Experimental Report

14/01/2014

Proposal: **8-04-663** **Council:** 4/2012

Title: Dynamics of phospholipid membranesaltered by fragments of the Alzheimer's disease peptide amyloid-beta

This proposal is a new proposal

Researh Area: Biology

Main proposer: **KARASTANEVA Hristina**

Experimental Team: HAUSS Thomas
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Samples: C36H18NO8PD54
c203h311n5o60s,
C34H65NO10P

Instrument	Req. Days	All. Days	From	To
IN5	7	2	01/12/2012	03/12/2012
IN16	7	6	23/11/2012	29/11/2012

Abstract:

The peptide Amyloid-ß (Aß is the main constituent of senile plaques and is a pathological hallmark in Alzheimer's disease. Recently, we have investigated how the fragment Aß(25-35) and Aß(22-40) influence the dynamics in phospholipid membranes [1,2]. Most important, we could demonstrate, that the insertion of Aß fragments into DMPC/DMPS membranes increases the lateral diffusion velocity, especially in the liquid-crystalline phase. This phase is the biologically most relevant one. The published results where obtained on the time-of-flight spectrometer NEAT with an energy-resolution 93 µeV. Here, we like to confirm and extend these results with a better energy-resolution of approx. 1 and 15 µeV.

Report: **ILL Experiment 8-04-663**
Instrument: **IN16/IN5**
Experiment Dates: **23/11/2013-03/12/2013**
Experiment Title: **Dynamics of Lipids + Amyloid – β**

Experimental Team:
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The emerging trend for the explanation of neurodegeneration in Alzheimer's disease imputes the cause of neurotoxicity to the interaction of soluble amyloid-β peptides with neural cells. Amyloid-β (Aβ) peptides are peptides naturally found in the cerebrospinal liquids, and little is known about their physiological function.

Previously, we have investigated the influence of fragments Aβ (22-40) and Aβ (25-35) on the lipid dynamics of phospholipid membranes [1,2]. We found that they accelerated the long-range translational diffusion of the lipid molecules on the ps time scale.

We conducted two quasi-elastic neutron scattering experiments, using IN16 and IN5. Two samples were observed, (1) an anionic lipid membrane consisting of 92 mg DMPC and 8 mg DMPS and (2) the same membrane with an added 4mg of amyloid – β (22-40) peptide fragment. The samples were ~100 mg of material on both sides of a thin quartz slide. The lipids form 2d bilayer stacks spontaneously, leading to well oriented samples. These two samples were scanned both in-plane (135° orientation to neutron beam) and out-of-plane (45° orientation to neutron beam), as is shown in Figure 1.

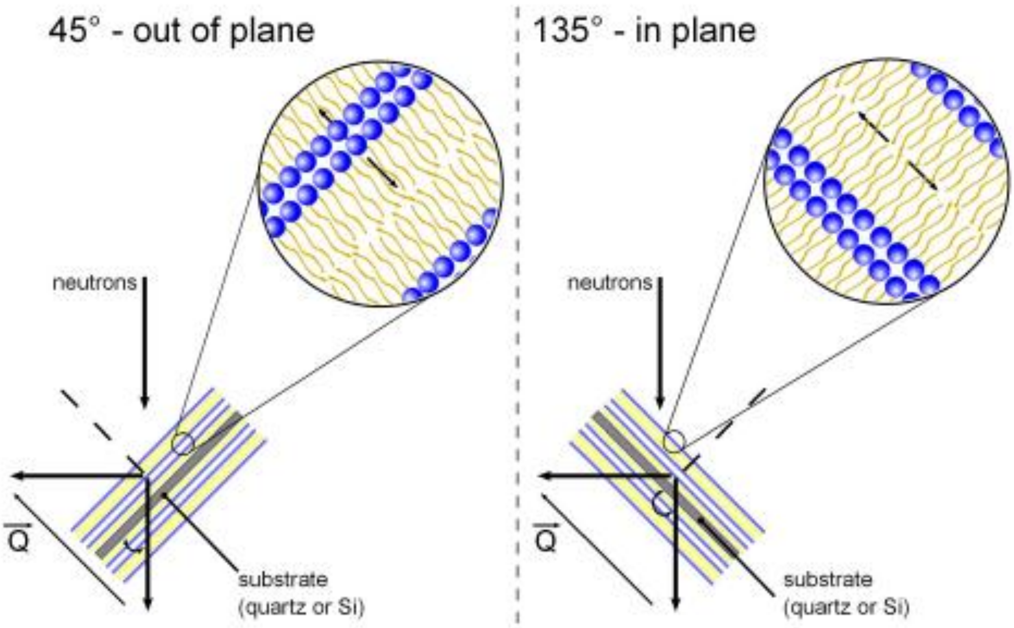


Figure 1. Out-of-plane and in-plane scattering geometries.

The samples were scanned at a low temperature, 15°C (288 K) and high temperature 30°C (303 K) to observe the membrane above and below the main phase transition temperature of 24°C (297 K). The lower temperature corresponds to a gel or ripple phase, and the high temperature to the liquid phase of the membrane.

Scans were taken with IN16 set to an energy resolution of 1 μeV, λ=6.3 Å^{-1}, and IN5 at 15 μeV and λ=10 Å^{-1}.

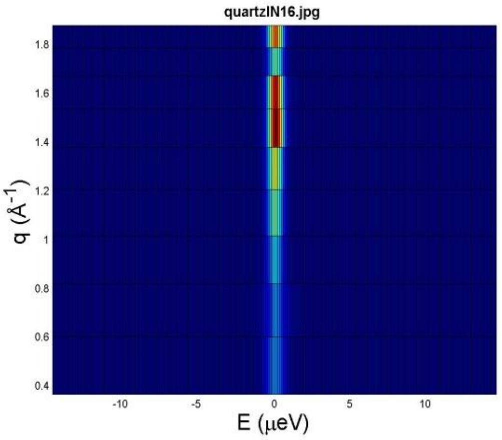


Figure 2. IN16 scan of quartz substrate without sample. Note the large elastic peak centered around 1.5 Å^{-1}.

The data was reduced using the standard procedure for IN16 and IN5 in LAMP, then imported to Matlab, where further analysis was performed. There was a broad peak observed around 1.5 Å^{-1}, thought to originate from an elastic peak from the quartz substrate, shown in Figure 2 This was fit and subtracted from the data during the analysis steps.

The general shape of the quasi-elastic broadening could be well fit with two Lorentzians convoluted with the elastic instrumental resolution (as determined by a scan of Vanadium). See an example of a typical fit in Figure 3.

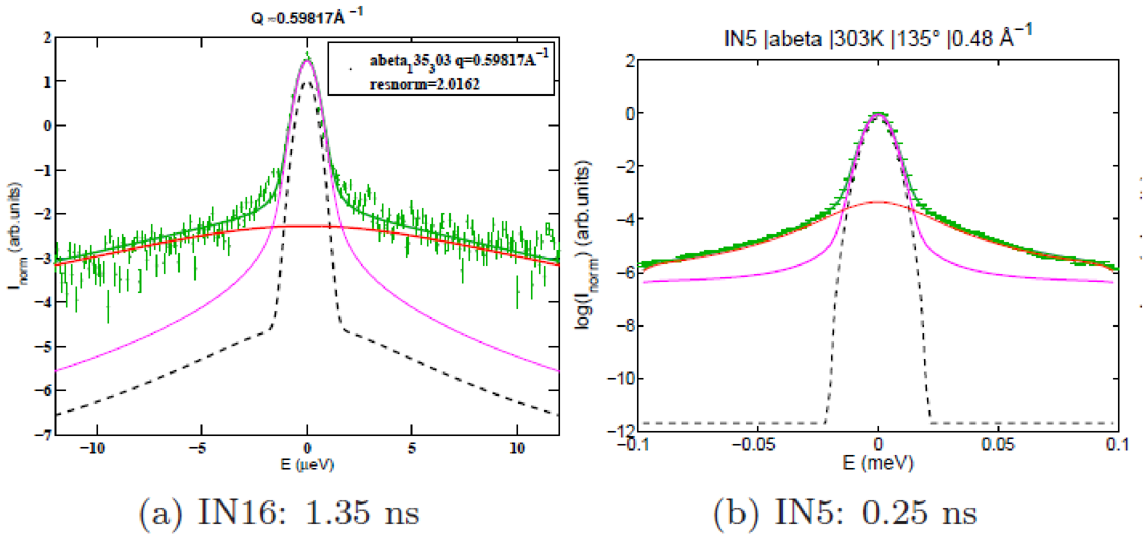
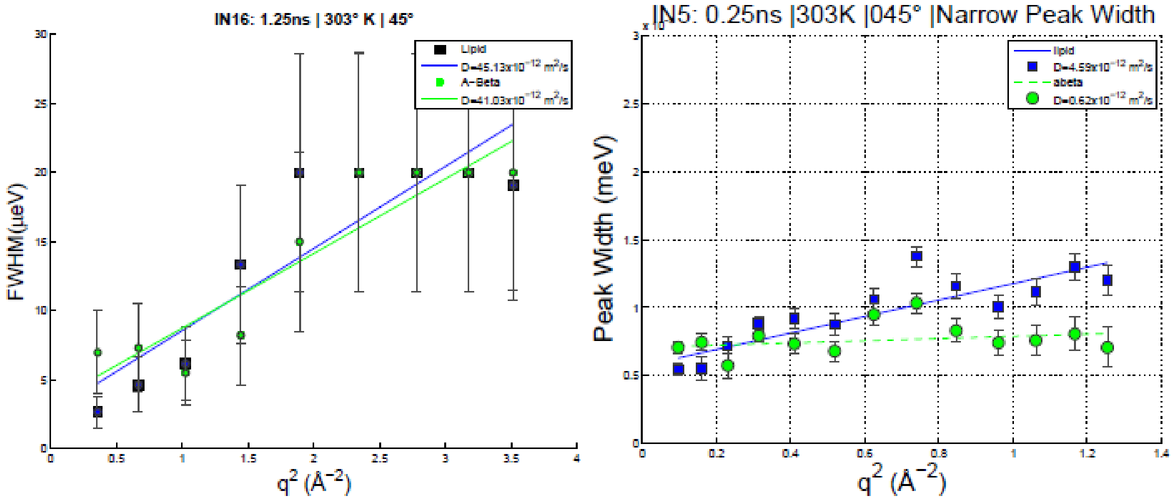


Figure 3. Exemplary fits of the quasi-elastic broadening at 303 K and 135°. (a) IN16, q=0.6 Å^{-1} and (b) IN5 at q=0.48 Å^{-1}. Note the y-axis (intensity) of both plots is displayed logarithmic.

The broadening of these fitted peaks, as a function of q-value was then plotted to calculate the diffusion constant corresponding to lipid tail motion, as shown in Figure 4.

A preliminary look at these diffusion constants shows that in the lower temperature range the addition of the amyloid-β peptide causes a small increase in the out of plane diffusion, but no significant change in-plane. For the high temperature scans, the addition of this peptide seems to lower the diffusion constant, as in Figure 4.



(a) IN16: 1.35 ns (b) IN5: 0.25 ns

Figure 4. Exemplary quasi-elastic broadening plotted against q^2 for 303 K and 45° orientation. The blue line is a linear fit to the pure lipid data, and the green a linear fit to the lipids with amyloid-β.

[1] A. Buchsteiner, *et.al.*, BBA-Biomembranes 1798, 1969-1976, 2010

[2] A. Buchsteiner, T. Haußß, N. A. Dencher, Soft Matter 8, 424-429, 2012