

MCH 501 - Principles of Medicinal Chemistry

University at Buffalo

Fall Semester 2016

<i>Lecturer</i>	<i>Location</i>	<i>Time</i>	<i>Days</i>
Dr. Qing Lin 679 NSC 645-4254 E-mail: qinglin@buffalo.edu Office Hours: 12:00-1:00 PM T, R or by appointment.	106 Talbert	8:00-9:20 AM	T, R

Text:

R. B. Silverman, "The Organic Chemistry of Drug Design and Action, 3rd Edition," Academic Press, 2014. Available at www.amazon.com.

Online Journal References:

- *Journal of the American Chemical Society*. (<http://pubs.acs.org/journals/jacsat/index.html>)
- *Angewandte Chemie-International Edition*. (<http://www3.interscience.wiley.com/cgi-bin/jhome/26737?CRETRY=1&SRETRY=0>)
- *Journal of Medicinal Chemistry* (<http://pubs.acs.org/journals/jmcmar/index.html>)
- *Nature Reviews Drug Discovery* (<http://www.nature.com/nrd/index.html>)

These Journals are available through UB Libraries electronic journals. *It is expected that each graduate student in a chemistry department read the chemical literature. These journals, and others that may be suggested during the semester, will serve as a supplement to the class. Each new issue should be perused by each student to become acclimated to the chemical literature.*

Mid Semester Exam – TBA during regular class time and place.

Final Exam – Tuesday Dec. 13th, 8:00 AM-11:00 AM, Talbert 115.

Each student is also required to make 2 presentations on a current publication of their choosing that is focused on medicinal chemistry (details below).

Outline for MCH 501 – This roughly follows “The Organic Chemistry of Drug Action and Design.” Supplemental materials in the form of literature articles will be made available through UBLearn. Coverage adjustments may be made as the semester proceeds.

- 1. Molecular Basis of Drug Action and Drug Design**
 - 1.1 Molecular properties, geometries, stereochemistry, conformation, energetics
- 2. Drug Discovery, Design and Development**
 - 2.1 Discovery without leads
 - 2.2 Lead discovery strategies
 - 2.3 Combinatorial chemistry: high throughput screening
 - 2.4 Principles of rational drug design
- 3. Lead Modification**
 - 3.1 Pharmacophores
 - 3.2 Functional group modification
 - 3.3 Bioisosterism, structure modification: homologation, chain branching,
 - 3.4 SAR

- 3.5 QSAR: Electronics, hydrophobicity, sterics
- 4. Receptor Targets**
- 4.1 Forces in Drug/Receptor complex
 - 4.2 Drug receptor theories: occupancy, rate, induced-fit, macromolecular perturbation, activation-aggregation
 - 4.3. Stereochemical consideration: chirality, geometric isomers, conformational isomers, ring topology
- 5. Enzyme Targets**
- 5.1 Enzyme catalysis: Approximation, covalent catalysis, general acid/base, electrostatic, desolvation, strain/distortion
 - 5.2 Coenzymes and prosthetic groups: PLP, THF, Flavin, Heme, ATP, CoA

About the Course:

Lecture:

Students should be properly registered and should attend all lectures. Students should read the text in advance of lecture to familiarize themselves with the material. Students are responsible for assigned materials and all materials presented in class whether they attend or not. Course grades will be determined by two examinations (a midterm and a final) and two presentations of journal articles selected by the student with approval from Dr. Lin. One article will describe new methods that can facilitate drug discovery and the other will be a recent research article describing a contemporary medicinal chemistry drug discovery effort.

Presentation:

Each student is also required to make presentations on current publications of their choosing that is focused on medicinal chemistry. *Each talk will be 25 min with 5 min for questions, assigned dates for these presentations will be provided later on Blackboard.*

This article will be a recent medicinal chemistry publication (i.e. within the last 3 years) focused on one of the topics covered in this course.

Grading:

<u>Midterm Exam</u>	20%
<u>Unannounced Quizzes</u>	10%
<u>Final Exam</u>	40%
<u>Presentations (2)</u>	15% Each

The presentations will be graded based on clarity, slide quality, knowledge of the materials, and proper use of the presentation time. The articles **MUST** be approved by Prof. Lin at least 1 week prior to the presentation and the presentation slides should be emailed to Prof. Lin by noon the day before the presentation. Presentations will be 20 min with 5 min for questions. *All articles and associated presentations are subject to being on the exams and will be posted on UB learns.*

Make-up Policy:

Students who are unavoidably absent from an exam must notify Dr. Lin in advance. For all absences, students must be prepared to document the reason for an absence if requested to do so (See incompletes for more detail). Since the final exam will be comprehensive, students who miss the midterm exam with a valid excuse will have their grade determined by the total points from their final exam and their two presentations, re-scaled accordingly to accommodate the missed midterm exam. ***If you are unable to make the date in which your class presentation was scheduled you must find another student to switch with.***

Incompletes:

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Students who present a valid written excuse for failure to take the Final Examination within 48 hours of that exam will be given a grade of I (incomplete) if they had a passing grade without counting the potential final exam points. The default grade for an incomplete will be computed with the final examination counting 0 points. Students with failing grades (before counting the final exam) are not eligible for incompletes and will be assigned a grade of F if they do not take the Final Examination. Incompletes must be removed by examination within 15 months, by taking a make-up exam at a time to be announced.

Students requesting an incomplete are hereby reminded that University regulations prohibit a second registration in a course for which they currently have an I-grade and that all I-grades must be removed before graduation. Students who stop attending, as judged by their absence from the Mid-Term and the Final Examination, without officially resigning, will be assigned the grade of F and their lack of attendance will be reported to the Office of Financial Aid at the end of the semester.

Handicapped Students:

The Chemistry Department works closely with the Office of Disability Services to make it possible for anyone wishing to take a Chemistry course to do so. Special arrangements can be made for handicapped students who cannot take examinations or quizzes in the normal manner and for those who cannot perform laboratory experiments unaided with the normal equipment. All such arrangements must be made well in advance of the event by contacting Mr. Randall E. Borst, Director of Accessibility Resources, 25 Capen Hall, and Dr. Lin.

Academic Integrity:

The University community depends upon shared academic standards. Academic dishonesty in any form represents a fundamental impairment of these standards. If, after consultation with the student, an instructor believes the student has committed an act of academic dishonesty, the instructor has the authority to impose sanctions in keeping with this principle. The MINIMUM sanctions to be imposed are as follows:

First infraction: The maximum point value for a test will be subtracted from the student's point total. A subsequent infraction will result in a minimum penalty of 20 total points.

Students should consult the Academic Regulations and Procedures section of the Graduate Education Bulletin for a more detailed discussion of possible harsher sanctions and the appeals process.

Academic dishonesty includes, but is not limited to, the following:

1. The possession of crib sheets or unauthorized notes at an examination or quiz, whether or not they are used. (Smart phone, calculator memory bank, calculator case or other articles are subject to inspection by the proctors.)
2. Copying from another person's examination paper or quiz, or deliberately allowing another person to copy from you.
3. Changing any of the answers on an examination paper or quiz, and then requesting that the paper be re-graded for additional credit.

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Miscellaneous:

1. Exam papers that students wish to have regraded must be turned in within one week after the paper has been received by the student. The nature of the problem must be specified on an attached sheet. Papers containing “white-out” corrections will not be re-graded. The entire exam is subject to being re-graded and the new grade reported.

Course Web Page:

The course web site is now available on Blackboard. You may access your course by navigating to:

<http://ublearns.buffalo.edu>

Each student’s username will be his or her UBIT name.

The final course grade (A – F, including +/-) will be determined solely on the basis of total points accumulated. Students missing a midterm examination, without a valid excuse, will receive a grade of “0” for that examination. There will be no makeup at anytime for unexcused absences. Students may receive an excused absence by providing a valid, written excuse within 48 h of the examination.

NOTE: During examinations, students may not use cell phones and cell phones must be kept out of sight and turned off. Violation of these rules will result in a grade of “0” for the examination.