Title: New computational frameworks to break down the complexity of protein-protein interactions: from geometrical arrangement of interface to interaction networks

Yasser MOHSENI BEHBAHANI*, Élodie LAINE, Alessandra CARBONE
The Laboratory of Computational and Quantitative Biology (LCQB), Sorbonne Université

Reliable prediction of protein-protein interactions (PPI) and how missense mutations affect these interactions would have tremendous implications for bioengineering and medicine. We developed novel computational frameworks to break down the complexity of PPI at both interface and network levels. At the interface level, we proposed Deep Local Analysis (DLA), a deep-learning approach based on invariant representation of interfacial residues to deconstruct and discover alternative interfaces, to discriminate near-native complex conformations from incorrect ones and to accurately estimate binding affinity changes upon mutation. At the network level, we created a versatile and interactive web-based tool, called LEVELNET, to visualise, explore and compare PPI networks. LEVELNET provides experimental and computational biologists with multiple functionality such as investigating whether and how a group of proteins interact, discovering the interactors for a given protein up to certain neighbouring depth-level and finding the interacting patches on the surface of a protein. The spectacular advances in protein 3D structure prediction has already paved the way for the future expansion of DLA and LEVELNET toward systematical assessment of mutational outcomes on PPI and the inference of their networks at a proteome-wide scale.