Physical Chemistry Seminar

Tuesday, March 2, 2010 | **11:00 a.m.** | **Room 1315 Chemistry Building**

Exploring the Earliest Stages of the Amyloid β Protein Aggregation Pathway

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The aggregation Amyloid β (Aβ) peptide has been linked to the neurodegenerative Alzheimer's Disease and implicated in other amyloid diseases including cerebral amyloid angiopathy. Aβ peptide is generated by cleavage of the amyloid precursor protein (APP) by transmembrane proteases. It is crucial to determine the structures of β -amyloid peptides in a membrane environment in order to provide a molecular basis for the cleavage mechanism. We report the structures of amyloid β peptide (Aβ1-40 and Aβ1-42) as well as the 672-726 fragment of APP (referred to as Aβ1-55) in a membrane environment determined by replica-exchange molecular dynamics simulation. A similar but distinct structural ensemble is observed for Aβ1-40 and Aβ1-42 at the membrane interface. The fragment of APP (Aβ1-55) is observed to have a long transmembrane helix. The position of the transmembrane region and ensemble of membrane structures are elucidated. A proposed conformational transition between the Aβ1-55 and Aβ1-40 structures provides insights into APP structure and cleavage mechanism that are essential to a complete understanding of the Aβ peptide aggregation pathways.

Refreshments will be available prior to the seminar at 10:45 a.m. outside room 1315

Graduate Students may meet with the speaker at 1:15 p.m. in Room 8305f