MASTER « *In Silico* Drug Design »

1ère année

PROPOSITION DE STAGE

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A envoyer à Mr Pr Taboureau

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Titre du stage : **Identification of amyloid patches on protein structures**

Description du sujet (quelques lignes):

The long-term purpose of the project is a better understanding of the molecular mechanisms driving specific fragments of proteins to interact in a compact manner leading to the production of amyloid fibres. Two groups are involved in this project, one in Krakow, Poland, and one in Paris. Each one developed a methodology and they are now used together in order to predict amyloid patches at the surface of globular proteins. Krakow group proposed to consider a protein as a fuzzy oil drop (FOD) model, for which a protein is a drop with the intrinsic hydrophobicity of the amino acids buried in the core of the globule. Paris group developed a coarse grain simulation of the folding process, which captures some of the physics of the distribution of the hydrophobic residues along the sequence. The prediction of the number of non-covalent neighbours in a discrete space allows determining positions important for the process of the folding, the Most Interacting Residues (MIR). Our previous collaboration succeeded to show that joint methods enhance the capacity of prediction of the nucleus of proteins.

We are now interested in fragments involved in protein-protein interfaces, which are usually hydrophobic. Because they are located at the surfaces, they should escape from both models, FOD and MIR. A database of structures of homo dimers is available, with MIR and interacting surfaces already calculated, and their quality has been evaluated. We expect that patterns that do not follow the FOD but are predicted as MIR should be some kind of footprint of the formation of amyloid complexes. The project is the thorough analysis of the accordance of both methods, MIR and FOD, to the dimers of the dataset. One expects to derive some rules from their behaviours. Then, they will be compared to some known experimental cases of amyloid fragments.

This internship is a follow-up of previous work, so the student must be skilled in python in order to re use existing scripts.

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