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Structure of Alzheimer's 10-35 β peptide from replica-exchange molecular dynamics simulations in explicit water ANDRIY BAUMKETNER, JOAN-EMMA SHEA, University of California Santa Barbara — We report a replica-exchange molecular dynamics study of the 10-35 fragment of Alzheimer's disease amyloid β peptide, Aβ10-35, in aqueous solution. This fragment was previously seen [J. Str. Biol. 130 (2000) 130] to possess all the most important amyloidogenic properties characteristic of full-length Aβ peptides. Our simulations attempted to fold Aβ10-35 from first principles. The peptide was modeled using all-atom OPLS/AA force field in conjunction with the TIP3P explicit solvent model. A total of 72 replicas were considered and simulated over 40 ns of total time, including 5 ns of initial equilibration. We find that Aβ10-35 does not possess any unique folded state, a 3D structure of predominant population, under normal temperature and pressure. Rather, this peptide exists as a mixture of collapsed globular states that remain in rapid dynamic equilibrium with each other. This conformational ensemble is seen to be dominated by random coil and bend structures with insignificant presence of α-helical or β-sheet structure. We find that, overall, the 3D structure of Aβ10-35 is shaped by salt bridges formed between oppositely charged residues.Of all possible salt bridges, K28-D23 was seen to have the highest formation probability, totaling more than 60% of the time.

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