New computational approaches to study the effect of genetic mutations on the topology of protein-protein interaction networks

Résumé du projet de recherche (Langue 1)

In this thesis, we wish to develop the necessary computational framework to reconstruct the annotated PPI network (more than 10000 nodes and hundreds thousands of interactions) for the human reference genome and annotated PPI (sub)networks for individual genomes. This means to provide an \textit{ab initio} method that reconstructs interaction networks and determine how mutations may affect the PPI topology. It will be based on the development of a deep learning approach discriminating protein docking conformations and protein partners' conformations, and on a novel docking algorithm especially designed for the protein partners discrimination problem. These approaches will be built on fundamental results developed in the last years in the team. Namely, the dataset of protein-protein interactions generated from Complete Cross-Docking (CC-D) (Sacquin-Mora et al 2009, Lopes et al 2013, Laine & Carbone 2015), and the algorithmic tools LISA (Raucci et al \textit{Structure}2018), CIPS (Nadalin & Carbone \textit{Bioinformatics} 2018), JET2 (Laine & Carbone \textit{PLoS Computational Biology}2016), which are the state-of-the-art in the field today. The reduction of the computational cost of the docking strategy (obtained by integrating the tools cited above), the deep learning model especially designed to discriminate conformational docking poses and the improved computational facilities available will allow us to realize a breakthrough on CC-D experiments and reach the size of the human proteome (the order of 10000 protein structures).