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# ProBiS-ligands Server

2014

## User's Guide

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Laboratory for Molecular Modeling  
National Institute of Chemistry  
Hajdrihova 19  
1000 Ljubljana, Slovenia  
[www.sicmm.org](http://www.sicmm.org)  
Support: [konc@cmm.ki.si](mailto:konc@cmm.ki.si)  
Collaborations: [dusa@cmm.ki.si](mailto:dusa@cmm.ki.si)

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# Background

ProBiS-ligands web server predicts binding of ligands to a protein structure. Starting with a protein structure or binding site, ProBiS-ligands first identifies template proteins in the Protein Data Bank that share similar binding sites. Based on the superimpositions of the query protein and the similar binding sites found, the server then transposes the ligand structures from those sites to the query protein.

# Software Requirement

ProBiS-ligands web server requires latest browsers that support HTML5 to use the Jsmol molecular viewer.

# Input

The screenshot shows the ProBiS-ligands web server interface. The main heading is "ProBiS ligands" with a logo on the left and "Protein Binding Sites Detection" on the right. Below the heading is a search bar with the placeholder "e.g., PDB ID" and a "Search" button. The main content area is titled "Predict Ligands by Similarity in Binding Sites" and contains several input fields and checkboxes. On the right side, there is a 3D molecular model of a protein structure with a binding site highlighted in yellow. The interface is annotated with six numbered steps: 1) PDB ID & Chain ID, 2) Select binding site (optional), 3) Change cutoff score for similar binding sites, 4) Search only for non-flexible similarities in binding sites, 5) Email (optional), and 6) Submit job. The "Local Alignments Only" checkbox is highlighted with an arrow pointing to step 4. The "Cutoff Z-Score" is set to 1.0 (default). The "Proteins to Compare Against" dropdown is set to "Non-redundant PDB". The "Your e-mail address (optional)" field is empty. The "Submit Job" button is at the bottom right.

1a) Get results from the ProBiS-Database

1) PDB ID & Chain ID

2) Select binding site (optional)

Loading of the protein in JSmol viewer may take a minute for the first time!

Binding site on chain A defined as a region within 3 Å of chain B (yellow)

3) Change cutoff score for similar binding sites

4) Search only for non-flexible similarities in binding sites

5) Email (optional)

6) Submit job

**Figure 1.** ProBiS-ligands input page. If the user checks the “Local Alignments Only” checkbox, ProBiS algorithm will run with the “-local” option, and will only find near perfect local structural alignments with about  $<2$  Å root mean square deviation (RMSD) between the aligned residues. Otherwise, residues with up to 7 Å

RMSD will be considered in the alignments, which allows to find similar, but flexible residues in compared proteins.

# Output

ProBiS-ligands output page is shown in Figure 2.

The screenshot displays the ProBiS-ligands web interface. On the left, a 3D JSmol viewer shows a protein structure with green ribbons representing invariant binding site residues and grey sticks representing transposed ligands. On the right, a table titled "1D0C, Chain A: 100 similar structures" lists predicted ligands. The table has columns for Structure, Cluster, Name, Source, BSite, and Ligand. Annotations with arrows point to specific features: "Invariant binding site residues" and "Transposed ligands" on the 3D model; "Click to view invariant binding site residues in JSmol viewer" pointing to the BSite column; "Click to view 3D model of transposed ligand in JSmol viewer" pointing to the Ligand column; "Show conservation scores on the query protein" pointing to the conservation bar at the bottom; and "Change representation of the query protein (currently shown as green ribbons)" pointing to the "Asymmetric Unit" dropdown menu.

Structure	Cluster	Name	Source	BSite	Ligand
	1	N-[(3s,4s)-4-[(6-amino-4-methylpyridin-2-yl) methyl]piperidin-2-yl]piperidine	3b3p	Remove 3D	Remove 3D
	1	N-[(3s,4s)-4-[(6-amino-4-methylpyridin-2-yl) methyl]piperidin-2-yl]piperidine	3yx5	View 3D	View 3D
	1	2-[[[2-[(3s,4s)-4-[(6-amino-4-methylpyridin-2-yl) methyl]piperidin-2-yl]piperidin-2-yl]amino]ethyl]pyridine	3yn3	Remove 3D	Remove 3D
	1	6-[[[(3r,4s)-4-[(2-[[[2-[(3s,4s)-4-[(6-amino-4-methylpyridin-2-yl) methyl]piperidin-2-yl]piperidin-2-yl]amino]ethyl]pyridin-2-yl]amino]ethyl]pyridin-2-yl]piperidin-2-yl]piperidine	3nb3	View 3D	View 3D
	1	6-[[[(3r,4s)-4-[(2-[[[2-[(3s,4s)-4-[(6-amino-4-methylpyridin-2-yl) methyl]piperidin-2-yl]piperidin-2-yl]amino]ethyl]pyridin-2-yl]amino]ethyl]pyridin-2-yl]piperidin-2-yl]piperidine	3jpe	View 3D	View 3D
	1	6-[[[(3r,4r)-4-[(5-(6-aminopyridin-2-yl) pentyl)oxy]pyrimidin-2-yl]piperidin-2-yl]piperidine	3ulw	View 3D	View 3D
	1	6,6'-[pyridine-2,6-diyldithane-2,1-diylbis(4-methylpiperidin-2-yl)]dipiperidine	3n5y	View 3D	View 3D
	1	N-[(3s,4s)-4-[(6-amino-4-methylpyridin-2-yl) methyl]piperidin-2-yl]piperidine	3jvs	View 3D	View 3D
	1	6,6'-[[[2s,3s)-2-aminobutane-1,3-diyl]bis(oxymethone)]dipiperidine	3rqn	View 3D	View 3D
	1	N-[(3s,4s)-4-[(6-amino-4-methylpyridin-2-yl) methyl]piperidin-2-yl]piperidine	3jvw	View 3D	View 3D
	1	6,6'-[[[2s,3s)-2-aminobutane-1,3-diyl]bis(oxymethone)]dipiperidine	4t5g	View 3D	View 3D

Figure 2. ProBiS-ligands output page. Left: Jsmol viewer. Right: predicted ligands (small molecule tab open).

# JSmol Help

Some key tips on how the user can manipulate the 3D protein model in JSmol are presented in Figure 3.

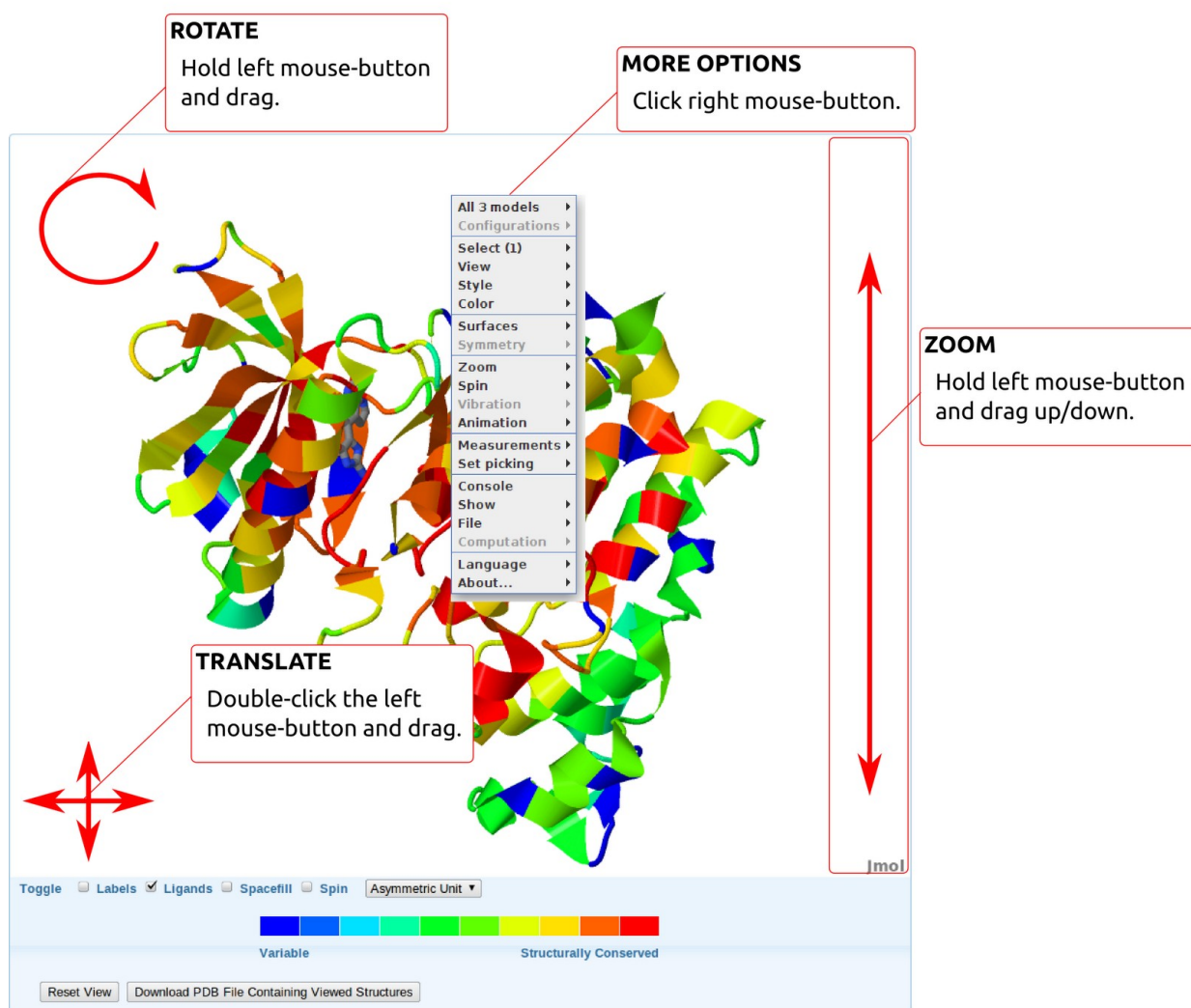


Figure 3. Mouse operations in JSmol.