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Myelin Structural Integrity in a Model for Human Early-Onset CMT1B
Michelle Crowther[1], Brian Shy[2], Adrienne M. Luoma[1], Lawrence Wrabetz[3], Michael E. Shy[2], Daniel A. Kirschner[1].
[1]Boston College, Chestnut Hill, MA, USA, [2]Wayne State University School of Medicine, Detroit, MI, USA, [3]San Raffaele Hospital, Milano, Italy.
Charcot-Marie-Tooth disease type 1B (CMT1B), a peripheral neuropathy, is caused by mutations in MPZ, the gene encoding protein zero (P0), the major integral protein of PNS myelin. An adhesive protein, P0 plays a significant role during elaboration and maintenance of multilamellar myelin. P0 mutation Arg69Cys (R69C) causes a severe early-onset form of CMT1B. To elucidate the pathogenesis of this neuropathy, an Arg69Cys knock-in mouse was generated by targeting the Arg69Cys mutation to one MPZ allele by homologous recombination in ES cells. Here we report our x-ray diffraction (XRD) measurements on the periodicity, membrane structure, and amount of myelin in unfixed, freshly-dissected nerves from wildtype (WT or +/+), heterozygous (R69C/+), and homozygous (R69C/ R69C) mice. CNS myelin (optic nerve) was also examined. The diffraction patterns showed decreasing strength of scattering intensity from myelin: WT > R69C/+ > R69C/R69C, indicating decreasing relative amounts of myelin. By contrast, optic nerves exhibited no such differences among genotypes. From the positions of the reflections the myelin periods of sciatic but not optic nerves were found to differ among the genotypes: 177.0 ± 0.4 Å for WT, 178.4 ± 0.5 Å for R69C/+, and 193.1 ± 4.2 Å for R69C/R69C. The calculated electron density profiles showed R69C/R69C's wider period derived from ~20 Å-swelling at the extracellular apposition. The extent of membrane packing distortion (Δ/d) in PNS myelin, calculated using Bragg order peak widths, was 25% greater in R69C/+ and doubled in R69C/R69C compared to WT. Differences in amount of myelin, period, and Δ/d among the genotypes were statistically significant at $p < 0.001$. Finally, comparison of R69C/+ with P0± and R69C/R69C with P0-/- suggested the small amount of mutant P0 that enters the myelin may detrimentally affect myelin-myelin interactions to produce less regular/unstable packing.

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Monolayers of a Mixed Phospholipid System
Carlos Luna[1], Helim Aranda-Espinoza[1], Amir Maldonado[2], Gerardo Paredes[2].
[1]University of Maryland, College Park, MD, USA, [2]Universidad de Sonora, Hermosillo, Sonora, Mexico.
Membranes formed with mixtures of phospholipids have interesting properties. Mixing the appropriate components can give rise to phenomena such as the rigidification of the membrane or the appearance of lipid rafs. It has been shown that hydration of a dryed SOPC:SOPS film produces vesciles whose shapes depend on the lipid composition.
This effect is probably due to different packing conditions of the phospholipid molecules in the membrane due to electrostatic interactions. In order to further understand this system, in this work we have investigated the packing of SOPC:SOPS Langmuir monolayers and AFM experiments as a function of phospholipid composition.

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Deposition of egg-PC to an Air/Water and Triolein/Water Interface
Matthew A. Mitsche, Donald M. Small.
Boston University Medical Center, Boston, MA, USA.
Phospholipid monolayers play a critical role in stabilization of biological interfaces including the alveoli of the lung, fat droplets in adipose tissue, and apolipoproteins. Behavior of phospholipids at an air-water interface is well understood. However, work at oil-water interfaces is limited due to technical challenges associated with a Langmuir trough. In this study, egg-phosphatidylcholine(PC) was deposited onto a drop of either air or triolein(TO) formed in a low salt buffer and the surface tension was measured using a drop tensiometer. The egg-PC was deposited by constituting it into SUVs and then allowing molecules to absorb to the surface. We observed that egg-PC binds irreversibly to both interfaces and at equilibrium exerts 15 and 12 mN/m at an air and triolein interface, respectively. To determine the surface concentration, which cannot be measured directly, compression isotherms from a Langmuir trough were compared to that of the drop tensiometer. The air-water interfaces had identical characteristics so the surface concentration of the drop can be determined by simply overlaying the two isotherms. Since TO is also surface active there will be triolein incorporated into the monolayer. Since TO is less surface active than PC as the pressure(Π) increases the triolein is progressively ejected. To understand the Π/area isotherm of PC on the TO drop a variety of TO-PC mixtures were spread at the air-water interface. The isotherms show an abrupt break in the curve at a specific Π caused by the ejection of TO from the monolayer into the bulk phase. A plot of these surface transition points against Π gives the monolayer surface composition at any Π. The oil drop experiment always contains bulk phase of TO, thus the 2-D phase rule predicts the monolayer composition of the droplet over a range of Π.

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Effects of Ether vs. Ester Linkage on Lipid Bilayer Structure and Water Permeability
Deren Guler[1], Dipon Ghosh[1], Jianjun Pan[1], John F. Nagle[1], John C. Mathai[2], Mark L. Zeidel[2], Stephanie Tristram-Nagle[1].
[1]Carnegie Mellon University, Pittsburgh, PA, USA, [2]Harvard Medical School, Cambridge, MA, USA.
The structure and the water permeability of bilayers composed of the ether linked lipid, dihexadecylphosphatidylcholine (DHPC), were studied and compared with the ester linked lipid, dipalmitoylphosphaditdylcholine (DPPC). Wide angle x-ray scattering (WAXS) on oriented bilayers in the fluid phase indicates that the area per lipid A is slightly larger for DHPC than for DPPC. Analysis of low angle x-ray scattering (LAXS) to 0.85 $Å^{-1}$ on the same fully hydrated bilayers yields area A=65.1 $Å^2$ for DHPC at 48°C and other structural quantities such as various bilayer thicknesses. The DHPC LAXS data provide the bending modulus, $K_C=4.2x10^{-13}$erg and the Hamaker parameter $H=7.2\times10^{-14}$erg for the van der Waals attractive interaction between neighboring bilayers. These quantities can be compared with the results for DPPC at 50°C: A=64.3 $Å^2$, $K_C=6.7x10^{-13}$erg and $H=8.2x10^{-14}$erg. For the low temperature phases with ordered hydrocarbon chains, use of oriented samples provides higher resolution than earlier studies. We confirm the transition from a tilted $L_{\beta'}$ gel phase to an untilted, interdigitated $L_{\beta}I$ phase as the sample hydrates at 20 °C, and WAXS data suggest that the drier, gel phase is an $L_{\beta'L}$ phase. These structural results for DHPC and DPPC are compared to new measurements of Pf, the water permeability, in both the fluid and gel phases.

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Electric Field Driven Conformational Changes of Gramicidin D in a Model Membrane Supported on a Au(111) Electrode Surface
Jacek Lipkowski, Slawomir Sek, Thamara Laredo, John R. Dutcher.
University of Guelph, Guelph, ON, Canada.
In this work, we show molecular resolution scanning tunnelling microscopy (STM) images of gramicidin, a model antibacterial peptide, inserted into a phospholipid matrix supported at a gold electrode surface. The resolution of the images is superior to that obtained in previous attempts to image gramicidin in a lipid environment using atomic force microscopy (AFM). This breakthrough has allowed visualization of individual peptide molecules surrounded by individual lipid molecules. We have observed several important features: the peptide molecules do not aggregate, the peptide molecules adopt a single conformation corresponding to a specific ion channel form, and the lipid molecules adjacent to the peptide molecules are systematically longer than those in the lipid matrix. These results constitute a new approach to obtain structural characteristics of antibiotic peptides in lipid assemblies that is necessary for the understanding of their biological activity.
We then applied the polarization modulation infrared reflection absorption spectroscopy (PM IRRAS) to investigate the effect of the electric field on the conformation and orientation of gramicidin molecules in a bilayer supported at the gold electrode surface. We observed potential controlled changes in the orientation and conformation of the gramicidin molecules in the supported bilayer. Careful analysis of the IR data indicated that the potential applied to the electrode affects the bilayer structure and these changes cause reorientation and conformational transformations of gramicidin molecules.

Inward Rectifier K Channels

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An Inter-intra Subunit Salt Bridge near the Selectivity Filter Stabilizes the Conducting State of Kir1.1
Henry Sackin[1], Mikheil Nanazashvili[1], Hui Li[1], Lawrence G. Palmer[2], D. Eric Walters[1].
[1]The Chicago Medical School, North Chicago, IL, USA, [2]Weill Medical College of Cornell Univ., New York, NY, USA.
ROMK (Kir1.1) potassium channels are normally closed by internal acidification with a pKa of 6.6. If this acidification occurs in the presence of low (1mM) external K, the channels also inactivate, such that channel activity is not recovered by realkalization until high K is returned to the external solution. Mutations in an inter-intra subunit salt bridge (E118-R128-E132-Kir1.1b) in the P-loop of the channel near the selectivity filter increased the K sensitivity of