

## Dynamics of full-length Amyloid $\beta$ peptides in monomeric and oligomeric states by classical and enhanced MD simulations.

Although intensive research in this field, no treatment is currently available for patients developing Alzheimer disease. This is due in particular to a poor understanding of the aggregation mechanism of Amyloid  $\beta$  ( $A\beta$ ) peptides, that plays a crucial role in the development of the pathology.

$A\beta$  peptides that are involved in Alzheimer disease exist in solution in a disordered state and are able to evolve dynamically among several structuration states :  $\alpha$ -helix  $\longleftrightarrow$  random coil  $\longleftrightarrow$   $\beta$ -sheet, the last state being able to oligomerize and then autoassembly in fibrils.

This internship has several goals:

- 1) Based on an extensive review of literature, identify structures of  $A\beta$  peptides that are relevant for molecular dynamics (MD) simulation
- 2) Perform long full-atom dynamics in order to sufficiently sample conformational space explored by these peptides and identify conformation suitable for autoassembly.
- 3) Perform full-atom, coarse-grained or enhanced sampling dynamics for oligomers assemblies (with variable number of monomers) and analyze their properties and stability during MD simulations.

The final idea is to build a library of relevant conformations of  $A\beta$  as monomers or oligomers that will be used as target for Alzheimer disease programs. The internship will be done in Sanofi Research Center (Chilly-Mazarin) in the Computer-Aided Drug Design team. Please note that this internship is a high priority for Sanofi but not yet finally approved.

Requirements:

The candidate should be familiar with peptides, proteins and have some knowledge on molecular modeling technics, molecular mechanics, molecular dynamics and structure handling: homology modelling and docking. Experience in scripting (R, knime, python, perl) would be a plus.

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