Protein interface classification by evolutionary analysis

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Macromolecular crystallography is currently producing a wealth of information about protein-protein interactions and often tackles very complex assemblies. Such complexity, however, often makes it difficult to distinguish which of the interfaces observed in the crystal lattice are biologically relevant and which are simply crystal contacts. To computationally address this issue, we have developed a general protein interface classification method (EPPIC, Evolutionary Protein Protein Interface Classifier [1]). EPPIC uses a simple geometric measure, number of core residues (defined as in Schärer et al. [2]) and two evolutionary indicators based on the sequence entropy of homolog sequences [3]. One indicator measures the difference in selection pressure between interface core and rim, while the other compares interface core and rest of the surface, minimizing bias with a Z-score like approach. EPPIC is available both as a command-line tool and as a web server (www.eppic-web.org). It provides a classification (biological contact or crystal contact) and a detailed analysis of each interface in a given crystal structure. We are currently extending our method to further applications, like the analysis of membrane protein interfaces. The EPPIC approach and the web server will be presented.

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