WISCONSIN
UNIVERSITY OF WISCONSIN–MADISON

BIOCHEM/CHEM 704: Chemical Biology Fall 2020

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

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

Course Time and Location: T/Th 11:00 AM- 12:15 AM Biochemistry 2131

Credit hours: Three. This class meets for two 75-minute class period each week over the semester and carries the expectation that students will work on course learning activities (reading, writing, problem sets, studying, etc) for about 3 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 focused on learning modern Chemical Biology by reading primary literature and writing an original research proposal. The class is (roughly) divided into two units. The first unit, comprising a third of the semester, will cover how chemistry was used to discover and now control the flow genetic information in cells. The second unit of the course will be an eclectic and student-guided mixture of modern chemical approaches to interrogating biological systems.

- **Canvas course URL available through:** https://learnuw.wisc.edu
- **Course designations:** 50% Graduate Coursework Requirement
- **Instructional mode:** Face-to-face

Office Hours: 4:45-5:45 PM on Mondays in Prof. Buller's office (5112a Chemistry). By appointment as well. Please come see me if you have questions!

Course Learning Outcomes: The goal of this course is to introduce students to fundamental concepts in Chemical Biology and modern methods 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, and an original figure.

4) Demonstrate knowledge of chemical biology by designing an original research project that focuses on answering a biological question or solving a biomedical problem.

Grading: Homework = 60%, Final Proposal = 30%, Participation = 10%.

Letter Grades: Grade cutoffs may shift as needed to accommodate new assignments.
A: >90% AB: 83-90% B: 75-83% BC: 68-75% C: 60-68% D: 53-60% F: <53%

Homework: The course is centered around reading primary literature and demonstrating your understanding through regular writing assignments. Professor Buller will lecture for a portion of 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 your reading. Portions of these worksheets 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.
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> **Cover Letters**: When a manuscript is submitted 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) See the Course canvas page for more detail.

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

Original Research Proposal

During the course of the semester, students will develop an original research proposal using chemical biology tools to probe the properties and principles of biological systems. No more than half of the proposal may involve methods development; *the goal is to focus on learning something new about biology*. As with all good science, ideas are not generated in a vacuum and the writing of the proposal will be deconstructed across the semester to facilitate peer-based editing of the constituent pieces. The assignment will be broken down into the following phases:

Idea Discussion *Specific Aims* *Outline* *First Draft* *Peer Editing* *Final Version*

If students are concurrently writing an NSF graduate fellowship, they are encouraged to adapt ideas from their proposal to fit the parameters of the assignment for this course. Note, a copy/paste job will not be sufficient, and students are expected to fully engage in the course writing process.

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)
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. It is my hope to move up reading assignments and discussions from the previous year, but rather than plan on a crunch, we will let things evolve according to the pace that feels right.

Class #	Date	Day	Reading For Class	Discussion Topic	Lecture Topic	Assignment Due? * = Graded
1	5-Sep	Th	Chemical Biology Background Refresher	Syllabus & Background Discussion. What is Chemical Biology?		Chemical Biology Background Refresher
2	10-Sep	T	"The Two Cultures: Chemistry and Biology" by Arthur Kornberg *Biochemistry* 1987, 26, 6888-6891 Van Vranken – Ch 2.1-2.3 (pg 27-36)	Chemical Structures; The Two Cultures	The Central Dogma: DNA & Replication	*Worksheet: Chemical structure correction*
3	12-Sep	Th	"Efficient replication between non-hydrogen-bonded nucleoside shape analogs" Morales J.C. and Kool E.T. *Nature Structural Biology*, 1998, 950-954	What drives double helix formation?	DNA Synthesis and Expanding the Alphabet	Readings Worksheet *DNA Modification*
4	17-Sep	T	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	Beyond four bases	The Central Dogma: Transcription	Readings Worksheet*
5	19-Sep	Th	Van Vranken – Ch 4.1 (pg 131-138)	What makes for a good Cover Letter?	RNA Folding, Catalysis, SELEX	*Cover Letter* Note: This assignment is due via Canvas on Saturday the 21st.
6	24-Sep	T	"RNA Structure Analysis at Single Nucleotide Resolution by Selective 2'-Hydroxyl Acylation and Primer Extension (SHAPE) " Merino EJ. *et al.*	Functional RNAs	The Central Dogma: Translation & the Genetic Code	*Readings Worksheet* Graded as a group.

			JACS, 2005, 127, 4223-4231 "Ribozyme-catalysed amino-acid transfer reactions" Lohse PA and Szostak JW *Nature*, 1996, 381, 422-444			
7	26-Sep	Th	PyMOL Installation	Figure making: ChemDraw and PyMol tutorials.		None
	28-Sep	Sat	11:30 AM – 3 PM Optional Figure Making Workshop	Original Figure Due Online Via Canvas by 5 PM on Sunday the 29th		
8	1-Oct	T	Van Vranken - Ch 4.6 – Part 1 (pg 156-166)	Figure Presentations	Lecture: Site Directed Mutagenesis	*Original Figure*
9	3-Oct	Th	Van Vranken – Ch 4.6 – Part 2 (pg 167-171)	Lecture: Directed Evolution and Expansion of the Genetic Code		None
10	8-Oct	T	Expanding the Genetic Code of *Escherichia coli* Wang L, et al. *Science*, 2001, 292, 498-500	Beyond 20 AAs!	***Brief discussion of original research proposal assignment***	*See Below*
11	10-Oct	Th	Van Vranken – Ch 6.2 (pg 236-240)	Lecture: Protein Chemistry & Enzyme Catalysis		*Readings Worksheet for Wang L et al. With PyMOL Figure* Due on Canvas
12	15-Oct	T	Regulation of the p300 HAT domain via a novel activation loop Thompson PR, et al. Nature Structural and Molecular Biology, 2004, 11, 308-315	Expressed Protein Ligation discussion		*Group Worksheet*
13	17-Oct	Th	None! Put your thinking caps on.	Biorthogonal Chemistry	***Original Research Group Brainstorming Session***	
14	22-Oct	T	Identification of secreted bacterial proteins by noncanonical amino acid tagging Mahdavi A. et al. *PNAS*, 2014, 111, 433-438	Paper Discussion and Whirlwind ChemBio	Small molecule fluorescence sensors (By Prof. Tina Wang)	*Readings Worksheet*
15	24-Oct	Th	*Paper TBD by Prof. Wang*	What makes a good sensor?		

16	29-Oct	T	Long-lived Engineering of Glycans to Direct Stem Cell Fate Pulsipher A. et al. *Angew. Chem. Int. Ed*, 2015, 54, 1466-1470	Discussion: Glycobiology	Lecture: More sugar please	
17	31-Oct	Th	*Paper TBD*	*Discussion*		***Proposal: Draft Aims Due On Canvas Nov 4th (Scored for completion)***
18	5-Nov	T	**Come with a printed or digital copy of your proposed aims that are ready for discussion.**	***Proposal: Specific Aims***	Lecture: Quorum Sensing!	18
19	7-Nov	Th	Pathogen elimination by probiotic *Bacillus* via signaling interference Piewngam P. et al. *Nature*, 2018, 562, 532	Discussion: Quorum sensing and human health	Lecture: Topic TBD	19
20	12-Nov	T	**Come with a printed or digital copy of your proposal in outline form.**	***Proposal: Outline Workshop; Come with computer and to use this time to work.***		
21	14-Nov	Th	*ABPP Paper by Prof. Weeks*	Discussion: Activity-based Protein Profiling		
22	19-Nov	T	*Paper TBD*	*Paper TBD*		
23	21-Nov	Th	*Paper TBD*	*Paper TBD*		***Proposal 1st Draft Due On Canvas by Sunday Nov. 24th. (Scored for completion)***
24	26-Nov	T	*No reading assignment*	***Proposal: In-Class Peer Editing; Come with computer and use this time to work.***		
25	28-Nov	Th		No Class – Happy Thanksgiving!		
26	3-Dec	T	*Paper TBD*	*Paper Discussion*	Intro to CRISPr/Cas9	26
27	5-Dec	Th	Paper TBD by Prof. Wang	Gene editing discussion		***Original Proposal Due***
28	10-Dec	T		**In Class Proposal Peer Scoring/Reviewing**		