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Coarse-Grained Model of Fragments of Amyloid-Beta peptides

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Amyloid-beta (Aβ) peptides are 36 to 43 amino acid residues, implicated by the amyloid cascade hypothesis as one of the cause of Alzheimer's disease (AD). In the brain, Aβ forms small peptide aggregates, called oligomers, leading to β-sheet fibrils that, with time, forms the 3D amyloid plaque that is the hallmark of AD. The structure of fibrils consists of parallel and/or anti-parallel sheets wound in a wide array of complex three-dimensional structures. Though parallel β-sheets are more common in AD, anti-parallel sheets are believed by some researchers to be associated with early onset AD.

This paper presents our effort in building a coarse-grained model of the formation of micro-crystal fibril of fragments of Aβ. For computational efficiency, an amino acid is represented as a spherical bead, located at the center of its C_α carbon.This allows the study of systems of up to 200 peptides. In the spirit of Go models, the intra-peptide dihedral and van der Waals interactions, as well as inter-peptide interactions are biased to the experimental crystal structures. Two C_α beads on different peptides can also interact by a Mercedes-Benz-type hydrogen bond,which stabilizes β-sheet. MD simulations observed that Aβ fragment models that are biased to anti-parallel β-sheets condensed to fibrils at lower temperature than models biased to parallel β-sheets. Finally the kinetics of fibril formations are presented, and the implication to AD are discussed.

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