nanodomains can form and exhibit coupling between inner and outer leaflets ordered domains. Methods to prepare a wider range of asymmetric membrane compositions and make more facile asymmetry measurements are being developed. In addition, cyclodextrin-catalyzed lipid exchange is being extended to studies of membrane domain structure and function in living cells. Substituting for cholesterol shows the subset of sterols having the ability to support the formation of lipid rafts are necessary and sufficient for them to support membrane domain formation in *Borrelia burgdorferi,* a bacteriumcontaining fatty acyl cholesterol glycosides.Interestingly,we find fatty acyl cholesterol glycosides are able to form ordered membrane domains without sphingolipids. Studies with cyclodextrin-catalyzed sterol exchange in mammalian cells show that sterols having an ability to promote the formation of ordered membrane domains are necessary and sufficient for them to support both clathrin-dependent and independent endocytosis provided they also contain a 3-beta OH. Efforts to carry out similar experiments with phospholipid and sphingolipid exchange are underway.

1691-Symp
The Biophysics of Living Membranes: Protein Partitioning and Functional Differentiation in Ordered Plasma Membrane Domains
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The lipid raft hypothesis posits that ordered, lateral membrane domains are important for the regulation of plasma membrane (PM) structure and function in eukaryotes. Giant Plasma Membrane Vesicles (GPMVs) are isolated plasma membranes that microscopically separate into coexisting ordered and disordered phases, facilitating experimental analysis of the composition and physical properties of ordered raft domains in biological membranes. In these studies, we analyze the biophysical and lipidomic differentiation of the plasma membrane in Mesenchymal Stem Cells (MSC) as the cells undergo differentiation into adipocytes and osteoblasts. During differentiation, dramatic remodeling the PM lipidome, including lipid acyl chain length and unsaturation, results inchanges to membrane order and phase separation. These observations elucidate the compositional determinants of biophysical properties in biological membranes, as well as identify lineage-specific PM features. These results facilitate rational remodeling of membrane phenotypes to direct differentiation, as supplementation with -3 docosahexaneoic acid (DHA) promoted the osteoblastic PM phenotype and potentiated osteogenic differentiation. The differences in the physical properties of the coexisting domains lead to preferential protein partitioning between them. We evaluate the structural determinants of raft partitioning of a model transmembrane protein, and find that raft phase partitioning is related to features of the protein's transmembrane domain (TMD), namely the hydrophobic length and surface area of the TMD. Longer TMDs impart greater raft association while TMDs with larger, bulkier amino acid side chains prefer the non-raft phase. We present a simple physical model wherein raft partitioning is driven by phase-dependent differences in interfacial energy between the TMD and its surrounding lipid matrix, and find excellent quantitative agreement with observations that provide the first predictions of protein-lipid surface tension. These results point the way to a general rule for raft partitioning of transmembrane proteins.

Platform: Voltage-gated K Channels, Mechanisms of Voltage Sensing and Gating II

1692-Plat
Molecular Dynamics Simulations of Hydrophobic Matching in KcsA
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Ion channels are regulated by many factors, including their interactions with lipids. While some lipid-protein interactions may be specific, acting as a ligand, membranes can also influence protein activity through their physiochemical properties, including hydrophobic thickness. Certain conformations of proteins can be preferentially stabilized or destabilized in a membrane-dependent fashion through matching of hydrophobic and hydrophilic portions of the surfaces of the protein and the membrane. Here, we examine atomic-scale molecular dynamics simulations of WT and E71A KcsA in heterogenous membranes of phosphatidylcholine and phosphatidylglycerol lipids of differing thickness supported by our experimental studies of electrophysiological activity and small angle X-ray scattering (SAXS).

1693-Plat
Insights into Ion Channel Selectivity with Ionic Coulomb Blockade
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The flow of ions through a biological ion channel can be considered as transitions between occupied energy levels in the channel and either of the connecting bulk reservoirs [2]. Discreteness of ions and an electrostatic exclusion principle ensure that the number of channel energy levels equals the number of occupying ions. Using these fundamental physical principles we have recently introduced [1] an ionic Coulomb blockade (ICB) theory developed by analogy with the similar phenomenon of electron tunnelling in quantum dots [2,3]. In this picture channel selectivity is governed by energy level changes [1].
We present details of the ICB theory for ion transitions through the channel. It incorporates physiological solutions and channel properties: physical dimension, voltage drop and fixed charge, and hence allows for comparison with physiological data. The set of kinetic equations obtained using ICB is analysed. The channel probability of occupancy as a function of transition rates (and hence fixed charge and number of ions) is obtained in the steady-state approximation. It is shown that this probability displays the staircase structure familiar from analysis of occupancy in quantum dots. It is also shown that current through the channel displays sharp peaks as a function of fixed charge, hence relating channel selectivity to the structure and position of energy levels.
The contribution of hydration energy is also discussed. We anticipate that inclusion of this energy into ICB theory will provide an important insight into the selectivity and conductivity of ion channels.
[1] Kaufman, I. K., McClintock, P. V. E., Eisenberg, R. S., New Journal of Physics. 17, 8, 15 (2015).
[2] Beenakker, C.W.J., Phys. Rev. B., 44, 4, (1991).
[3] Krems, M., Di Ventra, M., Phys. Condens. Matter, 25, 6, 065101 (2013).

1694-Plat
Ionic Basis of Repolarization of Atrial and Ventricular Specific Cell Types Derived from Human Induced Pluripotent Stem Cells
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Cardiomyocytes derived from human induced pluripotent stem cells (hIPSC-CMs) are an innovative cellular system for understanding human cardiac pathology and physiology. However, hIPSC-CMs express low levels of inward rectifying potassium channel (IK1) relative to native cardiac cells. The lack of this current deforms the action potential (AP) and leads to a depolarized or spontaneous diastolic potential. We used electronic expression of IK1 via dynamic clamp to restore the resting membrane potential back to physiological levels. This resulted in an improved AP morphology, including a reduction in variability and a rate dependent spike and dome shape. There were several significant differences between atrial and ventricular cells including differences in cell capacitance, sodium current magnitude and kinetics and most prominently differences in the transient outward currents. The late components of outward current, cells with atrial APs had a significantly larger sustained outward IKUR or Kv1.5-like component at +50 mV than ventricular shaped APs (in pA/pF: 3.71 $\pm$ 0.55 (n=5) vs 1.00 $\pm$ 0.10 (n=16),$P<0.05$) but similar peak outward currents: (6.89 $\pm$ 0.50 (n=5) vs. 6.58 $\pm$ 0 .67 (n=14),P=N.S). This plateau current is strongly inhibited by 50 micro molar 4-aminopyridine(4-AP). Similarly, atrial-like APs took on a ventricular like shape when treated with 4-AP while the ventricular myocytes APs were 4-AP insensitive. A cloned Kv1.5 current was expressed in oocytes and was used through the electronic expression system to add an IKur to the ventricular myocytes. Addition of this current changed the action potential morphology from ventricle to atrial like. This strongly suggests that IKur is the major determinant of atrial action potential morphology.

1695-Plat
Shaker-IR K Channel Gating in Heavy Water: Role of Structural Water Molecules in Inactivation
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It has been reported earlier that the slow (C-type) inactivated conformation in eukaryotic K_V channels is stabilized by a multipoint hydrogen-bond network