THE CHINESE UNIVERSITY OF HONG KONG
Department of Physics

SEMINAR

Computation-Guided Control of Peptide Self-Assembly

by

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ALL INTERESTED ARE WELCOME
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Abstract

Peptide self-assembly is a fundamental molecular process that can produce both disease-causing amyloid aggregates and functional peptide materials. It is thus important to know how to precisely control this process to prevent harmful outcomes and promote beneficial ones. Addressing this question hinges on the detailed knowledge about peptide self-assembly which, however, is difficult to obtain with current experimental characterization techniques. Molecular simulations could help to address this challenge but their application in peptide self-assembly has been stymied due to the lack of proper computation methods that can deal with the spatial complexity of this process in an efficient manner. Here I propose a multiscale approach that can overcome this limitation. Our approach combines an atomistic model of peptide molecules, carefully designed to reproduce peptide folding and self-assembly behaviors, with a simplified representation of environment that enhances simulation efficiency. I will show you how our approach can greatly improve our computational ability to study the aggregation of disease-associated peptides like amyloid-β peptide. Our results generate new atomic insights into the formation of high molecular-weight oligomers that are relevant to neurotoxicity but have never been computationally investigated before due to their large size. Based on these insights a potential strategy of aggregation prevention is proposed. Also, our approach can be applied to assist in the design of peptide-based materials by determining the relationship between conformations of peptide building blocks and assembly morphologies. Furthermore, by integrating our approach as a core component into a design framework combining experiment and computation, we design the first self-assembling stapled peptide that can form coiled coil-like nanofibers. Collectively, our computational approach is a promising tool for computation-guided control of peptide self-assembly.