Chemistry 4411/8411
Introduction to Chemical Biology

Tues/Thurs. 1 - 2:15 PM
231 Smith
Fall Semester, 2015

Instructor: Professor William Pomerantz, 312 Smith, wcp@umn.edu
Teaching Assistant: Steven Kirberger, kirbe004@umn.edu 439A Smith,
Office Hours: Pomerantz: Monday, Thursday: 2:30 – 3:30 PM and by appointment.
Kirberger: Wednesday, 10-11 PM, Kolthoff 151, and by appointment
Text: Essentials of Chemical Biology: Structure and Dynamics of Biological Macromolecules,
Supplemental Reading: (Available in Walter Library) 1) Fmoc Solid Phase Peptide Synthesis by
Chan and White, 2) Structure and Mechanism in Protein Science by Alan Fersht 3) Introduction to
Chemistry and Chemical Biology by Van Vranken and Weiss
For a review on the structure of proteins and peptides see “Biochemistry” by Stryer Chapters 1-2

Grading
4411 (3 credits) 8411 (4 credits)

Seminar and Literature Synopses: 10% 5%
Quizzes: 5% 5%
Individual Presentation/Assignments: 5% 10%
Problem Sets: 20% 20%
Midterms: 40% 40%
Final: 20% 20%

Course Overview: Chemical Biology is a rapidly developing field working at the interface of
chemical and biological sciences. Chemical biology in one form or another has evolved from
chemists’ desire to first recreate and ultimately mimic the structure and function of biological
molecules, followed by the development of new tools and application of physical organic principles
and biophysical methods to study them. In the current state of chemical biology, these new
chemical tools and molecular probes are being directly applied to address important questions in
biological systems. In this class we will follow a similar progression. We will begin by studying the
structure, function and synthesis (biological and chemical) of naturally occurring biopolymers. In
the second part of the course you will be introduced to biophysical methods for studying biological
systems. The course will then culminate by analysis of the most recent chemical biology research
being applied in state-of-the-art laboratories around the world.

Objective: Students taking this course will be able to appreciate and design syntheses of natural and
non-natural biopolymers, apply appropriate biophysical tools to study molecular recognition in
biochemical and cellular settings, critically analyze and interpret data in the primary literature,
present important findings in current-day chemical biology research, and effectively utilize
structural and bioinformatics databases available to chemical biologists as well as molecular
visualization software.
Seminar/Literature Synopses and Participation: Come to class prepared to participate. We will be using the textbook as a guide but much of the course will also be supplemented with research articles from the primary literature. Being able to interpret a scientific article and presentation in your own words is an important skill for developing your proficiency with the literature. 8411 students are responsible for writing up a two paragraph summary on one research seminar of their choosing related to chemical biology. Summaries are due up to two weeks following the seminar. Find seminar schedules on campus here:
https://sites.google.com/a/umn.edu/chemicalbiology/chembiosem

4411/8411 students are also responsible for writing a scientific abstract of one ACS Chemical Biology article (Due Tues Oct. 20th). Sign up ACS Chemical Biology ASAP alerts for the first part of the assignment! http://pubs.acs.org/page/follow.html

Problems Sets: Five problem sets will be assigned to supplement material covered in the class as well as provide you with a working knowledge of structural and bioinformatics database tools available to the chemical biologist as well as the visualization software PyMol. Software can be downloaded for free at: http://pymol.org/educational/ . Register for educational use only. An email will be sent with a prefabricated user name and password along with a URL to download the software from. Click on Educational use only. PyMol is also available in the microlab.

Individual Presentations: Students taking 8411 will be required to present a research article in class individually (15-20 minutes), and generate 2 stimulating questions for the class. Research presentations will be on Wed. or Fri at 5 pm. More details on the presentation to follow. Please contact me if a conflict arises. Chem 4411 students are not required but are encouraged to attend. To help with presenting, all presenters are required to watch the video by Susan McConnell on giving an effective presentation: https://www.youtube.com/watch?v=Hp7Id3Yb9XQ and use three points from the video in their talk.

Quizzes: Up to five short quizzes will be announced during the semester, and will be administered at the beginning of class. These may follow a “Just-in-Time” assignment (see slides on day 1 of class), or a follow-up to a reading or class assignment. The lowest score will be dropped.

Exams: Exams will be based on course material covered in class and on problem sets. In addition, content covered in research articles presented by 8411 students in class may be covered on exam (8411 only) if announced. These articles will be presented at least one week before each exam. Exams will be administered in the evening. An alternative time will be provided if there is an immediate conflict.

Contact Information: You must use your University of Minnesota x-500 email account so that I can send you information and updates regarding this course. Please keep Chem 4411/8411 in the subject heading of all of your emails.

Moodle: I will upload course powerpoint presentations and additional material to the Moodle site. By the end of the day before class starts. (by Mon/Wed. Midnight). Please print out the slides before class for taking notes.
My Expectations for students in my class
1) Coming to class prepared
2) Taking notes and actively participating
3) Staying up to date with reading and assigned problems. The book is a good reference, however the primary literature is also provided to solidify key concepts.
4) By the end of the semester to become proficient reading the chemical biology literature
5) Seeking help when a concept is not clear.

Two semesters of organic chemistry is a prerequisite for the course and several portions of the course may require a refresher, on reactivity and bonding and basic NMR. Please see me if additional resources are needed.

Academic Misconduct: Academic misconduct is not tolerated and may result in either a failed assignment or failure from the course. According to University policy scholastic misconduct is broadly defined as "any act that violates the right of another student in academic work or that involves misrepresentation of your own work. Scholastic dishonesty includes, (but is not necessarily limited to): cheating on assignments or examinations; plagiarizing, which means misrepresenting as your own work any part of work done by another; submitting the same paper, or substantially similar papers, to meet the requirements of more than one course without the approval and consent of all instructors concerned; depriving another student of necessary course materials; or interfering with another student's work."
## Important Dates

<table>
<thead>
<tr>
<th>Class Presentations 1</th>
<th>Wednesday, October 7th (5 PM)</th>
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<tbody>
<tr>
<td>Midterm 1</td>
<td>Thursday, October 15 (5 PM or 630 conflicts)</td>
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<tr>
<td>Class Presentations 2</td>
<td>Friday, November 6 (5 PM)</td>
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<tr>
<td>Midterm 2</td>
<td>Thursday, November 12 (5 PM or 630 conflicts)</td>
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<tr>
<td>Class Presentations 3</td>
<td>Monday, December 14 (5 PM)</td>
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<tr>
<td>Final Exam</td>
<td>Monday, December 21 (8:00 AM)</td>
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## Tentative Course Outline

*Portions taken from the current literature are subject to change*

<table>
<thead>
<tr>
<th>Day</th>
<th>Topic</th>
<th>ECB or related Lit.</th>
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<tbody>
<tr>
<td><strong>Part I Biopolymer Structure Function and Synthesis</strong></td>
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<tr>
<td>Thurs. Sept. 10</td>
<td>Amino acids, peptides, Fold it! 1-4</td>
<td>1.1-1.2 <a href="http://fold.it/portal/">http://fold.it/portal/</a> (download on computer)</td>
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<tr>
<td>Tues. Sept. 15</td>
<td>Peptides and Proteins ASAP Alert due</td>
<td>1.2-1.4 helical wheel exercise due Sept 22nd</td>
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<tr>
<td>Tues. Sept. 22</td>
<td>Synthesis in Chemical Biology (peptides I), PS1</td>
<td>2.1-2.2. See also: Van Vranken and Weiss pg. 185-196 reserved in library,</td>
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<tr>
<td>Thurs. Sept. 24</td>
<td>Synthesis in Chemical Biology (peptides II and DNA (short example time permitting) Quiz 1 Amino Acids</td>
<td>2.2-2.3. See also: Van Vranken and Weiss pg. 84-89 reserved in library</td>
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<tr>
<td>Tues. Oct. 6</td>
<td>Protein Purification</td>
<td>2.6-2.7. In class purification! <a href="http://media.oit.edu/ken">http://media.oit.edu/ken</a>. usher/</td>
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<tr>
<td>Wed. Oct. 7</td>
<td>8411 Student Presentations</td>
<td>5-7 pm</td>
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<tr>
<td>Date</td>
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<td>Notes</td>
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<tr>
<td>Tues. Oct. 13</td>
<td>Quiz 2 amino acid pKa In class review or catch up/Lit breakdown</td>
<td>Exam 1 up to here In class lit. breakdown. TBA</td>
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<tr>
<td>Thurs. Oct. 15</td>
<td>UV/circular dichroism Abstract Assignment</td>
<td>4.1 to 4.3</td>
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**EXAM 1 Thurs. Oct. 15 5-8 pm see me regarding time conflicts at least 2 days ahead**

*Part 2 Biophysical Methods for Studying Biological Systems*

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<th>Date</th>
<th>Event</th>
<th>Notes</th>
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<tbody>
<tr>
<td>Tues. Oct. 20</td>
<td>Fluorescence intro, chemical conjugation</td>
<td>4.4 to 4.5.5</td>
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<td><a href="http://www.youtube.com/watch?v=u63eZz8R0GI">http://www.youtube.com/watch?v=u63eZz8R0GI</a></td>
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<td>Thurs. Oct. 22</td>
<td>FRET and FP PS 3</td>
<td>4.5.4 and handout</td>
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<tr>
<td>Tues. Oct. 27</td>
<td>Receptor Ligand interactions: (K_d, K_a, IC_{50’s})</td>
<td>7.2 to 7.3</td>
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<td>Thurs. Oct. 29</td>
<td>NMR 1D and 2D NMR PS3 Due, PS4</td>
<td>5.1 to 5.5</td>
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**EXAM 1 Thurs. Oct. 15 5-8 pm**

*Part 3 Current Trends in Chemical Biology*

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<th>Date</th>
<th>Event</th>
<th>Notes</th>
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<tbody>
<tr>
<td>Tues. Nov. 3</td>
<td>NMR 2D and 3D NMR Quiz 3 Abstract Due</td>
<td>5.1 to 5.5</td>
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<td></td>
<td><a href="http://www.nmr.chem.uu.nl/~abonvin/tutorial/Assignment-Data/assignment.html">http://www.nmr.chem.uu.nl/~abonvin/tutorial/Assignment-Data/assignment.html</a></td>
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<tr>
<td>Thurs. Nov. 5</td>
<td>Luminescence Reporter Assays or ITC TBD PS4 Due Exam 2 up to here</td>
<td>TBD</td>
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**EXAM 2 Nov. 12th 5-7 pm**

**Mon. Dec. 21**

**FINAL EXAM 8-10:00**

Friday Nov. 6  **Student presentations**  5-7 pm

Tues. Nov. 10  **In class review/Lit breakdown**  In class lit. breakdown. TBA

Thurs. Nov. 12  **Proteomics MS**  9.1 to 9.3.2

**EXAM 2 Nov. 12th 5-7 pm see me regarding time conflicts at least 2 days ahead**
Primary Literature Referenced in Chem 4411/8411 last course (Fall 2014)
Below are some seminal and current references for chemical biology 4411/8411. We will not go over every article explicitly, but they will provide you with a deeper understanding of the material for the course and in your future studies. 4411/8411 F2015 may deviate slightly from this list

Part I
Class 1 What is Chemical Biology?

Amino acids, peptides, and proteins

Protein Translation

http://pubs.acs.org/cen/multimedia/85/ribosome/translation_bacterial.html

If link broken try:

http://cen.acs.org/media/video/2007/01/cen-translation_bacterial-vid1.html How translation occurs...Movie

Why Nature Chose Phosphates. Nucleic acid introduction


**Glycobiology:**


**Noncovalent interactions in biopolymers**


2. *Biochemistry, 1991*, 30, 7188 - Van der Waals effects on Lipid Melting

3. *Science, 1993*, 262, 1401-6 - Non-Covalent Interactions in Protein Folds

**Chemical synthesis of peptides**


**Chemical synthesis of proteins**


**Non-canonical Amino Acid Incorporation**


**Protein Expression**


**Nucleic Acid Synthesis**

In Class Literature Breakdown: Peptide Synthesis and NCL

Part II

Circular Dichroism and Protein Stability
3. *JACS*, 2007, 129 2456 - Understanding CD and determining % helicity
   Pace et al. *Biochemistry* 1979, 18, 288
5. Buer et al. *Biochemistry* 2009, 48, 10810 - Amino acid fluorination imparts stability due to packing preferences

Fluorescence
   [http://www.youtube.com/watch?v=u63eZz8R0GI](http://www.youtube.com/watch?v=u63eZz8R0GI) – Imaging the glycome movie (selective parts)

Fluorescence Polarization
1. *Chembiochem.* 2009, 10, 990-3 – Cell permeable β-peptide inhibitors of P53

FRET

EMSA
1. *Nat. Prot.* 2007, 2, 1849 - Electrophoretic mobility shift assay (EMSA) for detecting protein–nucleic acid interactions

Multidimensional NMR
   [http://www.nmr.chem.uu.nl/~abonvin/tutorials/Assignment-Data/assignment.html](http://www.nmr.chem.uu.nl/~abonvin/tutorials/Assignment-Data/assignment.html) - tutorial on HSQC $^1$H-$^{15}$N

Mass Spectrometry/Proteomic Analysis
2. Link et al. *Nature Biotech*, 1999, 17, 676, MuDPIT

**In Class Literature Breakdown: Fluorescent Aptamer Sensors**

**Part III**

**Activity-Based Protein Profiling**
   - *Nature Methods*, 2009, 6, 135- Activity Based Protein Profiling
   - *Nature Methods*, 2012, 9, 84 - Activity Based Protein Profiling
   - *ACS Chem. Biol.*, 2012, 7, 1653 - Activity Based Protein Profiling
   - *Nature Methods*, 2012, 9, 84 – Profiling palmitoylation using CLICK chemistry

**Brief In-class Literature Discussion and Homework Assignment**

**Aptamers and DNA Templated Synthesis**

**Protein Hot Spots and Disulfide Tethering**
2. Erlanson, *PNAS*, 2000, 97, 9367 -Applications of “disulfide tethering”
4. *PNAS*, 2006, 103, 15243 - Hot spot determination by site specific amino acid mutations for in class Pymol exercise

**Foldamers**
**14-Helix**

**12-Helix**
In Class Literature Breakdown on Foldamers
3. Biochemistry, 2007, 46, 14, 4356 - β-Galactocidase Assay; Example of Fusion Experiment

Epigenetics and the Histone Code Hypothesis