triggers local Rac-GTP hydrolysis, thus reducing local actin polymerization required for filopodia formation. ArfGAP44 expression increases as the neurons to their construction network is established and the frequency of exploratory filopodia formation is diminished, suggesting that ArfGAP44 may facilitate the transition of neurons from a dynamic exploratory mode to a mature more static state, a hallmark of nervous system development. Together, our data reveals a local and receptor-independent auto-regulatory mechanism that limits initiation of exploratory filopodia in neurons via protein recruitment to nanoscale membrane deformations.

1239-Pos Board B19
Role of Surface Tension in the Formation of Membrane Tubes
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The formation of tubular structures is a fundamental morphological change that takes place in biological and reconstituted lipid membranes. Mechanical tension in biological membranes is thought to potentially regulate a number of cellular processes, including cell migration. Here, we explore the impact of surface tension on the formation of membrane tubes using elastic and viscoelastic continuum models of lipid bilayers. In the elastic framework, we demonstrate that application of a point load is sufficient to drive the formation of a tube from an initially flat patch of membrane which undergoes a tent-to-tube transition as a region of negative Gaussian curvature develops at the base of the tube. We generate force vs. displacement curves over several orders of magnitude in the surface tension that display a characteristic overshoot of approximately 13% in the force required to maintain a tube at constant length for all values of surface tension. Additionally, we observe a larger (smaller) linear deformation of the patch relative to the tube radius for a membrane under greater (lesser) tension. We also develop a viscoelastic framework that accounts for lipid flow on the membrane surface on a time scale of a bilayer, affects the engulfment of nanoparticles by membranes. We present a model for the spontaneous curvature, which describes the asymmetry between the two leaflets of a bilayer, affects the engulfment of nanoparticles by membranes. We

1240-Pos Board B191
Biophysical Evaluation of Drug Impact on Pulmonary Surfactant Performance
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The respiratory surface of the mammalian lung is covered by a thin aqueous layer, and on top of it, by a lipid-protein surface active material, the pulmonary surfactant (PS). It is synthesised by type II pneumocytes and secreted in the form of multilamellar structures. Its main function is to form a film to reduce the surface tension at the air-liquid interface to values below 2mN/m, to prevent pulmonary collapse during expiration and to minimize the work during inspiration. PS has unique biophysical properties to adsorb very rapidly (in few seconds) into the air-liquid interface and, once there, to spread efficiently along it. The pulmonary surfactant system, historically considered as a barrier to drug delivery, could therefore offer novel opportunities to vehiculize different drugs efficiently, while hiding and protecting them from clearance in the lung. Nevertheless, drug impact on pulmonary surfactant performance needs to be considered in a case by case basis when different molecular entities are combined with PS.

In the present work we have investigated the effect of the interaction of an anti-inflammatory steroid and an anti-tuberculosis drug with different pulmonary surfactant preparations, and how drug effects depend on PS composition. After combining properly different surfactant systems with each drug at different drug/lipid ratios, we have evaluated their impact on surfactant function and mechanical properties of surfactant layers, as assessed in a captive bubble surfactometer. Furthermore, we have used the Langmuir-Blodgett technique to prepare supported films and analyse the structure of different drug-loaded surfactant layers in order to detect structural changes associated with the impact of drugs on surfactant activity.

1241-Pos Board B192
Multiscale Simulation of Concentration-Dependent Interaction of Hydrophobic Drug with Cell Membrane
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Cell membranes are often the main and often final barriers for drug delivery. Little is known how hydrophobic drugs such as paclitaxel penetrate through cell membranes. Here we investigate interactions between paclitaxel and a model cellular membrane of 1,2-dimyristoyl-sn-glycero-3-phosphocholine (DMPC) at the molecular level, using multiscale simulation with all-atomistic and coarse-grained models. We simulate several multiple systems of POPC bilayer membrane with several different paclitaxel concentrations in the membrane. Additionally, we calculate the free energy profile across the membrane interface, to compare with previously reported experimental measurements. Furthermore, coarse-grained models of the drug are refined to match the all-atomistic free energy profile. Along with the corresponding atomistic simulations, the coarse-grained models provide essential tools to investigate the concentration-dependent behavior of the drug in the membrane. For example, we examine the preferred positioning and orientation of the drug, anisotropic directional diffusion and aggregation over the extended timescale and system size. A better understanding of the interactions between hydrophobic drugs and model membranes and their transport will provide molecular-level insights of the drug delivery process.


1242-Pos Board B193
Stability Regimes and Engulfment Patterns of Nanoparticles at Membranes
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Understanding the interactions between nanoparticles and membranes is essential for many processes such as drug delivery, nano-toxicity and endo- and exocytosis of biological cells. Using a combination of local stability analysis and global energy minimization, we have studied how the membranes’ spontaneous curvature, which describes the asymmetry between the two leaflets of a bilayer, affects the engulfment of nanoparticles by membranes. We