Biochemistry/Chemistry 704: Chemical Biology Fall 2018

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
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- **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
Alberts, B. et al. *Molecular Biology of the Cell*. Routledge (2007)
Blackburn, G. M. et al. *Nucleic Acids in Chemistry and Biology*. RSC (2006)
Frey, P. A. & Hegeman, A. D. *Enzymatic Reaction Mechanisms*. Oxford University (2006)
Grossman, R. B. *The Art of Writing Reasonable Organic Reaction Mechanisms*. Springer (2007)
Jencks, W. P. *Catalysis in Chemistry and Enzymology*. Dover (1987)
McMurry J. & Begley, T. *The Organic Chemistry of Biological Pathways*. Roberts & Co. (2005)
Miller, A. & Tanner, J. *Essentials of Chemical Biology*. Wiley (2008)
Stanforth, S. P. *Natural Product Chemistry at a Glance*. Blackwell (2006)
Voet, D. & Voet, J. G. *Biochemistry*. John Wiley & Sons (2004)

Course Schedule

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

	Date	Day	Discussion Topic	Lecture Topic	Assignment Due * = Graded	Reading For Next Class
1	6-Sep	Th	Syllabus & Background Discussion. What is Chemical Biology?		Chemical Biology Background Refresher	"The Two Cultures: Chemistry and Biology" by Arthur Kornberg *Biochemistry* **1987**, 26, 6888-6891 Van Vranken – Ch 2.1-2.3 (pg 27-36)
2	11-Sep	T	Chemical Structures; The Two Cultures	The Central Dogma: DNA & Replication	*Worksheet: Chemical structure correction*	"Efficient replication between non-hydrogen-bonded nucleoside shape analogs" Morales J.C. and Kool E.T. *Nature Structural Biology*, 1998, 950-954
3	13-Sep	Th	What drives double helix formation?	DNA Synthesis and Expanding the Alphabet	Readings Worksheet	Van Vranken – Ch 3.3, 3.8 (pg 64-73, 97-102) A semi-synthetic organism with an expanded genetic alphabet Malyshev D.A. et al. *Nature*, 2014, 385-388
4	18-Sep	T	Beyond four bases	The Central Dogma: Transcription	*Readings Worksheet*	Van Vranken – Ch 4.1 (pg 131-138)
5	20-Sep	Th	Lecture: RNA Folding, Catalysis, SELEX		*Cover Letter*	"RNA Structure Analysis at Single Nucleotide Resolution by Selective 2'-Hydroxyl Acylation and Primer Extension (SHAPE) " Merino EJ. *et al.* *JACS*, 2005, 127, 4223-4231 "Ribozyme-catalysed amino-acid transfer reactions" Lohse PA and Szostak JW *Nature*, 1996, 381, 422-444
6	25-Sep	T	Functional RNAs	The Central Dogma: Translation & the Genetic Code	*Readings Worksheet*	Ch 4.6 (pg 156-166) PyMOL Installation
7	27-Sep	Th	Figure making: ChemDraw and PyMol tutorials		None	None
-	29-Sep	Sat	11:30 AM – 3 PM Optional Figure Making Workshop			
8	2-Oct	T	Figure Presentations	Synthetic Methods for Protein Construction	*Original Figure*	Van Vranken – Ch 4.6 (pg 167-171)

9	4-Oct	Th	Lecture: Directed Evolution and Expansion of the Genetic Code		None	Expanding the Genetic Code of *Escherichia coli* Wang L, et al. *Science*, 2001, 292, 498-500
10	9-Oct	T	Beyond 20 AAs!	Protein Chemistry	Readings Worksheet	Van Vranken – Ch 6.2 (pg 236-240)
11	11-Oct	Th	Lecture: Protein Chemistry & Enzyme Catalysis		*Cover Letter* (For Wang L, et al.)	Evaluating the Catalytic Contribution form the Oxyanion Hole in Ketosteroid Isomerase Schwans JP, et al. *JACS*, 2011, 133, 20052-20055
12	16-Oct	T	How do we think about mutations?	Protein Engineering	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	T	Discussion: Bioorthogonal Chemistry		*Readings Worksheet*	Bioorthogonal Chemistry Paper (TBD)
15	25-Oct	Th	Paper Discussion (TBD)	Protein Engineering II	None	"Directed evolution of a monomeric, bright and photostable version of *Clavularia* cyan fluorescent protein: structural characterization and applications in fluorescence imaging" Al H-W, et al. *Biochem J*, 2006, 400, 531 ----------Two Papers---------- "Nox2 redox signaling maintains essential cell populations in the brain" Dickinson BC. et al. *Nat Chem Biol*, 2011, 7, 106-112
16	30-Oct	T	What makes a good sensor?	Bioimaging	*Readings Worksheet*	TBD
17	1-Nov	Th	Flex time!	Flex Time & Presentation Guidelines	None	
18	6-Nov	T	In-Class Presentations	Glycobiology		Long-lived Engineering of Glycans to Direct Stem Cell Fate Pulsipher A. et al. *Angew. Chem. Int. Ed*, 2015, 54, 1466-1470
19	8-Nov	Th	A sugar code?	Quorum sensing		
20	13-Nov	T	In-Class Presentations	Activity Based Protein Profiling		ABPP Paper, TBD

21	15-Nov	Th	Ligandability?	In-Class Presentations		
22	20-Nov	T	In-Class Presentations			
23	Thanksgiving	Th	*No Class*			
24	27-Nov	T	Poster Session I – Location TBD			
25	29-Nov	Th	Poster Session II – Location TBD			
26	4-Dec	T	Special Topics Discussion			
27	6-Dec	Th	Special Topics Discussion			
28	11-Dec	T	What is Chemcial Biology?			