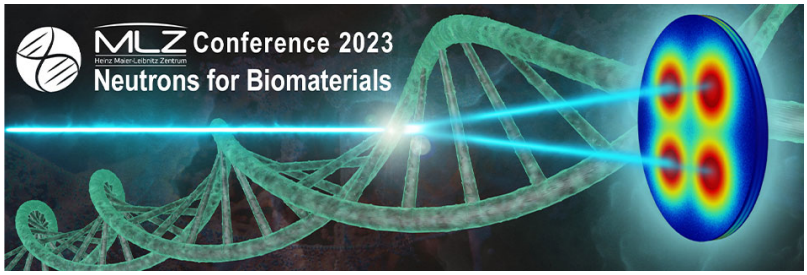

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Understanding the Aggregation Kinetics and Conformational Changes in Amyloid-β42 (Aβ42) in Presence of Neuronal Phospholipids

Tuesday, 23 May 2023 17:20 (1h 10m)

Amyloid β42 (Aβ42) is predominantly found in the form of plaques in the brain tissues and stems the cognitive dysfunctionality in Alzheimer's. Aβ depending upon aggregation states Aβ42-monomer (M)/β-sheets/oligomer (O)/fibril (F), and amino acid lengths affect the model membrane mimetic systems [1-4]. The plasma membrane is the first biological structure encountered by Aβ42 and can play a vital role in Aβ42 fibrillation. Here, we have extracted the brain phospholipids which mainly involve Sphingomyelins (SM), Phosphatidylcholines (PC), Phosphatidylethanolamines (PE), Hexosylceramides (HCER) and Free Fatty Acids (FFA). We have studied the Aβ42 fibrillation and conformational changes in the presence of neuronal phospholipid unilamellar vesicles (ULV). The ULVs are characterized by dynamic light scattering (DLS) and Cryo transmission electron microscopy (CryoTEM). The hydrodynamic radius of ULVs was 65±15 nm and the diameter was 90 nm, averaged over all the CryoTEM images, using DLS and CryoTEM respectively. The monomeric Aβ42 (Aβ42-M) mixed with ULVs at 0.3w/v% and characterized by CryoTEM. ULVs bilayer remains intact with the freshly prepared Aβ42-M. However, Aβ42-M strongly interact with the ULVs and aggregate to form Aβ42-fibril (F). CryoTEM images showed that Aβ42-M aggregates and encapsulates the ULVs forming a necklace structure and also impairment of the ULVs bilayer was observed. Furthermore, Aβ42 mainly remains in β-sheet form, however, with neuronal phospholipids, it transforms into α-helix. This suggests that Aβ42 strongly associated with neuronal phospholipids which can play an important role in Aβ fibrillation and conformation.
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