Generalized-ensemble and nonequilibrium molecular dynamics simulations of protein aggregates

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Protein aggregates such as spherical substances called oligomers and acicular substances called amyloid fibrils cause more than 40 kinds of diseases. For example, Alzheimer's disease is thought to be caused by aggregated amyloid-β (Aβ) peptides. I give a talk on our molecular dynamics (MD) simulation studies to understand the aggregation and disaggregation mechanisms of Aβ peptides [1-9]. We performed Hamiltonian replica-permutation MD simulations for Aβ40 and Aβ42 to investigate the dimerization process [7], which is the early oligomerization process. We identified the key residue, Arg5, for the Aβ42 dimerization and revealed why Aβ42 aggregates faster than Aβ40. I also present nonequilibrium MD simulations for the disruption of the protein aggregates by supersonic wave and infrared laser irradiation. We revealed different roles of water molecules in disrupting protein aggregates by supersonic wave [8] and infrared laser irradiation [9].

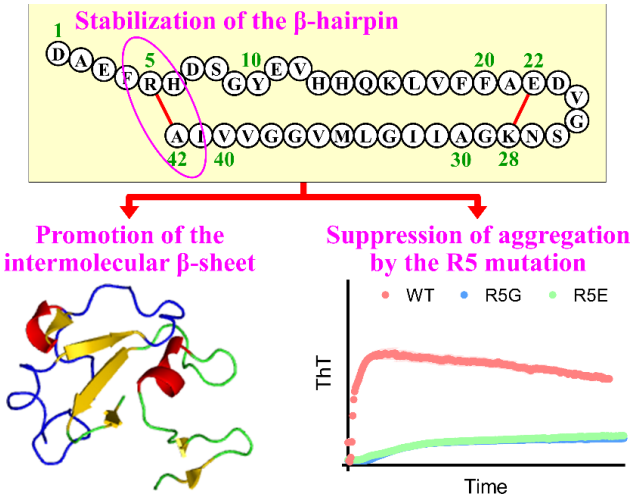

Fig. 1. Arg5 is the key residue for aggregation of amyloid-β peptides [7]. It stabilizes the β-hairpin structure and promotes the intermolecular β-sheet.

References

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