

Systematic analysis of atomic protein-ligand interactions in the PDB

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We compiled a list of 11 016 unique structures of small-molecule ligands bound to proteins in the Protein Databank - 6444 of which have experimental binding affinity - representing 750 873 protein-ligand atomic interactions, and analyzed the frequency, geometry and impact of each interaction type. We find that hydrophobic interactions are generally enriched in high-efficiency ligands, but polar interactions are over-represented in fragment inhibitors. While most observations extracted from the PDB will be familiar to seasoned medicinal chemists, less expected findings, such as the high number of C-H \cdots O hydrogen bonds or the relatively frequent amide- π stacking between the backbone amide of proteins and aromatic rings of ligands, uncover underused ligand design strategies.