Anesthetics, in general, are a big discussion topic when it comes to describe their way of action. There are two main models that portray such process. The first and more accepted one states a direct effect over the proteins receptors of the membrane that regulates the nervous impulse. The second gives more emphasis on the membrane lipids, in which more tangible properties are taken in consideration, such as its compressibility. This model poses a more general and less specific way of action that the one suggested by the membrane protein receptors.
In our work, we study the electrostatic properties of the interaction of a drug and a membrane model by solving the Poisson-Boltzmann equation. Moreover, we also simulate the dynamics of the system by Molecular Dynamics (MD). As a final approach we estimate the configurational entropy in order to understand how the system behaves and evolves in time.
We build five systems whose main component is a bilayer membrane of the saturated lipid Dipalmitoylphosphatidylcholine (DPPC), in presence of four different drugs: caffeine, lidocaine, procaine and tetracaine. One for each molecule and a fifth as a control.
From the positions and energies results of the MD, it was possible to see how the caffeine posses a certain preference for the polar region of the membrane model and the anesthetics for the apolar region. These last ones produced a destabilization effect over the lipid tails of the membrane, which we were able to measured by means of a configurational entropy. Each molecule, lidocaine, procaine and tetracaine, gave increasing values of entropy; this is a direct effect of the membrane disorganization, offering a possible explanation on how different anesthetics provide such different effectiveness.

3403-Pos Board B558
Coarse-Grained Molecular Dynamics Simulations Reveal the Membrane Dependence of MscL Gating
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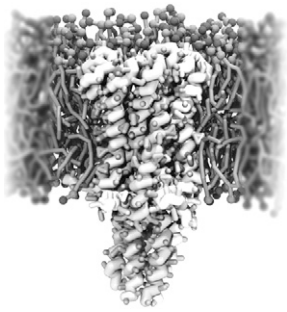
Membrane proteins are solvated in a lipid bilayer; with the proteins' hydrophobic area covered by the bilayer's hydrophobic core. The strong bilayer-protein hydrophobic interactions effectively couple the protein to the bilayer and vice versa. Therefore, membrane protein function can be influenced with changes in bilayer properties.
A coarse-grained MARTINI molecular dynamics model is used to explore the lipid bilayer influence on the mechanosensitive channels of large conductance (MscL). Among the mechanosensitive channels MscL is the most studied and often used as a model for how proteins sense membrane tension. We characterize the MscL gating kinetics dependence on bilayer properties by simulating MscL embedded in bilayers of different composition and with systematic addition of straight chain alcohols. Both bulk bilayer properties and local properties/deformation around the proteins are analysed in addition to MscL time to opening after applied tension (k_o). The *in-silico* predictions are compared with experimental data determined using reconstituted MscL in a liposomal fluorescent efflux assay. The *in-silico* model correctly predicts known MscL behaviour, like longer k_o in thicker bilayers. Surprisingly, the model also predicted longer k_o with the addition of octanol, a finding which was experimentally confirmed.



3404-Pos Board B559
Molecular Dynamics Simulations of Pegylated Compounds in Dopc Lipid Bilayer
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Lipids constitute the primary structural element of biological membrane and they play a central role in biochemical and biophysical processes of the cells. Because of their obvious biocompatibility, lipids and their derivatives are of great importance in pharmaceutical applications. Lipids can self-assemble into a variety of structures such as bilayers, micelles, and liposomes. Liposomes are the key structure for drug delivery because they can transport hydrophilic and hydrophobic compounds embedded in their interior and in the bilayer respectively. Liposomes are vulnerable to attack from the immune system and after a first adhesion to the proteins in the blood plasma they are recognized and removed from the blood. The circulation time of liposomes in the bloodstream can be prolonged using lipids with hydrophilic polymers attached to their headgroups, which form a protective steric barrier.
In this study, we performed molecular dynamics simulations to analyze the effect of the Polyethylene glycol (PEG) as polymer coatings. Here we analyze different biophysical properties of the equilibrated mixed bilayers to determine how the presence of PEGylated compounds in varying chain lengths and concentration affects the lipid bilayer. Short PEG chains (< 20 PEG units) are unstable in the water phase and after aggregation, diffuse in the lipid bilayer rapidly increasing the disorder and the area of the lipid bilayer. This behavior is not unexpected because PEG is soluble in several nonpolar as well as polar solvents. On the other hand, longer PEG chains (> 20 PEG units) are more stable in the water phase and their aggregates do not show the tendency to diffuse from the water to the hydrophobic core of the lipid bilayer. These simulations reveal that PEG chain length is an important factor in the development of functionalized liposomes for drug delivery.

3405-Pos Board B560
Physical Properties of Model Phosphatidylcholine Bilayers containing Diacylglycerol (DAG): A Molecular Dynamics Simulations Study
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DAGs are lipid molecules capable of triggering a wide range of biological responses. They serve as second messengers by regulating both the translocation to the membrane compartment and the activation of C1 domain-bearing proteins. They are also involved in the activation of certain TRPC channels, the facilitation of membrane fusion and other phenomena of great biophysical interest. DAG-mediated processes are associated with diseases such as cancer, diabetes, immune system disorders and Alzheimer's disease, thus further motivating studies that would provide deeper insight in the physical properties of DAG-containing membranes.
We developed a GROMOS force field-based description of biologically relevant DAG isoforms at the atomic level and incorporated the DAG molecules into model phosphatidylcholine bilayer systems developed earlier [1]. We subsequently employed molecular dynamics simulations of the mixed hydrated bilayer systems. Our studies allowed us to observe overall thermodynamic and structural effects as a function of increasing DAG concentration and varying chain composition. The effects could then be compared with experimental observations. Moreover, we obtained information related to the mobility of DAG and its local effects that are not readily accessible by experimental means.
Our study highlights the importance of the modulation of several physical properties of lipid bilayers by DAG in a local level. It also provides a valid model for studying the interactions of lipid bilayers with DAG-responsive proteins by computational means.
[1] Poger, D., and A. E. Mark. J. Chem. Theory Comput. 6 (2010) 325.

3406-Pos Board B561
Rate Estimates from Sampling Sparse Transitions: TRNA Motion Limits Transitions between Ribosomal Translocation Intermediates
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During the elongation cycle, after peptide-bonds are formed in the ribosome, transfer RNAs translocate to their new binding sites. Resting on extensive MD simulations of 13 near-atomistically resolved translocation intermediates of the fully solvated ribosome, we have estimated the rates from transition state theory for the motions of the tRNAs, 30S head and body, as well as the L1-stalk. The Kramers pre-factor and transmission coefficient were determined from a statistical analysis of transitions observed in the simulations.
To that aim, we first estimated all free energy barrier heights from a multidimensional quasi-harmonic approximation derived from local fluctuation analysis. Second, we introduced two model parameters, an attempt rate and a constant scaling factor for the estimated barrier heights. using the assumption that all barrier crossings occur at the same attempt rate, scaling factor and attempt rate were obtained through a least squares fitting of the transition probabilities observed in our simulation times to the respective transition probabilities from Kramers theory.
The obtained rate estimates range from ns to ms and suggest that tRNA movement, rather than body and head rotation, is rate-limiting for most transitions between intermediate states of tRNA translocation.

3407-Pos Board B562
Barriers to SIRNA Transfection through a Phospholipid Bilayer
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Small interfering RNA (siRNA) molecules play a pivotal role in silencing gene expression via the RNA interference (RNAi) mechanism. SiRNA offers considerable promise for gene therapy, and substantial effort has gone into developing