Physics

Mechanics
  Kinematics
  Newton's Laws
  Work & Energy
  Harmonic Motion
  Fluid Mechanics

Gravitation

Waves

Thermodynamics
  Heat & Temprature
  Ideal Gas
  1st Law
  2nd Law

Electricity and Magnetism
  Electrostatics
  DC Current
  Magnetism

Light and Optics
  Properties of Light
  Geometric Optics
  Wave optics

Modern Physics

Nuclear Physics

Kinematics

- Definitions: displacement (m), velocity (m/s), acceleration (m/s^2)
  - vectors and scalars

$$\bar{v} = \frac{\Delta x}{\Delta t} \qquad \bar{a} = \frac{\Delta v}{\Delta t}$$

- constant acceleration

$$v = v_0 + at \qquad \Delta x = \tfrac{1}{2}(v + v_0)\Delta t$$

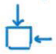
$$\Delta x = v_0 t + \tfrac{1}{2}at^2 \qquad v^2 = v_0^2 + 2a\Delta x$$

- 2 dimensional motion
  - projectile motion $\quad t_{peak} = \frac{V_{y0}}{g}$
  - uniform circular motion $\quad a_r = \frac{v^2}{r}$

Newton's Laws

$F = N = kg\,m/s^2$

- Law of inertia
- $F = ma$
- $F_{12} = -F_{21}$

- Free body diagrams and static equilibrium
  - 
  - static equilibrium - no net force & no net torque
    torque - (force)(moment arm)

- Friction

$$F_s \leq \mu_s N \qquad F_k = \mu_k N$$

- Fundamental Forces
  - Gravitation $\quad F_g = \frac{G m_1 m_2}{r^2}$
  - Electromagnetism

$$F_e = \frac{k q_1 q_2}{r^2} \qquad F_m = qvB\sin\theta$$

electrostatic   magnetic

Work and Energy

$Joule = N \cdot m = kg\frac{m^2}{s^2}$

- Work = $(force_{\parallel})(distance)$ $\quad [W = F\cos\theta\,\Delta x]$
- Work = ΔKE
- $KE = \frac{1}{2}mv^2$

$$PE = mgh$$

$$\left(U = \tfrac{1}{2}kx^2,\ U = \frac{kq_1q_2}{r},\ U = \frac{-Gm_1m_2}{r}\right)$$

- Power
  1 Watt = J/s
  $P = F_{\parallel}v$

Harmonic Motion

- mass spring $\quad F = -kx \quad U = \frac{1}{2}kx^2$

spring constant

$$f = \frac{1}{2\pi}\sqrt{\frac{k}{m}}$$

$$\mu = \frac{m_1 m_2}{m_1 + m_2} \qquad f = \frac{1}{2\pi}\sqrt{\frac{k}{\mu}}$$

- pendulum

$$f = \frac{1}{2\pi}\sqrt{\frac{g}{L}}$$

Fluid Mechanics

- Properties of a fluid
  - density $\quad \rho_{H_2O} = \frac{1000kg}{m^3} \quad \rho_{H_2O} = \frac{1g}{cm^3} = \frac{1g}{cc} = \frac{1g}{mL} = \frac{1kg}{L}$
  - Pressure $\quad Pascal = \frac{1N}{m^2} \quad$ 1 atm = 101,000 Pa ~ 1 bar
    = 1×10^5 Pa
    = 760 mmHg = 760 torr

- Static Fluids
  - $P = P_{atm} + \rho g h$
  - $B = W_{fluid\ displaced}$

- Pascal's Law

- Flow of an Ideal Fluid

$$A_1 v_1 = A_2 v_2 = Q \quad \text{volume flux}$$

$$P + \rho g y + \tfrac{1}{2}\rho v^2 = constant$$

- Real Fluids
  Viscosity = η
  turbulence = $RN = \frac{\rho v d}{\eta}$

Poiseuille's Law

$$Q = \frac{\Delta P r^4 \pi}{L \eta 8}$$

Waves

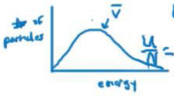
- longitudinal or transverse
- stretched string $v = \sqrt{\frac{F}{\mu}}$ ← tension, ← mass/length
- harmonic waves
  $\lambda = \text{m/cycle}$ (m) $k = \frac{\text{cycle}}{\text{m}}$ (m^{-1}) $v = \lambda f$
  $T = \text{s/cycle}$ (s) $f = \frac{\text{cycle}}{\text{s}} = \text{Hz}$ (s^{-1})
- sound $v = \sqrt{\frac{B}{\rho}}$ ← bulk modulus, ← density
  - $\beta = 10 \log \left(\frac{I}{I_0}\right)$ ↗ loudness
  - Doppler Effect $f' = f\left(\frac{v \pm v_s}{v \mp v_o}\right)$
- standing waves
  - stretched string $\lambda = \frac{2L}{n}$ (n=1, 2, 3 etc)
  - air column ·
    open at both ends $\lambda = \frac{2L}{n}$ (n=1, 2, 3.)
    closed at one end $\lambda = \frac{4L}{n}$ (n = 1, 3, 5 ...)

Heat and Temperature

- Temperature scales
  $K = C + 273$
  - standard T : 273 K
  - Standard state T : 298 K
- Heat capacity
  - specific heat
    $c_{H_2O} = \frac{1 \text{ cal}}{\text{g °C}}$ $Q = mc\Delta T$
    1 cal = 4.18 J
  - molar heat capacity
    $C_{H_2O} = \frac{18 \text{ cal}}{\text{mol °C}}$
- Heat flow
  - conduction $\frac{Q}{t} = kA\frac{\Delta T}{\Delta x}$
  - radiation $\frac{Q}{t} = A\sigma\varepsilon T^4$ emissivity $\varepsilon = 1$, blackbody

Ideal Gas

- assumptions · point masses, no action-at-a-distance, only elastic collisions
- internal energy · only the kinetic energy of the particles · thermal energy
  $U = \frac{3}{2}nRT$
- Macrostate · P, V, T $PV = nRT$
- Gas Laws
  $P_1V_1 = P_2V_2$ (constant T)
  $\frac{V_1}{T_1} = \frac{V_2}{T_2}$ (constant P)
  $\frac{P_1V_1}{T_1} = \frac{P_2V_2}{T_2}$
- Kinetic theory



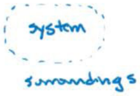
$U = \frac{3}{2}NkT$

$\frac{U}{N} = \frac{1}{2}m\bar{v}^2 = \frac{3}{2}kT$

$\frac{1}{2}m_A\bar{v}_A^2 = \frac{1}{2}m_B\bar{v}_B^2$

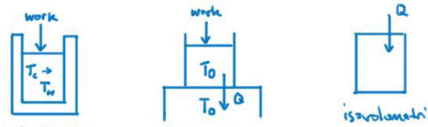
$\frac{\bar{v}_A}{\bar{v}_B} = \sqrt{\frac{m_B}{m_A}}$

1st Law of Thermodynamics



$\Delta U = Q - W$ $(W = P\Delta V)$

- Model Transformations



adiabatic (no heat flow)
$Q = 0$
$\Delta U = -W$

isothermal (constant T)
$\Delta U = 0$
$Q = W$

isovolumetric
$W = 0$
$\Delta U = Q$

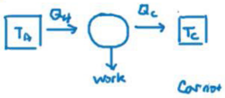
2nd Law of Thermodynamics

- The entropy of the universe always increases
- Entropy

spontaneous (not reversible)

$S = k \ln X$ ↑ # of microstates

- ΔS due to heat flow $\Delta S = \frac{Q}{T}$
  $\boxed{T_H} \xrightarrow{Q} \boxed{T_C}$
  $\Delta S_H = \frac{Q}{T_H}$ $\Delta S_c = \frac{Q}{T_c}$
  spontaneous
  cold body gains more entropy than the hot body loses
  $\Delta S_{universe}$ ⊕
  $\boxed{T_H} \rightleftarrows \boxed{T_H}$ thermal equilibrium
- Heat engines



$W = Q_H - Q_c$

$\varepsilon = \frac{W}{Q_H}$

Carnot cycle: $\frac{Q_H}{T_H} = \frac{Q_c}{T_c}$

$\Delta S_{universe} = 0$

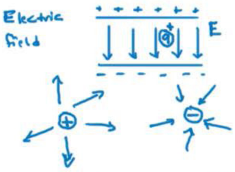
$\varepsilon = 1 - \frac{T_c}{T_H}$

Electricity

electric charge : Coulombs

electric field : N/C

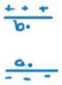
- Electrostatic force
  Coulomb's Law $F = \frac{kq_1q_2}{r^2}$
- Electric field



$F = Eq$

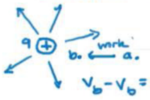
$E_q = \frac{kq}{r^2}$

- Potential difference



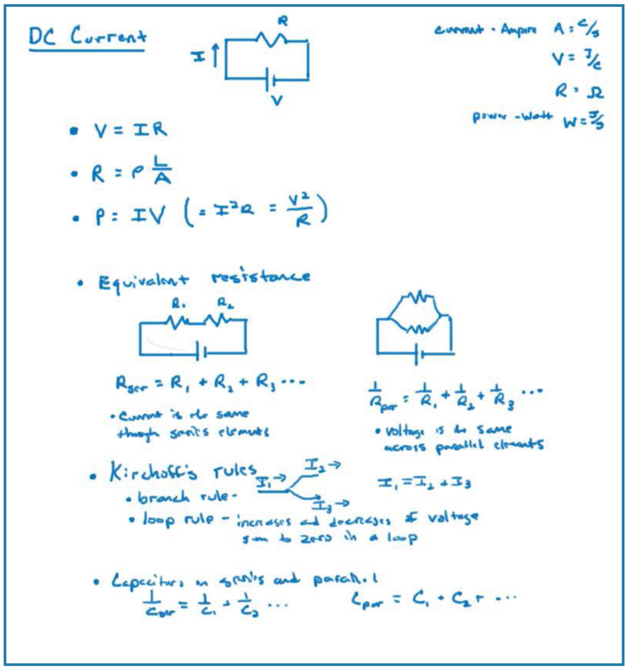
volt = J/C

$V = Ed$



$V_b - V_b = kq\left[\frac{1}{r_b} - \frac{1}{r_a}\right]$

- Capacitance
  $C = \frac{Q}{V}$



DC Current

current - Ampere $A = C/s$

$V = J/C$

$R = \Omega$

power - Watt $W = J/s$

- $V = IR$
- $R = \rho \frac{L}{A}$
- $P = IV \left(= I^2R = \frac{V^2}{R} \right)$
- Equivalent resistance

$R_{ser} = R_1 + R_2 + R_3 \cdots$

- current is the same through series elements

$\frac{1}{R_{par}} = \frac{1}{R_1} + \frac{1}{R_2} + \frac{1}{R_3} \cdots$

- voltage is the same across parallel elements

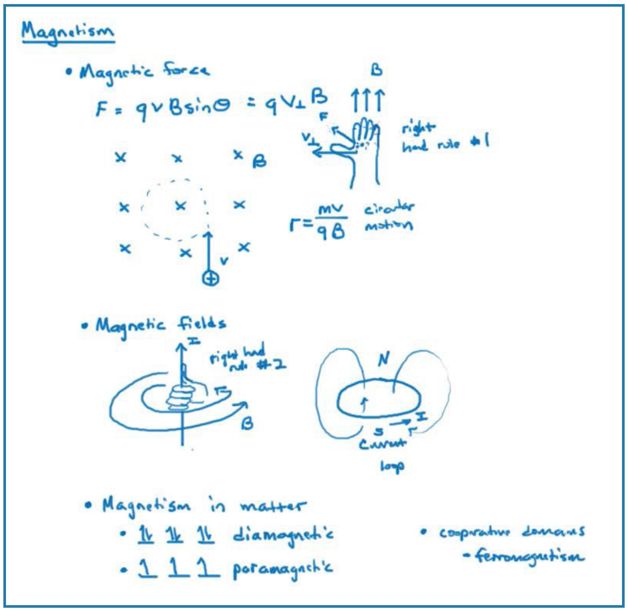
- Kirchoff's rules
  - branch rule -

$I_1 = I_2 + I_3$

  - loop rule - increases and decreases of voltage sum to zero in a loop

- Capacitors in series and parallel

$\frac{1}{C_{ser}} = \frac{1}{C_1} + \frac{1}{C_2} \cdots \qquad C_{par} = C_1 + C_2 + \cdots$



Magnetism

- Magnetic force

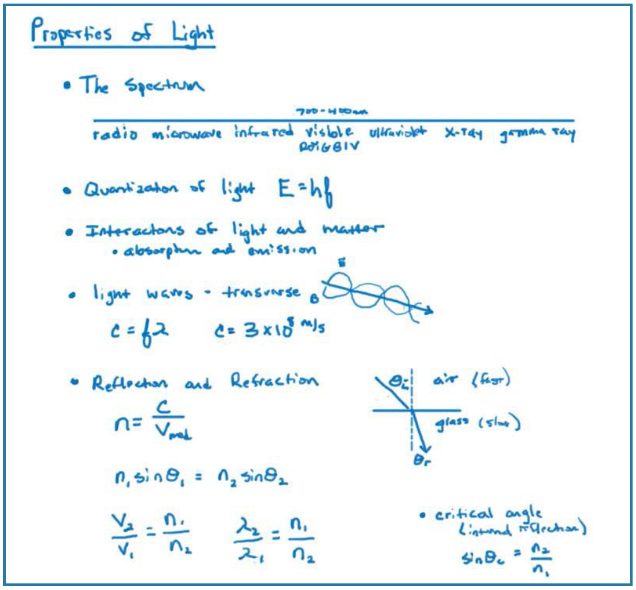
$F = qvB\sin\theta = qv_\perp B$

$r = \frac{mv}{qB}$ circular motion

- Magnetic fields

- Magnetism in matter
  - $\underline{\uparrow\downarrow}\ \underline{\uparrow\downarrow}\ \underline{\uparrow\downarrow}$ diamagnetic
  - $\underline{\uparrow}\ \underline{\uparrow}\ \underline{\uparrow}$ paramagnetic

- cooperative domains
  - ferromagnetism



Properties of Light

- The Spectrum

700-400nm

radio microwave infrared visible ultraviolet X-ray gamma ray

ROYGBIV

- Quantization of light $E = hf$
- Interactions of light and matter
  - absorption and emission
- light waves - transverse

$c = f\lambda \qquad c = 3\times10^8\ m/s$

- Reflection and Refraction

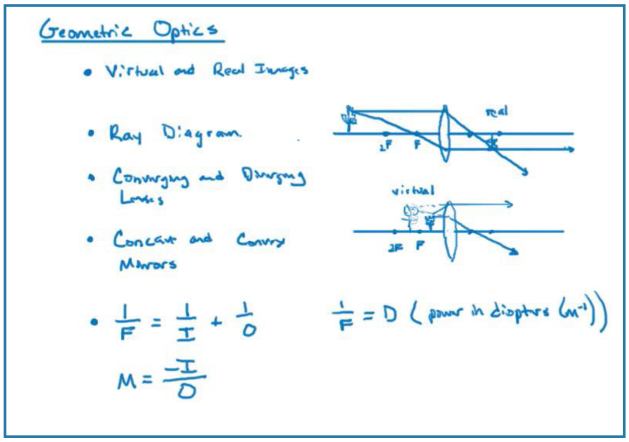
$n = \frac{c}{V_{med}}$

$n_1 \sin\theta_1 = n_2 \sin\theta_2$

$\frac{V_2}{V_1} = \frac{n_1}{n_2} \qquad \frac{\lambda_2}{\lambda_1} = \frac{n_1}{n_2}$

- critical angle (internal reflection)

$\sin\theta_c = \frac{n_2}{n_1}$



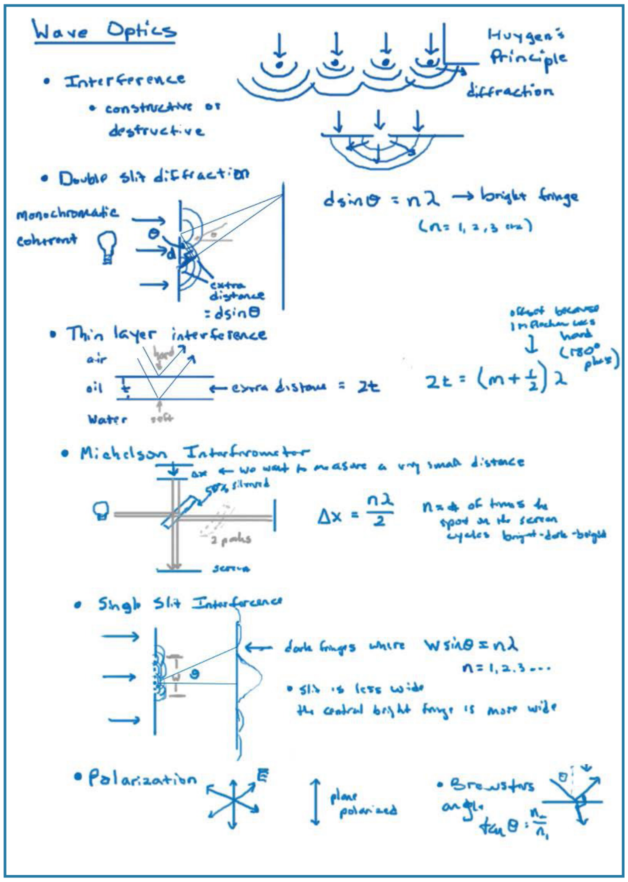
Geometric Optics

- Virtual and Real Images
- Ray Diagram
- Converging and Diverging Lenses
- Concave and Convex Mirrors

- $\frac{1}{F} = \frac{1}{I} + \frac{1}{O}$

$\frac{1}{F} = D$ (power in diopters (m^{-1}))

$M = \frac{-I}{O}$



Wave Optics

- Interference
  - constructive or destructive

- Double slit diffraction

$d\sin\theta = n\lambda \rightarrow$ bright fringe

$(n = 1, 2, 3$ etc$)$

- Thin layer interference

← extra distance = $2t$

offset because reflection was hard (180° phase)

$2t = \left(m + \frac{1}{2}\right)\lambda$

- Michelson Interferometer

Δx ← we want to measure a very small distance

$\Delta x = \frac{n\lambda}{2}$ n = # of times the spot on the screen cycles bright-dark-bright

- Single Slit Interference

← dark fringes where $W\sin\theta = n\lambda$

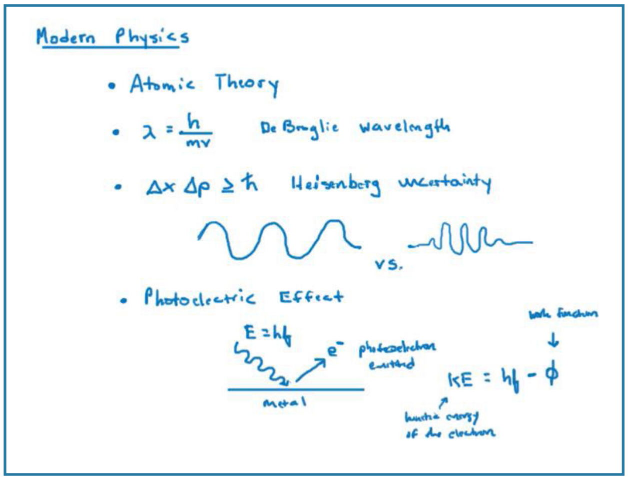
$n = 1, 2, 3 \ldots$

- slit is less wide the central bright fringe is more wide

- Polarization

plane polarized

- Brewsters angle $\tan\theta = \frac{n_2}{n_1}$

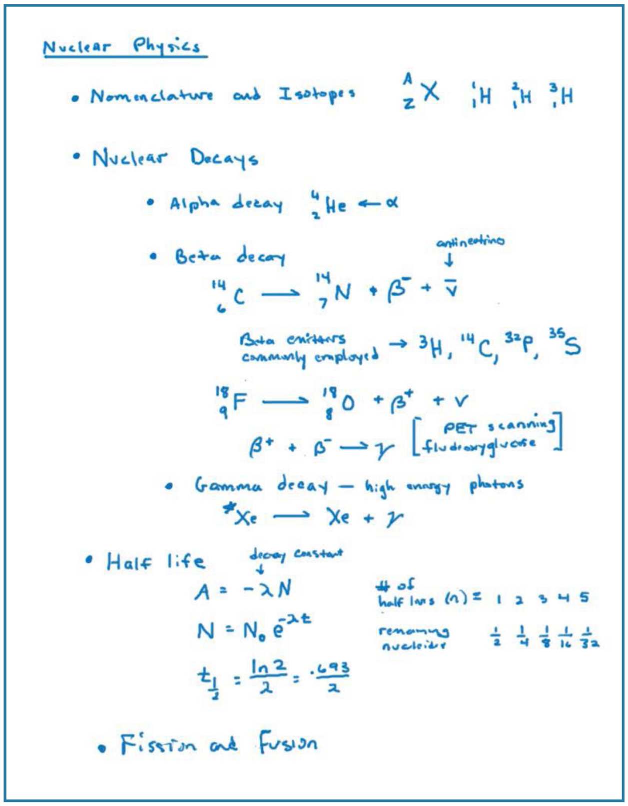


Modern Physics

- Atomic Theory
- $\lambda = \frac{h}{mv}$ De Broglie wavelength
- $\Delta x \, \Delta p \geq \hbar$ Heisenberg uncertainty

vs.

- Photoelectric Effect



Nuclear Physics

- Nomenclature and Isotopes $^{A}_{Z}X$ $^{1}_{1}H$ $^{2}_{1}H$ $^{3}_{1}H$
- Nuclear Decays
  - Alpha decay $^{4}_{2}He \leftarrow \alpha$
  - Beta decay

$$^{14}_{6}C \longrightarrow {}^{14}_{7}N + \beta^- + \overset{\text{antineutrino}}{\bar{\nu}}$$

Beta emitters commonly employed → ^{3}H, ^{14}C, ^{32}P, ^{35}S

$$^{18}_{9}F \longrightarrow {}^{18}_{8}O + \beta^+ + \nu$$

$$\beta^+ + \beta^- \longrightarrow \gamma \quad \left[\begin{matrix}\text{PET scanning} \\ \text{fludeoxyglucose}\end{matrix}\right]$$

  - Gamma decay — high energy photons

$$^{*}Xe \longrightarrow Xe + \gamma$$

- Half life

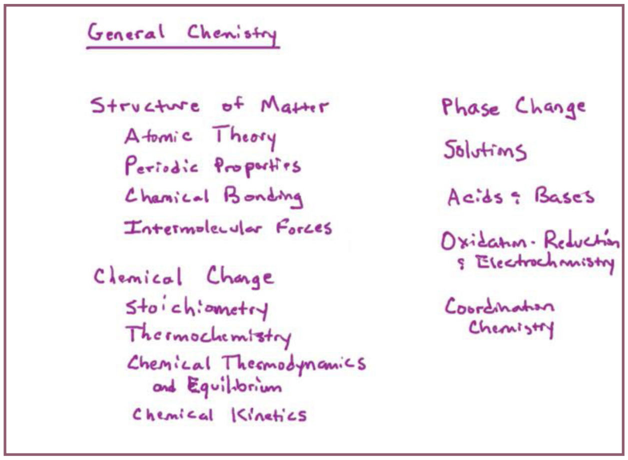
$$A = -\overset{\text{decay constant}}{\lambda} N$$

$$N = N_0 e^{-\lambda t}$$

$$t_{\frac{1}{2}} = \frac{\ln 2}{\lambda} = \frac{.693}{\lambda}$$

# of half lives (n) =	1	2	3	4	5
remaining nucleotide	$\frac{1}{2}$	$\frac{1}{4}$	$\frac{1}{8}$	$\frac{1}{16}$	$\frac{1}{32}$

- Fission and Fusion



General Chemistry

Structure of Matter
- Atomic Theory
- Periodic Properties
- Chemical Bonding
- Intermolecular Forces

Chemical Change
- Stoichiometry
- Thermochemistry
- Chemical Thermodynamics and Equilibrium
- Chemical Kinetics

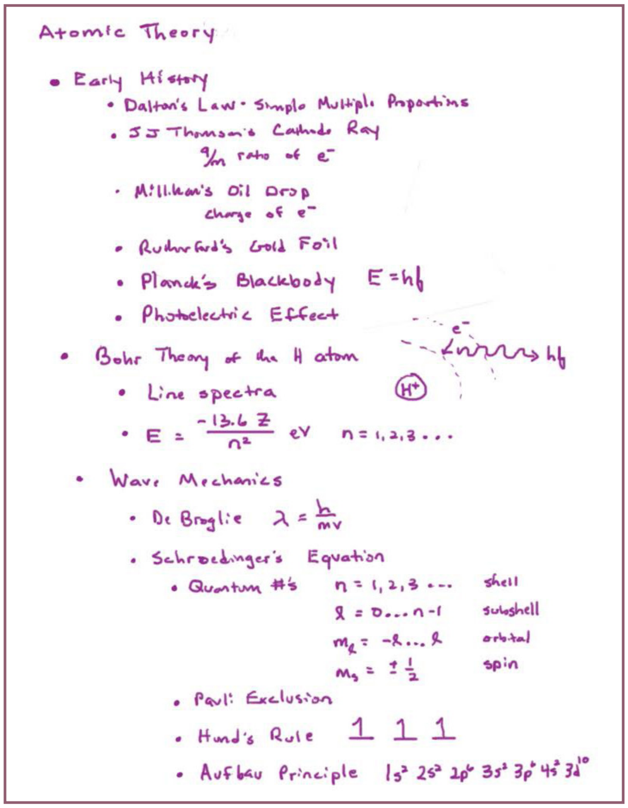
Phase Change

Solutions

Acids & Bases

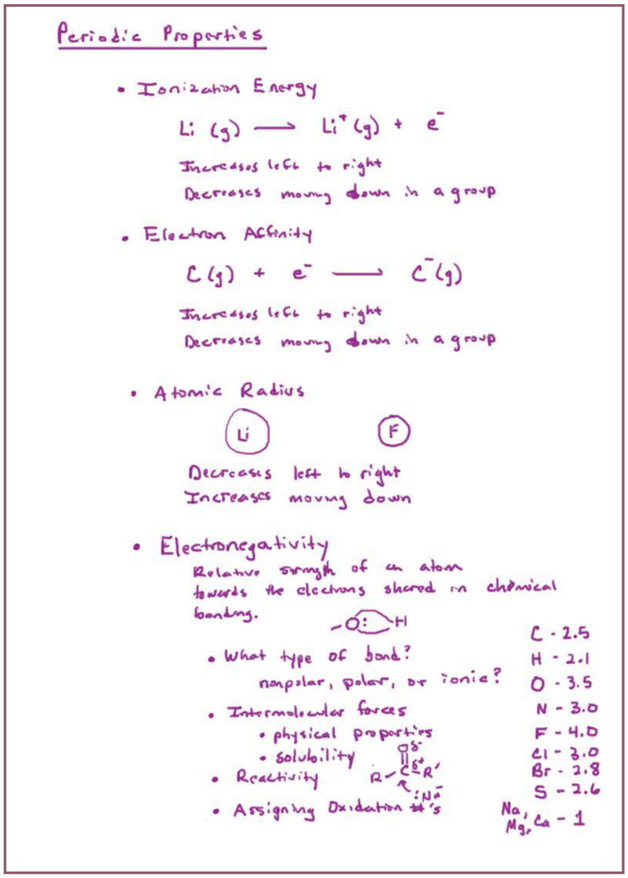
Oxidation-Reduction & Electrochemistry

Coordination Chemistry



Atomic Theory

- Early History
  - Dalton's Law · Simple Multiple Proportions
  - JJ Thomson's Cathode Ray
    q/m ratio of e^-
  - Millikan's Oil Drop
    charge of e^-
  - Rutherford's Gold Foil
  - Planck's Blackbody $E = hf$
  - Photoelectric Effect
- Bohr Theory of the H atom
  - Line spectra
  - $E = \frac{-13.6\,Z}{n^2}$ eV $n = 1, 2, 3 \ldots$
- Wave Mechanics
  - De Broglie $\lambda = \frac{h}{mv}$
  - Schroedinger's Equation
    - Quantum #'s
      $n = 1, 2, 3 \ldots$ shell
      $\ell = 0 \ldots n-1$ subshell
      $m_\ell = -\ell \ldots \ell$ orbital
      $m_s = \pm \frac{1}{2}$ spin
    - Pauli Exclusion
    - Hund's Rule 1 1 1
    - Aufbau Principle $1s^2\ 2s^2\ 2p^6\ 3s^2\ 3p^6\ 4s^2\ 3d^{10}$



Periodic Properties

- Ionization Energy

$$Li\,(g) \longrightarrow Li^+(g) + e^-$$

Increases left to right
Decreases moving down in a group

- Electron Affinity

$$C\,(g) + e^- \longrightarrow C^-(g)$$

Increases left to right
Decreases moving down in a group

- Atomic Radius

Li F

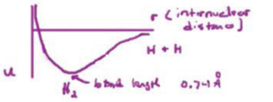
Decreases left to right
Increases moving down

- Electronegativity
  Relative strength of an atom towards the electrons shared in chemical bonding.
  - What type of bond?
    nonpolar, polar, or ionic?
  - Intermolecular forces
    - physical properties
    - solubility
  - Reactivity
  - Assigning Oxidation #'s

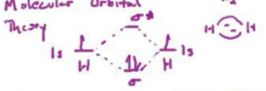
C - 2.5
H - 2.1
O - 3.5
N - 3.0
F - 4.0
Cl - 3.0
Br - 2.8
S - 2.6
Na, Mg, Ca - 1

Chemical Bonding

- Lewis Symbols
- Nonpolar, Polar, Ionic
- The Covalent Bond
  - Bond Energy



  - Molecular Orbital Theory



  - Simple Oscillator Model

    - partition for thermal energy
    - IR spectroscopy

- Intra-atomic Hybridization

C $\frac{1\downarrow}{2s}$ $\underbrace{\frac{1}{}\frac{1}{}}_{2p}$ __ ⟶ $\underbrace{\frac{1}{}\ \frac{1}{}\ \frac{1}{}\ \frac{1}{}}_{sp^3}$

- Bond Order

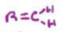
⟶ $\underbrace{\frac{1}{}\ \frac{1}{}\ \frac{1}{}}_{sp^2}$ $\underset{p}{\frac{1}{}}$

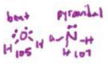
- 

$R\text{-}\overset{\overset{O}{\|}}{C}\text{-}O^- \longleftrightarrow R\text{-}\overset{\overset{O^-}{|}}{C}{=}O$

Resonance

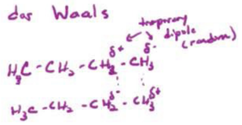
- VSEPR - valence shell electron pair repulsion

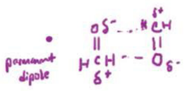
# of regions		Geometry	Bond Angle
2	O=C=O	linear	180°
3		trigonal planar	120°
4		tetrahedral	104.5
6		octahedral	90° or 180°



Intermolecular Force

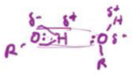
- Van der Waals — Weakest



- 

Dipole - Dipole — Stronger

- H Bonding — strongest



- Physical Properties
- Solubility - Like Dissolves Like

Stoichiometry

- The Mole 6.02×10^{23} particles
- Molecular Weights and Formula Weights

$$MW_{H_2O} = \frac{18\,g}{mol}$$

- Percent Composition
- Empirical and Molecular Formulas
- Balancing Chemical Equations
- Limiting Reagent Calculations
  - Involves comparing molar ratio actually present with the stoichiometric ratio in the reaction
- Theoretical Yield and Percentage Yield

Thermochemistry

- 1st Law of Thermodynamics

$$\Delta U = Q - W \qquad (W = P\Delta V)$$

- Enthalpy

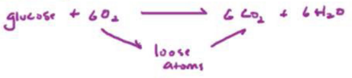
$$H = U + PV$$

Enthalpy is a state function whose change (as long as P is constant) equals heat flow, Q.

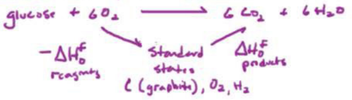
$$\Delta H = Q \quad (\text{when } P \text{ is constant})$$

ΔH is path independent - Hess' Law of Heat Summation

- Hess' Law
  - Born Haber cycle
  - Bond Energies



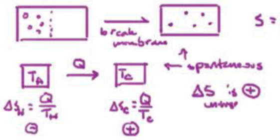
  - Standard Enthalpies of Formation



$$\Delta H = \Delta H^f_{0\ \text{products}} - \Delta H^f_{0\ \text{reagents}}$$

Chemical Thermodynamics and Equilibrium

- 2nd Law of Thermodynamics - The entropy of the universe always increases.
- Basic system changes



$$S = k \ln X$$

$$\Delta S = \frac{Q}{T}$$

- 

Universe = system + surroundings

$$\Delta S_{universe} = \Delta S_{system} + \Delta S_{surroundings}$$

$$= \Delta S_{system} - \frac{\Delta H}{T} \quad \left(\frac{Q}{T}\right)$$

- Gibbs Free Energy

$$G = H - TS$$

$$\Delta G = \Delta H - T\Delta S$$

$$\underset{\Delta S_{universe}}{-\frac{\Delta G}{T}} = \underset{\Delta S_{surroundings}}{-\frac{\Delta H}{T}} + \underset{\Delta S_{sys}}{\Delta S}$$

Free energy, G, is a state function that when it changes means that the entropy of the universe changed.

- Standard Free Energy

$$3H_2 + N_2 \rightleftharpoons 2NH_3 \qquad \ominus\ \Delta G^\circ$$

Standard free energy change for $A \rightleftharpoons B$ describes the difference for [A] = [B] = 1M

$$\overset{\oplus}{\Delta G} = \overset{\ominus}{\Delta G^\circ} + 2.3RT\,\overset{\oplus}{\log}\,Q \qquad Q = \frac{[B]}{[A]}$$

if we had high $[NH_3]$ and very low $[H_2] + [N_2]$

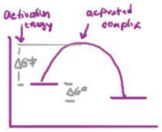
Then what happens: $\Delta G \underset{\text{goes to}}{\longrightarrow} 0$ as $Q \to K$ | Then ΔG is actually ⊕

$$\left[K = e^{-\Delta G^\circ/RT}\right] \qquad \Delta G^\circ = -2.3RT\log K$$

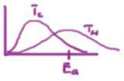
- Le Chatlier's Principle - If a system at equilibrium is disturbed, the system will respond in the direction that undoes the disturbance.
  - concentration • temperature • pressure
    - Increasing T favors the endothermic direction
    - Increasing P favors the lower volume (fewer moles of gas)

Chemical Kinetics

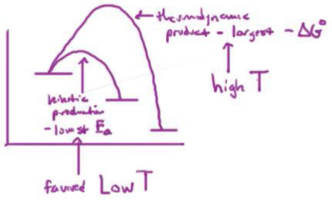
- Reaction rates
- Rate laws $\quad rate = k[A]^x[B]^y$ (from experiment)
  reaction order = x + y
- Half Life
  - 1st order - independent of initial concentration
    $t_{\frac{1}{2}} = \frac{0.69}{k}$
- Collision Theory
- Transition State Theory



- Effect of Temperature
  Arrhenius equation : $k = Ae^{-E_a/RT}$



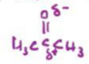
- Catalysts
- Kinetic vs. Thermodynamic Control



Phase Change

- Solids, Liquids, Solids
- Intermolecular Forces
- Vapor Pressure of Liquids
  - Vapor pressure increases with temperature

  - Volitility - property of liquid. volatile liquid has a high vapor pressure at a given T. • smaller molecular weight and weaker intermolecular forces



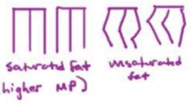
$H_3C\overset{\overset{O\,\delta^-}{\parallel}}{\underset{\delta^+}{C}}CH_3$

dipole - dipole

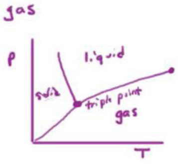
$CH_3CH_2CH_2CH_3$

Van der Waals
more volatile • lower BP

- Boiling Point - Temperature at which the vapor pressure comes to equal external pressure
- Freezing Point - Crystallization (Melting Point)



- Heat of fusion : solid → liquid
  Heat of vaporization : liquid → gas
  Sublimation : solid → gas
- Phase Diagrams



Solutions

- Types of Solutions
  - Solutions vs. mixtures (emulsions, colloids, sols, gels)
- Concentration expressions
  - mole fraction $\frac{\#\text{ moles component}}{\text{total }\#\text{ moles}}$ • gases, Raoult's Law
  - molarity(M) $\frac{\text{Moles}}{\text{L solution}}$ • reaction quotients, equilibrium constants rate expressions
  - molality (m) $\frac{\text{Moles}}{\text{kg solvent}}$ • colligative properties
- Solubility
  - Like dissolves like
  - Solubility and Temprature
    If solubility increases with T, solution process is endothermic
- Electrolytes
  - The dielectric properties of water

  - Strong vs. weak Electrolytes
    (soluble) (insoluble - sparingly soluble)
    - Solubility rules
- Weak Electrolytes - Heterogeneous Solution Equilibria

$$PbSO_4(s) \rightleftharpoons Pb^{2+}(aq) + SO_4^{2-}(aq)$$

Equilibrium state - saturation

- Solubility Product $K_{sp} = [Pb^{2+}][SO_4^{2-}]$ at saturation
  - Common Ion Effect

$$AgCl_2(s) \rightleftharpoons Ag^{2+}_{(aq)} + 2Cl^-_{(aq)}$$ saturated solution

Add KBr $\qquad K_{sp}(AgBr_2) << K_{sp}(AgCl_2)$

$$Ag^{2+}_{(aq)} + 2Br^-_{(aq)} \longrightarrow AgBr_2(s)$$

  - Complex Ions

- Henry's Law
  $C_g = kP_g$
- Raoult's Law
  $P_{vap} = XP^\circ_{vap}$
- Colligative Properties
  BP elevation
  FP depression $\quad \Delta T = kim$
  - Osmotic Pressure

Acids : Bases

- Arrhenius • Lewis ★ • Brønsted - Lowry

$$\underset{\text{conj acid}}{HA} + H_2O \rightleftharpoons \underset{\text{conj base}}{A^-} + H_3O^+$$

Strong vs. weak acids : bases

$$B + H_2O \rightleftharpoons BH^+ + OH^-$$

The equilibria are coupled with autoprotolysis

- Autoprotolysis of Water

$$2H_2O \rightleftharpoons H_3O^+ + OH^-$$

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

$$K_w = [H^+][OH^-] = 1 \times 10^{-14}$$

- pH → $pH = -\log[H^+]$
  → $pH + pOH = 14$
- Common acids and Bases
- Acid - Base Equilibria

$$K_a = \frac{[A^-][H^+]}{[HA]} \qquad pK_a = -\log K_a$$

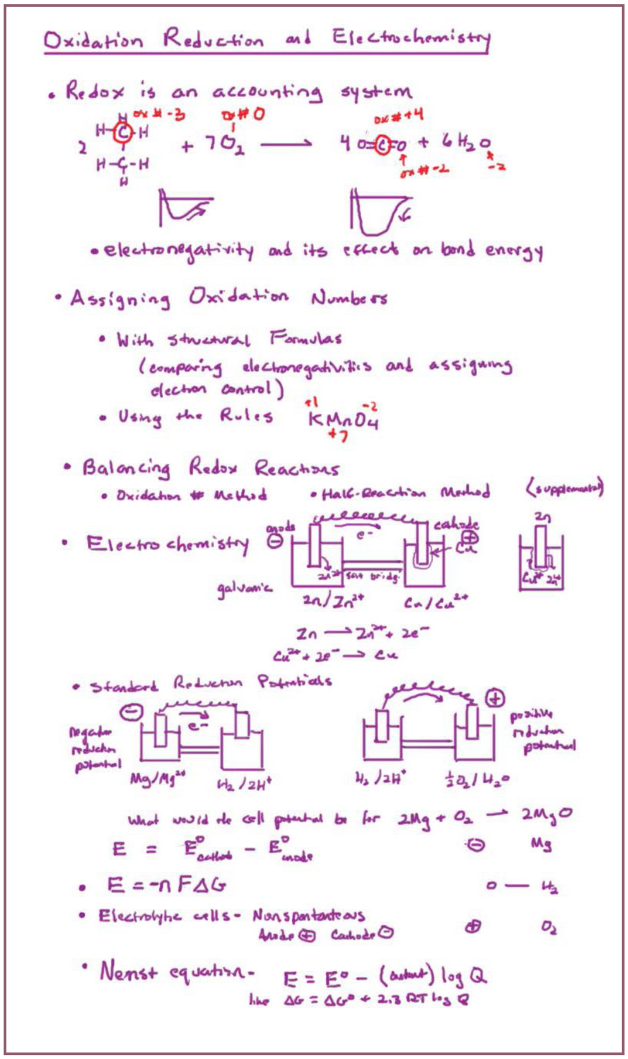
$$K_b = \frac{[HA][OH^-]}{[A^-]} \qquad pK_b = -\log K_b$$

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

- Henderson - Hasselbach

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

  - To determine the pH of a buffer solution (mixture of a weak acid and its conjugate base)
  - To determine the state of ionization of a solution component.
    pKa - Aspartate = 4.
    $7 = 4 + \log\left(\frac{[A^-]}{[HA]}\right) \qquad \frac{[A^-]}{[HA]} = \frac{1000}{1}$



Oxidation Reduction and Electrochemistry

- Redox is an accounting system

$2\,C_2H_6 + 7O_2 \longrightarrow 4\,O{=}C{=}O + 6H_2O$

ox # -3 ox # 0 ox # +4 ox # -2 -2

  - electronegativity and its effect on bond energy
- Assigning Oxidation Numbers
  - With structural Formulas (comparing electronegativities and assigning electron control)
  - Using the Rules $\overset{+1}{K}\underset{+7}{Mn}\overset{-2}{O_4}$
- Balancing Redox Reactions
  - Oxidation # Method
  - Half-Reaction Method
- Electrochemistry

$Zn \longrightarrow Zn^{2+} + 2e^-$

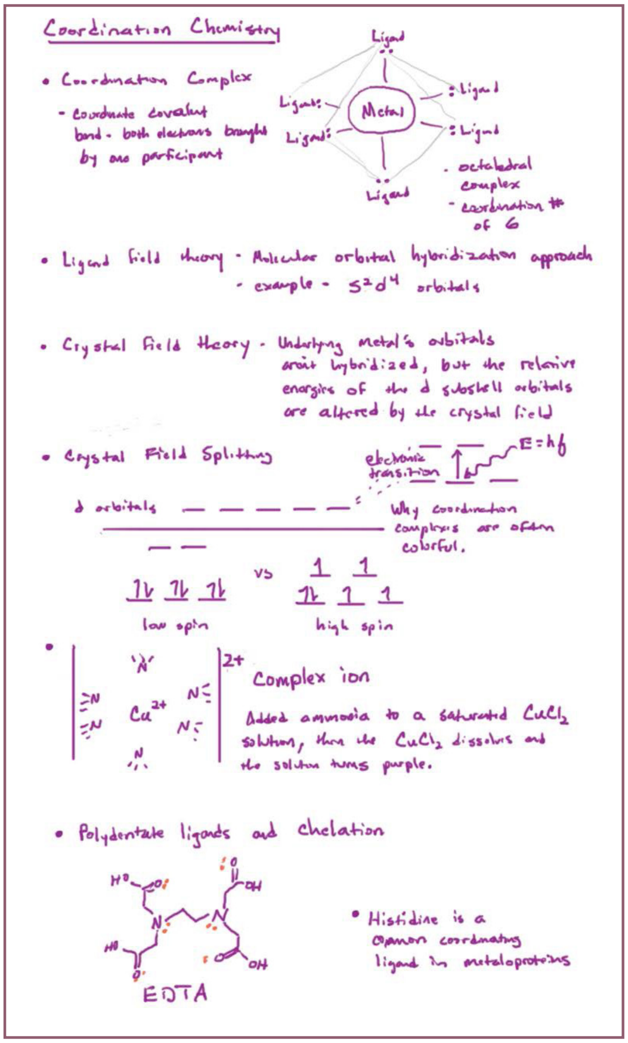
$Cu^{2+} + 2e^- \longrightarrow Cu$

- Standard Reduction Potentials

What would the cell potential be for $2Mg + O_2 \rightarrow 2MgO$

$E = E^\circ_{cathode} - E^\circ_{anode}$

- $E = -nF\Delta G$
- Electrolytic cells - Nonspontanteous
  Anode ⊕ Cathode ⊖
- Nenst equation - $E = E^\circ - (constant) \log Q$
  like $\Delta G = \Delta G^\circ + 2.3\,RT \log Q$



Coordination Chemistry

- Coordination Complex
  - coordinate covalent bond - both electrons brought by one participant

- octahedral complex
- coordination # of 6

- Ligand field theory - Molecular orbital hybridization approach
  - example - s^2d^4 orbitals
- Crystal field theory - Underlying metal's orbitals aren't hybridized, but the relative energies of the d subshell orbitals are altered by the crystal field
- Crystal Field Splitting

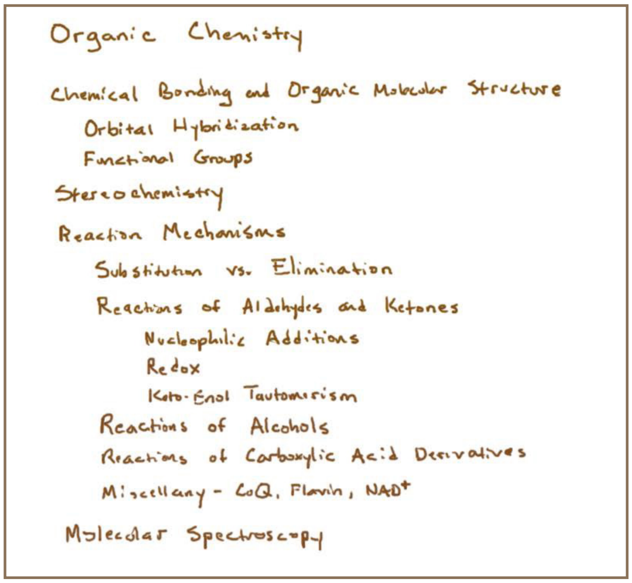
Why coordination complexes are often colorful.

- $[Cu(NH_3)_6]^{2+}$ Complex ion

Added ammonia to a saturated $CuCl_2$ solution, then the $CuCl_2$ dissolves and the solution turns purple.

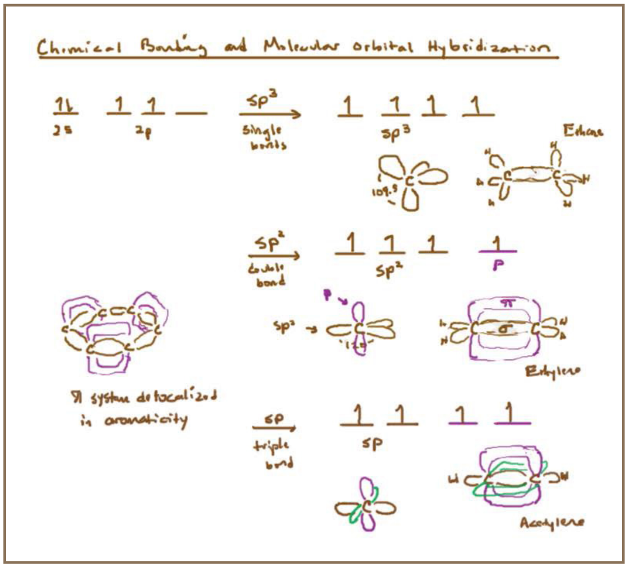
- Polydentate ligands and chelation

- Histidine is a common coordinating ligand in metaloproteins

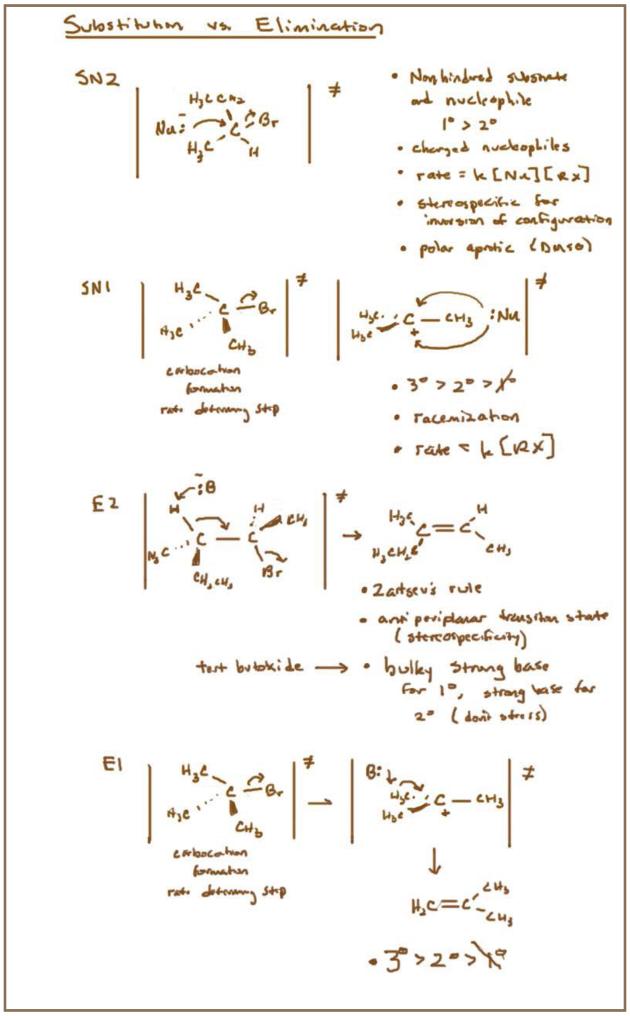


Organic Chemistry

- Chemical Bonding and Organic Molecular Structure
  - Orbital Hybridization
  - Functional Groups
- Stereochemistry
- Reaction Mechanisms
  - Substitution vs. Elimination
  - Reactions of Aldehydes and Ketones
    - Nucleophilic Additions
    - Redox
    - Keto-Enol Tautomerism
  - Reactions of Alcohols
  - Reactions of Carboxylic Acid Derivatives
  - Miscellany - CoQ, Flavin, NAD^+
- Molecular Spectroscopy



Chemical Bonding and Molecular orbital Hybridization



Substitution vs. Elimination

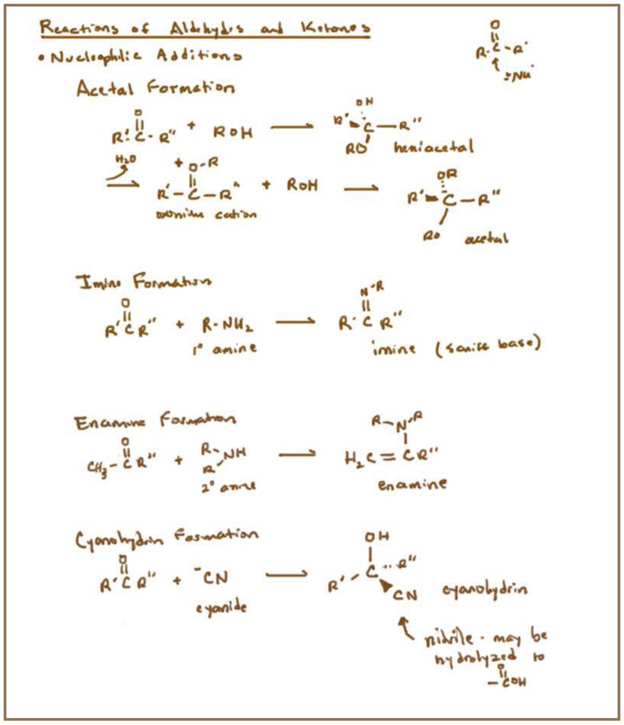
- Non hindered substrate and nucleophile 1° > 2°
- charged nucleophiles
- rate = k [Nu] [RX]
- stereospecific for inversion of configuration
- polar aprotic (DMSO)

- 3° > 2° > ~~1°~~
- racemization
- rate = k [RX]

- Zaitsev's rule
- anti periplanar transition state (stereospecificity)

tert butoxide → • bulky strong base for 1°, strong base for 2° (don't stress)

- 3° > 2° > ~~1°~~



Reactions of Aldehydes and Ketones

- Nucleophilic Additions

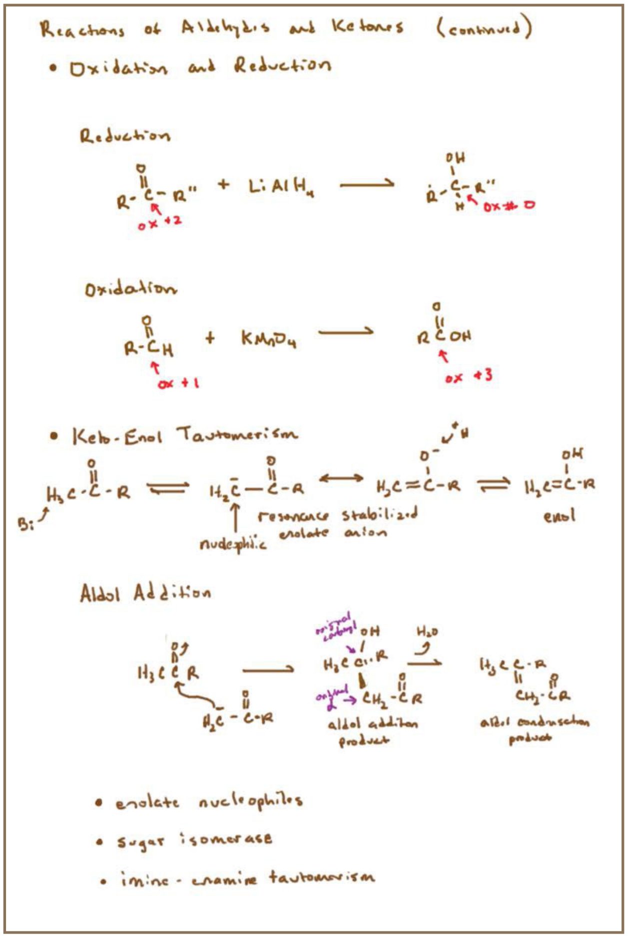
Acetal Formation

Imine Formation

Enamine Formation

Cyanohydrin Formation

nitrile - may be hydrolyzed to −C(=O)OH



Reactions of Aldehydes and Ketones (continued)

- Oxidation and Reduction

Reduction

Oxidation

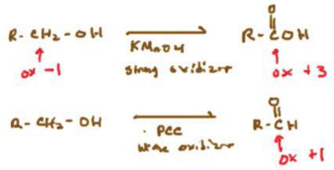
- Keto-Enol Tautomerism

Aldol Addition

- enolate nucleophiles
- sugar isomerase
- imine - enamine tautomerism

Reactions of Alcohols

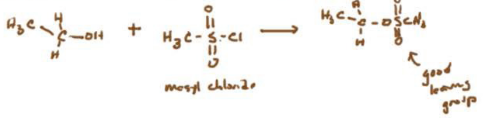
Oxidation of Alcohols



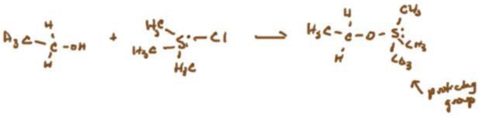
SN1 and SN2 substitution

- Requires acid catalysis
  - -OH is a poor leaving group

Mesylate and Tosylate Leaving Groups

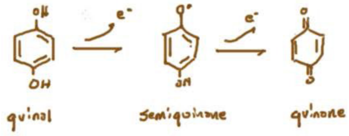


Silyl Protecting Groups

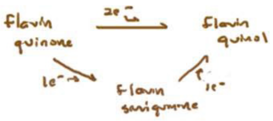


Miscellany

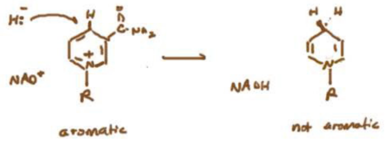
Quinol- Quinone Oxidation Reduction



Flavin

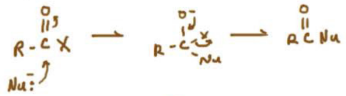


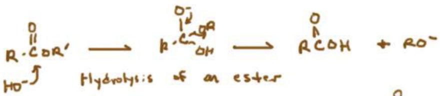
Nicotinamide



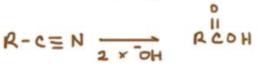
Carboxylic Acid Derivatives

Nucleophilic Acyl Substitution

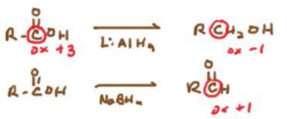


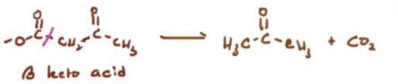


Nitrile Hydrolysis



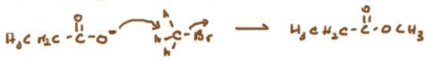
Reduction of Carboxylic Acids





Decarboxylation of β keto acid

Use of Carboxylate Nucleophile

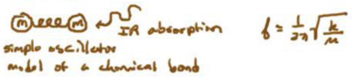


Lactones and Lactams

Molecular Spectroscopy

Infrared Spectroscopy

- Mechanism

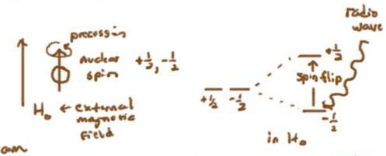


- Characteristic Absorbances

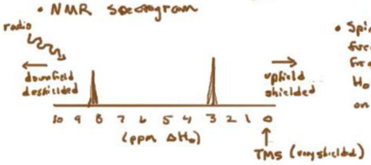
-C-H stretch	sp^3	$<3000\ cm^{-1}$	(k) wave number (cycles/cm ½)
	sp^2	$>3000\ cm^{-1}$	
	sp	$\sim 3200\ cm^{-1}$	
$\overset{O}{\overset{\|}{C}}$ stretch		$\sim 1700\ cm^{-1}$	(big)
-O-H stretch		>3200	(broad) H bonding
-N-H		>3200	(sharper)
aromatic overtone		~2000	
fingerprint region		below 1400	

NMR - ^1H and ^{13}C

- Mechanism

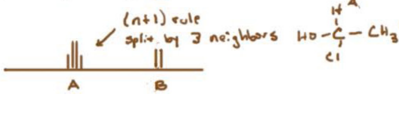


- NMR Spectrogram



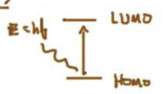
- Spin flip occurs when radio frequency = precessional frequency of the nucleus in H_0. Resonance f will depend on H_0 and gyromagnetic ratio.

- Causes of Deshielding
  - electronegative neighbor
  - magnetic anisotropy
    - aromatic ring current
- Spin-Spin Coupling



Molecular Spectroscopy (cont.)

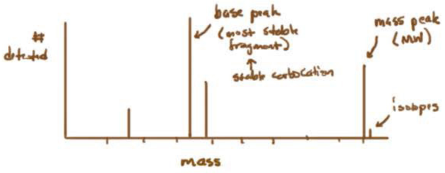
Ultraviolet Spectroscopy



- Conjugation C=C−C=C
  lowers transition energy HOMO → LUMO (bathochromatic shift)
  - Pigments absorb visible light

Mass Spectroscopy

$r = \frac{mv}{qH_0}$



Biochemistry

Proteins
- Amino Acids
- Protein Structure
- Protein Lab
- Oxygen Transporters
- Enzymes
  - Enzyme Activity
  - Enzyme Kinetics
  - Enzyme Inhibition
  - Allosteric Enzymes
  - Enzyme Mechanisms
  - Zymogens
- Connective Tissue Proteins

Carbohydrates

Lipids

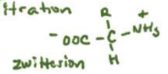
Nucleic Acids

Pathways
- Glycolysis
- Pyruvate Dehydrogenase
- β-Oxidation of Fatty Acids
- Citric Acid Cycle
- Oxidative Phosphorylation
- Glycogen Metabolism
- Gluconeogenesis
- Ketone Bodies
- Pentose Phosphate Pathway
- Urea Cycle

Amino Acids

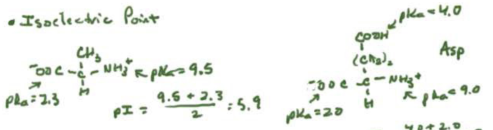
- Structure and Stereochemistry
- Categories
  - Hydrophobic vs. Hydrophilic
  - Ionizable vs. Not

  (glucogenic vs. ketogenic, essential vs. nonessential, etc)
- Titration



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

  - Isoelectric Point



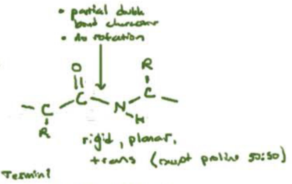
$pI = \frac{9.5 + 2.3}{2} = 5.9$

$pI = \frac{4.0 + 2.0}{2} = 3$

- Single Letter Codes
- Personalities
  - Metabolic Profile
    - Glucogenic vs. Ketogenic
    - Amino acids with prominent α keto acid conversions
      alanine — pyruvate
      aspartate – oxaloacetate (transaminase)
      glutamate – α ketoglutarate
    - Targets of phosphorylation
    - Targets of glycosylation (N-linked and O-linked)
    - Special
      proline – α helix disruptor
      glycine – empty space, achiral
      serine – nucleophile, serine protease
      lysine – forms Schiff base with substrate
      tyrosine, tryptophan – precursors of neurotransmitters
      histidine – acid-base catalyst, coordinates metals
      cysteine – forms disulfide

Protein Structure

- The Peptide Bond

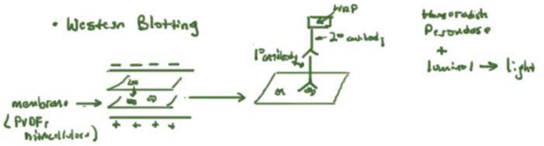


- Orienting with a Polypeptide
  - Identify N and C Termini
  - Follow the backbone N-C-C-N-C-C
- 1°, 2°, 3°, 4° structure
- Secondary structure Motifs
  - α helix
  - β pleated sheet
- Protein Folding
  - Anfinsen's Dogma
    - Exceptions - chaperones (heat shock protein) prions, amyloid
- Posttranslational Modification

Protein Lab

- Centrifugation

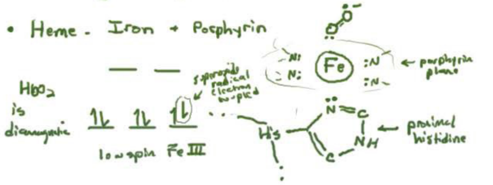
- Dialysis
- Chromatography
  - Basic Principle - Stationary and Mobile Phases
  - Techniques
    - TLC and Paper
    - Column
      - Size Exclusion - Large particles move faster
      - Ion Exchange
        - Anion exchange resin like DEAE is ⊕ charged
        - Gradient elution buffer 0.01M NaCl → 1.0M NaCl
      - Affinity
        - antibody antigen
        - enzyme substrate
        - polyhistidine - nickel
        - biotinylation - avidin
    - HPLC
- SDS-PAGE
  - Sodium Dodecyl Sulfate - denatures, uniform q/m
  - Polyacrylamide Gel Electrophoresis
- Western Blotting



- Protein Mass Spec
  - trypsin digest mass spectrum

Oxygen Transporters

- Myoglobin
  - Structure
    - 6 α helices
    - hydrophobic interior
  - Function
  - Binding Affinity - P^{50} ~ 2 torr
- Heme - Iron + Porphyrin



- Hemoglobin
  - Structure
    - Quaternary structure

      HbA – $\alpha_2\beta_2$ HbF - $\alpha_2\gamma_2$
  - Oxygen Saturation Curve
    - p50 - 26 torr
    - sigmoidal - positive cooperativity, multisubunit, Hill coefficient > 1
  - Mechanism of Cooperativity
    - When O_2 binds Fe, pulls proximal histidine triggering conformational shift opening the other 3 sites for O_2

      Jacob Monod Model $R \rightleftharpoons T$
  - Effects of H^+, CO_2, DPG

$$R \underset{\text{DPG}\rightarrow}{\overset{\substack{\leftarrow O_2\\ H^+\rightarrow\\ CO_2\rightarrow}}{\rightleftharpoons}} T$$

$$CO_2 + H_2O \rightleftharpoons H_2CO_3$$

$$H_2CO_3 \rightleftharpoons HCO_3^- + H^+$$

$$H^+ + HbO_2 \rightleftharpoons HbH^+ + O_2$$

- HbF has less affinity for DPG

Enzyme Activity

- Biological Catalysts
- Lock and Key Hypothesis
- Induced Fit
- Stereospecificity
- Active Sites
  - Essential Residues
  - Mechanisms
- Modes of Catalysis
  - Proximity of Substrates
  - Acid-Base Catalysis
  - Stabilizing a Transition State or Intermediate
  - Imposing a Conformational Change
- Coenzymes - organic substance that helps enzyme function
  - NAD^+ · FAD · CoA · Ubiquinone (CoQ)
  - TPP · ascorbate · biotin · PLP · $NADP^+$
  - cobalamin · folate

Enzyme Kinetics

- With increasing [S] reaction rate approaches V_{max}
- Elementary Reaction

turnover #

$$E + S \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} ES \xrightarrow{k_2} E + P \qquad \left(k_2 \xleftarrow{\text{elementary}} k_{cat}\right)$$

$$V = k_2[ES]$$

- Steady State Assumption [ES] = constant

formation = breakdown

$$k_1[E][S] = (k_{-1}+k_2)[ES]$$

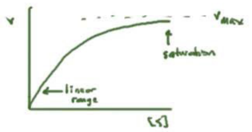
$$[ES] = \frac{[E][S]}{(k_{-1}+k_2)/k_1}$$

$$[ES] = \frac{[E][S]}{K_M} \qquad K_M = \frac{k_{-1}+k_2}{k_1}$$

$$[ES] = [E_T]\left(\frac{[S]}{[S]+K_M}\right) \leftarrow \text{\% saturation}$$

$$V = V_{max}\frac{[S]}{[S]+K_M} \quad \text{Michaelis Menten Equation}$$

- When $[S] >> K_M$: $V \approx V_{max}$
- $[S] << K_M$: $V = \frac{V_{max}}{K_M}[S]$
- $[S] = K_M$: $V = \frac{1}{2}V_{max}$



- Enzymes are tuned by evolution

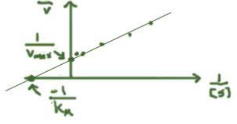
  If an enzyme has a low K_M compared to typical [S]
  - saturation
  - steady state

  An enzyme with a high K_M compared to [S]
  - linear range
  - responsive

- Lineweaver Burk Plot

$$\frac{1}{V} = \frac{1}{V_{max}} + \left(\frac{K_M}{V_{max}}\right)\left(\frac{1}{[S]}\right)$$

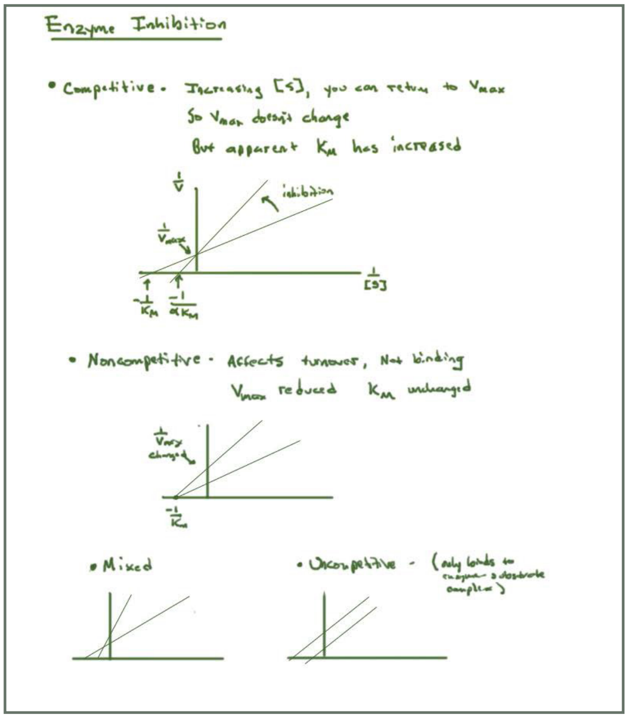
$$y = b + mx$$



- Catalytic Efficiency

$$\text{catalytic efficiency} - \frac{k_{cat}}{K_M}\left(\text{or } \frac{k_2}{K_M}\right)$$

- If high, binds easily, doesn't go backwards, turns over fast
- natural limit (dictated by diffusion) enzymatic perfection

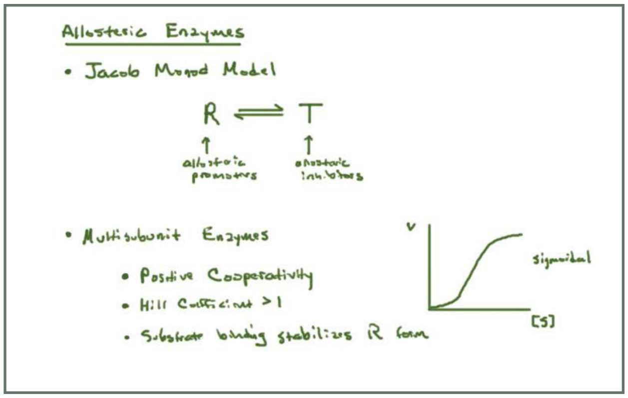


Enzyme Inhibition

- Competitive - Increasing [S], you can return to V_{max}
  So V_{max} doesn't change
  But apparent K_M has increased

- Noncompetitive - Affects turnover, Not binding
  V_{max} reduced K_M unchanged

- Mixed
- Uncompetitive - (only binds to enzyme-substrate complex)



Allosteric Enzymes

- Jacob Monod Model

$$R \rightleftharpoons T$$

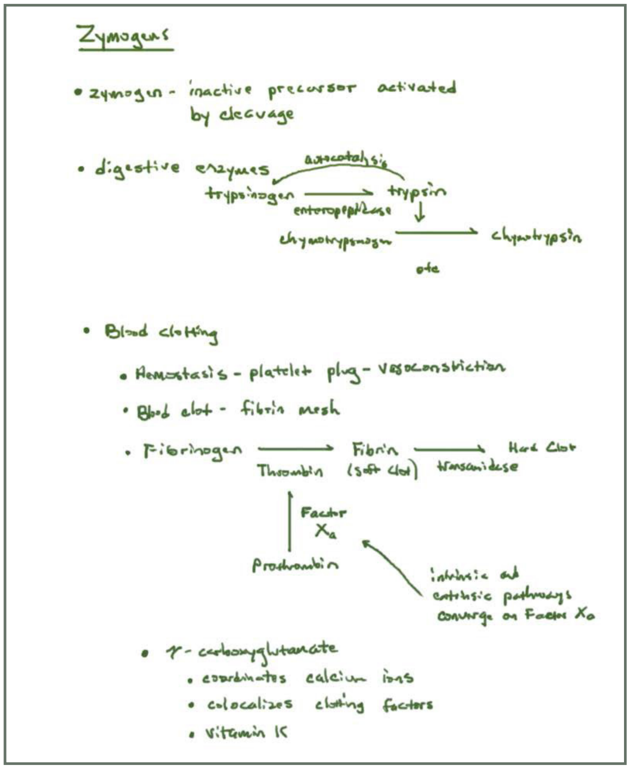
R ↑ allosteric promoters

T ↑ allosteric inhibitors

- Multisubunit Enzymes
  - Positive Cooperativity
  - Hill Coefficient > 1
  - Substrate binding stabilizes R form

Enzyme Mechanisms (Models for Reference)

- Chymotrypsin
  - Serin protease
  - catalytic triad Asp - His - Ser
  - 1st nucleophilic acyl substitution
    - formation of enzyme ester
  - 2nd nucleophilic acyl substitution
    - hydrolysis of the enzyme ester
- Carboxypeptidase
  - Zinc protease
  - Hydrolysis of C-terminal residue
  - Zn stabilizes tetrahedral intermediate
- Lysozyme
  - Degrades peptidoglycan
  - Peptidoglycan - Carbohydrate - chains of NAM and NAG
    - peptide crosslinks
  - Breaks glycosidic bond
  - Binding cleft for portion of chain
    - Energy in binding fuels conformational change for 1 residue to half-chair - proper orbital overlap to form oxonium cation in breaking the glycosidic bond
  - Glutamate in a hydrophobic pocket - raised pKa
    - protonated



Zymogens

- zymogen - inactive precursor activated by cleavage
- digestive enzymes

$$\begin{tikzcd} \text{trypsinogen} \arrow[r, "\text{enteropeptidase}"'] & \text{trypsin} \arrow[l, bend right, "\text{autocatalysis}"'] \arrow[d] & \\ \text{chymotrypsinogen} \arrow[rr] & {} & \text{chymotrypsin} \end{tikzcd}$$

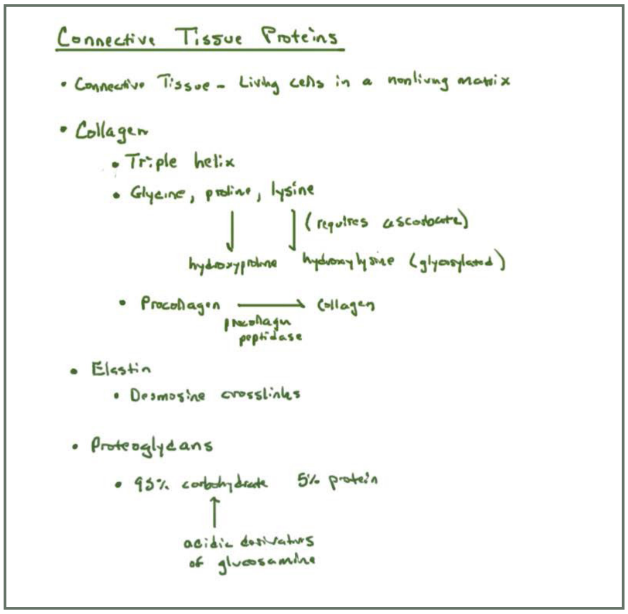
etc

- Blood clotting
  - Hemostasis - platelet plug - vasoconstriction
  - Blood clot - fibrin mesh
  - Fibrinogen $\xrightarrow[\text{Thrombin}]{}$ Fibrin (soft clot) $\xrightarrow[\text{transamidase}]{}$ Hard Clot

$$\begin{tikzcd} \text{Thrombin} \\ \text{Prothrombin} \arrow[u, "\text{Factor } X_a"'] \end{tikzcd}$$

intrinsic and extrinsic pathways converge on Factor X_a

  - γ-carboxyglutamate
    - coordinates calcium ions
    - colocalizes clotting factors
    - vitamin K



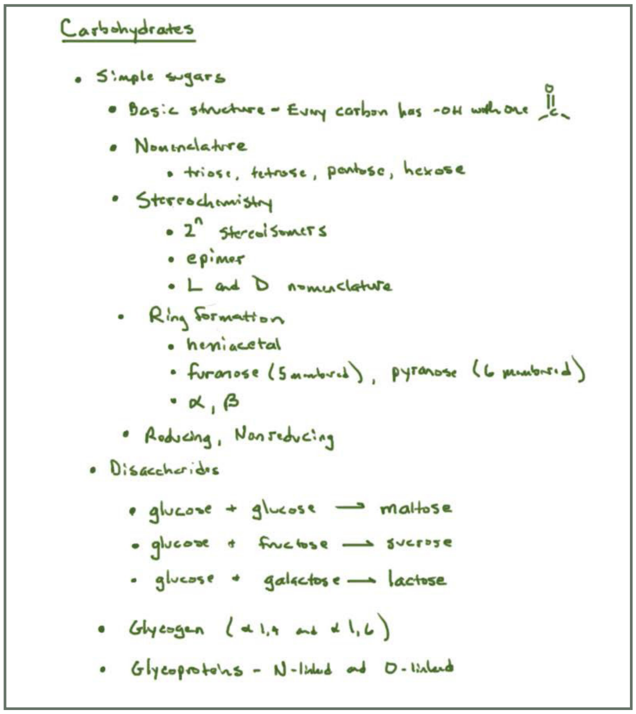
Connective Tissue Proteins

- Connective Tissue - Living cells in a nonliving matrix
- Collagen
  - Triple helix
  - Glycine, proline, lysine
    - proline ↓ hydroxyproline
    - lysine ↓ (requires ascorbate) hydroxylysine (glycosylated)
  - Procollagen $\xrightarrow[\text{peptidase}]{}$ Collagen

procollagen peptidase

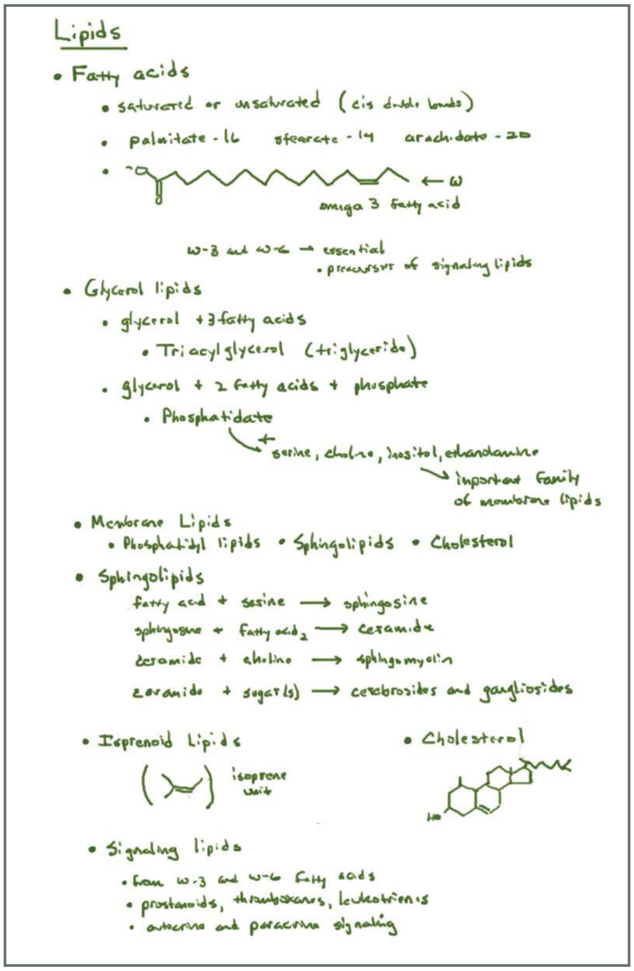
- Elastin
  - Desmosine crosslinks
- Proteoglycans
  - 95% carbohydrate 5% protein

↑ acidic derivatives of glucosamine



Carbohydrates

- Simple sugars
  - Basic structure - Every carbon has -OH with one C=O
  - Nomenclature
    - triose, tetrose, pentose, hexose
  - Stereochemistry
    - 2^n stereoisomers
    - epimer
    - L and D nomenclature
  - Ring formation
    - hemiacetal
    - furanose (5 membered), pyranose (6 membered)
    - α, β
  - Reducing, Nonreducing
- Disaccharides
  - glucose + glucose → maltose
  - glucose + fructose → sucrose
  - glucose + galactose → lactose
- Glycogen (α 1,4 and α 1,6)
- Glycoproteins - N-linked and O-linked



Lipids

- Fatty acids
  - saturated or unsaturated (cis double bonds)
  - palmitate - 16 stearate - 14 arachidate - 20
  - ← ω

omega 3 fatty acid

ω-3 and ω-6 → essential
- precursors of signaling lipids

- Glycerol lipids
  - glycerol + 3 fatty acids
    - Triacylglycerol (triglyceride)
  - glycerol + 2 fatty acids + phosphate
    - Phosphatidate

+ serine, choline, inositol, ethanolamine → important family of membrane lipids

- Membrane Lipids
  - Phosphatidyl lipids
  - Sphingolipids
  - Cholesterol
- Sphingolipids

fatty acid + serine ⟶ sphingosine

sphingosine + fatty acid$_2$ ⟶ ceramide

ceramide + choline ⟶ sphingomyelin

ceramide + sugar(s) ⟶ cerebrosides and gangliosides

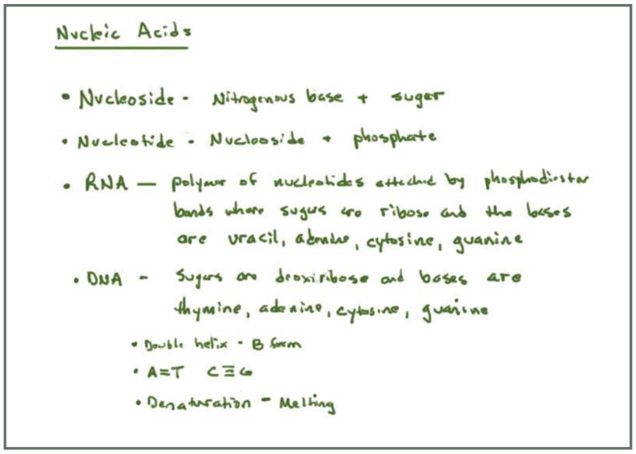
- Isprenoid Lipids

isoprene unit

- Cholesterol

HO

- Signaling lipids
  - from ω-3 and ω-6 fatty acids
  - prostanoids, thromboxanes, leukotrienes
  - autocrine and paracrine signaling



Nucleic Acids

- Nucleoside - Nitrogenous base + sugar
- Nucleotide - Nucleoside + phosphate
- RNA — polymer of nucleotides attached by phosphodiester bonds where sugars are ribose and the bases are uracil, adenine, cytosine, guanine
- DNA - Sugars are deoxiribose and bases are thymine, adenine, cytosine, guanine
  - Double helix - B form
  - A=T C≡G
  - Denaturation - Melting

Glycolysis

- Glucose + 2ADP + 2NAD$^+$ + 2Pi $\longrightarrow$ 2 Pyruvate + 2ATP + 2NADH
- Substrate Level Phosphorylation
- Steps
  - Hexokinase

    glucose + ATP $\longrightarrow$ glucose-6-phosphate + ADP
    - ⊖ΔG (glucose-6-phosphatase in gluconeogenesis)
    - phosphorylation traps glucose in the cell
    - G6P - crossroads - also feeds PPP and glycogen synthesis
    - Glucokinase in liver (high K_M)
    - Induced fit
  - Phosphoglucose Isomerase

    glucose-6-phosphate $\rightleftharpoons$ fructose-6-phosphate
    - Through keto-enol tautomerism
  - Phosphofructokinase I

    fructose-6-phosphate $\xrightarrow{ATP \to ADP}$ fructose 1,6 bisphosphate
    - ⊖ΔG (fructose-bis-phosphatase I in gluconeogenesis)
    - Committed step
      - Allosteric Promoters

        AMP (low energy charge)

        F2,6P (formed by PFK II)
      - Inhibitors - ATP, citrate
  - Aldolase

    fructose 1,6 bisphosphate $\rightleftharpoons$ dihydroxyacetone-phosphate + glyceraldehyde-3-phosphate
    - retroaldol cleavage (actually goes through iminium anion)
  - Triose Phosphate Isomerase

    dihydroxyacetone-phosphate $\rightleftharpoons$ glyceraldehyde-3-phosphate

(continued)

Glycolysis (continued)

- Glyceraldehyde-3-Phosphate Dehydrogenase

  glyceraldehyde-3-Phosphate + NAD$^+$ + Pi $\rightleftharpoons$ 1,3 Bisphosphoglycerate + NADH
- Phosphoglycerate Kinase

  1,3 Bisphosphoglycerate + ADP $\rightleftharpoons$ 3-Phosphoglycerate + ATP
- Phosphoglyceromutase

  3-phosphoglycerate $\rightleftharpoons$ 2-Phosphoglycerate
- Enolase

  2-Phosphoglycerate $\rightleftharpoons$ Phosphoenolpyruvate
- Pyruvate Kinase

  Phosphoenolpyruvate + ADP $\longrightarrow$ Pyruvate + ATP
  - ⊖ΔG (Pyruvate carboxylase + PEP carboxykinase in gluconeogenesis)
  - Inhibited by ATP and alanine
- Fermentation

  pyruvate $\xrightarrow{NADH \to NAD^+}$ lactate

Pyruvate Dehydrogenase Complex

- TPP attacks and decarboxylates pyruvate
- Then passes the two carbon unit to lipoamide, which oxidizes it.
- Transthioesterification with CoA forming acetyl CoA → TCA
- FAD oxidizes lipoamide.
- NAD$^+$ oxidizes FADH$_2$ forming NADH → electron transport

pyruvate $\xrightarrow[\text{CoA}]{NAD^+}$ acetyl CoA + NADH + CO$_2$

β Oxidation of Fatty Acids

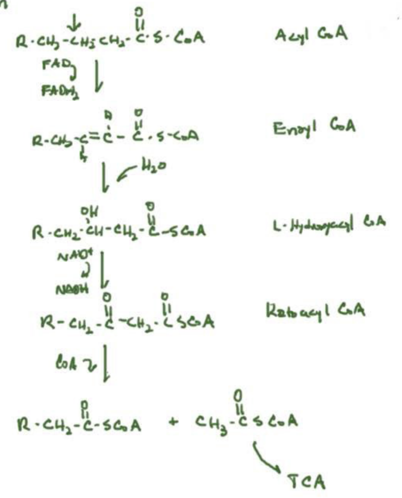
Triglyceride $\xrightarrow{\text{lipases}}$ Glycerol + Fatty Acids

Glycerol ↓ dihydroxy acetone phosphate

Fatty Acids ↓ β oxidation

- Activation of Fatty Acyl Carboxylates

  Acyl Carboxylate $\xrightarrow{ATP \to PPi}$ Acyl AMP $\xrightarrow{CoA \to AMP}$ Acyl CoA
- Acyl CoA shuttled to mitochondria by Carnitine
- β oxidation



$R\text{-}CH_2\text{-}CH_2CH_2\text{-}\overset{O}{\overset{\|}{C}}\text{-}S\text{-}CoA$ Acyl CoA

$\downarrow$ FAD → FADH$_2$

$R\text{-}CH_2\text{-}\overset{}{C}H{=}\overset{H}{C}\text{-}\overset{O}{\overset{\|}{C}}\text{-}S\text{-}CoA$ Enoyl CoA

$\downarrow$ H$_2$O

$R\text{-}CH_2\text{-}\overset{OH}{CH}\text{-}CH_2\text{-}\overset{O}{\overset{\|}{C}}\text{-}SCoA$ L-Hydroxyacyl CoA

$\downarrow$ NAD$^+$ → NADH

$R\text{-}CH_2\text{-}\overset{O}{\overset{\|}{C}}\text{-}CH_2\text{-}\overset{O}{\overset{\|}{C}}SCoA$ Ketoacyl CoA

$\downarrow$ CoA

$R\text{-}CH_2\text{-}\overset{O}{\overset{\|}{C}}\text{-}SCoA + CH_3\text{-}\overset{O}{\overset{\|}{C}}SCoA$ → TCA

Citric Acid Cycle

- Citrate synthase

  $\text{oxaloacetate} + \text{acetyl CoA} \longrightarrow \text{citrate}$

  - central carbon of citrate is achiral (prochiral) but subsequent reactions forming CO_2 are never the acetyl CoA carbons.
- Aconitase

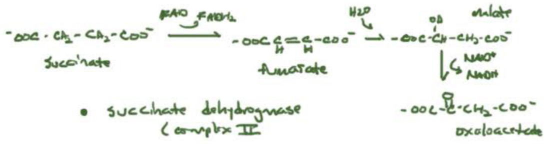
  $\text{citrate} \xrightarrow{H_2O} \text{aconitate} \xrightarrow{H_2O} \text{Isocitrate}$
- Isocitrate Dehydrogenase

  $\text{isocitrate} \xrightarrow{NAD^+ \ NADH} \text{oxalosuccinate} \xrightarrow{CO_2} \alpha\text{ ketoglutarate}$
- α-ketoglutarate Dehydrogenase
  - same mechanism as pyruvate dehydrogenase

  $\alpha\text{ketoglutarate} \xrightarrow{NAD^+ \ CoA} \text{succinyl CoA} + NADH + CO_2$
- Succinyl CoA Synthase

  $\text{Succinyl CoA} + P_i + GDP \longrightarrow \text{succinate} + GTP + CoA$

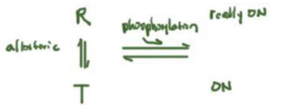
  - substrate level phosphorylation



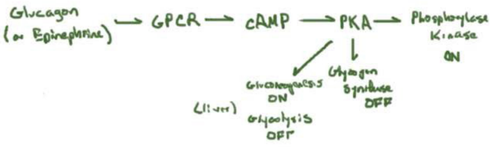
- succinate dehydrogenase (complex II
- fumarase
- malate dehydrogenase

Glygogen Metabolism

- Structure and Function of Glycogen
  - storage form of glucose - liver and muscle
  - Structure
    - α 1,4 and α 1,6
    - large, highly branched, granules, hydrophilic
    - glycogenin core - branch ends - nonreducing ends
- Glycogen Breakdown
  - Phosphorylase cleaves α 1,4 linkages liberating glucose 1-phosphate
  - Debranching enzyme and transferase
  - Phosphoglucomutase G1P → G6P
  - Glucose-6 phosphatase G6P → glucose (liver, kidney)
- Glycogen Synthesis
  - Glycogen synthase
  - G1P is activated to UDP-glucose before synthase
  - Branching enzyme
- Allosteric and Covalent Modes of Regulation of Glycogen Phosphorylase



- Allosteric
  - AMP ↑
  - G6P ↓
- Covalent - Phosphorylation by Phosphorylase Kinase



Insulin ⟶ Protein Phosphatase

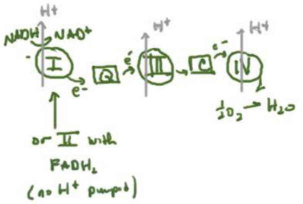
Oxidative Phosphorylation

Electron transport + Chemiosmosis

- Electron Transport

  $NAD^+ + H^+ + 2e^- \rightleftharpoons NADH \qquad E_o = -0.32V$

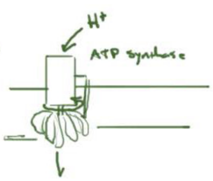
  $\frac{1}{2}O_2 + 2H^+ + 2e^- \rightleftharpoons H_2O \qquad E_o = 0.82V$



- Iron Sulfur Centers and Cytochromes
- Ubiquinone

  $\text{ubiquinone} \xrightarrow{1e^-} \text{ubisemiquinone} \xrightarrow{1e^- \ 2H^+} \text{ubiquinol}$

- Chemiosmosis



Gluconeogenesis

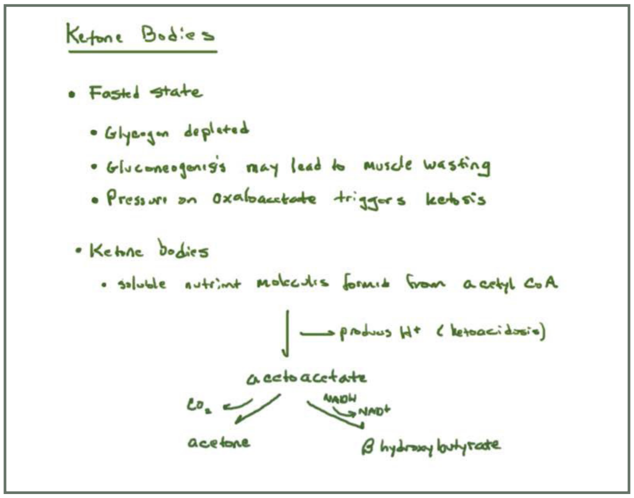
- Synthesis of glucose from noncarbohydrate precursors
  - amino acids, lactate, glycerol
  - principle points of entry - pyruvate, oxaloacetate, dihydroxyacetone phosphate
  - liver (also kidney cortex)
- Not a reversal of glycolysis
  - replacement of the irreversible steps of glycolysis -
    - hexokinase - replaced with glucose-6-phosphatase
    - PFK I - fructose-bis-phosphatase I
    - pyruvate kinase - 1) pyruvate carboxylase
      2) PEP carboxykinase
- Pyruvate Carboxylase - mitochondria
  - activation of biotin ⟶ carboxybiotin (requires ATP)

  pyruvate + carboxybiotin ⟶ oxaloacetate + biotin

  - Pyruvate carboxylase is activated by acetyl CoA, not only for gluconeogenesis but also for TCA intermediates
    - high ATP → gluconeogenesis
    - low ATP → TCA
- PEP carboxykinase - cytosol (sometimes mitochondria)

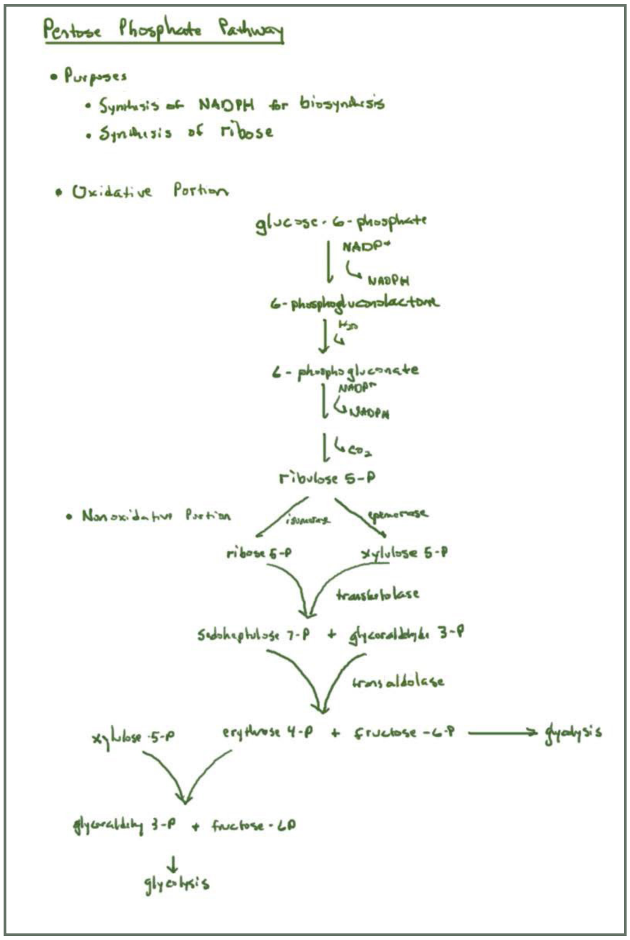
  $\text{oxaloacetate} + GTP \longrightarrow \text{phosphoenolpyruvate} + CO_2 + GDP$

  - oxaloacetate is shuttled as malate to cytosol
  - stimulated through PKA (glucagon) at the level of gene expression.
- Gluconeogenesis and Glycolysis are Reciprocally Regulated



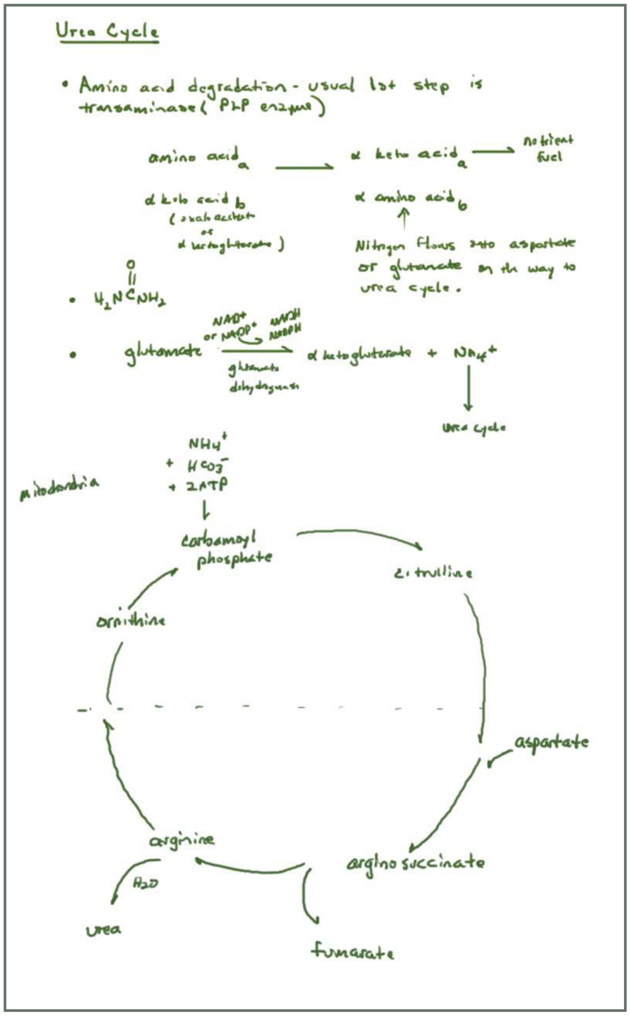
Ketone Bodies

- Fasted state
  - Glycogen depleted
  - Gluconeogenisis may lead to muscle wasting
  - Pressure on oxaloacetate triggers ketosis
- Ketone bodies
  - soluble nutrient molecules formed from acetyl CoA



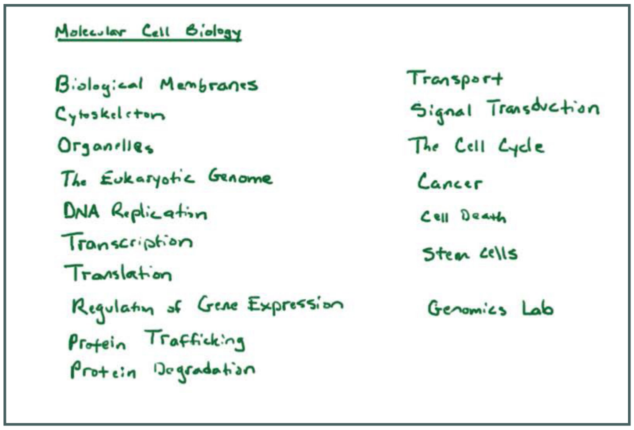
Pentose Phosphate Pathway

- Purposes
  - Synthesis of NADPH for biosynthesis
  - Synthesis of ribose
- Oxidative Portion
- Nonoxidative Portion



Urea Cycle

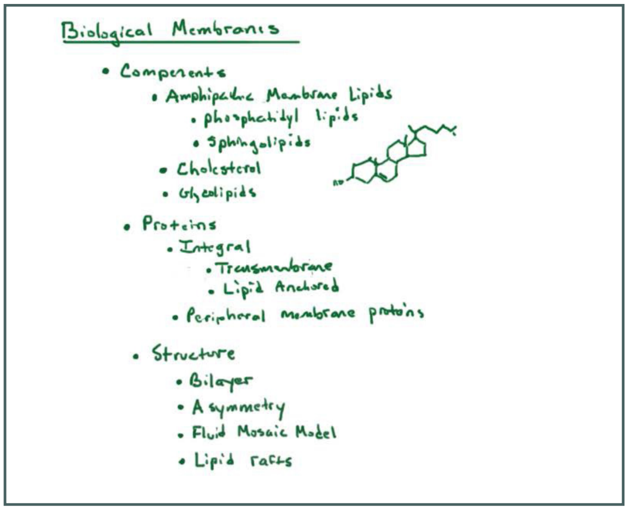
- Amino acid degradation - usual 1st step is transaminase (PLP enzyme)
- $H_2N\overset{O}{\overset{\|}{C}}NH_2$
- glutamate $\xrightarrow[\text{glutamate dehydrogenase}]{NAD^+ \text{ or } NADP^+ \quad NADH\ NADPH}$ α ketoglutarate + NH_4^+



Molecular Cell Biology

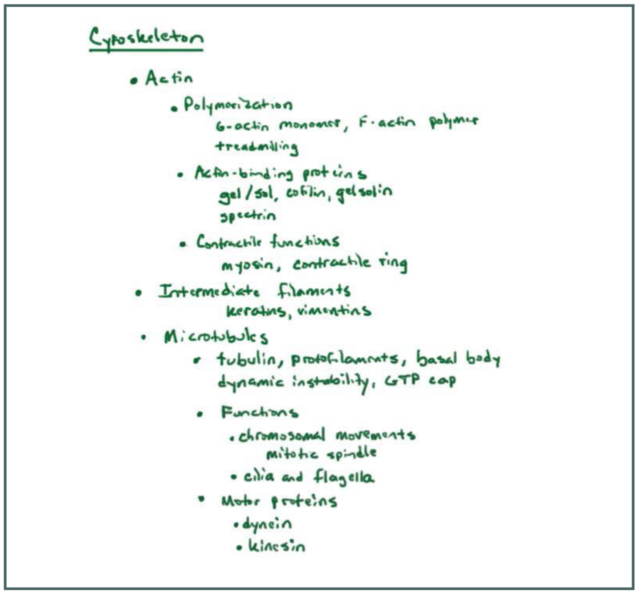
Biological Membranes
Cytoskeleton
Organelles
The Eukaryotic Genome
DNA Replication
Transcription
Translation
Regulation of Gene Expression
Protein Trafficking
Protein Degradation

Transport
Signal Transduction
The Cell Cycle
Cancer
Cell Death
Stem Cells
Genomics Lab



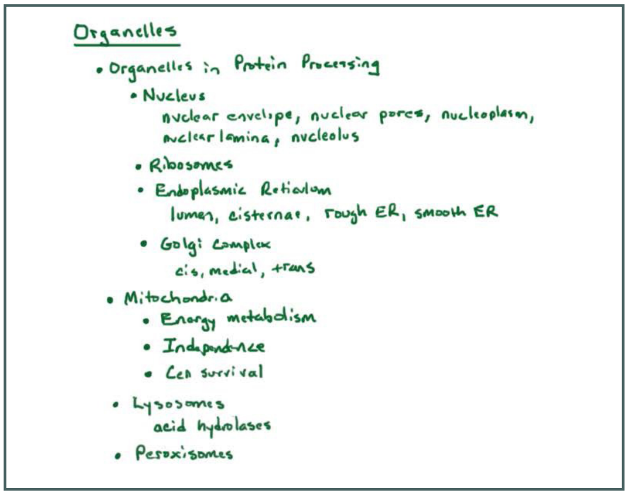
Biological Membranes

- Components
  - Amphipathic Membrane Lipids
    - phosphatidyl lipids
    - Sphingolipids
  - Cholesterol
  - Glycolipids
- Proteins
  - Integral
    - Transmembrane
    - Lipid Anchored
  - Peripheral membrane proteins
- Structure
  - Bilayer
  - Asymmetry
  - Fluid Mosaic Model
  - Lipid rafts



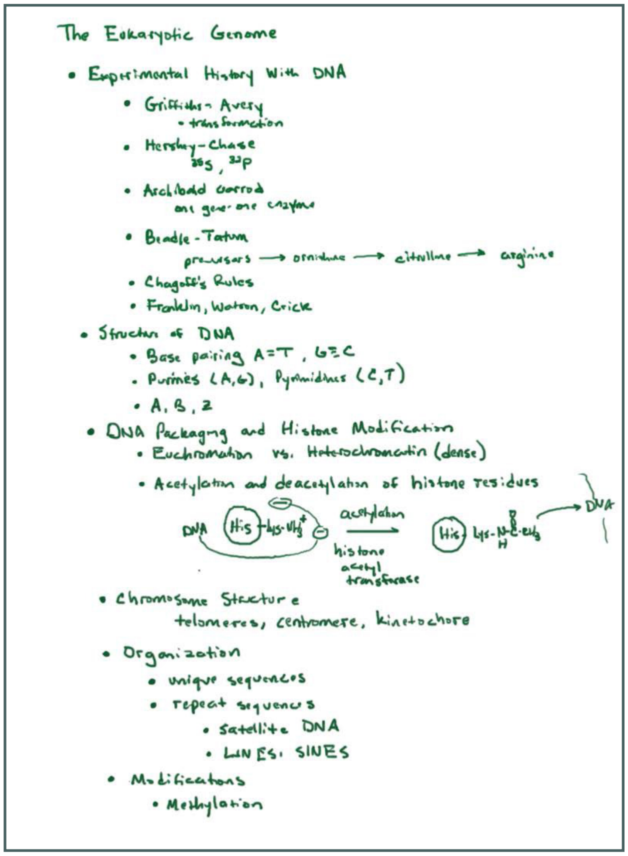
Cytoskeleton

- Actin
  - Polymerization
    G-actin monomer, F-actin polymer
    treadmilling
  - Actin-binding proteins
    gel/sol, cofilin, gelsolin
    spectrin
  - Contractile functions
    myosin, contractile ring
- Intermediate filaments
  keratins, vimentins
- Microtubules
  - tubulin, protofilaments, basal body
    dynamic instability, GTP cap
  - Functions
    - chromosomal movements
      mitotic spindle
    - cilia and flagella
  - Motor proteins
    - dynein
    - kinesin



Organelles

- Organelles in Protein Processing
  - Nucleus
    nuclear envelope, nuclear pores, nucleoplasm,
    nuclear lamina, nucleolus
  - Ribosomes
  - Endoplasmic Reticulum
    lumen, cisternae, rough ER, smooth ER
  - Golgi complex
    cis, medial, trans
- Mitochondria
  - Energy metabolism
  - Independence
  - Cell survival
- Lysosomes
  acid hydrolases
- Pesoxisomes

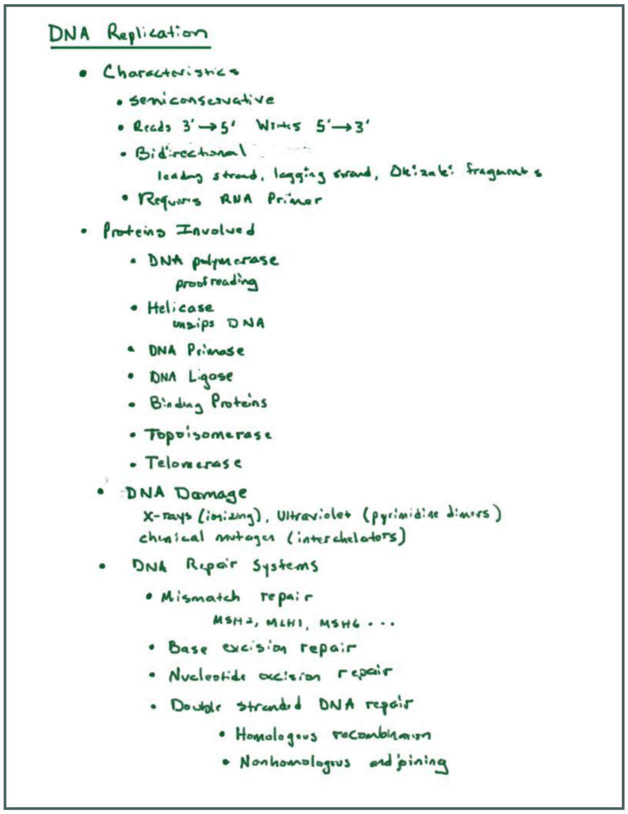


The Eukaryotic Genome

- Experimental History With DNA
  - Griffiths - Avery
    - transformation
  - Hershey-Chase
    ^{35}S, ^{32}P
  - Archibald Garrod
    one gene-one enzyme
  - Beadle-Tatum
    precursors → ornithine → citrulline → arginine
  - Chagoff's Rules
  - Franklin, Watson, Crick
- Structure of DNA
  - Base pairing A=T, G≡C
  - Purines (A,G), Pyrimidines (C,T)
  - A, B, Z
- DNA Packaging and Histone Modification
  - Euchromatin vs. Heterochromatin (dense)
  - Acetylation and deacetylation of histone residues

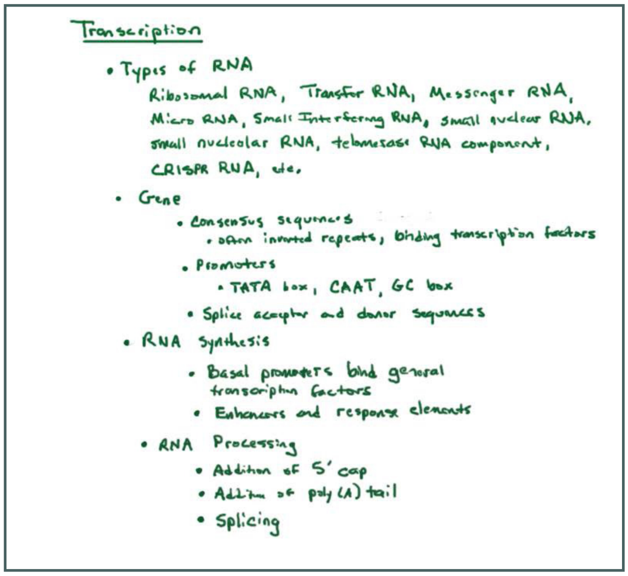
$$\text{DNA}\ \boxed{\text{His}}\text{-lys-}NH_3^+ \ominus \xrightarrow[\text{histone acetyl transferase}]{\text{acetylation}} \boxed{\text{His}}\text{-Lys-}\underset{H}{N}\text{-}\overset{O}{\overset{\|}{C}}\text{-}CH_3 \rightarrow \text{DNA}$$

- Chromosome Structure
  telomeres, centromere, kinetochore
- Organization
  - unique sequences
  - repeat sequences
    - Satellite DNA
    - LINES, SINES
- Modifications
  - Methylation



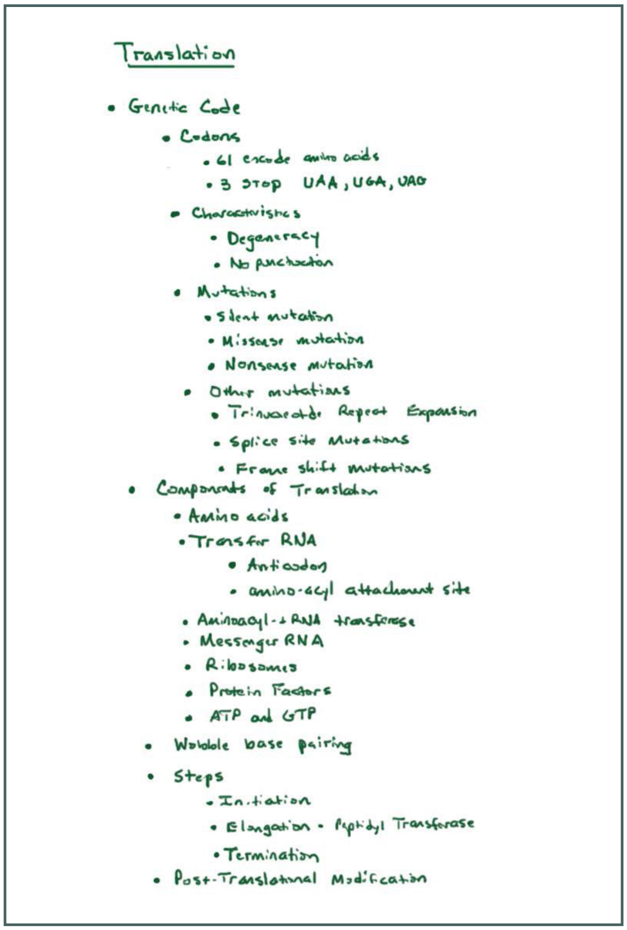
DNA Replication

- Characteristics
  - semiconservative
  - Reads 3'→5' Writes 5'→3'
  - Bidirectional
    leading strand, lagging strand, Okizaki fragments
  - Requires RNA Primer
- Proteins Involved
  - DNA polymerase
    proofreading
  - Helicase
    unzips DNA
  - DNA Primase
  - DNA Ligase
  - Binding Proteins
  - Topoisomerase
  - Telomerase
- DNA Damage
  X-rays (ionizing), Ultraviolet (pyrimidine dimers)
  chemical mutagen (interchelators)
- DNA Repair Systems
  - Mismatch repair
    MSH2, MLH1, MSH6 ...
  - Base excision repair
  - Nucleotide excision repair
  - Double stranded DNA repair
    - Homologous recombination
    - Nonhomologous end joining



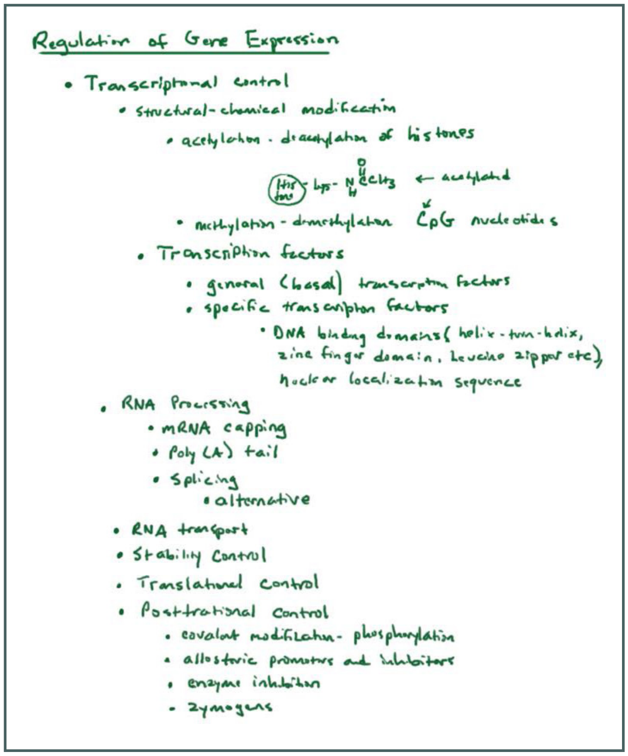
Transcription

- Types of RNA
  Ribosomal RNA, Transfer RNA, Messenger RNA, Micro RNA, Small Interfering RNA, small nuclear RNA, small nucleolar RNA, telomerase RNA component, CRISPR RNA, etc.
- Gene
  - Consensus sequences
    - often inverted repeats, binding transcription factors
  - Promoters
    - TATA box, CAAT, GC box
  - Splice acceptor and donor sequences
- RNA synthesis
  - Basal promoters bind general transcription factors
  - Enhancers and response elements
- RNA Processing
  - Addition of 5' cap
  - Addition of poly (A) tail
  - Splicing



Translation

- Genetic Code
  - Codons
    - 61 encode amino acids
    - 3 stop UAA, UGA, UAG
  - Characteristics
    - Degeneracy
    - No punctuation
  - Mutations
    - Silent mutation
    - Missense mutation
    - Nonsense mutation
  - Other mutations
    - Trinucleotide Repeat Expansion
    - Splice site Mutations
    - Frame shift mutations
- Components of Translation
  - Amino acids
  - Transfer RNA
    - Anticodon
    - amino-acyl attachment site
  - Aminoacyl-tRNA transferase
  - Messenger RNA
  - Ribosomes
  - Protein Factors
  - ATP and GTP
- Wobble base pairing
- Steps
  - Initiation
  - Elongation - Peptidyl Transferase
  - Termination
- Post-Translational Modification



Regulation of Gene Expression

- Transcriptional control
  - structural-chemical modification
    - acetylation - deacetylation of histones

      $\boxed{\text{Histone}}-\text{lys}-\underset{H}{N}\overset{O}{\overset{\|}{C}}CH_3$ ← acetylated

    - methylation - demethylation CpG nucleotides
  - Transcription factors
    - general (basal) transcription factors
    - specific transcription factors
      - DNA binding domains (helix-turn-helix, zinc finger domain, Leucine zipper etc), nuclear localization sequence
- RNA Processing
  - mRNA capping
  - Poly (A) tail
  - Splicing
    - alternative
- RNA transport
- Stability Control
- Translational control
- Posttrational control
  - covalent modification - phosphorylation
  - allosteric promoters and inhibitors
  - enzyme inhibition
  - zymogens

Protein Trafficking

- Trafficking of Proteins Synthesized on Bound Ribosomes
  N-terminal signal sequence, signal recognition particle (SRPs)
  - ER - N-linked glycosylation (dolichol), transport vesicles
  - Golgi complex - cis, medial, trans - phosphorylations, O-linked glycosylation, protease, mannose-6-phosphate tag (targets to the lysosome)
    - Lysosome - acid hydrolases, endosome, clathrin
    - Secretion
- Trafficking from Free Ribosomes
  - Cytosolic Proteins
  - Nuclear Proteins - nuclear localization sequence (NLS), importin
  - Mitochondrial Proteins - chaperones, TOM, TIM, N-terminal mitochondrial import sequence
  - Peroxisomes - C-terminal tripeptide signal

Protein Degradation

- lysosomal - autophagy, autophagosomes (from ER)
- Proteosomal Degradition
  - Modes of recognition - protein half life
  - Ubiquitination - Ubiquitin-activating enzyme (E1), ubiquitin-conjugating enzyme (E2), ubiquitin-ligase (E3)
  - Proteosome

Transport

- Basics of Diffusion and Osmosis
  - Membrane permeability
  - Osmotic pressure, cell volume
- Passive Transport
  - Catalyzed transport (Facilitated transport)
    Km (50% saturated), V_{max}
  - ion channels, gated channels
- Active Transport
  - Primary Active Transport (direct ATP cleavage)
    P-class pumps, F-class, V-class, ABC-class
  - Secondary Active Transport (cotransport)
    symport, antiport
- Glucose Transport
  - Facilitate Transport (GLUT)
    glucose concentration, # of carriers
    - Role of insulin
      insulin sensitive and insulin insensitive
  - Active transport of glucose
    - proximal convoluted tubule, intestine
- Drug Transport
  - Solute carriers
  - ABC transporters

G Protein Signaling

- GPCR signaling
  - Mechanism

CAMP
↓
PKA

  - Other 2nd Messengers
    - Phospholipase C

$$\text{phosphatidyl inositol 4,5-bisphosphate (PIP}_2\text{)} \xrightarrow{PLC} IP_3 + DAG$$

inositol triphosphate — diacylglycerol

↓ IP_3
release of Ca^{++} from ER
↓ DAG
PKC (+ calmodulin)

- Ras G Proteins
  - Context is usually downstream from a catalytic receptor
  - Signaling Mechanism
    - Transautophosphorylation of receptor Y residues
    - SH2 domains (to bind phosphorylated sites) of effector molecules
    - SHC - SOS - Ras complex

GTP GDP
↓
Ras-GTP
Raf
MEK
MAPK
↙ ↓ ↘
targets transcription factors
↓
expression of cyclins, etc

Catalytic Receptor Signaling

- Receptors with Intrinsic Tyrosine Kinase (Growth Factor)

  - After tyrosine activity, binding of proteins with SH2 domains occurs
  - Important Adapter Molecules
    - Ras → MAP kinase cascade
    - STATs (more typically associated with JANUS kinase)
    - PI3 kinase (not PLC)

$$PIP_2 \longrightarrow PIP_3$$

↓
Akt (also called protein kinase B)

- Receptors utilizing Nonreceptor Tyrosine Kinase (cytokine receptor)
  - Src Family
  - Janus Kinase (JAK)
    - JAK-STAT
- Insulin signaling
  - insulin receptor substrates (IRS)

Steroid Receptor Signaling

- Structure
- Nuclear-Initiated steroid Signaling
  - Intracellular receptor
    hormone binding domain, nuclear localization sequence,
    DNA binding domain (zinc finger motifs)
  - steroid hormone receptors
    vitamin A, vitamin D, retinoid, thyroid hormone
- Membrane Initiated

The Cell Cycle

- Interphase
  - G_1 and G_0
    restriction point
  - S phase
  - G_2 phase
- Mitosis
  - Prophase - chromosomes condense, centromere, kinetochores, mitotic spindle
  - Prometaphase - disassembly of nuclear envelope, spindles attach to kinetochores
  - Metaphase - metaphase plate, karyotype analyses
  - Anaphase - centromeres split, sister chromatids split
  - Telophase - nuclear envelope reforms
- Cytokinesis - cleavage furrow, aurora kinases
- Assessment of cell proliferation
  - DNA synthesis - ^3H thymidine
  - Dilution of cytoplasmic probe
  - Cell Cycle Analysis

Regulation of the Cell Cycle

- Cell cycle regulators
  cyclins, cyclin-dependent kinases (CDKs),
  cyclin-dependent kinase inhibitors
- Checkpoint Regulation
  - Tumor suppressors
    - G_1 checkpoint
    - Retinoblastoma (RB) protein
      - hypo- or hyper phosphorylation
        ↑ ← (cyclin D-CDK4/6, active MAPK)
        activity cycling
    - p53 - DNA damage leads to phosphorylation
      of p53 → activates p21
      → cell arrest and perhaps aptosis
    - cyclin dependent kinase inhibitors
      p21, INK4A, CIP/KIP
    - G_2 checkpoint
    - CDK1 - controls entry into mitosis
    - cdc25C phosphatase - removes inhibitory phosphorylations from CDK1
  - DNA damage and cell cycle checkpoints
    ATM, ATR inactivate cdc25C

Abnormal Cell Growth

- Protooncogenes and oncogenes
  - mechanism of conversion
- Tumor suppressor genes
  - p53
    - senses DNA damage
    - cell cycle arrest
    - activates apoptosis
  - Dominant and recessive nature of oncogenes
    and tumor suppressor genes
  - Molecular basis of cancer
  - Tumor progression
  - Inherited mutations
  - Mutations in Drug-Metabolizing Enzymes

Cell Death

- Necrosis - inflammatory response
- Apoptosis - bleb, phosphatidylserine (inner → outer leaf)
  - Functions - elimination of damaged cells - p53 → Bax
    development
    homeostasis
  - Initiation
    - Apoptosome
      p53 → Bax
      → exit of cytochrome C from mitochondria
      → formation of apoptosome
      → caspase cascade
    - Death receptors
      tumor necrosis factor receptor (TNRF)
      - death domain (cytoplasmic sequence),
        FADD, TRADD, Fas death receptor,
        Fas ligand, T-cytotoxic
  - Caspase family of proteases
    - classification - initiator and effector
    - targets
  - Bcl-2 Family
    - proapoptotic and anti apoptotic
      Bak, Bax　　　Bcl-2, Bcl-xL
  - Apoptosis in Disease
  - Laboratory assessment of apoptosis
    DNA laddering, TUNEL, Annexin, Flow Cytometry

Aging and Senescence

- Cellular Senescence
  - Phenotype
    - Irreversible cell cycle arrest
    - Senescence-associated heterochromatin
  - Induction
    - DNA replication stress
    - Mitochondria - ROS
    - Stem cell theory of aging
  - Molecular Mechanisms
    - p53
    - pRB

Genomics Laboratory

- Molecular cloning
  - Forming recombinant DNA
    - Restriction Endonuclease
    - Restriction site - AAGCTT
      AAGCTT ← sticky end
      TTCGAA
  - Vectors
    - Plasmids - restriction sites
      antibiotic resistance genes for screening
      origin of replication
      - Constructing a library
      - Expression vectors
    - λ Phage - stuffer region
      - cohesive ends - direct reassembly
- PCR - thermal cycler, Taq polymerase
  - Steps
    1) denaturation
    2) annealing (primers)
    3) elongation
  - RT-PCR - reverse transcriptase
  - real time PCR (quantitative PCR)
    - fluorescent probe - lights up in elongation
    - # of cycles required to get a detectable signal depends on the initial amount
- Electrophoresis
  - Denaturing (urea) and nondenaturing (native)
  - PAGE and agarose
  - postelectrophoretic - autoradiography, staining,
    blotting - Southern - DNA
    Northern - RNA
  - Sanger Sequencing
    - Carry out replication with di-deoxy chain terminators that are fluorescent (ddNTP) - then electrophoresis