

0515 Applying spatially conserved motifs of specific ligand binding sites to predict hitherto unknown protein function

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There are a considerable number of proteins for which the structure has been determined but full function remains unknown. Using training sets of 3D coordinates of known ligand binding sites, we can identify fingerprints of spatially conserved features associated with specific ligand binding function. We apply these 3D motifs of functional elements to searching for that binding site in any PDB structure file. We have applied the fingerprinting algorithm in our software, TMSite, to PDBs containing protein-ligand complexes to detect these binding site fingerprints. The approach requires that PDBs containing the specific ligand binding are available.

The greater the number of fingerprint features (components of conserved residues) successfully identified in the "known" protein set, the more specific subsequent searches in the "unknown" test group will be with fewer erroneous matches. Results are improved by iteratively validating matches as being proximal to accessible pockets and can be broadened by maintaining spatial conservation but searching for similar, not identical, amino acids which may carry out the same function as those in the fingerprint. This method allows location of single/ multiple binding sites in proteins where the ligand has not been co-crystallised or identified.