

User's Guide

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INTRODUCTION

Candock web server offers a web-based, easy to use interface that handles all aspects of molecular docking. It is designed to predict how small molecules, such as substrates or drug candidates, bind to a receptor of known 3D structure. User friendly interface provides full control over the input settings of ligands and protein, for more advanced users it offers a choice of algorithm parameters. The application can be used for docking and analysis of single ligand as well as for docking ligands databases to target protein. Results are shown in three-dimensional graphics which allows users to explore potential drug - protein interactions effortlessly.

In the background of the Candock web server is the Candock algorithm, an advanced fragment-based molecular docking algorithm enabling both protein and ligand flexibility, and running in parallel on a cluster of computers. More information about the algorithm can be found at <http://tyr.cmm.ki.si/candock-server/?what=algorithm>.

Web server is available at <http://tyr.cmm.ki.si/candock-server/>.

The screenshot displays the Candock web server interface. The main heading is "Predict the preferred orientation of ligands to a protein." The interface includes several input fields: "PDB ID:" with a dropdown menu set to "all", "Chain ID(s):" with a dropdown menu set to "A, AB", and an "Upload a PDB file" button. Below these are options for "Upload a ligand database in file (mol2 or smi)" and "Draw ligands structure". There is a "Select Binding Site (mandatory)" section showing "0 selected binding sites" and an "Advanced Parameters (optional)" section. At the bottom, there is a field for "Your e-mail address (optional):" with a note: "A link to the results page will be sent to you by e-mail. Computation for a medium sized database will take a few hours." The left sidebar contains "Introduction", "Download", "Help", and "Related Citations". The right sidebar contains a "Video Tutorial" section with a video player and a "Contact" section with a form for suggestions, questions, comments, or bug reports. Two yellow arrows with red outlines point to the "User's Guide" link in the sidebar and the "Video Tutorial" section.

Figure 1: Web Server

INPUT

The screenshot shows the input form for the CANDOCK SERVER. It includes several input fields and buttons, with yellow arrows pointing to specific parts:

- Protein Input:** Points to the "PDB ID" field (containing "1all") and the "Chain ID(s)" field (containing "A, AB").
- Ligands Input:** Points to the "Ligands to Compare Against" dropdown menu (set to "Test Database") and the "Upload a ligand database in file (mol2 or smi)" button.
- Binding Site Selection:** Points to the "Select Binding Site (mandatory)" button.
- Algorithm Parameters:** Points to the "Advanced Parameters (optional)" button.
- E-mail:** Points to the "Your e-mail address (optional)" field.
- Submit Job for Docking:** Points to the "Submit Job" button.

The form contains the following text and elements:

PDB ID: Chain ID(s):

[Upload a PDB file](#)

Ligands to Compare Against:
Source: test-database

[Upload a ligand database in file \(mol2 or smi\)](#)

[Draw ligands structure](#)

Select Binding Site (mandatory)
0 selected binding sites

Advanced Parameters (optional)

Your e-mail address (optional):

A link to the results page will be sent to you by e-mail.
Computation for a medium sized database will take a few hours.

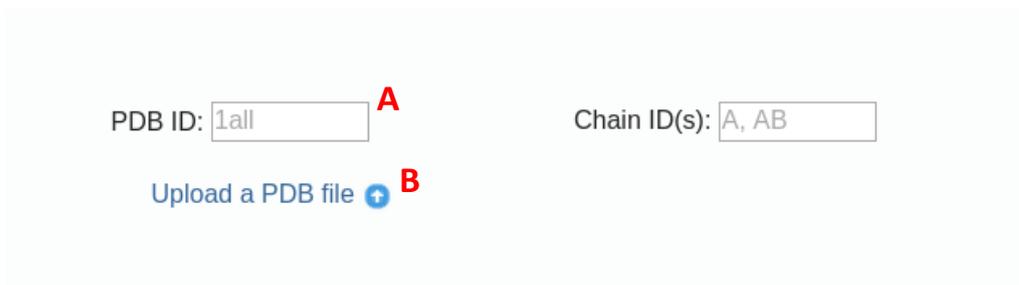
[Submit Job for Docking](#)

Figure 2: Input

PROTEIN INPUT

Select input protein and it's chain(s).

- Write PDB ID and Chain ID(s)
- or Upload a PDB file



PDB ID: **A** Chain ID(s):

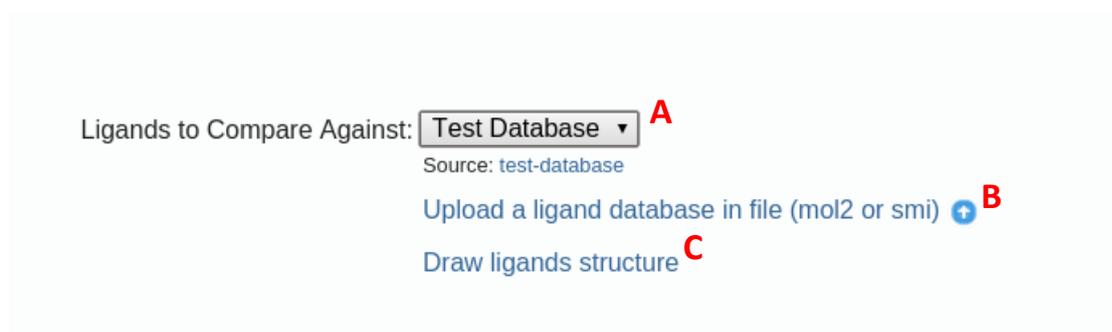
[Upload a PDB file](#) **B**

Figure 3: Protein Input

INPUT OF LIGANDS

Select ligands for docking with one of the following methods:

- Select ligands database from [ZINC](#)
- Upload a ligand database in file. File with suffix mol2 or smi can be accepted
- Draw custom ligands structure with [MarvinSketch](#) tool



Ligands to Compare Against: **A**
Source: test-database

[Upload a ligand database in file \(mol2 or smi\)](#) **B**

[Draw ligands structure](#) **C**

Figure 4: Input of Ligands

If you click on **Draw ligands structure** window shown in Figure 5 will pop up. Help is available by hovering with mouse over blue info icon (Figure 5, A).

It enables drawing ligand structure with MarvinSketch application. To add ligand for docking click blue button with green plus icon in top toolbar (Figure 5, B). Ligands will be shown in the right side under "Ligands:" (Figure 5, C). They can be removed with click on red x icon (Figure 5, D). When finished click on exit button (Figure 5, F).

If you are not familiar with MarvinSketch you can see [user guide](#).

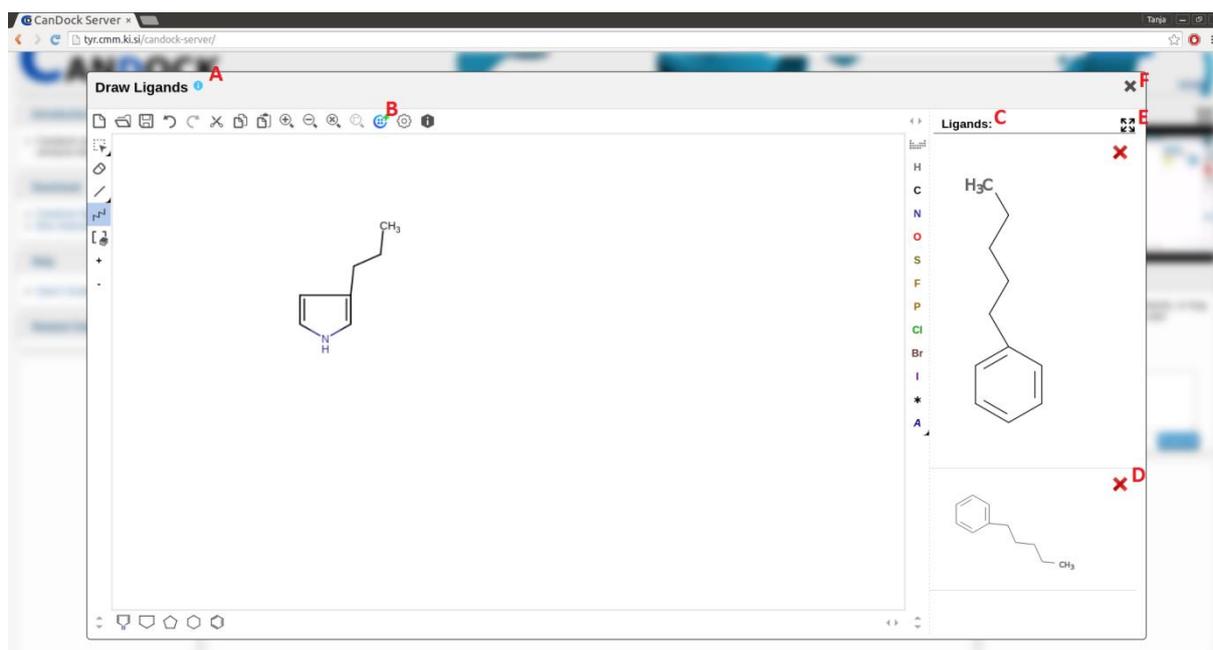


Figure 5: Input of Ligand with MarvinSketch Tool. A: Help, B: Add ligand for docking C: List of drawn ligands, D: Remove ligand, E: Full Screen, F: Exit

BINDING SITES SELECTION

Click **Select Binding Site (mandatory)** and window in Figure 6 will be shown.

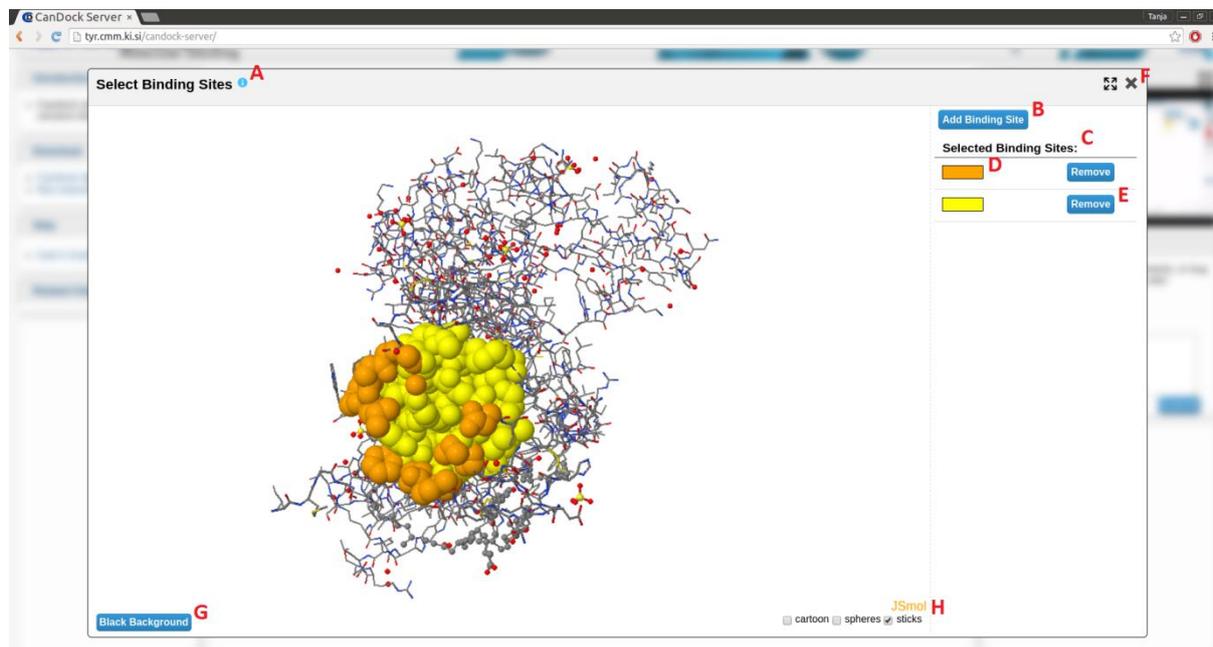


Figure 6: Binding Sites Selection A: Help, B: Add binding site button, C: List of selected binding sites, D: Precalculated binding site, E: Remove binding site, F: Exit, G: Change background color, H: Set protein view

Under the **Selected Binding Sites** (Figure 6, C) are shown predicted binding sites using ProBiS binding sites detection algorithm. These binding sites were predicted for the representative protein of the selected protein and mapped onto the selected protein. On default predicted binding sites are already selected for docking. Click **Remove** (Figure 6, E) button if you want to change that.

In addition, you can also add custom binding sites by selecting atoms and pressing **Add binding site** button (Figure 6, B). Small window (Figure 7) will pop up in which you have to set radius of binding site. Depending on what atoms were selected their geometric center will be calculated. Binding site will include all atoms whose distance to geometric center is smaller than the chosen radius. Click **Add Binding Site** button to add selected binding site for docking. Click **Cancel** to cancel adding.

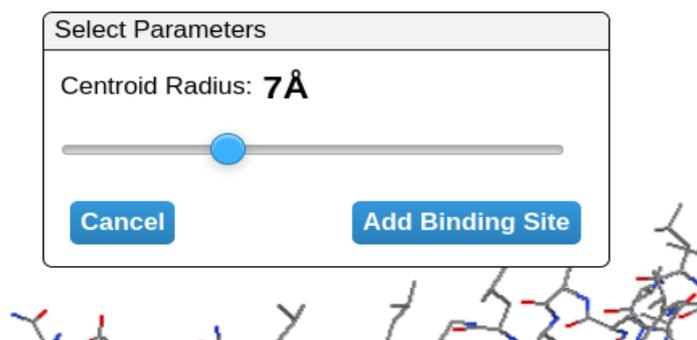


Figure 7: Set centroid radius

When finished selecting binding sites click on exit button in the top right corner (Figure 6, F).

SETTING ALGORITHM PARAMETERS

Click on **Advanced Parameters (optional)** to change algorithm settings. Hover with mouse over blue info icon to see a brief description of parameter. Default values are already written in the input boxes.

Advanced Parameters (optional) 

Algorithm Parameters

Num Iter:	<input type="text" value="1000"/>		Max Seeds To Cluster:	<input type="text" value="2000"/>	
Max Num Clus:	<input type="text" value="500"/>		Min Pts:	<input type="text" value="5"/>	
Clus Rad:	<input type="text" value="1.0"/>		Top Percent:	<input type="text" value="0.80"/>	
Interatomic	<input type="text" value="8.0"/>		Excluded:	<input type="text" value="0.8"/>	
Grid:	<input type="text" value="2.0"/>		Num Bsites:	<input type="text" value="1"/>	
Radial:	<input type="text" value="10.0"/>		Max Iter:	<input type="text" value="0"/>	
Mini Tol:	<input type="text" value="0.1"/>		Fftype:	<input type="text" value="kb"/>	
Docked Min Pts:	<input type="text" value="3"/>		Docked Max Num Clus:	<input type="text" value="10"/>	
Docked Clus Rad:	<input type="text" value="2.0"/>		Tol Min Coeff:	<input type="text" value="0.7"/>	
Tol Max Coeff:	<input type="text" value="1.0"/>		Tol Dist:	<input type="text" value="3.0"/>	
Spin:	<input type="text" value="15"/>		Max Num Ligands:	<input type="text" value="1000"/>	
Scale:	<input type="text" value="0.01"/>		Step:	<input type="text" value="0.1"/>	
Cutoff:	<input type="text" value="8"/>		Func:	<input type="text" value="radial"/>	
Comp:	<input type="text" value="reduced"/>		Ref:	<input type="text" value="mean"/>	
Probis Min Pts:	<input type="text" value="10"/>		Probis Clus Rad:	<input type="text" value="2.0"/>	
Neighb:	<input type="text"/>				

Figure 8: Algorithm Parameters

E-MAIL ADDRESS

Your e-mail address (optional):

A link to the results page will be sent to you by e-mail.
Computation for a medium sized database will take a few hours.



Figure 9: Email input

A link to the results page will be sent to you by e-mail. Docking for a medium sized database will take a while.

SUBMIT JOB FOR DOCKING

Click on blue **Submit Job** button.

AFTER SUBMITTING JOB FOR DOCKING

Moving rectangle (Figure 10, A) shows current state of your Candock job. You can close this window if you want to.

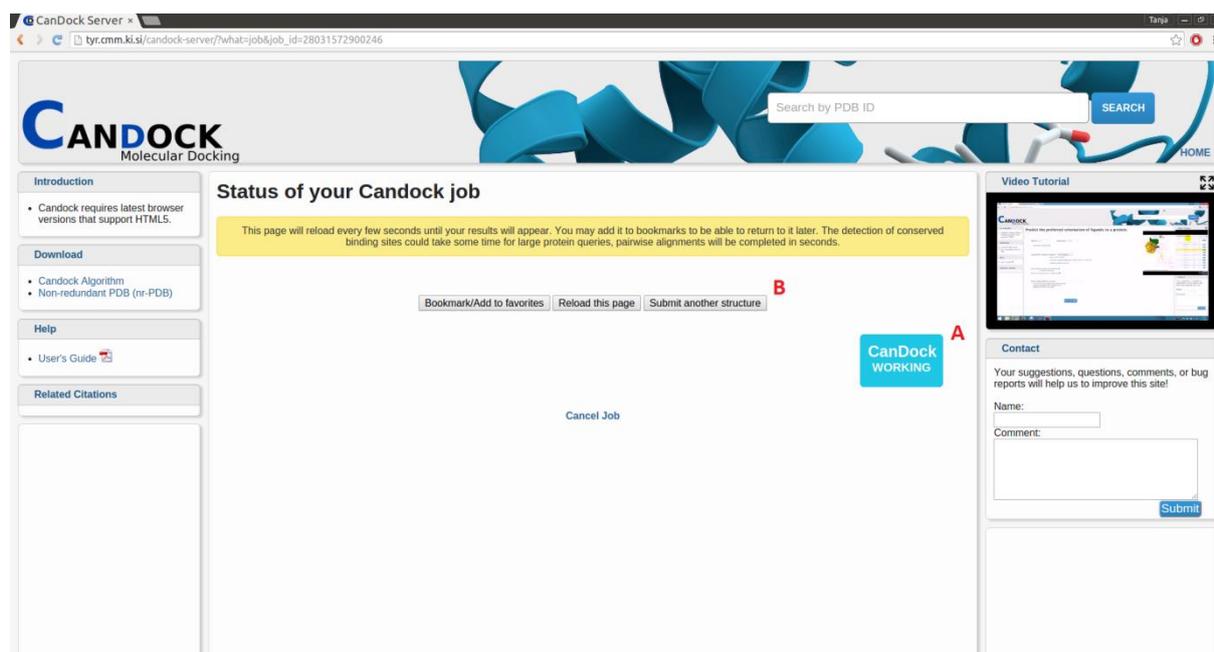


Figure 10: Status of your Candock job

Check your email. Two emails will be sent to you. One after submitting job for docking and the other when your job will be finished.

In Figure 10, B you can see 3 buttons. If you didn't write down your email we strongly recommend you that you click on **Bookmark/Add to favorites** button to save the url address of the web page where results will be shown. For submitting new job click on **Submit another structure**.

You'll be redirected to results page when your job is done.

RESULTS

On the right side is table with results. By default, the predicted ligands' poses are sorted by interaction energy values.

The screenshot shows the Candock server interface. On the left, a 3D ribbon model of a protein is displayed in red. On the right, a table lists 68 ligands for chain A. The table columns are 'structure', 'ligand', 'total', 'interaction', and '3D'. The first row is highlighted in yellow and shows a ligand with ID CHEMBL480556_7, a total score of 25604.25, and an interaction energy of -0.10. A 'View 3D' button is next to it. A yellow starburst labeled 'Results' points to the table. A yellow arrow labeled 'Add Ligand to 3D View' points to the 'View 3D' button. Other annotations include 'Menu' pointing to the top navigation bar and 'Full Screen' pointing to the top right corner.

Figure 11: Results Page

Click on + button to expand a ligand's line to see SMILES code and source of this ligand. Click on the **Source** and drop-down menu with links to webpages will be shown.

The table shows the expansion of the first row. The 'structure' column has a minus sign and a chemical structure icon. The 'ligand' column contains the ID CHEMBL480556_7. The 'total' column shows 25604.25 and the 'interaction' column shows -0.10. A 'View 3D' button is in the '3D' column. Below the main row, a yellow bar contains 'SMILES: COCCOc1ccc(cc1)N1CCN(CC1)CCOc1cc2nc(nn2c(n1)N)c1ccc01' and a 'Source' dropdown menu. The dropdown menu is open, showing 'CHEMBL' and a 'close' button.

structure	ligand	total	interaction	3D
-	CHEMBL480556_7	25604.25	-0.10	View 3D
SMILES: COCCOc1ccc(cc1)N1CCN(CC1)CCOc1cc2nc(nn2c(n1)N)c1ccc01				
Source				
close				
+	CHEMBL480556_2	25801.71	-0.07	CHEMBL

Figure 12: Source

Click on picture of ligand in order to see a bigger one. Hide pop up window with picture by clicking on it.

3EML , Chain A : 68 ligands »

Download Table

structure	ligand	total	interaction	3D
	CHEMBL480556_7	25604.25	-0.10	View 3D
SMILES: <chem>COCOC1CC(CO1)N1CCN(CO1)CCCC1CC2NC(NN2C(N1)N)C1CCCO1</chem> Source ▼				
	CHEMBL480556_2	25801.71	-0.09	View 3D
	CHEMBL480556_1	25748.15	-0.08	View 3D
	CHEMBL480556_8	25674.92	-0.08	View 3D

Figure 13: Bigger Picture

Click on **View 3D** button to add ligand's three-dimensional pose to Jsmol viewer. Zooming in and out is enabled by mouse scroll wheel.

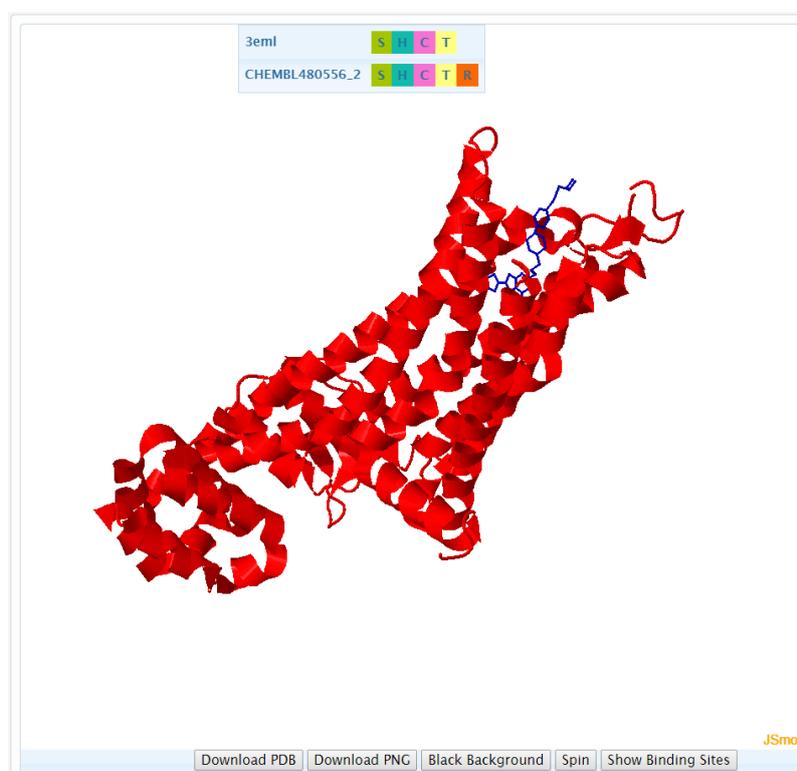


Figure 14: Ligand and protein in Jsmol

Click on **Show Binding Sites** to see the selected binding sites to which docking was performed in JSmol.

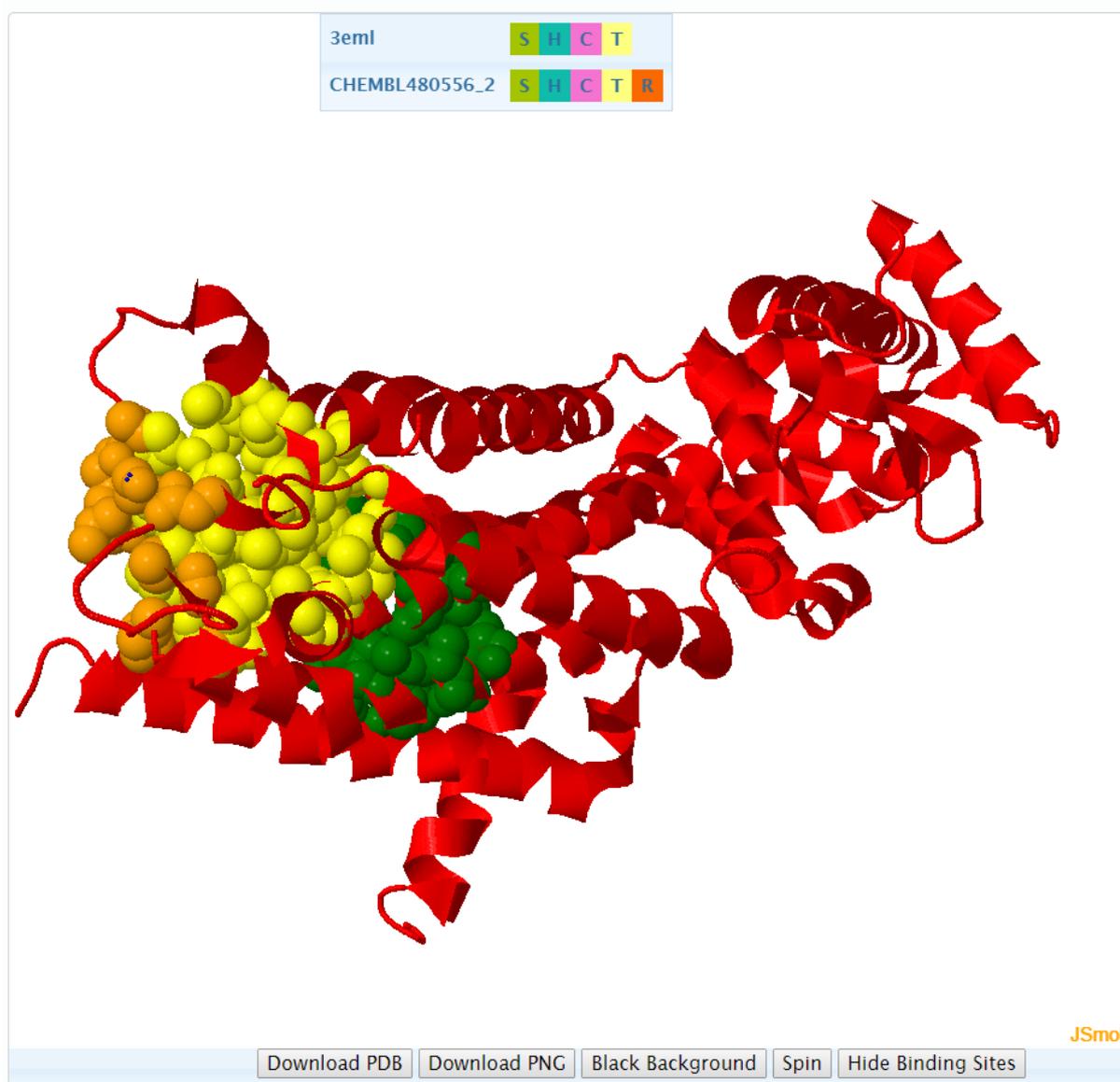


Figure 15: Shown binding sites

Click on **Download PDB** to download pdb file with protein and currently shown ligands. With **Download PNG** button png picture of JSmol can be downloaded.

JSMOL CONTROL

A menu box inside the Jsmol viewer lists the ligands and the protein that are currently shown in JSmol. You can remove ligand from 3D view by clicking on orange **R** button in menu or on blue **Remove 3D** button in right table.

Menu legend: **S** – show, **H** – hide, **C** – color, **T** – tools.

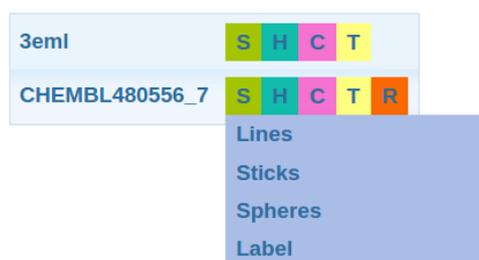


Figure 16: Menu: Show

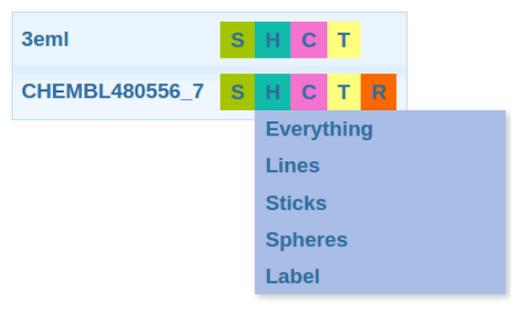


Figure 17: Menu: Hide

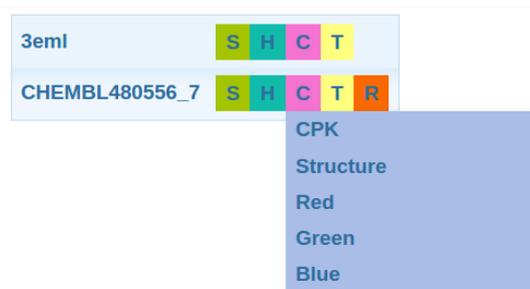


Figure 18: Menu: Color

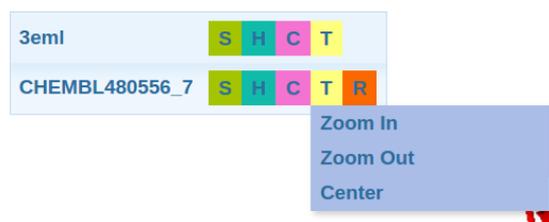
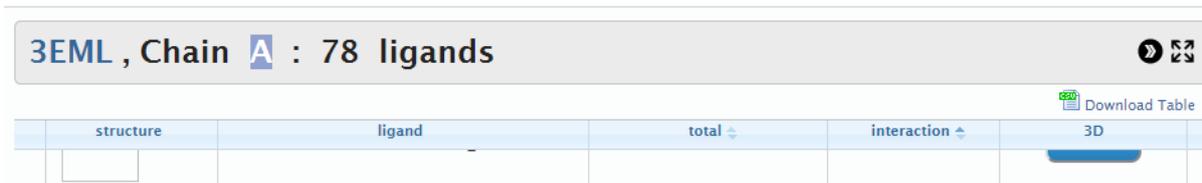


Figure 19: Menu: Tools

On the right top side of the results table are three buttons.



structure	ligand	total	interaction	3D

Figure 20: Table Control

Click on >> to hide or show table. Button  enables full screen view. Click on **Download Table** to download results table in CSV.

SEARCH FOR PAST RESULTS



CANDOCK
Molecular Docking

Search by PDB ID **SEARCH**

Search Results

PDB ID	Chain	Ligand Database	Time
1AZE	A	test-database.mol2	19.03.15

Introduction
• Candock requires latest browser versions that support HTML5.

Download
• Candock Algorithm
• Non-redundant PDB (nr-PDB)

Help

Video Tutorial

Contact
Your suggestions, questions, comments, or bug reports will help us to improve this site!

You can check if someone already docked the same job that you want to. Write PDB ID in search box and click **SEARCH** button. Past jobs are listed under »Search Results«. Click on PDB ID (example: 1AZE) to be redirected to the existing results page.