Title:

Through the Computational Lens: Exploring Key Molecular Mechanisms in Neurodegeneration and Actin Networking

Abstract:

This presentation delves into the molecular dynamics that underpin critical biological processes in neurodegeneration and actin networking. In the first part of our study, we use molecular dynamics simulations to investigate the interactions of Abeta42 monomers with fibrillar surfaces, a pivotal factor in Alzheimer's disease progression. Employing coarse-grained simulations, we focus on the diffusion behaviors of freely diffusing Abeta42 monomers across various fibril surfaces, considering their structural orientations—parallel and perpendicular. Our results reveal significant correlations between the monomers' diffusion coefficients and their orientations on these surfaces. Notably, differences in diffusion coefficients between N-terminal and C-terminal surfaces highlight the impact of surface roughness on monomer dynamics.

In the second part, we explore the role of cofilin, an essential actin-binding protein, in actomyosin network dynamics. Our molecular dynamics simulations identify new cofilin dimer structures facilitated by disulfide bond formation through thiol post-translational modifications (PTMs). These structures, absent in current databases, provide insights into the potential formation of cofilin tetramers, underscoring a novel mechanism for actin filament regulation. These computational studies offer crucial insights into molecular interactions that could inform future therapeutic strategies and deepen our understanding of cellular dynamics.