

NMRLipids IV: Other than PC headgroups

O. H. Samuli Ollila^{1,*}

¹University of Helsinki

(Dated: February 16, 2017)

Primarily measured but also simulated NMR order parameters will be collected also for other than phosphatidylcholine (these are discussed in NMRLipids I) headgroup. The information will be used to understand structural differences between different lipid molecules in bilayers.

INTRODUCTION

Phospholipids containing various polar headgroups and acyl chains are essential building blocks of biological membranes. Atomistic level structural details of lipids and lipid-ion interactions are considered highly important in several biological processes. The lipid structure and ion binding can be studied in detail with NMR spectroscopy. However, the structural interpretation of NMR data requires usage of models. The combination of classical molecular dynamics simulations with NMR data, especially with C-H bond order parameters, can potentially give atomistic resolution interpretation of structure and dynamics of molecules [1–3].

Our recent studies concluded that MD models are capable to give structural interpretation for phosphatidylcholine hydrophobic acyl chain region, while hydrophilic headgroup, glycerol backbone and cation binding posed a major challenge for current force fields [1–4]. These conclusions were reached by reviewing extensively available experimental data from various sources and using NMRLipids Open Collaboration project to collect massive amount of simulation data [1, 4].

Here we apply the same approach in search of MD simulation models which would reproduce glycerol backbone and headgroup structures of lipids with PE, PG and PS headgroups. In addition, we attempt to find a MD simulation model that would be able to correctly describe cation binding in bilayer containing negatively charged PG and PS lipids.

EXPERIMENTAL GLYCEROL BACKBONE AND HEADGROUP ORDER PARAMETERS FOR PE, PG AND PS LIPIDS

Experimental order parameters for different lipid headgroups are collected in Fig. 1.

GLYCEROL BACKBONE AND HEADGROUP ORDER PARAMETERS FOR PE, PG AND PS LIPIDS IN SIMULATIONS

1.Simulation data for lipids with different headgroups to be collected

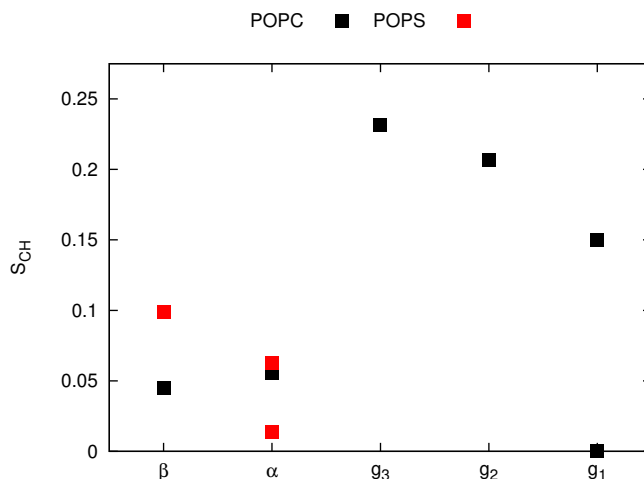


FIG. 1: Order parameters for headgroup and glycerol backbone with different headgroups

CA²⁺ BINDING IN BILAYERS WITH NEGATIVELY CHARGED PG AND PS LIPIDS

Ion binding affinity in lipid bilayer containing PC lipids can be measured by using C-H bond order parameters for headgroup α and β carbons by using the electrometer concept. The decrease of these order parameters is linearly proportional to the amount of bound charge in bilayer [4?]. The electrometer concept can be used also for bilayers containing PC lipids mixed with charged lipids [7? ?]. This is demonstrated in Figs 2, 3 and 4, where PC headgroup order parameters as a function of CaCl_2 concentration are shown from experiments with POPC and PS or PG.

Order parameters increase when PS or PG are mixed with PC in the absence of additional ions, as seen from Figs. 2 and 3. In electrometer concept this is explained by the tilting of headgroup more parallel to membrane normal [?]. The order parameter decrease with increasing CaCl_2 concentration is explained by the tilting of headgroup more perpendicular to membrane normal. This decrease is shown to be a good measure for the amount of bound ions in lipid bilayer with PC lipids [4?].

The order parameter decrease as a function of added CaCl_2 for systems with different amount of negative charge are shown in Fig. 4. As expected, the order parameter decrease is more pronounced with increasing amount of negatively

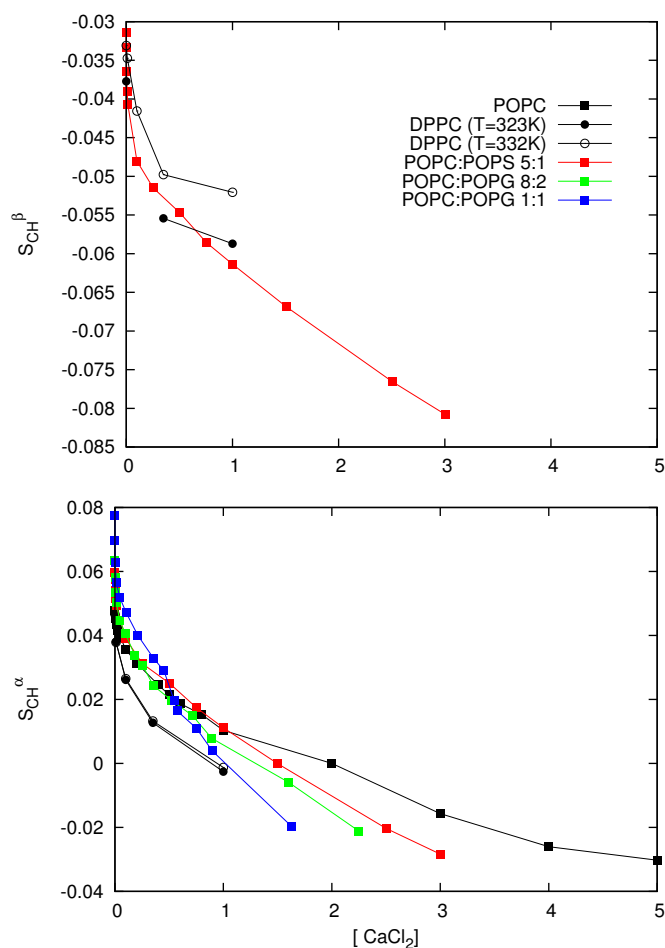


FIG. 2: PC headgroup order parameters as a function of CaCl_2 concentration from experiments containing charged lipids. Pure DPPC data from [5], pure POPC data from [6], POPC:POPS mixture data from [7] and POPC:POPG mixture data from [8].

2. Check the NaCl concentrations in the samples.

charged lipids in bilayer. This is explained by the increase of cation concentration in proximity of bilayer containing negatively charged lipids [?].

In addition to the changes in PC headgroup order parameters with ion binding, also changes in PS and PG headgroup order parameters are measured. 3. Add this data.

CA²⁺ BINDING IN BILAYERS WITH NEGATIVELY CHARGED PG AND PS LIPIDS IN SIMULATIONS

4. Simulation data for systems with negatively charged lipids and CaCl_2 to be collected

CONCLUSIONS

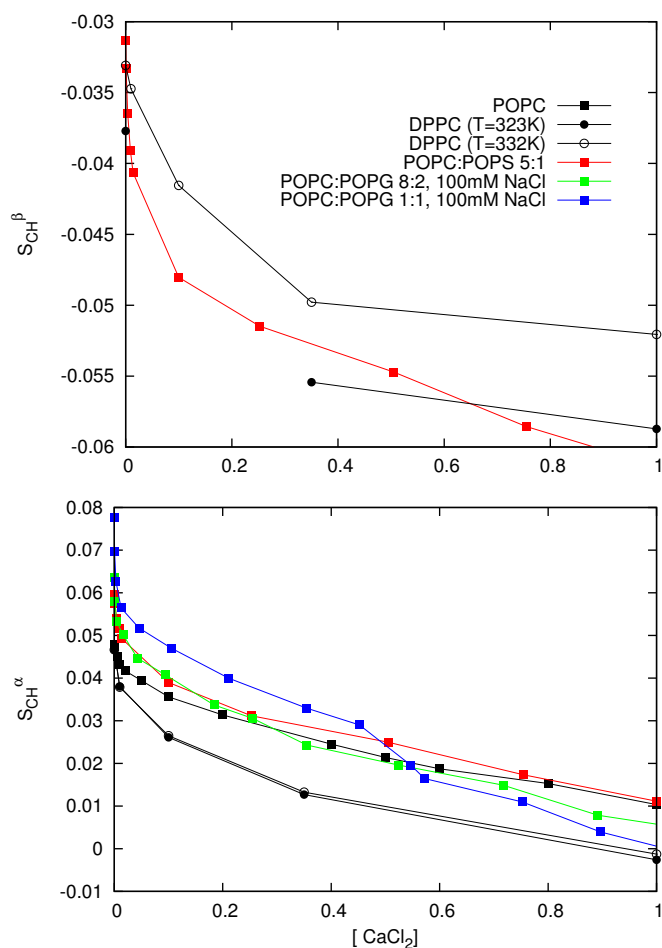


FIG. 3: Figure 2 zoomed to smaller concentrations.

SUPPLEMENTARY INFORMATION

* samuli.ollila@helsinki.fi

- [1] A. Botan, F. Favela-Rosales, P. F. J. Fuchs, M. Javanainen, M. Kanduč, W. Kulig, A. Lamberg, C. Loison, A. Lyubartsev, M. S. Miettinen, et al., *J. Phys. Chem. B* **119**, 15075 (2015).
- [2] O. S. Ollila and G. Pabst, *Biochimica et Biophysica Acta (BBA) - Biomembranes* **1858**, 2512 (2016).
- [3] T. M. Ferreira, R. Sood, R. Bärenwald, G. Carlström, D. Topgaard, K. Saalwächter, P. K. J. Kinnunen, and O. H. S. Ollila, *Langmuir* **32**, 6524 (2016).
- [4] A. Cate, M. Girych, M. Javanainen, C. Loison, J. Melcr, M. S. Miettinen, L. Monticelli, J. Maatta, V. S. Oganessian, O. H. S. Ollila, et al., *Phys. Chem. Chem. Phys.* **18**, 32560 (2016).
- [5] H. Akutsu and J. Seelig, *Biochemistry* **20**, 7366 (1981).
- [6] C. Altenbach and J. Seelig, *Biochemistry* **23**, 3913 (1984).
- [7] M. Roux and M. Bloom, *Biochemistry* **29**, 7077 (1990).
- [8] P. M. Macdonald and J. Seelig, *Biochemistry* **26**, 1231 (1987).

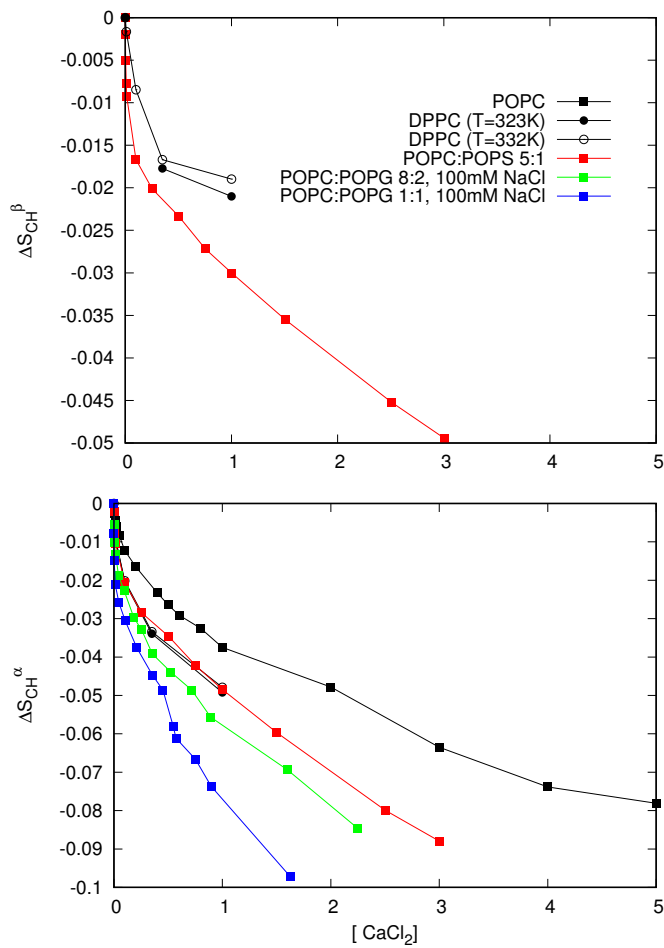


FIG. 4: Changes in order parameters

ToDo

P.

- 1. Simulation data for lipids with different headgroups to be collected 1
- 2. Check the NaCl concentrations in the samples. 2
- 3. Add this data 2
- 4. Simulation data for systems with negatively charged lipids and $CaCl_2$ to be collected 2