[BIOINFO 2023]

Reweighted ensemble structures of Aβ42 monomer using maximum entropy approach

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Amyloid β (Aβ) aggregation is a key feature of Alzheimer's disease. Although complex aggregation mechanisms have been increasingly revealed, the complex nature of Aβ monomers makes it challenging to study the early events of amyloidogenesis. In this study, we introduced a novel mathematical tool based on the maximum entropy approach. This tool reweights structural ensembles by fitting molecular dynamics simulation data to solution experiment. Our approach successfully yielded ensemble weights that best matched two-dimensional NMR chemical shift data. We also confirmed that the reweighted ensembles are consistent with circular dichroism and dynamic light scattering analyses. An application of maximum entropy with experimental findings holds great promise for advancing our understanding of protein misfolding diseases and their functions, providing a template structure for further research.