CHEM106 General Chemistry II Course Competencies

Lsn 1: General Chemistry Review: *Electronegativity, Electron Configuration, Lewis Structures, Molecular Geometry, Hybridization, Double Bonds, Aromatic Structure, Kinetic Energy Molecular Distribution, and Vapor Pressure*

- *Electronegativity, charge distribution, and molecular bonding structure*
  - Demonstrate an understanding of electronegativity; understand and be able to clearly explain the basis for electronegativity periodic trends in terms of fundamental laws of electrostatic interactions (Coulomb's Law).
  - Understand how to use relative electronegativities of atoms to clearly depict charge distribution across chemical bonds. Be able to quickly predict the important partial charges on atoms within given molecules.
- *Electron configuration*
  - For a given atom or ion, use the periodic table to quickly list its specific electron configuration
  - Understand the valence electron configuration of atoms and ions
- *Molecular structure*
  - Draw molecular structures showing all bonds from a given molecular representation
  - Quickly draw complete Lewis structures, to include all nonzero formal charges, for a given molecule or ion
  - Predict electron arrangement, molecular geometry, hybridization, and bond angles around given atoms in molecules
- *Multiple bond structure*
  - Know and discuss double/triple bond geometry and hybridization
  - Outline and diagram cis/trans geometry about carbon-carbon double bonds
  - Outline, discuss, and use aromatic electronic structure and geometry
- *Distribution of molecular kinetic energies*
  - Calculate fractions of molecules having kinetic energies greater than a given energy at a given temperature
  - Graphically represent and be able to clearly explain the distribution of kinetic energies of a collection of molecules at various temperatures
  - Understand the kinetic energy conversions into potential energy necessary to separate molecules, to break bonds, or to react molecules
- *Vapor pressures*
  - Use molecular structures to predict relative vapor pressures of given substances
  - Use the kinetic molecular distributions to explain how vapor pressures change with temperature

Lsn 2: Intermolecular Forces (Noncovalent Interactions)*: Ionic Interactions, Hydrogen Bonds, Van der Waals Interactions, Dipole-Dipole and Ion-Dipole Interactions, Repulsive Interactions, Water Solvation, and Hydrophobic Interactions*

- *Noncovalent interactions and intermolecular forces*
  - Understand and be able to clearly discuss and diagram the basis for attractions between molecules/ions to include ion hydration, hydrogen bonding, London dispersion, dipole-dipole, ion-dipole, and cation-π electron interactions.
  - Understand and use the relative magnitude (in kJ/mole) of chemical bonds (e.g. ionic, covalent and metallic) vs intermolecular forces (hydrogen bonding, London dispersion, dipole/dipole) interactions.
  - Quickly draw diagrams that clearly show appropriate partial charges and intermolecular interactions among a given set of molecules or ions.
  - Predict points of potential H-bond donors and acceptors for any given molecular structure.
  - Predict and discuss relative boiling points (also vapor pressure, melting points, viscosity, surface

tension) from molecular structure

Lsn 3: <u>Solubility and Lipids</u>: *Thermodynamics of Liquid-Liquid Solubility, Octanol-Water Distribution Equilibrium Constants [Partition Coefficients (P)], Phospholipid Components and Structure, Cell Membrane Structure and Properties*

- *<u>Solubility, thermodynamics, and equilibria</u>*
  - Understand and be able to clearly explain the thermodynamics of solution formation
  - Know what equilibria constants are; be able to relate equilibria constants to changes in Gibbs Free Energy
- *<u>Partition coefficients (P)</u>*
  - Understand what is meant by the octanol-water partition coefficient (P) and clearly describe its significance
  - Solve problems involving P, log P, and drug concentrations or amounts distributed across water and 1-octanol phases
  - Be able to predict relative polarities and solubilities (hydrophilic/hydrophobic, lipophilic/lipophobic) of a given molecular structure
- *<u>Phospholipids</u>*
  - Understand and be able to quickly draw molecular structures of components within phospholipid molecules
  - Relate the structure of phospholipids molecules to solubility
- *<u>Membranes</u>*
  - Understand and draw the molecular structure of membranes
  - Understand and describe the forces that hold membranes together
  - Predict and explain how membrane fluidity changes with temperature, degree of saturation, and fatty acid chain length.
  - Clearly outline the role of cholesterol in cell membranes
  - Predict relative membrane permeability for a variety of types of molecules or ions
- *<u>Fats, oils, and fatty acids</u>*
  - Know the structure of saturated, monounsaturated, polyunsaturated, and trans fats; describe associated health effects
  - Relate the melting points of fats and oils to molecular structure
  - Understand and explain what is meant by omega fatty acids

Lsn 4: <u>Condensation and Hydrolysis Reactions</u>: *Alcohols and Carboxylic Acids, Triglyceride Formation, Polyphosphate and Phospholipid Formation*

- *<u>Molecules: carboxylic acids, fatty acids, amino acids, and alkaloids</u>*
  - Outline the structure of a carboxylic acid functional group and diagram its acid/conjugate base forms
  - Be able to draw the structure for fatty acids, to include those having one or more points of unsaturation
- *<u>Condensation reactions</u>*
  - Use partial charges within molecules to outline the basic mechanism for condensation reactions
  - Outline the chemical reactions and mechanisms for the formation of phospholipids from molecular subcomponents
  - Predict and outline fundamental mechanisms for condensation reactions such as those between
    - Acids and alcohols
    - Phosphates and alcohols
    - Amino acids
- *<u>Hydrolysis reactions</u>*
  - Outline the reactions involved in phospholipid hydrolysis

- Outline peptide hydrolysis chemical equations

Lsn 5: <u>Amino Acids</u>: *Structure, Chirality, Side Chain Polarity, Peptide Bond and Resonance, Peptide Condensation and Hydrolysis, Henderson-Hasselbalch Equation, Charge and pH, Solubility and P*

- *<u>Amino acids</u>*
  - Know and be able to quickly draw the general molecular structure of amino acids and be able to clearly diagram the acid/conjugate base forms for both the carboxylic acid and the amine functionalities
  - Be able to quickly draw the complete molecular structure showing all bonds for all of the following amino acids:
    - AA's with nonpolar side chains [Alanine(Ala,A), Valine(Val,V), Leucine(Leu,L), Isoleucine(Ile,I), Phenylalanine(Phe,F)]
    - AA's with polar uncharged side chains [Glycine(Gly,G), Serine(Ser,S), Threonine(Thr,T), Tyrosine(Tyr,Y), Cysteine(Cys,C), Asparagine(Asn,N), Glutamine(Gln,Q)]
    - AA's with carboxylic acid side chains [Aspartic Acid(Asp,D), Glutamic Acid(Glu,E)]
    - AA's with basic side chains [Lysine(Lys,K), Arginine(Arg,R), Histidine(His,H)]
  - Understand and explain amino acid chirality
- *<u>Peptides</u>*
  - Understand how peptide bonds are formed and draw appropriate resonance structures to explain peptide bond geometry
  - Diagram and understand the mechanisms for condensation and hydrolysis reactions of peptides
- *<u>Acid-base systems</u>*
  - Predict reactions of acids with water; predict reaction of bases with water.
  - Write and use equilibria expressions for dissociation of weak acids and bases, K_a and K_b; pKa's
  - Know the Henderson-Hasselbalch equation: be able to understand and use.
  - Predict predominant (and relative amounts) of acid/base forms (e.g. $COOH/COO^-$, $NH_3^+/\text{-}NH_2$) present at a given pH.
  - Know what an alkaloid is and be able to quickly draw acid/conjugate forms of a given alkaloid.
- *<u>Acid-base properties of amino acids</u>*
  - Predict acid-base forms of amino acids present at various pH's
  - Relate pH to amino acid functional group solubility in lipids or water

Lsn 6: <u>Protein Structure</u>*: Primary Structure, Disulfide Bonds, Secondary Structure - Alpha Helices and Beta Sheets, Tertiary/Quaternary Structures and Associated Noncovalent Interactions, Prions, PostTranslational Protein Modifications*

- *<u>Protein structure</u>*
  - Know the primary structure of peptides
  - Understand protein secondary structure; draw diagrams to represent the underlying reason for the formation of alpha helices and beta sheets
  - Understand the various types of interactions that can occur between side chains; draw appropriate diagrams and clearly discuss these
  - Understand protein tertiary and quaternary structures
  - Understand the underlying reasons for the structure of globular proteins

Lsn 7: <u>Enzymes: Structure and Function</u>: *Enzyme Catalysis, Mechanism of Action, Active Site, Substrate Binding, Catalytic Roles, Michaelis-Menton Kinetics, Lineweaver-Burk Plots, Km and Vmax Determination, Turnover Numbers, K_M and Substrate-Enzyme Affinity, Factors Affecting Reaction Rates, Rate Law, Arrhenius Equation, Activation Energy, Kinetic Molecular Distribution*

- *<u>Enzyme-substrate interactions</u>*
  - Be able to draw and to clearly explain reaction energy diagrams for enzyme-substrate interactions

- Understand the effects of inhibitors and what is specifically meant by IC50
- Understand and clearly explain the basis for important types of noncovalent enzyme-substrate interactions
- Clearly describe the enzyme inhibition process

- *Michaelis-Menton kinetics*
  - Write equilibria associated with enzyme-substrate interactions
  - Understand how reaction order changes with substrate concentration
  - Be able to use the Lineweaver-Burke relationship to calculate V_{max}, turnover number, and K_M
  - Understand the significance of K_M; understand the relation of K_M to enzyme-substrate complex stability and to maximum reaction rate
- *Chemical kinetics*
  - Understand the two fundamental requirements for a chemical reaction to occur…
  - Draw reaction coordinate-energy profiles and clearly label activation energies, and heat gained or lost
  - Understand and be able to clearly explain the role of catalysts
  - Understand and be able to use fundamental principles to clearly describe the dependence of reaction rate changes with temperature
- *Arrehenius equation*
  - Know and be able to use the Arrehenius equation for rate constant determination
  - Demonstrated the ability to calculate relative rates of reactions for different activation energies or temperatures
  - Understand and be able to calculate a reaction's activation energy from given rate constants at different temperatures
  - Understand relative impacts of temperature changes on rates for chemical reactions with low and high activation energies
  - Be able to use activation energies to predict rate constants at different temperatures
- *Rate law*
  - Understand what is meant by the rate law and outline the experimental procedures and methodology to determine reaction order
  - Use a given rate law to calculate rate constants and their associated units

Lsn 8: Enzymes as Drug Targets: *Active Site Inhibitors, Allosteric Inhibition, Competitive / Uncompetitive / Non-Competitive*
Inhibitors, Suicidal Substrates

- *Enzyme inhibition*
  - Understand and fully explain the basis for competitive enzyme inhibition
  - Understand and fully explain the basis for noncompetitive enzyme inhibition
  - Illustrate and discuss the effects of various types of inhibition on maximum reaction velocities and on substrate concentrations required to achieve half of the maximum reaction velocities
  - Discuss what is meant by suicidal inhibitors and use your understanding of condensation reactions to predict the specific mechanism of action for a given active site and inhibitor structures.

Lsn 9: Medical Approaches to Inflammation I: Nonsteroidal Anti-Inflammatory Drugs (NSAID's)

- *Inflammation*
  - Understand the overall molecular basis of inflammation
- *Cyclooxygenase (COX) inhibitors*
  - Understand the mechanism of action of cyclooxygenase (COX) inhibitors
  - Identify key structural features of NSAIDs and understand of specific important interactions with COX enzymes

    - Understand the specific interaction between the NSAID carboxylic group and the COX Arg-120 side chain; describe and effectively explain the effect upon K_M values that occur when neutral glutamine is substituted for Arg-120
    - Understand and clearly discuss aspirin's unique mechanism of action for irreversible COX inhibition
- *COX-2 Inhibitors*
    - Understand key differences between COX-1 and COX-2 enzymes, their physiological roles, and their respective inhibitors
    - Clearly describe the rationale for the development of COX-2 inhibitors
    - Explain the structure differences between nonspecific COX inhibitors and COX-2 specific inhibitors; relate these differences to active site geometries of thee two enzymes
    - Use COX-1 and COX-2 IC50 values for various substances to evaluate their respective potential for therapeutic development

Lsn 10: Medical Approaches to Inflammation II: Steroidal Anti-Inflammatory Drugs

- *Steroid structure and properties*
    - Understand and draw the skeletal structure for steroids
    - Discuss and predict the lipophilic/lipophobic properties of steroids
    - Outline where steroids are produced, what their sources are, and how they work hormones in the human body
- *Inflammation and steroids*
    - Understand the overall molecular basis of inflammation
    - Explain the molecular mechanism of action for steroids as anti-inflammatories
    - Understand the emerging relevance of inflammatory processes in various diseases
- *Central dogma*
    - Understand and clearly describe how genetic information is encoded in DNA
    - Explain what a gene is, what it does, and the two roles of the major regions (promoter and coding) of DNA gene templates
    - Generate a possible DNA sequence for the coding of a given peptide
    - Interpret a DNA or RNA sequence to generate an amino acid sequence that is coded for by this
- *Complex ions*
    - Understand the structure of complex ions and be able to explain the basis for their interaction
    - Relate Lewis acid/base chemistry to complex ion components
    - Clearly explain why complexes are colored and demonstrate an understanding of relevant molecular orbital energies
    - Understand and describe the structure of important biochemical complexes such as iron in hemoglobin.
- *Intracellular Receptors and Zinc fingers*
    - Diagram and discuss the structure of zinc fingers; clearly show the amino acid residues that interact with the zinc ion and how zinc fingers affect protein shape
    - Explain the underlying basis for the zinc finger mechanism of action in steroidal interactions with DNA
    - Discuss a new area of drug research that targets the zinc fingers in estrogen receptors to treat breast cancer

Lsn 11: Receptors as Drug Targets I*: Neurotransmitters and Hormones, Receptor-Ligand Interactions, Agonists, Antagonists, Partial Agonists, Inverse Agonists, Treatment of Hormone-Dependent Breast Cancers, Mechanisms of Actions for active ingredients in Advair*

- *Drug-receptor binding*
    - Understand and clearly discuss the ligand-receptor interactions; know the underlying physical

principles that govern these interactions
    - Understand chirality, enantiomers, racemic mixtures, and the chiral specificity of many drug receptors
    - Know, diagram, and explain the equilibrium constant expression for K_d, the dissociation constant for drug-receptor complex dissociation
- *Receptors*
    - Understand and describe some of the various classes of drug receptors present within the human body
    - Understand the various types of receptor responses
    - Understand receptor response differences to agonists, partial agonists, antagonists, and inverse agonists

Lsn 12: Receptors as Drug Targets II: *Affinity, Efficacy, and Potency; Sensitization, Tolerance, and Dependence, Dissociation Binding Equilibria, EC50, IC 50*

- *Affinity, Efficacy and Potency*
    - Define, illustrate and demonstrate an understanding of affinity, efficacy, and potency
- *Sensitization, Tolerance, and Dependence*
    - Illustrate, describe, and discuss the mechanism of action of the desensitization process that can occur due to prolonged receptor activation by an agonist
    - Illustrate, describe, and discuss the mechanism of action of the sensitization process that can occur due to prolonged receptor binding of antagonists
    - Discuss the molecular basis for tolerance and dependence.
- *Neurotransmitter molecular structures*
    - Acetylcholine
    - Dopamine, norepinephrine, epinephrine, and serotonin [5-Hydroxytryptamine (5-HT)]
    - Glutamate, GABA (gamma-aminobutyric acid)

Lsn 13: Nucleic Acids as Drug Targets

- *Nucleic acid structure*
    - Understand the structure of DNA and RNA to include the major components and specific features
    - Understand the condensation mechanism of action to form phosphate diester polynucleotides
    - Clearly explain the underlying physical basis for the attractions between the two strands of double helix DNA
- *Cancer Chemotherapy Treatments*
    - Outline the mechanism of action for platinum compounds [e.g. cisplatin $PtCl_2(NH_3)_2$] as chemotherapeutic agents for cancer patients
    - Describe the historical development of and outline the mechanism of action for nitrogen mustards as chemotherapeutic agents for cancer patients
    - Describe the mechanism of action for 5-Fluorouracil (5-FU) as a chemotherapeutic agent for cancer patients

Lsns 1-13: Mid-Term Examination

Lsn 14-15: Receptor Structure and Signal Transduction I-II - Overview and Thermodynamics of Ion Channels: *Ion Concentration Gradients, Cell Membrane Potentials, Nernst Equation and Membrane Equilibrium Potentials, Ion Movements and Resulting Inhibitory/Excitatory Potential Changes Ion Channels, Sodium-Potassium-ATP Pump Mechanism, Free Energy Changes of Ion Movement across Voltage and Concentration Gradients*

- *Ion Channels*

- Understand the relative intracellular and extracellular concentrations of sodium, potassium, calcium, and chloride ions
- Understand the sodium-potassium pump mechanism to maintain ion concentration gradients and the array of energetics associated with this
- Describe what an ion channel is and the specific properties of the substance that forms the channel
- Outline the difference and define what is meant by voltage-gated and ligand-gated ion channels.
- Describe the structure of voltage gated sodium ion channels and potassium ion channels to explain how they work. Understand the role of these ion channels in moving nerve pulses down an axon
- Understand the role and the basic general mechanism of G-Protein Coupled Receptors (GPCR) in cell signaling processes; explain the importance of these receptors in the pharmaceutical industry
- Understand and be able to clearly explain the physical basis for the selectivity of sodium and potassium ion channels
- Understand how increased permeability can affect voltage-gated ion channels

- *Neurochemistry*
  - Be able to relate concentrations to associated electric potentials (e.g. Nernst Equation) and changes in Free Energy
  - Demonstrate the ability to calculate Free Energy changes, equilibrium constants, and electric potentials associated with given reactions
  - Explain and calculate cell membrane potentials associated with ion concentration gradients
  - Relate resting membrane potential to ion permeability and to intracellular/extracellular concentrations
  - Calculate Free Energy changes necessary to move substances across concentration gradients and to move ions across potential gradients
- *Thermodynamics*
  - Understand and be able to use the Second Law of Thermodynamics to predict reaction spontaneity
  - Clearly explain how spontaneity is related to Free Energy change.
  - *Explain Free Energy changes associated with ATP-ADP interconversion; discuss and effectively use the concept of coupled reaction energetics*

Lsn 16: Receptor Structure and Signal Transduction III – GPCR's: *G-Protein Coupled Receptors Signaling Mechanism of Action*

- Understand the role and the basic general mechanism of G-Protein Coupled Receptors (GPCR) in cell signaling processes; explain the importance of these receptors in the pharmaceutical industry

Lsn 17: Receptor Structure and Signal Transduction IV – Kinase-Linked Receptors: *General Principles, Structure and Activation Mechanism of Tyrosine-Kinase Receptors, Tyrosine Kinase-Linked Receptors, Signal Transduction Involving Kinase-Linked Receptors*

Lsn 18: Cholinergics I: *Nervous System, Cholinergic System, Acetylcholine Structure & Receptor Binding*

- Outline and clearly explain the steps that occur to pass a nerve impulse from one neuron to another
- Know the structure of acetylcholine and explain how it is synthesized and hydrolyzed
- Clearly explain the two major mechanisms used to reduce neurotransmitter concentration levels at nerve synapses
- Understand the two (nicotinic and muscarinic) major classes of cholinergic (acetylcholine) receptors and the mechanism of action for each

Lsn 19: Cholinergics II: *Cholinergic Antagonists, Acetylcholinesterase Inhibitors*

Lsn 20: Adrenergics: *Geometry of adrenergic receptors, main types of norepinephrine receptors, interaction of adrenergic receptors with neurotransmitters, MOA of activated receptors*

- Describe the geometry of adrenergic receptors
- Classify the role of the three main types of norepinephrine receptors (alpha, beta 1, and beta 2)
- Describe the interaction of adrenergic receptors with neurotransmitters
- Discuss the mechanism of action of activated adrenergic receptors
- Be familiar with medications that target adrenergic receptors and discuss their mechanism of action

Lsn 21: <u>Psychoactive Drugs I -- Stimulants and Tranquilizers</u>:

Lsn 22: <u>Psychoactive Drugs II – Anti-Depressants</u>:

- Understand how PCP (angel dust) and Memantine (Namenda) affect the glutamate receptor NMDA (N-Methyl-D-Aspartate)
- Understand the synthesis steps involved in the production of L-DOPA, dopamine, norepinephrine, and epinephrine
- Understand the role of glycine and GABA receptors
  - Be able to explain the electrochemical basis for their inhibitory effects
  - Clearly explain how each of the following substances affects the GABA-ergic system: ethanol, barbiturates, strychnine, diazepam (valium), and caffeine
- Explain the role of monoamine oxidase (MAO) for catecholamine neurotransmitters; identify the role of MAO inhibitors.
- Explain the effect of dopamine levels on brain activity
  - Explain the effects of cocaine and of amphetamines on the dopaminergic system
  - Outline the role of seratonin and identify the substance from which it is produced
    - Explain what SSRI's are and what they are used for

Lsn 23: <u>Psychoactive Drugs III – Anti-Psychotics and Hallucinogens</u>:

Lsn 24: <u>Psychoactive Drugs IV – Cannabinoids, Opium & Opioid Analgesics</u>:

- Relate the structure of opioid receptors to opioid ligand geometry and identify key features of each
- Understand the history of opioid use and development by humans
- Understand the side-effects of opioids
- Describe the structure of natural opioids found in the human body and be familiar with its historical discovery

Lsn 25: <u>Chemistry of Local and General Anesthetics</u>:

- Understand the mechanism of action for local anesthetics
- Relate pK_a's to local pain anesthetics
- Understand the history of cocaine use by humans
- Describe the mechanism of action for general anesthetics
- Be familiar with the molecular structures for the more widely used general anesthetics

Lsns 14-25: Second Half-Term Examination

Lsns 1-25: Comprehensive Final Examination