

# Chemistry 694 – RNA Structure and Catalysis

## Portland State University, Spring 2009

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### General Information

Class meetings (**required**) – Monday and Wednesday 5:00 – 6:30 pm.

Text – Gesteland RF, Cech TR, Atkins JF (eds.) (2006) *The RNA World*, 3<sup>rd</sup> edition.

Dr. Lehman's Office Hours – Mon and Fri 10 am to 11 am; and by appt.

Best way to contact Dr. Lehman – by email! ([niles@pdx.edu](mailto:niles@pdx.edu))

### Prerequisites

The prerequisite for enrollment in Chem 694 is completion of or concurrent enrollment in Chem 492 at PSU, or consent of the instructor. I will assume you have taken a full year of organic chemistry and at least one term of physical chemistry. If you have taken biochemistry elsewhere, please talk to me before enrolling in this class. This is an advanced upper-division/graduate course and I will not be reviewing the basics of biochemistry that you may need to succeed in this class. Undergrad students may not enroll in Chem 694, but may, after consultation, enroll in 3 units of Chem 405 with me instead for the same class.

### Course Overview

Chem 694 will focus on the structure of RNA and how that structure relates to its function, both *in vivo* and *in vitro*. Through discoveries in the past 25 years, RNA (ribonucleic acid) has skyrocketed as a pivotal molecule in the storage and transmission of genetic information, in the control of gene expression, in cellular metabolism, in protein translation, and in the origins of life on the Earth. In October 2006, for example, the Noble Prize was awarded to Craig Mello and Andrew Fire for the discovery of RNA interference (RNAi). As such, we are in the midst of an exciting phase of elucidation about the biochemistry of RNA, both in terms of structure and function. This course will use a combination of lecture-style teaching with primary literature reading and presentation to allow the students to gain a solid introduction into this fascinating and rapidly moving field of study. During roughly the first two-thirds of the course, I will lead the students through the basic chemistry of RNA, moving through nucleotide structure, to RNA secondary and tertiary structure, and finally to RNA enzyme structure and mechanisms of catalysis. During the last third of the course, the students will read and present to the group some selected recent papers in the primary literature on RNA structure and catalysis.

### Grading

Grading will be done on a straight scale. There are 100 points possible for the term, and if you accumulate 85 points or greater, you will earn an A. If you accumulate 80 points or greater you will earn an A-. If you accumulate 75 points or greater, you will earn a B+. If you accumulate 70 points or greater, you will earn a B. If you accumulate 60 points or greater you will earn a C. If you accumulate 50 points or greater, you will earn a D (undergraduate students) or fail (graduate students). Undergraduate students who earn fewer than 50 points will fail. I will not give grades of B-, C+, C-, D+ or D- in this course. Graduate students will be required to do more for their presentation scores. Sources & sinks of points are:

- Midterm – 30 points
- Quiz 1 – 10 points; Quiz 2 – 10 points
- Presentation – 20 points
- Final Project – 30 points
- Attendance – 0 points (but up to 20 points can be *subtracted* from your total; see below)
- Extra credit – 2 points for attendance at Sid Altman lecture on Friday, May 8<sup>th</sup> at 5 pm

## Course Policies

This is senior/grad level course and I will treat you like adults and expect that you respond in kind; approaching the course and the other students with respect. Cheating or plagiarism will be grounds for an F grade. Because we meet only ten times during the course, attendance is critical. *Two points will be subtracted from your point total for any missed class sessions (for whatever reason, good or bad, including medical school interviews, illness, etc.). This especially applies to days of student presentations.*

## Examination & Project Policies

During the first 15 minutes of lectures #4 and #10 there will be quizzes worth 10 points each, covering the material from the previous few lectures. These quizzes will ensure that all students are keeping up with the reading and lecture material. The Midterm exam, worth 30 points, will be given in class during the seventh week. Students will have 1.5 hours maximum to answer essay questions dealing with the material presented in the first six weeks of class. This will be a closed book, but **open note** exam. A take-home final project, worth 30 points, will be due on Wednesday of finals week (by 9 am, June 10<sup>th</sup>, 2009). The final project will be a 5 page written report on a stable RNA of your choice. Students must choose one RNA from the following list to research (with the caveat that no two students can do the same RNA):

- Yeast phenylalanyl tRNA
- *E. coli* 5S rRNA
- *Xenopus laevis* 5.8S rRNA
- *B. subtilis* RNase P
- *Azoarcus* tRNA<sup>le</sup> group I intron
- Hammerhead ribozyme
- Hairpin ribozyme
- HDV ribozyme
- *B. subtilis glmS* riboswitch ribozyme
- Class I ligase ribozyme

Each student will choose one of these RNA and present a well-referenced report that describes its discovery, biological role (if any), 2° structure, 3° structure, substrate binding properties (if any), catalytic mechanism (if any), and evolutionary history. Reports will be graded for coverage of the above points, clarity, and demonstration of understanding of the current state of knowledge regarding the RNA. All reports must include -- within the 5-page limit -- a student-drawn diagram of the best current estimate of the secondary structure of the RNA; this aspect of the report alone will be worth 10 points.

## Student Presentations

During the last 3 class sessions, students will give in-class oral presentations based on their readings in the primary literature, which I will help assign. The graduate students will go first, during the eighth and ninth weeks of the term. The undergrads will present last, during the tenth week of the term. All students will prepare presentations that summarize the main goals, experiments, and findings of each of two papers that focus on one topic. The topics may, at the students' discretion, be the same as the RNA for which they have chosen to study for their written report. The presentations may use overhead transparencies, PowerPoint slides, or any other media that may be appropriate. Each student should plan on presenting two papers, and devote 30 minutes of presentation time to each paper. Each presentation should be clearly organized, with enough background material so that all listeners can follow the rationale and experimental design of the paper. I will assign up to 20 points for each student, with the following weighting scheme:

- Introduction and general explanations – 5 points
- Coverage of salient points in the papers – 10 points
- Clarity of oral presentation and of presentation materials – 5 points

## Class Schedule – Ch405/694 Sp 2009

Date*	Reading	Topic
Mon, Mar 30 Wed, Apr 1	Chapter 2 in <i>The RNA World</i> Chapter 2 in Neidle*	Introduction to course, RNA and nucleotides Nucleotide structure
Mon, Apr 6 Wed, Apr 11	Handout: pp. 89-111 from Neidle*	RNA/DNA–small molecule interactions <b>NO CLASS</b>
Mon, Apr 13 Wed, Apr 15	Chapter 22 in <i>The RNA World</i> Chapter 22 in <i>The RNA World</i>	<b>quiz 1</b> ; Global RNA 2° and 3° structure Global RNA 2° and 3° structure
Mon, Apr 20 Wed, Apr 22	Chapter 23 in <i>The RNA World</i> ** Chapter 23 in <i>The RNA World</i> **	Base pairing and base triples Base pairing and base triples
Mon, Apr 27 Wed, Apr 29	Chapter 22 in <i>The RNA World</i> Chapter 22 in <i>The RNA World</i>	Comparative & computer analysis of structure Comparative & computer analysis of structure
Mon, May 4 Wed, May 6 Fri, May 8	Chapters 5 & 6 in <i>The RNA World</i> Chapters 5 & 6 in <i>The RNA World</i> <b>SID ALTMAN LECTURE 5:00 pm IN HOFFMAN HALL</b>	<b>quiz 2</b> ; RNA-directed catalysis RNA-directed catalysis
Mon, May 11 Wed, May 13	Chapters 5 & 6 in <i>The RNA World</i> <b>Midterm exam</b> (covering all lectures + chaps. 2, 5, 6, 22, & 23 in <i>The RNA World</i> )	RNA-directed catalysis
Mon, May 18 Wed, May 20	Chem 694 student presentations: Chem 694 student presentations:	
Mon, May 25 Wed, May 27	Chem 694 student presentations: <b>NO CLASS</b>	
Mon, Jun 1 Wed, Jun 3	Chem 694 student presentations: Chem 694 student presentations:	
Wed, Jun 10	<b>FINAL PROJECT DUE</b>	

\*on a couple of occasions I will hand out additional readings from the book:

Neidle S (2002). *Nucleic Acid Structure and Recognition*, Oxford University Press

\*\*supplement your reading with Leontis NB *et al.* (2002). *Nucleic Acids Research* 30, 3497-3531.