Chemistry 564
Bioorganic Chemistry
California State University Northridge

Lecture:

Instructor:	Thomas Minehan
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Class Meetings	TuTh 5-6:15, EH 2222
Office hours:	Tu 12:30-2:00 pm, EH2314
Required Texts:	Van Vranken and Weiss, *Introduction to Bioorganic Chemistry and Chemical Biology*
Supplementary Texts:	Hecht, *Bioorganic Chemistry: Nucleic Acids; Peptides and Proteins; Carbohydrates*

Prerequisite for Enrollment in Chemistry 564
A passing grade in Chemistry 334 or its equivalent
Strongly recommended: Chem 461 or Chem 464, or instructor approval

Course Focus: **"Bioorganic Chemistry is a rapidly growing scientific discipline that seeks to apply the useful principles and techniques of organic chemistry – including organic synthesis / synthetic methodology, mechanistic, and structural analysis – toward solution of problems in biology**." – Nelson J Leonard. This course will focus on the organic chemistry of biooligomers, which are responsible for every main function of the cell, including control, communication, and manufacturing. Addressing four classes of biooligomers - DNA, RNA, lipids/terpenes, and glycans- we will study their synthesis/biosynthesis, structure, and covalent and non-colvalent interactions with small molecules. Although there is a textbook for the course, the emphasis will be on material from the primary literature, and so the student should gain an early familiarity with how to access journals such as *Organic and Biomolecular Chemistry, ACS Chemical Biology, Journal of Medicinal Chemistry, Bioorganic and Medicinal Chemistry, Bioorganic and Medicinal Chemistry Letters, Journal of Organic Chemistry, Journal of the American Chemical Society, and Biochemistry*. Students should also be familiar with how to access/view structures from the protein databank (www.rcsb.org) as well as the nucleic acids database (http://ndbserver.rutgers.edu).

Student Learning Outcomes for Chem 564 (B.S. and M.S. Program):
SLO1(m): Demonstrate basic knowledge in the area of organic/biological chemistry. (Assessment tool: course exams).
SLO2(m): Organize and communicate scientific information clearly and concisely, both verbally and in writing (Assessment tool: final project / oral presentation / rubric).

SLO3(m): Effectively utilize the scientific literature to research a chemistry topic (Assessment tool: final project / written presentation / rubric).

Grading:

- Midterm Exams 1+2: (100 pts)
- Final Exam (cumulative): 30% (100 pts)
- Presentation: 30% (100 pts)
- Class Participation: 10% (50 pts)

Total: 350 pts.

*Grades: 100-85%: A, 84-70% B, 79-60% C, 50-60% D

Exams: The midterms will focus on lecture/textbook material from the first half of the course. The final exam will focus on articles selected from the current literature reviewed in class in the second half of the course.

Class Participation: After the midterm, the class will break up into groups to discuss representative publications from the current literature in bioorganic chemistry, and the results of these discussions will then be presented to the class. Appropriate literature references will be given to the groups beforehand via the course website. It is critical that all members of a group download the literature references and read them before coming to class!

Final Project/Presentation: Each student will choose a current topic in the field of bioorganic chemistry from the original literature and, after instructor approval, research the background and provide the current perspective and understanding of that topic using no less than 5 literature articles. The topic will be presented to the class (~15 minutes) *via* powerpoint during the last two weeks of class. In addition to the presentation, students will turn in a *JACS* communication style paper (2 pages max) on their research, complete with appropriate literature references.

*__Attendance:__ Attendance in the lecture is **mandatory**

*__Drop/ Withdrawal Policy:__ The chemistry department adheres to the university policy concerning withdrawal from the course. A full description is published in the university catalog for the dates fixed for adding, withdrawal, etc. **Academic failure does not constitute a clear and compelling reason for withdrawal from class** or for the assignment of an incomplete grade after the date for withdrawal, as specified in the University catalog, is passed.

Make up exams are normally not given, and will be considered only under very compelling and unusual circumstance and when proper documentation is provided in support of such a request.

Cheating: Cheating on an exam will result in failure on that exam plus possible disciplinary action by the Dean of Students. In any instance of academic dishonesty the University's disciplinary procedures will be followed.

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List of Course Topics

1. DNA

•Chemical structure of DNA: ribose/2-deoxyribofuranose conformation, Watson-Crick base-pairing, aromaticity/tautomerism, modified bases, non-natural base-pairing, π-stacking, major and minor grooves, Hoogsteen base pairing, A, B, and Z-form DNA, duplex melting, DNA hairpins, DNA superstructures.

Reading: V&W, Chapter 3, sections 3.1-3.4; 3.9
Problems: 3.25-3.27, 3.29, 3.30, 3.36

•Chemical synthesis of DNA: Caruthers phosphoramidite couplings/solid phase methods. (Enzymatic synthesis of DNA: DNA polymerases.) DNA sequencing: Maxam-Gilbert, Sanger methods

Reading: V&W, Chapter 3, sections 3.5-3.6
•Interactions of DNA with small molecules: DNA as a nucleophile toward alkylating functional groups: epoxides, cyclopropanes, aziridines. The reactivity of DNA toward free radicals: enediyne antitumor antibiotics/bleomycin. Non-covalent major and minor groove binding small molecules, DNA intercalators.

Reading: V&W, Chapter 3, sections 3.10
Problems: 3.38, 3.39, 3.43, 3.44, 3.45, 3.47, 3.49, 3.54, 3.55, 3.56, 3.59

2. RNA

•Chemical structure of RNA: differences with DNA: uracil, ribofuranosides; phosphodiester cleavage under basic conditions, ribonucleases. RNA secondary structure: A-form helical structure; folding, stem-loop (hairpin) formation; bulges; internal loops; tRNA: pseudouridine, inosine. Tertiary structure.
•Chemical synthesis of RNA: Solid phase RNA synthesis; 2'-O-TBS, TOM protected nucleoside phosphoramidites; orthogonal base/carbohydrate protecting groups. RNA polymerase I and II; transcription factors; control of transcription by small molecules.
•Interactions of RNA with small molecules: groove-binding aminoglycosides: neomycin-HIV TAR sequence; Tobramycin. Intercalators: 2-phenylquinolines; threading intercalators; recognition of hairpin loops: deoxystreptamine dimers. Internal loop binders: neamine derivatives. Bulge binders: ethidium, DAPI, netropsin; aminoquinolines.

Reading: V&W, Chapter 4, sections 4.10-4.4
Problems: 4.24, 4.29, 4.30

3. Glycans

•Chemical Structure of oligosaccharides: monosaccharide building blocks, pyranose conformations, α and β anomers, stereoelectronic effects. Types of polysaccharides: cellulose, starch, chitin, hyaluronan, polysialic acids. Proteoglycans, glycosaminoglycans, glycolipids. Cyclodextrins. Human blood group antigens.

•Chemical Synthesis of oligosaccharides: neighboring group participation, chemical activation of glycosyl donors: halides, imidates, pentenyl glycosides, thioglycosides, sulfoxides, glycals, phosphates. Selective hydroxyl group protection/deprotection. Solid phase oligosaccharide synthesis. Examples of total synthesis of oligosaccharides

•Interactions of oligosaccharides with other molecules: DNA-binding glycoconjugates, cyclodextrin complexes, carbohydrate interactions with antibodies/lectins.

Reading: V&W, Chapter 7, sections 7.1-7.3, 7.5, 7.7, 7.8
Problems: 7.23, 7.25, 7.27, 7.29, 7.30, 7.33

4. Polyketides, Terpenes, Lipids

•Structures of polyketides and terpenes: fatty acids and their biosynthesis. Phospholipids, sphingolipids. Phospholipases. Prostaglandins, leukotrienes. Aromatic polyketides; polypropionate natural products. Terpenes from isoprene: isopentyl pyrophosphate and dimethylallyl pyrophosphate. Mono-, sesqui-, di-, and triterpenes. Cholesterol. Retinoids, terpene natural products from microorganisms

•Synthesis of polyketides and terpenes: polyketides from repeated Claisen condensations of two-carbon and three-carbon units; terpene biosynthesis; polyene cyclizations. Biosynthesis of nonhuman terpene natural products

Reading: V&W, Chapter 8, sections 8.1-8.4, 8.6, 8.7
Problems: 8.24, 8.26, 8.30, 8.32, 8.35, 8.36, 8.38, 8.40, 8.42

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Course Schedule

Dates	Topics	Reading
Aug 29, 31	Review of Peptide/Protein structure	V&W Ch. 5
Sept. 5, 7, 12, 14	DNA	V&W Ch. 3
Sept. 19, 21, 26	RNA	V&W Ch. 4
Sept. 28	Midterm 1	
Oct 3, 5, 10	Glycans	V&W Ch. 7
Oct. 12, 17, 24	Lipids, terpenes, polyketides	V&W, Ch. 8
Oct. 26	Midterm 2	
Oct. 31, Nov. 2	Literature Group presentations	website papers
Nov. 7, 9	Literature Group presentations	website papers
Nov. 14, 16, 21	Literature Group presentations	website papers
Nov. 28, 30	Student Individual Presentations	
Dec. 5, 7	Student Individual Presentations	
Dec. 12	Final Exam 5:30-7:30pm	