Chemical Biology - Chem 370 (3 credits)

Spring Semester 2014

Instructors:

Dr. Jeff Jones, Fulmer 406/408, 335-5983, jpj@wsu.edu
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Class Meeting: M/W/F 11:10-12:00 PM, Fulmer 432
Office Hours M/W/F 2:10-3:00 PM, Fulmer 408 Jones and by appointment

Prerequisites:

Chem 345 with a C or better

Required Textbook:

Principles of Biochemistry, 5th Edition
Laurence A. Moran, Robert A Horton, Gray Scrimgeour, Marc Perry, ISBN-10: 0321707338 ISBN-13: 9780321707338

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 and energy production. This course is designed 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 exam I; comprehensive final exam
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 exam II; comprehensive final exam
Write clearly and articulate core concepts with regard to structure/function relations, metabolism, and energy production.	Lecture 21-30 and throughout the course	Hourly exam II; comprehensive final exam
Write clearly and articulate core concepts with regard to metabolism specific to amino and nucleic acids.	Lectures 31-33	Comprehensive final exam.
Reason quantitatively by evaluating kinetic and structural data and devise reasonable mechanisms that account for experimental outcomes.	All lectures will focus on mechanism	Hourly exam I, II, and comprehensive final exam.

Grading Scheme:

Course letter grades will be based on two quizzes (50 points total), two hourly exams and a comprehensive final. Each hourly exam is worth 100 points and the final exam is worth 150 points. Letter grades will be based on the following scale:

A	90%	B	80%	C	70%	D	60%
A-	87 %	B-	77%	C-	67%	F	50%
B+	83 %	C+	73%				

Make up exam policy. There are no make-ups for missed exams. If you are ill during a scheduled exam, your final exam will be worth 250 points. If 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)

Week 1	Starting	Monday	Wednesday	Friday	
Week 2	Jan 13	Lecture 1	Lecture 2	Lecture 3	
Week 3	Jan 20	MLK holiday	Lecture 4	Lecture 5	
Week 4	Jan 27	Lecture 6	Lecture 7	Lecture 8	
Week 5	Feb 3	Lecture 9	Lecture 10	Lecture 11	
Week 6	Feb 10	Lecture 12	Test Review	**Test 1**	
Week 7	Feb 17	President's day holiday	Lecture 13	Lecture 14	
Week 8	Feb 24	Lecture 15	Lecture 16	Lecture 17	
Week 9	Mar 3	Lecture 18	Lecture 19	Lecture 20	
Week 10	Mar 10	Lecture 21	Lecture 22	Lecture 23	
	Mar 17				Spring vacation
Week 11	Mar 24	Lecture 24	Test Review	**Test 2**	
Week 12	Mar 31	Lecture 25	Lecture 26	Lecture 27	
Week 13	Apr 7	Lecture 28	Lecture 29	Lecture 30	
Week 14	Apr 14	Lecture 31	Lecture 32	Lecture 33	
Week 15	Apr 28	Lecture 34	Review	Review	
Finals		TBA			

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. Ramachandran plots and the stereochemistry of the alpha carbon: an enantiomeric versus diastereomeric peptide.
    d. Rational for fixed conformational space in proteins versus organic polymers in solution: Secondary structure.
    e. Common polymer conformations lead to common structures.
    f. 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 in organic and biochemistry.
    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 disacharides.
    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 – 34)

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. Nucleic Acids and DNA/RNA
    b. Nucleotide synthesis
    c. Reduction of RNA to DNA

d. Stable sugar radicals for one electron chemical reactions.
e. Metabolizing Purines and pyrimidines and disease states.

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