This result was unexpected since it was assumed that the SDPC would be present only in the liquid disordered phase. FRET measurements using di-16:0-PE labeled with NBD and di-18:1 PE labeled with rhodamine were performed in order to monitor changes possible changes in domain size induced by the exchange of POPC for SDPC. Initial results show similar transfer efficiency between these two probes in 1/1/1 POPC/SM/chol and in 1/2/3/3 POPC/SDPC/SM/chol, suggesting the presence of SDPC does not greatly perturb domain size and structure.

3040-Pos Board B195

Improved Charmm Force Field for Polyunsaturated Fatty Acid Chains, a Study on DAPC Membranes

Viviana Monje[1], Taehoon Kim[2], Wonpil Im[2], Jeffery B. Klauda[1].
[1]University of Maryland, College Park, College Park, MD, USA, [2]The University of Kansas, Lawrence, KS, USA.

The present research is a part of a collaborative effort to improve the CHARMM[i] force field (FF) parameters, referred to as C36p, for accurate prediction of the properties of polyunsaturated fatty acid (PUFA) chains in lipid membranes. The focus of our study was to test the accuracy of C36p FF. Molecular dynamics (MD) simulations were used to study the behavior of 1,2-diarachidonyl-phosphatidylcholine (DAPC), a PUFA with two hydrophobic tails with identical degree of unsaturation. CHARMM and NAMD[ii] software packages were used to equilibrate and analyze the bilayer systems. The system consisted of a DAPC bilayer formed by 72 fully hydrated lipids with periodic boundary conditions. The simulations were performed in the NPT (constant particle number, pressure, and temperature) ensemble at 1 bar and 323.15 K for 100 ns. Simulations with the C36p FF resulted in more accurate membrane properties such as surface area per lipid, deuterium order parameters, electron density profiles, and C-H spin-lattice relaxation times.[iii] Efforts continue to improve the FF for accurate prediction on the rigidity of PUFA lipid membranes and orientation of cholesterol within these bilayers.

Endnotes

[i]CHARMM(Chemistry ar HARvard Macromolecular Mechanics). http://www.charmm.org

[ii]NAMD, Scalable Molecular Dynamics. http://www.ks.uiuc.edu/Research/namd/

[iii]Klauda, J.B.; Monje, V; Kim, T; Im, W. Improving the CHARMM Force Field for Polyunsaturated Fatty Acid Chains. *J. Phys. Chem,* **2012**, 116, 9424−9431.

3041-Pos Board B196

Interaction of α-Tocopherol with a Polyunsaturated Lipid Studied by MD Simulations

Xiaoling Leng[1], Justin A. Williams[1], Drew Marquardt[2], Norbert Kučerka[3], John Katsaras[4], Jeffrey Atkinson[2], Thad A. Harroun[2], Scott E. Feller[5], Stephen R. Wassall[1].
[1]IUPUI, Indianapolis, IN, USA, [2]Brock University, St. Catharines, ON, Canada, [3]National Research Council, Chalk River, ON, Canada, [4]Oak Ridge National Laboratory, Oak Ridge, TN, USA, [5]Wabash College, Crawfordsville, IN, USA.

Polyunsaturated phospholipids are essential components of neural membranes and their effect on membrane architecture is proposed to be the molecular origin of a myriad of health benefits. A downside of polyunsaturated phospholipids is that they are highly susceptible to oxidation due to the presence of multiple double bonds. α-Tocopherol is the most biologically active component in a family of phenolic compounds that comprise vitamin E, which is the major lipid soluble antioxidant in cell membranes. To investigate whether α-tocopherol preferentially interacts with polyunsaturated phospholipids to optimize protection against oxidation, we performed MD simulations on 1-stearoyl-2-docosahexaenoylphosphatiylcholine (SDPC, 18:0-22:6PC) and 1-stearoyl-2-oleoylphosphatidylcholine (SOPC, 18:0-18:1PC) bilayers containing α-tocopherol. SDPC with a docosahexaenoyl sn-2 chain is polyunsaturated, while SOPC with an oleoyl sn-2 chain serves as a monounsaturated control. The simulations were run under constant pressure for 200 ns on a system that comprised 80 phospholipid molecules, 20 α-tocopherol molecules and 2165 water molecules. We discovered significant differences between the two systems. Notably, α-tocopherol produces a greater increase in order parameters for the stearoyl sn-1 chain of SDPC than SOPC, suggesting stronger interaction with the polyunsaturated phospholipid, and the flip-flop of α-tocopherol across the bilayer is much faster in SDPC than SOPC. We have further quantified the interaction of α-tocopherol with phospholipid by calculating the van der Waals interaction energy between α-tocopherol and the individual lipid chains (sn-1 and sn-2) in SDPC and SOPC. Solid state NMR, neutron scattering and complementary experiments are now underway to test the predictions from the MD simulations.

3042-Pos Board B197

Cholesterol/Phospholipid Bilayer Phase Diagrams from Coarse Grained Simulations

Olle Edholm, Richard Tjörnhammar, Qaiser Waheed.
Royal Institute of Technology, Stockholm, Sweden.

Coarse grained simulations of membranes containing mixtures of phospholipids and cholesterol at different concentrations and temperatures (below and above the main transition) have been performed. Random mixing without formation of domains was observed. On the contrary, we observed that phase separated fluid systems with different cholesterol concentrations mix into uniform systems in less than 200 nsec. For the gel phase the results are less conclusive due to the two orders of magnitude slower dynamics. The gel to liquid crystalline phase transition is successively weakened by cholesterol while the phase transition temperature increases slightly.

The gel phase system undergoes a transition with increasing amounts of cholesterol from a solid ordered phase into a liquid ordered one. In the solid phase, the amplitude of the oscillations in the radial distribution functions decays algebraically with a pre-factor that goes to zero at the two-dimensional solid-liquid transition. The liquid ordered phase is characterized by liquid-like pair correlation functions that decay exponentially to one and have just one detectable peak. Angular correlation functions that measure how the orientation of the lattice vectors in the membrane plane decorrelates with distance were also calculated. They show an algebraic decay with exponent 0.15-0.25 in large regions of the solid ordered phase. This indicates that the liquid ordered phase has more structure than a two-dimensional liquid and may be a hexatic phase.

To explore further whether phase segregation into cholesterol-rich and cholesterol-poor domains is favorable from a free energy point of view, the chemical potential for cholesterol insertion into lipid bilayers at different cholesterol concentrations was calculated from simulations. This shows a small bulk free energy of about 0.3kT per lipid that favors phase separation while a small line tension (a few pN) between cholesterol-rich and -poor regions favors mixing.

3043-Pos Board B198

Molecular View of Phase Coexistence in Model Membranes

Svetlana Baoukina, Eduardo Mendez-Villuendas, D. Peter Tieleman.
University of Calgary, Calgary, AB, Canada.

We used computer simulations to investigate phase transformations in lipid monolayers. This is important for understanding lipid-lipid interactions underlying lateral organization in biological membranes, and the role of phase coexistence in the regulation of surface tension by lung surfactant. Molecular dynamics simulations with the coarse-grained force field MARTINI were employed to achieve large length (~80 nm in lateral dimension) and time (tens of microseconds) scales. Lipid mixtures containing saturated and unsaturated lipids and cholesterol were investigated under varying surface tension and temperature. We reproduced compositional lipid de-mixing and transformation into liquid-expanded (LE) and liquid-condensed (LC) phases, and into liquid-ordered (Lo) and liquid-disordered (Ld) phases. Transformation proceeded via either nucleation and growth, or spinodal decomposition, with distinct coarsening kinetics. Nucleation rate and growth exponents were calculated. Partial lipid areas and phase composition showed a different dependence on surface tension. The domain boundary length increased and the line tension decreased with reducing surface tension. Domains of Lo phase manifested spontaneous curvature at low surface tensions. The surface viscosity of monolayers with phase coexistence increased due to domain reorganization under shear. In the Lo/Ld mixture, strong compositional fluctuations were observed at higher temperatures. Monolayer collapse occurred in the disordered phase (LE or Ld), which then transferred into bilayer folds and monolayer-bilayer connection. Domains of coexisting phased either increased or reduced monolayer stability. We also investigated lipid bilayers of the same composition. Decreasing surface tension in monolayers and temperature in bilayers had similar effects on the properties of coexisting phases.

3044-Pos Board B199

Improved Coarse-Grained Modeling of Cholesterol Activation in Lipid Bilayers

Michael D. Daily[1], Brett N. Olsen[2], Paul H. Schlesinger[2], Daniel S. Ory[2], Nathan A. Baker[1].
[1]Pacific Northwest National Laboratory, Richland, WA, USA, [2]Washington University in St. Louis, St. Louis, MO, USA.