CHEM 480/680: Computer Aided Drug Design

Instructor: Dr Dora Schnur
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Office hours: TBA and by appt but usually available MWF afternoons and before class.

Meeting times: Thur 6:00pm -8:50 pm: first hour is lecture; remainder is lab

Required Text: Young, "Computational Drug Design: a Guide for Computational and Medicinal Chemists", Wiley, 2009 plus handouts.

Reserved texts: Since there really are no good texts for this type of course, several additional texts will be on reserve in the library to cover topics of interest in more detail. Reading these additional texts is optional, but will be helpful. Cramer is only for those interested in the theoretical underpinnings of the methods used. The other texts are applications oriented and depending on the topic, one or more will be very informative.

1. Holtje, Sipplel, Rognan and Folkers, Molecular Modeling: Basic Applications and Principles, 3rd Edition, Wiley, 2008.

2. Leach, "Molecular Modelling: Principles and Applications", 2nd Edition, Pearson Prentice-Hall, 2001

3.Schneider and Baringhaus, "Molecular Design: Concepts and Applications", Wiley, 2008

4. Cramer, "Essentials of Computational Chemistry", 2nd Edition, Wiley, 2004.

Software: Schrodinger Maestro Suite 2013 for Windows. Possibly other software programs where appropriate. Please note, that the program has extensive help manuals which include theory. We will be using the tutorials.

Other: a flash or pen drive is strongly recommended for storing your data

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Syllabus (subject to modification since this is a new course…)

January 9: intro to Computer Aided Drug Design and Maestro software

January 16: Molecular mechanics, Semi Empirical and *ab initio* calculations;

January 23: Targets and target classes I; docking and scoring

January 30: Targets and target classes 2: pharmacophores and virtual screening

February 6 : Midterm exam; catch up on tutorials; notebook check

February 13: QSAR methods

February 20: Combinatorial and Parallel Library Design, Bioisosteres and scaffold hopping

February 27: Sequences, homology modeling;

March 6: Project presentations; written project reports due.

March 13: Final exam, notebook check and remaining presentations

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In the laboratory, we will explore how these topics are applied using Maestro from Schrodinger, Inc., a commercial software package commonly used in the pharmaceutical industry and possibly also with various other specialized programs. Our goal will be to study and apply the basic methods and protocols used for drug design. Students will perform experiments based on both commercially provided software tutorials and using real data from the literature. A student designed modeling project will be part of the course requirements.

GRADING:
Mid Term 20%
Final Exam 25%
Project 30%------20% written 10% oral presentation
Lab notebook 15%
Attendence 5%
Assignments 5%

STUDENT SPECIAL PROJECTS: The topic will be selected by the student with approval of the instructor and may be part of an ongoing student research project with another faculty member, if desired. A short description of the approved project topic, software to be used and goal should be handed in no later than **Feb 10** and the final report is due on **March 6** as a 10 minute presentation/poster plus a written report in the form of a publication.
ATTENDANCE POLICY: Attendance is mandatory, especially at scheduled exams, in lab, and on days when homework or projects are due. Please be on time for class.
Attendance will be noted at all sessions. All of the material in the lectures, readings, projects, workshops and other laboratory activities, and homework assignments are fair game for the examinations. Material will be introduced in lecture which is not in the textbooks. Active classroom discussions are very important in order to gain a good understanding of the material. Please participate!
ORGANIZATION AND REQUIREMENTS: There will be weekly laboratory projects and tutorials, a mid-term examination and a final exam. Homework assignments, projects and reading assignments will be given in class. Homework may be collected and reviewed for completeness and accuracy. You should attempt all problems and show all of your work.
I will be glad to help you with homework and laboratory questions before or after the assignment or report is due. You must do your own work, but you may of course consult with other students on individual problems (note: "consult with" is not the same as "copy from." Please see the Drexel University plagiarism policy for details.)
Missed examinations will merit a grade of zero unless the absence is due to a documented medical emergency or other unforeseeable circumstances. Please note that documentation from a relative is not acceptable. Makeup exams are at the instructor's discretion.
WORKSHOPS AND PROJECTS: The laboratory consists of "projects/experiments" and /or "workshops/tutorials." Please keep either a written or enotebook recording your experiments. These will be checked periodically in class and graded as excellent, satisfactory or unsatisfactory.
The format for project work is discussed below.

READING MATERIALS:

Lecture 1

- Young: Chapter 1, 2,3, 18.1-18.3
- Optional:
  - Holtje: Chapter 1
  - Leach Chapter 1
  - Schneider and Baringhaus: chapter 1

Lecture 2 Molecular mechanics, QM

- Young : chapter 10 (molecular mechanics), 16 (QM)
- Optional much more in depth on MM, etc.
  - Holtje: Chapter 1, Chapter 2 through section2.4.3
  - Leach: chapter 2, and 9 ; chapter 4 through4.13 and 3.7
  - Cramer: chapters 1 and 2 through 2.5, 4, 5, 6, 8; note: this text is very theoretical!

Lecture 3 Docking

- Young: Chapter 5,12
- Optional
  - Holtje: Chapter 5 and 6
  - Leach: chapter 12.6
  - Schneider and Baringhaus: chapter 3

Lecture 4 Pharmacophores and virtual screening

- Young: Chapter 13, 18.4-18.6
- Optional
  - Holtje: Chapter 5 and 6
  - Leach: chapter 12.1-12.5
  - Schneider and Baringhaus: chapter 4

Lecture 5 QSAR

- Young: Chapter 6, 14 and 15
- Optional
  - Holtje: Chapter 2.6 thru end of chapter, 3
  - Leach: chapter 12.1-12.5, 12.13
  - Schneider and Baringhaus: chapter 2

Lecture 6 Library design,etc.

- Young: Chapter 8
- handouts
- Optional
  - Holtje: Chapter 2.6 thru end of chapter, 3
  - Leach: chapter 12.10 and 12.14

Lecture 6 Homology modeling.

- Young: Chapter 9, 11
- Optional
  - Holtje: Chapter 4
  - Leach: chapter 10

KEEPING A PROFESSIONAL NOTEBOOK: FORMAT for ENotebook: (or bound notebook)—mostly maintained during lab

The first page contains your name, the course number/title and the dates of the course

The second page will be an index of the experiments performed (which you update as you go) with page numbers

The third page contains the list of any lab partners and/or project "witnesses"

***Format for Experimental pages**---does not have be completely prose---bullets and partial sentences ok*

Page Number of Enotebook

Date:

Project Title and Number:

Purpose of the experiment or tutorial---can be referenced if from a tutorial

Software version used, including specific modules

Reference list---you may refer to previous experiments in your enotebook in addition to other reference materials

List of compounds studied if applicable

Procedure---if using a tutorial, list deviations from the described procedure.

Observations/Calculations/Data

Results and Conclusions

List of compounds designed (if applicable)

"I certify that the above experiment is completed." Your name and date of completion------Once you certify completion, you are not permitted to make any alterations to these pages. You have to add an addendum to the experiment referencing the certified one to report any changes. If you work on a project over multiple days, you enter each date before entering additional information. This means you could have a date in the middle of a procedure or data section or even results section. If an experiment produces a lot of data, you may specify file names (if the files are saved) instead of incorporating pages of numbers in your notebook.

If you have a lab partner, include their name and date of signing***. NOTE: if you have a lab partner since computers seats are limited, each student must keep an individual enotebook. If a joint notebook is kept, each student will receive ½ the total points as their grade!!!!!***

(In industry, you would formally sign and date the experiment electronically and a colleague would witness your experiment electronically. If using a bound notebook, you should sign and date every page at the bottom and a "witness" would do the same. We are emulating this practice in the course.)