Chemical Biology - Chem 370 (3 credits)

Spring Semester 2017

Instructors:

Dr. Jeff Jones, Fulmer 408, jpj@wsu.edu

Class Meeting: M/W/F 12:10-1:00 PM, Fulmer 438
Office Hours M/W/F 1:10-2:00 PM, Fulmer 408 (Jones)

Prerequisites:

Chem 345 with a C or better

Required Textbooks:

Principles of Biochemistry, Custom Edition For Washington State
Laurence A. Moran, Robert A Horton, Gray Scrimgeour, Marc Perry, ISBN-10: 1-323-58921 ISBN-13: 978-1-323-58921-2

Course Description:

This course is designed to provide advanced undergraduates with a foundational knowledge of chemical biology as it relates to graduate and professional programs requirements, more advanced coursework, and research needs. The first half of the course will focus on structure and function of the chemistry of biological systems while the second half of the course will concentrate on metabolic cycles, energy production, and the flow of biological information. This course is designed in part to extend the chemical reactions and mechanisms studied in undergraduate organic chemistry to biological systems. Particular emphasis will be placed on the connection between functional groups and oxidation/reduction reactions.

Course Objectives

To familiarize students with the chemical mechanisms that underlies biological systems.

Learning Outcomes

Student Learning Outcomes. At the end of this course, students will be able to:	Course Topics/Dates. The following topic(s)/date(s) will address this outcome	Evaluation of Outcome. This outcome will be evaluated by:
Describe biochemical reactivity in terms of organic functional group chemistry.	Lecture 1-12; and throughout course	Hourly Quiz I; comprehensive tests; homework
Interpret structural changes within a chemical framework considering bond making and bond breaking, specifically with regard to reduction/oxidation reactions.	Lecture 13-20 and throughout the course.	Hourly Quiz I; comprehensive tests; homework
Write clearly and articulate core concepts with regard to structure/function relations, metabolism, and energy production.	Lecture 21-24 and throughout the course	Hourly Quiz I; comprehensive tests; homework
Write clearly and articulate core concepts with regard to metabolism specific to amino, and nucleic acids.	Lectures 18-24	Hourly Quiz I; comprehensive tests; homework
Understand core concepts with regard biological information flow and human genetics: chromosome/DNA/RNA structures and chemistry and DNA/RNA processing.	Lectures 25-34	Hourly Quiz I; comprehensive tests; homework

Reason quantitatively by evaluating kinetic and structural data and devise reasonable mechanisms that account for experimental outcomes.	All lectures will focus on mechanism	Hourly Quiz I; comprehensive tests; homework

Grading Scheme:

Course letter grades will be based on two hourly exams, two hourly quizzes and homework. Each hourly exam is worth 100 points and the quiz is worth 50 points (Exams and quizzes are 80% of your grade) and homework worth 20%. Letter grades will be based on the following scale with possible adjustments:

A	93	B	83	C	73	D	65
A-	90	B-	80	C-	68	F	50
B+	87	C+	77				

Make up exam policy. There are no make-ups for missed exams. If you are ill during a scheduled exam or you are away from campus on a university sponsored event, notify the course instructor to schedule a proctored exam.

Attendance policy. Attendance will not be taken and will not count towards your letter grade. All the material necessary for success in this course will be presented in lecture therefore you are strongly encouraged to attend all lectures. If you miss a lecture, see the course instructor as soon as possible.

Lecture Schedule & Topics:

Lecture Schedule (tentative)

	Starting	Monday	Wednesday	Friday	
Week 1	Aug 21	Lecture 1	Lecture 2	Lecture 3	
Week 2	Aug 28	Lecture 4	Lecture 5	Lecture 6	
Week 3	Sept 4	Labor Day	Lecture 7	Lecture 8	
Week 4	Sept 11	Lecture 9	Lecture 10	Lecture 11	
Week 5	Sept 18	Lecture 12	Lecture 13	Lecture 14	
Week 6	Sept 25	No Class	Quiz 1	Lecture 15	
Week 7	Oct 2	Lecture 16	Lecture 17	**Lecture 18**	
Week 8	Oct 9	Lecture 19	Lecture 20/Review	**Test 1**	
Week 9	Oct 16	Lecture 21	Lecture 22	Lecture 23	
Week 10	Oct 23	Lecture 24	Lecture 25	Lecture 26	
Week 11	Oct 30	Lecture 27	Lecture 28	Lecture 29	
Week 12	Nov 6	Lecture 30	Lecture 31	Veteran's Day	
Week 13	Nov 13	Lecture 32	Lecture 33	Quiz 2 ?	
Week 14	Nov 20	Thanksgiving	Break		
Week 14	Nov 27	Lecture 34	Lecture 35	Lecture 36	
Week 15	Dec 4th	Lecture 37	Lecture 38	**REVIEW**	
		Test 2 Monday			
Finals					

Lecture Topics:

Part One: Introduction (Lectures 1 – 4)

1. Introduction to Chemical Biology.
2. Water.
    a. Polar covalent bonds, hybridization, and the structure of water and water clusters.

b. Buffers, ions in solution, micelles, and membranes.
c. Bonding: covalent, ionic, and hydrophobic effects.
d. Water as a nucleophile.
e. Water as an acid or base: organic functional groups in biological systems and under physiological pH, qualitative and quantitative analysis of acid/base equilibria

Part Two: Structure and Function (Lectures 5 – 20)

3. Amino Acids and the Primary Structures of Proteins.
    a. Review of amine and carboxylic acid functional group chemistry.
    b. Polyfunctional molecules: alpha amino acid, polar alpha amino acids, hydrophobic (aliphatic) amino acids
    c. Extending pKa tables to physiological pH: the qualitative and quantitative analysis of acid/base equilibria for amino acids.
    d. Amide bond synthesis and hydrolytic stability at physiological pH.
    e. Peptides and proteins: polymers linked by amide bonds.
    f. Purification and characterization of peptides and proteins: mass spectrometry, electrophoresis, and primary sequence.

4. Proteins: Three-Dimensional Structure and Function
    a. Conformational analysis of amide bonds: Relating butane and aliphatic conformations to peptides and proteins.
    b. Determining conformation in peptides and proteins: X-ray diffraction.
    c. Rational for fixed conformational space in proteins versus organic polymers in solution: Secondary structure.
    d. Common polymer conformations lead to common structures.
    e. Non-covalent interactions of proteins: Protein-protein interactions, structural proteins, and oxygen binding to heme proteins.

5. Properties of Enzymes - Enzymes as catalysts
    a. Relating catalytic reduction with metal catalysts (Pd, Pt) to enzymatic reduction.
    b. Hydrolysis reactions.
    c. Nucleophilic substitution and imine formation in organic and biological systems.
    d. Kinetics: From nucleophilic substitution to catalytic saturable processes.
    e. Rate constants in organic and biological reactions.
    f. Inhibition of a catalytic process, modulating activity in a biological systems and drug discovery.

6. Mechanisms of Enzymes
    a. Extensions of carbonyl functional group chemistry to biological nucleophilic substitutions.
    b. Converting bond energy to storable energy by oxidation of functional groups.
    c. Comparisons of solution phase acid/base chemistry with catalytic acid/base chemistry: the utility of having a strong acid and a strong base for a given reaction.
    d. Entropic versus enthalpic catalysis.
    e. Examples of rate acceleration by catalysis.

7. Coenzymes and Vitamins
    a. Lewis acids used to alter pKa of functional groups.
    b. Cofactor for storing reducing equivalents: NADH compared to $NaBH_4$.
    c. Revisiting imine formation in biological and organic systems: Vitamin B6.
    d. Other ways to alter pKa using vitamins.
    e. Making and braking carbon-carbon bonds: a Grignard type reaction in water! Forming enols.
    f. Radical reactions: controlled chaos of very reactive intermediates.

8. Carbohydrates
    a. Cyclohexane and cyclic hemiketals- review of the hydration of an aldehyde and ketone.
    b. Connecting sugars by an ethers linkage at the hemiketal carbon to form polysaccharides.
    c. More complex carbohydrate polymers: energy storage and altered protein function

9. Lipids and Membranes
    a. Review of carboxylic acids, aliphatic chains, and esters.
    b. Stereochemistry of carbon-carbon double bonds.

c. Review of the saponification reaction and the formation of a carboxylic acid and an alcohol.
d. triacylglyceride esters: lipids
e. Charged lipids.
f. Steroids as lipids.
g. Long chain carboxylic acids.
h. Lipid bilayers, the ionic state based on pKa for passive diffusion and its relationship to the extraction of organic compounds
i. Transporters to facilitate membrane crossing
j. Moving signals by a chemical cascade.

Part Three: Metabolism and Bioenergetics- The making and breaking of carbon-carbon bonds connected to oxidation (Lectures 21 – 26)

10. Introduction to Metabolism
    a. Review of thermodynamics.
    b. The energetic of a phosphorus-oxygen bond.
    c. Storing reducing equivalents to make phosphorus-oxygen bonds.

11. Glycolysis
    a. SN2 reaction- phosphorylation.
    b. Intramolecular oxidation of an alcohol and reduction of an aldehyde. Breaking carbon-carbon bonds followed by oxidation.

12. Gluconeogenesis, The Pentose Phosphate Pathway, and Glycogen Metabolism
    a. Making glucose
    b. Regulation of glucose synthesis.
    c. The pentose pathway.
    d. Glycogen formation and breakdown
    e. Maintenance of glucose levels and diabetes.

13. The Citric Acid Cycle
    a. Thiamine diphosphate: imine stabilization of an anion.
    b. Reduction of the disulfide bond of lipoamide to make a thioacylester
    c. Transfer of the acyl group to Acetyl CoA.
    d. Oxidation of dihydrolipoamide to lipoamide.
    e. Reduction of NAD+
    f. Oxidation of acetyl CoA: the citric acid cycle: a series of oxidation and decarboxylation reactions

14. Electron Transport and ATP Synthesis: Using the reducing equivalents produced by the citric acid cycle.
    a. Electron transfer
    b. Establishing a proton gradient.
    c. A very cool molecular machine that makes ATP.

15. Photosynthesis
    a. Converting light to energy.

16. Lipid Metabolism
    a. Synthesis of fatty acids.
    b. Prostaglandins and leukotrienes: Oxidations of double bonds, and peroxy cycloadditions.
    c. Cholesterol biosynthesis and isoprene chemistry: Multiple Claisen condensations.
    d. Oxidation of fatty acids.
    e. Lipids in disease states.

17. Amino Acid Metabolism
    a. Nitrogen fixation
    b. Amino acid synthesis: More imine chemistry
    c. Aromatic amino acids from the Claisen rearrangement.

18. Nucleotide Metabolism
    a. Nucleotide synthesis
    b. Reduction of RNA to DNA
    c. Stable sugar radicals for one electron chemical reactions.
    d. Metabolizing Purines and pyrimidines and disease states.

Part Four: Biological Information Flow (Lectures 26 – 39)

19. Nucleic acids
    a. DNA structure
    b. Nucleosomes and chromatin
    c. Nucleases and nucleic acid hydrolysis
    d. Restriction endonucleases
    e. DNA sequencing and synthesis, human genetics and genome project
20. DNA Replication, Repair, and Recombination
    a. DNA polymerases, DNA replication
    b. Model of the replisome
    c. Initiation and termination of DNA replication
    d. The polymerase chain reaction, DNA sequencing
    e. DNA repair, homologous recombination, topoisomerase
    f. Epigenetics
21. Transcription and RNA Processing
    a. RNA polymerase
    b. Transcription initiation and termination
    c. Regulation of transcription
    d. Post-transcriptional modification of RNA, transfer and ribosomal RNA processing
22. Protein Synthesis
    a. The Genetic Code
    b. Transfer RNA
    c. Aminoacyle-tRNA Synthetases
    d. Ribosomes
    e. Initiation, chain elongation, and termination of translation
    f. Regulation of protein synthesis
    g. Post translational processing, the "signal" hypothesis, protein glycosylation

Students with Disabilities:

Reasonable accommodations are available for students with a documented disability. If you have a disability and need accommodations to fully participate in this class, please either visit or call the Access Center (Washington Building 217; 509-335-3417) to schedule an appointment with an Access Advisor. All accommodations MUST be approved through the Access Center.

Academic Integrity:

Academic integrity will be strongly enforced in this course. Any student caught cheating on any assignment will be given an F grade for the course and will be reported to the Office Student Standards and Accountability. Cheating is defined in the Standards for Student Conduct WAC 504-26-010 (3). It is strongly suggested that you read and understand these definitions: http://conduct.wsu.edu/default.asp?PageID=338

Safety Statement:

The following websites detail the WSU Safety policy and plan. The content of these sites will be discussed on the first day of the term

- http://safetyplan.wsu.edu
- http://alert.wsu.edu
- http://oem.wsu.edu