MED-SuMo

Target-based Drug Design at PDB Scale

Overview

MED-SuMo is a very powerful target-based drug design software. The core engine makes it possible to compare any interaction surface against the full Protein Data Bank in a few minutes.

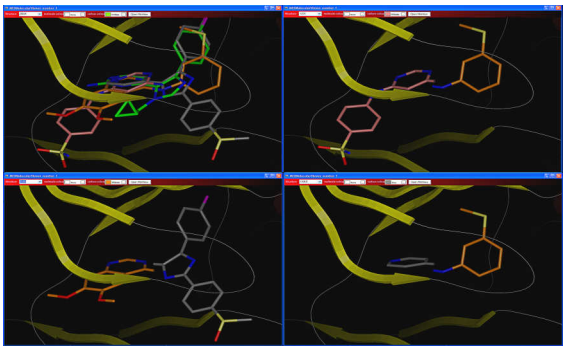
Independent to the notion of protein sequence or fold, *MED-SuMo* detects and compares biochemical functions on protein surfaces such as H-Bonds, Charges, Hydrophobic and Aromatic groups. In order to rapidly browse hundreds of hits, the *MED-SuMo* scoring function takes into account biochemical functions and shape overlaps.

This unique chemo-proteomic component bridges the protein and the ligand diversity spaces together by identifying all local similarities on interaction surfaces. Applications include (1) functional annotation, (2) allosteric site detection, (3) binding site characterization, (4) off-target identification, (5) scaffold hopping, (6) drug repurposing,,and in conjunction with *MEDP-Fragmentor* (7) fragment-based drug design, (8) bioisoteric replacement.

Compared to other methods in molecular modelling, *MED-SuMo* predictions are valuable because they are essentially based on experimental data from the PDB.

Fragment-Based Drug Design

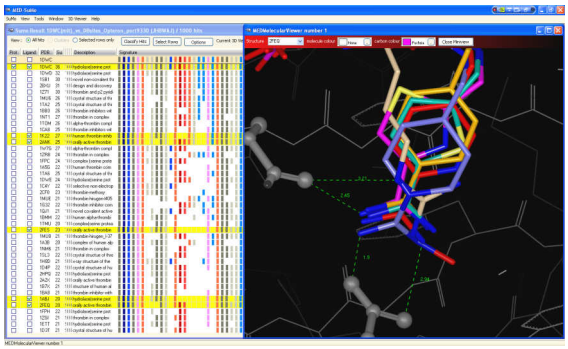
MED-SuMo generates hundreds of hits, i.e. protein-ligand complexes sharing some surface interaction features with the query. These chemical entities are exported into the 3D coordinates of the query. Therefore it's a very valuable starting point for any fragment-based drug design approach.



Overlay of 3 co-crystallized ligands from p38 MAP kinase (1DI9 in orange, 1A9U in grey, 1BMK in green)

Bioisosteric Replacement

From a standard *MED-SuMo* protein-ligand site comparison, it is possible to focus the hit list analysis on a local area by selecting a subset of the *MED-SuMo* signatures in the result table. Browsing suggested ligands provides a source of bioisosteric replacement candidates.

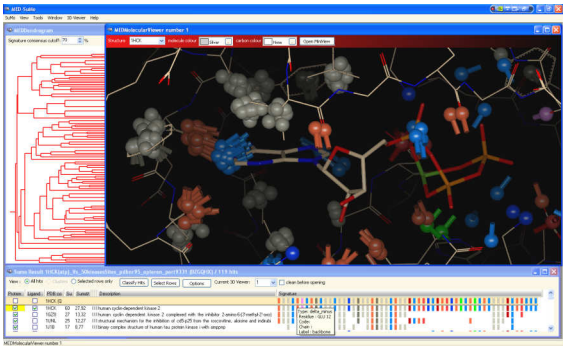


Thrombin enzyme1DWC is compared to the PDB. Hits with interaction in the P1 pocket show bioisosteric replacement to benzamidine

MED SuMo

Binding Site Characterization

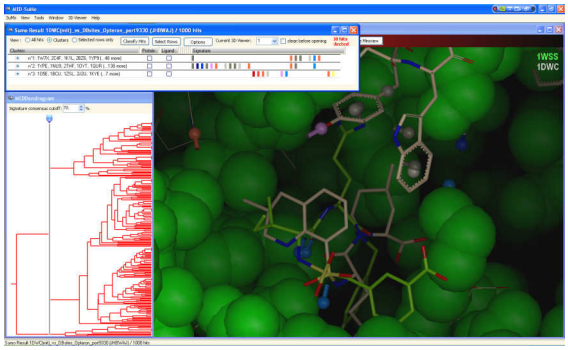
By comparing an active site of interest against the whole PDB, *MED-SuMo* makes it possible to characterize the binding pocket and assess interactions that contribute to affinity and selectivity. Such knowledge can be used as constraints in any virtual screening campaign to enrich the quality of predictions.



Comparison of 1HCK (CDK2) toward 50 kinases from PDB-nr95. Very frequent SuMo objects are related to similar binding pocket.

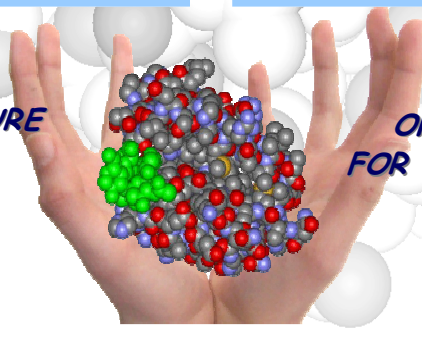
Functional Annotation

By submitting any whole protein surface against the binding site database, *MED-SuMo* retrieves all local chemical similarities between its surface and other candidates in the PDB. High performance makes it possible to include such valuable annotations into any functional genomic pipeline.



Thrombin enzyme (in white) 1DWC against the PDB. The 3 clusters highlight P2/P3-pockets, 60loop, and P1-pocket pocket. Trypsin is in green.

3D protein structure in your hand ?



Take Full advantage of this Unique Material for your Drug Design Process with MED-SuMo

MED-SuMo — Structure-Based Comparison of Protein-Ligand Interactions

MED-SuMo heuristic

The core *MED-SuMo* algorithm is based on the representation of macromolecular structures using a set of chemical functional groups. The detected functional groups on the protein surface environment are grouped into triplets, which are considered as the minimal unit for a biological function. The triplets form a graph which can be treated powerfully and quickly thanks to the graph theory. The result of comparisons consists of several matching sites. Each site is a set of pairs of matching functional groups.

Full protein and protein-ligand interaction surfaces are automatically detected. In addition, Protein-Fragment interaction surface are accessible into the *MEDP-Fragmentor* module by cross mining chemical library of small molecule onto pdb files

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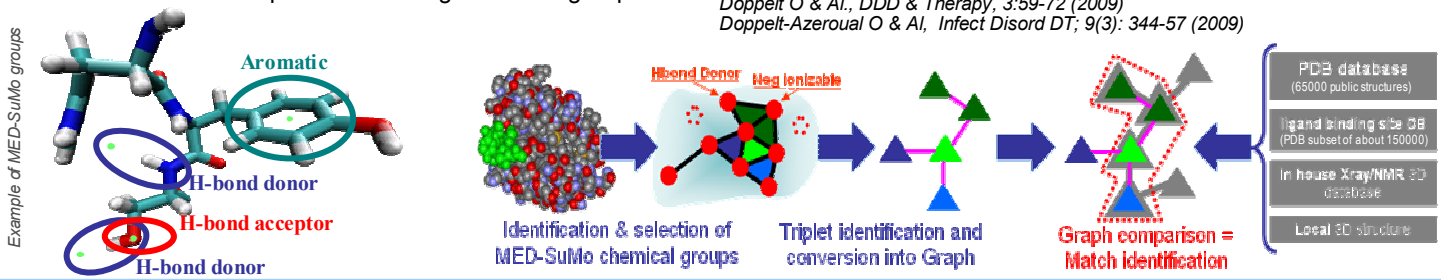
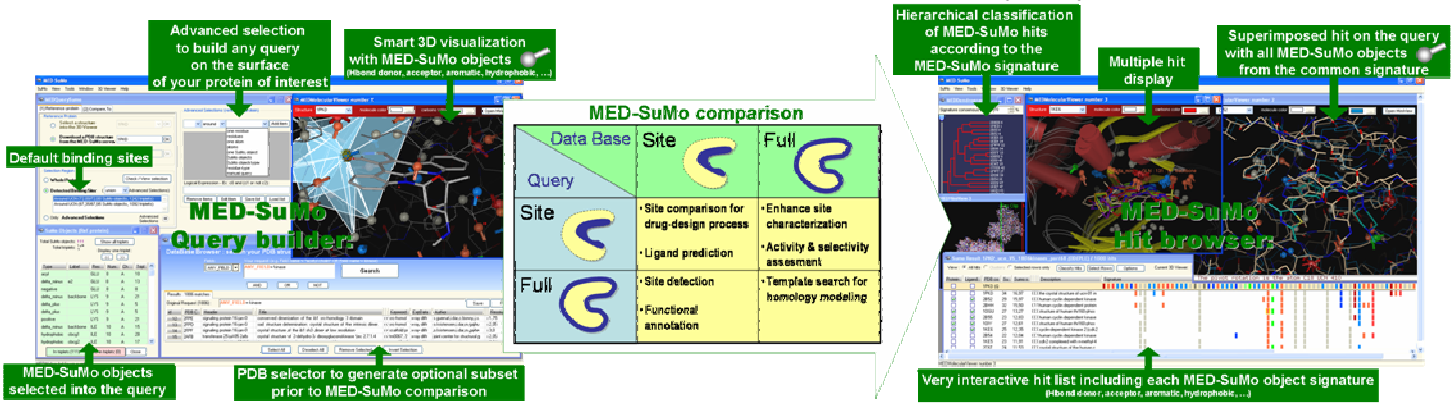


Working with MED-SuMo

MED-SuMo is based on a client-server architecture. The server works on Linux systems and takes advantage of multiprocessor platforms. The client interface (Windows and Linux versions) provides support to prepare and analyze any *MED-SuMo* surface comparison.



Summary

- **Powerful Chemo-Proteomic technology to compare interaction surfaces in the PDB (Protein Data Bank)**
- **Patented and published method**
- **Detect convergent or divergent function evolutions**
- **Leadability and Selectivity assessment**
- **Account for flexibility upon comparison**
- **Multiple ranking scores**
- **Full interaction between 3D superimposed protein-ligand, spreadsheet hit list, clustering window, and pharmacophoric signature**
- **Innovative starting point for structure-based drug design methods such as virtual screening**
- **Export protein and/or ligand hits into query coordinates**
- **Support PDB and/or proprietary databases**

Request further information about MED-SuMo today!

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