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Experimental Report

The interaction between amyloid-β peptides and model membrane containing cholesterol and/or melatonin

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The changes to the structural properties of membrane - most likely underlying its functionalities - are known to be accompanied by the changes in membrane physico-chemical properties. The cholesterol increases the order of lipid hydrocarbon chains and increases the stiffness of membrane.[1] On the other hand, melatonin increases the fluidity of membrane and counteracts the effect of cholesterol.[2] Intriguingly, decreasing levels of melatonin in the brain tissue were correlated with the aging, suggesting the melatonin's potential role in preventing the development of Azheimer's disease (AD) whose probability also increases with age.[3]

We followed up on our previous studies investigating the effect of the addition of cholesterol and/or melatonin on the structural properties of model phospholipid membranes.[4] The current measurements have attempted to investigate the interactions of such membranes with amyloid-β (Aβ) peptides, which are one of the hallmarks of AD. Based on the previous results, we have focused on the system with high levels of cholesterol and melatonin - separately as well as together - which revealed the considerable changes to the membrane structural properties previously, while not resulting in any disruptions of the system.

The samples of DOPC bilayers, and those with 29 mol% cholesterol, melatonin, and cholesterol and melatonin, with the addition of 3 mol% of transmembrane Aβ segment A$\beta_{25\text{-}35}$ were prepared according to the well established procedure. The time-of-flight (TOF) small angle neutron diffraction (SAND) measurements however provided images of a very low quality that did not allow to reconstruct the neutron scattering length density profiles. The existence of a single diffraction order, which is spread over a wide range of omega angles (omega being an angle of sample) – a long diagonal line in Figure 1 – suggests a high misorientation of stacked bilayers.

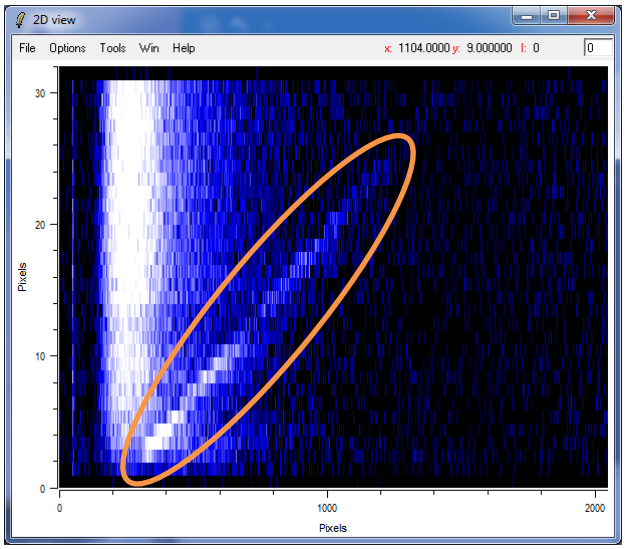

Figure 1: 2D TOF image obtained in 1 hour acquisition. The X axis corresponds to the detector TOF channels (i.e., neutron wavelength), and the Y axis corresponds to its horizontal position (i.e., diffraction angle).

The samples were subjected to the further annealing that improved their mosaicity, and the acquisition times were extended up to 15 hours in order to improve the statistics of data. The resulting diffraction curves nevertheless display up to 2 diffraction orders only, while the Fourier transform based analysis requires 4 peaks at a minimum.[5]

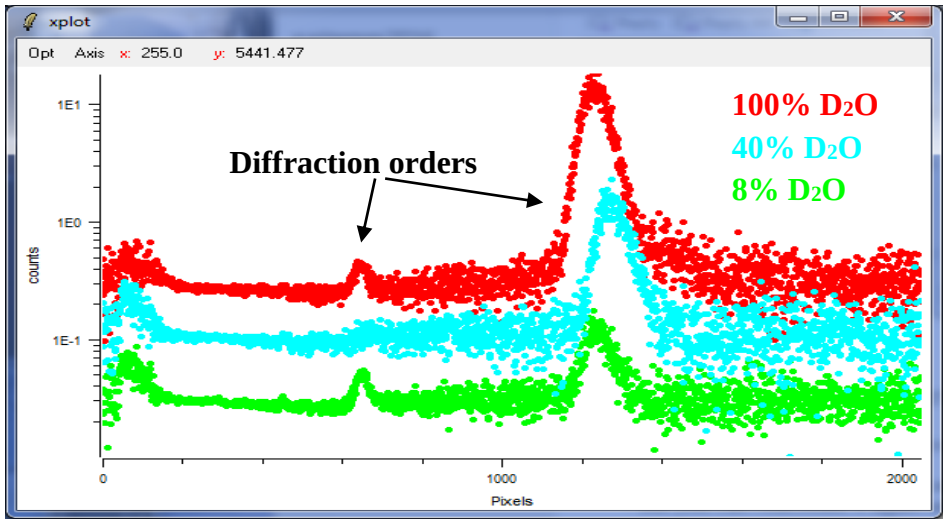

Figure 2: 1D diffraction curves reduced from 2D TOF images and normalized per neutron spectrum using vanadium standard. The X axis corresponds to the diffraction angle, while Y axis depicts the diffraction intensities. The example shows data obtained for the stacked bilayers hydrated with various D_2O/H_2O contrasts (shifted vertically for the clarity of presentation).

Conclusions

Our observations suggest that the addition of Aβ peptide affects the structure of stacked bilayers by increasing their mosaicity. We will focus in future on improving the sample preparation procedure to overcome this difficulty. In addition, the acquisition times utilized in this study appears to suggest low neutron flux on the DN2 instrument, which may require a substantial extension of exposures in future measurements.

References

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