



Utah State
UNIVERSITY

Principles of Biochemistry Chemistry 5700, Fall 2005

Section 1, M W F, 10:30-11:20 AM, NR 105

Professor Scott A. Ensign

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- Office Hours:** Tue., 9AM-10AM, Thurs.10:30AM-11:30 AM; Friday 12:30-1:30 PM, other times by appointment.
- Text:** "Lehninger Principles of Biochemistry", 2005, Nelson and Cox, 4th ed.
- WebCT** I will be using WebCT (Web Course Tools) for the management of Chem. 5700. All reserve materials (class standings, current exam keys, previous exams, problem set solutions, material from previous years, lecture overheads, kinemage files, and other material relevant to the course) will be posted on WebCT. The reserve materials will be provided to you as downloadable PDF files, which require AcrobatReader, a free program available for both IBM and mac platforms at the Adobe web site. Importantly, *you will take your weekly quizzes using WebCT*. To log on to WebCT, go to the web address: <http://webct.usu.edu/>. Your **USERNAME** is your BANNER login and your default **PASSWORD** is your BANNER password. The class ID is CHEM5700_SE. WebCT has many useful features (your assignment scores, a chat room, bulletin board, e-mail, etc.) and you should take the time to explore them from within our course page. I will provide more instructions on using WebCT in class.
- Lecture Overheads** Copies of my lecture overheads will be posted on WebCT. I strongly recommend downloading and printing the appropriate overheads BEFORE lecture and using them to take your notes in class.
- Kinemages** Kinemages are illustrations of macromolecules that can be viewed, rotated and manipulated using the free kinemage software MAGE. Kinemages and MAGE are excellent resource for visualizing complex molecules- while many graphics visualization programs have been developed, this one is still my favorite due to it's simplicity and ease of use. Listed on the course schedule are kinemage files that correlate with lecture topics. You may download these kinemage files from the course WebCT site; the free MAGE software can be downloaded from the kinemage web site:
<http://kinemage.biochem.duke.edu/kinemage/kinemage.php>
- Prerequisites:** A full year of organic chemistry (Chem 2310-2320, or equivalent)
Course Withdrawal: Withdrawal from the course after Sept. 19 will result in a "W" notation being placed on your transcript. No withdrawal is permitted after Nov. 16.
- Provisions:** The administration of Chem 5700 will adhere strictly to the regulations outlined in the Fall Semester Schedule of Classes, pp. 104-109. Per recent instructions from the Dean's office, no assignments will be accepted or graded from students

not formally enrolled in the course. Students not enrolled in the course may sit in only with instructor approval.

Course Content: Chemistry 5700 is the first of a two semester course sequence in Biochemistry. The intent of this sequence is to provide a thorough and comprehensive survey of biochemistry for science majors (undergraduates and graduates). No prior exposure to biochemistry is required nor expected. The focus of the course will be the molecular structure and function of biomolecules, principles of bioenergetics, and catabolism. Chemistry 5710 will focus on anabolism, signalling and information pathways. On the following pages is a tentative outline of the topics to be covered in the M W F 10:30 AM class meetings.

Quizzes Quizzes will cover material presented in the previous week's lecture. The quizzes are to be taken on-line using WebCT. The quizzes are open book but must be worked individually (i.e. no help from classmates, etc). The intent of the quizzes is to keep you on top of the course material- i.e. not waiting until exam time to cram. Quiz 1, the Organic Chemistry Competency Quiz, may be repeated as many times as you like over the course of the semester, and your HIGHEST score on this quiz will be recorded. You MUST obtain a score of 7 or better on this quiz -if your score is lower than that, you'll have to retake it until you receive a 7 or better. Quizzes 2-10 can be taken only once, and must be taken before 11 P.M. Friday of the week indicated on the schedule.

Problems: Problem sets and study questions will be periodically distributed during the course of the semester. I also recommend that you work the study questions and problems found at the end of each chapter of your textbook.

Exams: Three hourly exams (100 points each) will be given during class on the dates indicated on the course schedule. The final exam is in-class and counts 150 points (75 points on material presented since exam 3; 75 points comprehensive). The exam formats (i.e. short answer, short essay, problem solving) will be similar to the exams given in past years, which are on reserve with solution keys. The *comprehensive section only* of the final exam will be multiple choice. I strongly encourage you to work the past years exams as part of your exam preparation.

Grading:

| | |
|--------------------------------------|-------------------|
| 10 quizzes worth 10 points each..... | 100 points |
| Three hourly exams | 300 points |
| Comprehensive Final exam | 150 points |
| Total | 550 points |

In accordance with the Americans with Disabilities Act, reasonable accommodations will be provided for all persons with disabilities in order to ensure equal participation in Chem 5700. In cooperation with the Disability Resource Center, reasonable accommodation will be provided for students with disabilities. Please meet with the instructor during the first week of class to make arrangements. Alternative format print materials, large print, audio, diskette or Braille, will be available through the Disability Resource Center.

Class schedule

| Week | Day | Date | Lecture | Topic | Chapter, Lehninger | Kinemage exercise | Quiz |
|------|-----|-------|------------------------------|---|--------------------|-------------------|------|
| 1 | M | 8/29 | 1 | Introduction to the course | 1 | | 1 |
| | W | 8/31 | 2 | Water: properties, ionization, hydrophobic effects | 2 | | |
| | F | 9/3 | 3 | Amino acids and peptides | 3 | 1 | |
| 2 | M | 9/5 | | Holiday--no class | | | 2 |
| | W | 9/7 | 4 | Proteins: purification, composition, quantitation; amino acid sequence | 3 | | |
| | F | 9/9 | 5 | Proteins: secondary structures; fibrous proteins | 4 | 2 | |
| 3 | M | 9/12 | 6 | Proteins: tertiary and quaternary structure; common structural patterns | 4 | 3 | 3 |
| | W | 9/14 | 7 | Protein function: ligand binding; allostery; regulation | 5 | 4 | |
| | F | 9/16 | 8 | Enzymatic catalysis | 6 | | |
| 4 | M | 9/19 | 9 | Enzymes (cont.) | 6 | 5 | 4 |
| | W | 9/21 | 10 | Enzyme kinetics | 6 | | |
| | F | 9/23 | 11 | Enzyme kinetics (cont.) | 6 | | |
| 5 | M | 9/26 | 12 | Enzyme mechanisms | 6 | 6 | none |
| | W | 9/28 | 13 | Enzyme regulation | 6 | 7 | |
| | F | 9/30 | Exam 1: covers Lectures 1-13 | | | | |
| 6 | M | 10/3 | 14 | Carbohydrates: structure, nomenclature, stereochemistry, disaccharides | 7 | 8 | none |
| | W | 10/5 | 15 | Polysaccharides: structure, analysis, physical properties. | 7 | | |
| | F | 10/7 | 16 | Nucleotides and nucleic acids: structure and physical properties | 8 | 9 | |
| 7 | M | 10/10 | 17 | Nucleic acids (cont.) | 8 | | 5 |
| | W | 10/12 | 18 | Lipids | 10 | 10 | |
| | F | 10/14 | 19 | Lipids (cont.) | 10 | | |
| 8 | M | 10/17 | 20 | Membranes: bilayers, composition and structure; fluid mosaic model | 11 | 11 | 6 |
| | W | 10/19 | 21 | Transport across membranes | 11 | | |

| | | | | | | | |
|----|---|-------|---|--|----|----|------|
| | F | 10/21 | 22 | catch up; prepare for Exam 2 | | | |
| 9 | M | 10/24 | Exam 2: covers Lectures 14-22 | | | | none |
| | W | 10/26 | 23 | Introduction to metabolism, biochemical thermodynamics, bioenergetics | 13 | | |
| | F | 10/28 | 24 | High energy compounds and phosphoryl group transfer | 13 | | |
| 10 | M | 10/31 | 25 | Oxidation/reduction reactions in biology, electron transfer cofactors | 13 | | 7 |
| | W | 11/2 | 26 | elimination/isomerization/rearrangement; C-C bond breakage and formation | 13 | 12 | |
| | F | 11/4 | 27 | Glycolysis and catabolism of hexoses | 14 | 13 | |
| 11 | M | 11/7 | 28 | Glycolysis and catabolism of hexoses (cont.) | 14 | 14 | 8 |
| | W | 11/9 | 29 | Introduction to metabolic regulation: glycolysis | 15 | | |
| | F | 11/11 | 30 | pyruvate oxidation, citric acid cycle, cofactor role of TPP | 16 | 15 | |
| 12 | M | 11/14 | 31 | citric acid cycle (cont.) | 16 | | 9 |
| | W | 11/16 | 32 | oxidation of fatty acids, cofactor role of B12 | 17 | | |
| | F | 11/18 | 33 | finish fatty acid oxidation; prepare for Exam 3 | 17 | | |
| 13 | M | 11/21 | Exam 3: covers Lectures 23-33 | | | | none |
| | W | 11/23 | | holiday, no class | | | |
| | F | 11/25 | | holiday, no class | | | |
| 14 | M | 11/28 | 34 | amino acid catabolism | 18 | | 10 |
| | W | 11/30 | 35 | amino acid catabolism (cont.) | 18 | | |
| | F | 12/2 | 36 | mitochondrial electron transfer reactions | 19 | 16 | |
| 15 | M | 12/5 | 37 | ATP synthesis | 19 | | none |
| | W | 12/7 | 38 | ATP synthesis (cont.) | 19 | | |
| | F | 12/9 | 39 | Review for final | | | |
| | W | 12/14 | Final Exam (Lectures 1-39) 9:30-11:20 AM | | | | |

Chemistry 5700 Learning Objectives

Where a term is written with no explanatory comment, you should be able to define that term and its relevance in biochemistry.

GENERAL AND ORGANIC CHEMISTRY, WATER AND ACID/BASE EQUILIBRIA

- meaning of G, H, S
- know your organic functional groups
- Explain the features of water that make it suitable for supporting life
- Explain the thermodynamics of the dissolving process
- Explain the hydrophobic effect
- acid/base properties of water and weak acids/bases; meaning of and relation between K_a and pK_a
- composition of a buffer, interpretation of a titration curve, meaning of equivalence point, polyprotic acids
- buffer problems: calculate values of $[HA]$, $[A^-]$, pH, etc. given the necessary data for a buffer problem; be able to predict/calculate outcome of titration of a buffer solution with a weak acid or base.

AMINO ACIDS AND PROTEINS

- Properties of α -amino acids: chirality, numbering/lettering; acid/base properties; isoelectric point; know the names and structures of the 20 standard amino acids; reactivity of side chains; classify amino acids on the basis of "R" group
- peptide bond, nomenclature for naming polypeptides, disulfide bonds
- Protein composition: subunits, homo and hetero
- Protein purification: principles of ion exchange, size exclusion, affinity chromatography, nondenaturing and SDS-PAGE and the information they provide
- Specific activity, enzyme recovery, fold purification, estimate % of total protein based on fold purification
- 1°, 2°, 3°, 4° structure
- the nature of the peptide bond; cis vs. trans
- phi and psi angles and polypeptide conformation; Ramachandran plot
- Secondary structure: properties of the α -helix, β -sheet, β -turn, random coil
- fibrous proteins: α -keratin and collagen: structural features; use of nonnatural amino acids and why
- common structural motifs: globin fold, 4-helix bundle, α/β motifs (e.g. α/β barrel and saddle)
- motif vs. domain
- principles of ligand binding to proteins
- cooperativity vs. noncooperativity; hyperbola vs. sigmoidal binding curve
- oxygen binding properties of Mb and Hb; distal and proximal His
- Allosteric of hemoglobin; CO_2 , H^+ , and 2,3-BPG effects and physiological significance
- Basis for transition from T to R hemoglobin; importance of salt bridges (DON'T memorize specific ones!), O_2 binding, N-terminal carbamylation, protonation. Understand how nearby groups can perturb the pK_a of another functional group and how this is important in hemoglobin
- Molecular explanation for sickle cell anemia
- Homology between proteins: conserved vs. nonconserved residues; identical, similar, radical amino acid substitutions and possible consequences (think sickle cell anemia)

ENZYMATIC CATALYSIS

- Enzymes: features, cofactors vs coenzymes vs prosthetic groups
- Reaction coordinate diagram, activation energy, transition state, G, H, S

- Principles of enzyme catalysis: proximity, orientation, general acid/base, metal ion catalysis, covalent catalysis
- Understand and explain binding energy and transition state theory
- Enzyme kinetics: kinetic mechanism, reaction order, elementary steps, rate constant, Michaelis-Menten kinetics
- steady state assumptions, pre-steady state, post-steady state
- Michaelis-Menten equation; V_{max} , K_m , k_{cat} , K_D , catalytic efficiency. v vs. S plot and double-reciprocal plots
- Reversible inhibitors: competitive, noncompetitive, and uncompetitive. How they work and determining inhibitor type from kinetic data
- strategies for enzymatic rate enhancement, general acid/base, metal ion catalysis, covalent catalysis, nucleophiles and electrophiles in catalysis
- be able to push electrons properly when drawing an enzymatic mechanism
- Schiff base formation, and role of Schiff base in catalysis, as illustrated by acetoacetate decarboxylase
- metal ion catalysis as illustrated by carbonic anhydrase. What role(s) does the metal ion play in catalysis?
- charge shielding vs. charge stabilization
- features of chymotrypsin catalysis. Be able to draw the complete mechanism for chymotrypsin, and explain how the enzyme illustrates general principles of catalysis (general acids/bases, covalent catalysis, changing an amino acids pKa, transition state stabilization, substrate specificity)

ENZYME REGULATION

- covalent vs. allosteric regulation of enzymes
- allosteric enzyme regulation: principles, multiple binding sites, heterotropic and homotropic positive and negative modulators (effectors)
- product inhibition vs. feedback inhibition

CARBOHYDRATES

- Draw structures of D-glyceraldehyde, dihydroxyacetone, D-ribose, 2-deoxyribose, D-glucose, D-fructose in linear forms
- Draw fischer projections for alpha- and beta-D-glucopyranose, D-fructofuranose, D-ribofuranose, 2-deoxyribofuranose
- N-acetyl-D-glucosamine, N-acetylmuramic acid
- Define the terms monosaccharide, polysaccharide, aldose, ketose
- hemiacetal, hemiketal, acetal, ketal
- epimers, anomers, mutarotation, equatorial, axial
- reducing end, nonreducing end
- O-glycosidic, N-glycosidic
- amylose, amylopectin, glycogen
- cellulose, chitin, peptidoglycan, glycosaminoglycan, proteoglycan

NUCLEIC ACIDS

- Draw structures for adenine, thymine, guanosine, uracil, cytosine
- Draw the nucleosides and nucleotides of above bases, and name them properly
- nucleotide, nucleoside, nucleic acid, polynucleotide, 5' and 3' ends
- Chargaff's rules
- DNA double helix, B-DNA, base pairing, anti parallel, pitch

- major groove, minor groove
- base tilt, sugar pucker, anti vs. syn
- palindrome, mirror repeat, hairpin, cruciform
- RNA structure: single stranded vs. double stranded
- denaturation, annealing, hybridization, melting temperature

LIPIDS/MEMBRANES

- Draw structures of palmitic, stearic, oleic, linoleic acid, glycerol, a triacylglycerol, a glycerophospholipid
- Draw the structures of sphingosine, ceramide, sphingomyelin
- Describe GENERALLY the structural features of cholesterol (don't memorize all the subtleties)
- micelle, bilayer, liposome, vesicle
- soap, detergent
- phosphodiester
- lipase, phospholipase
- lateral, transverse diffusion
- cholesterol function
- order-disorder bilayer transition, transition temperature
- general mechanisms of hormone action
- hormone/cofactor functions of prostaglandin, vitamins D, A, K

MEMBRANE PROTEINS

- integral and peripheral membrane proteins
- hydrophathy plot
- passive transport
- permease, transporter
- synport, antiport, uniport
- active transport: primary, secondary, proton, sodium pumps
- Sodium-potassium ATPase
- ionophores
- galactoside permease
- chloride-bicarbonate exchanger
- bacteriorhodopsin
- porin
- ion channels

BIOENERGETICS

- Be able to use the Nernst equation, gibb's free energy equation, and tabulated E° and ΔG° values to calculate electromotive force/free energy values for reactions under standard state and nonstandard state conditions given the proper equations and constants.
- Define and explain:
 - high energy compounds
 - reduction potential
 - strong and weak reductant and oxidant
- electron transfer reactions; single e^- , hydrogen atom, hydride transfer, direct electron transfer

BIOLOGICAL REACTION MECHANISMS

- Explain the meaning of the term “high energy compound”
- Understand and explain the features that make certain organophosphates “high energy compounds” and function in phosphoryl group transfer in biological systems
- Understand the mechanisms of action and associated strategies for lowering activation energy barriers for representative enzymes of the kinase, mutase, isomerase, aldolase, dehydrogenase, and enolase families.
- Outline the mechanism of action of the α -keto acid (pyruvate, α -KG) dehydrogenase multienzyme complexes and understand the roles of the five cofactors involved.
- Understand how general acids/bases, electron sinks, metal ions, etc. contribute to the mechanisms.
- Recognize/explain the importance of the following mechanistic terms: nucleophile, electrophile, cis-enediolate, Schiff base, tetrahedral and pentavalent intermediates, keto/enol tautomerization, control of stereochemical outcome (cis vs trans, R vs S, pro R vs Pro S)
- homolytic vs. heterolytic bond cleavage

ORGANIC COFACTORS

- Recognize the structures of the following cofactors, and be able to demonstrate/explain how the cofactors are used in central catabolism: thiamine pyrophosphate, lipoic acid, NAD^+ / NADH , NADP^+ , NADPH (know full name-i.e. oxidized or reduced nicotinamide adenine dinucleotide), biotin, FAD/FADH_2 (know full name, not just abbreviation), coenzyme A, biotin, pyridoxal phosphate, tetrahydrofolate, S-adenosylmethionine, CoQ, FMN, iron-sulfur clusters, cytochromes

CATABOLIC PATHWAYS

- group transfer reactions: acyl, phosphoryl
- phosphatase, mutase, kinase, phosphodiesterase
- isomerization, elimination, rearrangement
- aldol condensation, claisen condensation
- Be able to draw structures for all glycolytic intermediates, oxidative pentose pathway intermediates, and citric acid cycle intermediates
- Outline the sequences of reactions and name the enzymes in glycolysis, the citric acid cycle, the oxidative pentose pathway, and β -oxidation of even chain fatty acids.
- Explain substrate level phosphorylation
- Function and strategy of alcohol and lactic acid fermentation
- epinephrine, glucagon, cAMP; hormonal regulation of glycogen metabolism
- product inhibition, feedback inhibition, allosteric regulation, covalent regulation
- myocyte, hepatocyte, adipocyte
- oxidative vs. nonoxidative decarboxylation
- linear vs. cyclic pathways
- prochiral molecules
- dietary fat absorption and catabolism
- stored fat mobilization and catabolism
- ketone bodies: structures and reactions of
- Describe pathways of dietary amino acid assimilation
- function and mechanism of action of pyridoxal phosphate in transamination reactions.
- oxidative deamination; glutamate dehydrogenase
- transport of amino groups from tissue to liver; gln vs. ala transport
- glutamine synthetase
- nitrogen excretion: carbamoyl phosphate synthetase, ornithine transcarbamylase, urea cycle
- outline how the urea cycle and citric acid cycle are linked

- ketogenic vs. glucogenic AAs
- Cofactor roles of tetrahydrofolate, S-adenosylmethionine, oxidation states of C1 compounds carried by C1 cofactors
- features of mitochondrion

THE ELECTRON TRANSFER CHAIN AND OXIDATIVE PHOSPHORYLATION

- electron transfer cofactors: NAD, FAD, CoQ, FMN, iron-sulfur clusters, cytochromes
- complexes I-IV
- Q cycle
- chemiosmotic hypothesis
- proton pumping, transmembrane electrical potential, protonmotive force
- protonophores, ionophores, uncouplers, respiratory chain inhibitors
- ATP synthase, F_1 , F_0
- adenine nucleotide translocase
- malate-aspartate shuttle
- glycerol-3-phosphate shuttle