of charged groups plays a role in modulating the selectivity of the pore for either anions or protons. To elucidate the molecular mechanism of permeation and selectivity, we are conducting free energy simulations for the translocation of protons and other ions in both wild-type and mutant forms of hHv1.

2191-Plat
Regulation of CatSper Channel through Non-Conventional Lipid Signaling
Melissa R. Miller[1,2], Yuriy Kirichok[2], Polina Lishko[1].
[1]University of California, Berkeley, Berkeley, CA, USA, [2]Department of Physiology, University of California, San Francisco, San Francisco, CA, USA.
The sperm-specific cation channel, CatSper, regulates intracellular calcium levels and is crucial for male fertility, both in mice and humans. CatSper triggers hyperactivation, a type of inducible motility that enables sperm to penetrate the egg's protective vestments. For this motility change, human CatSper requires elevation of intracellular pH with simultaneous extracellular stimulation by progesterone which sperm encounter during their journey to the oocyte. In the absence of these stimuli, CatSper retains some basal activity which can be reversibly inhibited by mild lipid extraction. Here we report that basal CatSper activity, as recorded using whole-cell patch clamp technique from mature human spermatozoa, requires a lipid signaling molecule produced within the sperm plasma membrane. Furthermore, treatment with the female hormone progesterone up-regulates the production of this lipophilic signal. Development of a novel lipid extraction technique has provided a method for concentration, isolation, and identification of this lipid signaling molecule providing a better understanding of the lipidic pathways regulating male fertility in humans.

Symposium: Awards Symposium

2192-Symp
Phases and Fluctuations in Biological Membranes
Sarah Veatch.
University of Michigan, Ann Arbor, MI, USA.
The thermodynamic properties of plasma membrane lipids play a vital role in many functions that initiate at the mammalian cell surface. Some functions are thought to occur, at least in part, because plasma membrane lipids have a tendency to separate into two distinct liquid phases, called liquid-ordered and liquid-disordered. We propose that at least some of aspects of lipid mediated functions occur because plasma membrane composition is tuned close to a critical point at physiological temperature. This hypothesis is supported by our observations of micron-sized and dynamic critical fluctuations in isolated plasma membranes near their critical temperature of roughly room temperature. In this talk, I will discuss our ongoing efforts to probe for consequences of criticality in the plasma membranes of intact cells.

2193-Symp
Structural and Mechanistic Diversity of ABC Transporters
Douglas C. Rees.
Chemistry, California Institute of Technology/HHMI, Pasadena, CA, USA.
ATP Binding Cassette (ABC) transporters constitute a ubiquitous superfamily of integral membrane proteins responsible for the ATP powered membrane translocation of a wide variety of substrates. The highly conserved ABC domains defining the superfamily provide the nucleotide-powered engine that drives transport. In contrast, the transmembrane domains creating the translocation pathway are more variable, with three distinct folds currently recognized. Structural analyses of the high affinity methionine MetNI importer and of a bacterial homologue of the mitochondrial Atm1 exporter will be discussed within the mechanistic framework of the alternating access model. The interconversion of outward and inward facing conformations of the translocation pathway is coupled to the switching between open and closed interfaces of the ABC subunits that are associated with distinct nucleotide states. As observed for MetNI, additional domains may be present that can regulate transport activity. Building on this qualitative molecular framework for deciphering the transport cycle, an important goal is to develop quantitative models that detail the kinetic and molecular mechanisms by which ABC transporters utilize the binding and hydrolysis of ATP to power substrate translocation.

2194-Symp
Role of Membrane Lipids in Activating G-Protein-Coupled Receptors
Michael F. Brown[1,2], Udeep Chawla[1], Suchithranga M.D.C. Perera[1], Andrey V. Struts[1].
[1]Department of Chemistry and Biochemistry, University of Arizona, Tucson, AZ, USA, [2]Department of Physics, University of Arizona, Tucson, AZ, USA.
The role of lipid-protein interactions in membrane function has long attracted the attention of researchers in the field of lipid membrane biophysics. Effects of membrane lipids on G-protein-coupled receptors (GPCRs) are revealed by UV-visible and FTIR spectroscopic studies of the conformational energetics of rhodopsin in visual signaling [1]. During rhodopsin photoactivation, the photoreactive 11-*cis*-retinylidene chromophore is isomerized to all-*trans* yielding an equilibrium between inactive Meta-I and active Meta-II states. Modulation of the metarhodopsin equilibrium depends on the polar head groups and the lipid acyl chain length and polyunsaturation. Membrane lipids can forward or backshift the metarhodopsin equilibrium due to their chemically non-specific material properties [2]. A flexible surface model (FSM) describes elastic coupling of membrane lipids to the conformational energetics of rhodopsin. The new biomembrane model challenges the standard fluid mosaic model. Based on data first introduced for rhodopsin [2] the idea of a curvature stress field bridges theory and experiment. According to the FSM, membrane lipids whose spontaneous curvature stabilizes the activated state within the membrane are involved in regulating protein function. The new biomembrane model explains the effects of bilayer thickness, nonlamellar-forming lipids, detergents, and osmotic stress on visual signaling. An ensemble-mediated activation mechanism is proposed for rhodopsin in a natural membrane lipid environment, which includes a role for bulk water in the activation of rhodopsin-like GPCRs [4]. Ion channels, transporters, and membrane-bound peptides can all be affected by curvature forces due to elastic deformation of the bilayer, thus giving a new paradigm for membrane lipid-protein interactions in structural biology.
[1] M.F. Brown (2012) *Meth. Mol. Biol.***914**, 127-153.
[2] M.F. Brown (1997) *Curr. Top. Membr.***44**, 285-356.
[3] M.F. Brown (2012) *Biochemistry***51**, 9782-9795.
[4] A.V. Struts (2011) *PNAS* **108**, 8263-8268.

2195-Symp
Deconstructing the Physical and Molecular Basis of Touch and Pain Sensation
Miriam B. Goodman.
Molecular and Cellular Physiology, Stanford University, Stanford, CA, USA.
Touch is the first sense to develop and the last to fade. To investigate the molecular and physical basis of this crucial sensory modality, we exploit the nematode C. elegans and in vivo cellular physiology.

Platform: Optical Microscopy and Super Resolution Imaging II

2196-Plat
Watching Gene Regulation by Small RNA in Bacteria with Super-Resolution Imaging
Jingyi Fei[1], Digvijay Singh[2], Qiucen Zhang[1], Seongjin Park[1], Ido Golding[1,3], Carin K. Vanderpool[4], Taekjip Ha[5,6].
[1]Department of Physics, Center for the Physics of Living Cells, University of Illinois, Urbana, IL, USA, [2]Center for Biophysics and Computational Biology, University of Illinois, Urbana, IL, USA, [3]Baylor College of Medicine, Houston, TX, USA, [4]Department of Microbiology, University of Illinois, Urbana, IL, USA, [5]University of Illinois, Urbana, IL, USA, [6]Howard Hughes Medical Institute, Urbana, IL, USA.
Small RNAs play important roles in regulating gene expression. Here we describe a new approach for characterization and quantification of small regulatory RNAs as well as targeting mRNA at single-cell level by combining single-molecule in situ hybridization and super-resolution imaging. We apply this approach to investigate a stress-induced bacterial small RNA, which is the central regulatory effector of the glucose-phosphate stress response. The quantitative analysis and localization information allow us to establish a kinetic model to describe the sRNA-induced target mRNA degradation in the cell. More importantly, our results demonstrate very promising application of this technique in studying other bacterial small RNA systems, and potentially microRNAs in eukaryotes.

2197-Plat
The Topological Organization of the Inactive X Chromosome in its Native State
Elizabeth A. Smith[1], Gerry McDermott[1], Karen Leung[2], Barbara Panning[2], Carolyn A. Larabell[1], Mark A. Le Gros[1].
[1]Anatomy, UCSF, San Francisco, CA, USA, [2]Biochemistry and Biophysics, UCSF, San Francisco, CA, USA.
The three-dimensional topology and compaction profile of an individual chromosome likely influences the expression of its genes. We present the first high-resolution description of the structure of an individual chromosome, the inactive X chromosome (Xi), in its native state. Female mouse pre-B cells were vitrified and then imaged using a pair of emerging imaging techniques, cryogenic confocal fluorescence tomography and soft x-ray tomography