

Research projects 2018-2019 – Master Internships

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In silico structural analysis of a bacterial amyloid peptide

Project description:

Hfq is a bacterial regulator with key-roles in the control of genetic expression. The protein noticeably regulates translation efficiency and RNA decay. This property is of primary importance for bacterial adaptation and virulence. Our collaborators at the CEA of Saclay and SOLEIL synchrotron have previously shown that Hfq *E. coli* protein, and more precisely its C-terminal region, self-assembles into an amyloid structure. Hfq function depends on this self-assembly, which is based on the formation of intermolecular β -sheets, which result in the formation of fibrils. Such a structure is often found associated to neurodegenerative pathologies, but in this case the self-assembly helps to maintain the physiological state of the cell and are called functional amyloid.

A peptide composed by 11 amino acids residues, derived from the Hfq C-terminal region has been shown to be the nucleation site of the amyloid. This peptide therefore offers a model to understand how Hfq self-assembly occurs. The goal of this internship project is to characterize, at the atomic level, the structure of Hfq peptide self-assembly. The perspective of this work is to design compounds with antibacterial properties, by preventing the formation of Hfq amyloid fibers. Indeed, some compounds have already been identified experimentally (*in vitro* and *in vivo*), but need to be optimized for antibacterial applications. For this goal we aim to study the folding and dynamical behavior of the Hfq peptide and to compare our results with the experimental data obtained by our collaborator (circular dichroism, infrared spectroscopy, SAXS, electron microscopy and AFM imaging). We will use molecular modeling approaches to understand the folding events, in particular replica exchange molecular dynamic (REMD) simulations, which allows performing sampling of the peptide motions to investigate accurately its dynamic and its structure-activity relationship. Ultimately, the perspectives of this work are to study the effect of the compounds mentioned above for their optimization for antibacterial purpose.

Profile of the candidate: Strong interest in bioinformatics, programming and molecular modeling. Basic skills: experience in molecular modeling and protein structures.