entrapment efficiency and spontaneous release of anti-cancer drug doxorubicin is studied by using absorption spectroscopy and fluorescence de-quenching method. These physical measurements are performed on liposomes with varying PLFE molar ratios at different temperatures. The obtained results may help to optimize and design liposomal drugs with greater stability and higher therapeutic efficacy. (supported by NSF DMR1105277)

1272-Pos Board B164
PLFE Lipids Stabilize Liposomal CA4P
Varsha Daswani.
Temple University, Philadelphia, PA, USA.
Liposomal encapsulation using bipolar tetraether lipids such as the polar lipid fraction E (PLFE) isolated from the archaeon Sulfolobus acidocaldarius offer many advantages over conventional phospholipid mediated or free drug delivery. PLFE provide increased stability to lipid vesicles. Liposome mediated drug delivery can reduce the off target effects caused by anti-cancer drugs. Therefore, we hypothesize that PLFE archaeosomes, offer the anti-cancer drug combretastatin A4 disodium phosphate (CA4P) a higher therapeutic efficacy by increasing the drug's stability, circulation time, and targeting. In this study, the fluorescent properties of CA4P have been utilized for drug leakage assays with different compositions of PLFE/POPC in unilamellar vesicles of varying sizes. We have found that PLFE lipids stabilize liposomes and decrease rate of CA4P leakage. We have also shown that this effect is manifested in the cytotoxicity assay against human MCF-7 breast cancer cells. (supported by NSF DMR1105277)

1273-Pos Board B165
Hydrodynamic Co-Localization of Molecules in Supported Lipid Bilayers Detected by Secondary Ion Mass Spectrometry
Monica M. Lozano[1], Krishna Kumar[2], Steven G. Boxer[1].
[1]Stanford University, Stanford, CA, USA, [2]Tufts University, Medford, MA, USA.
Here we report on the use of secondary ion mass spectrometry (SIMS) to study the hydrodynamic co-localization of membrane components in supported lipid bilayers formed by the fusion of multi-component giant unilamellar vesicles to oxidized silicon substrates. In these experiments, hydrodynamic drag forces arising from flow above the supported lipid bilayer (SLB) results in the directed motion of molecules protruding from the SLB. In this particular case, protrusion of the cholera toxin B into the aqueous layer serves as a handle for the directed motion of its natural ligand, ganglioside GM1, and any other molecule (i.e. cholesterol) strongly associated with it. Orthogonal isotopic labeling or fluorination of every lipid bilayer component allowed generation of molecule-specific images, using a nanoSIMS, that map the lateral redistribution of molecules in a lipid bilayer as a result of hydrodynamic flow. Furthermore, simultaneous detection of up to seven different ion species, including secondary electrons, allowed generation of ion ratio images whose signal intensity values could be correlated to composition through the use of calibration curves from standard samples.

1274-Pos Board B166
Interaction of 1,4-Naphtoquinone with Cell Membranes Models Studied with Tensiometry and Vibrational Spectroscopy
Luciano Caseli, Nadia Hussein.
Universidade Federal de Sao Paulo, Diadema-SP, Brazil.
Antineoplastic drugs are natural or synthetic compounds that act against the development of cancer cells, whose chemical interactions with cell membranes have a mechanism of action not sufficiently known so far. For this reason, it is imperative the understanding at the molecular level of drug-cell interactions, and using models for cell membranes is a suitable strategy for that. In this study, we employed Langmuir monolayers of lipids as cell membrane models, and 1,4-Naphthoquinone, which is a potent inhibitor of human cancer cell growth and angiogenesis, was investigated. The drug was incorporated in monolayers of zwitterionic lipids such as DPPC (dipalmitoyl phosphatidyl choline), and negative ones, such as DPPS (dipalmitoyl phosphatidyl choline). Surface pressure-area isotherms showed that the drug induces to a condensation of the monolayer, influences the first-order transition of the lipid from liquid-expanded to liquid-condensed phases, and alters the visco-elastic properties of the monolayers. Also, Polarization Modulation Infrared Absorption-Reflection Spectroscopy (PM-IRRAS) indicated that the drug acts in a first moment in the polar heads of the phospholipids, which causes further distortion of the alkyl chains of the phospholipids. These results are important not only because brings information on drug-membrane interactions at the molecular level, but also because envisage the enhancement of the use of antioneoplastic drugs in cancer treatment.

1275-Pos Board B167
Lipid Membrane Phase Dynamics
Michael S. Kessler, Susan Gillmor.
The George Washington University, Washington, DC, USA.
We study lipid phase behavior using giant unilamellar vesicles to model cell membrane dynamics. In our system, we investigate the effects of cross-linking in the head groups position via biotinylated lipids, avidin, and its analogues. Cross-linking is the linking of two molecules (biotinylated lipids) via a crosslinking agent (avidin). Vesicles allow us to isolate the lipid rearrangement due to cross-linking, a common activity on cell surfaces. By comparing specific binding strength of the coupling and self-adhesion, we study the role that cross-linking plays in membrane behavior. Using anti-avidin we attempt to induce aggregation of the membrane bound protein, producing micron size phase domains from initial one-phase vesicles. Confocal microscopy enables us to image this change in the membrane dynamics. Using phase specific dyes, we probe phase segregation on the nanometer scale from the addition of a cross-linker to the system. Förster Resonance Energy Transfer (FRET) enables us to detect clustering on the submicron (1-10 nm) scale, beyond the limits of conventional microscopy. Both techniques allow us to quantify the phase behavior due presence of the cross-linking agent. Using FRET we detect lipid rearrangement associated with the transition from one-phase vesicles to two-phase vesicles using two different fluorescent dyes, a donor and acceptor. From judicious choice of donor and acceptor dyes, we detect the changes in fluorescence acceptor signal as a function of clustering. We are pursuing lifetime studies to complement our current FRET analyses. From this simple cross-linking system, we model membrane responses to protein complex formation and oligomerization.

1276-Pos Board B168
Meta-Cresol Affects Lipid Raft Organization in Membrane-Model Systems and Increases Membrane Leakage in Neural Cells
Joaquim M. Trigo Marquês, André E.P. Bastos, Ana S. Viana, Pedro A. Lima, Rodrigo F.M. de Almeida.
Centro de Química e Bioquímica, Faculdade de Ciências da Universidade de Lisboa, Lisboa, Portugal.
m-cresol is an excipient stabilizer used in numerous pharmaceutical formulations, including injectable insulin and vaccines. Therefore, we studied the effects of *m*-cresol in a range of concentrations from 10nM to 3mM on membrane model systems mimicking lipid-rafts and living neural-cells.
First, the intrinsic fluorescence of *m*-cresol was studied. Both its fluorescence lifetime and anisotropy increased in the presence of liposomes, indicating a decreased mobility of the molecule. This interaction was dependent on membrane lipid composition. To elucidate this process, liposomes were labeled with several membrane probes spanning a range of in-depth locations and with preference for distinct lipid domains. For the probes located in the bilayer core (DPH and trans-parinaric acid), no effect was detected even for an *m*-cresol concentration of 300M, whereas for the more superficial NBD-DOPE and NBD-DPPE, >30M *m*-cresol induced a significant fluorescence lifetime decrease.
Atomic force microscopy experiments were performed on ternary supported lipid bilayers containing raft-like liquid ordered domains (Lo). Indeed, it was observed that upon addition of *m*-cresol in the M range, a reduction of the Lo occurs without changing their thickness. For higher *m*-cresol concentrations, raft-like domains are not detected at all.
Whole-cell voltage-clamp recordings from pyramidal-neurons isolated from the CA1 region of rat hippocampus (p21-p29) and from N1E-115 neuroblastoma cells were also performed. *m*-Cresol was applied during constant superfusion and the following parameters were monitored: series-resistance, whole-cell capacitance, holding-current (Vm=-70 mV), and another read-out for the leak-current. Results show that only the leak current was altered by *m*-cresol (>100 M).
As a whole, we show that *m*-cresol interacts with the membrane, affecting lipid raft organization, with functional implications on neural-cell integrity.
We thank F.C.T. Portugal for financial support (Ciência2007, SFRH/BD/64442/2009, PEst-OE/QUI/UI0612/2011).

1277-Pos Board B169
Two- Dimensional Macroscopic Protein Domains Induced by the Interplay between Lipid- Protein and Protein- Protein Interactions
Wan-Ting Hsieh, Zhengzheng Liao, Chih-Jung Hsu, Ivan J. Dmochowski, Tobias Baumgart.
University of Pennsylvania, Philadelphia, PA, USA.
It has been suggested that lipids and proteins are not homogeneously distributed in cell membranes; they can segregate into dynamic micro/ nanodomains, serving as centers for signal transduction, membrane trafficking, and cytoskeletal organization. Here we ask the question whether two- dimensional protein