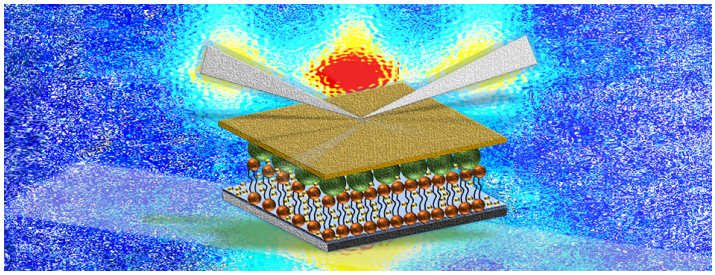

Beitrag ID: **58** Typ: **Talk**

The Influence of Charge on the Interaction Between Intrinsically Disordered Proteins and Phospholipid Membranes: A Neutron Reflectometry Examination of α-Synuclein and Synaptobrevin-2

Donnerstag, 10. Oktober 2024 13:45 (15 Minuten)

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]. NMR and molecular dynamics (MD) simulation revealed that αSyn can interacts with the membrane by forming α-helices at its N-terminus, which include a kink in the helical structure. The fraction of αSyn in the bound α-helical state at the N-terminal increases with the amount of charged lipids in the membrane [2], while the disordered C-terminal region remains 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 (TMR) 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 [3].
Further characterization of αSyn and Syb2 with membrane interactions using neutron reflectometry revealed insights into the protein's configuration both within the membrane and in the adjacent solution. We examined membranes with varying charge compositions to understand how different lipid environments influence the protein's behavior.

[1] Gitler et al., Proc. Natl. Acad. Sci. U. S. A., 105(1), 145-150 (2008)
[2] Viennet et al., Commun. Biol., 1, 44 (2018).
[3] Lakomek et al., Proc. Natl. Acad. Sci. U. S. A., 116, 8699–8708 (2019)

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