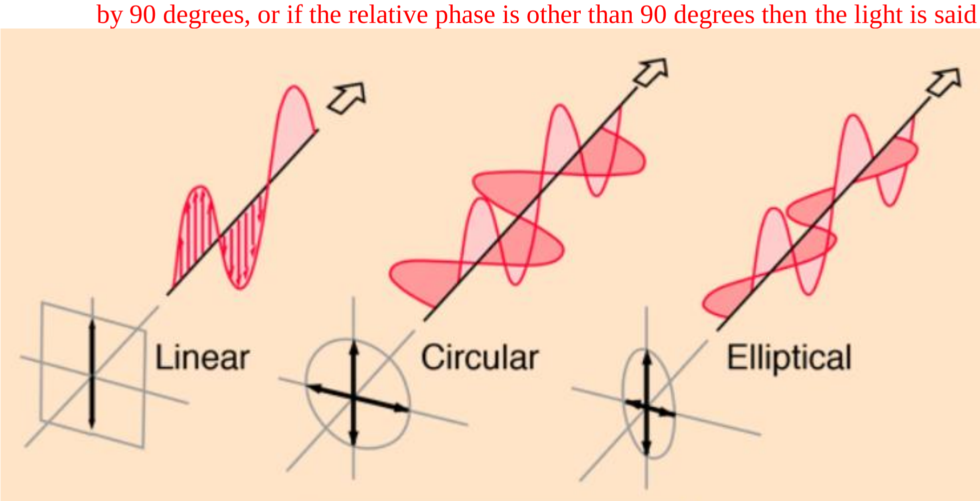
- usually, whole integers for lambda gives constructive interference, but in this case, it's destructive
- 

Other diffraction phenomena, X-ray diffraction

- X-ray diffraction: x-rays projected at a crystal scatter and produce patterns unique to the structure of the crystal

Polarization of light: linear and circular

- Polarized light – light oscillating in only one direction
- Most light is not polarized – all overlapping
- Polarizer – lets light only in one direction
  - Sunglasses
    - Light that reflects off the sun is polarized, defined by the plane of the surface that it hi
      - if it hits the floor, then it's polarized horizontally
      - sunglasses will only let in vertically polarized light
- Light in the form of a plane wave in space is said to be linearly polarized. However, natural light is generally unpolarized, all planes of propagation being equally probable. If light is composed of two plane waves of equal amplitude differing in phase by 90 degrees, then the light is said to be circularly polarized. If two plane waves fo differing amplitude are related in phase by 90 degrees, or if the relative phase is other than 90 degrees then the light is said to be elliptically polarized.



Properties of electromagnetic radiation

- Velocity equals constant c, in vacuo

- Electromagnetic radiation consists of perpendicularly oscillating electric and magnetic fields; direction of propagation is perpendicular to both

Classification of electromagnetic spectrum, photon energy E = hf

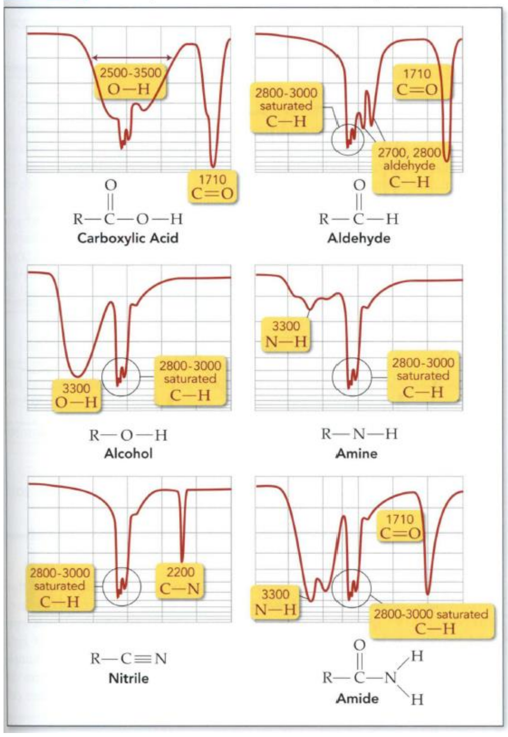
Visual spectrum, color

Molecular Structure and Absorption Spectra (OC)

Infrared region

- Intramolecular vibrations and rotations
- Recognizing common characteristic group absorptions, fingerprint region
- IR spectroscopy
  - uses molecular dipoles to find information about functional groups
  - infrared region – causes polar bonds within compound to stretch and contract
  - Atoms with greater mass resonate at lower frequencies
    - that's why mostly X-H bonds show up
  - Stiffer bonds, such as double and triple bonds, resonate at higher frequencies

FIGURE 4.11 IR Absorption of Common Functional Groups



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Visible region (GC)

- Absorption in visible region gives complementary color (e.g., carotene)
- Color—opposite or not?
  - If it is a source (can be seen in the dark), then it is straightforward
  - If it is not a source (can't be seen in the dark, then use color wheel
    - R-G, B-O, Y-V
  - For absorbance spectra, the color is opposite
  - For emission spectra, the color is the same
- Effect of structural changes on absorption (e.g., indicators)

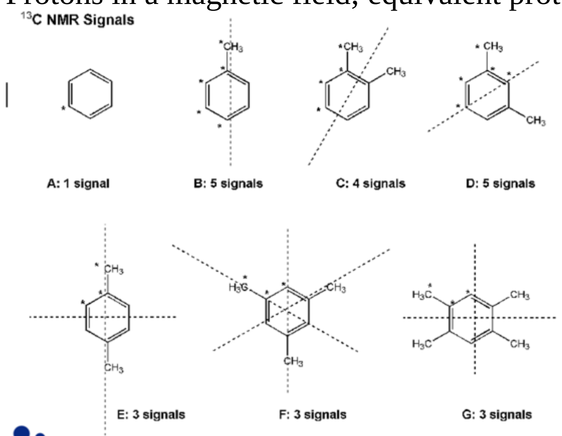
Ultraviolet region

- π-Electron and non-bonding electron transitions
- Conjugated systems
- UV Spectroscopy
  - detects conjugated systems by comparing the intensities of two beams of light from the same monochromatic light source
    - one beam is shone through a sample cell and the other is shown through a reference cell
  - when photon collides with electron in molecule, the photon may be absorbed, bumping an electron up to a vacant molecular orbital

        - typically pi-electron movements from bonding to nonbonding orbitals
        - electrons in sigma-bonds usually require more energy to reach the next highest orbital
        - **conjugated systems with pi bonds have vacant orbitals at energy levels (LUMO) close to their HOMO**
    - The longer a chain of conjugated double bonds, the greater the wavelength (less frequency) of absorption
        - each additional conjugated double bond increases the wavelength by about 30-40 nm
        - additional alkyl group attached to any atom involved in the conjugated system increases spectrum wavelength by about 5 nm
    - If a compound has eight or more double bonds, its absorbance moves into the visible region of the electromagnetic spectrum
        - they have the opposite color that they absorb
-

NMR spectroscopy

- Protons in a magnetic field; equivalent protons



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- Spin-spin splitting

Spectrocscopy

- Nuclear Magnetic Resonance (NMR) spectroscopy
    - study of interaction between atomic nuclei and radio waves
    - nuclei with odd atomic or mass number possess a mechanical property called nuclear spin
        - as spinning proton, like any other rotating sphere of charge, generates a magnetic field around the nucleus
    - when subject to an external magnetic field, the field of a nucleus aligns either with or against the external field
        - aligning with = α = lower energy spin state
        - aligning against = β = higher energy spin state
        - the stronger the magnetic field, the greater the difference in energy between these states
        - when protons return to their original spin state, they release electrical impulses generated by NMR spectrometer
    - In NMR, the frequency of the electromagnetic radiation is held constant while the magnetic field strength is varied
    - in absence of any electrons, all protons absorb electromagnetic energy from a given magnetic field at the same frequency
        - electrons shield protons from the magnetic field, so the external field must be strengthened for a shielded proton to achieve resonance
    - Downfield = low magnetic field strength = deshielded
    - upfield = high magnetic field strength = shielded
    - Splitting, integration

Geometrical Optics (PHY)

Reflection from plane surface: angle of incidence equals angle of reflection

Refraction, refractive index n; Snell's law: $n1 \sin \theta 1 = n2 \sin \theta 2$

- $n = c / v$ (always greater than 1)
    - glass: 1.5
    - water: 1.3

Dispersion, change of index of refraction with wavelength

Conditions for total internal reflection

- $\theta_{critical} = \sin^{-1} (n_2 / n_1)$
- Can only occur if the material is denser than what it's reflecting against ($n_1 > n_2$).

Spherical mirrors

- Center of curvature
- Focal length
- f = R / 2
- Real and virtual images
- Real images are always inverted, and are on the same side of the mirror/lens as the observer (+)
- virtual images are always upright and are on the opposite side of the observer (-)
- Diverging: SUV
- Converging: RI

Thin lenses

- Converging and diverging lenses
  - Convex = converging, concave = diverging (opposite for mirrors)
- Use of formula $1/p + 1/q = 1/f$, with sign conventions
  - Focal point: converging (+), diverging (-)
  - Object – always positive
  - Image:
    - Diverging: SUV, negative
    - Converging: RI, except within focal length (where rules for diverging apply
  - Magnification
    - dverging: always smaller
    - Converging:
      - object > R: smaller
      - Object = R: same size
      - Object < R: larger
    - = - di / do
- Lens strength, diopters
- The **diopter** is the unit of measure for the refractive**power** of a **lens**. The **power** of a **lens** is defined as the reciprocal of its focal length in meters, or D = 1/f, where D is the **power** in **diopters** and f is the focal length in meters. **Lens** surface **power** can be found with the index of refraction and radius of curvature.
- Combination of lenses
- image of one is the object of the second
- Lateral magnification M = m1m2
- P(eff) = effective power = P1 + P2

Lens aberration

- Chromatic – higher frequency light bends more
  - The higher frequency waves are able to interact with the atoms of the material more so because they match the resonant frequencies of the electrons, this slows down the wave. So, the high frequency waves slow down because they are preoccupied with exciting electrons of atoms as they pass through the material
  - they thus have bigger indices of refraction
- Spherical: rays further from the center focus at different points than rays at the center
  - it is only for parabolas that they focus on a single point

Optical Instruments, including the human eye

- Eye: cornea and lends bends light
  - near objects: lens contracts, focal length reduces
  - Nearsighted: lens bends too much
    - corrected by diverging lens
- Note: microscope inverts, which means top to bottom and left to right

Content Category 4E: Atoms, nuclear decay, electronic structure, and atomic chemical behavior

Atomic Nucleus (PHY, GC)

Atomic number, atomic weight

Elements

- Atomic number – number of protons
  - provides identity of the element
  - may have any number of neutrons or electrons, but only one number of protons

- Mass Number, A, is the number of protons plus neurons
    - approximately equal to its atomic weight

Atomic weight – weighted average of the naturally occurring isotopes of that element

Neutrons, protons, isotopes

- Isotopes – two or more atoms of the same element that contain different numbers of neuron
    - Hydrogen: Protium (^1H), deuterium (^2H), tritium (^3H)
- Ion – not electrically neutral
    - **cations** – positive, more protons than electrons
        - loss of electron - **smaller**
        - positive charge of nucleus exerts greater attractive force on each valence electron, pulling them closer to the nucleus
            - loss of electrons reduces repulsive forces, further contributing to the decrease in size
    - **anions** – more electrons that protons
        - Gain of an electron – **larger**
            - positive charge pulls less strongly on each individual valence electron
            - addition of electron increases repulsive forces

Salt – neutral compound composed of a positive and negative ion together

Nuclear forces, binding energy

Binding energy is the energy that holds a nucleus together, equal to the mass defect of the nucleus

- Minimum energy required to disassemble a system of particles into separate parts

Nuclear force is a force that acts between the protons and neutrons of atoms.

Radioactive decay

Radioactive Decay

- concerns atoms that spontaneously break apart
    - all atoms other than hydrogen are subject to some type of spontaneous decay
- Nuclear decay – degradation of particles within nucleus of an atom
- Half-life
    - length of time necessary for one half of a given amount of substance to decay
    - Follows first-order kinetics
        - $A_t = A_0 e^{(-kt)}$
            - A_t = amount at time t
            - A_o = original amount
            - k = rate constant
            - t = time

α, β, γ decay

- Types of radioactive decay
    - On all these following processes, the sum of the atomic numbers and the sum of the mass numbers on the left answers must equal to the right side
    - alpha decay – loss of an alpha particle (helium nucleus, 2 protons and neutrons)

    $$^{238}_{92}U = {}^{4}_{2}\alpha + {}^{234}_{90}Th$$

    - Beta decay – **breakdown of a neutron into a proton and electron**, and the expulsion of the newly created electron

    $$^{234}_{90}Th \rightarrow {}^{234}_{91}Pa + {}^{0}_{-1}e$$

        - mass number stays the same, but atomic number increases by one
        - neutrino (not shown) is also emitted during beta decay
    - Positron emission – emission of a positron when **a proton becomes a neutron**

    $$^{22}_{11}Na \rightarrow {}^{0}_{1}e + {}^{22}_{10}Ne$$

        - positron is like an electron with a positive charge
        - proton is transformed into a neutron and a positron is emitted
    - Electron capture

    $$^{201}_{80}Hg + {}^{0}_{-1}e \rightarrow {}^{201}_{79}Au + {}^{0}_{0}\gamma$$

        - capture of an electron and the merging of that electron with a proton to create a neutron

All forms of beta decay are simply the breakdown or formation of a single neutron (n) within the nucleus. This creates a proton (p^+) in the former and eliminates a proton in the latter.

If you keep this in mind, you do not need to memorize the reactions, as they make sense accordingly.

$$n \rightarrow p^+ + e^-$$

$$p^+ + e^- \rightarrow n$$

Using positrons (e^+) instead of electrons (e^-)

$$n + e^+ \rightarrow p^+$$

$$p^+ \rightarrow n + e^+$$

- Gammay ray – high frequency photon
    - no mass or charge, does not change the identity of the atom from which it is given off
    - Gamma decay often accompanies the other types of radioactive decay
        - **can occur when an electron and positron collide**

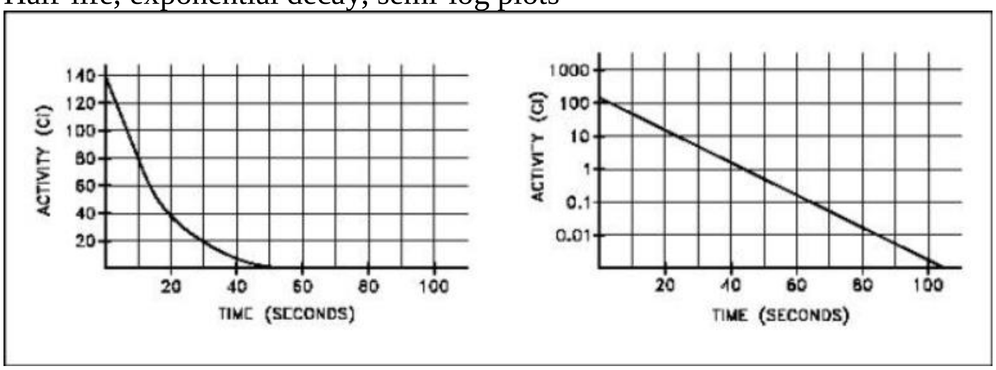
$${}^{0}_{-1}e + {}^{0}_{1}e \rightarrow {}^{0}_{0}\gamma + {}^{0}_{0}\gamma$$

- matter-antimatter collision – annihilation, mass is destroyed, converted to energy in the form of gamma rays

TABLE 1.11 > Types of Radioactive Decay

Type of Decay	Process	Change in Mass #	Change in Atomic # (change in number of protons)	New Element Name
α (Alpha) Decay	Lose helium nucleus	-4	-2	2 to left on periodic table
β (Beta) Decay	Neutron becomes proton, electron emitted or positron absorbed	No change	+1	1 to the right on the periodic table
Electron Capture*	Proton becomes neutron, electron is absorbed	No change	-1	1 to the left on the periodic table
Positron Emission*	Proton becomes neutron, positron is emitted	No change	-1	1 to the left on the periodic table
γ (Gamma) Decay	Emit high energy gamma ray (neutron becomes proton and electron)	No change	No change	No change

Half-life, exponential decay, semi-log plots



Mass spectrometer

- Mass Spectrometry
    - Used to determine a compound's molecular weight
    - molecules of a sample are bombarded *with electrons*, causing them to break apart and ionize
        - the largest ion is the size of the original molecule but has one less electron
            - molecular ion – this largest cation
    - After molecule is broken apart, ions are accelerated through a curved path
        - radius of curvature depends on mass to charge ratio (m/z)
    - Largest peak = **base peak**
    - Peak made by molecular ion = **parent peak**

Electronic Structure (PHY, GC)

Orbital structure of hydrogen atom, principal quantum number n, number of electrons per orbital (GC)

Quantum Mechanics

- elementary particles can only gain or lose energy in discrete units
- The Four Quantum Numbers
    - Principle Quantum Number – n – **shell** level
    - Second quantum number (angular momentum) – l – **subshell**, which has a distinct shape
        - l = 0, s subshell
        - l = ±1, p subshell
        - l = ±2, d subshell
        - l = ±3, f subshell
        - n-1
    - Third quantum number (magnetic) – m_l – precise **orbital** within a given subshell

        - Each orbital holds 2 electrons
        - from –l to +l
        - total number of orbitals within a shell = n^2
            - total number of electrons = $2n^2$
    - Fourth Quantum number – m_s – spin
        - ±1/2

Ground state, excited states

- Ground state vs Excited state vs ions

$$Na^{+} \Rightarrow 1s^2\,2s^2\,2p^6 \text{ or } [Ne]$$
$$Fe^{3+} \Rightarrow [Ar]\,3d^5$$
$$Br^{-} \Rightarrow [Ar]\,4s^2\,3d^{10}\,4p^6 \text{ or } [Kr]$$
$$Be_{\text{with an excited electron}} \Rightarrow 1s^2\,2s^1\,2p^1$$

Absorption and emission line spectra

Absorption and Emission Line Spectra

- When excited electrons fall from a higher energy state to a lower energy state, energy is released
    - creates an emission line spectrum that is characteristic of the given element
    - Absorption line spectrum – measures the radiation absorbed when electrons absorb energy to move to a higher energy state
- Max Planck: if energy is transferred from one point to another via an electromagnetic wave, and we wish to increase the amount of energy transferred, the energy can only change in discrete increments by:

$$\Delta E = hf$$

    - h = Planck's constant = 6.6×10^{-34} J s
    - f = frequency (s^{-1})
- Einstein - If light is considered as a particle phenomenon, where each photon is one particle, *the energy of a single photon is given by the same equation*
- Bohr – electrons rotate around the nucleus on a path characterized by a certain energy level
    - model worked for line spectra for hydrogen only
- de Broglie – expanded this model:

$$\lambda = \frac{h}{mv}$$

    - m = mass, v = velocity
- When electron falls from higher energy to lower energy, energy is released from the atom in the form of a photon
    - has a wave frequency which corresponds to $\Delta E = hf$
    - Reverse is also true: when a photon collides with an electron, it can only bump that electron to another energy level if its energy corresponds to the energy difference between rungs

Use of Pauli Exclusion Principle

Paramagnetism and diamagnetism

Paramagnetic and Diamagnetic

- Hund's rule – electrons will not fill any orbital in the same subshell until all orbitals in that subshell contain at least one ion
    - like charges repel each other
- Paramagnetic elements – elements with unpaired electrons
    - subshell is not completely filled
    - The spin of each unpaired electron is parallel to the others
        - as a result, the electrons <u>will align with an external magnetic field</u>
- Diamagnetic elements – elements with no unpaired electrons
    - subshells completely filled
    - unresponsive to external magnetic field

Conventional notation for electronic structure (GC)

Bohr atom

Heisenberg Uncertainty Principle

Heisenberg Uncertainty Principle

- inherent uncertainty in the product of the ***position*** of a particle and its ***momentum***
- arises from the dual nature (wave-particle) of mater

$$\Delta x \Delta p \geq \frac{h}{2}$$

Effective nuclear charge (GC)

- Effective nuclear charge (Z_{eff}) – the amount of charge felt by the most recently added electron
  - Z_{eff} – generally increases going left to right across the periodic table
    - while more protons are added across a period, the new electrons added are in roughly the same energy level and therefore do not experience significantly more shielding than the previous electron
  - Z_{eff} – generally decreases going from top to bottom down the periodic table
  - When an atom gains an electron, Z_{eff} decreases, and when an atom loses an electron, Z_{eff} increases
    - this is why cations are smaller and **anions** are **larger**

Photoelectric effect

- Photoelectric effect
  - Einstein demonstrated the existence of a one-to-one photon-to-electron collision
  - proved that light is made up of particles
  - Intensity of light by increasing the number of photons does not matter in increasing the kinetic energy of an emitted electron
    - this kinetic energy only increases when intensity is increased by increasing the frequency of each photon
  - The minimum amount of energy required to eject an electron – **work function**
  - Kinetic energy of ejected electron is given by the energy of the photon minus work function:
  - $(K.E. = hf - \Phi)$

The Periodic Table - Classification of Elements into Groups by Electronic Structure (GC)

Alkali metals

- Group 1 – alkali
  - soft metallic solids with low densities and melting points
  - easily form 1+ cations
  - highly reactive – react with most nonmetals to form ionic compounds
  - All react with hydrogen to form hydrides, such as NaH
  - react exothermically with water to produce the respective metal hydroxide and hydrogen gas
  - In nature, only exist as compounds

Alkaline earth metals: their chemical characteristics

- Group 2 – alkaline earth metals
  - harder, more dense, and melt at higher temperatures than alkali metals
  - form 2+ cations
  - less reactive than alkali metals because their highest energy electron completes the s orbital
  - Only exist in compounds in nature

Halogens: their chemical characteristics

- Group 17 – Halogens
  - highly reactive
  - Fluorine and Chlorine – diatomic gases
  - Bromine – diatomic liquid
  - Iodine – diatomic solid
  - Likely to gain an electron to attain a noble gas configuration
  - Fluorine always has an oxidation state of -1 in compounds
    - can only make one bond
    - the others can take on oxidation states as high as +7
  - Other halogens besides fluorine can make more than one bond, though this is rare
  - All can combine with hydrogen to make gaseous hydrogen halides
    - soluble in water, forming hydrohalic acids

Noble gases: their physical and chemical characteristics

- Group 18 – Noble gases (inert)
  - nonreactive
  - unlike other elements, are normally found in nature as isolated atoms

Transition metals
Representative elements
Metals and non-metals
Oxygen group

- Group 16 – chalcogens, or oxygen group
  - Oxygen – second most electronegative element
  - can make double bonds
  - in nature, exists as O_2 and O_3
  - typically reacts with metals to form metal oxides
  - Sulfur – most common: S_8
  - Metal sulfides – most common form of sulfur found in nature
    - Sulfur can form between 2 to 6 bonds
    - ability to pi bond, forming strong double bonds

The Periodic Table - Variations of Chemical Properties with Group and Row (GC)

Valence electrons
First and second ionization energy

- Definition
- Prediction from electronic structure for elements in different groups or rows
- Ionization energy – energy needed to detach an electron from an atom
  - Across period: **increases**
    - moving across a period to the right – Z_{eff} increases, pull electrons more strongly toward the nucleus
  - Down Group: **Decreases**
    - moving down a group – Z_{eff} also increases, but r also increases as well
      - due to the exponent on coulomb's law ($F = kq_1q_2 / r^2$), r has a bigger effect
        - you plug in Z_{eff} to q_1
  - When an electron is more strongly attracted to the nucleus, more energy is required to detach

Electron affinity

- Definition
- Variation with group and row
- Electron Affinity – willingness of an atom to accept an additional electron
  - energy released when an electron is added to an isolated atom
  - Across period: **increases**
  - Down Group: **decreases**
  - Electron affinity is **more exothermic** to the right and up on the periodic table
  - electron affinity values for noble gases are endothermic, because noble gases are stable
-

Electronegativity

- Definition
- Comparative values for some representative elements and important groups
- Electronegativity – tendency of an atom to attract electrons shared in a covalent bond
  - Across period: **increases**
  - Down Group: **Decreases**
  - Fluorine is the most electronegative atom
  - The electronegativity of hydrogen falls between that of boron and that of carbon
    - When bonded with hydrogen, carbon and elements to the right of carbon will carry a partial negative charge while hydrogen will carry a partial positive charge
    - Boron and elements to the left of boron will carry a partial positive charge, hydrogen will carry a partial negative charge
      - think of the hydrides
  - Atoms with large differences in electronegativity (1.6 or larger on the Pauling scale) will form ionic bonds
    - Moderate differences (0.5-1.5) – generally form polar covalent bonds
    - Atoms with very minor electronegativity differences (0.4 or smaller) will form nonpolar covalent bonds

Electron shells and the sizes of atoms

Electron shells and the sizes of ions

- cations are smaller, anions are larger

Stoichiometry (GC)

Molecular weight

Empirical versus molecular formula

Metric units commonly used in the context of chemistry

Description of composition by percent mass

Mole concept, Avogadro's number $N_A = 6.02 \times 10^{23}$

Definition of density

Oxidation number

- Common oxidizing and reducing agents
- Disproportionation reactions

Chemical Potential and Redox Reactions

- Oxidized atoms lose electrons, reduced atoms gain electrons
- Oxidation states – possible charge values that an atom can hold within a molecule
    - do not truly exist, simply provides a system for tracking movement of electrons

Oxidation State	Atom
0	Atoms in their elemental form
-1	Fluorine
+1	Hydrogen (except when bonded to a metal, like NaH; then -1.)
-2	Oxygen (except when it is in a peroxide like H_2O_2; then -1.)

Oxidation State	Group on Periodic Table
+1	Group 1 elements (alkali metals)
+2	Group 2 elements (alkaline earth metals)
+3	Group 15 elements (nitrogen family)
-2	Group 16 elements (oxygen family)
-1	Group 17 elements (halogens)

- These two tables gives oxidation states of elements when they are in a compound
- When these two tables conflict, the table on the left is given higher priority
    - For example, the oxidation state of nitrogen in NO_3^- is +5 because of the -2 oxidation state of oxygens
- Redox reaction: $2H_2 + O_2 \rightarrow 2H_2O$
    - Both H and O start at 0
    - O becomes -2 (reduced)
    - H becomes +1 (oxidized
- Reducing agent (reductant) becomes oxidized, oxidizing agent (oxidant) becomes reduced
    - in the above example, H was the reducing agent, giving electrons to O
    - O was the oxidizing agent, accepting electrons from H
    - The reducing agent contains the atom being oxidized, the oxidizing agent contains the atom being reduced

$$CH_4 + 2O_2 \rightarrow CO_2 + 2H_2O$$

Carbon goes from −4 to +4 and **Oxygen** goes from 0 to −2

- Methane is the reducing agent, O_2 is the oxidizing agent
- Note: the reducing agents and oxidizing agents in the example are compounds
    - *the atom is oxidized or reduced; the compound is the oxidizing or reducing agent*
- **Disproportionation** is a chemical **reaction**, typically a redox **reaction**, where a molecule is transformed into two or more dissimilar products. In a redox **reaction**, the species is simultaneously oxidized and reduced to form at least two different products

Description of reactions by chemical equations

- Conventions for writing chemical equations
- Balancing equations, including redox equations
- Balance elements in the equation other than O and H.
- Balance the oxygen atoms by adding the appropriate number of water (H_2O) molecules to the opposite side of the equation.
- Balance the hydrogen atoms (including those added in step 2 to balance the oxygen atom) by adding H^+ ions to the opposite side of the equation.
- Add up the charges on each side. Make them equal by adding enough electrons (e^-) to the more positive side. (Rule of thumb: e^- and H^+ are almost always on the same side.)

- The e^- on each side must be made equal; if they are not equal, they must be multiplied by appropriate integers (the lowest common multiple) to be made the same.
- The half-equations are added together, canceling out the electrons to form one balanced equation. Common terms should also be canceled out.
- (If the equation is being balanced in a basic solution, through the addition of one more step, the appropriate number of OH^- must be added to turn the remaining H^+ into water molecules.)
-
- Limiting reactants
- Theoretical yields

Foundational Concept 5: The principles that govern chemical interactions and reactions form the basis for a broader understanding of molecular dynamics of living systems

Content Category 5A: Unique nature of water and its solutions

Acid/Base Equilibria (GC, BC)

Brønsted–Lowry definition of acid, base

Ionization of water

- Kw, its approximate value (Kw = [H+][OH–] = 10–14 at 25°C, 1 atm)
- Definition of pH: pH of pure water

Water and Acid-Base Chemistry

Autoionization of water:

$$H_2O + H_2O \rightleftharpoons H_3O^+ + OH^-$$

- In pure water at 25° C, the equilibrium H^+ and OH^- concentrations are equal at 10^{-7}
- If a weak acid is added, the following thee reactions occur simultaneously:

$$HA + H_2O \rightleftharpoons A^- + H_3O^+$$

$$A^- + H_2O \rightleftharpoons HA + OH^-$$

$$H_2O + H_2O \rightleftharpoons H_3O^+ + OH^-$$

  - The first reaction will shift towards the products (Because we added HA)
    - concentration of H_3O^+ increases
  - The second reaction will shift to the reactants (Because we added HA), causing OH^- to decrease
    - Since the amount of conjugate base A is small for a weak acid, the rate of the second reaction will be insignificant compared to the first
  - Thus, we have a significant increase in H_3O^+ concentration and a relatively insignificant decrease in OH^- concentration
  - This results in an excess of products for the third reaction, so the reaction equilibrium is driven toward the left
    - the concentration of H_3O^+ will be greater than OH^-
- Even though the addition of an acid or base shifts the equilibrium, the equilibrium constant for the autoionization of water will remain the same as long as the temperature remains constant
  - Since liquids do not participate in the equilibrium constant,

$$K_w = [H_3O^+][OH^-]$$

    - At 25°C and 1 atm, the equilibrium of this reaction lies far to the left:
      - $K_w = 10^{-14}$
    - Thus,

$$pH + pOH = pK_w \qquad\qquad pH + pOH = 14$$

(For an aqueous solution at 25°C)

- An acid has its own equilibrium constant in water, K_a
  - The equilibrium constant for any reaction in which an acid reacts with a hydronium ion and a conjugate base
  - The larger the K_a, the smaller the pKa, the stronger the acid
- For $HA + H_2O \rightarrow H_3O^+ + A^-$,

$$K_a = \frac{[H_3O^+][A^-]}{[HA]}$$

- For every K_a, there is a K_b,
  - For $A^- + H_2O \rightarrow OH^- + HA$,

$$K_b = \frac{[OH^-][HA]}{[A^-]}$$

- Relationships:

$$K_a K_b = K_w \qquad pK_a + pK_b = 14$$

(At 25°C)

-

Conjugate acids and bases (e.g., NH4 + and NH3)

  - Stability of the conjugate base
    - H-F bond is most polar, but HF is the least acidic out of the hydrogen halides
      - due to instability of F^- - its small charge causes its negative charge to be more concentrated than that of chloride
    - When there is conflict between the three rules, look primarily at the stability of the conjugate base

Conjugate Acids and Bases

- $HA + H_2O \leftrightarrow H_3O^+ + A^-$
- A^- is the conjugate base of HA and HA is the conjugate acid of A^-
- The stronger the acid, the weaker its conjugate base
  - weak acid can have a strong or weak conjugate

Strong acids and bases (e.g., nitric, sulfuric)

Strong Acids and Bases

- Acids stronger than H_3O^+ and bases stronger than OH^-
- In water, there isn't really a difference for strong acids that are stronger than H_3O^+
  - acetic acid (a weaker base than H2O) can distinguish between stronger acids.

ABLE 7.1 › Strong Acids and Bases

Strong Acids		Strong Bases	
Hydroiodic acid	HI	Sodium hydroxide	NaOH
Hydrobromic acid	HBr	Potassium hydroxide	KOH
Hydrochloric acid	HCl	Amide ion	NH_2^-
Nitric acid	HNO_3	Hydride ion	H^-
Perchloric acid	$HClO_4$	Calcium hydroxide	$Ca(OH)_2$
Chloric acid	$HClO_3$	Sodium oxide	Na_2O
Sulfuric acid	H_2SO_4	Calcium oxide	CaO

Weak acids and bases (e.g., acetic, benzoic)

- Dissociation of weak acids and bases with or without added salt
- Hydrolysis of salts of weak acids or bases
- Calculation of pH of solutions of salts of weak acids or bases

Finding the pH

- For strong acids, since [HA] is nearly zero, there is no K_a (same goes for strong bases
- Finding the pH: since the entire concentration of acid or base is assumed to dissociate, the concentration of H_3O^+ is the same as the original concentration of acid
  - For instance, a 0.01 molar solution of HCl will have 10^{-2} , and the pH of the solution will be 2
  - A 0.01 molar solution of NaOH will have a 10^{-2} concentration of OH, and the pH of the solution will be 12
- For weak acids and bases:
  - Ex: Find the pH of 0.01 M HCN:

$$HCN + H_2O \rightleftharpoons H_3O^+ + CN^-$$

$$K_a = \frac{[H_3O^+][CN^-]}{[HCN]} = 6.2 \times 10^{-10} \qquad \frac{[x][x]}{[0.01 - x]} = 6.2 \times 10^{-10} \qquad \frac{[x][x]}{[0.01]} \approx 6.2 \times 10^{-10}$$

  - x must be less than 5% of 0.01 for us to make this exception
- $x = 2.5 \times 10^{-6}$
- $-\log (2.5 \times 10^{-6}) = 5.6$
- For weak base, find Kb, find concentration, find pOH, subtract from 14
- The pH of an acid or base can be thought of as its "natural state"
  - can be shifted away from its natural state by the addition of a base, or even a different acid
- Shortcut:
  - pH = ½ pKa – ½ log [HA]

Equilibrium constants Ka and Kb: pKa, pKb

Buffers

- Definition and concepts (common buffer systems)

Buffers

- Combinations of acids and salts that are used to keep pH of solution within a certain range
- we want to start with an acid whose pKa is close to our desired pH
  - then, mix equal amounts of that acid with its conjugate base
  - **the concentration of the buffer solution should greatly exceed the concentration of outside acid or base that could affect the pH of the solution**
- Consider a one liter buffered solution created by combining 1 M each of carbonic acid and sodium bicarbonate (pKa = 6.37)
  - if 0.01 mol HCl were added,

$$pH = 6.37 + \log\frac{[1 - 0.01]}{[1 + 0.01]}$$

  - This give pH = 6.36
- Influence on titration curves

Ions in Solutions (GC, BC)

Anion, cation: common names, formulas and charges for familiar ions (e.g., NH4 + ammonium, PO4 3– phosphate, SO4 2– sulfate)

- Polyatomic ions to know:

Nitrite	NO_2^-	Sulfate	SO_4^{2-}	Chlorate	ClO_3^-
Nitrate	NO_3^-	Hypochlorite	ClO^-	Perchlorate	ClO_4^-
Sulfite	SO_3^{2-}	Chlorite	ClO_2^-	Carbonate	CO_3^{2-}

Bicarbonate	HCO_3^-
Phosphate	PO_4^{3-}
Ammonium	NH_4^+

Hydration, the hydronium ion

Adding Salts to Water to change pH

There is a general rule in chemistry as to how salts affect solution pH. If the salt of a strong base and weak acid is dissolved in water it will form an alkaline solution, whereas, the salt of a weak base and strong acid will form an acidic solution. The salts of a strong acid and strong base or a weak acid and weak base will both form a neutral or near neutral solution. For example, sodium sulfate (Na2SO4) will form a neutral solution when dissolved in water because it is the salt of a strong base and strong acid, whereas, tri-sodium phosphate (Na3PO4) will form an alkaline solution because it is the salt of a strong base and weak acid. Sodium chloride is table salt and when it is added to water it breaks down into ions of sodium and chloride. Neither of them reacts to water so adding it to water will only change the volume, not the pH. In order for a type of salt to affect the pH it has to react with water to release or bind the hydrogen atoms from the water.

Solubility (GC)

Units of concentration (e.g., molarity)

- Several ways to measure concentration of a solution
  - molarity (M), molality (m), mole fraction (χ), mass percentage, and parts per million

$$M = \frac{\text{moles of solute}}{\text{volume of solution}} \quad m = \frac{\text{moles of solute}}{\text{kilograms of solvent}} \quad \chi = \frac{\text{moles of solute}}{\text{total moles of all solutes and solvent}}$$

$$\text{mass \%} = \frac{\text{mass of solute}}{\text{total mass of solution}} \times 100\% \quad \text{ppm} = \frac{\text{mass of solute}}{\text{total mass of solution}} \times 10^6$$

  - **Note: Parts per million is NOT the number of solute molecules per million molecules. It is the mass of the solute per mass of solution times 1 million.**
  - Another Note: solution concentrations are always given in terms of the form of the solute before dissolution
    - when 1 mol NaCl is added to 1 liter of water, the resulting solution is approximately 1 molar, NOT 2 molar, even though one mole of NaCl dissociates into two moles of ions
  - Normality measures the number of equivalents per liter of solution
    - only likely to appear in the context of an acid-base reaction
    - defined as the mass of acid or base that can donate or accept one mole of protons
      - Ex: 1 molar H_2SO_4 is called a 2 normal solution because it can donate 2 protons for each H_2SO_4 molecule
- Density of Solution
  - mass solution / volume

Solubility product constant; the equilibrium expression Ksp

Solubility

- quantifies a solute's tendency to dissolve in solvent
- reverse reaction: precipitation
- As the concentration of dissolved salt increases, the rates of dissolution and precipitation equilibrate
  - solution is saturated at this point
- Equilibrium of a solvation reaction: Solubility product K_{sp}
  - Remember that solids and pure liquids have an approximate mole fraction of one and can be excluded from the equilibrium expression
  - Ex:

$$Ba(OH)_2(s) \rightleftharpoons Ba^{2+}(aq) + 2OH^-(aq)$$
$$K_{sp} = [Ba^{2+}][OH^-]^2$$

- Solubility vs solubility product
  - Solubility – number of moles of solute per liter of solution that can be dissolved in a given solvent
  - Solubility product – used to calculate solubility of a substance in a given solvent
    - independent of ion concentrations and can be found in a reference book
- Using the Solubility Product

$$BaF_2(s) \rightleftharpoons Ba^{2+}(aq) + 2F^-(aq) \quad K_{sp} = [Ba^{2+}][F^-]^2 \quad 2.4 \times 10^{-5} = (x)(2x)^2 \quad x \approx 1.8 \times 10^{-2}$$

  - 1.8×10^{-2} mol/L is the solubility of BaF_2 in one liter of water at 25°C
  - To determine S for an ion, multiply S (that is, x) by its coefficient
    - **The solubility of Fluorine is 2x**
- What is the molar solubility, given the Ksp?
  - MX --> x^2
  - MX_2 --> $4x^3$
  - MX_3 --> $27x^4$
  - What is molar solubility? - x

Common-ion effect, its use in laboratory separations

- Complex ion formation
- Adding other ions (NaF)
  - spectator ions: not included in the equilibrium expression, so they would have no effect on the equilibrium

        - Ex (still using BaF ex above: Na^+
    - Common ion effect – disturbance of equilibrium by adding ion in common with an ion in equilibrium expression
        - adding F – decreases solubility of BaF_2
        - A common ion added to a saturated solution shifts the equilibrium
            - if added to a solution that is not saturated, it does not shirt the equilibrium
        - Determining the extent of the shift

$$2.4 \times 10^{-5} = (x)(2x + 1)^2$$

        - Simplification:

$$2.4 \times 10^{-5} \approx (x)(1)^2$$
$$x \approx 2.4 \times 10^{-5}$$

-
- Complex ions and solubility

Key Points

- A complex ion is an ion comprising one or more ligands attached to a central metal cation (typically a transition metal) with a dative covalent bond.
- The number of lone pairs of electrons which a cation can accept is known as the **coordination number** of the cation.
- The equilibrium constant of a complex ion can be determined by monitoring a change of color that typically takes place during formation of a complex ion.
- **Formation of a complex ion can increase the solubility of a salt.**

Key Terms

- **ion product constant for water**: The result of multiplying the concentration of hydroxide times the concentration of hydronium ion, typically equal to 10−14.
- **formation constant**: A measure of the strength of the interaction between the reagents that come together to form the complex.
- **Dative bond**: Two-center, 2-electron covalent bond in which the two electrons derive from the same atom.
- **ligand**: An ion, molecule, or functional group that binds to another chemical entity to form a larger complex.
- **coordination number**: In chemistry and crystallography*, the number of ligands surrounding a central metal atom in a coordination compound.*

Complex Ion Formation and Solubility

Formation of a chemical complex has an effect on solubility. A well-known example is the addition of a concentrated solution of ammonia (NH_3) to a suspension of silver chloride (AgCl), in which dissolution is favored by the formation of an ammine (NH_3) complex.

AgCl(s)+2NH3(aq)→[Ag(NH3)2]+(aq)+Cl−(aq)AgCl(s)+2NH3(aq)→[Ag(NH3)2]+(aq)+Cl−(aq)

The equilibrium constant for this reaction is:

Kc=[Ag(NH3)+2][Cl−][NH3]2Kc=[Ag(NH3)2+][Cl−][NH3]2

This equation shows that as the ammonia forms a complex with the AgCl, more of the solid will dissolve as the reaction proceeds toward the products. This will increase the solubility of AgCl in solution.

- Solubility and pH
    - $[H^+]$ can be a common ion

Titration (GC)

Indicators

Indicators and the Endpoint

- Indicator is usually a weak acid whose conjugate base is a different color
- In order for the human eye to detect a color change, the new form of the indicator *must reach 1/10 of the concentration* of the original form

$$pH = pK_a + \log\frac{[In^-]}{[HIn]}$$

$$\text{lower range of color change} \Rightarrow \quad pH = pK_a + \log\frac{1}{10} \Rightarrow pH = pK_a - 1$$

$$\text{upper range of color change} \Rightarrow \quad pH = pK_a + \log\frac{10}{1} \Rightarrow pH = pK_a + 1$$

- The point where the indicator changes color is called the endpoint (not equivalence)
- If asked which indicator to use for a titration, you should choose an indicator with a pKa as close as possible to the pH of the titration's equivalence point

Note that indicator papers turn color as pH goes higher. If an indicator has a range of color change from orange to red from the pH of 4.4-4.8, that means that if it turns red, the pH may be higher than 4.8

Neutralization

Neutralization

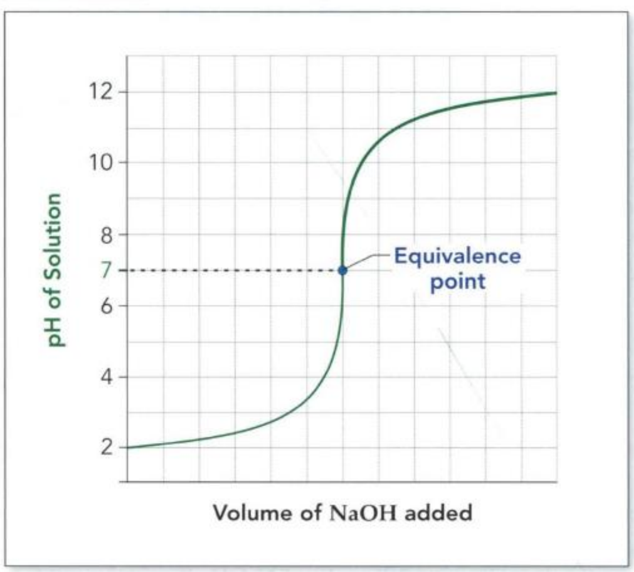
- Acid + Base → Water + Salt
  - HCl + NaOH → NaCl and H_2O
- Are typically highly exothermic
  - Since $K_w = 10^{-14}$, the reverse reaction (neutralization) will have $1/K_w = 10^{14}$
- We can use $\Delta G = -RT \ln(K)$ to solve for free energy

Interpretation of the titration curves

Titration curves

- Suppose a 1 L aqueous solution contains 0.01 moles of HCl. Theoretically, the addition of 0.01 moles of NaOH all at once would cause the neutralization reaction to occur and run to completion, and the pH of the resulting solution would be 7
- If the base were added slowly? – Titration
- Performed for one of two reasons:
  - Find the concentration of a substance by comparing it with the known concentration of the titrant
  - Find the pKa or pKb of an acid or base

FIGURE 7.9 Titration of Strong Acid with Strong Base

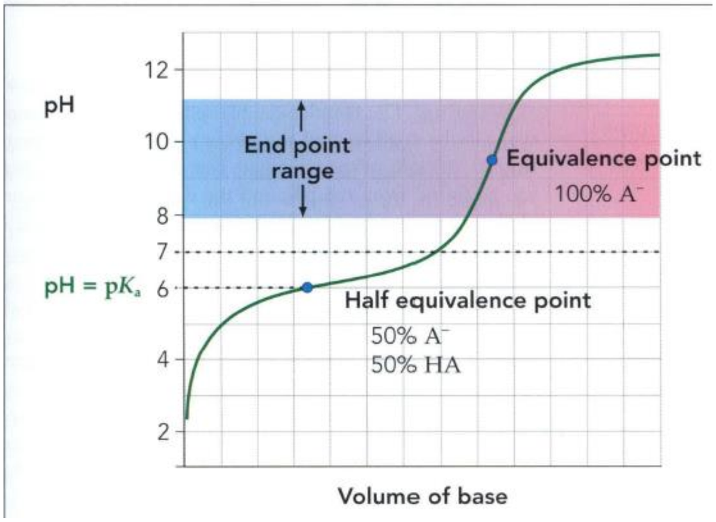


- equivalence point – there are equal equivalents of acid and base in solution

Weak Acid –Strong Base

- The main difference with strong-acid-base titration is that the degree of protonation will differ based on what the pH is
- Equivalence point will be above 7
- At equivalence point, there will be a molecule of strong base for every molecule of weak acid

FIGURE 7.10 Titration of Weak Acid with Strong Base



- Half equivalence point: exactly one half of the acid has been neutralized by the base
- the concentration of the acid is equal to the concentration of its conjugate base
  - spot where the largest amount of base or acid could be added with the least amount of change in pH
- Henderson-Hasselbalch equation:

$$pH = pK_a + \log\frac{[A^-]}{[HA]}$$

  - Cannot typically be used to find the pH at the equivalence point. Instead, the pK_b of the conjugate base must be used

Finding the pH at the equivalence point is a good exercise, even though you probably won't have to do it on the MCAT®. Here are the steps:

Use K_a and K_w to find the K_b. $$K_b = \frac{K_w}{K_a}$$

Set up the K_b equilibrium expression. $$K_b = \frac{[OH^-][HA]}{[A^-]}$$

Solve for the OH^- concentration, and find the pOH.

Subtract the pOH from 14 to find the pH.

$$14 - pOH = pH$$

  - concentration of the conjugate base at the equivalence point is equal to the number of moles of acid divided by the volume of acid plus the volume of base used to titrate

Weak Acid-Weak Base

- Proceeds similarly to a weak acid-strong base titration
- one major difference in the titration curve is that he range of pH is compressed
  - there are no strong acids or bases, so it is impossible to reach the extreme pH values
  - as a result, it is more difficult to identify where the equivalence point lies because the change in pH is less pronounced
- If the acid is stronger than the base, the equivalence point will fall at pH of below 7, and if the base is stronger than the acid, the pH will be greater than 7 at the equivalence point

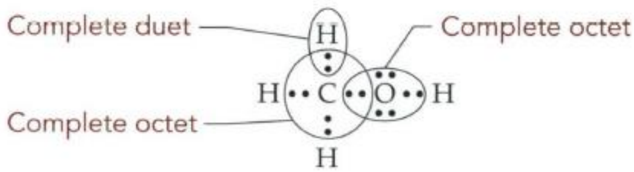
Redox titration

Content Category 5B: Nature of molecules and intermolecular interactions

Covalent Bond (GC)

Lewis Electron Dot formulas

- Resonance structures
- Formal charge
- Lewis acids and bases
- Lewis structure – valence electrons



The Lewis Structure for methanol with 14 valence electrons

  - 3 rules
    - Find total number of valence electrons for all atoms in the molecule
    - Use on pair of electrons to form a single bond between each pair of atoms
    - arrange the remaining electrons in lone pairs and double or triple bonds to satisfy octet rule
  - Exceptions:
    - boron and Beryllium do not contain full octets
    - Atoms from the third period or higher may be able to hold more than 8 valence electrons
- Lewis structure can be used to determine the formal charge of an atom
  - (# of valence electrons) – [(# of bonds) + (# of nonbonding electrons)]
    - double bond = 2, triple bond = 3
  - the sum of the formal charges for each atom represents the total charge on the molecule or ion
    - however, the formal charge on a given atom does not represent an actual charge on that atom

Partial ionic character

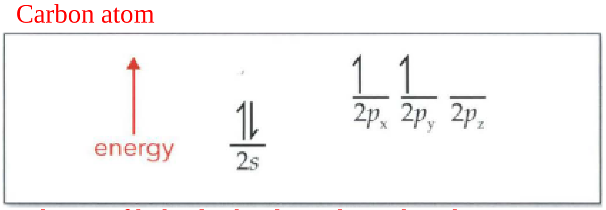
- Role of electronegativity in determining charge distribution
- Dipole Moment

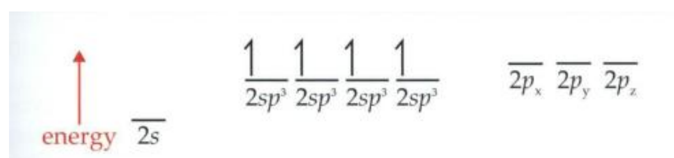
σ and π bonds

- Hybrid orbitals: sp3 , sp2 , sp and respective geometries

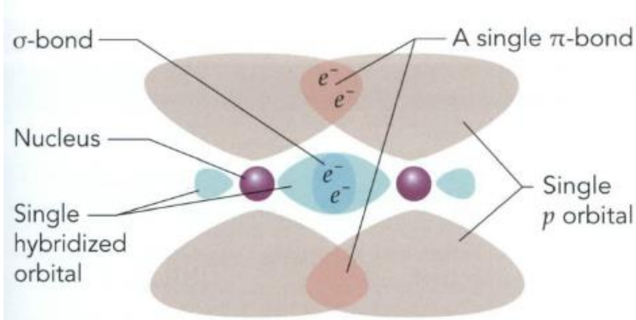
Hybridization

- Carbon atom





- Theory of hybrid orbitals explains this phenomenon
  - σ- bond is formed in the area where the hybrid orbitals of two atoms overlap
  - π - bonds are formed by the overlap of pure p orbitals

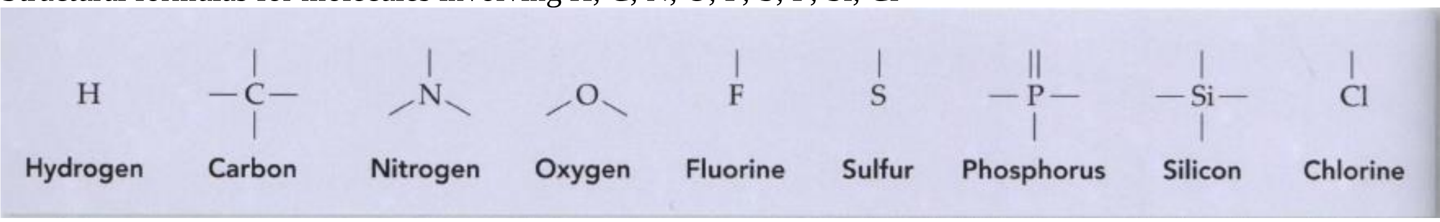


- To determine the type of hybridization (sp, sp^2, sp^3), count the number of sigma bonds and lone pairs of electrons on the atom
  - Ex: Oxygen on H_2O makes two sigma bonds and two lone pairs of electrons
    - the oxygen atom must have four hybrid orbitals, or sp^3 hybridization
- sp hybrid orbital has 50% s character and 50 % p character

- VSEPR

Hybridization	Bond angles	Shape	Example
sp	180°	Linear	Ethyne C_2H_2
sp^2	120°	Trigonal planar	The carboxylic acid part of acetic acid CH_3COOH
sp^3	109.5°	Tetrahedral, pyramidal, or bent	Methane CH_4, ammonia NH_3, water H_2O
sp^3d	90°, 120°	Trigonal-bipyramidal, see-saw, t-shaped or linear	Phosphorus pentachloride
sp^3d^2	90°, 90°	Octahedral, square pyramidal, or square planar	Sulfur hexaflouride

  - Lone pairs and pi electrons require more room than bonding pairs, which means that they can distort the predicted bond angles (as can ring strain)
- While the bond-dissociation energy is the energy of a single chemical bond, *bond energy is the average of all the bond-dissociation energies of the bonds in a molecule*
  - both correlate positively to bond strength
- Valence shell electron pair repulsion and the prediction of shapes of molecules (e.g., NH3, H2O, CO2)
- Structural formulas for molecules involving H, C, N, O, F, S, P, Si, Cl



- Delocalized electrons and resonance in ions and molecules

Resonance and Electron Delocalization

- Delocalized electrons – bonding electrons that are spread out over *three or more atoms*
  - *only result from pi-bonds and lone pairs*
  - can be represented by resonance structures
- Resonance energy – difference between the energy of the real molecule and the energy of the most stable Lewis structure
- Resonance structure rules:
  - Atoms must not be moved
  - Number of unpaired electrons must remain the same
  - Resonance atoms must lie in the same plane
- The contribution made to the actual molecule by any given structure is roughly proportional to that structure's stability
  - the most stable structure has the lower formal charges on most atoms
    - separation of charges within a molecule also decreases stability
- Two conditions must be present for resonance to occur:
  - species must contain an atom with either a p orbital or an unshared pair of electrons
  - that atom must be single bonded to an atom that possesses a double or triple bond
    - the adjacent p-orbital in a conjugated system may contain zero, one, or two electrons
    - the p-orbital allows the adjacent pi bond from the double or triple bond to extend and encompass more than two nuclei
- Aromaticity – increased stability of a cyclic molecule due to electron delocalization (resonance)
  - must be cyclic, planar, and follow Huckel's rule ($4n + 2$ π electrons)

Multiple bonding

- Effect on bond length and bond energies
- Rigidity in molecular structure

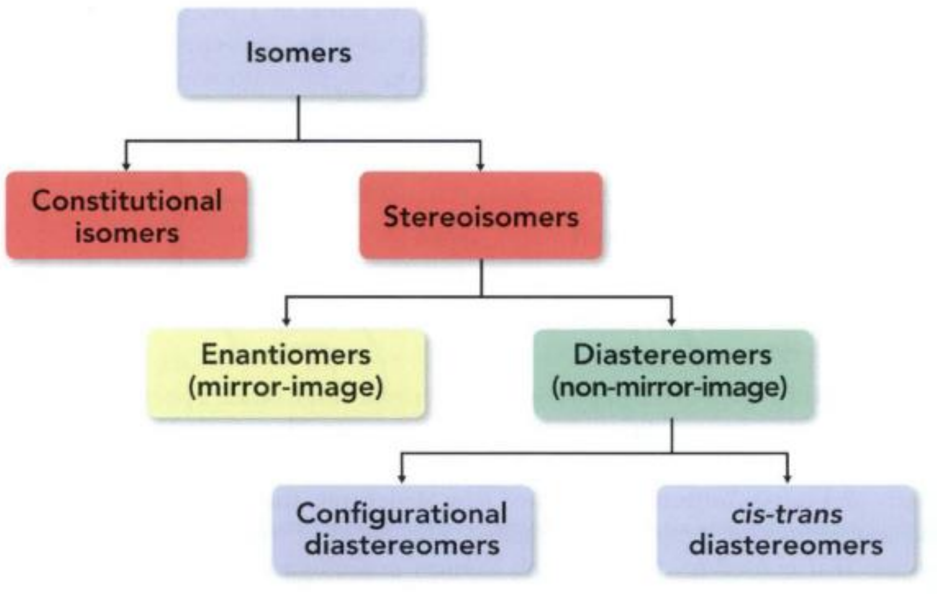
Bonds

- σ bond (sigma bond) forms when the bonding pair of electrons are localized to the space directly between the two bonding atoms
  - the electrons in this bond are as close as possible to the two nuclei

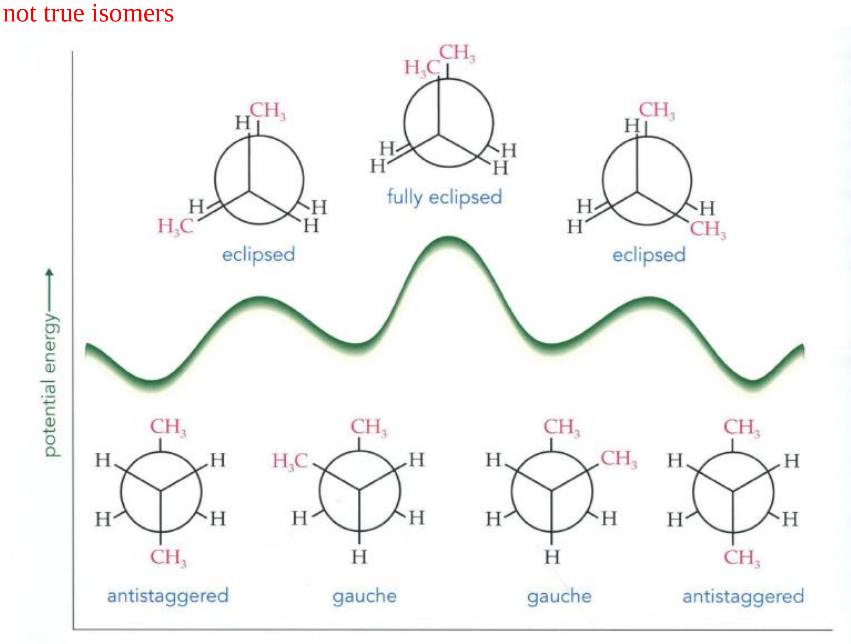
    - lowest energy, strongest, most stable type of covalent bond
    - always the first type of covalent bond to be formed between two atoms
- π bond (pi bond) – created by overlapping p orbitals
    - Double and triple bonds are made by adding pi bonds to a sigma bond
        - the first pi bond forms above and below the sigma bonding electrons, forming a double bond
            - double bond = π bond + σ bond
            - triple bond = 2 π bonds + σ bond
    - π bond itself is weaker than a σ bond, but π bonds are always added to an existing σ bond, strengthening the overall bond
    - shorten the overall bond length
        - triple > double > single
- Atoms bound by a single bond can rotate freely around the bond, changing the overall shape of the molecule
    - when pi bonds are present, free rotation is no longer possible
    - introduces rigidity in molecular structure

Stereochemistry of covalently bonded molecules (OC)

- Isomers
    - Structural isomers
- Isomers – unique molecules that share the same molecular formula
    - Structural – different connectivity
    - Stereoisomers (e.g., diastereomers, enantiomers, cis/trans isomers)
    - Stereoisomers – same molecular formula and connectivity
        - enantiomers and diastereomers
            - enantiomers – non-superimposable mirror images
                - chiral molecules – have “handedness”
                    - bonded to four different substituents
                - only differ in their reactivities to chiral molecules.
- Diastereomers
    - same molecular formula and connectivity, but are not mirror images
        - have multiple chiral centers
    - **differ in physical properties**
    - *can be salts*
    - Meso compound – has multiple chiral centers, but is optically inactive
        - plane of symmetry through their center
        - achiral
        - *does not rotate ppL*
    - Epimers – diasteroemers that differ in configuration at only one chiral carbon
        - still aren’t mirror images
        - Anomers – cyclic diastereomers that are formed when a ring closure occurs at an epimeric carbon
            - (glucose: alpha and Beta anomers)
    - Cis-trans isomers (geometric isomers) – *special type of diastereomer* that exist due to hindered rotation created by multiple bonds or a ring structure
        - have different physical properties
        - cis – have dipole moment, stronger intermolecular forces, higher boiling points
            - lower melting points due to difficulty in forming crystals
            - steric hindrance in cis-molecules raises their energy levels, decreasing stability
        - E/Z
            - Zame Zide



- Conformational isomers
- Conformational – different spatial orientations of the same molecule
  - not true isomers



- Polarization of light, specific rotation
- Observed Rotation
  - R and S enantiomers differ in their rotation of plane-polarized light
  - knowing the absolute configuration of the molecule does not indicate the direction in which each configuration rotates the light
    - *must be determined through experiment*
  - Chiral molecules are optically active
    - if the compound rotates pp-light clockwise, it is "+" or "d"
    - If the compound rotates pp-light counterclockwise, it is "-" or "l"
  - Specific rotation – standardized form of observed rotation that is calculated from the observed rotation and experimental parameters
  - *Except for interactions with plane-polarized light and reactions with other chiral compounds, enantiomers have the same physical and chemical properties*
- racemic mixture – enantiomers mixed together in equal concentrations
- does not rotate pp-light

- Absolute and relative configuration
    - chiral molecules – have "handedness"
        - bonded to four different substituents
        - R and S – absolute configuration
            - when the lowest priority group is oriented into the page, a circle drawn with a clockwise motion is R, counterclockwise is S
    - **Relative configuration** – two molecules have the same relative configuration about a chiral carbon if they differ by only one substituent and the other substituents are oriented identically about the carbon
-
    - Conventions for writing R and S forms
    - Conventions for writing E and Z forms

Liquid Phase - Intermolecular Forces (GC)

Hydrogen bonding - improves water solubility

Dipole Interactions

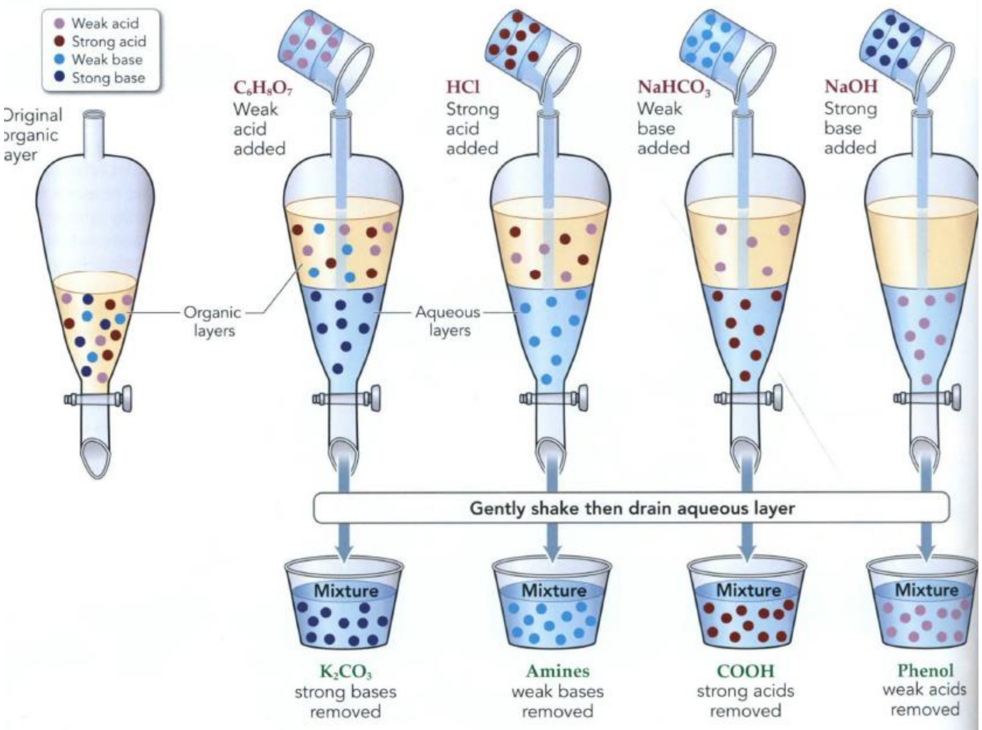
Van der Waals' Forces (London dispersion forces)

Content Category 5C: Separation and Purification Methods

Separations and Purifications (OC, BC)

Extraction: distribution of solute between two immiscible solvents

- Extraction
    - based on solubility
    - involves two immiscible phases, most commonly an aqueous layer and a less dense organic layer



- weak acid protonates strong bases, making them polar and causing them to move to the aqueous layer
- strong acid protonates remaining weak bases
- weak base deprotonates only strong acids
- strong base reacts with any remaining weak acid

- Two layers, aqueous and organic
    - aqueous – charged molecules
        - how to make molecules charged? Add acids and bases
            - phenols – add NaOH, (quench with NaOH)
- Note: aqueous phase will not always be more dense than organic

- Also, some water molecules can seep into organic phase and surround organic molecules. Drying agents (inorganic anhydrous salts) can remove these water molecule

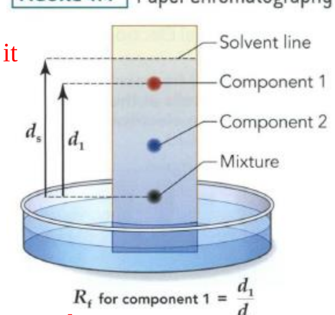
Distillation

- Distillation
    - based on boiling points (at least 20° C)
    - compound with lower boiling point will boil off first and can be captured and condensed in a cool tube
    - Fractional distillation – more precise method of distillation
        - vapor is run through glass beads, allowing compound with higher boiling point to repeatedly condense and fall back into the solution
    - Cannot completely separate two compounds
- Vacuum – lowers pressure, makes it easy to vaporize
-

Chromatography: Basic principles involved in separation process

- Column chromatography
- Chromatography
    - can be used to purify a compound from a mixture and/or to identify the ratio of compounds in a mixture
    - separation of a mixture by passing it over through a matrix that adsorbs different compounds more or less strongly according to their properties
        - matrix surface – stationary phase, mixture dissolved in solution is mobile phase
            - Mobile phase may be benzene, stationary phase may be silica gel (polar)
            - polar phase will have higher Rf and longer eluting time
        - typically, stationary phase is polar, causing more polar compounds to elute more slowly
    - column chromatography
        - solution containing mixture dripped down a column containing the solid phase
    - Gas-liquid chromatography
    - Gas-liquid chromatography
        - liquid phase is the stationary phase
        - mixture is dissolved into a heated carrier gas (usually helium or nitrogen)
            - passed over a liquid phase bound to a column
            - compounds in mixture equilibrate with the liquid phase at different rates, pass through exit ports as individual components
    - High pressure liquid chromatography
- Paper chromatography
    - paper chromatography
        - small portion of sample to be separated is spotted onto paper
        - the end of paper placed into a non-polar solvent
        - solvent moves up the paper and dissolves the sample as it passes over it
        - most polar near the bottom, least polar near the top
        - Rf factor
            - lower for polar, higher for nonpolar

FIGURE 4.4 Paper Chromatography



- Thin-layer chromatography
    - Thin-layer chromatography
        - similar to paper except that a coated glass plate is used
- Separation and purification of peptides and proteins (BC)
- Specific activity is a measure of enzyme purity and is quoted as units/mg. The value becomes larger as an enzyme preparation becomes purer since the amount of protein (mg) is typically less, but the rate of reaction stays the same (or may increase due to reduced interference or removal of inhibitors
- Activity units provide the best measurement of yield. The total number of activity units is equal to specific activity (units / mg) x total protein (mg)
- Electrophoresis
    - gel electrophoresis
        - nucleic acids are negatively charged, migrate through gel
        - larger particles move more slowly
        - Proteins are separated by a different type of gel
            - usually denatured in the presence of a detergent before they are placed in the gel
            - detergent coats each protein with negative charge proportional to its length
            - proteins can also be separated based on isoelectric points
        - Ladder – mixture of DNA, RNA , or polypeptide fragments of known sizes or quantities

            - used for comparison
    - Blotting – after gel electrophoresis, for visualization purposes
        - molecules transferred from gel onto membrane, allowing for easier manipulation or visualization
        - Southern Blotting – target fragments of known DNA sequence in a large population of DNA
            - gel placed in basic solution to denature DNA fragments (double to single strand)
            - nitrocellulose placed on top or below gel, transferred to this membrane
            - labeled probe with complementary nucleotide sequence is added
            - visualize
        - Northern Blot – identifies RNA fragments
        - Western blot – detect a particular protein in a mixture of proteins
            - visualization usually occurs through antibodies
                - primary antibody specific to protein in question used first
                - secondary antibody-enzyme conjugate added
                    - recognizes and binds the primary antibody and marks it with an enzyme for visualization
                    - reaction catalyzed by enzyme attached to the secondary antibody produces color or something
    - Agarose – for bigger fragments of DNA
    - SDS page – small DNA or protein
    -
-
- Quantitative analysis
- Chromatography
    - Size-exclusion
    - Ion-exchange
    - Affinity
        - size-exclusion chromatography – separation by size and weight, often thru gel filtration
            - interestingly, smaller takes longer
        - ion-exchange chromatography – separation based on net surface charge
            - utilizes cationic or anionic "exchangers" that slow down the movement of charged molecules
            - cationic exchange column binds cations, anionic exchange column binds anions
        - affinity chromatography – uses highly specific interactions to slow down select molecules
            - can make use of receptor-ligand, enzyme-substrate, and antigen-antibody
        - Histidine tagging is where you modify primary sequence by adding 6 or more histidines to the end. Nickel column has an affinity to a histidine tag. Affinity chromatography is specific interactions occurring between the column and target, such as antibody + antigen, or magnetic + iron. Ni^{2+} will coordinate with two molecules of histidine.
            - As a note: Chelation is when an ion or molecule will bind through coordinate bonds to a metallic ion. Takes it out of solution, effectively
    -

Racemic mixtures, separation of enantiomers (OC)

- Separation of enantiomers from a racemic mixture
    - chiral resolution – 3 ways
        - Use *differences in crystallization* of the enantiomers
        - add stereospecific enzymes that will only react with one enantiomer
        - convert to diastereomers

Content Category 5D: Structure, function, and reactivity of biologically relevant molecules

Nucleotides and Nucleic Acids (BC, BIO)

Nucleotides and nucleosides: composition

- Sugar phosphate backbone
- These are made up of phosphodiester bonds
- Pyrimidine, purine residues

Deoxyribonucleic acid: DNA; double helix

Chemistry (BC)

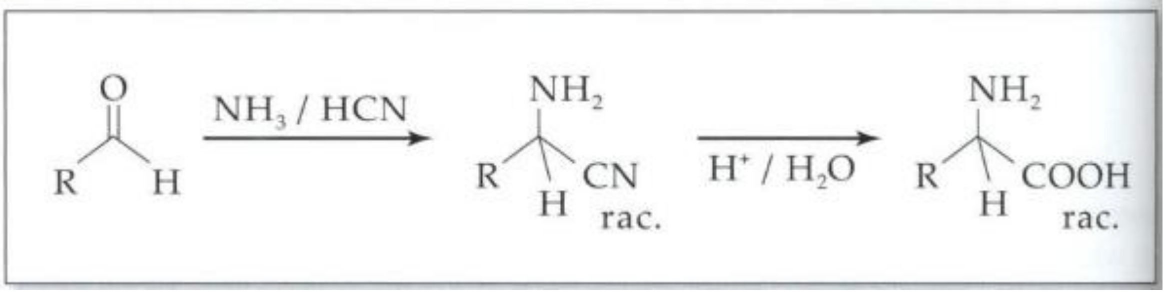
Other functions (BC)

Amino Acids, Peptides, Proteins (OC, BC)

Amino acids: description

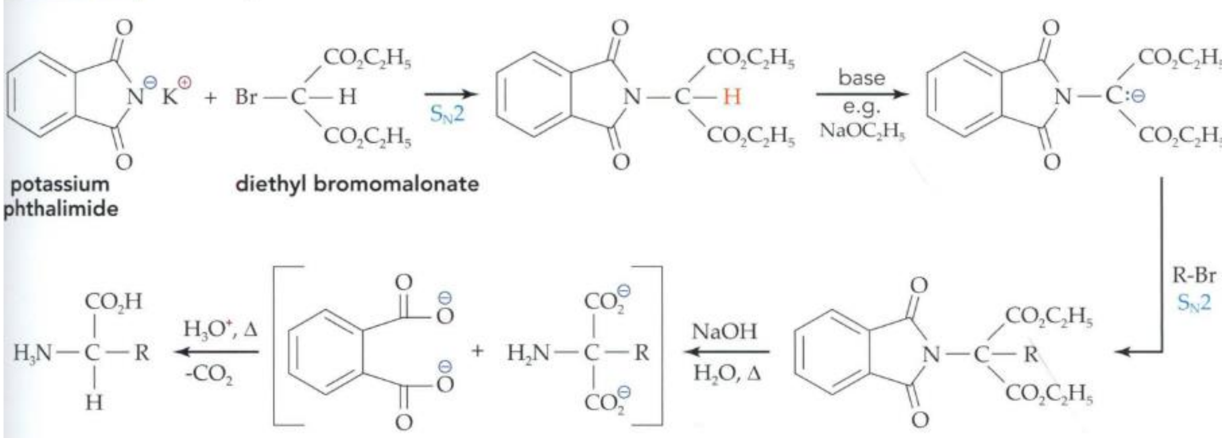
- Absolute configuration at the α position
- Dipolar ions
- Classification
  - Acidic or basic
  - Hydrophilic or hydrophobic
- Synthesis of α-amino acids (OC)
  - Strecker Synthesis - starts with aldehyde

FIGURE 3.52 Strecker Synthesis



  - Gabriel Synthesis

FIGURE 3.51 Gabriel Synthesis



Peptides and proteins: reactions

- Sulfur linkage for cysteine and cystine
- Peptide linkage: polypeptides and proteins
- Hydrolysis (BC)

General Principles

- Primary structure of proteins
- Secondary structure of proteins
- Tertiary structure of proteins
- Isoelectric point

The Three-Dimensional Protein Structure (BC)

Conformational stability

Hydrophobic interactions

Solvation layer (entropy)

Quaternary structure

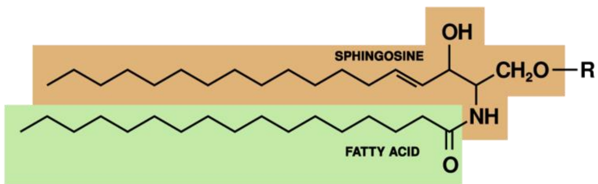
Denaturing and Folding

Non-Enzymatic Protein Function (BC)

Binding

Immune system
Motor

Lipids (BC, OC)
Description, Types

- Storage
  - Triacyl glycerols
  - Free fatty acids: saponification
  - Soaps are sodium or potassium salts of long chain fatty acids. When triglycerides in fat/oil react with aqueous NaOH or KOH, they are converted into soap and glycerol. This is called alkaline hydrolysis of esters. Since this reaction leads to the formation of soap, it is called the **Saponification** process.
- Structural
  - Phospholipids and phosphatids
  - Sphingolipids (BC)
  - 

  - Waxes - esters
- Signals/cofactors
  - Fat-soluble vitamins
  - ADEK
  - Steroids
  - Prostaglandins (BC)
  - The **prostaglandins** (**PG**) are a group of physiologically active lipid compounds having diverse hormone-like effects in animals. Prostaglandins have been found in almost every tissue in humans and other animals. They are derived enzymatically from fatty acids. Every prostaglandin contains 20 carbon atoms, including a 5-carbon ring. They are a subclass of eicosanoids and of the prostanoid class of fatty acid derivatives.
  - They act as autocrine or paracrine factors with their target cells present in the immediate vicinity of the site of their secretion. Prostaglandins differ from endocrine hormones in that they are not produced at a specific site but in many places throughout the human body.

Carbohydrates (OC)
Description

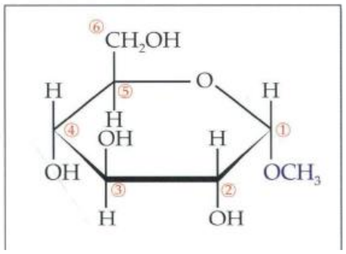
- Nomenclature and classification, common names
- Absolute configuration
- Cyclic structure and conformations of hexoses
- Epimers and anomers

Bonding and Reactions of Biological Molecules

- Glucose is an aldohexose
- Alpha and Beta-glucose
  - Alpha – OH pointed down
- Furanose – 5, pyranose – 6 membered ring

- Sugars formed when a sugar is attacked by an alcohol to create an acetal are given names that end in –oside

Methyl α-glucopyranoside



- Sucrose: 1,1' glycosidic linkage: glucose and fructose This linkage is alpha with respect to glucose and beta with respect to fructose. It is more accurately called a 1,2' linkage because the anomeric carbon on fructose is numbered 2, not 1 like glucose.
- Maltose: α–1,4' glycosidic linkage: two glucose molecules
- Lactose: β–1,4' galactosidic linkage: galactose and glucose
- Cellulose: β–1,4' glycosidic linkage: a chain of glucose molecules
- Amylose (Starch): α–1,4' glycosidic linkage: a chain of glucose molecules
- Amylopectin: α–1,4' glycosidic linkage: a branched chain of glucose molecules with α–1,6' glucosidic linkages forming the branches
- Glycogen: α–1,4' glycosidic linkage: a branched chain of glucose molecules with α–1,6' glucosidic linkages forming the branches

-
- Humans don't possess enzymes for B-1,4
- Reducing sugars are either hemiacetals in their ring form or ketones or aldehydes in straight-chain form
  - acetals do not open easily because they contain blocking groups
  - Reducing sugars pass the Tollens test and form silver

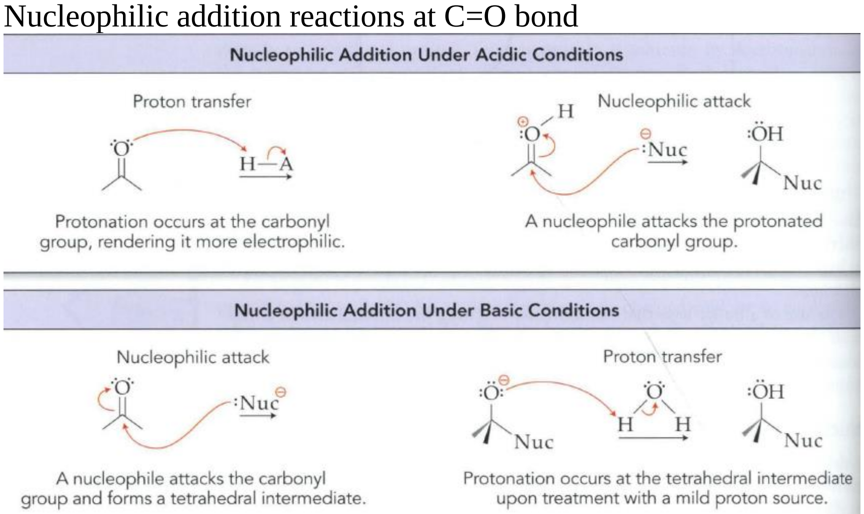
Hydrolysis of the glycoside linkage
Keto-enol tautomerism of monosaccharides
Disaccharides (BC)
Polysaccharides (BC)

Aldehydes and Ketones (OC)
Description

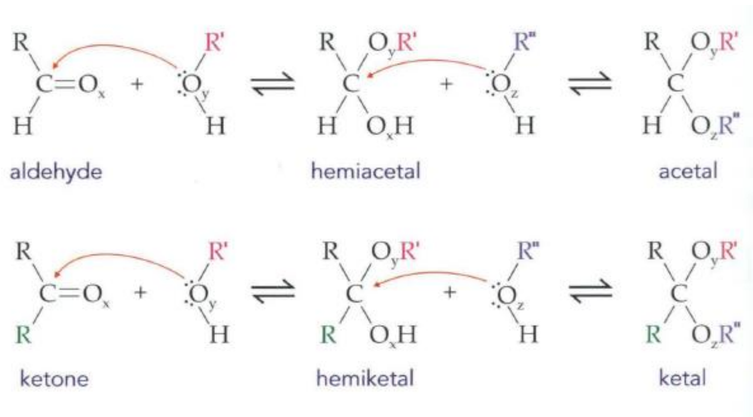
- Nomenclature
- Two of the most reactive carbonyls
  - *carbonyls are better electron withdrawing groups than OH*
- no leaving group
- Ketones: indicated by the ending –one
- Aldehydes: indicated by the ending –al
- Physical properties
- Aldehydes and ketones are more polar and have higher boiling points than alkanes of similar molecular weight
  - cannot h-bond, so have lower boiling points than corresponding alcohols
  - are soluble in water up to four carbons

Important reactions

- Nucleophilic addition reactions at C=O bond

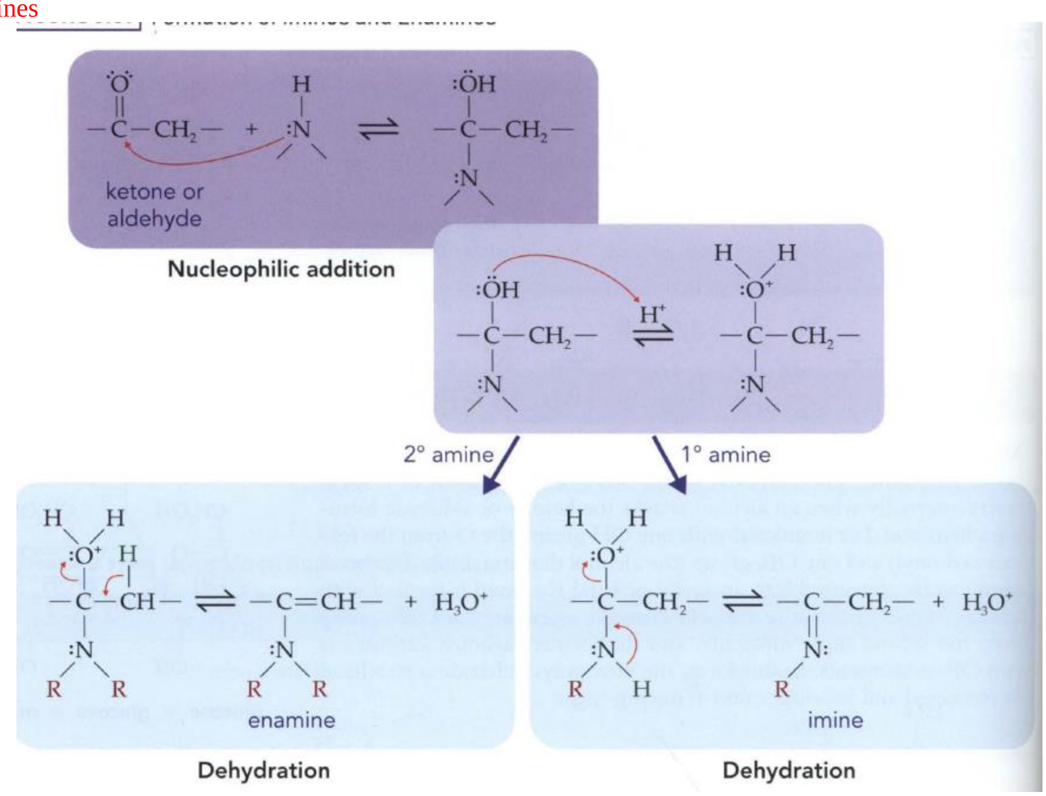


- Acetal, hemiacetal



-
- Acetals can be used for protection
- Monosaccharides are examples of hemiacetals and hemiketals that occur in nature
  - hemi form achieved when internal alcohol attacks ketone/aldehyde
  - hemi form can be converted into an acetal or ketal if a bond is formed with another sugar
- Distinguishing
  - Hemiacetals and acetals have lone hydrogen attached to former carbonyl carbon (ketals don't)
  - Both hemi products have an OH, while both full acetals and ketals have two –OR groups
- **The reaction will stop at the hemi form in base-catalyzed conditions**
- Imine, enamine

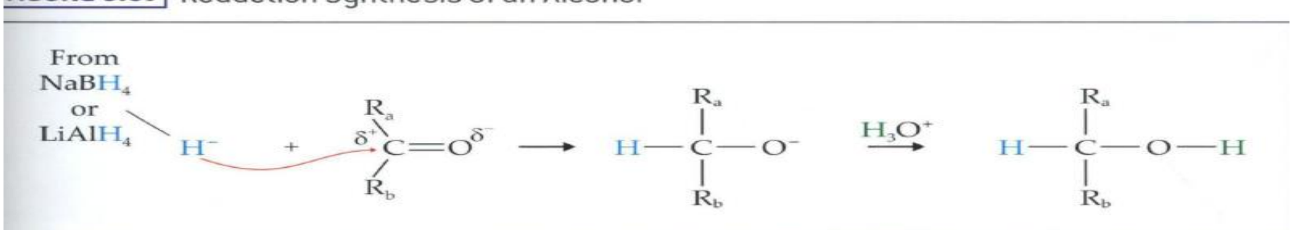
Imines and Enamines



- The tautomer of an imine is an enamine, although this can only happen when the original amine is primary
- **Enamines – not as stable due to the electron-withdrawing nitrogen of the pi bond**
  - more stable than enols, as nitrogen is less electron withdrawing than oxygen
- Hydride reagents

Hydride reagents

FIGURE 3.39 Reduction Synthesis of an Alcohol



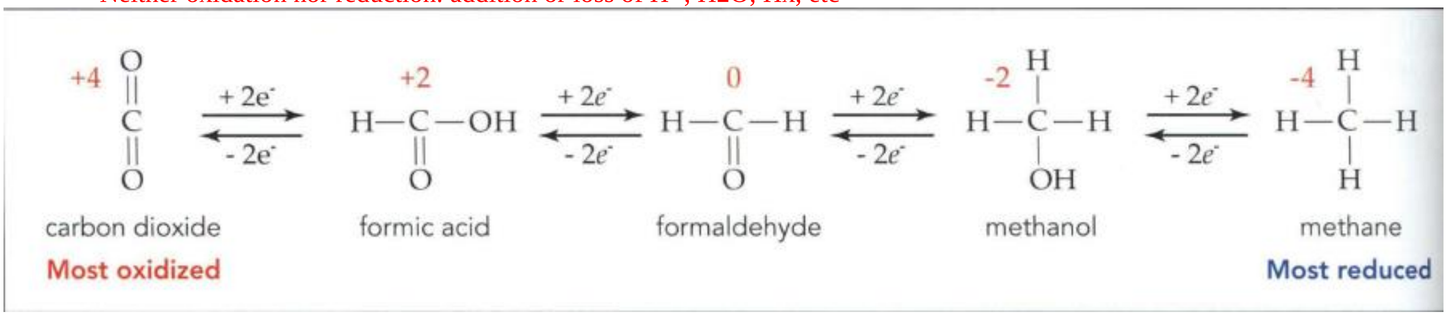
- H- is such a strong base that it is too unstable to exist in isolation
- **Only LAH is strong enough to reduce carboxylic acids and esters and acetates**
- **Both NaBH4 and LAH can reduce ketones and aldehydes**
- Cyanohydrin

Cyanohydrins – (CN^-)

- nucleophiles that produce cyanohydrins (nitrile and alcohol attached to the same carbon)
  - **when exposed to acid and water, converted to a carboxylic acid**
- Oxidation of aldehydes

Oxidation and Reduction of Oxygen Containing Compounds

- Oxidation – increase in bonds to oxygen or halogen, loss of C-H bonds
- Reduction – increase in bonds to hydrogen or R groups, loss of bonds to oxygen or halogen
- Neither oxidation nor reduction: addition or loss of H+, H2O, Hx, etc



- Carboxylic acids and their derivatives are usually reduced first to aldehydes, then to alcohols
  - alcohols converted to alkenes through dehydration
  - fully reduced when it becomes an alkane
- **Primary alcohols oxidize to aldehydes, which in turn, oxidize to carboxylic acids**
- **secondary alcohols oxidize to ketones**
- **tertiary alcohols cannot be oxidized**
- Two equivalents of LAH can be used to reduce carboxylic acids and their derivatives *to alcohols*
  - Reduction of ketones and aldehydes requires only a single portion of LAH, or NaBH4

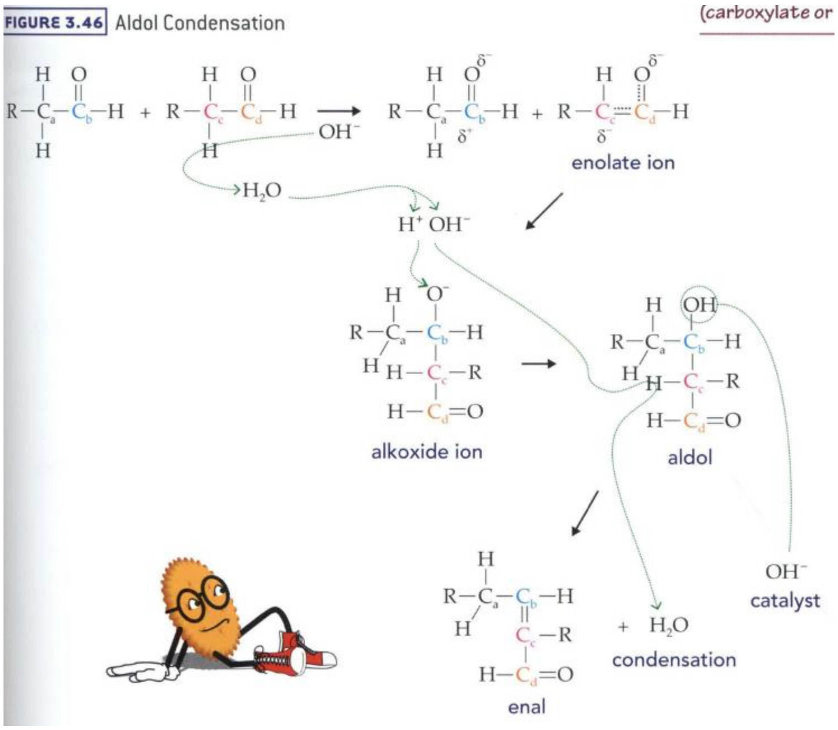
TABLE 3.1 › Oxidizing and Reducing Agents

Oxidizing Agents	Reducing Agents
$K_2Cr_2O_7$	$LiAlH_4$
K_2MnO_4	$NaBH_4$
H_2CrO_4	H_2 + pressure
O_2	
PCC	

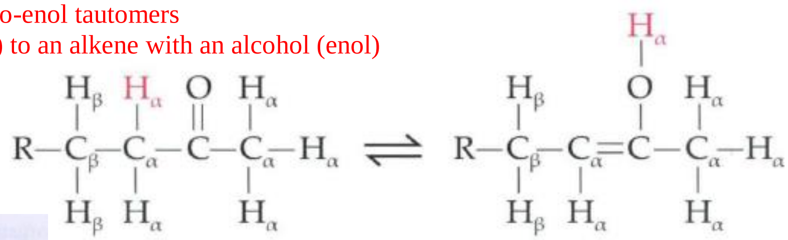
-
- PCC is a gentler oxidizing agent that will oxidize primary alcohols to aldehydes and secondary alcohols to ketones
- **the other will oxidize alcohols all the way to carboxylic acids**
  - **oxidation goes all the way, reduction doesn't**
- Reactions at adjacent positions: enolate chemistry

Carbonyls as Nucleophiles: Aldol Condensation

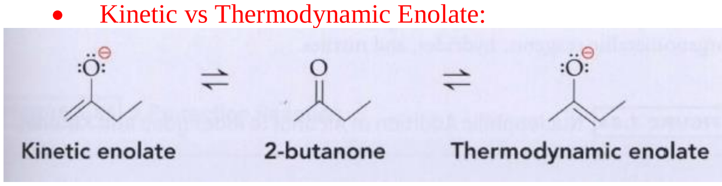
- Carbonyl nucleophile attacks another carbonyl
- alpha carbon acts as a nucleophile
- can be catalyzed with an acid or base
  - base: removal of alpha-hydrogen, leaving enolate ion
  - **aldols** are unstable and are easily dehydrated by heat or a base to become an **enal**
- Keto-enol tautomerism (α-racemization) Aldol condensation, retro-aldol



- Kinetic versus thermodynamic enolate
- Ketones and aldehydes eist at room temperature as keto-enol tautomers
  - tautomerization – shift from a carbonyl (keto) to an alkene with an alcohol (enol)
  - *keto is more stable than enol*
  - enolate – negatively charged enol
    - can act as nucleophiles
    - formed in basic conditions



- Kinetic vs Thermodynamic Enolate:



- Kinetic reaction has lower Ea but forms less stable product
  - favored by use of a bulky base or *low temperatures*
- Thermodynamic reaction has a higher Ea, but forms a more stable product

General principles

- Effect of substituents on reactivity of C=O; steric hindrance
- **Aldehydes** are usually **more reactive** toward nucleophilic substitutions **than ketones** because of both steric and electronic effects. In **aldehydes**, the relatively small hydrogen atom is attached to one side of the carbonyl group, while a larger R group is affixed to the other side.
- Acidity of α-H; carbanions

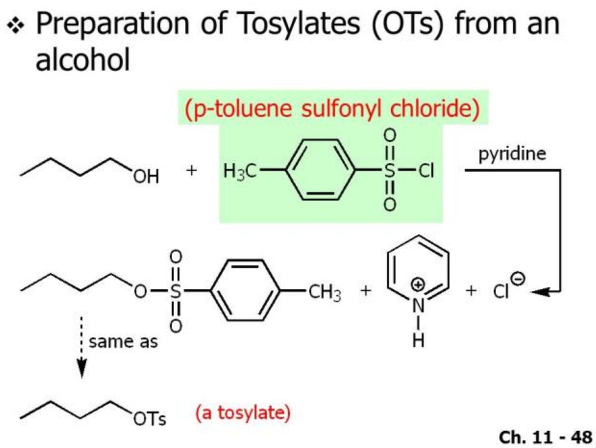
Alcohols (OC)

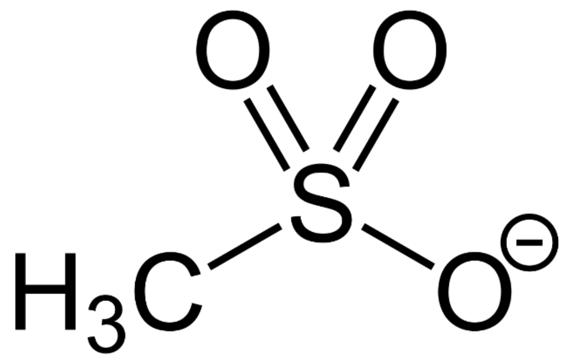
Description

- Nomenclature
- R-OH
- parent chain: -ol
- commonly act as nucleophiles
- Physical properties (acidity, hydrogen bonding)
- General properties
  - boiling point goes up with molecular weight and down with branching
  - melting point less clear
  - bp and mp much higher than similar-size alkanes due to their ability to hydrogen bond

Important reactions

- Oxidation

- Substitution reactions: SN1 or SN2
- Protection of alcohols
- Preparation of mesylates and tosylates
    - tosylates and mesylates are also useful for the protection of alcohols
        - prevents the alcohol from acting as an acid or undergoing other reactions
- 



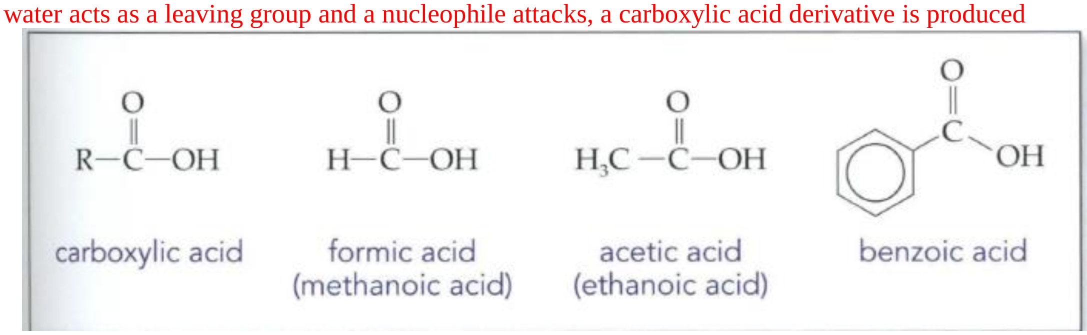
Carboxylic Acids (OC)

Description

- Nomenclature
- Physical properties

Substitution Reactions: Carboxylic Acids and Their Derivatives

- Expect carboxylic acids to act either as acids, losing a proton from their –OH group, or as substrates attacked by nucleophiles in substitution reactions
- planar quality makes it vulnerable to nucleophilic attack
- When water acts as a leaving group and a nucleophile attacks, a carboxylic acid derivative is produced



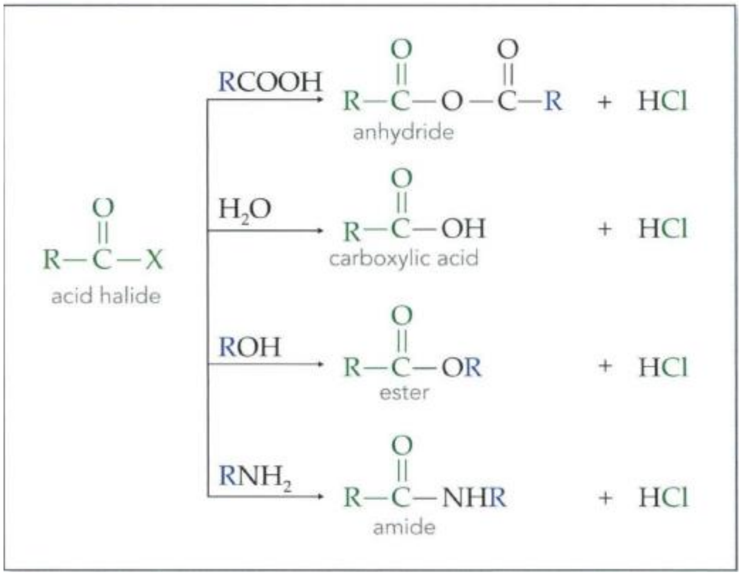
- Alipathic acids – carboxylic acids where R group is an alkyl group
    - salts of carboxylic acids are named with suffix –ate
        - “acetic” becomes “acetate”
- Carbonyl carbon of a carboxylic acid takes priority over all other groups
- Carboxylic acids are able to make two strong H-bonds with each other to form dimers
    - significantly increase the boiling point
    - double bonds in unsaturated carboxylic acids impede the crystal lattice, lowering the melting point
- Carboxylic acids with four or fewer carbons are miscible with water
    - the more carbons, the less soluble in water
    - also soluble in nonpolar solvents because they are able to solvate in the dimer form without the h-bonds being disrupted
- Very strong compared to other organic acids
    - When proton is removed, conjugate base is stabilized by resonance
    - EWGs on the alpha-carbon help to further stabilize the conjugate base and increase the acidity further
-

Important reactions

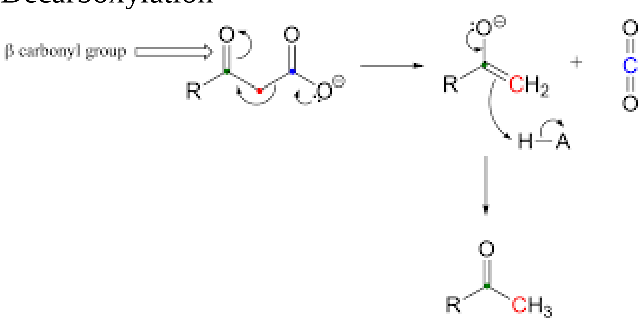
- Carboxyl group reactions
    - Amides (and lactam), esters (and lactone), anhydride formation

Substitution Reactions

- More reactive acyl derivatives can be made easily into less reactive ones but not the other way around



- All carboxylic acid derivatives hydrolyze to give the carboxylic acid
  - can occur under acidic conditions (yielding the acid) or basic conditions (yielding the carboxylate anion)
  - hydrolysis of amides only possible under extreme chemical conditions
  - Reduction
    - First reduced to aldehydes, then alcohols
  - Decarboxylation



  -

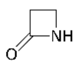
Reactions at 2-position, substitution

Acid Derivatives (Anhydrides, Amides, Esters) (OC)

Description
- Nomenclature
- Physical properties

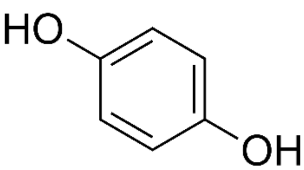
Important reactions
- Nucleophilic substitution
- Transesterification
- Hydrolysis of amides

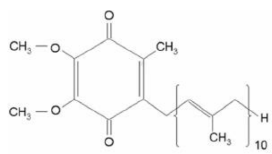
General principles
- Relative reactivity of acid derivatives
- Steric effects
- Electronic effects
- Strain (e.g., β-lactams)
- Acyl halides
  - OH – replaced with halide
- Anhydrides – leaving group is carboxylate anion
  - to name: name each of the two acids from which it is derived and drop the word “acid”
    - list them alphabetically, then follow with the word “anhydride”
    - If both sides of the molecule are identical, the name is not repeated
      - acetic anhydride
- Esters
  - to name: start with alcohol, change ending to –yl

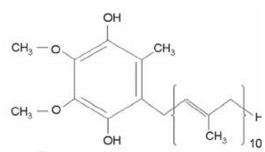
    - then name the carboxylic acid as its carboxylate salt
        - ethyl acetate
- Alcohols can react with carboxylic acids through nucleophilic substitution to form esters
    - strong acid catalyzes this reaction by protonating the hydroxyl group
    - yield is low because strong acids also catalyze reverse reaction
        - yield can be adjusted using Le-Chatelier's principle – add more water or alcohol
- Transesterification – trading alkoxy groups on an ester
- Lactones
    - intramolecular ester
    - when an alcohol attacks COOH on the same carbon chain
- Amides
    - Naming – replace –ic with –amide
        - acetamide
        - N-ethylacetamide
    - are less basic than amines due to EWG properties of the carbonyl
    - Under nucleophilic attack, the C-N bond is preserved
        - the C=O oxygen can be repeatedly protonated and become the leaving group
    - lactams – cyclic amides
        - unstable in small ring sizes (Beta lactam:
        - 
        - nucleophiles can react

Phenols (OC, BC)

Oxidation and reduction (e.g., hydroquinones, ubiquinones): biological 2e– redox centers


Hydroquinone

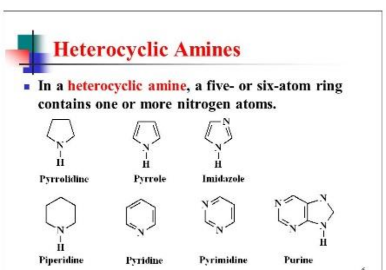

Ubiquinone


Ubiquinol

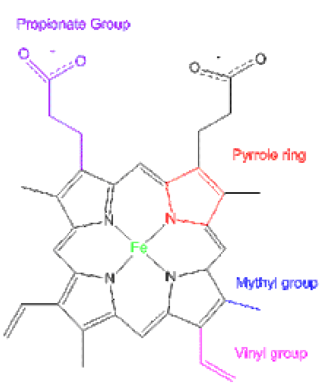
Ubiquinone = coenzyme Q

Polycyclic and Heterocyclic Aromatic Compounds (OC, BC)

Biological aromatic heterocycles



Heme (a porphyrin – any class of pigments whose molecules contain a flat ring of four linked heterocyclic groups, sometimes with a central metal atom)



Content Category 5E: Principles of Chemical Thermodynamics and Kinetics

Enzymes (BC, BIO)

Classification by reaction type

Mechanism

- Substrates and enzyme specificity
- Active site model
- Induced-fit model
- Cofactors, coenzymes, and vitamins

Kinetics

- General (catalysis)
- Michaelis–Menten
- Cooperativity
- Effects of local conditions on enzyme activity

Inhibition

Regulatory enzymes

- Allosteric
- Covalently modified

Principles of Bioenergetics (BC)

Bioenergetics/thermodynamics

- Free energy/Keq
- Concentration

Phosphorylation/ATP

- ATP hydrolysis $\Delta G \ll 0$
- ATP group transfers

Biological oxidation–reduction

- Half-reactions
- Soluble electron carriers
- Flavoproteins

Energy Changes in Chemical Reactions – Thermochemistry, Thermodynamics (GC, PHY)

Thermodynamic system – state function

Zeroth Law – concept of temperature

First Law − conservation of energy in thermodynamic processes

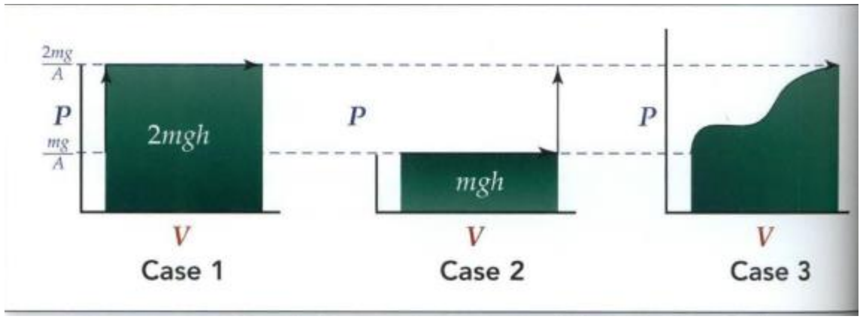
First Law of Thermodynamics

- Total energy of system and surroundings is always conserved
- Energy change for a system must equal heat flow and work done
  - $\Delta E = q + w$

PV diagram: work done = area under or enclosed by curve (PHY)

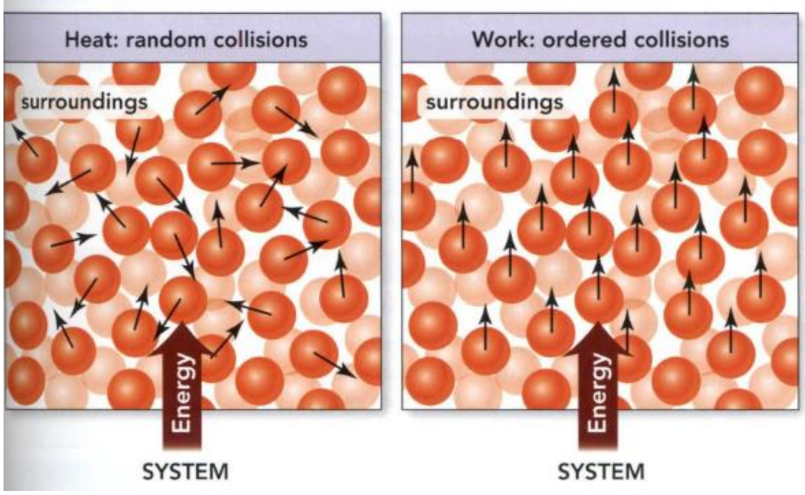
Work

- PV work (through force) and nonPV work (electrical)
- Under constant pressure: $W = - P\Delta V$
  - *When a system does work on its surroundings, work is negative*
- Different pathway = different amount of work
  - Changing pressure – requires calculus
    - assume that if volume does not change, no work is done
- Represents area under the pressure-volume graph



- Can be described at a molecular level
  - directional collisions of molecules to push piston up
  - directional collisions are the defining feature that distinguishes work from heat on a molecular scale

FIGURE 4.8 | Molecular Collisions in Heat and Work



  - Energy transfer as heat or work? look at the effect on the surroundings
    - if energy transfer into surroundings causes random collisions, then its heat
    - if energy transfer into surroundings causes ordered collisions, then its work

Second Law – concept of entropy
- Entropy as a measure of "disorder"
- Relative entropy for gas, liquid, and crystal states

Entropy
- Nature's tendency to create the most probably arrangement that can occur in a system
  - spreading energy evenly between system
  - leads to greater disorder
  - Second Law of Thermodynamics – the Entropy of an isolated system will never decrease
    - since the universe is also an isolated system, and is composed of the system and surroundings,
      - $\Delta S_{system} + \Delta S_{surroundings} = \Delta S_{universe} \geq 0$
- State function, extensive property
  - increases when the amount of substances increases
- At the end of the day, entropy is what drives reactions
  - entropy MUST be increased
    - (of the universe, not necessarily of the system)
- Entropy increases with number, size, volume, and temperature
  - Ex: if a reaction increases number of gas molecules, it has positive entropy
    - gas molecules are more free to move than solid or liquid particles
      - liquids are higher than solids
  - Among molecules that are in the same phase, the larger molecule (more bonds) has a higher entropy)
- Third Law of Thermodynamics – Entropy is zero at Absolute Zero
  - only in theory
  - Zero point enthalpy is relative and arbitrary, Zero point entropy is absolute
- $\Delta S = q_{rev} / T$
  - Units: J/K
  - q_{rev} = infinitesimal change in heat per Kelvin in a reversible process

    - T = temperature (initial)

Reversibility

- In an isolated system (the universe), the entropy change has to be zero for reversibile reactions
- In the real world, they do not happen
- Alternate definitions of reversibility
    - at the microscopic level, where Second Law does not apply
        - all reactions considered reversible
            - collisions between molecule
        - macroscopic principles of thermodynamics should not be applied to the microscopic world, but microscopic conditions can be used to make predictions about the macroscopic world
- Equilibrium is achieved when the rate of forward reaction equals to the rate of reverse reaction
    - at this point, the entropy is the greatest
- $\Delta S^o_{reaction} = \Delta S^o_{fproducts} - \Delta S^o_{freactants}$
-

Measurement of heat changes (calorimetry), heat capacity, specific heat

Calorimetry

- Heat Capacity
    - Added energy required to increase temperature of a given substance by 1 K
    - differs per substance
    - $C = q / \Delta T$
- Two heat capacities for any substance
    - C_v – constant volume heat capacity
        - no work, all energy change must be in the form of heat
        - none of the energy going into the system can escape as work done by the system
    - C_p – constant pressure heat capacity
        - some of the energy can leave the system as PV work done by the surroundings as the volume changes
- Thus, at constant pressure, a substance can absorb energy with less change in temperature by expelling some of the energy to the surroundings as work
    - $C_p > C_v$
    - However, this difference is only significant for molecules in the gas phase
        - liquids and solids are fairly resistant to changes in volume
- Large molecules tend to have higher heat capacities than those of smaller molecules
    - not all of the energy goes into increasing temperature of compound
        - can go into bond stretching
- Water has a higher heat capacity because of its strong intermolecular bonds
    - hydrogen bonds must first be broken for kinetic energy (and therefore temperature) to increase
- Heat capacity will always be positive
- 1 cal = 4.184 J
    - approximately equal to the amount of energy needed to raise on gram of water by one degree Celsius
    - 1 Cal = 4184 J
- Specific heat capacity – intrinsic proprety that represent the heat capacity per unit mass
    - $q = mc\Delta T$

Calorimeters

- studies relationship between heat transfer and temperature change, associated with chemical or physical reaction
- highly insulated from their surroundings
- For Endothermic reactions
    - temperature of water decreases
    - as long as amount of water is known, the heat transferred away from water can be calculated with $q = mc\Delta T$
- Essentially,
    - $q_{water} = -q_{reactants}$
- Two types: Constant Pressure and Constant Volume
    - Constant Pressure
        - Coffee cup calorimeter – measures energy change at atmospheric pressure
        - cannot contain expanding gases because they are open at the top
        - $q = \Delta H$
            - change in enthalpy can be measured, along with entropy if Free energy is known
    - Constant Volume
        - Bomb calorimeter
        - $q = \Delta U$

- internal energy change can be calculated

Heat transfer – conduction, convection, radiation (PHY)

- Energy transfer through heat can occur in three ways
  - Conduction – through molecular collisions
  - Convections – through the motion of fluids (gases and liquids)
    - Ex: Hot air rising
  - Radiation – through electromagnetic waves
    - Stefan-Boltzman law:
      - $P = \sigma\varepsilon AT^4$
        - P = power = rate at which an object radiates electromagnetic waves
        - σ = Stefan-Boltzman constant = 5.67×10^{-8} W m^{-2} K^{-4}
        - A = surface area
        - T = temperature in Kelvins
        - ε = emissivity
          - between 0 and 1
            - 1 – 1 – black body – absorbs all radiation
    - only type of heat transfer that can occur through a vacuum

Endothermic/exothermic reactions (GC)

- Enthalpy, H, and standard heats of reaction and formation
- Hess' Law of Heat Summation

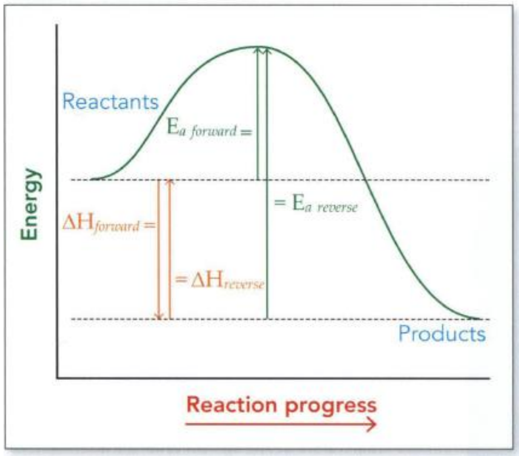
Enthalpy and Entropy

- Enthalpy – defined as an equation rather than as a description of a property
  - $H = U + PV$
  - depends only on temperature for an ideal gas
  - extensive property
- $\Delta H = \Delta U + P\Delta V$
  - can be derived to $\Delta H = W_{non\text{-}PV} + q_{(constant}$ pressure, closed system at rest, PV work only)
  - Thus, if only PV work is performed, **enthalpy change is the heat transfer into the system at constant pressure**
- Standard state
  - reference form of a substance at any chosen temperature T and a pressure of 1 bar (10^5 pascals)
    - reference form is usually the form that is most stable at 1 bar and the chosen temp
  - Ana element in its standard state at 25 C is assigned an enthalpy value of 0 kJmol
  - Enthalpy values of compounds based on the change in enthalpy when they are formed from raw elements in their standard states at 25 C
    - Standard enthalpy of formation (ΔH^o_f) – for one mole of compound
  - standard state is different from STP
    - temperature is probably 25 C, but doesn't have to be
  - $\Delta H^o_{reaction} = \Delta H^o_{fproducts} - \Delta H^o_{freactants}$
- Endothermic – reaction with positive enthalpy change
  - produces heat flow to the system
  - Anabolic reactions (building a large molecule from several smaller ones) are usually endothermic
    - photosynthesis – uses energy to build glucose
- Exothermic – reaction with negative enthalpy change
  - produces heat flow to the surroundings
  - Catabolic reactions (breaking down a large molecule into several smaller molecules)) are usually exothermic
    - cellular respiration – breaks down glucose to release energy

Accounting for Energy: Hess's Law

- Based on the fact that enthalpy is a state function, and the change in enthalpy depends only on the identities and thermodynamic states of the initial and final compounds
- "The sum of the enthalpy changes for each step is equal to the total enthalpy change regardless of the path chosen"
- Also indicates that a forward reaction has exactly the opposite change in enthalpy as the reverse reaction

FIGURE 4.11 One Step Reaction



- Activation energy is based on the kinetics of a reaction
- enthalpy change is based on the thermodynamics

Bond dissociation energy as related to heats of formation (GC)

- Bonds broken – bonds formed

Free energy: G (GC)

Spontaneous reactions and ΔG° (GC)

Energy and Reactions: Gibbs

- $\Delta G = \Delta H - T\Delta S$
  - all three state functions refer to the system, but the equation also provides information about the surroundings
    - Heat transferred into the surroundings (exothermic) increases entropy of surroundings
    - Heat transferred into system (endothermic) increases entropy of system
      - thus, accounts for entropy change of both system and surroundings
  - Algebraic manipulation to $\Delta G = -T\Delta S$
    - S must be positive for G to be negative – both required for spontaneous reaction
    - Both S and G must be 0 at equilibrium
- Extensive property and a state function
- Not conserved – can change for an isolated system
- **represents maximum non-PV work available for a reaction**
  - contracting muscles, transmitting work, batteries

TABLE 4.3 › Effect of Enthalpy and Entropy on Gibbs Free Energy

ΔH	ΔS	$\Delta G = \Delta H - T\Delta S$	
−	+	−	Always spontaneous
−	−	− or +	Spontaneous at low temperatures; non-spontaneous at high temperatures
+	+	+ or −	Non-spontaneous at low temperatures; spontaneous at high temperatures
+	−	+	Never spontaneous

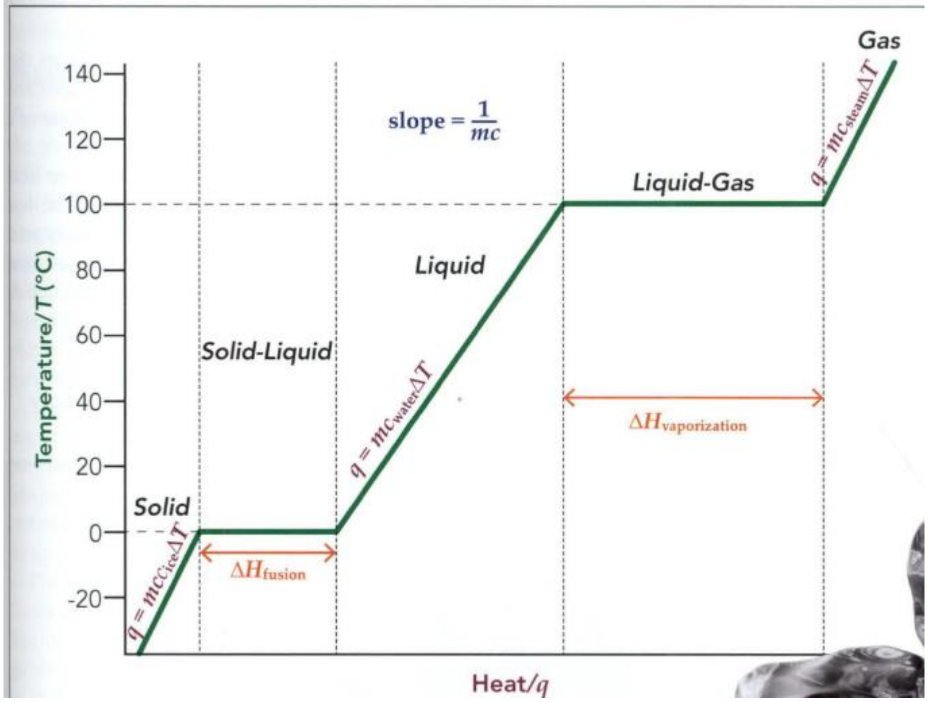
Coefficient of expansion (PHY)

- Thermal expansion is the tendency of matter to change in shape, area, and volume in response to a change in temperature.[1]
- Temperature is a monotonic function of the average molecular kinetic energy of a substance. When a substance is heated, the kinetic energy of its molecules increases. Thus, the molecules begin vibrating/moving more and usually maintain a greater average separation. Materials which contract with increasing temperature are unusual; this effect is limited in size, and only occurs within limited temperature ranges (see examples below). The relative expansion (also called strain) divided by the change in temperature is called the material's coefficient of thermal expansion and generally varies with temperature.

Heat of fusion, heat of vaporization

Phase Changes

FIGURE 5.11 Phase Changes

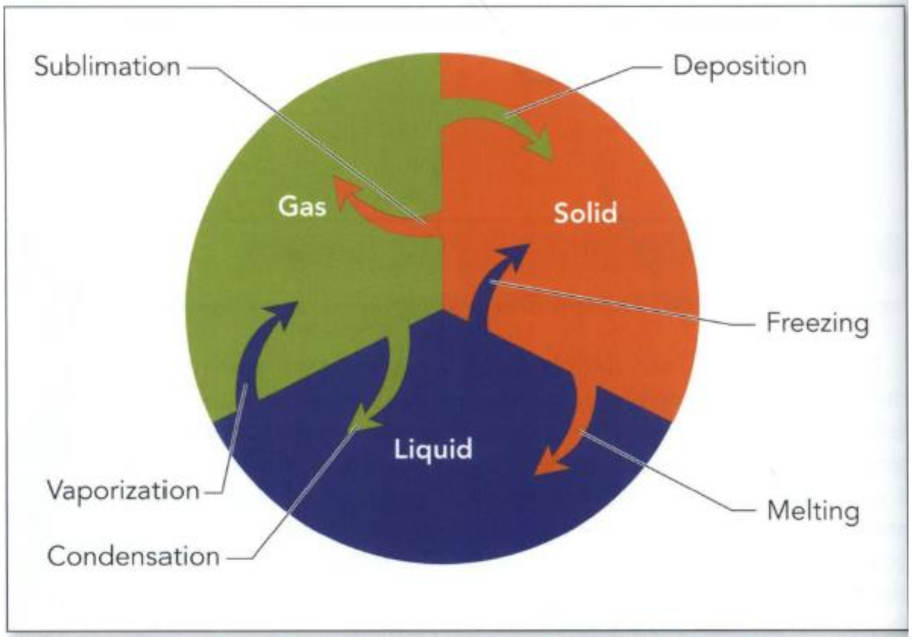


- Notice that at phase changes, heat capacity is technically infinite
- Since pressure is constant, q = ΔH
  - enthalpy change associated with melting is called heat of fusion
  - enthalpy change associated with boiling is called heat of vaporization
- Amount of heat absorbed during melting is exactly the same as the amount released during freezing
- Different compounds have different heats of fusions and heats of vaporization based on how tightly the molecules are held together within the compound
- Heats of vaporization are usually larger than the heats of fusion because the transition from liquid to gas requires more significant intermolecular bond breaking than the transition from solid to liquid
- $$\Delta T = \left(\frac{1}{mc}\right)q$$

Phase diagram: pressure and temperature

- $$\Delta T = \left(\frac{1}{mc}\right)q$$

FIGURE 5.12 Phase Changes

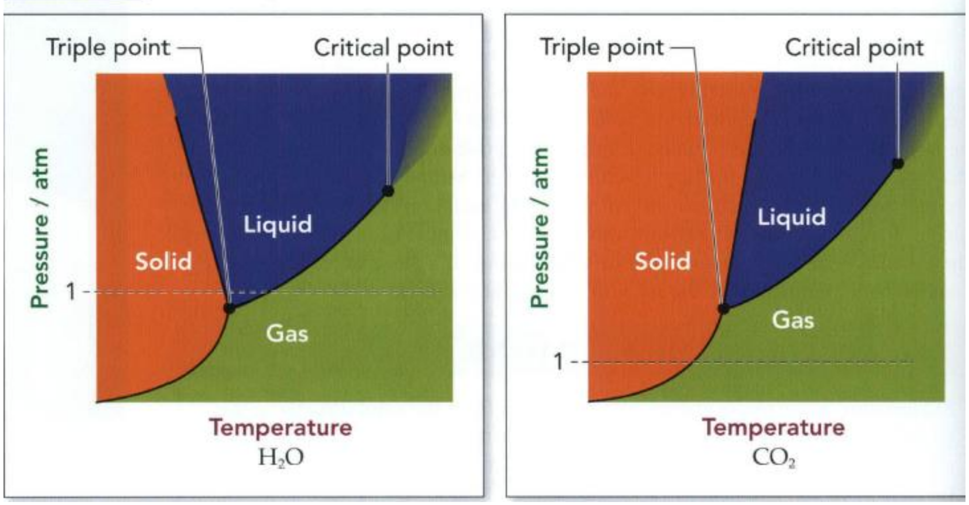


-
- Specific heats
  - gases tend to have much lower specific heats than their respective solids and liquids
- Melting, boiling, and sublimation are endothermic and increase entropy
  - entropy and enthalpy are positive for melting, boiling, and sublimation
    - negative for freezing, condensation, and deposition
    - Thus, temperature dictates whether reaction will be spontaneous

Phase Diagrams

- lines – equilibrium
- triple point – substance can exist in equilibrium between the solid, liquid, and gas phases
- critical temperature – temperature above which a substance cannot be liquefied regardless of the pressure applied
- Critical pressure – pressure required to produce liquid phase when the substance is at the critical temperature
  - critical point is composed of the crucial temperature and pressure
  - fluids beyond this point has characteristic of both gas and liquid – supercritical fluid (cannot be distinguished)

FIGURE 5.13 Phase Diagrams



  - notice **negative slope** for water solid-liquid line
    - indicates that **ice is less dense than water**
    - H-bonds form crystal structure, more space than random arrangement of liquid molecules

Rate Processes in Chemical Reactions - Kinetics and Equilibrium (GC)

Reaction rate

Activation Energy and the Effect of Temperature on Reaction Rate

- reacting molecules must collide for a chemical reaction to occur

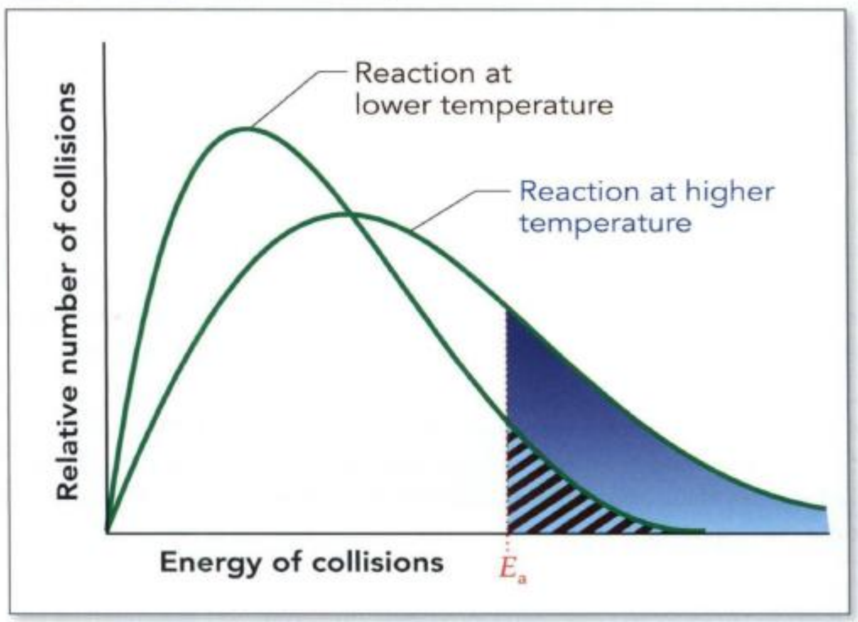
- since the rate of a given reaction is slower than frequency of collisions, most collisions do not result in a reaction
  - must meet a certain criteria
    - proper energy, proper orientations
  - The relative kinetic energies of colliding compounds must be greater than or equal to a certain threshold energy—the activation energy
  - Particles must also align in a certain way
- Arrhenius equation:

$$k = zpe^{-E_a/RT}$$

-
  - k = rate constant
  - z = collision frequency
  - p = fraction of collisions having the effective spatial orientation p (steric factor)
  - $e^{-Ea / RT}$ – fraction of collisions having sufficient relative energy
    - increase in Ea will reduce value of K
- value of rate constant is affected by **pressure, catalysts, and temperature**
  - pressure dependence is typically relevant only for gases
    - higher pressure increases rate constant
  - Higher temperature means increasing rate constant
    - increases both forward and reverse reactions

FIGURE 1.23 Temperature Dependence of Reaction Rates

Each curve represents the energy distribution of a sample of particles. Since temperature is a proxy for kinetic energy, as the temperature increases, the average kinetic energy of the sample increases. This means there will be more collisions with enough energy to overcome the activation energy. The point is that the proportion of collisions (area under the curve) with energy greater than E_a will increase as temperature increases.



- In reality, the activation energy itself changes slightly depending on temperature, but this effect is so slight that it can be ignored

Dependence of reaction rate on concentration of reactants

- Rate law, rate constant

Determining Reaction Rate

- describes how quickly the concentration of the reactants or products are changing over the course of the reaction
- Questions will generally apply to gases or dilute solutions at constant temperature
- Remember: the rate constant is proportional, not identical, to the rate of reaction
- Rates expressed in **M s^{-1}** or mol L^{-1} s^{-1}
- Do not assume that a reaction is elementary (occurring in one step) unless stated so
- Rate can be expressed as the disappearance of reactants or the appearance of products:

$$rate = -\frac{1}{a}\frac{\Delta[A]}{t} = -\frac{1}{b}\frac{\Delta[B]}{t} = \frac{1}{c}\frac{\Delta[C]}{t} = \frac{1}{d}\frac{\Delta[D]}{t}$$

-

- strictly correct only for an elementary reaction, but is also a good approximation for a multistep reaction if the concentrations of any intermediates are low
- Reaction rates are usually determined using only the concentrations observed during the initial moments of the reaction
  - when concentration of reactants is very high relative to the concentration of products, and the rate of reverse reaction is zero
- Rate Law:

$$\text{rate}_{\text{forward}} = k_f[\text{A}]^{\alpha}[\text{B}]^{\beta}$$

- α and β are the reaction order of each reactant, and $\alpha + \beta$ = overall order of the reaction
  - related to the number of molecules that must collide for a particular elementary reaction
  - **if reaction is elementary, α = a and β = b**
- never assume that you can use the coefficients of the balanced equation in a rate law unless you know the reaction is elementary
- Rate law is used to determine how changes in initial concentration affect reaction rate

Determining the Rate Law by Experiment

- Consider the reaction: 2A + B + C → 2D

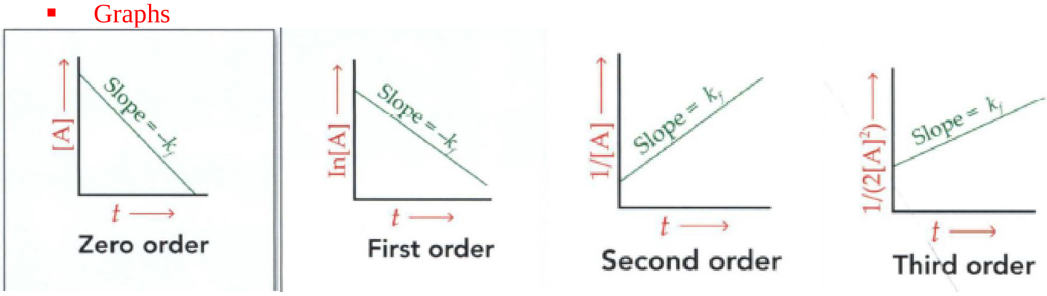
TABLE 1.6 > Experimental Data

Trial	Initial Concentration of A (mol L^{-1})	Initial Concentration of B (mol L^{-1})	Initial Concentration of C (mol L^{-1})	Initial Rate of D (mol L^{-1} sec^{-1})
1	0.1	0.1	0.1	8.0×10^{-4}
2	0.2	0.1	0.1	1.6×10^{-3}
3	0.2	0.2	0.1	6.4×10^{-3}
4	0.1	0.1	0.4	8.0×10^{-4}

- When A doubles: Rate doubles; When B doubles, rate quadruples; When C doubles, rate stays the same
- $\text{rate}_{\text{forward}} = k_f[\text{A}][\text{B}]^2$
  - third order reaction
  - we can solve for k
- shows that the rate can be increased by increasing concentration of reactants
- Reaction order

Reaction Order

- indicate how changes in the reactant concentrations influence the reaction rate
- For multistep reactions, the overall reaction can be broken down into two or more elementary reactions
  - the slowest of these elementary reactions determines the rate equation
- Graphs



- slopes are equal to the rate constant for a given rate law
  - is constant

Rates of Multiple Step Reactions

- Slowest step = rate-determining step
  - if the first step is the slow step, he rate law is derived from this step
  - if another step is the slow step, it is still the rate-determining step, but the steps prior to this rate-determining step will also contribute to the rate law
    - **steps after the slow step do not contribute to the rate law**
    - **intermediate not present in the overall reaction may appear**

Rate-determining step

In chemical kinetics, the overall rate of a reaction is often approximately determined by the slowest step, known as the **rate determining step** (RDS) or **rate-limiting step**. For a given reaction mechanism, the prediction of the corresponding rate equation (for comparison with the experimental rate law) is often simplified by using this approximation of the rate determining step.

Dependence of reaction rate upon temperature

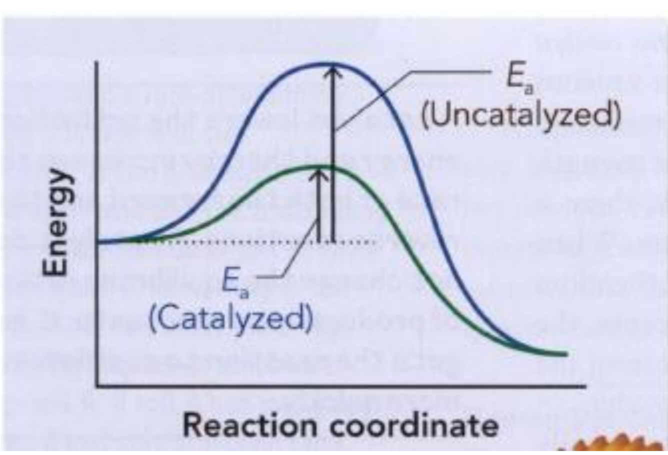
- Activation energy
  - Activated complex or transition state
  - Interpretation of energy profiles showing energies of reactants, products, activation energy, and ΔH for the reaction
- Use of the Arrhenius Equation

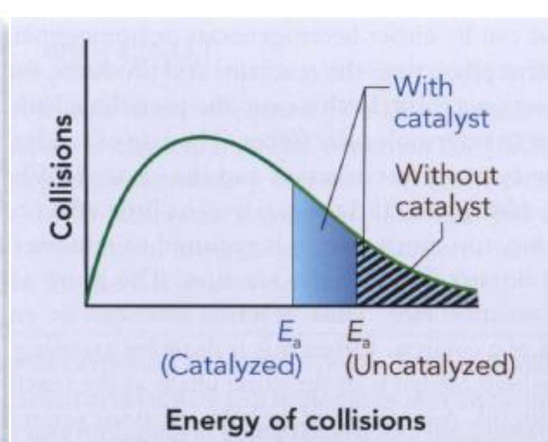
Kinetic control versus thermodynamic control of a reaction

Catalysts

Catalysis

- catalyst – substance that increases the rate of a reaction without being consumed or permanently altered
- increases the rate of both forward and reverse reactions
- may lower E_a, increase steric factor, or both
  - increasing steric factor increases the number of favorable collisions
  - most catalysts work by lowering E_a
- catalyst provides an alternative reaction mechanism that competes with the uncatalyzed mechanism
  - creates different pathway
- Homogeneous vs heterogeneous
  - Heterogeneous catalyst – different phase than reactants and products
    - particles adsorb to the surface of the solid due to intermolecular forces
    - rate of catalysis depends on the strength of attraction between the reactant and the catalyst
      - can't be too weak or too strong
    - r**eaction rates can be enhanced by increasing the surface area of a catalyst**
      - grinding a solid into a powder
  - Homogenous catalyst – same phase as the reactants and products
    - some reactions exhibit autocatalysis, where a product of the reaction acts as a catalyst for the reaction
- If increasing the concentration of a catalyst increases the rate of the reaction (such as when the concentration of the catalyst is small compared to the concentrations of reactants and products), it can be included in the rate law
  - reactions with catalysts will then require separate rate constants
  - since the catalyst does not prevent the original reaction from proceeding, the total rate is given by the sum of the rates of both reactions
    - typically, the rate of the original reaction is negligible compared to the rate of the catalyzed reaction



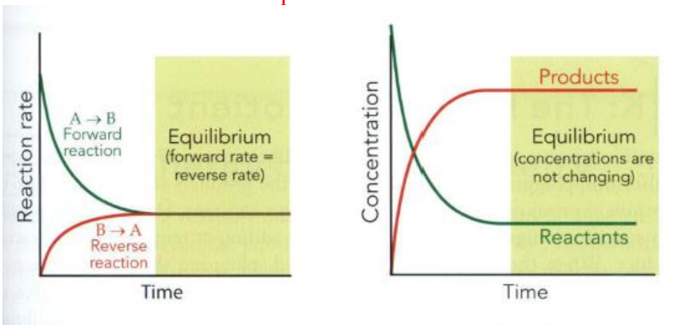


Equilibrium in reversible chemical reactions

- Law of Mass Action

Equilibrium

- rate of forward reaction equals rate of reverse reaction



- The point of greatest entropy
- For a homogenous reaction, where all products and reactants are in the same phase, there will always be some of each species present at equilibrium
  - in other words, at equilibrium, there will be a mixture of both reactants and products
- for aA + bB → cC + dD,

$$K = \frac{[C]^c[D]^d}{[A]^a[B]^b} = \frac{\text{Products}^{\text{cofficients}}}{\text{Reactants}^{\text{cofficients}}}$$

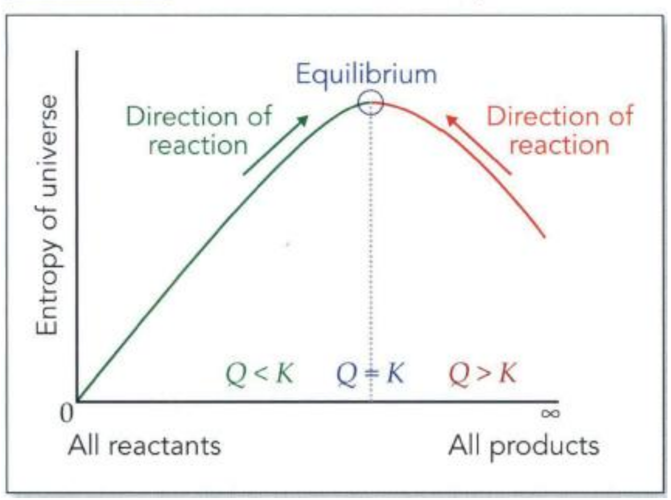
  - **Law of Mass Action**
  - K allows us to determine relative amounts of each species at equilibrium
  - Concentration of a pure liquid or pure solid is given a value of 1
    - do not contribute to the value of the equilibrium constant
  - Note that any equilibrium constant (solubility, ionization, etc) only changes with temperature.

K: the Reaction Quotient

$$Q = \frac{\text{Products}^{\text{coefficients}}}{\text{Reactants}^{\text{coefficients}}}$$

- Q = reaction quotient
  - same thing as K, but not at equilibrium
- If:
  - Q = K, reaction is at equilibrium
  - Q >K, reverse reaction rate will be greater than the forward rate
  - if Q <K, forward reaction rate will be greater than reverse reaction rate

FIGURE 4.13 Nature Trends Toward Equilibrium



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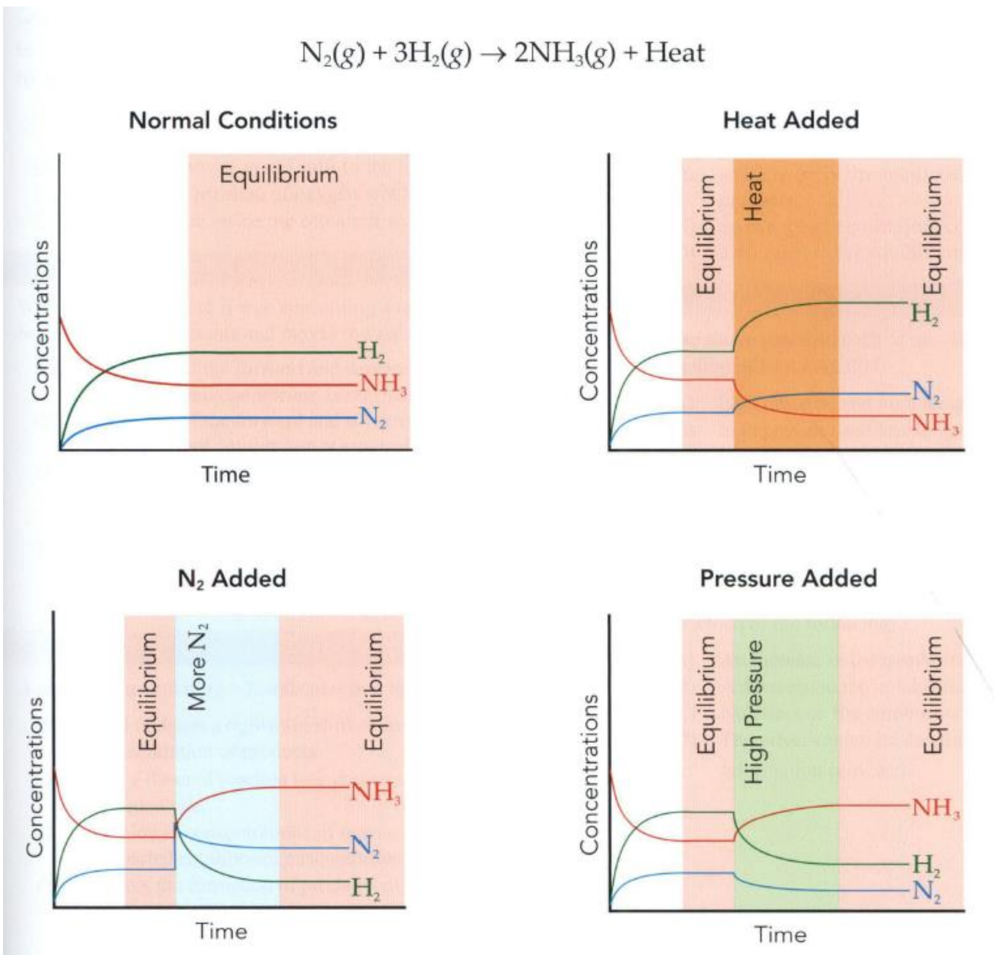
- Equilibrium Constant
- Application of Le Châtelier's Principle

Le Chatelier's Principle

- When a system **at equilibrium** (only works for a system in equilibrium) is stressed, the system will shift in a direction that will reduce that stress
  - Three stresses
    - addition or removal or product or reactant
    - changing the pressure or volume of the system
    - heating or cooling the system
  - The Haber Process: $N_{2(g)} + 3H_{2(g)} \rightarrow 2NH_{3(g)}$ + Heat
    - If we add N_2, the reaction is pushed to the right
    - If we add heat (analogous to adding more product), then the reaction is pushed to the left
    - If pressure is increased, equilibrium shifts to the right
      - there are four gas molecules on the left side and two on the right
      - A similar effect is found when a solution in equilibrium is concentrated or diluted
        - equilibrium shifts to the side with fewer moles when the solution is concentrated
- Notable exceptions
  - Increase of pressure due to the addition of a nonreactive gas (no effect)
  - For solvation reactions, the solubility of a salt generally increases with increasing temperature, even when the reaction is exothermic



Relationship of the equilibrium constant and ΔG°

Free Energy and Spontaneity

- Spontaneity of a reaction under specific conditions can be predicted using the relationship between the equilibrium constant K and ΔG
- The difference between ΔG° and ΔG
  - ΔG° – under specific case of standard state conditions

$$\Delta G^\circ = -RT\ln(K)$$

- ΔG – far less specific, represents the energy change for any given reactions under any attainable conditions

$$\Delta G = \Delta G^{\circ} + RT\ln(Q)$$

- Relationship between K and ΔG:
  - if K = 1, then $\Delta G^{o} = 0$
  - if K > 1, then $\Delta G^{o} < 0$
  - if K < 1, then $\Delta G^{o} > 0$
    - This does not mean that a reaction is always spontaneous if it has an equilibrium constant greater than one
      - spontaneity of a reaction depends on starting concentrations of products and reactants
    - The relationship between K and ΔG^{o} does say that if a reaction has an equilibrium constant greater than one, the reaction is spontaneous at the temperature used to derive that particular equilibrium constant and standard state

$$\Delta G^{o} = -RT\ln K_{eq} = -nFE^{o}_{cell}$$