

# Bio207: The Life and Death of Proteins

Stanford University, Spring 2009

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Bio207 is a graduate level course aimed at understanding how protein conformation is controlled in the cell. The primary emphasis will be on experimental design and critical reading and discussion of primary literature. We will focus on selected "case studies" and read the fundamental papers that have led to a greater understanding of that particular question. By following the historical development of specific topics we will evaluate how different experimental approaches can contribute to our understanding of a biological problem. Topics will include (see the outline for a complete list): How do proteins fold? How do chaperones function? How does protein misfolding link to disease?

This year the emphasis of the class will be on interdisciplinary approaches to understand protein folding and misfolding in the cell. The class will feature a stellar cast of top researchers in the protein folding and misfolding field. Each class will start with a lecture by one of these researchers, followed by a discussion of papers chosen by the lecturing professor. For each topic you will be asked to read a few (2-3) related research papers. At each class you will hand in a written assignment on that day's papers. This written assignment will be a short (less than one page) critique of these papers (as if you would be reviewing them for publication). The papers will be then be discussed in class. For the end of the class, you will be expected to write a short proposal on one topic related to the class. The proposal should be in NIH format (like a grant or fellowship) but should be **no longer than five pages**. The proposals should be handed on May 30 and will be evaluated in an NIH style panel.

By the end of the quarter you should:

- a) be familiar with approximately 40 research papers and reviews focused on protein folding and misfolding (these papers form the core of a working understanding of the field)
- b) be familiar with many of the techniques used to address questions related to protein folding and misfolding
- c) practice writing a grant/fellowship application and reviewing it in an NIH-panel format

d) (and most important) be able to apply your newly developed understanding to the analysis of biological problems, in the classroom as well as in your future studies and research.

### **Requirements**

- 1) attendance at all classes
- 2) *ACTIVE* participation in class discussions
- 3) 7 written assignments
- 4) Grant application: writing and evaluation

### **Grading** (approximate percentage of final grade)

class participation	40%
written assignment	20%
grant writing/evaluation	40%

### **Written Assignments**

The written critiques of the papers should be terse and specific. They should include a brief description of the problem addressed by the paper (1-3 sentences) and how the authors propose to answer these questions. It should then evaluate how successfully their experiments support their conclusions, point out the flaws in experimentation or logic and determine whether this paper is an important contribution or not. The maximum length of each critique is one double spaced page (12 point font only).

### **Grant Application and Evaluation**

NIH style grant/fellowship applications typically consist of a Research Problem divided into 2-4 Specific Aims, with a clear hypothesis to be tested. The evaluation will be carried out in a NIH Study Section format, with two primary reviewers for each proposal, and a group discussion. Primary reviewers must write a short critique of each proposal (less than a page) evaluating a number of criteria. The final score is assigned after a group discussion.

## Schedule

Week 1: April 8

Judith Frydman, Biology Department, Stanford University

**General introduction to protein folding in the cell**

Week 2: April 15

Jonathan King, Biology Department, MIT

**Protein Folding, Misfolding and Aggregation**

Week 3: April 22

Vijay Pande, Chemistry Department, Stanford University

**Folding@Home: computational approaches to the folding problem**

Week 4: April 29

Paul Adams, Laurence Berkeley Lab

**Structural Biology of Chaperonins**

Week 5: May 6

W.E. Moerner, Chemistry Department, Stanford University

**Application of Single Molecule Approaches to folding and misfolding**

Week 6: May 13

William Mobley, Dept of Neurology, Stanford University School of Medicine

**Alzheimers Disease and other neurodegenerative diseases:  
Clinical aspects and cellular pathology**

Week 7: May 20

Judith Frydman

**Molecular chaperones, cancer and aging**

Week 8: May 27

Isabella Graef, Dept of Pathology, Stanford University School of Medicine

**Small molecules and therapeutic approaches to folding disease**

Week 9: June 3

**Study Section Evaluation of Student Grant Proposals**

## **Course Director**

Dr. Judith Frydman  
Associate Professor, Department of Biology  
Co-Director, Center for the Protein Folding Machinery  
Stanford University  
<http://www.stanford.edu/group/frydman>

## **Invited Lecturers:**

Jonathan King Ph.D.  
Prof of Molecular Biology  
MIT  
<http://web.mit.edu/king-lab/www/>

Vijay Pande PhD  
Associate Professor of Chemistry and, by courtesy, of Structural Biology  
Chair, Biophysics Program  
Stanford University  
[folding.stanford.edu/Pande/Main](http://folding.stanford.edu/Pande/Main)

Paul Adams PhD  
Deputy Division Director, Physical Biosciences Division, Lawrence Berkeley Lab  
Adjunct Professor, Department of Bioengineering, U.C. Berkeley  
Head, Berkeley Center for Structural Biology  
Lawrence Berkeley Laboratory  
<http://cci.lbl.gov/paul>

W. E. Moerner PhD  
Harry S. Mosher Professor of Chemistry and, by courtesy, of Applied Physics  
Stanford University  
[www.stanford.edu/group/moerner/](http://www.stanford.edu/group/moerner/)

William C. Mobley M.D., Ph.D.  
Professor, Department of Neurology and Neurological Sciences and  
Director, Center for Research and Treatment of Down Syndrome  
Stanford University  
<http://mobleylab.stanford.edu/>

Isabella Graef M.D., Ph.D.  
Assistant Professor, Department of Pathology  
Stanford School of Medicine, Stanford University  
<http://graeflab.stanford.edu/>