enhanced-dynamics HMMM membrane model. For each protein, we have performed a total of 30 independent simulations with different lipid compositions (1:1 PC:PS and 7:3 PC:PS), providing robust statistics to characterize the membrane-bound form of these proteins. The results suggest that, despite the overall structural similarity, TIM1 and TIM3 establish different interactions with the membrane upon binding. Moreover, simulations show that in addition to the PS-binding pocket found in TIM proteins, other specific protein-membrane ionic interactions can be formed in each case, suggesting a molecular basis for their different biological roles.
In addition to MD simulations, the orientation of TIM1 and TIM3 in model PS-containing membranes has been characterized using X-ray scattering. The agreement between the X-ray experiments and the MD simulations provide a detailed description of the membrane-binding mechanism of TIM proteins.

1257-Pos Board B208
Anomalous Dynamics of Pleckstrin Homology Domains on Lipid Membrane Surfaces
Eiji Yamamoto[1], Antreas C. Kalli[2], Takuma Akimoto[1], Kenji Yasuoka[1], Mark S.P. Sansom[2].
[1]Keio University, Yokohama, Japan, [2]University of Oxford, Oxford, United Kingdom.
Association and diffusion of peripheral proteins to the cell membrane during many signaling and trafficking events in the cell occurs via lipid-binding modules e.g. pleckstrin homology (PH) domains. PH domains are a highly structurally conserved family of proteins which is believed to associate with various phosphatidyl inositol phosphates (PIPs) molecules in the plasma membrane thus initiating multiple signaling cascades. Despite the available structural and functional data for a variety of different PH domains the diffusive and interacting dynamics of these proteins with the lipid membrane and in particular with PIP molecules has been veiled. Using a coarse-grained molecular dynamics simulation approach, we investigate the localization and dynamic of different PH domains on a lipid bilayer surface of complex phospholipid composition. Our results demonstrate that the different PH domains associate with the PIP molecules in the membrane via a highly positively charged loop in good agreement with available experimental data. We also show that translational and rotational diffusion of PH domains on the lipid membrane surface exhibit transient sub-diffusion. Moreover, we find that fluctuations of the number of PIPs binding with the PH domains exhibit 1/f noise. Constructing a dichotomous process for the number of the PIPs, we find that the process can be regarded as a correlated renewal process where residence times are correlated.

1258-Pos Board B209
Molecular Dynamics Simulation Studies of Interactions of E. coli-K12 with OmpF in Outer Membranes: Effects of LPS Structures on Monoclonal Antibodies Binding
Dhilon S. Patel[1], Emilia L. Wu[1], Phillip E. Klebba[2], Wonpil Im[1].
[1]Center for Bioinformatics, MRB, The University of Kansas, Lawrence, KS, USA, [2]Department of Biochemistry and Molecular Biophysics, Kansas State University, Manhattan, KS, USA.
Gram-negative bacterial outer membrane, which is a highly asymmetric lipid bilayer, is composed of an outer membrane protein along with phospholipids (PLs) forming the inner leaflet and lipopolysaccharides (LPSs) forming the outer leaflet. Outer membrane protein F (OmpF) porin is a trimeric integral membrane protein responsible for the passive transport of small hydrophilic molecules such as nutrients and waste products across the outer membrane of Escherichia coli (E. coli). Here, we report the structural properties of a model of the E. coli-K12 outer membrane and its interaction with OmpF using molecular dynamics simulations. Immunochemical and other experiments suggested several cell-surface exposed epitopes (antibody binding sites), which were recognized by various monoclonal antibodies (MAbs). Molecular details of interaction between LPS core sugars and surface of OmpF suggest the importance of LPS core sugars in shielding of these epitopes. Results are compared with experimental evidence, which showed that with shortening of the LPS core sugars (rfa E. coli-K-12 mutants), the number of MAbs, that recognized porin surface epitopes, increased sequentially. To check the stabilizing effect of LPS structure on the extracellular loop conformations, results of interaction between OmpF and asymmetric E. coli-K12 bilayer are compared to those from OmpF simulations in a DMPC bilayer. In addition, overall membrane properties such as, electron density profiles, per-lipid surface area of each lipid type, and chain order parameters are compared with E.coli-K12 outer membrane in absence of OmpF. These results are also compared to our previous molecular dynamics results with E. coli-R1 outer membrane with OmpLA. Overall, membrane structural properties are comparable, however, individual lipid properties showed slight variations.

1259-Pos Board B210
Modelling Protein-Micelle Systems in Implicit Water
Rodney E. Versace, Themis Lazaridis.
Chemistry, City College of New York, New York, NY, USA.
The hydrophobic nature of membrane proteins requires their study in a membrane-mimicking environment that maintains their stability and function. This is typically accomplished using detergents above their critical micelle concentration (CMC). The ones most commonly used are dodecylphosphocholine (DPC) and sodium dodecyl sulfate (SDS). Hundreds of membrane-active peptide and protein structures have been determined by solution NMR in these detergents. However, the structure of these protein-micelle complexes is not known in atomic detail. Atomistic simulations of detergent self-assembly are computationally expensive and involve long time scales. Here, we propose modeling detergent-protein complexes using an implicit water approach. The CHARMM36 force field is used to treat the surfactant and the protein in atomic detail and the EEF1 implicit solvation model is used for water. Solvation parameters for the surfactants are adjusted to reproduce experimental aggregation numbers and CMC values for the pure micelles. To validate the approach, additional molecular dynamics simulations were performed on small membrane-active peptides to confirm the stability of their experimentally determined structures in the micellar environment. This approach provides atomically detailed information on protein-surfactant complexes at a modest computational cost.

1260-Pos Board B211
Simulations Predict 18:0-22:6 Phosphatidylserine Drives α-Synuclein into the Liquid-Disordered Phase in Synaptic Vesicle Lipid Composition
Benjamin E. Brummel.
Biomedical Engineering, University of Minnesota, Minneapolis, MN, USA.
Because α-Synuclein binds to anionic lipids and synaptic vesicles consist of 12% 18:0-22:6 phosphatidylserine (SDPS), we asked where this asymmetric lipid partitions, and how it affects α-Synuclein partitioning in a lipid raft system. Our coarse-grained molecular dynamics simulations of SDPS in a lipid raft composition show that 18:0-22:6 PS partitions to the liquid disordered phase (Ld). Additional simulations of lyso-18:0 and lyso-22:6 and subsequent energy fluctuations analysis demonstrate that SDPS partitioning to Ld is due to the 22:6 acyl-chain's greater affinity for Ld than the 18:0 chain's affinity for Lo. Furthermore, we show that α-synuclein's preference for anionic lipids drives it to join SDPS in the Ld phase. Knowing that the remainder of the synaptic vesicle composition is largely uncharged, we propose that SDPS will drive α-synuclein to Ld regions of the synaptic vesicle mixture.

1261-Pos Board B212
The Structure of a Melittin Stabilized Toroidal Pore
John M. Leveritt III.
Chemistry, The City College of New York, New York, NY, USA.
Melittin is a 26-residue lytic peptide that is more effective at degrading zwitterionic membranes than membranes containing anionic lipids. At high peptide/lipid ratios there is evidence that melittin forms toroidal pores lined by peptides and lipid head groups, as opposed to the ''barrel-stave'' model where transmembrane peptides fully line the pore in a cylindrical manner. However, the detailed structure of these pores remains unknown. Microsecond all atom molecular dynamics simulations of a closely packed tetramer were performed in an effort to determine a well-equilibrated stable pore structure. The trajectory in DMPC shows early formation of a toroidal pore which remains stable for the remainder of the 9 μs simulation. An additional 9 μs simulation from the same starting structure was performed in membranes containing 25% anionic lipids (DMPG). In that case, despite a limited initial entry of water and head groups in the membrane hydrophobic core, no stable pore was observed.

1262-Pos Board B213
Membranome: A Database of Single-Spanning Transmembrane Proteins
Andrei L. Lomize, Irina Pogozheva.
College of Pharmacy, University of Michigan, Ann Arbor, MI, USA.
The Membranome database (http://membranome.org) has been created. The database is focused on structural models of single-spanning (bitopic) transmembrane (TM) proteins and their oligomeric complexes. Current version of Membranome collects data on bitopic proteins of six model organisms, Methanococcus jannaschii, Escherichia coli, Saccharomyces cerevisiae, Dictyostelium discoideum, Arabidopsis thaliana and Homo sapiens that represent different kingdoms of life. It provides comprehensive information on more than 4,500 bitopic proteins, including their three-dimensional (3D) structures, interactions, biological functions, topology, localizations, and classification. The structural data comprise available experimental structures and 3D models of TM alpha-helices that were generated using our new thermodynamic model