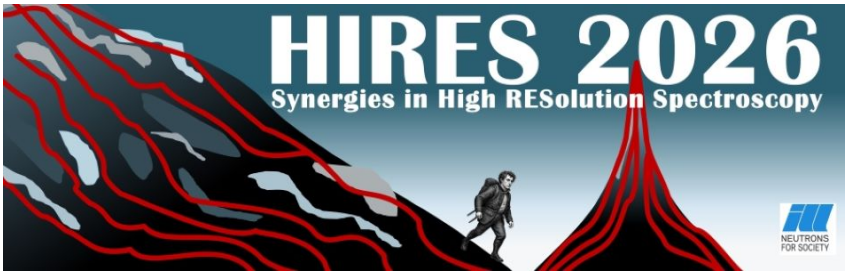

Contribution ID: **10** Type: **Invited**

Dynamics and structure of proteins and lipids in context of diseases using neutron scattering and synchrotron radiation

A hallmark of amyloidosis such as Alzheimer's disease is the deposition of amyloid fibrils, which are self-assembled protein filaments with core regions rich in β-sheets, in various organs. Cytotoxicity underlying the pathogenesis of amyloidosis is partly caused by the disruption of cell membranes by binding of amyloid fibrils. Since amyloidogenic proteins form polymorphic fibrils with different levels of cytotoxicity, it is crucial to understand the structural and dynamical features of these fibrils and lipid membranes to gain insights into their physical properties leading to higher cytotoxicity. For this purpose, we have employed model systems of polymorphic amyloid fibrils of hen egg white lysozyme and membranes of DMPG and DMPC, and utilized elastic incoherent neutron scattering (EINS) and quasi-elastic neutron scattering (QENS) to characterize the molecular dynamics at the sub-nanosecond timescale while we have utilized vacuum ultraviolet circular dichroism (VUVCD) and small-angle X-ray scattering (SAXS) to characterize the structure of the fibrils and monomers.

In addition, we are now working on another protein, Notch2nl-B, which is involved in the expansion of the cerebral cortex and related to brain tumors. The modern-type (197I) is known to promote the brain tumor formation compared with the ancestral-type (197T), suggesting that possible changes in its structure and dynamics are associated with the pathogenesis of the brain tumor. We have employed VUVCD and SAXS to obtain structural information on this protein containing flexible regions, for which application of EINS/QENS is expected.

In this talk, we will present our recent findings on molecular dynamics and structure of the above systems relevant with the pathogenesis of the corresponding diseases.

Session

Biology/Health

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Session Classification: Biology/Health