Seminar

Integrated Cryo-EM and Solid-State NMR Structure of Amyloid-β Fibrils from Alzheimer's Disease Brain

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Amyloid fibril formation by various polypeptides is a biophysically interesting and biomedically important phenomenon, any understanding of which depends on molecular structural information. The aggregation of amyloid-β (Aβ) peptide in the brain as amyloid fibrils is a pathological hallmark of Alzheimer's disease. Structural studies of these aggregates are important in understanding their formation, spreading, and for development of therapeutic and diagnostic approaches. In this talk, I will describe the structural studies of Aβ-fibrils from the postmortem brain of an individual with Alzheimer's disease. Here we have integrated both solid-state NMR (ssNMR) and cryoEM to solve the structure of the most common polymorph of Aβ-fibrils that develop in the brain of Alzheimer's disease patients. Here we present the cryoEM map of Aβ-fibril at 2.7 Å resolution. The information from both ssNMR and cryoEM are combined in a single structure calculation to obtain the structure of brain-derived Aβ-fibrils. In the case of Aβ fibrils, we have found a surprising two-fold symmetric polymorph with a mass-per-length value of 27 kDa/nm (indicating three Aβ molecules per β-sheet repeat spacing). The integration of cryoEM and ssNMR pave the way for structural studies of complex systems.

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4:10 PM
Room 136 – Chemistry
David Weliky – Host