GERSTEIN GROUP AT YALE ADDS NEW DIMENSION TO PROTEIN INTERACTION NETWORKS

Protein interaction network (PIN) studies in different organisms have provided a wealth of data. However, the reliability of the datasets and the predicted interactions have become clear concerns in evaluating these studies. Therefore, most studies of protein networks neglect the structural and chemical aspects of each interaction. [1]

A new study [2] by Mark Gerstein's group at Yale University provides an additional dimension to protein interaction networks in the form of structural modeling that characterizes interactions by using atomic-resolution information from three-dimensional protein structures. This more rigorous approach (see figure) is intended to increase the reliability of the reported protein interactions.

Beginning with the yeast protein interaction network, the approach involves first removing low confidence interactions, and then incorporating structural and chemical information on protein interactions. 3D structural modeling also is applied to exclude possible configurations of complexes that appear mutually exclusive, and thus narrow the range of possible interactions.

The result is termed the structural interaction network (SIN), which consists of 873 proteins and1269 interactions, 438 which were found to be mutually exclusive. In initial analyses of the SIN, notable properties include a maximum of 14 interaction partners per "hub" protein, in contrast to earlier interactome studies reporting much higher ranges. The approach also distinguishes between "multi-interface" hubs that involve simultaneously possible interactions and "singlish-interface" hubs with mutually exclusive interactions, and shows that the former are more likely to be essential, co-expressed, and show lower evolutionary rate (dN/dS). The SIN dataset and updates can be found at http://sin.gersteinlab.org.

References

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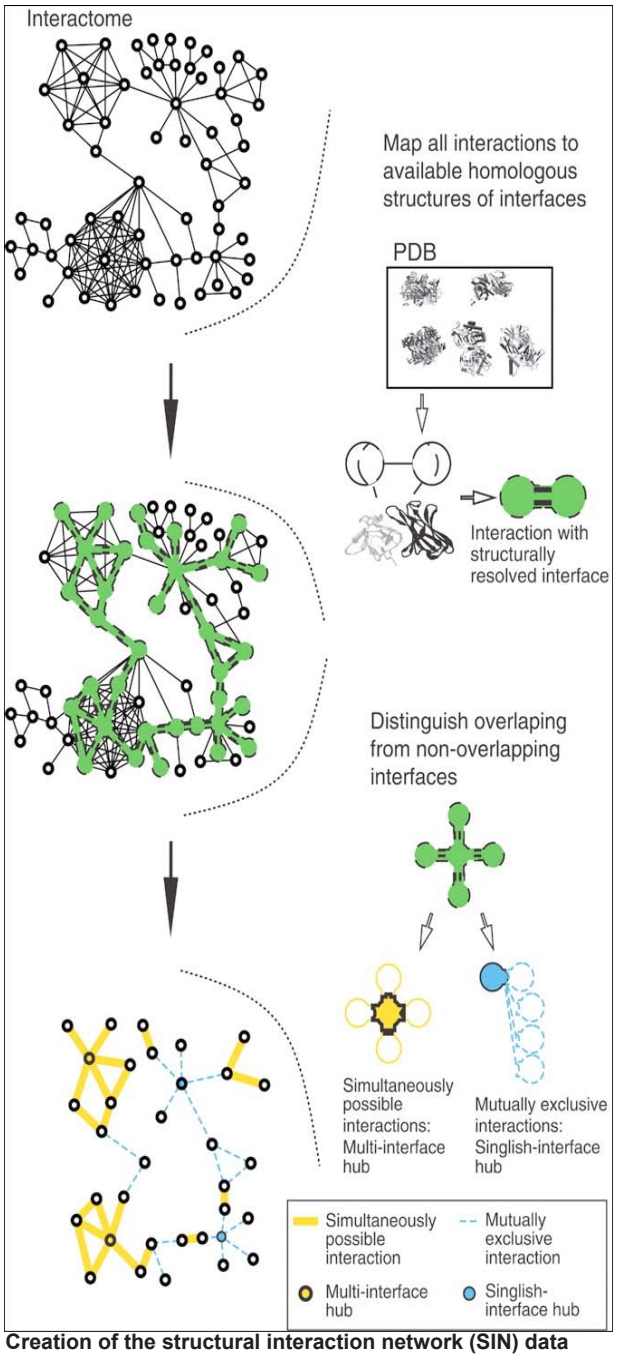

Creation of the structural interaction network (SIN) data set. All interactions from the filtered protein interaction data set are mapped to Pfam domains [3]. Pham is a large collection of protein multiple sequence alignments and profile hidden Markov models [3]. The Pfam domains are mapped to known structures of protein interactions by means of iPfam [4]. Most resources that contain information about protein interactions focus only on binary interactions between proteins; iPfam includes these as well as interactions between domains in a single protein [4]. In creating the SIN data set, only those interactions are kept in which both interaction partners (or a homologous domain of either) can be found in a 3D structure of a protein complex. All interactions are then classified into mutually exclusive and simultaneously possible by 3D structural exclusion. When a protein has more than one simultaneously possible interaction, the number of interaction interfaces is counted. (Figure from Kim et al [2])