Syllabus for MCB 4009 / 5013: Structure and Function of Macromolecules

11:00-12:15 pm Tuesday/Thursday
Torrey Life Science Building Rm 301

Instructors

Dr. Andrei Alexandrescu
Office: BPB, Room 209
Phone: 486-4414
E-mail: andrei.alexandrescu@uconn.edu
Office Hours: Tu 1-2 pm, Th 1-2 pm

Dr. Victoria Robinson
Office: BPB, Room 204
Phone: 486-4353
E-mail: victoria.robinson@uconn.edu
Office Hours: Tu 4-6 pm, Wed 4-6 pm

Part 1: Survey of protein structure		
Jan 20	AA	Introduction. [1]
22	AA	Protein Folding & Forces [2] [1-3, 1-4, 1-5, 1-9, 1-12, U1-3, U1-4]
27	AA	Protein building blocks, secondary structure. [3] [1-6, 1-7, 1-8]
29	AA	Supersecondary structure, tertiary structure, domains. [4] [1-10, 1-7, 1-8]
Feb 3	AA	Examples of structure superfamilies [5, 6] [1-15,1-16,1-17,1-18]
5	AA	Protein Structure and Evolution [7,8]
10	AA	Oligomeric Proteins [9,10] [1-19,1-20,1-21]
12	AA	Fibrous Proteins and Amyloids [11]
17	AA	Protein Dynamics [12] [1-22, 2-2]
19		**EXAM I**
Part 2: Introduction to structure determination techniques		
24	AA	Structure Determination by NMR [13]
26	AA	Structure Determination by NMR
Mar 3	AA	Structure Prediction and Design [14]
5	AA	High resolution microscopy: TEM, SEM, STEM, AFM [15]
Spring recess: No Classes March 8-13		
17	VR	Structure Determination by Crystallography [16, 17] [5-2, 5-3]
19	VR	Structure Determination by Crystallography
24	VR	Macromolecular Machines: The Ribosome [18, 19]
26	VR	Macromolecular Machines: Sec Complex [20]
31		**EXAM II**
Part 3: Control of Protein Function **(Selections from P&R Chapter 3; supplementary readings are listed)**		
Apr 2	VR	Overview of regulatory mechanisms [21, 22]
7	VR	Location and targeting
9	VR	Effectors and Ligands
Apr 14	VR	Phosphorylation
16	VR	Kinases and Cell Signaling Pathways in Bacteria [23]
21	VR	Protein switches: GTPases [24, 25]
23	VR	Modifications; methylation, glycosylation etc.
28	VR	Regulation by proteolysis and degradation [26]
30	VR	Membrane Proteins

Final Exam – to be announced

Exams, Assignments and Grades:

Exam 1 will cover part 1, exam 2 will cover part 2 and the final exam will cover part 3. The exams will count equally and contribute 75% towards your course grade. Two homework assignments will be distributed for each section, for a total of six, and will count for 25% of your course grade. Class participation will also be considered in cases of borderline grades.

Plagiarism will not be tolerated!!! Copying from a famous source (e.g. Nobel Prize winner) is not being deferential and respectful it is intellectual theft! If you use other people's ideas make sure you describe the concepts IN YOUR OWN WORDS, and that you properly cite your sources! Please don't insult your professors by assuming that they don't know enough to be able to spot plagiarism! If caught plagiarizing, you will fail the class and be subject to disciplinary action that could include dismissal from the university. Please see the definitions below, and if you have any further questions ask your instructors.

"Plagiarism is using others' ideas and words without clearly acknowledging the source of that information."

http://www.lib.uconn.edu/using/tutorials/LILT/plagiarism.htm

Readings:

To save students money, we decided to go without a textbook this year. However, there are selected readings listed from a wonderful on-line text:

Protein Structure and Function
By Gregory A Petsko and Dagmar Ringe
http://www.new-science-press.com/browse/protein

Selected readings from this site are shown in red e.g. [**1-5**] means chapter 1, section 5.

In addition, we compiled a list of background papers that we feel are appropriate introductions to the topics described in the lectures. Another motivation for doing this is that real scientists read research papers and reviews, not textbooks. You should develop the skills to read the scientific literature at this stage. The articles will be placed on electronic reserve in HuskyCT. You are expected to read the assigned papers! Additional material for the class may include handouts from other papers and books. If you receive a handout you ARE expected to read it! We will include our slides for all the lectures on HuskyCT. All in all this is a lot of information, and you will have to invest time to do the background reading, to get as much as possible out of the lectures. Most of the exams in this class are essay questions that test how much you know about a subject. When we grade the questions we look at how eruditely you can discuss the subject. The more you read, the more you'll know.

1. Perutz, M. (1964). The hemoglobin molecule. *Sci. Amer 211*: 64-76.
2. Anfinsen, C.B. (1973). Principles that govern the folding of protein chains. *Science 211*: 64-76.
3. Eisenberg, D. (2003). The discovery of the a-helix and b-sheet, the principal structural features of proteins. *Proc. Natl. Acad. Sci. 100*: 11207-11210.
4. Baldwin, R.L. & Rose, G.D. (1999). Is protein folding hierarchic? I. Local structure and peptide folding. *TIBS 24*: 26-33.
5. Murzin, A.G. (1993). OB(oligonucleotide/oligosaccharide binding)-fold: common structural and functional solution for non-homologous sequences. *EMBO J. 12*: 861-7.

6. Lupas, A. (1996). Coiled coils: new structures and new functions. *Trends Biochem. Sci. 21*: 375-382.
7. Chothia C & Lesk AM (1987) The Evolution of Protein Structures. *Cold Spring Harb. Symp. Quant. Biol. 52:* 399-405.
8. Orengo, C., Jones, D.T. & Thornton, J.M. (1994) Protein superfamilies and domain superfolds. *Nature 372:* 631-634.
9. Goodsell, D.S. & Olson, A, J. (2000) Structural symmetry and protein function. *Annu. Rev. Biophys. Biomol. Struct. 29:* 105-153.
10. Ali, M.H & Imperiali, B. (2005) Protein oligomerization: how and why. *Bioorganic & medicinal Chem. 13:* 5013-5020.
11. Cohen, F.E. & Kelly, J.W. (2003). Therapeutic approaches to protein-misfolding diseases. *Nature 426*: 905-909.
12. Karplus, M. & McCammon, J.A. (2002). Molecular dynamics simulations of biomolecules. *Nature Struct. Biol. 9*: 646-652.
13. Wüthrich, K (2003). NMR studies of structure and function of biological macromolecules. *Angew. Chem. Int. Ed. 42*: 3340-3363.
14. Kuhlman, B., Dantas, G., Ireton, G.C., Variani, G., Stoddard, B.L., & baker, D. (2003). Design of a novel globular protein fold with atomic-level accuracy. Science 302: 1364-1368.
15. Baumeister, W & Steven, A.C. (2000). Macromolecular electron microscopy in the era of structural genomics. *TIBS 25*: 624-631.
16. Chayen, N. E., and Saridakis, E. (2008) Protein crystallization: from purified protein to diffraction-quality crystals. *Nat. Methods* 5:147-153.
17. Wlodawer, A., Minor, W., Dauter, Z. and Jaskolski, M. (2008) Protein crystallography for non-crystallographers, or how to get the best (but not more) from published macromolecular structures. *FEBS J.* 275(1):1-21.
18. Steitz, T.A. (2008) A structural understanding of the dynamic ribosome machine. *Nat. Rev. Mol. Cell Biol.* 9:242-53.
19. Bashan, A. and Yonath, A. (2008) Correlating ribosome function with high-resolution structures. *Trends in Micro.* 16:325-335.
20. Driessen, A.J. and Nouwen, N. (2008) Protein translocation across the bacterial cytoplasmic membrane. *Ann. Rev. Biochem.* 77:643-67.
21. Petsko and Ringe (2008) Protein Structure and Function. Chapter 3. http://www.new-science-press.com/browse/protein
22. Witze, E.S., Old, W.M., Resing, K.A. and Ahn, N.G. (2007) Mapping protein post-translational modifications with mass spectrometry. *Nat. Methods* 4:798-806.
23. Robinson, V.L., Buckler, D.R. and Stock, A.M. (2000) A tale of two components: a novel kinase and a regulatory switch. *Nat. Struct. Biol.* 7:626-33.
24. Vetter, I.R. and Wittinghofer, A. The guanine nucleotide-binding switch in three dimensions. (2001) *Science* 294:1299-304.
25. Bos, J.L., Rehmann, H. and Wittinghofer, A. (2007) GEFs and GAPs: critical elements in the control of small G proteins. *Cell* 129:865-77.
26. Hunter T. (2007) The age of crosstalk: phosphorylation, ubiquitination, and beyond. *Mol Cell*. 28:730-8.