Algorithm for the alignment of 3D molecular graphs

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Internship presentation :

Structure-based drug design [1] relies on knowledge of the three dimensional structure of the biological target obtained through methods such as X-ray crystallography, which is used as a basis for designing new ligands by applying accepted principles of molecular recognition. Currently, the most successful methods for protein-ligand docking use crystal structures obtained with the same or similar ligands as a starting point [2]. One of the most widely used methods to compare the structure of ligands is LigAlign[3], which iteratively uses the Hungarian combinatorial optimization algorithm with $O(N^3)$ complexity. However, it often makes mistakes in ligands with symmetric groups. Thus, the goal of the internship will be to develop a robust method to align flexible ligands starting from $O(N^3)$ combinatorial optimization methods.

Internship objectives :

The overall research topic of the proposal is to extend the state-of-the art methods for ligand-based protein-ligand docking. More precisely, it includes the development of a robust flexible ligand alignment method with a careful validation on a diverse set of crystallographic structures. Specific attention will be drawn to a subset of ligands with symmetric groups, such 6-membered aromatic rings. On the final step, we will integrate the method as an individual module in the SAMSON software platform developed in our team.

Requirements :

We are looking for creative, passionate and hard-working individuals from applied math / computer science background with exceptional talent for computer science and mathematics. Excellent oral, written and interpersonal communication skills are essential (working language will be English – knowledge of French is a plus). Good knowledge of C++ will be an asset.

References :

[1] T. L. Blundell, “Structure-based drug design,” Nature, (1996), 384, 23.

[2] https://drugdesigndata.org/about/grand-challenge-2015.

[3] Heifets, A., Lilien, R., LigAlign: Flexible ligand-based active site alignment and analysis. Journal of Molecular Graphics and Modelling. Volume 29, Issue 1, 24 August 2010, Pages 93-101.