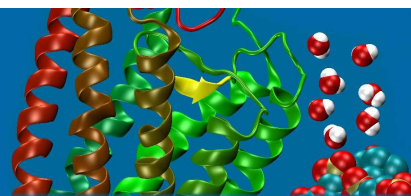


# Structural Biology of Membrane Proteins



## KICK-OFF MEETING PROGRAMME Toulouse, France - September 18<sup>th</sup>-20<sup>th</sup> 2008

### **Observing membrane proteins in water and ice** – Andreas Engel, University of Basel, Switzerland

Biological membranes composed of proteins and lipids delineate cells and their compartments, and provide vital cellular functions. Electron microscopy (EM) has made it possible to assemble the biochemical and atomic scale structural information from X-ray crystallography into a meaningful model of the biological membrane and to place it in a cellular context. Cryo-EM is used to acquire high-resolution structural information from two-dimensional (2D) crystals of membrane proteins embedded in a lipid bilayer, and of single protein complexes embedded in a vitrified layer of buffer solution. Small cells can be vitrified as well, and their 3D structure is elucidated to a resolution of a few nm by electron tomography. While EM produces projections of vitrified samples from which their 3D structure can be computationally reconstructed, the atomic force microscope (AFM) depicts the 3D surface topography of native biological membranes directly in buffer solutions. The atomic structure of different aquaporins, and the surface topography of bacteriorhodopsin, the disc membrane of rod outer segments, as well as photosynthetic membranes demonstrate the power of these microscopy methods and their advances in the observation of membrane proteins.

### **Membrane proteins at Sanofi-Aventis** – Vincent Mikol

**Structure/function studies of Mitochondrial carriers and GPCRs** – Eva Pebay-Peyroula, Institut de Biologie Structurale, Grenoble

**Structural investigations on porins and ABC-transporters by solid-state NMR** – Hartmut Oschkinat, Forschungsverbund Berlin e.V, Germany

**Molecular dynamics simulations of rhodopsin and other GPCRs. Mechanical unfolding and mechanisms of activation** – Slawomir Filipek, International Institute of Molecular and Cell Biology, Poland

**Imaging and sensing native membrane proteins** – Daniel Mueller, University of Technology, Germany

**pH-Dependent Transmembrane Peptide Insertion: Mechanism and Uses** – Donald Engelman, Yale University

**News surfactants for the biochemistry of membrane proteins** – Cécile Breyton, Institute of Physical Chemical Biology, France

We are developing new surfactants for the biochemistry of membrane protéines: in one case, the original idea was to modify classical detergents so as to make them non-intrusive, and their micelles poor solvents for lipids and hydrophobic cofactors. This lead to the conception of fluorinated surfactants. In the second case, that of amphipols, the initial predicament was to get rid of micelles altogether, devising molecules having such a high affinity for the surface of the protein that they would never dissociate. In both cases, the concept has been validated, and we will present applications for which these new surfactants can be particularly useful.

**Biophysical characterization of lipid-protein and drug-membrane receptor interactions** – John Baenziger, University of Ottawa, Canada

We are interested in characterizing the mechanisms of membrane protein function with a focus on a number of targets including a neurotransmitter receptor, the muscle-type nicotinic acetylcholine receptor (nAChR). For the latter, we are particularly interested in defining the mechanisms by which lipids modulate nAChR function and to eventually understand the role of lipid-protein interactions in neurotransmitter receptor function *in vivo*. We use a variety of biophysical tools, including protein crystallization, fluorescence, solid-state NMR,

dynamic light scattering, and FTIR spectroscopy, to probe both membrane and membrane protein structure and conformational change. We have developed a novel FTIR *difference* approach that allows one to monitor subtle changes in the vibrations and thus structures of the nAChR and other membrane proteins upon ligand binding. The technology has been used to characterize the nature of receptor-ligand interactions and can do so at a residue-specific level. We discuss the nature of the approaches utilized to study membrane protein function in light of recent advances in the 3D structural characterization of integral membrane proteins.

**Applications of cell-free expression systems for the production of membrane proteins** – Frank Bernhard, J.W. Goethe-University, Germany

To be announced – Przemyslaw Nogly, Margarida Archer's applicant, Universidade Nova de Lisboa, Portugal

**NMR structure determination of kpOmpA** – Alain Milon, Centre National de la Recherche Scientifique, France

**Novel technologies for investigating membrane proteins** – Horst Vogel, Ecole polytechnique fédérale de Lausanne, Switzerland

**Gating of a K(+) channel studied by solid-state NMR spectroscopy** – Christian Ader, Utrecht University, The Netherlands

We have studied structure and function of the chimeric ion channel KcsA-Kv1.3 in lipid bilayers by solid-state NMR (ssNMR) spectroscopy. We discuss structural changes of this protein associated with pH induced gating based on water-edited ssNMR spectroscopy and high-resolution dipolar correlation spectroscopy. Our results provide structural insight into potassium channel activation and inactivation gating on a global and local scale.

**Molecular dynamics simulations of rhodopsin and other GPCRs. Mechanical unfolding and mechanisms of activation** – Valentin Gordeliy, Institute of Structural Biology, Grenoble

A general overview of our current activity in the field of membrane protein crystallization and high resolution structures will be given. Two specific projects: on molecular mechanism of signal transduction and ion transport will be discussed in more details. One of the goals of this presentation is to establish cooperation's with other participants of ITN SBMPs in the field under discussion.