Biochemistry/Chemistry 704: Chemical Biology

Official Course Description: Chemistry and biology of proteins, nucleic acids and carbohydrates; application of organic chemistry to problems in cell biology, biotechnology, and biomedicine.

Requisites: Declared in Biochemistry or Chemistry graduate program or consent of instructor.

Instructor: Professor Andrew Buller (arbuller@wisc.edu) 5112a Chemistry

Course Time and Location: T/Th 8:50 AM- 9:40 AM 175 DeLuca Biochemistry Labs

Credit hours: 2. This class meets for two 50-minute class period each week over the fall/spring semester and carries the expectation that students will work on course learning activities (reading, writing, problem sets, studying, etc) for about 2 hours out of classroom for every class period. This syllabus includes additional information about the use of class time and expectations for student work.

This graduate level course is divided into two sections. The first, comprising a third of the class, will cover how chemistry was used to discover and now control the flow genetic information. The second section of the course is an eclectic mix of modern chemical approaches to interrogating biological systems.

- Canvas course URL available through: https://learnuw.wisc.edu
- Course designations: Graduate level; physical science breadth; counts as L&S credit
- Instructional mode: Face-to-face
- Official Course Description: Chemistry and biology of proteins, nucleic acids and carbohydrates; application of organic chemistry to problems in cell biology, biotechnology, and biomedicine.
- Requisite: Enrollment as a graduate student or as an undergraduate with the permission of the instructor

Office Hours: 5-6 PM on Wednesdays in Prof. Buller’s office (5112a Chemistry). By appointment as well. Please come see me if you have questions!

Grading: Assignments are weighted as follows, Homework = 50%, Presentation = 30%, Participation = 20%

Letter Grades: A: >90%  AB: 83-90%  B: 75-83%  BC: 68-75%  C: 60-68%  D: 53-60%  F: <53%

Homework: Professor Buller will lecture for roughly half the class period to introduce the class to concepts that will be explored in one/two papers that everyone will read prior to the next class. Periodic assignments will accompany the papers and are due at the end of each class period. We will discuss content in a small group and whole-class format where your active participation is expected.
Graded Worksheets: Navigating your way through primary literature in a new field is difficult. I have prepared brief questionnaires that are designed to help guide you through the process. Portions of these will be graded throughout the semester. Each questionnaire, graded or otherwise, will contain Discussion questions that will be used to seed conversation in the subsequent class period.

Cover Letters: When one submits a manuscript for publication in a journal, one prepares a cover letter that explains to the editor the significance of the work. For very competitive journals, such as Science and Nature, the editorial staff sends only a small fraction of manuscripts out to reviewers; most manuscript are rejected without review. Therefore, the cover letter is especially important for competitive journals, as the authors must convince the journal editor that the manuscript deserves a full review. Pretend that you are the authors of a paper we have discussed and you are preparing to send the manuscript for publication. Write a one-page cover letter to the Editor explaining why your manuscript is important. (Adapted from Prof. Gellman)

Research Presentation: Instead of an in-class exam, students will select a recent paper (past five years) in the field of Chemical Biology and present the work to the class. These presentations will take one of two forms, an oral presentation with slides to the whole group or, alternatively, a poster

Course Learning Outcomes: The goal of this course is to introduce students to fundamental concepts in Chemical Biology and methods of chemistry used to solve problems in molecular and cell biology. After completion of this course, successful students will:

1) Be able to describe the chemical basis for replication, transcription, translation and how each of these central processes can be expanded to include new chemical matter.

2) Develop skills to critically read the literature and effectively communicate research in a peer setting.

3) Describe the substance and importance of chemical biology research in the format of a cover letter to a journal editor, an original figure, an oral presentation, and in a written commentary.

Diversity, Equity, and Inclusion are important throughout campus life, and these principles are particularly immediate in a discussion-based class. It is worth re-reading and reflecting on the official UW statement:

Diversity is a source of strength, creativity, and innovation for UW-Madison. We value the contributions of each person and respect the profound ways their identity, culture, background, experience, status, abilities, and opinion enrich the university community. We commit ourselves to the pursuit of excellence in teaching, research, outreach, and diversity as inextricably linked goals.

ACADEMIC INTEGRITY
By enrolling in this course, each student assumes the responsibilities of an active participant in UW-Madison’s community of scholars in which everyone’s academic work and behavior are held to the highest academic integrity standards. Academic misconduct compromises the integrity of the university. Cheating, fabrication, plagiarism, unauthorized collaboration, and helping others commit these acts are examples of academic misconduct, which can result in disciplinary action. This includes but is not limited to failure on the assignment/course, disciplinary probation, or suspension. Substantial or repeated cases of misconduct will be forwarded to the Office of Student Conduct & Community Standards for additional review. For more information, refer to studentconduct.wiscweb.wisc.edu/academic-integrity/.
ACCOMMODATIONS FOR STUDENTS WITH DISABILITIES

McBurney Disability Resource Center syllabus statement: “The University of Wisconsin-Madison supports the right of all enrolled students to a full and equal educational opportunity. The Americans with Disabilities Act (ADA), Wisconsin State Statute (36.12), and UW-Madison policy (Faculty Document 1071) require that students with disabilities be reasonably accommodated in instruction and campus life. Reasonable accommodations for students with disabilities is a shared faculty and student responsibility. Students are expected to inform faculty [me] of their need for instructional accommodations by the end of the third week of the semester, or as soon as possible after a disability has been incurred or recognized. Faculty [I], will work either directly with the student [you] or in coordination with the McBurney Center to identify and provide reasonable instructional accommodations. Disability information, including instructional accommodations as part of a student’s educational record, is confidential and protected under FERPA.”

http://mcburney.wisc.edu/facstaffother/faculty/syllabus.php

Resources:

Supplementary readings will be assigned from:
Van Vranken D. & Weiss G. Introduction to Bioorganic Chemistry and Chemical Biology (2013)
Excerpts will be posted to the course Canvas website.

Additional content is available from:
www.khanacademy.org
## Course Schedule

I have tried to include as much detail into our schedule as possible, but changes should be expected as the semester proceeds.

<table>
<thead>
<tr>
<th>Date</th>
<th>Day</th>
<th>Discussion Topic</th>
<th>Lecture Topic</th>
<th>Assignment Due * = Graded</th>
<th>Reading For Next Class</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>6-Sep</td>
<td>Syllabus &amp; Background Discussion. What is Chemical Biology?</td>
<td>Chemical Biology Background Refresher</td>
<td>“The Two Cultures: Chemistry and Biology” by Arthur Kornberg</td>
<td>Van Vranken – Ch 2.1-2.3 (pg 27-36)</td>
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<tr>
<td>2</td>
<td>11-Sep</td>
<td>Chemical Structures; The Two Cultures</td>
<td>The Central Dogma: DNA &amp; Replication</td>
<td><em>Worksheet: Chemical structure correction</em></td>
<td>Van Vranken – Ch 3.3, 3.8 (pg 64-73, 97-102) A semi-synthetic organism with an expanded genetic alphabet</td>
</tr>
<tr>
<td>4</td>
<td>18-Sep</td>
<td>Beyond four bases</td>
<td>The Central Dogma: Transcription</td>
<td><em>Readings Worksheet</em></td>
<td>Van Vranken – Ch 4.1 (pg 131-138)</td>
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<tr>
<td>6</td>
<td>25-Sep</td>
<td>Functional RNAs</td>
<td>The Central Dogma: Translation &amp; the Genetic Code</td>
<td><em>Readings Worksheet</em></td>
<td>Ch 4.6 (pg 156-166) PyMOL Installation</td>
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<tr>
<td>7</td>
<td>27-Sep</td>
<td>Figure making: ChemDraw and PyMol tutorials</td>
<td></td>
<td>None</td>
<td>None</td>
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<tr>
<td>8</td>
<td>2-Oct</td>
<td>Figure Presentations</td>
<td>Synthetic Methods for Protein Construction</td>
<td><em>Original Figure</em></td>
<td>Van Vranken – Ch 4.6 (pg 167-171)</td>
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- Optional Figure Making Workshop on 29-Sep, 11:30 AM – 3 PM
<table>
<thead>
<tr>
<th>Week</th>
<th>Date</th>
<th>Day</th>
<th>Topic</th>
<th>Reading/Worksheet</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>9</td>
<td>4-Oct</td>
<td>Th</td>
<td>Lecture: Expansion of the Genetic Code</td>
<td>None</td>
<td>None</td>
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</tbody>
</table>
|      |       |      |                                              | Expanding the Genetic Code of *Escherichia coli*  
  Wang L, et al.  
  Expressed protein ligation: A general method for protein engineering  
  Muir TW, Sondhi D, and Cole PA  
  *PNAS*, 1998, 95, 6705-6710 |                                            |
| 10   | 9-Oct | Th   | Beyond 20 AAs!                               | Protein Chemistry  
  *Readings Worksheet*  
  *Cover Letter* | Van Vranken – Ch 6.2 (pg 236-240) |
| 11   | 11-Oct| Th   | Lecture: Protein Chemistry & Enzyme Catalysis| None                                    | Evaluating the Catalytic Contribution form the Oxyanion Hole in Ketosteroid Isomerase  
  Schwans JP, et al.  
  *JACS*, 2011, 133, 20052-20055 |                                            |
| 12   | 16-Oct| Th   | How do we think about mutations?             | Protein Engineering I  
  *Readings Worksheet* | None                                       |
| 13   | 18-Oct| Th   | Lecture: Bioorthogonal Chemistry             | *Paper Selection Due*                  | Identification of secreted bacterial proteins by noncanonical amino acid tagging  
  Mahdavi A. et al.  
  *PNAS*, 2014, 111, 433-438 |                                            |
| 14   | 23-Oct| Th   | Discussion: Bioorthogonal Chemistry         | *Readings Worksheet*                  | Bioorthogonal Chemistry Paper (TBD)       |
| 15   | 25-Oct| Th   | Paper Discussion (TBD)                       | Protein Engineering II  
  *Readings Worksheet* | “Directed evolution of a monomeric, bright and photostable version of *Clavularia* cyan fluorescent protein: structural characterization and applications in fluorescence imaging”  
  *Biochem J*, 2006, 400, 531  
  “Nox2 redox signaling maintains essential cell populations in the brain”  
  Dickinson BC, et al.  
| 16   | 30-Oct| Th   | What makes a good sensor?                    | Bioimaging  
  *Readings Worksheet* | TBD                                        |
| 17   | 1-Nov | Th   | Flex time!                                   | Flex Time & Presentation Guidelines  
  *Readings Worksheet* | None                                       |
| 18   | 6-Nov | Th   | In-Class Presentations                       | Glycobiology  
  *Readings Worksheet* | Long-lived Engineering of Glycans to Direct Stem Cell Fate  
  Pulsipher A. et al.  
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<tr>
<th></th>
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<th>A sugar code?</th>
<th>Activity Based Protein Profiling</th>
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<tbody>
<tr>
<td>19</td>
<td>8-Nov</td>
<td>Th</td>
<td>Quorum sensing</td>
<td>ABPP Paper, TBD</td>
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<tr>
<td>20</td>
<td>13-Nov</td>
<td>T</td>
<td>In-Class Presentations</td>
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<tr>
<td>21</td>
<td>15-Nov</td>
<td>Th</td>
<td>Ligandability?</td>
<td>In-Class Presentations</td>
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<tr>
<td>22</td>
<td>20-Nov</td>
<td>T</td>
<td>In-Class Presentations</td>
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<tr>
<td>23</td>
<td>Thanksgiving</td>
<td>Th</td>
<td>No Class</td>
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<tr>
<td>24</td>
<td>27-Nov</td>
<td>T</td>
<td>Poster Session I – Location TBD</td>
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<tr>
<td>25</td>
<td>29-Nov</td>
<td>Th</td>
<td>Poster Session II – Location TBD</td>
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<tr>
<td>26</td>
<td>4-Dec</td>
<td>T</td>
<td>Special Topics Discussion</td>
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<tr>
<td>27</td>
<td>6-Dec</td>
<td>Th</td>
<td>Special Topics Discussion</td>
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<tr>
<td>28</td>
<td>11-Dec</td>
<td>T</td>
<td>What is Chemical Biology?</td>
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