Experimental report

04/05/2017

Proposal: 8-04-782 **Council:** 4/2016

Title: Hydration dependend QENS studies of phopholipid membranes to validateand improve MD simulatons at the short-time regime

Research area: Physics

This proposal is a new proposal

Main proposer: Lisa LAUTNER

Experimental team: Marvin BERLINGHOF
Lisa LAUTNER

Local contacts: Tilo SEYDEL

Samples: C36H72NO8P
C42H82NO8P

Instrument	Requested days	Allocated days	From	To
IN16B	2	2	01/06/2016	03/06/2016
IN5	1	2	30/05/2016	01/06/2016

Abstract:

MD simulations are often used for intensive studies on complex biological systems as for example membranes, where experiments are limited. In order to validate the simulations on atomistic time scales complementary methods are necessary. Here, on this scales the neutron scattering experiments are ideally suited to verify the simulations and improve the force fields.
We intend to study the short-time dynamics in mimic membranes and use the calculated intermediate scattering functions to validate our MD simulations. Therefore, we compared our QENS measurements from the time-of-flight spectrometer TOFTOF (MLZ, Garching) and from IN16B (ILL, Grenoble) on different membrane systems to MD simulations. With decreasing times and distances the simulation data increasingly deviate from the experimental scattering functions due to the incorrectly reproduced water dynamics. The aim of the proposed experiment is to measure the contribution of the hydration and bulk water to the scattering function in order to extract the lipid dynamics from the data and compare it to the corresponding dynamics of the simulation which is believed to describe the lipid dynamics correctly.

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EXPERIMENTAL REPORT

Experiment Title

Hydration dependent QENS study of phospholipids

Proposal number	**8-04-782**
Instrument	**IN5, IN16B**
Date of Experiment	**30.05.16-03.06.16**
Local Contact	**Tilo Seydel, Jacques Ollivier**

Experimental Team

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Molecular Dynamics (MD) simulations are used for intensive studies on complex biological system as i.a. biological membrane mimics. The simulations mostly are validated with different experiments On large time and length scales, simulations are validated with experimental parameters and are able to reproduce the structure and dynamics very well. But at atomistic scales a complementary method which is sensitive in this regime is necessary. Quasielastic Neutron Scattering (QENS) experiments are ideally suited due to their high spatial as well as temporal resolution to validate the simulations and develop the force fields further. Nevertheless, there are so far almost no comparisons of MD simulation data with neutron scattering experiments for the pico- to nanosecond dynamics of biological membranes. Although many important biological processes i. a. signal transport or interactions between lipids and proteins take place in this short-time regime.

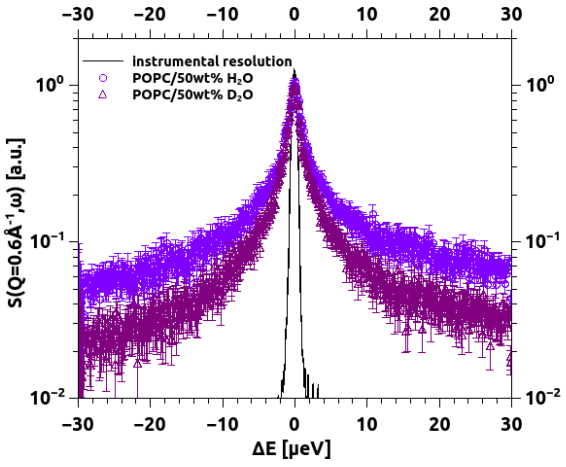

Figure 1: Scattering functions of POPC hydrated with 50 wt% of H_2O (bright violett) and 50 wt% of D_2O (violett). The hydrogen molecules of the POPC/H_2O samples cause the increase of the scattering.

We used the backscattering spectrometer IN16B (ILL, Grenoble, France) in combination with the time-of-flight instrument IN5 (ILL) to measure the scattering function of D_2O and H_2O. In order to analyse the contribution of the bulk water in the scattering function, we performed QENS experiments on multilamellar phospholipid 1-palmitoyl-2-oleoyl-sn-glycero-3-phosphocholine (POPC) bilayers in the liquid-crystalline L_α-phase (cf. Fig. 1) with three different D_2O as well as the same three H_2O concentrations. Below, at and above the fully hydrated state. Furthermore, H_2O and D_2O were measured. For the

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IN5 measurements, wavelengths of 5 Å and 10 Å and a chopper speed of 12000 rpm, respectively, were chosen. These led to energy resolutions of approximately 80 µeV and 10 µeV. At IN16B a wavelength of 6.271 Å and a chopper speed of 7100 rpm was adjusted which results in a energy resolution of about 0.75 µeV. The samples were measured in thin-walled aluminum hollow cylinders. Vanadium foil in a hollow aluminium cylinder was measured to determine the instrumental resolution. The samples were kept at 300 K during the measurements. Using both instruments enables to obtain a large time range which is best-suited to validate the MD simulations by comparing the intermediate scattering functions from both, experiment and simulation.

The software package lamp [https://www.ill.eu/instruments-support/computing-for-science/cs-software/all-software/lamp/] was used to treat both, the IN5 and the IN16B raw data. The measured spectra were treated according to [1]. The spectra were normalized using the vanadium standard, than corrected for self-absorption effects and detector efficiency, the empty can was subtracted, and finally ,in the case of the IN5 data, the corresponding spectra were converted to $S(Q,\omega)$ with the same Q-values as obtained by IN16B.

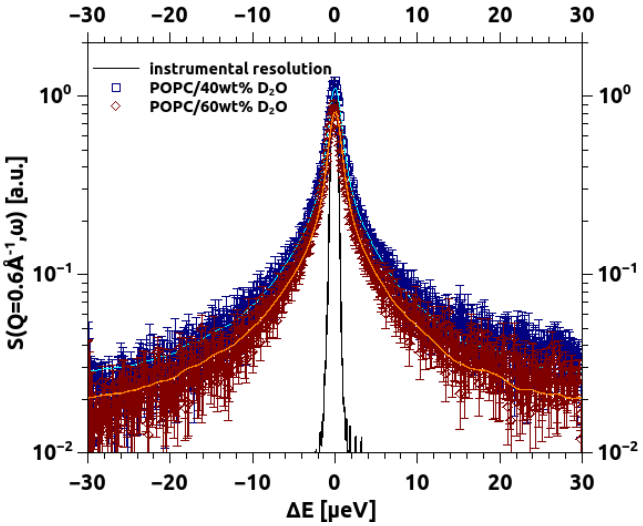

Figure 2: QENS data of a POPC multilamellar liquid-crystals with 40 wt% D_2O (blue squares) and POPC with 60 wt% D_2O at 300 K. The red curve represents the best Lorentzian fit. The solid lines represent the best fits.

In a first step the POPC/D_2O samples with the three different hydration amounts were fitted using the fit program fabada [2]. The POPC data were fitted using two Lorentzian functions, one for the fast internal lipid motions, and one for the lateral lipid motion, and convoluted with the instrumental resolution. Figure 2 displays the IN16B measurement of POPC with two different D_2O concentrations, namely 40 wt% and 60 wt%. The solid lines represent the best fits. The fit results indicate, that the lower hydration results in a lower lipid long-range diffusion ($D_{40wt\%}$ = 28 cm²/s and $D_{60wt\%}$ = 30 cm²/s). The thereby determined scattering function of the lipid dynamics will be used to subtract the lipid contribution in the POPC/H_2O samples to determine the proportion of bound water molecules to the lipid head groups and the bulk water. Finally, the results can be used to improve our MD simulations.

[1] S. Busch *et al.*, *J. Am. Chem. Soc.*, 2010, **132**, 3232-3233
[2] L. C. Pardo *et al.*, *J. Phys.: Conf. Ser.* 2011, **325**, 012006