

chains order parameter dependence on coordinate for 40% cholesterol - 60% DPPC membrane, measurable in NMR experiments, is calculated analytically and compared with molecular dynamics simulation data [5]. The order parameter calculation allows for DPPC tilt angle. The model parameters found by fitting the MD data are used further to calculate lateral pressure distribution and coefficient of thermal area expansion. The microscopic model allows one to study other thermodynamic coefficients and diffusion phenomena in multi-component bilayers. 1. Mukhin S.I., S. Baoukina, Analytical derivation of thermodynamic characteristics of lipid bilayer from a flexible string model. *Phys. Rev. E*. 71: 061918 (2005). 2. Mukhin S.I., B.B. Kheifets, Analytical approach to thermodynamics of bilipid membranes. *Phys. Rev. E*. 82: 051901 (2010). 3. Mukhin S.I., B.B. Kheifets, Pore formation phase diagrams for lipid membranes. *JETP Lett.* 99: 358-362 (2014). 4. Edholm O., J.F. Nagle. Areas of Molecules in Membranes Consisting of Mixtures. *Biophys. J.* 89: 1827-1832 (2005). 5. Hofsass C., Lindahl E., and Edholm O. Molecular Dynamics Simulations of Phospholipid Bilayers with Cholesterol. *Biophys. J.* 84: 2192-2206 (2003).

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Simulation Study of Composition Fluctuations in Lipid Bilayers

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Lipid bilayers constitute the basis of biological membranes. Understanding lipid mixing and phase behavior can provide important insights into membrane lateral organization (the raft hypothesis). Here we investigate model lipid bilayers below and above the miscibility transition temperatures. Molecular dynamics simulations with the MARTINI coarse-grained force field are employed to model bilayers on a length scale approaching 100 nm laterally and a time scale of tens of microseconds. We simulate lipid mixtures containing saturated and unsaturated lipids, and cholesterol at different concentrations and temperatures between 270 and 340 K. The coexistence of liquid-crystalline and gel, as well as liquid-ordered and liquid-disordered phases is reproduced. We induce a gradual transition from phase separation to mixing by raising the temperature and adding hybrid lipids (with a saturated and an unsaturated chains). The evolution of bilayer properties along this transition is analyzed. Domain size and phase boundary length, the length and time scales of composition fluctuations, and inter-leaflet coupling are quantified. The results allow characterizing partitioning of hybrid lipids between the coexisting phases, their role in composition fluctuations, and also the effect of spontaneous curvature on composition fluctuations. Curved domains are observed in both symmetric and asymmetric bilayers (with different composition of the two leaflets).

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Fatty Acid Interactions with RNA Building Blocks: Origin of Life Implications

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Several experimental and computational methods have been used to address important questions regarding fatty acid interactions with RNA building blocks that have implications in the origins of life^{1,2,3}. A recent study by Keller et al.² showed that nucleobases can bind to and stabilize the aggregation of prebiotic amphiphiles, which could support a possible mechanism for the emergence of protocells. Some nucleobases were found to bind stronger to the aggregates of putative prebiotic amphiphiles. Among carbohydrates, ribose has shown a greater potential to permeate through bilayers compared to its diastereomers. This is fundamentally interesting; as ribose/deoxy ribose are sugars found in RNA and DNA. The mechanisms, however, are not fully understood. We use molecular dynamics simulation to systematically study the permeation of furanose and pyranose carbohydrates as well as RNA nucleobases through different fatty acid bilayers as models of prebiotic conditions. The membrane fluidity and hydrogen bonding interactions have found to play significant roles in selective permeability. References:

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Open Collaboration that uses NMR Data to Judge the Correctness of Phospholipid Glycerol and Head Group Structures in Molecular Dynamics Simulations

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Tampere, Finland, ⁴Department of Chemical Engineering, Kyoto University, Kyoto, Japan, ⁵Fachbereich Physik, Freie Universität Berlin, Berlin, Germany, ⁶IBCP, CNRS UMR 5086, Lyon, France, ⁷Aalto University, Espoo, Finland, ⁸Max Planck Institute for Chemical Energy Conversion, Mülheim an der Ruhr, Germany, ⁹INSERM, U1134, DSIMB; Institut National de la Transfusion Sanguine (INTS); Laboratoire d'Excellence GR-Ex, Paris, France.

We compare the C-H order parameters measured by Nuclear Magnetic Resonance (NMR) experiments to those predicted by 12 different molecular dynamics (MD) simulation models. We focus on the order parameters of the lipid headgroups and glycerol backbones in phospholipid bilayers.

Only two of the models (CHARMM36 [1] and Maciejewski-Rog [2]) give a reasonable agreement with experiments for a fully hydrated lipid bilayer.

We then compare (for the two best-performing models at full hydration and for the Berger model [3], the most used lipid model in the literature) to NMR experiments the changes in the order parameters as a function of hydration level, NaCl and CaCl₂ concentrations, and cholesterol content. The results clearly show that the glycerol and headgroup structures in the Berger model are not realistic, the Na ion partitioning is significantly too strong and cholesterol-induced structural changes are overestimated. The CHARMM36 and Maciejewski-Rog perform better, but the Na partitioning is too strong at least in the latter.

This is an open science project that is progressed at nmrlipids.blogspot.fi. All the results and discussions are available at that address.

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Solid-State 2H NMR Investigation of Transducin Activation by Rhodopsin

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X-ray structures of active-state rhodopsin (Meta-II) and the cognate G-protein transducin are available, yet the transducin activation mechanism by rhodopsin is still obscure due to lack of atomistic dynamical information. We are studying the conformations of retinal in active Meta-II, and how the presence of the all-trans retinal agonist yields substantial differences in activation of transducin compared to opsin. Solid-state NMR spectroscopy gives information pertaining both to structures and dynamics, and is a powerful method to study how rhodopsin activates transducin. Experiments are currently underway with selectively deuterated retinal in aligned membrane samples containing active Meta-II [1]. Simulation of the 2H NMR lineshape of the aligned samples in terms of a static uniaxial distribution reveals the bond orientations of retinal methyl groups and mosaic spread, which represents the alignment disorder of the stacked membranes [2,3]. Comparison with the solid-state 2H NMR spectra predicated by published X-ray results enables proposed structures for active Meta-II to be tested [4]. Moreover, the solid-state 2H NMR spectral lineshapes show the role of dynamical fluctuations of the protein. We are also conducting solid-state 2H NMR experiments with deuterated C-terminal peptide of transducin to study the interaction between the G-protein and the rhodopsin transmembrane helices. Our hypothesis is that association and dissociation cycles of transducin depend on the relationship between the local dynamics of peptide and the fluctuations of rhodopsin helices. Solid state 2H NMR experiments can not only tell us how rhodopsin activates transducin, but also can reveal the general mechanisms whereby GPCRs activate the cognate G-proteins. [1] A.V. Struts et al. (2011) *PNAS* 108, 8263. [2] X. Xu et al. (2014) *Encycl. Mag. Res.* 3, 275-286. [3] B. Mertz et al. (2012) *BBA* 1818, 241-251. [4] A.V. Struts et al. (2007) *JMB* 372, 50-66.

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n-3 PUFA-Containing Phospholipids Studied by MD Simulations: A Comparison of EPA, DPA and DHA

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A wide range of health benefits is associated with consuming omega-3 polyunsaturated fatty acids (n-3 PUFA) from marine oils. Eicosapentaenoic acid