QUBIC
The Australian Research Council Centre of Excellence in Quantum Biotechnology

How Does Chirality Patterning Influence Amyloid Assembly Stability?

Institution	The University of Wollongong
Project details	Amyloid aggregation is a hallmark of numerous protein-misfolding diseases, including Alzheimer's disease, Parkinson's disease, and type II diabetes. Although naturally occurring amyloidogenic peptides consist almost exclusively of L-amino acids, both L- and D-enantiomeric peptides have been shown to independently form amyloid fibrils. Experimental studies of the amyloidogenic core region of human islet amyloid polypeptide (IAPP20-29) further revealed strong chiral selectivity during fibril propagation and secondary nucleation, with limited cross-seeding between peptides of opposite chirality. However, the molecular basis of this chiral recognition remains poorly understood. In particular, it remains unclear whether amyloid stability is governed primarily by the overall chirality composition or by the specific arrangement of L- and D-peptides within an assembly. Different chirality patterns, including homochiral, alternating heterochiral, and block-segregated organizations, may produce distinct intermolecular interactions and packing geometries. This project will employ all-atom molecular dynamics simulations to investigate how chirality patterns affect the structural and dynamic properties of minimal amyloid assemblies derived from the IAPP20-29 core region, providing molecular-level insights into chiral recognition and amyloid stability. **Expected aims and outcomes**: The project aims to identify the molecular interactions responsible for chiral selectivity in amyloid assembly and determine whether specific arrangements of L- and D-peptides stabilise or destabilise fibrillar structures. The findings will improve our understanding of chiral recognition in biomolecular self-assembly and may contribute to the future design of aggregation modulators and peptide-based functional materials. The student will develop skills in computational modelling, data analysis and scientific communication.
Who can apply	Students with a background in chemistry, physics, biochemistry, materials science, mathematics, computer science or related disciplines are encouraged to apply. Basic programming experience is desirable but not required. Training in molecular simulation and data analysis will be provided.
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