Simulations of the early steps of protein aggregation

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More than 20 human diseases, including Alzheimer's disease and dialysis-related amyloidosis, are associated with the pathological self-assembly of soluble proteins into transient cytotoxic oligomers and amyloid fibrils. Because protein aggregation is very complex, the detailed aggregation paths and structural characterization of the intermediate species remain to be determined.

Here, we first review our current understanding of the dynamics and free energy surface of the assembly of small amyloid-forming peptides [KFFE, Abeta(16-22), Abeta(11-25), NGAIL and beta2m(83-89)] using a coarse-grained protein force field (OPEP) coupled to the activation-relaxation technique, molecular dynamics (MD) or replica exchange MD (REMD).

Next, we present REMD-OPEP simulations on the dimers of Alzheimer's peptides Abeta(1-40) and Abeta(1-42) and discuss the role of amino acids 23-28 in fibril formation.

Finally, we analyse MD-OPEP simulations of Abeta(16-22) oligomers with multiple copies of an N-methylated inhibitor.

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