Objectives

This class will serve as an overview of biochemical principles and methodologies, and is intended to prepare senior biochemistry majors for graduate studies in biochemistry, or for future careers in science and medicine. Three hours of course credit will be awarded for completion of this class, consisting of two 1-hour lectures (MW) and 3 h of laboratory per week. The overall topic of the course is drug design, a topic important to the pre-medical and pre-graduate student alike. The course will broadly cover the topic from target selection to preparation for clinical trials. The laboratory will make use of the computer and will include familiarization and manipulation of the small molecule and protein data-bases, working with protein three-dimensional structures, and ultimately docking small molecules into a protein structure.

The class will include a significant written component, including a mid-term paper, and the compilation of an accurate and detailed research notebook, describing all activities in the laboratory. It will also include an oral component. The results of the laboratory portion of the course will be presented to the class. All of the written and oral components of the course will build upon the laboratory portion of the course.

There is no TEXTBOOK for this class, but the following text can be obtained from the instructor for an hour at a time.


Additional reference texts:


The FINAL GRADE for the class will derive from four components:

1. Midterm Paper 150
2. Laboratory evaluation 150
3. Oral Presentation 150
1) The Midterm paper will consist of a 5-7 page literature overview of your target protein. It should answer the following questions.

What is the metabolic context in which the target protein operates, and what is its reaction (include structures of reactants)?

Why is the protein a good target for drug development?

Has the protein been cloned and expressed in a stable form (provide details briefly)?

What is known of the mechanism of action - kinetic and chemical?

How would you go about rationally designing an inhibitor of the target protein?

Each reference, including reviews, books, etc., used in the preparation of your written paper must be included in your list of references at the end of the report. Further, all appropriate material appearing in the text must have appropriate reference annotation — anything less is plagiarism* and will be treated in the most severe manner possible (i.e., for Dr. Cook, this will generate a recommendation of a grade of "F" for the class and expulsion from the University of Oklahoma). In particular, this means that any material(s) (i.e., paragraphs, sentences, phrases, ideas, concepts, figures, tables) which is/are, for the most part, directly taken from a particular reference should be appropriately annotated (reference number and/or authors/dates listed according to referencing method being employed and the complete reference citation given in the “References” and/or “Literature Cited” section at the end of the paper). Further, these same material(s) (i.e., paragraphs, sentences, phrases, ideas, concepts, figures, tables) which is/are, for the most part, directly taken from a particular reference should be placed in quotes and/or indented. With the exception of data base information, the Web is inappropriate for this assignment.

Likewise, you should be sure to properly reference material that was only viewed through a secondary source. If, e.g., you only saw a summary of an original article in Chemical Abstracts but were unable to actually view the original document itself, your reference should contain references to both the Chem. Abstr. article and the original publication.


The mid-term paper will serve as the introductory material for the oral presentation toward the end of the semester.

2) Evaluation of the laboratory exercise will be based on your laboratory notebook. This will be described in more detail in a separate handout.

3) An oral presentation will be made by each student (group) and will consist of the following:

a) An overview of the protein and why it is a good target - include biological context (the term paper should serve to provide most of this information).

b) Bioinformatics - including multiple sequence alignment, identification of key
catalytic and binding groups, etc. (from the laboratory exercises).
c) Structure of apoenzyme and ligand bound forms. Results of docking experiments (from the laboratory exercises).

4) The final exam will be comprehensive for the course. The format will be discussed later in the semester.

**LATE ASSIGNMENTS.** All assignments must be turned in at the beginning of class on the due date. Assignments will be accepted if late, but at a cost. If the assignment is turned in late on the same day, the equivalent of a letter grade will be lost. Assignments that are 1, 2, and 3 days late will lose the equivalent of 2, 3, and 4 letter grades. Assignments more than 3 days late will not be accepted. For example, an assignment turned in late on the due date will be graded on the basis of 90 points instead of 100.

*Plagiarize - to steal and pass off (the ideas or works of another) as one's own: use (a created production) without crediting the source: present as new and original an idea or product derived from an existing source*

*Webster's 9th New Collegiate Dictionary*

**LECTURE SCHEDULE**

<table>
<thead>
<tr>
<th>Date</th>
<th>Lecture Topic</th>
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<tbody>
<tr>
<td>Aug. 22</td>
<td>Overview - History</td>
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<tr>
<td>24</td>
<td>Overview - Procedure</td>
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| 29 | "Genomics and Target Selection"  
Dr. Fares Najar |
| 31 | "Natural Products"  
Dr. Robert Cichewicz |
| Sept. 5 | LABOR DAY |
| 7 | Combinatorial Chemistry/Libraries |
| 12 | "Importance of Stereochemistry"  
Dr. Kenneth Nicholas |
| 14 | Quantitative Structure Activity Relationship |
| 19 | Receptors as Targets |
| 21 | “G-Protein Coupled Receptors”  
Dr. Augen Pioszak |
| 26 | Enzymes as Targets  
Deliberate Rational drug Design |
| 28 | Ion Channels and other Transporters |
"Siderophore Transport/Trojan Drugs"
Dr. Phillip Klebba

Oct. 3
"Metals in Medicine"
Dr. Richard Taylor
5 Transition State Theory
6-7 TX Holiday - NO LAB

10 "Small Molecule Structural Data Base"
Dr. Douglas Powell
12 Enzyme Mechanism

17 "Protein X-ray Crystallography: The Prospect of Structure-based Rational Drug Design"
Dr. Ann West
19 Enzyme Mechanism

24 Examples of Rational Drug Design
26 "Defense against Malaria"
Dr. Jun Li

31 Student Presentations
Nov. 2 Student Presentations

7 Student Presentations
9 Student Presentations
14 Student Presentations
16 Student Presentations

21 OPEN
23-25 THANKSGIVING
28 Student Presentations
30 Student Presentations

Dec. 5 Student Presentations
7 Student Presentations

15 Final Exam - PHSC 114 – 9:30-10:30

The University of Oklahoma is committed to providing reasonable accommodation for all students with disabilities. Students with disabilities who require accommodations in this course are requested to speak with the instructor as early in the semester as possible. Students with disabilities must be registered with the Office of Disability Services prior to receiving
accommodations in this course. The Office of Disability Services is located in Goddard Health Center, Suite 166, phone 405/325-3852 or TDD only 405/325-4173.

Each student should acquaint her or his self with the University's codes, policies, and procedures involving academic misconduct, grievances, sexual and ethnic harassment, and discrimination based on physical handicap.

The instructor reserves the right to change this syllabus by modification, addition and/or subtraction of assignments, course content, due dates, and grading policies, as she deems necessary.