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Proteins*Plus*: On-The-Fly Structure-Based Design on the Web

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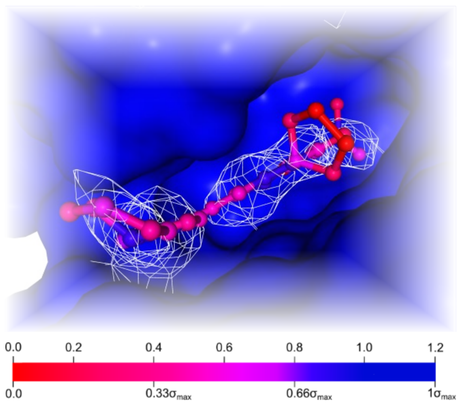
Proteins*Plus* (https://proteins .plus)[1] offers modelling support for numerous challenges in drug design. Its tools provide easy access for interdisciplinary researchers and students through an intuitive user interface without installation hurdles. Users can perform computational analyses with approx. 195k protein structures from the Protein Data Bank (PDB)[2] and millions of predicted AlphaFold Protein Structure Database[3] models at their fingertips. Capabilities include structure quality analyses for X-ray models, structure preparation (hydrogen and water placement, metal coordination assignment), pocket prediction, binding site comparisons, mutation analysis, automated molecular docking, 2D interaction visualization and editing, protein-protein complex analyses, and solvent channel visualization. All results are downloadable for further studies. With more than 600k page views per year, Proteins*Plus* is an internationally highly visible resource of the German Network for Bioinformatics Infrastructure (de.NBI).

Proteins*Plus* Services in a Nutshell

EDIA

X-ray structure **quality analyses** with the $EDIA_m$ for electron density fit assessment[4]



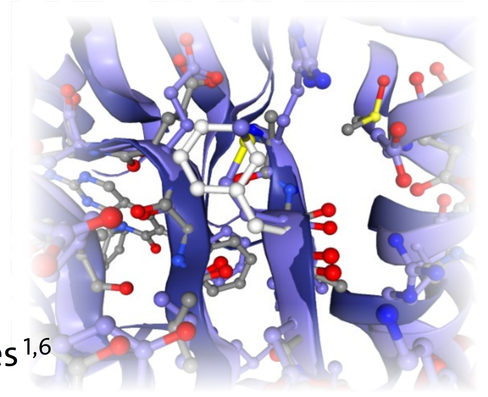
StructureProfiler

Checking protein-ligand complexes for compatibility with typical **quality criteria** in structure-based design[5]

Name	ACT_B_309	LQQ_B_401	DMS_B_402
HET-Code	ACT	LQQ	DMS
Chain	B	B	B
ID	309	401	402
Maximum atomic B factor	100	100	100
Occupancy	0	0	0
Crystal symmetry contacts	0	0	0
OWAB	83.9	53.8	72.2
$Edia_m$	0.61	0.5	0.47
Intramolecular clash	0	0	0
Unusual bond lengths	0	0	33.3
VSEPR bond angles	0	9.09	33.3
Torsion angles	0	0	0

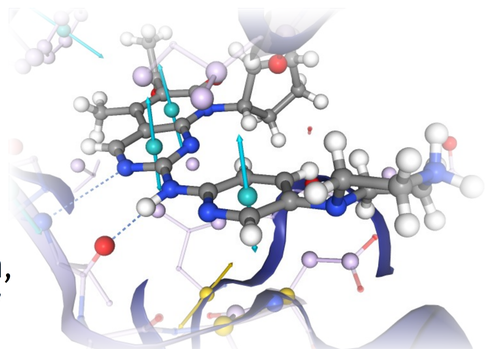
MicroMiner

Analyzing and visualizing the structural **impact of single-residue mutations** on binding sites and protein complexes[1,6]



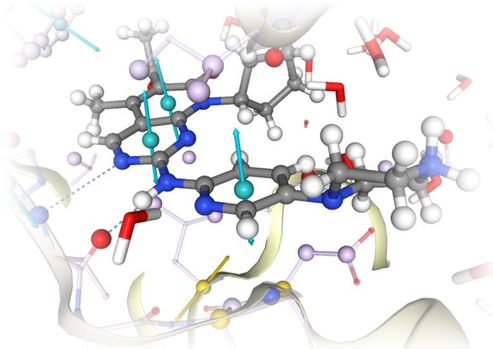
Protoss

Hydrogen atom coordinate assignment considering hydrogen bonds, metal coordination, repulsive contacts[7]



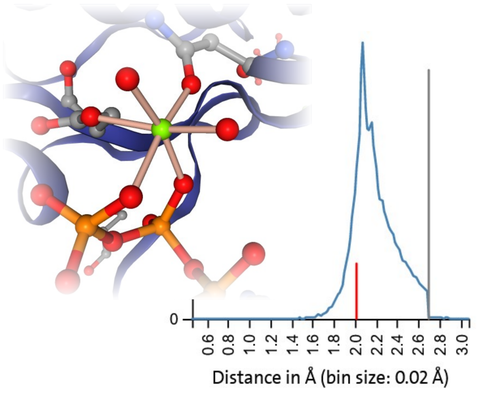
WarPP

Water placement for binding sites, efficiently and reliably optimizing hydrogen bond networks[8]



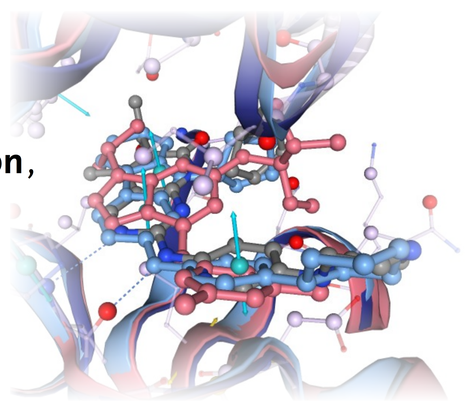
METALizer

Analyzing **metal coordination** geometries exploiting the knowledge of metal binding in the PDB[9]



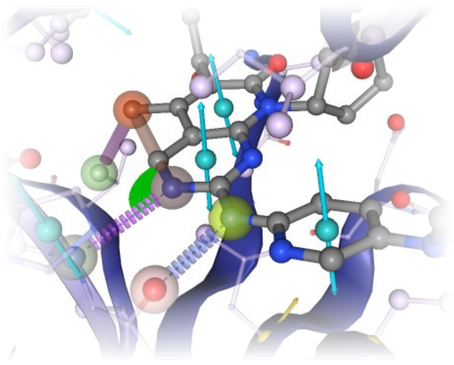
SIENA

Binding site **ensemble generation**, flexibility analyses and ligand pose comparisons for related sites[10]



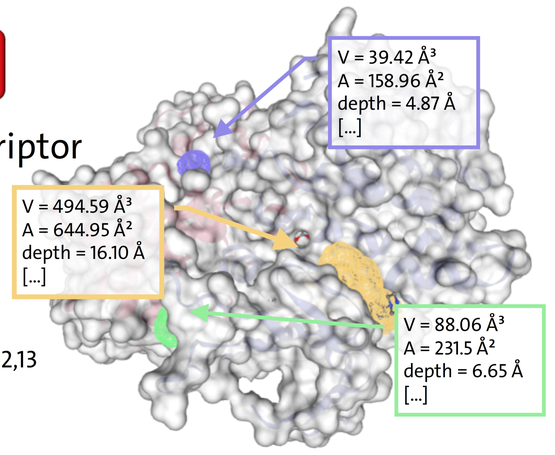
GeoMine

Binding site comparison based on user-specific textual, numerical, chemical and geometrical queries[11]



DoGSite3

Binding site descriptor calculation, **pocket prediction**, function annotation and virtual screening[12,13]



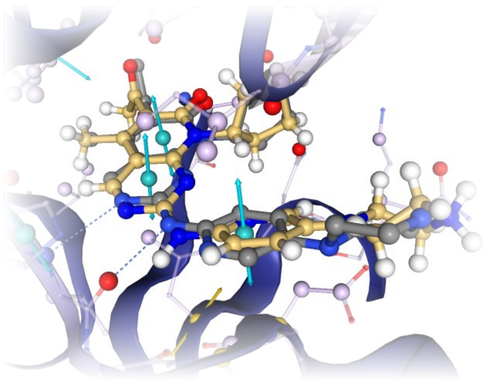
ActivityFinder

Annotating protein-ligand complexes by **activity data** from the ChEMBL database[14] (version 23) of bioactive molecules

PDB		ChEMBL 23	
Target ID	Compound ID	pChEMBL value	Type
2euf	ACT	4.44	Ki
2euf	ACT	4.97	Ki
2euf	LQQ	5.46	IC50
2euf	LQQ	6.05	IC50
2euf	LQQ	6.1	IC50
2euf	LQQ	7.2	IC50
2euf	LQQ	7.8	IC50
2euf	LQQ	7.96	IC50

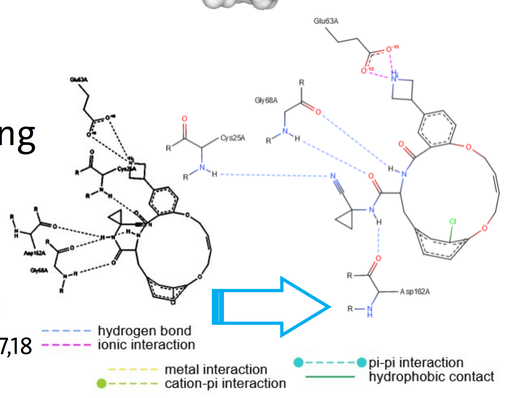
JAMDA

On-the-fly **molecular docking** for pose prediction, compound optimization and SAR analyses[1,15,16]



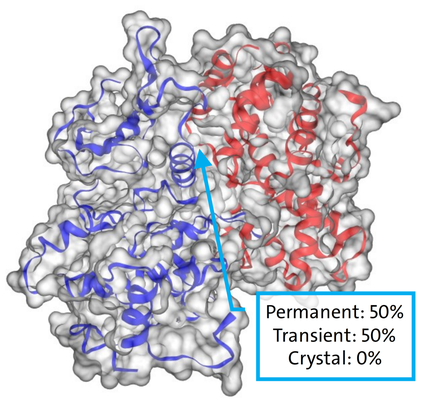
PoseEdit

Visualizing and editing protein-ligand **interactions in 2D** to pinpoint important binding site residues and ligand moieties[17,18]



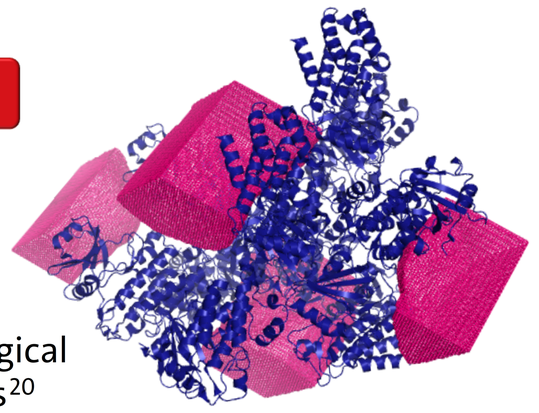
HyPPI

Protein-protein interface classification for permanent and transient complexes, and crystallographic interfaces[19]



LifeSoaks

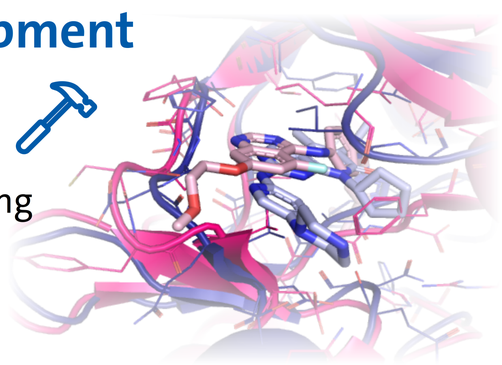
Exploring and visualizing **solvent channels in crystals** of biological macromolecules[20]



Under Development

SiteMine

Automated screening for **protein-ligand binding site similarities**



References

[1] Schöning-Stierand *et al.* (2022). Nucleic Acids Res, 50: W611-W615.
[2] Berman *et al.* (2000). Nucleic Acids Res, 28(1): 23542.
[3] Jumper *et al.* (2021). Nature, 596: 583-89.
[4] Meyder *et al.* (2017). J Chem Inf Model, 57(10): 2437-47.
[5] Meyder *et al.* (2018). Bioinformatics, 35(5): 874-6.
[7] Bietz *et al.* (2014). J Cheminf, 6(12): 1-12.
[8] Nittinger *et al.* (2018). J Chem Inf Model, 58(8): 1625-37.
[9] Schöning-Stierand *et al.* (2020). Nucleic Acids Res, 48: W48-W53.
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[11] Graef *et al.* (2022). J Med Chem, 65(2): 1384-95.
[12] Volkamer *et al.* (2010). J Chem Inf Model, 50(11): 2041-52.
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[19] Fährrolfes *et al.* (2017). Nucleic Acids Res, 45: W337-W343.