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Docking protein domains in contact space

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Short Abstract: We present a novel method that attempts to dock protein domains using a contact map representation. It is based on a scoring function that combines structural, physicochemical and evolutionary information. The method correctly predicts some contacts across the interface and can complement effectively other computational methods.

Long Abstract:
Many biological processes involve the physical interaction between protein domains. Understanding these functional associations requires knowledge of the molecular structure. Experimental investigations though present considerable difficulties and there is therefore a need for accurate and reliable computational methods.

In this work we present a novel method that seeks to dock protein domains using a contact map representation. Rather than providing a full three dimensional model of the complex, the method predicts contacting residues across the interface. It works therefore at an intermediate level between binding site predictions and standard docking algorithms. The former methods attempt to identify the interface residues on a protein without specifying the contacts they actually form, the latter aim to provide a detailed atomic model of the putative complex.

We use a scoring function that combines structural, physicochemical and evolutionary information (e.g. local shape complementarity, conservation, interaction potential, etc.). Each potential residue contact is assigned a value according to the scoring function and the hypothesis is that the real configuration of contacts is the one that maximizes the score. The search is performed with a simulated annealing algorithm directly in contact space.

We have tested the method on interacting domain pairs that are part of the same protein (intra-molecular domains). We show that it correctly predicts some contacts and that predicted residues tend to be significantly closer to each other than other pairs of residues in the same domains. Moreover we find that predicted contacts can often discriminate the best model (or the native structure, if present) among a set of optimal solutions generated by a standard docking procedure.

Overall, contact docking appears feasible and able to complement effectively other computational methods for the prediction of protein-protein interactions. With respect to more standard docking algorithms it might be more suitable to handle protein conformational changes and to predict complexes starting from protein models.