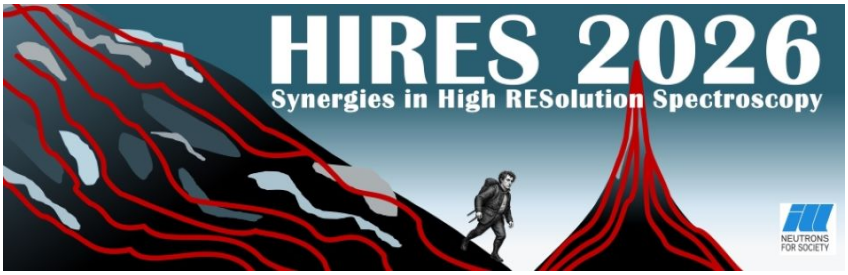

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Using QENS to Probe the Dynamics of the Tau Protein under Liquid-Liquid Phase Separation

Tau is an intrinsically disordered protein (IDP) expressed in neurons. In contrary to well-folded proteins, IDPs lack a distinct stable 3D structure and sample a vast conformational space instead. Tau's biological function lays in its interaction with the microtubules. In patients with Alzheimer's disease, however, it is found to be part of protein filaments in the brain.
Solutions of tau can spontaneously demix into a dense phase (enriched in protein) and a light phase(depleted in protein) in a process called liquid-liquid phase separation (LLPS). In the presence of LLPS, tau has been found to aggregate more easily [1]. To understand diseases such as Alzheimer's disease on a molecular level, it might be important to shed light on the protein dynamics during LLPS and aggregation. Previously, we studied the dynamics of tau and its hydration water in monomers and fibers [2]. Here, we extend our efforts to elucidating tau dynamics under LLPS by quasi-elastic neutron scattering (QENS). The measured QENS signal represents the superimposed contributions of the protein center-of-mass translational diffusion, of the protein tumbling, of internal protein fluctuations on the level of the protein backbone and side chains, and of the solvent [3].
We will discuss results from a first experiment at the back-scattering spectrometer IN16B at the Institut Laue Langevin (ILL), in which we compared two tau solution (80 mg/mL), namely a homogeneous solution and a solution that underwent LLPS. Initial QENS data analysis indicates tau under LLPS is less mobile.

[1] Lin Y., et al., ACS Chem. Neurosci., 11, 615-627 (2020)
[2] Fichou Y., et al. Proc. Natl. Acad. Sci. U.S.A., 112, 6365-6370 (2015)
[3] Grimaldo M., et al. Quart. Rev. Biophys., 52, e7 (2019)

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