2760-Pos Board B190
Polystyrene Nanoparticles Alter the Stability of Model Cell Membranes
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Due to their small size, nanoparticles have the ability to penetrate pulmonary and vascular tissue, and as a result, are classified as potential human carcinogens. On the other hand, nanoparticle insertion into targeted cells can play a key role in drug delivery and gene therapy applications, prompting a need to more thoroughly characterize nanoparticle/membrane interactions. Because nanoparticle interactions with biological membranes exist, but have not been fully characterized, the stability of model cell membranes was observed in the presence of particles. Giant unilamellar vesicles (GUVs) composed of canonical ternary mixture of lipids of dipalmitoylphosphatidylcholine (DPPC)/ 1,2-dioleoyl-sn-glycero-3-phosphocholine (DOPC)/cholesterol (1:1:1) with 0.8% mol fluorescent lipid were made in the presence of functionalized polystyrene nanoparticles at varying concentrations. A change in the vesicle size distribution in the presence of NP indicates that inclusion of particles affects the stability of bilayer curvature. Aminated polystyrene particles were shown to limit the size of stable GUVs even at low particle concentrations of 0.025 wt%. Association of the positively charged particles at the lipid/water interface resulted in extruded lipid tubules from the vesicle surface. Carboxylated particles produced a less dramatic effect. This may be attributed to the greater charge density of the carboxylated particles, compared to those with amine functionalization, such that a higher inter-particle repulsion could prevent nanoparticle arrangement on the surface. In both cases, high nanoparticle concentration completely prevented the formation of GUVs, indicating a concentration dependent effect. The effect of the nanoparticles on the membrane material properties of the vesicles will also be discussed.

2761-Pos Board B191
How Nsaids Affect Lipid Monolayer and Bilayer Properties
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Non-steroidal anti-inflammatory drugs (NSAIDs) inhibit prostaglandin synthesis by blocking cyclooxygenase and influence gramicidin channel lifetimes in planar lipid bilayers. In the past we studied how the NSAIDs salicylic acid, acetylsalicylic acid, acetaminophen, ibuprofen and diclofenac influenced the pressure-area curve in the aqueous subphase on dipalmitoyl-PC pressure-area curves at modestly supratheraputic dosages (1 mM concentrations in the subphase). We observed consistent changes that imply these NSAIDs interact strongly with the lipid head groups of monolayers. Here we report subsequent findings using umbrella sampling molecular dynamics. Each titratable NSAID was simulated, both protonated and unprotonated, with DPPC bilayers. The neutral NSAIDs have free energy wells as deep as −10 kcal/mol in the headgroup region, whereas charged molecules were uniformly repulsed from the bilayer. These findings call for further experiments on the pH dependency of drug-bilayer interactions and suggest that neutral NSAIDs, including protonated aspirin in the low pH chyme of the stomach, interact with cell membranes and could cause adverse side effects.

2762-Pos Board B192
Studies of Zwitterionic Lipoplexes - Nanosystem Based on Phospholipids and Surfactants as Innovative Delivery Systems for Gene Therapy
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The gene therapy is the one of the most promising method of treatment in contemporary medicine. This way of therapy is very useful in the treatment a dozen of incurable or fatal diseases. This method of treatment is leaned on implement a gene into patient's cells with the use of dedicated delivery systems (vectors). The main problem of gene therapy is to find the best vector which will be effective and will be not toxic for human cells. A good approach seems to be use of non-viral vectors like delivery system based on lipid-surfactant mixtures.
The aim of this study was to examine the possible application of selected amphoteric surfactants (zwitterionic alkyl derivatives of sulfobetaine) as complexing agents (with and without helper lipid) for nucleic acids (siRNA, low and high-molecular weight DNA).
The studies of DNA conformation in selected DNA - zwitterionic surfactant lipoplexes were performed using the circular dichroism (CD) spectroscopy. CD spectra were recorded in the spectral range 350 - 200 nm by using J-815 spectrometer (Jasco). The results obtained indicate that the DNA maintains the B-form for wide range of surfactant concentrations in the solution. The structure and organization of lipoplexes was also independently analyzed by the Fourier transform infrared spectroscopy. The absorption spectra for lipoplexes were collected by using FTIR spectrometer BRUKER Tensor 27 in the temperature range 2-40°C. The phase transitions in examined systems were studied by using the differential scanning calorimetry (DSC). Ability of creating of stable complexes in DNA-surfactant systems studied was confirmed using electrophoresis on agarose gel. For all formed stable lipoplexes the complete reduction of electrophoretic mobility was observed. Finally the transfection efficiency of selected systems were also tested on HeLa cells.

2763-Pos Board B193
Photothermal Manipulation of Membranes
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There is emerging evidence that highly controlled nanoscale heating processes can be used to manipulate biological membrane events such as pore formation, bilayer translocation, and fusion. These processes may have diverse applications in triggered drug release, gene transfection, and hybridoma formation. The goal of this work is to devise new methods of producing nanoscale heating and to exploit this phenomenon as a way to manipulate biomembrane structure and function. Photothermal gold nanoparticles have been explored for these purposes but suffer from size-restricted diffusion limitations and poor clearance profiles, while many photothermal organic dyes are susceptible to photobleaching. Our lab has developed high performance near infrared (NIR) dyes and dye loaded nanoparticles which generate heat upon absorption of NIR laser light, making them ideal for *in vivo* applications.[1,2] These photothermal agents were incorporated into cells and artificial membranes, and heat was produced with precise spatiotemporal control. Membranes sensitive to temperature were shown to release encapsulated contents and to have increased bilayer translocation rates. Recent work with artificial temperature insensitive membranes and cell membranes is also discussed.
(1) Spence, G. T.; Hartland, G. V.; Smith, B. D. *Chem. Sci.***2013**, *4*, 4240
(2) Spence, G. T.; Lo, S. S.; Ke, C.; Destecroix, H.; Davis, A. P.; Hartland, G. V.; Smith, B. D. *Chem. Eur. J.***2014**, *20*, 12628

2764-Pos Board B194
Theoretical and Experimental Insights into Lipopolysaccharides-Polymyxin B Interactions Using Genetically Modified Enterobacterial Strains
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The Gram-negative Outer Membrane Lipopolysaccharides (LPS) is the first molecular barrier of the antimicrobial peptide (AMP). Each LPS monomer is composed of a lipid-A and a polysaccharide chain of multiple modular-subunits with defined chemical structure and properties. There is great interest in understanding how AMP, like Polymyxin-B, associate and permeabilizate bacterial membranes; nevertheless, this process is poorly understood and further studies are needed. To understand the Polymyxin-B interaction with the LPS, we have combined molecular dynamics simulations of LPS containing-bilayers and in vivo and in vitro experimental assays using genetically modified Escherichia coli and Salmonella Typhimurium strains to display LPS of controlled chemotypes. The dynamical characterization of the Polymyxn-B interactions with LPS-subunits gives a new insight of their contribution to the outer membrane destabilization process, which is essential to develop new antibiotics strategies. Granted by FONDECYT N° 11130576.

2765-Pos Board B195
Interaction of Thymol with Cell Membranes Models Studied with Tensiometry, Vibrational Spectroscopy and Molecular Simulation
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Thymol (2-isopropyl-5-methylphenol) is a natural compound that acts as a microbicide, with a probable effect on cell membrane surfaces. However, the mechanism of action when it interacts with lipid surfaces is not sufficiently known. For this reason, it is important to understand at the molecular level interactions between the drug and biointerfaces, and using models for cell membranes can be an appropriate strategy for this purpose. In this study, we employed Langmuir monolayers of lipids as cell membrane models, with the drug incorporated in monolayers of zwitterionic lipids, namely DPPC (dipalmitoyl phosphatidyl choline), and negative lipids, namely DPPS (dipalmitoyl phosphatidyl serine), and compared to data obtained with Molecular Simulation. Combining data on Surface Pressure-Area Isotherms with Polarization Modulation Infrared Reflection-Absorption Spectroscopy (PM-IRRAS), the effect of the thymol on lipid monolayers was compared by in view of the chemical and molecular