Table 1: Summary of Applications for Protein Functional Annotation

Method	Advantages/Disadvantages	Website
FAST-NMR [22]	*Advantages* • experimentally identifies ligands that bind protein • experimentally identifies ligand binding site • uses entire description of ligand binding site for functional assignment *Disadvantages* • slower than pure computational methods • requires NMR assignments for protein	http://bionmr-c1.unl.edu
eF-seek [69]	*Advantages* • compares electrostatic surfaces of functional sites to identify ligand binding sites *Disadvantages* • results may identify multiple ambiguous ligand binding sites • protein size limitation • Slow (1-2 days)	http://ef-site.hgc.jp/eF-seek
JAFA [70]	*Advantages* • meta-server to sequence-based methods for functional annotation • does not require a structure *Disadvantages* • redundant with ProcFunc, but lacks structure analysis • sequence similarity, even at the 50% level, is not sufficient to confer function [15]	http://jafa.burnham.org
PDB-UF [27]	*Advantages* • assigns E.C. number to hypothetical proteins in PDB • uses global structural similarity to known enzymes *Disadvantages* • limited to enzymes and accuracy of E.C. assignments • majority of proteins still unassigned	http://pdbuf.bioinfo.pl
ProcFunc [71]	*Advantages* • uses a series of structure-based methods to identify ligand binding sites and potential homologues • comprehensive results from a variety of common methods • fast *Disadvantages* • results may be ambiguous, inconclusive or contradictory • reduced description of ligand binding site, 3-5 amino acids • uncertainty in identifying ligand binding site increases uncertainty in functional annotation	http://www.ebi.ac.uk/thornton-srv/databases/profunc
SuMo [72]	*Advantages* • does not use structure or sequence similarity • accounts for protein flexibility *Disadvantages* • results may identify multiple ambiguous ligand binding sites • uses a reduced description of ligand binding site, searches by triplets of chemical groups • biased to common ligand binding sites in PDB	http://sumo-pbil.ibcp.fr