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Elongation affinity of Aβ-42 via molecular dynamics simulations[1]

ROBERTO RODRIGUEZ, LIAO CHEN, Department of Physics and Astronomy, University of Texas at San Antonio, GEORGE PERRY, Department of Biology, University of Texas at San Antonio — A number of diseases including Alzheimer's, Parkinson's, and Huntington's are characterized by the presence of fibrillar aggregations of amyloid-β (Aβ) peptides. The 42-residue variant Aβ-42 has emerged as a key factor in the pathology of Alzheimer's disease. Very recently, the functional structure of Aβ-42 fibrils has been elucidated via high-quality NMR studies. We conducted molecular dynamics simulations on this recently published structure and calculated the free energy needed to elongate an Aβ-42 fibril, finding excellent agreement with experimental measurements. We also studied the effect of the mature amyloid fibrils on the conformational stability of free peptides attached to their surface, and find that at least a dimer is needed for the free peptides to retain their fibrillar conformation, in support of the well-known second-order secondary nucleation mechanism.

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