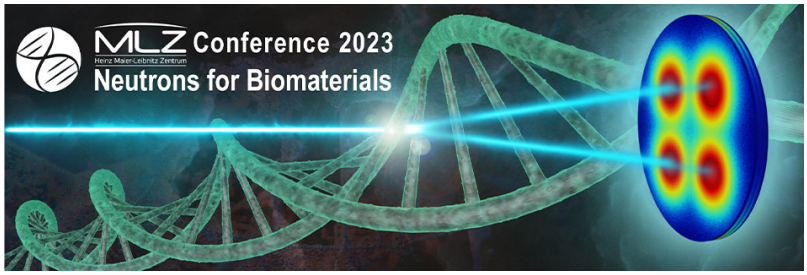

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The role of charge for interactions intrinsically disordered proteins with bio-membranes.

Thursday, 25 May 2023 11:00 (20 minutes)

Intrinsically disordered proteins (IDPs) are a class of proteins that do not have a defined three-dimensional structure but may fold if a binding partner is present. In our current research we focus on the interaction of two neuronal IDPs with bio-membranes where binding to the membrane induces configurational changes or folding:
α-Synuclein (αSyn) is associated with various neurogenerative disorders, including Parkinson's disease, which is characterized by fibril formations in the human brain. αSyn plays an important role in synaptic vesicle trafficking and is involved in membrane interactions[1,2]. NMR and MD simulation showed that αSyn interacts with the membrane by partially forming α-helices, starting at the N-terminus and including a kink in the alpha helix. The fraction of αSyn in the bound α-helical state at the N-terminal increases with the amount of charged lipids in the membrane [3]. While the disordered C-terminal region stays disordered. Interaction of αSyn with differently charged lipid bicelles was measured by Circular Dichroism (CD) Spectroscopy at SOLEIL and showed increasing of α-helical structure for charged membranes.
Synaptobrevin-2 (Syb2) is a vesicle-associated integral membrane protein. Syb2 plays an important role in vesicular membrane fusion at the neuronal synapse by participating in the dynamic formation of the SNARE complex. Syb-2 anchors with a short transmembrane region to the membrane and has a large intrinsically disordered soluble region (1-96) which shows a gradually increasing rigidity from the N to C terminus that correlates with an increase in lipid binding affinity.
One of the techniques is Neutron Reflectometry, which we plan to use to investigate the interaction of αSyn and Syb2 with membranes (DMPC/DMPG) of varying charge composition (fraction of negative DMPG in neutral DMPC) to examine the configuration in/at the membrane and in the adjacent solution.

[1] Gitler et al., Proc. Natl. Acad. Sci. U. S. A. 2008, 105, 145.
[2] Bellani et al., Common. Integr. Biol. 2010, 3, 106.
[3] Viennet et al., Commun. Biol. 2018, 1, 1.

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