

CHEMISTRY 491: Special Topics in Biochemistry – Membrane Proteins in Health and Disease

Term: Spring, 2007
Prerequisites: CHEM 351 (or equivalent)
Class time: 1.00 p.m. - 3.45 p.m. Mondays
Class location: UNIV 271
Instructor: S. Jayasinghe (Jay), Ph.D.
Inst. Office: Sci II, 229
Inst. Office hours: Mondays and Wednesdays from 10:00 a.m. to 11:30 a.m. or by appointment
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Course Objective: In this course we will discuss the principles that govern the structure and function of membrane proteins. Students will be introduced to the different classes of membrane proteins using examples that play important roles in human health and disease. Concepts of membrane protein structure and function will be investigated while learning how to manipulate three-dimensional structure models using computer software.

Student Learning Outcomes:

Upon completion of this course students should:

- (1). Be able to describe the difference between soluble and membrane proteins, be able to describe the importance of membrane proteins in health and disease, and be able to describe important structural and sequence features of membrane proteins.
- (2). Be able to identify the various classes of membrane proteins, and be able to describe the differences between them.
- (3). Be able to use the Protein Data Bank (PDB) to retrieve coordinate files of proteins whose 3D structures are known.
- (4). Be able to use software (Visual Molecular Dynamics, VMD) to manipulate and visualize 3D protein structures.

Textbook: No required textbook. We will refer to 'Biochemistry' by Garrett and Grisham as the need arises (especially in the introductory/review sections).

Readings: Course discussion will focus on relevant articles from the literature and on relevant chapters from 'Biochemistry' by Garrett and Grisham.

Topic Schedule: **1/22/07** **Introduction to the course**

Introduction to the Protein Data Bank (PDB)
Introduction to Visual Molecular Dynamics (VMD)

Readings:
(1). 'VMD Molecular Graphics' – by the University of Illinois at Urbana Champaign
(2). 'Visualizing Molecules with VMD' – by Christoph Weber.

(3). 'A short guide to the Visualization of Membrane Protein systems using Visual Molecular Dynamics (VMD) – by Alfredo Freites.

1/29/07

Review of protein structure and protein folding

Readings:

(1). Chapter 4 (4.1, 4.2); Chapter 5 (5.1, 5.2, 5.8, 5.9); Chapter 6 (6.1, 6.2, 6.3, 6.4) of Garrett and Grisham.

(2). Dobson, C.M., The structural basis of protein folding and its link to human disease, *Philos. Trans. R. Soc. Lond. B. Biol. Sci.*, **356**(1406), 133-145.

2/05/07

Review of lipids and lipid membranes

Readings:

(1). Chapter 8 (8.1, 8.2, 8.3, 8.4); Chapter 9 (9.1) of Garrett and Grisham.

(2). Vereb, G., *et.al.*, Dynamic, yet structured: The cell membrane three decades after the Singer-Nicolson model, *PNAS*, 100(14), 8053-8058.

2/12/07

**Classification of membrane proteins
The folding of membrane proteins**

Readings:

(1). Chapter 9 (9.2) of Garrett and Grisham.

(2). White, S.H., and von Heijine, G., The machinery of membrane protein assembly, *Curr. Opin. Struct. Biol.*, **14**, 397-404.

(3). White, S.H., *et.al.*, How Membranes Shape Protein Structure, *JBC*, **276**(35), 32395-32398.

(4). White, S.H., Translocons, thermodynamics, and the folding of membrane proteins, *FEBS Lett.*, **555**, 116-121.

2/19/07

**Membrane Proteins of Known Structure
Identification of Membrane proteins**

Readings:

(1). Jayasinghe, S., Hristova, K., and White, S.H., Mptopo: A database of membrane protein topology, *Prot. Sci.*, **10**, 455-458.

(2). http://blanco.biomol.uci.edu/Membrane_Proteins_xtal.html

2/26/07

Ion Channels and Pumps

Readings:

(1). Dworakowska, B., and Dolowy, K., Ion Channels-related diseases, *Acta Biochimica Polonica*, **47**(3), 685-703.

(2). Yu, F.H., Yarov-Yarovoy, V., Gutman, G.A., and Catterall, W.A., Overview of Molecular Relationships in the Voltage-Gated Ion Channel Superfamily, *Pharmacol. Rev.*, **57**(4), 387-395.

(3). MacKinnon, R., Potassium Channels, *FEBS Letters*, **555**, 62-65.

3/05/07 Ion Channels and Pumps Cont...

Readings:

(1). Yu, F.H., and catterall, W.A., Overview of the voltage-gated sodium channel family, *Genome Biology*, **4**(3), 207.

(2). Jentsch, T.J., Maritzen, T., and Zdebik, A.A., Chloride channel diseases resulting from impaired transepithelial transport or vesicular function, *J. Clin. Invest.*, **115**(8), 2039-2046.

3/12/07 Other Channels

BtuB: the Cobalamine Transporter

Readings:

(1). Agre, P., The Aquaporin Water Channels, *Proc. Am. Thorac. Soc.*, **3**(1), 5-13.

(2). Yasui, M., Molecular Mechanisms and Drug Development in Aquaporin Water Channel Diseases: Structure and Function of Aquaporins, *J. Pharmacol. Sci.*, **96**, 260-263.

(3). Chimento, D.P., Mohanty, A.k., Kadner, R.J., Wiener, M.C., Substrate-induced transmembrane signaling in the cobalamin transporter BtuB, *Nat. Struct. Biol.*, **10**(5), 394-401.

3/19/07 G-Protein Coupled Receptors

Readings:

(1). Ballesteros, J., and Palczewski, K., G protein-coupled receptor drug discovery: Implications from the crystal structure of rhodopsin, *Curr. Opin. Drug Discov. Devel.*, **4**(5), 561-574.

(2). Rhodopsin: Strcutural basis of molecular physiology, *Physiol. Rev.*, **81**(4), 1659-1688.

3/26/07 No Class – Spring Break

4/02/07 Peripheral membrane Proteins

Readings:

(1). Overduin, M., Cheever, M.L., and Kutateladze, T.G., Signaling with phosphoinositides: better than binary, *Mol. Interv.*, **1**(3), 150-159.

(2). Prestwich, G.D., Phosphoinositide signaling: From Affinity Probes to Pharmaceutical Targets, *Chemistry & Biology*, **11**, 619-637.

(3). Legendre-Guillemin, V., Wasiak, S., Hussain, N.K., Angers, A., McPherson, P.S., ENTH/ANTH proteins and clathrin-mediated membrane budding, *J. Cell Sci.*, **117**(Pt 1), 9-18.

4/09/07 Toxins

Reading:

(1). Montoya, M., and Gouaux, E., β -Barrel membrane protein folding and structure viewed through the lens of α -hemolysin, *Biochim. Biophys. Acta*, **1609**, 19-27.

4/16/07 Diseases of Protein Misfolding (Alzheimer's, Type II Diabetes): Implications of polypeptide membrane interactions.

Reading:

(1). Kaye, R., et.al., Permeabilization of lipid bilayers is a common conformation-dependent activity of soluble amyloid oligomers in protein misfolding diseases, *J. Biol. Chem.*, **279**(45), 46363-46366.

4/23/07

4/30/07

5/07/07 Last day of Class: Projects Due

Course web site: www.csusm.edu/jayasinghe/Classes/CHEM491/CHEM491.html

In Class presentations: Working in groups, students will lead class discussion on the following topics: Ion, and other, channels, G-protein coupled receptors, peripheral membrane proteins, toxins, and diseases of protein misfolding.

Students will be responsible for reading the assigned reports (see above), summarizing the information, and presenting this information to the class. Students are encouraged to read and integrate additional information from the primary literature as needed. Student presentations should (at least) include the following information:

Importance of the particular class of membrane protein (to human health) – Background information

Current understanding of the structural details of members of the class of membrane protein – Are 3D structures available? How were they obtained? Number of TM segments, Helical?

Structural features that play critical roles in the function of the class of membrane protein – Critical residues, in the case of channels selectivity filters etc.

All members of a team must participate in the presentation.

Semester Project: Working in groups students will develop a website detailing the structural aspects of a membrane protein with known 3D structure. Your web page should be an informative resource on your selected membrane protein.

Your webpage **must** include images that you generated using VMD to illustrate the important structural information on your selected protein.

In developing your webpage use the following site as a guide:
http://www.rcsb.org/pdb/static.do?p=education_discussion/molecule_of_the_month/index.html

Your websites should be 'clean' (as in the examples in the above website, white backgrounds are best) and should not contain elements (such as animations etc.) that distract from the scientific information.

Consider the website to be an online version of a written paper.

Final websites are due on the last day of class.

Grading (points):	Attendance and class participation	50
	In class presentations	100
	Final project	150

Writing Requirement: The University Writing Requirement will be satisfied upon successful completion of the semester project.

Students with Disabilities: Students with disabilities who require accommodation must be approved by the Office of Disabled Student Services (DSS). Please contact this office as soon as possible and should meet with the instructor during office hours (or at some other mutually agreeable time). The DSS office is located in Craven hall 5205. Their telephone number is (760) 750-4905 or TTY (760) 750-4909.

Academic Honesty: All students are expected to maintain academic honesty. **All submitted work must be your own and must be written in your own words.**

All students should be familiar with the university policies and procedures concerning academic honesty as detailed in the university catalog. An online version of these policies and procedures can also be found at:
http://lynx.csusm.edu/policies/procedure_online.asp?ID=187