structure of the lipids and the drug. The adsorption of the drug at the monolayers decreases the order of the lipid film, in a molecular mechanism that involves both polar head groups and alkyl tails from the lipids. Also the adsorption of thymol is modulated by the lipid monolayer composition since it adsorbed in a higher extend in negative charged lipid monolayers. Data obtained from Molecular Simulation corroborate with Langmuir monolayer experiments suggesting specific sites of interaction between lipid and drug. A model is then proposed in which thymol interacts with lipids at the air-water in such a way that the interactions are maximized owing to geometrical adaptations on behalf of the contact between specific groups between the lipid and the drug.

2766-Pos Board B196

Effects of Cations on the Material Properties of Model Cell Membranes

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The outer leaflet of a cell membrane can be modeled with a lipid monolayer, of which structure and material properties can be measured as a function of lipid composition, insertion of macromolecules (peptides or nanoparticles), and ion presence, among other variables. Cation effects on these monolayers are not fully characterized, especially at higher ion concentrations, and due to the greater variety of multivalent cations promise to be more complex than well-understood anion effects. Since biological processes take place in buffered environments, an understanding of ion effects on lipid macromolecular structures is necessary to study fundamental cell membrane interactions.

These experiments investigated effects that cations of different charge (NaCl, $MgCl_2$, and $CaCl_2$) and concentration (0.1 M to 1.0 M) have on the structure and material properties of dipalmitoylphosphatidylcholine (DPPC) lipid monolayers. To determine trends due to ion type and concentration, isotherm features were quantified and compared, namely: area per molecule at liftoff, surface pressure at the phase transition plateau, layer compressibility prior to collapse, and area per molecule and surface pressure upon collapse into the subphase. Small ion concentrations (0.1 M) allowed lipids in the monolayer to pack more closely compared to a model membrane on a pure water subphase due to electrostatic screening. At higher concentrations, the surface pressure at defined areas per molecule was greater compared to pure water (indicating expansion of the structure), and the monolayer underwent an additional structural transition, likely a rearrangement of the lipid tails with respect to the air-water interface before collapse. The divalent salts caused a decrease in monolayer compressibility, indicating fluidization, and faster increase of liftoff area at higher salt concentrations. These trends were noticeably different compared to the monovalent cations. These effects can be explained by considering local electrostatic interactions.

2767-Pos Board B197

A Study of How Chelating Agents Interact with Neutral Lipid Membranes

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Chelating agents are used in a range of areas, from treating metal poisoning in medicine to removing unwanted heavy metal ions from a given solution in biochemistry. Specifically, ethylenediaminetetraacetic acid (EDTA) is widely used in biochemistry and other areas of science to sequester polyvalent cations such as Ca^{2+} and Fe3+ from solutions. Small angle x-ray scattering [1] has shown that low concentrations (mM range) of EDTA in solution introduce a phase coexistence in homogeneous 1-palmitoyl-2-oleoyl-sn-glycero-3-phosphocholine (POPC) multilamellar vesicles. This suggests that there are interactions taking place between EDTA and the lipid head group. We investigate the interaction of EDTA with lipids in the presence of various cations, using 1H NMR. A discussion of the interactions present between EDTA and lipids will be formulated based on observed proton chemical shifts and relaxation rates.

[1] Johnson et al, Langmuir 2014.

2768-Pos Board B198

Specificity and Competitive Cation Association to Phosphatidylinositol-4,5-Bisphosphate Model Membranes

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Phosphatidylinositol-4,5-bisphosphate (PIP_2) is an active signaling lipid implicated, among other functions, in the regulation of cell growth by activating the tumor suppressor PTEN. Using synchrotron surface-sensitive x-ray diffraction and fluorescence techniques we determined the preferential cation binding to PIP_2 monolayers. The natural, highly unsaturated PIP_2 was spread as a Langmuir monolayer on a physiological buffer containing 100 mM KCl at pH 7.2 to which divalent cations (Ca^{2+} and Mg^{2+}) were added. X-ray fluorescence of the PIP_2 monolayer on the buffer shows an eight fold surface enhancement (within the x-ray penetration depth below the critical angle, ~5 nm) of monovalent K^+ compared to its bulk concentration. When physiological levels of calcium are added (1-100 μM), the Ca^{2+} gradually replaces bound K^+ ions, leading to a significant change in the organization of the PIP_2 model membrane. At higher concentrations (100-1000 μM), which might be achieved during calcium signaling, we observe a 1000 fold surface enhancement of Ca^{2+}. Similar experiments with Mg^{2+} ions also show strong ion binding to PIP_2 at physiological levels (1 mM) with a lesser structural effect on the monolayer compared to that induced by Ca^{2+}. For mixed solutions of Mg^{2+} and Ca^{2+} we find that Ca^{2+} occupies the majority of binding sites, and at mM concentrations completely removes the Mg^{2+} ions from the interface. Surprisingly, with both 1 mM Mg^{2+} and 1 mM Ca^{2+} in the subphase there is still a fourfold surface enrichment of K^+ ions at the headgroup region.

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Charge Dependence of POPG:POPC-Liposome Repulsions in Deionized Water

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Shear moduli of deionized suspensions of electrostatically interacting 100 nm POPG:POPC liposomes were measured by microrheological methods. Liposome compositions spanned the entire range of POPG:POPC ratios. The liposomes were sized by extrusion and diluted in deionized water at volume fractions between 0.094 and 0.167. Liposome mean size, polydispersity, and electrophoretic mobility were also measured. Polydispersity indices ranged from 0.08 to 0.15, indicating quite monodisperse suspensions. When illuminated by white light, POPG:POPC =20:80 suspensions displayed optical Bragg scattering, indicative of particle ordering. At volume fraction 0.167 the dependence of shear modulus on composition was non-monotonic, first increasing to 6000 d/cm^2 at POPG:POPC ~20:80, then decreasing to 1000 d/cm^2 at POPG:POPC =100:0. Other concentrations behaved similarly. This effect may be attributed to the screening behavior of fully deionized suspensions, where counterion screening due to dissociated protons depends exponentially on particle charge. A 100 nm POPG liposome has ~50,000 phosphate groups on its outer surface, each bearing 1 negative charge when dissociated. Since shear moduli reflect the mean particle charge of an interacting suspension, they provide information on interaction-mediated surface-charge regulation (protonation). Shear moduli were analyzed by the DLVO theory of screened Coulomb repulsions between charged spheres. Liposomes are well-suited to such studies since their titratable charge can be accurately controlled.

2770-Pos Board B200

The Effect of Compartmentalization on the Kinetics of Transition Metal Ion-Induced LDL Peroxidation

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The typically observed kinetic profiles of transition metal ion-induced lipid peroxidation can be described in terms of a limited number of characteristic time-points derived from experimental time-dependencies and presented in terms of rate constants and concentrations, as calculated based on mechanistic considerations. The critical part of such analysis is that it is valid only if the experimental system behaves as if it is homogeneous, i.e. as if the reaction occurs in a solution. In spite of the uncertainties due to the latter assumptions, we obtained a reasonable agreement between the experimental data and the theoretically predicted dependencies, which supports our previous theoretical treatment. Yet, several previous findings could not have been explained in terms of our (''quasi-homogeneous'') model, indicating that the model is valid not under all conditions. One example is that under certain conditions, rapid peroxidation of lipids occurs prior to complete consumption of LDL-associated Tocopherol. We think that uninhibited (''rapid'') peroxidation becomes apparent when considerable fractions of the particles lose all their Tocopherol (i.e. before the time predicted for ''homogeneous'' system). The lack of Tocopherol is an essential but insufficient demand for rapid peroxidation. Another demand is that the particle should contain at least a critical number of hydroperoxides molecules. In the present investigation, we show that the results of all our kinetic studies can be understood if we consider compartmentalization. Specifically, for any given composition of the particles (LDL and/or HDL), the kinetic results are probably governed by the distribution and rate of exchange of antioxidants and hydroperoxides between particles. Our analysis is of special importance for systems containing more than one population of lipoprotein particles. The possible effects of compartmentalization should be considered in other reactions that occur in inhomogeneous systems.