PPI-signature: detecting similar interactions among homologous proteins and distinct partners

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About 80% of proteins are only capable of performing their functions through associations with other proteins. Different types of interactions are responsible for making such associations, and they are fundamental for stabilizing complexes and to ensure proteins will function properly. Furthermore, to optimize their functional roles, proteins interact with a spectrum of binding affinities, making these interactions the heart of most biological processes. Although there are a variety of affinities, Protein–Protein Interactions (PPIs) maintain a high degree of specificity for their partners. Thereby, the underlying premise is that there is a limited set of residues which participate in protein binding sites, and they are well-conserved to keep a specific way of interaction with other set of proteins.

Understanding how PPIs occur, and which are the specific interactions between a protein and their binding partner are crucial for explaining the structural and physicochemical determinants. Thus, we can shed light on how protein recognition and binding affinity takes effect. Moreover, this understanding can help in some applications. For instance, in proteins engineering, it can improve the design of resistant proteins to inhibition, and in prioritizing drug targets. Many works address their subject to discover a pattern in a protein family; however, few of them are concerned about the semantic of this pattern. The task of determining patterns in a complex is more complicated than in a monomer; thus, the existing methods are not good enough to identify patterns among interfaces.This failure occurs because most of the algorithms do not to consider the whole protein complex, and the intrinsic features that a protein needs to bind in another one.

Finding a signature that describes which interactions are common in proteins, which belong to the same family, is vital. A signature can have significant implications for understanding the nature and function of PPIs, especially those that are considered to have "promiscuity." Hence, we proposed a multi-objective genetic algorithm to find patterns that are not straightforward. The algorithm pruposed uses types of interactions that amino acids establish with their neighbors in three-dimensional space; also, it compares the residue identity and the environment associated with each of them. Consequently, we can point out what and how important the similar interactions among a set of interfaces are. The results have shown that this methodology is more appropriate to embrace characteristics that are relevant in interface comparisons, and on the identification of a functional signature.