BIOL 647 – **Structure-Function of Membrane Proteins**
Syllabus, Spring, 2016

I. Lipid Environment of Membrane Proteins.

General properties of biological membranes; physical-chemical and biological hydrophobicity scales; hydrophobic mismatch. bacterial vs. eukaryotic membranes.

Biomedical Applications: lipid-related diseases, cardiolipin, Barth's disease; lipid rafts; cholesterol/amyloid rafts.

Lipid phase transitions; lipid fluidity; lipid, protein diffusion; measurement by spectroscopy (e. g., epr, fluorescence).

Lipid-mediated lateral pressure in membranes.

Detergent mimics of lipids

Nanodiscs;

II. General Architecture of Membrane Proteins

α-helical and β-barrel (gram-negative bacterial outer membrane) structures; the OM BAM complex

Intra-protein lipids.

Membrane protein topology; rules for topology, the *cis*-positive rule; dependence of topology on lipid (e. g., PE).

III. Structure Determination

Properties of detergents; extraction and purification of integral membrane proteins; the detergent problem.

Crystallization: (i) use of antibodies to improve crystallization; (ii) in detergent; (iii) lipid cubic phase; (iv) bicelles.

Femtosecond cruystallography: "diffraction before destruction"

Cryo- Electron Microscopy.

Mass spectroscopy; lipid-protein interactions.

IV. Biogenesis

Sec-dependent and Sec-independent processes; protein insertion; the translocon;

Folding of outer membrane proteins.

V. Membrane Proteins; Structure and Function:

First crystallized membrane proteins: bacteriorhodopsin in 2-D, porin and photosynthetic reaction center (PRC) in 3-D; major structure motifs, β-barrel (gram-negative bacterial Omps), α-helical; hetero-oligomeric complexes.

A) β-barrel bacterial Omps; OmpF, nutrient receptors; LamB; Fe siderophores, Tol, Ton proteins; parasitization of nutrient receptors by phages and colicins;

Biomedical applications: Neisseria; Yersinia; Folate receptor as a drug target; NMDA receptor in the brain.

(**B**) α-Helical Proteins. Biomedical applications, GPCR proteins; drug action; mechanism of action of caffeine, the circadian clock – GPCR adenosine receptor; chemokine receptor-cancer.

C) Energy transduction, respiratory, photosynthetic hetero-oligomeric membrane protein electron transport complexes; H^+-, Na^+-ATPase, ATP synthase.

D) Active transport; symporters and anti-porters; lactose symporter, sodium-proton antiporter; ABC transporters; bacterial homologues of eukaryotic proteins; the glutamate transporter; cystic fibrosis trans-membrane regulator (CFTR); concept of “alternating access.”

E) Ion channels; water (aquaporin); the potassium channel K^+; Biomedical application: influenza virus M2 channel.