our group. It was found that both local and general anesthetics display very similar effects on stimulation-response curves of the median nerve. Our findings support the recent thermodynamic theory for nerve pulse generation and propagation (electromechanical solitons, Heimburg & Jackson, PNAS 2005).

1241-Pos Board B133
Why are the Actions of Anesthetics on GABA-A Universal?
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There is a long-standing debate on whether general anesthetics act through a non-specific perturbation of bilayer physical properties or through binding to specific sites within ion channels, particularly the GABA-A receptor. In this study, we demonstrate that a series of liquid n-alcohol general anesthetics lower phase transition temperatures in giant plasma membrane vesicles, which have previously been shown to sit close to a miscibility critical point. All n-alcohols depress critical temperatures (Tc) by $4 \pm 1^{\circ}C$ when added to vesicles at their anesthetic dose. Current work is investigating if transition temperatures are also depressed when n-alcohols are added to synthetic vesicles with critical lipid compositions. We also performed simulations of simplified receptors embedded in a nearly-critical membrane. In this model, receptor channels can be in two distinct internal states (conducting or non-conducting), and the occupancy of these states is allosterically regulated by their local lipid environment as well as the availability of ligand. We show that model channels with dimensions comparable to that of GABA-A could have their conductance increased by 50% when Tc is lowered by $4^{\circ}C$ in the limit of low ligand concentration. This is in good agreement with experimental observations of GABA-A channels in the presence of general anesthetics (compare to Figure 2b in [1]). Taken together, these findings suggest that general anesthetics can have dramatic effects on the internal states of membrane bound proteins without requiring that they directly bind to specific sites. Instead, we propose that anesthetics may act by lowering the critical temperature of the membrane which in turn allosterically regulates ion channel function.
1. N. Franks and W. Lieb, Molecular and cellular mechanisms of general anesthesia. Nature, 367, 607 (1994).

1242-Pos Board B134
Small Molecule Interaction with Lipid Bilayers: A Molecular Dynamics Study of Chlorhexidine
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Chlorhexidine is a chemical antiseptic shown to be effective against a wide range of bacteria. It is therefore used in a wide range of industries in products such as: surgical hand washes, mouthwash, industrial sterilization and many other similar applications. It acts specifically against the plasma membrane, causing leakage leading to cell death. Chlorhexidine presents an interesting modelling challenge with a hydrophobic hexane connecting two biguanides (arginine analogues) and two aromatic rings. We conducted molecular dynamic simulations to reproduce the experimental environment of chlorhexidine in a 1,2-dimyristoyl-sn-glycero-3-phosphocholine (DMPC) bilayer to produce atomic-level information. We constructed an all-atom force field of chlorhexidine from the CHARMM36 force field using well established parameters of certain amino acids. Partial charges were treated differently, which were calculated using GAUSSIAN software. Using GROMACS simulation software we were able to determined that chlorhexidine resides inside of the membrane around the headgroup region of the lipids in a wedge shape. This concurs with previous studies done by this lab using neutron diffraction which have determined that chlorhexidine was located at the membrane aqueous interface.

1243-Pos Board B135
Role of Lipid Composition in Gas Permeation across Biological Membranes
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Gas molecules dissolved in an aqueous environment are pre-dominatly in their hydrophilic charged state because of their respective acid/base equilibria. Overton's rule suggests that permeation of small charged molecules across the membrane boundary is highly restricted and must occur either in their neutral form or through a dedicated transport mechanism. There has been experimental evidence to the effect that the water channel family, Aquaporins, may be responsible for the permeation of neutral gas molecules such as CO2, NH3 , and O2 across biological membranes. This is in apparent contrast to the observation that the permeation rate of neutral gas molecules across pure lipid bilayers is mostly unhindered. It is hence of interest to test the hypothesis the lipid composition of biological membranes may result in a vastly different in gas permeability as composed to pure model membranes.
The lipid composition of physiological membranes is highly complex and further involves asymmetry in the two leaflets. Also, a major component of the cellular lipid bilayers involved in gas permeation, such as those surrounding Red Blood Cells (RBCs), is cholesterol. Cholesterol is known to have a strong clustering effect that increases the packing of the lipids in the membrane. It is possible to study the role of lipid composition and asymmetry through molecular dynamics (MD) simulations by reconstructing atomistically the important characteristics of physiological membranes. Here we present preliminary results of the permeability of model physiological membranes based on atomistic MD simulations.

1244-Pos Board B136
Cardiolipin's Impact on Model Membranes Thermodynamic: Drug-Lipid Interactions and Protein Conformation Implication
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Steady-state fluorescence anisotropy and dynamic light scattering (DLS) were used to determine the thermotropic properties of lipid model systems of bacterial membranes. Diferent lipid proportions of PE:PG:CL were used in order to mimic *Yersinia kristensenii*, *Proteus mirabilis* and *Escherichia Coli* membranes. Cardiolipin's inclusion as a third lipid component of any PE:PG mixture considerably changes the system's properties. The results obtained by these two techniques were shown to be reproducible and were the same within experimental errors, suggesting that either technique can be used to obtain accurate values to characterize the thermotropic behavior of such systems. Moreover they show that the main transition temperatures obtained are undoubtedly cardiolipin dependent. Additionally AFM experiments were performed and these results show that even at small concentration cardiolipin produces important changes not only in the membrane thermotropic properties, but also in the bilayer structure. Moxifloxacin and enrofloxacin's interaction studies with these model systems were also performed and show that cardiolipin's absence greatly influence the conclusions obtained. Preliminary circular dichroism results of an *E. coli* membrane protein, OmpF, reconstituted in different model system membranes, with and without cardiolipin, also point out for its influence on protein's conformation.
Taken all together these results show that cardiolipin's incorporation in model system membranes can have a significant impact on the membrane's properties and its inclusion should be considered when the aim is to construct model system of bacterial membranes.

1245-Pos Board B137
Stressing Lipid Membranes: Effects of Polymers on Membrane Structural Integrity
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Cell membrane dysfunction due to loss of structure integrity is the pathology of tissue death in trauma, muscular dystrophies, reperfusion injuries and some common diseases. It is now established that certain poly(ethylene oxide) (PEO)-based biocompatible polymers, such as Poloxamer 188, Poloxamine 1107, and PEO homopolymers, are effective in sealing of injured cell membranes, and thus prevent acute necrosis. Despite the highly potential application of PEO-based polymers for these medical problems, the fundamental mechanism of how these polymers interact with cell membranes are still under debate. Here, the effects of these polymers on structural integrity of lipid vesicles were explored under osmotic and oxidative stress. Through fluorescence leakage assays, time-lapse fluorescence microscopy, dynamic light scattering and isothermal titration calorimetry, we identified that the surface-adsorbed hydrophilic polymers efficiently inhibits the loss of structural integrity of lipid vesicles under external stimuli, while the insertion of the hydrophobic polymers increases membrane permeability. To elucidate the mechanism by which hydrophilic polymers help restore membrane integrity while their hydrophobic counterparts disrupt it, 1H Overhauser Dynamic Nuclear Polarization (ODNP)-NMR spectroscopy, a newly developed NMR technique that is highly effective in differentiating weak surface adsorption versus translocation of polymers to membranes, was employed to detect polymer-lipid membrane interactions through the modulation of local hydration dynamics in lipid membranes. Our study shows that P188, the most hydrophilic poloxamer known as a membrane sealant, weakly adsorbs onto the membrane surface, yet effectively retards