P-1.34

Solvent-dependent Conformational Behavior of Aß Monomers: Insights from Atomistic Simulations

Irene Cadenelli [1], Andrea Ciccolo [2], Andrea Tagliabue [1], Valeria Conti Nibali [2], Davide Bochicchio [1], Giulia Rossi [1]

[1] Università di Genova, Genova, Italy

[2] Università di Messina, Messina, Italy

Amyloid beta (Aβ) peptides, especially Aβ40 and Aβ42, play a central role in the pathogenesis of Alzheimer's disease, with small oligomers identified as the most toxic species. Their aggregation pathway, strongly influenced by the environment, remains difficult to characterize experimentally due to their intrinsic disorder and dynamic nature. In this study, we employed atomistic molecular dynamics simulations to investigate the conformational preferences of Aβ40 and Aβ42 monomers in different solvents: water at physiological concentration, dimethyl sulfoxide (DMSO), hexafluoroisopropanol (HFIP), and trifluoroethanol (TFE). For each system, three 3-μs replicas were performed using well-tempered metadynamics. We analyzed secondary structure content, hydrophobic solvent-accessible surface area, hydrogen bonding, radius of gyration, and other structural descriptors to obtain a comprehensive picture of monomeric behavior. Our results highlight the strong influence of the solvent on secondary structure propensity and peptide flexibility. Preliminary differences between Aβ40 and Aβ42 also emerged. These insights contribute to a deeper understanding of their conformational landscape and support the development of a transferable coarse-grained model for future studies of aggregation and peptide–membrane interactions.