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Multiscale Molecular Dynamics Simulations of Beta-Amyloid Interactions with Neurons LIMING QIU, MARK VAUGHN, KELVIN CHENG, Texas Tech University — Early events of human beta-amyloid protein interactions with cholesterol-containing membranes are critical to understanding the pathogenesis of Alzheimer's disease (AD) and to exploring new therapeutic interventions of AD. Atomistic molecular dynamics (AMD) simulations have been extensively used to study the protein-lipid interaction at high atomic resolutions. However, traditional MD simulations are not efficient in sampling the phase space of complex lipid/protein systems with rugged free energy landscapes. Meanwhile, coarse-grained MD (CGD) simulations are efficient in the phase space sampling but suffered from low spatial resolutions and from the fact that the energy landscapes are not identical to those of the AMD. Here, a multiscale approach was employed to simulate the protein-lipid interactions of beta-amyloid upon its release from proteolysis residing in the neuronal membranes. We utilized a forward (AMD to CGD) and reverse (CGD-AMD) strategy to explore new transmembrane and surface protein configuration and evaluate the stabilization mechanisms by measuring the residue-specific protein-lipid or protein conformations. The detailed molecular interactions revealed in this multiscale MD approach will provide new insights into understanding the early molecular events leading to the pathogenesis of AD.

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