2516-Pos
Do Cation-PI Interactions Occur in Lipid Bilayers Between Phosphatidylcholine Headgroups and Interfacially Localized Tryptophans?
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Lipids can modulate membrane protein activity in many different ways. To understand the basic priciples governing this complex lattice of interactions between lipids and membrane proteins, simple model peptides have been created. Among those are the families of WALP and KALP peptides, which consist of a poly-(leucine-alanine) stretch flanked by tryptophans and lysines, respectively.
Here we focused on studying how electrostatic interactions between these flanking residues and the lipid polar head groups can affect the behavior of the peptides and the lipids. We used 2H NMR on Ala-d4 labeled peptides to map changes in the orientation of the peptides in phosphatidylcholine bilayers in the absence and presence of the anionic lipid phosphatidylglycerol and we used 14N NMR to monitor changes in structure and dynamics of the phosphocholine head groups. Surprisingly, we found that WALP peptides, which are uncharged, are more sensitive to incorporation of negatively charged lipids, than their positively charged equivalents, the KALP peptides. As a possible explanation we raised the hypothesis that WALP peptides are sensitive to the concentration of phosphatidylcholine lipids in the membrane, due to favorable cation-pi interactions between the tryptophans and the choline moieties of the lipids. This hypothesis was supported by results from high resolution solid state NMR experiments, designed to monitor Trp-choline interactions. The existence of such a favorable interaction may shed new light on understanding the behavior of membrane proteins, in particular since in such proteins Trp frequently occurs as flanking residue at the lipid/water interface.

2517-Pos
Single Tryptophan Mutants of Galleria Mellonella Apolipophorin III: Binding Interaction to Lipopolysaccharides
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Apolipoproteins have been shown to interact with lipopolysaccharides, thereby providing protection against sepsis. To gain insight in the binding interaction, apolipophorin III (apoLp-III) from the Greater wax moth, Galleria mellonella, was used as a model. The protein bears a unique tyrosine residue which has been used to monitor LPS binding interaction. To improve the binding analysis, single tryptophan mutants were engineered. The introduction of a tryptophan in apoLp-III provides a stronger fluorescence signal, allowing for less protein and decreasing light scatter problems when determining the binding interaction with the three components of LPS (Lipid A, core and O-antigen polysaccharides). Five single-tryptophan mutants (F20W, L80W, L119W, I138W and F145W) were designed and produced in a bacterial expression system. The secondary structure of the mutant proteins was similar to that of the wild-type protein. The protein stability, measured as the resistance to Gdn-HCl induced denaturation, was slightly decreased. This indicates that the overall α-helical structure was not affected by the introduction of tryptophan. Upon LPS binding, the tryptophan fluorescence emission increased for I138W and F145W-apoLp-III, decreased for F20W and L119W-apoLp-III, and no significant difference was observed for L80W-apoLp-III. Thus the tryptophan residues relocate into distinct environments, indicating that the apoLp-III helices bind to different parts of LPS.

2518-Pos
Simulations of Surfactant and Lipid Assemblies with Generalized Born Implicit Solvent Models
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In recent years, all-atom and coarse-grained models have been developed for theoretical studies of surfactant and lipid assemblies. Here we describe the development of hybrid models incorporating atomic-level representation of surfactant molecules and continuum description for solvent. Specifically, we show that atomistic simulations of neutral, anionic and cationic surfactants can be performed using the generalized Born implicit solvent model by careful parameterization of atomic input radii. We applied the new models to constant pH molecular dynamics simulations of acid-base titration of fatty acid solubilized in dodecyl triehyleneglycol either (DE3), dodecylsulfaphate (SDS) and dodecyl tetramethylammonium (DTA) micelles. We show that simulation results are able to reproduce the experimental data and offer atomically detailed explanation for the abnormal titration behavior of fatty acid in cationic micelles. The combined atomistic solute and continuum solvent models significantly reduce computational and represent an attractive alternative approach for theoretical studies of interfacial phenomena involving surfactant and lipid assemblies.

2519-Pos
Voronoi Analysis of Lipid Surface Area in Protein-Membrane Systems
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All-atom molecular dynamics (MD) simulations are powerful tools to study dynamics and functions of membrane proteins at the atomic level. In these simulations, NPAT ensemble, where the cell area is fixed, has been widely used to reproduce the experimental value of lipid surface area around proteins. However, the surface area for each lipid molecule can be under- or overestimated due to the deformation of membranes. It may cause artificial conformational deviations of membrane proteins during log MD simulations. To overcome this problem, we proposed a novel algorithm to calculate the lipid surface area in protein-membrane systems using Voronoi tessellation. We analyzed 100-ns MD trajectory data of the SecY channel of *Thermus thermophilus* (ttSecYE) and *Methanococcus jannaschii* (mjSecYEβ), Fab-ttSecYE complex, and sarcoplasmic reticulum (SR) Ca^{2+}-pump in the NPAT ensemble. We found that in the simulations of Fab-ttSecYE and Ca^{2+}-pump the averaged surface area for 'bulk' lipids, which are located more than 18 Å away from the proteins, agreed with the experimental values, while slightly larger surface areas were obtained in the simulations of ttSecYE and mjSecYEβ. In order to reproduce more reliable membrane environment, we performed a short NPT simulation until the lipid surface areas only for 'bulk' lipids were converged to the experimental values, and then the cell area was fixed with the NPAT ensemble as a production dynamics. By this procedure, a more valid MD trajectory data was obtained, where the membrane thickness and order parameter of bulk lipid molecules were also consistent with the experimental values.

2520-Pos
Potential of Mean Force Between Ionizable Amino Acid Side Chains in Lipid Bilayer
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Potentials of mean force (PMF) between ionizable amino acid side chains (Arg, Lys, His, Glu/Asp) in different protonation states in palmitoyl oleoyl phosphatidylcholine lipid bilayer were obtained from all-atom explicit solvent molecular dynamics simulations and the adaptive biasing force approach available with NAMD.[1,2] Side chains (SC) were constrained in different orientations: collinear, stacked and T-shaped and placed into the bilayer interface. The most structured PMFs were observed for unlike-charged ions or pairs with neutral SCs in collinear orientation. Contact pairs (CP) occurred at a distance of 2.6-3.1 Å with the strongest interaction of −9.6 kcal/mol between Arg^+ and Glu^- ions. Like-charged SCs in this orientation displayed less stable contact minima at greater distances or solvent separated minima. All pairs in stacking approach showed similar, well-structured PMF profiles with CPs at ~3.8 Å. The strongest interaction between like-charged pairs was observed for stacked arginines. Like-charged pairs constrained in T-shaped geometry mostly displayed slightly stable solvent separated minima. A relationship between water and phosphate coordination numbers, contact pair minima and free energy barriers was found. There is also dependence of PMF shapes on H-bonding between amino acids. Generally, interactions between ionizable SCs are more attractive and the PMFs are more structured in a lipid bilayer than in water.[3]
[1] Darve, E.; Pohorille, A. *J. Chem. Phys*. **2001**, *115*, 9169.
[2] Darve, E.; Wilson, M.; Pohorille, A. *Mol. Simul*. **2002**, *28*, 113.
[3] Masunov, A.; Lazaridis, T.*J. Am. Chem. Soc.* **2003** *125*, 1722.

2521-Pos
Water Under the BAR
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The generation of high-curvature membranes by Bin/amphiphysin/Rvs (BAR) domain containing proteins is a topic of intense current interest. Details regarding the mechanism of curvature generation are debated, with some emphasizing for the importance of electrostatic attraction between the protein and the membrane, and others pointing to the insertion of amphipathic N-terminal helices. Here, we present evidence from molecular simulations of single amphiphysin N-BAR domains that, even when tightly bound to highly curved membranes, a considerable amount of water is found between the protein in the membrane.