Amino acid empirical contact energy definitions for fold recognition in the space of contact maps - (session: Structural Genomics)

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Contradicting evidence has been presented in the literature concerning the effectiveness of empirical contact energies for fold recognition. Empirical contact energies are calculated on the basis of information available from selected protein structures, with respect to a defined reference state, according to the quasi-chemical approximation. Protein-solvent interactions are estimated from residue solvent accessibility.

In the approach presented here contact energies are derived from the potential of mean force theory, several definitions of contact are examined and their performance in fold recognition is evaluated on sets of decoy structures. The best definition of contact is tested, on a more realistic scenario, on all predictions including sidechains accepted in the CASP4 experiment. In 30 out of 35 cases the native structure is correctly recognized and best predictions are usually found among the 10 lowest energy predictions.

The definition of contact based on van der Waals radii of alpha carbon and side chain heavy atoms is seen to perform better than other definitions involving only alpha carbons, only beta carbons, all heavy atoms or only backbone atoms. An important prerequisite for the applicability of the approach is that the protein structure under study should not exhibit anomalous solvent accessibility, compared to soluble proteins whose structure is deposited in the Protein Data Bank. The combined evaluation of a solvent accessibility parameter and contact energy allows for an effective gross screening of predictive models.