Molecular recognition as information transfer system — possible applications

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The development and validation of a new knowledge based scoring function (ScoreJE) to predict binding affinity between proteins and ligands is described. ScoreJE efficiently predicts binding affinity between small molecule ligand and protein receptor. ScoreJE also discriminates between near-native like docked ligand binding orientations from those that deviate from native crystal structures. Protein-ligand atomic contact information was derived from a “nonredundant dataset” (NRD) of over 3000 X-ray crystal structures of protein-ligand complexes. This information was classified for individual “atom contact pairs” (ACP) before calculating mutual atomic contact preferences. The preferences were calculated on information theoretic relationship of joint entropy for “ScoreJE Atom Type set-2” (SATs2). ScoreJE was validated using a primary evaluation dataset of 75 protein-ligand complexes (many of which were also part of NRD) with known binding affinities. The robustness of ScoreJE was further demonstrated via cross-validation of the results. Single body solvation-desolvation measures (SDMs) were derived from atomic contacts between protein atom types and modelled water molecules. ScoreJE was then modified by incorporation of SDMs. During validation on an extended dataset of 145 protein-ligand complexes of known binding energies, though “SDM included ScoreJE” (SIScoreJE) outperformed ScoreJE in predicting the binding affinity between protein carbohydrate-moiety containing ligands, ScoreJE predicted binding affinity of hydrophobic ligands better. We find that ability of ScoreJE and SIScoreJE was relatively better than other scoring functions like Chem-Score, Gold-Score and X-Score.