The Scripps Research Institute
Graduate Program
Structural Biology

## Contact Information

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## Course Information

Semester, Year: Fall 2009
Meeting day, time: Monday, Wednesday, Friday, 9:45am – 11:15am
Meeting Location: The Committee Lecture Hall, Molecular Biology
The location for the practical sessions will be announced prior to the class.

## Course Description

This course covers all aspects of structural biology from primary to quaternary structure and deals with the 3D structure of proteins, nucleic acids, carbohydrates, and lipids. The enzyme section deals with kinetics, mechanism and drug design. Macromolecular assemblies and higher order structures include oligomers, viruses, the immune system, molecular machines, metalloproteins, membrane proteins and biological complexity.

## Background Preparation (Prerequisites)

Students are encouraged to review background material relevant to each class that can be found in 'Intro to Protein Structure', Second Edition by Carl Branden and John Tooze. Students typically have taken an undergraduate-level course in biology or biochemistry, but this is not required.

## Texts and Journal References

Intro to Protein Structure, Second Edition by Carl Branden and John Tooze

## Course Learning Outcomes

By the end of this course, students will be able to

- analyze and evaluate the basic building blocks of biological macromolecules
- consider how structure leads to function
- discuss the evolution of biological structure and function
- understand the architecture and building blocks of proteins
- evaluate protein folds and the nature of the protein universe

- understand protein folding and misfolding
- understand the architecture and building blocks of nucleic acids
- understand the architecture and building blocks of carbohydrates
- understand the architecture and building blocks of lipids
- understand how enzymes function and the basis of structure-based drug design
- understand the basics of enzyme kinetics
- construct homology models of proteins
- computationally dock ligands to proteins
- build models of proteins and nucleic acids
- understand protein-nucleic acid interactions
- understand the structure and function of membrane proteins
- understand the structure of some molecular machines
- understand how viruses assemble
- evaluate biological complexity

## Course Requirements & Assignments

### Grading

Grading will be based on two exams: a midterm and final. Normally, 4 to 5 questions are set for each exam that cover the material presented in the course. The overall recorded grade is a composite of the two exams and is usually equally weighted, or otherwise proportional to the number of questions on each exam. Letter and numerical grades will be assigned to each exam and the overall grade will be entered for the permanent record.

| Letter Grade | Outcome | Description | Learning Outcome |
|---|---|---|---|
| A | Pass | Superior achievement | Exemplary |
| B | Pass | Demonstrated a good knowledge and grasp of the course material | Proficient |
| C | Fail | Below average, not at level expected for letter grade. | Developing |
| C | Pass | Acceptable only for taking as Pass/Fail | Developing, but adequate as a survey course |
| F | Fail | Not acceptable | Not sufficient knowledge or understanding |

### Attendance

All classes and practicals must be attended to complete class, unless specific permission is granted for absence by the course director or TAs due to personal or business reasons. Unapproved absence or late attendance for 3 or more classes may result in a lower grade being assigned or an incompletion recorded.

**Scientific and Professional Ethics**

The work you do in this course must be your own. You must be aware when you are building on someone else's ideas, including ideas of classmates, professors, and authors you read. You must explicitly acknowledge the ideas of others. Feel free to build on, react to, criticize, and analyze the ideas of others but, when you do, make it known whose ideas you are working with. If you ever have questions about drawing the line between others' work and your own, ask me and I will give you clear guidance. Exams must be completed independently. Any collaboration on answers to exams, unless specified explicitly in the exam, will result in an automatic failing grade and possible expulsion from the graduate program.

**Expectations and Logistics**

The course is intended to provide an advanced level understanding of macromolecular structure and function and is taught by experts for every topic covered. While some of the topics may have been covered at a superficial level in undergraduate or other survey courses, the intent here is to provide instruction by true experts and leaders in the field for every single topic covered. The course is suitable for biologists, immunologists, biophysicists, and chemists alike. The course changes each year to reflect any new developments in the structural biology field. The intent is to come out with a good grasp of the principles of macromolecular structure, function and evolution and to be able to search structural databases, generate homology models, grasp the concepts and principles in molecular modeling and docking and to be able to computationally explore macromolecular structures to understand the design principles with regard to biological function. Students are expected to actively participate in the course by asking questions and engaging with the lecturers and TAs so as to individually probe deeper into the topics and gain the maximum benefit. A question and answer session at the end of each lecture is recommended. The TAs will attend all the lectures, provide assistance to the lecturers, provide guidance on the course to the students in the class, address questions, and will organize review sessions on request.

## Schedule

| Lecture Date | Topic | Lecturer (TSRI, unless indicated) |
|---|---|---|
| Mon, Sept 14 | **Please note early start time for overview on the first day of class!** | |
| 9:15 AM | Overview of Structural Biology | Wilson |
| 9:45 AM | Alphabet 1: Proteins-Primary Structure, Chemistry And Covalent Modifications | Dawson |
| Wed, Sept 16 | Protein Secondary and Supersecondary Structure | Wilson |
| Thur, Sept 17 12:00 – 3:00pm | Introduction to Molecular Graphics | Johnson, G./Ward |
| Fri, Sept 18 | Model Building Practical: Protein Secondary and Tertiary Structure | Pique/Getzoff/Olson |
| Mon, Sept 21 | Structural Classification of Proteins, Profiles and Protein Families | Godzik, Burnham |
| Wed, Sept 23 | Molecular Modeling I: Homology and Comparative Modeling | Godzik, Burnham |
| Fri, Sept 25 | Molecular Modeling "How to" Practical/Tutorial | Godzik, Burnham |
| Mon, Sep 28 | Protein Folding – Experimental & Theoretical | Dyson |
| Wed, Sept 30 | Macromolecular Machines in Protein Folding | Chapman |
| Fri, Oct 02 | Macromolecular Machines in Protein Unfolding | Chapman |
| Mon, Oct 5 | Protein Misfolding, Disease, *in vivo* Folding and Degradation | Kelly |
| Wed, Oct 7 | Alphabet 2: Nucleic Acids – Chemistry and Secondary Structure | Joyce |
| Fri, Oct 9 | Model Building Practical – Nucleic Acids | MacRae |
| Mon, Oct 12 | RNA Catalysis | Fedor |
| Wed, Oct 14 | Tertiary Structure of Nucleic Acids | Williamson |
| Fri, Oct 16 | RNA – Protein Interactions | Williamson |
| Mon, Oct 19 | DNA – Protein Interactions | Wright |

| Lecture Date | Topic | Lecturer (TSRI, unless indicated) |
|---|---|---|
| Wed, Oct 21 | Nucleic Acid Tutorial | MacRae |
| Fri, Oct 23 | Autodock | Johnson, G./Huey |
| | Midterm Take-home Exam October 23-26 | |
| Mon, Oct 26 | Enzyme Kinetics I | Romesberg |
| Wed, Oct 28 | Enzyme Kinetics II | Romesberg |
| Fri, Oct 30<br>8:00am – 9:30am | Enzyme Kinetics Practical | Romesberg |
| Mon, Nov 2 | Enzyme Structures I – Mechanism and Inhibition | Stevens |
| Wed, Nov 4 | Enzyme Structures II – Drug Design | Wolan, UCSF |
| Fri, Nov 6 | Enzyme Structures Practical/Tutorial | Stevens |
| Mon, Nov 9 | Metalloproteins – Chemistry, Structure & Mechanism | Goodin |
| Wed, Nov 11 | Metalloenzymes – Structure & Mechanism | Goodin |
| Fri, Nov 13 | Structural Basis of Immune Recognition | Wilson |
| Mon, Nov 16 | Alphabet 3: Carbohydrates – Structure, Biosynthesis and Glycoprotein Families | Paulson |
| Wed, Nov 18 | Carbohydrate Binding Proteins: Structure and Function | Paulson |
| Fri, Nov 20 | Carbohydrate Tutorial | Paulson |
| Mon, Nov 23 | Biological Networks | TBA |
| Wed, Nov 25 | *Thanksgiving Holiday* | |
| Fri, Nov 27 | *Thanksgiving Holiday* | |
| Mon, Nov 30 | Alphabet 4: Lipids, Lipid Binding Proteins, Lipid Biochemistry, Lipid Enzymes and Lipidomics | Dennis, UCSD |
| Wed, Dec 2 | Membrane Proteins | Ward |
| Fri, Dec 4<br>***9:45 – 11:45*** | Complexity: A Central Problem of 21st Century Biology | Edelman |

| Lecture Date | Topic | Lecturer (TSRI, unless indicated) |
|---|---|---|
| Mon, Dec 7 | Virus Assembly and Structure | Johnson, J. |
| Wed, Dec 9 | Protein Quaternary Structure and Cooperativity | Olson |
| Fri, Dec 11 | Virus/Protein Assemblies Practical/Graphics | Johnson, J./Olson |

Final Take-Home Exam December 11-14th

Winter Break December 18 – January 4th