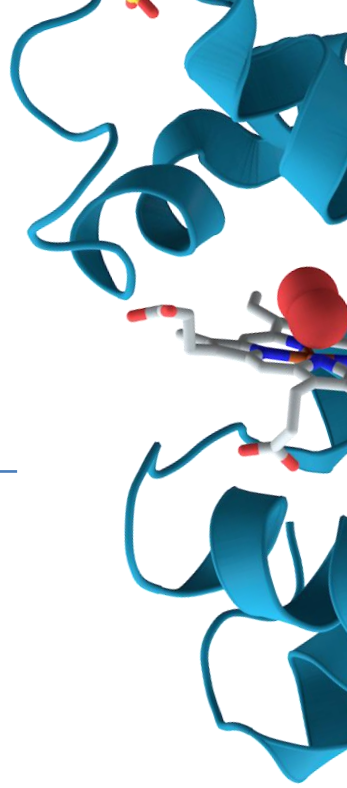

CANDOCK WEB SERVER

Molecular Docking

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/.

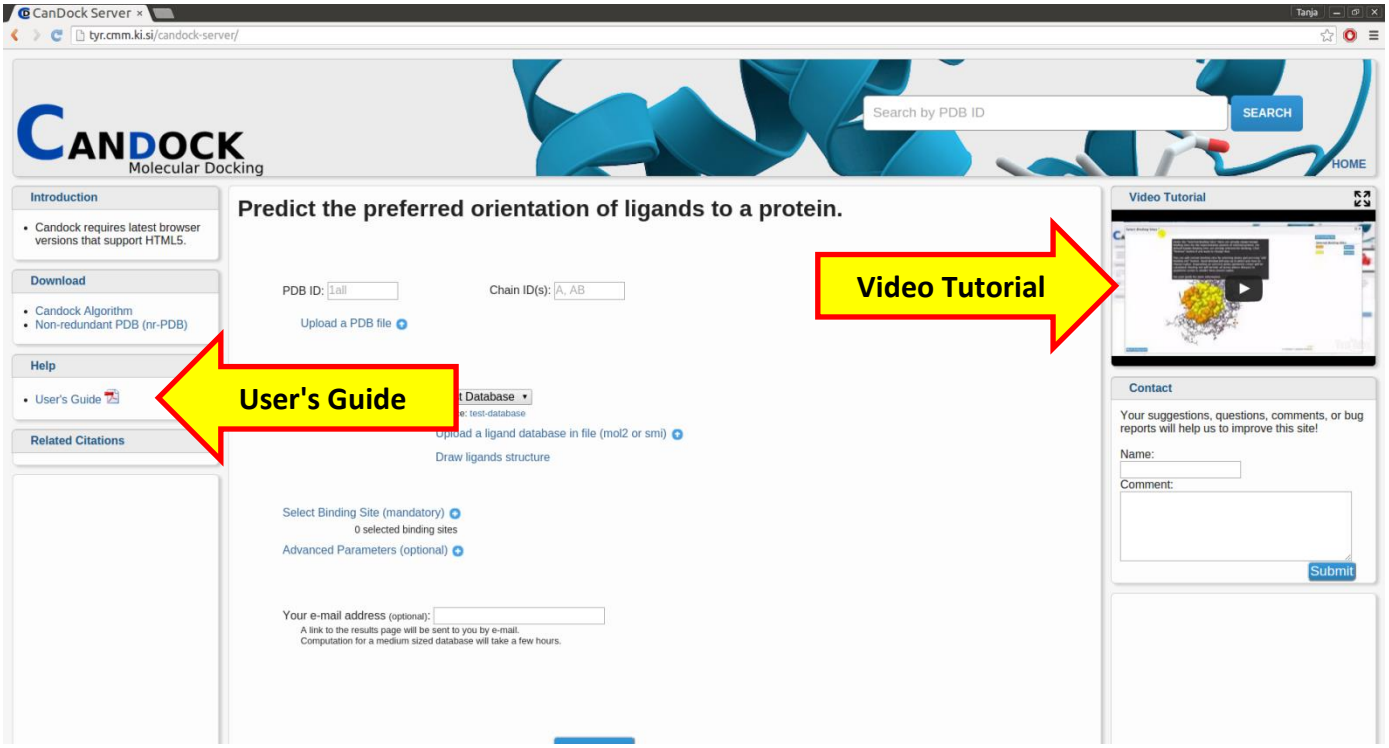


Figure 1: Web Server

INPUT

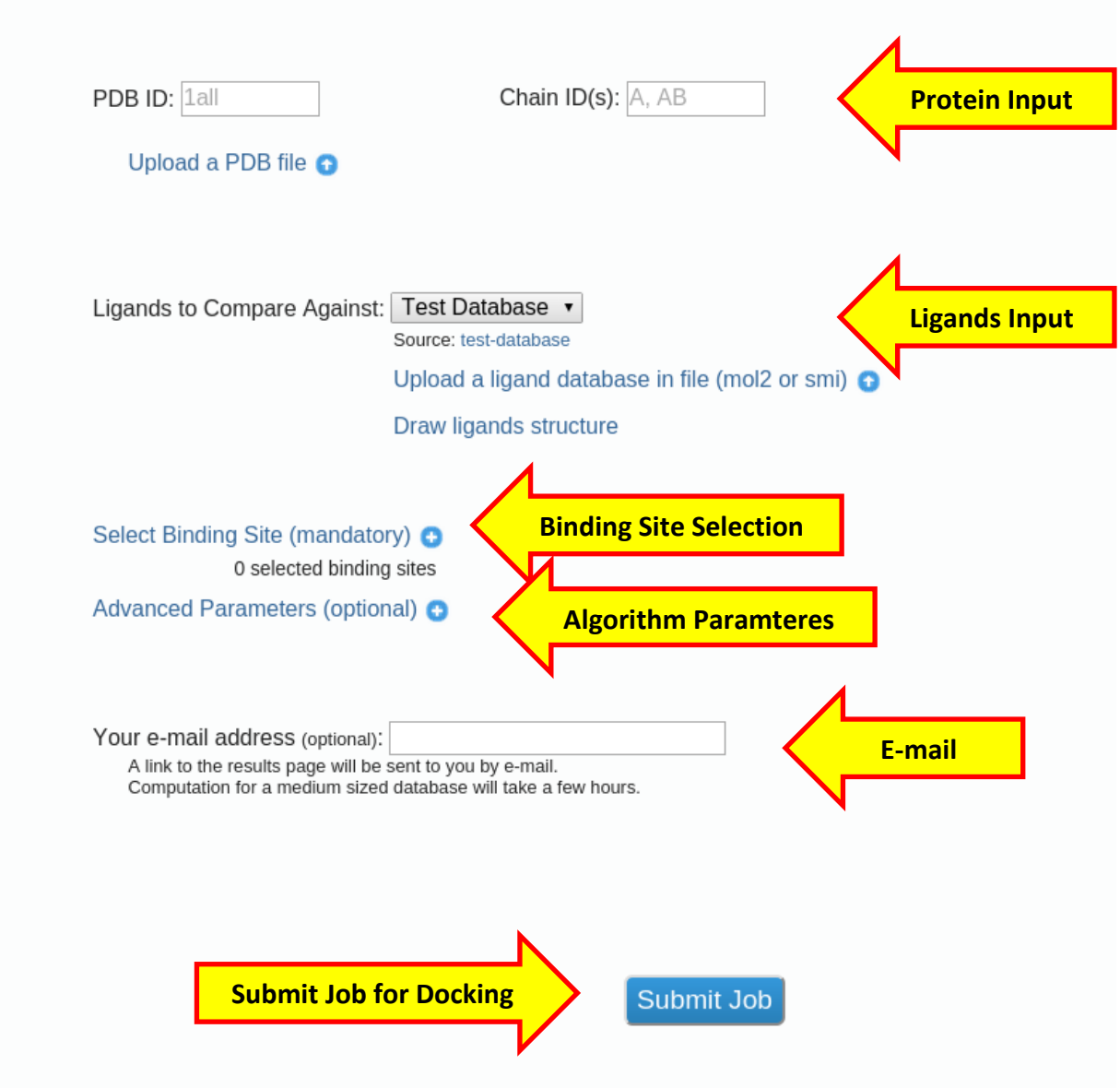


Figure 2: Input

PROTEIN INPUT

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

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

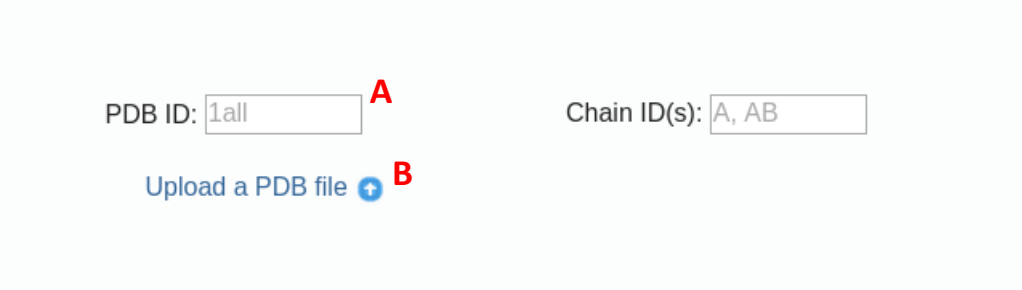


Figure 3: Protein Input

INPUT OF LIGANDS

Select ligands for docking with one of the following methods:

a) Select ligands database from ZINC
b) Upload a ligand database in file. File with suffix mol2 or smi can be accepted
c) Draw custom ligands structure with MarvinSketch tool

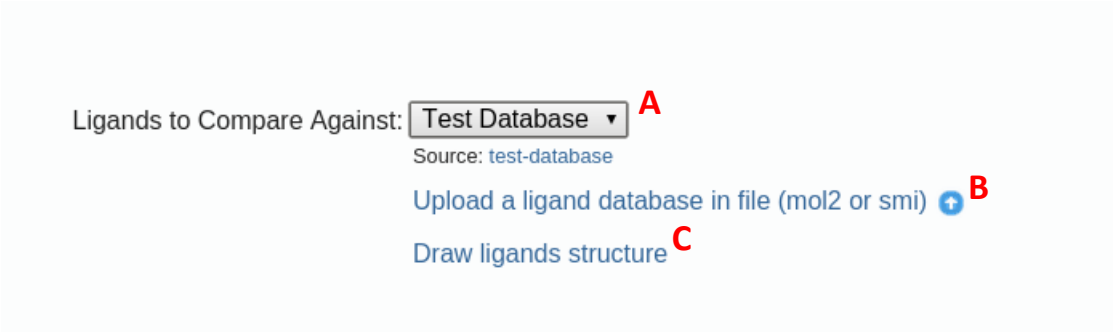


Figure 4: Input of Ligands

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.

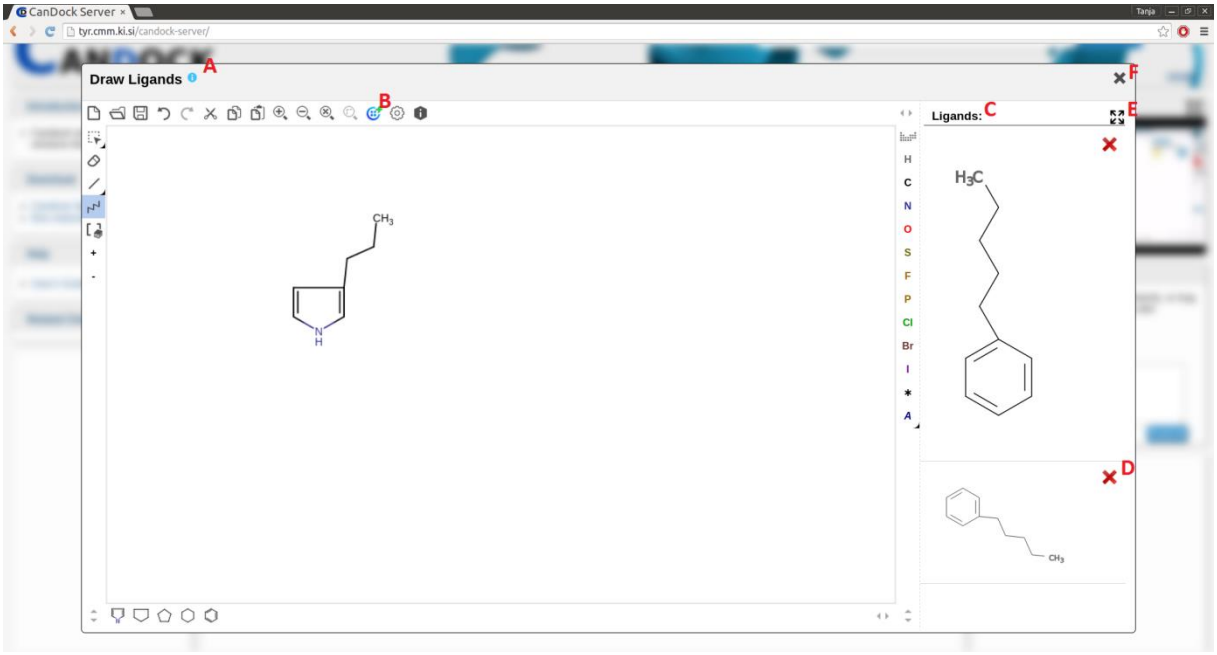


Figure 5: Input of Ligand with MarvinSketch Tool. A: Help, B: Add ligand for docking C: List of drawn ligands, D: Remove ligand, E: Full Screen, F: Exit

BINDING SITES SELECTION

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

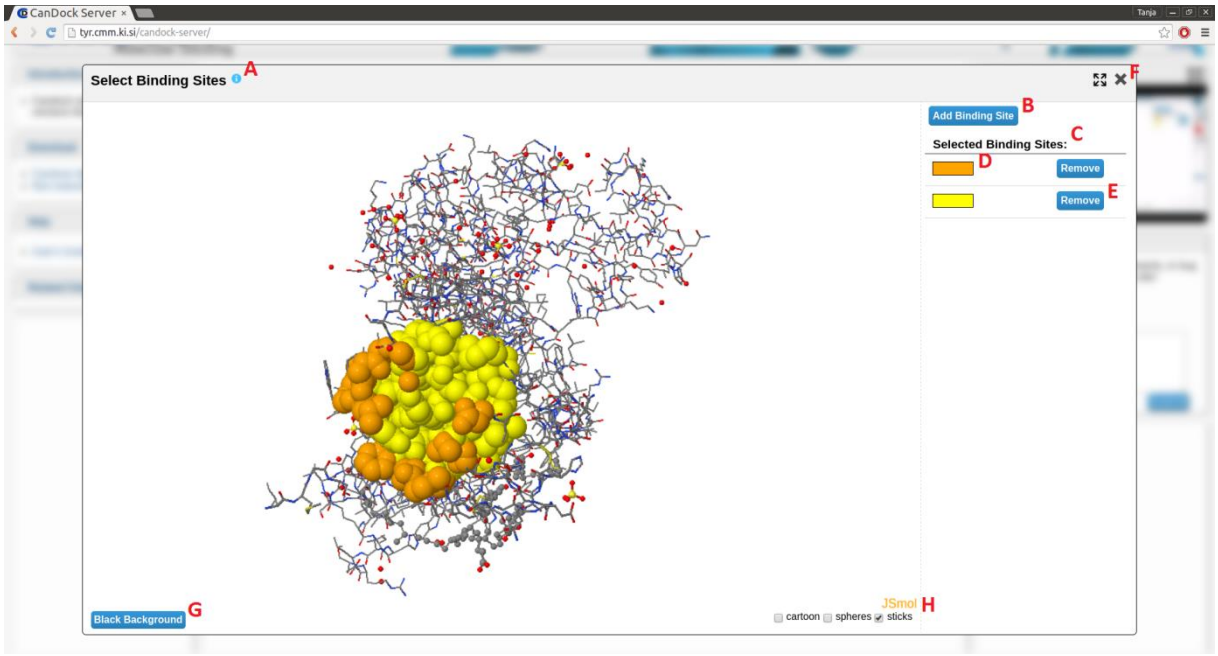


Figure 6: Binding Sites Selection A: Help, B: Add binding site button, C: List of selected binding sites, D: Precalculated binding site, E: Remove binding site, F: Exit, G: Change background color, H: Set protein view

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.

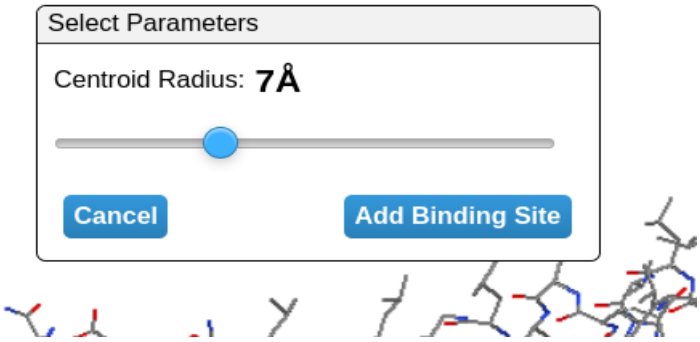


Figure 7: Set centroid radius

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.

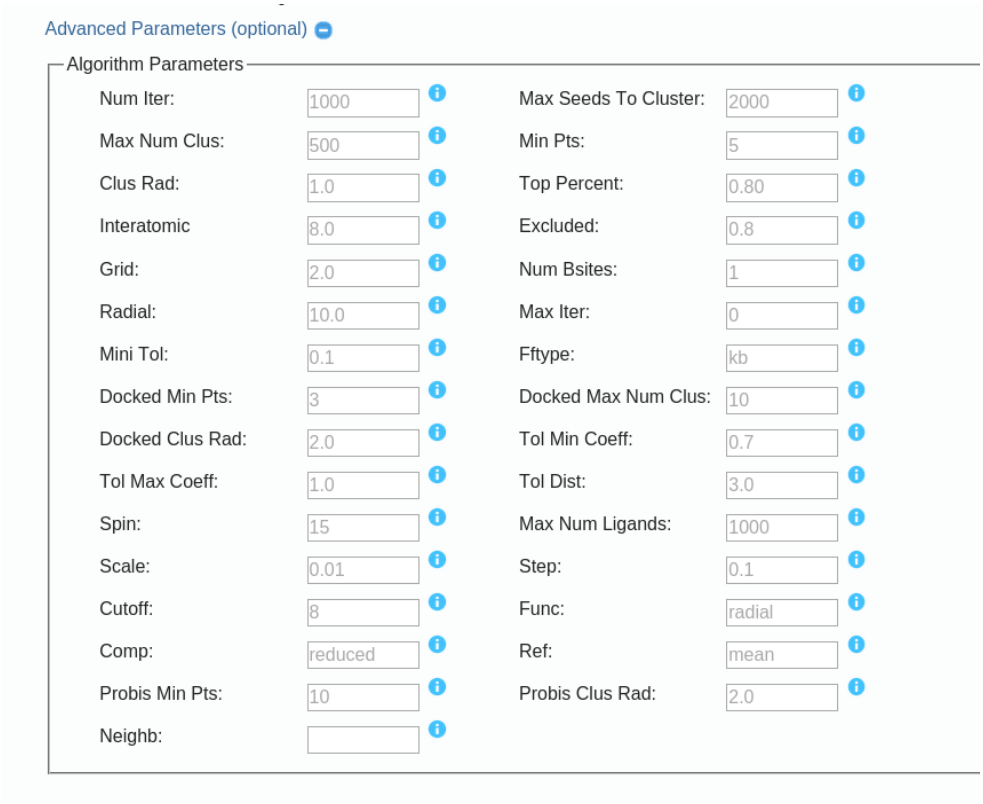


Figure 8: Algorithm Parameters

E-MAIL ADDRESS

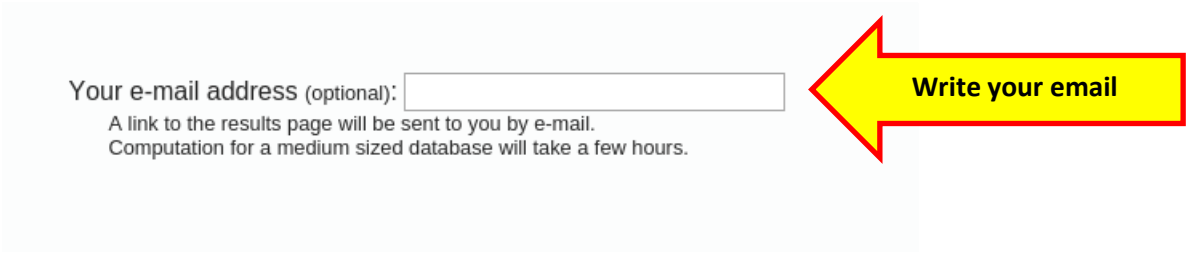


Figure 9: Email input

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.

ATER SUBMITING JOB FOR DOCKING

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

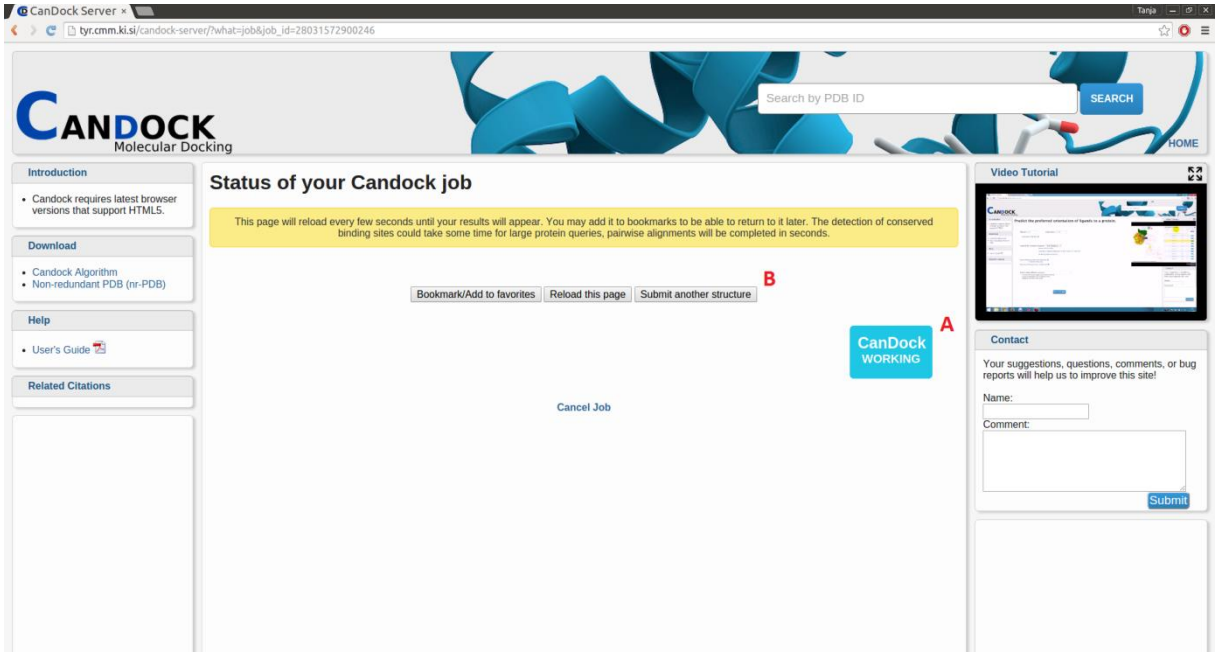


Figure 10: Status of your Candock job

Check your email. Two emails will be send to you. One after submiting 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.

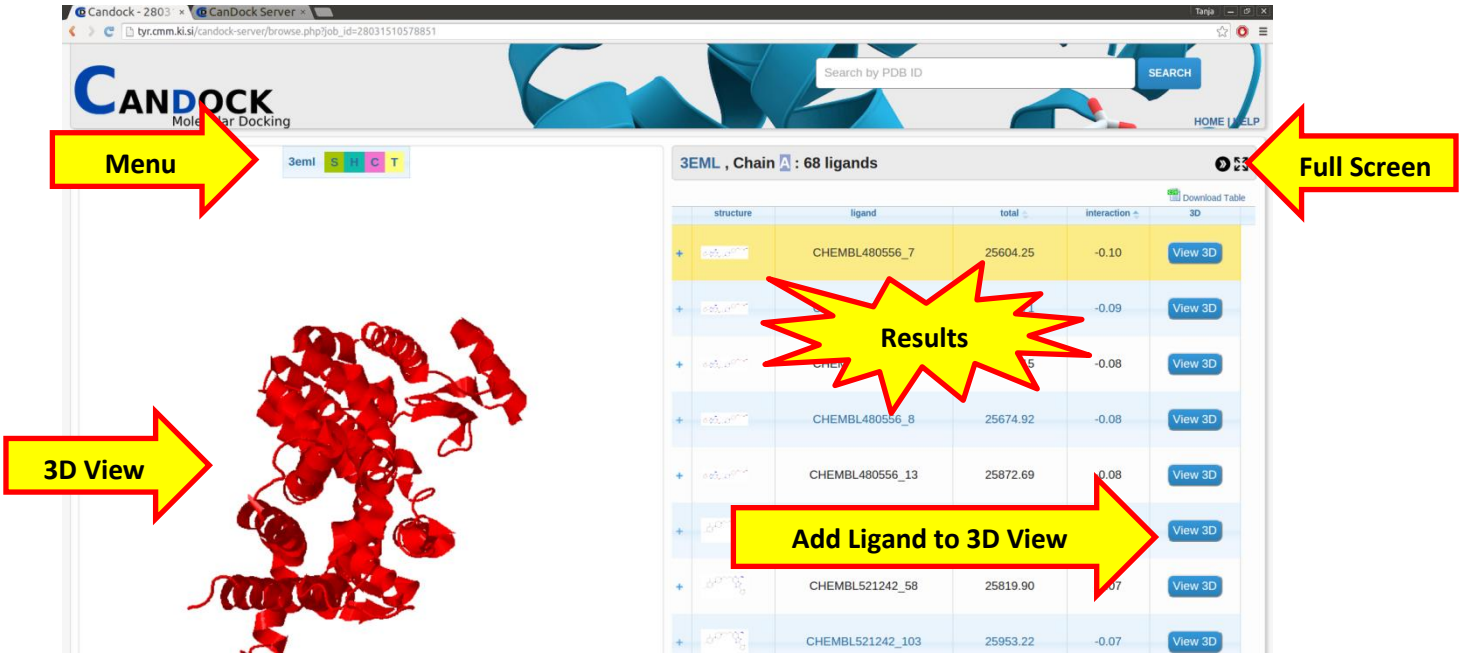


Figure 11: Results Page

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.

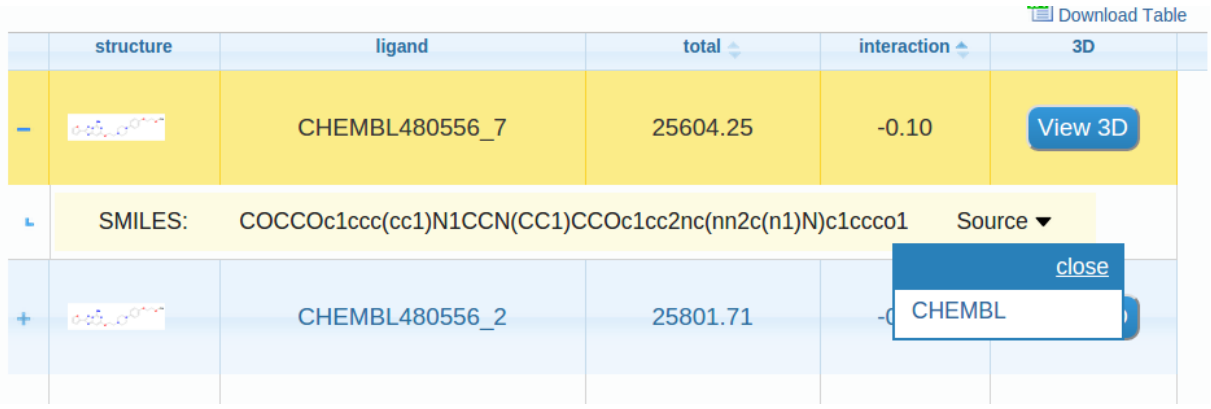


Figure 12: Source

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

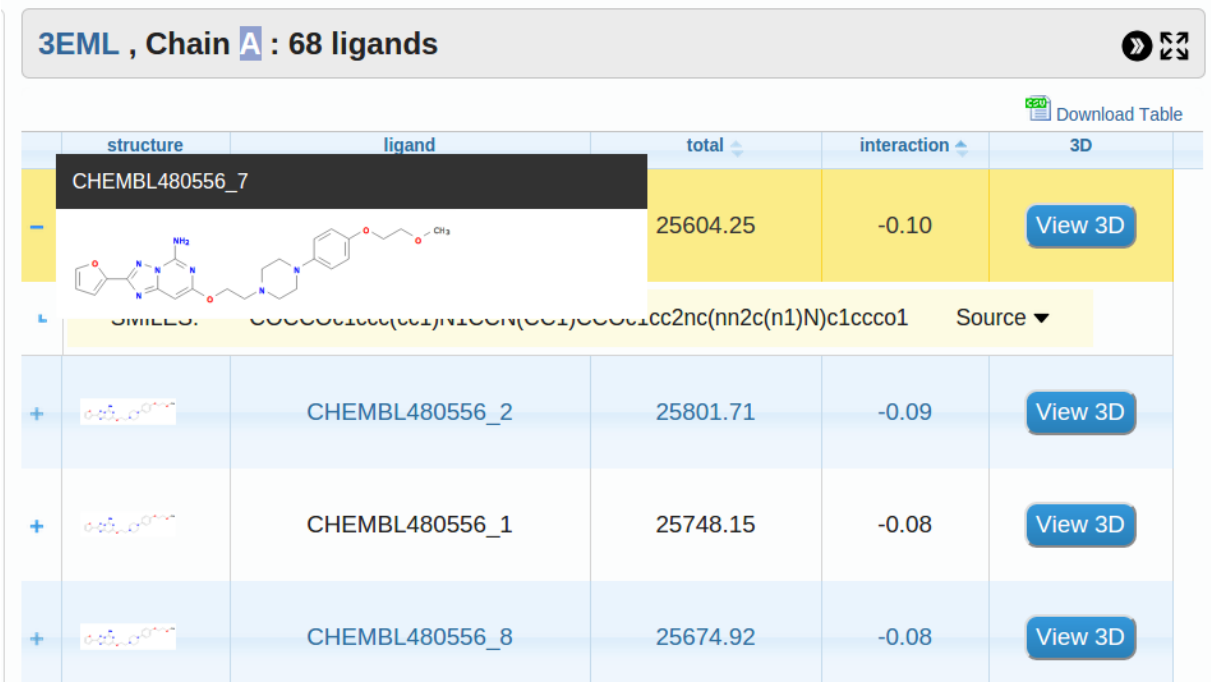


Figure 13: Bigger Picture

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.

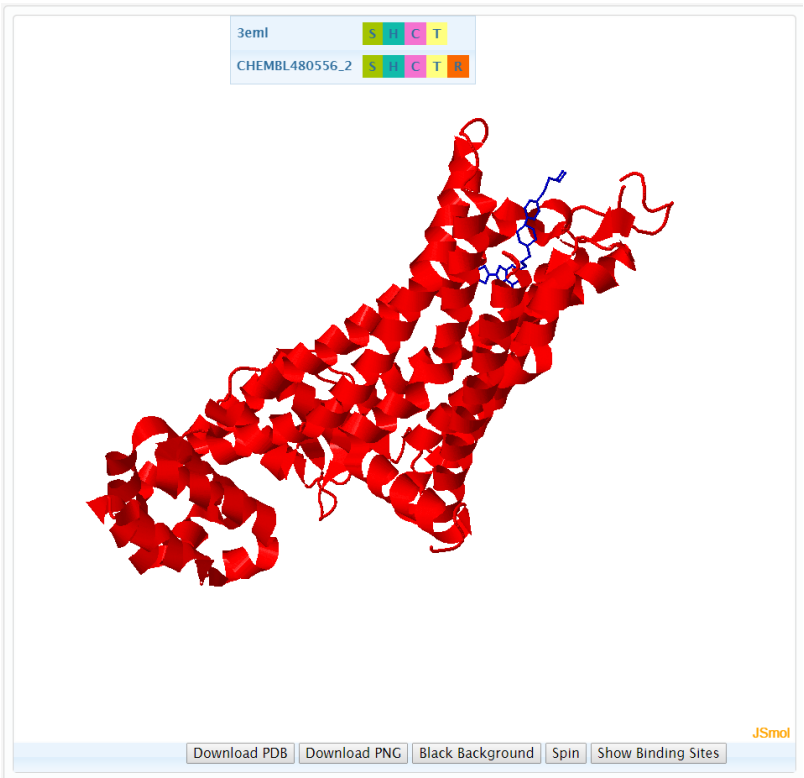


Figure 14: Ligand and protein in Jsmol

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

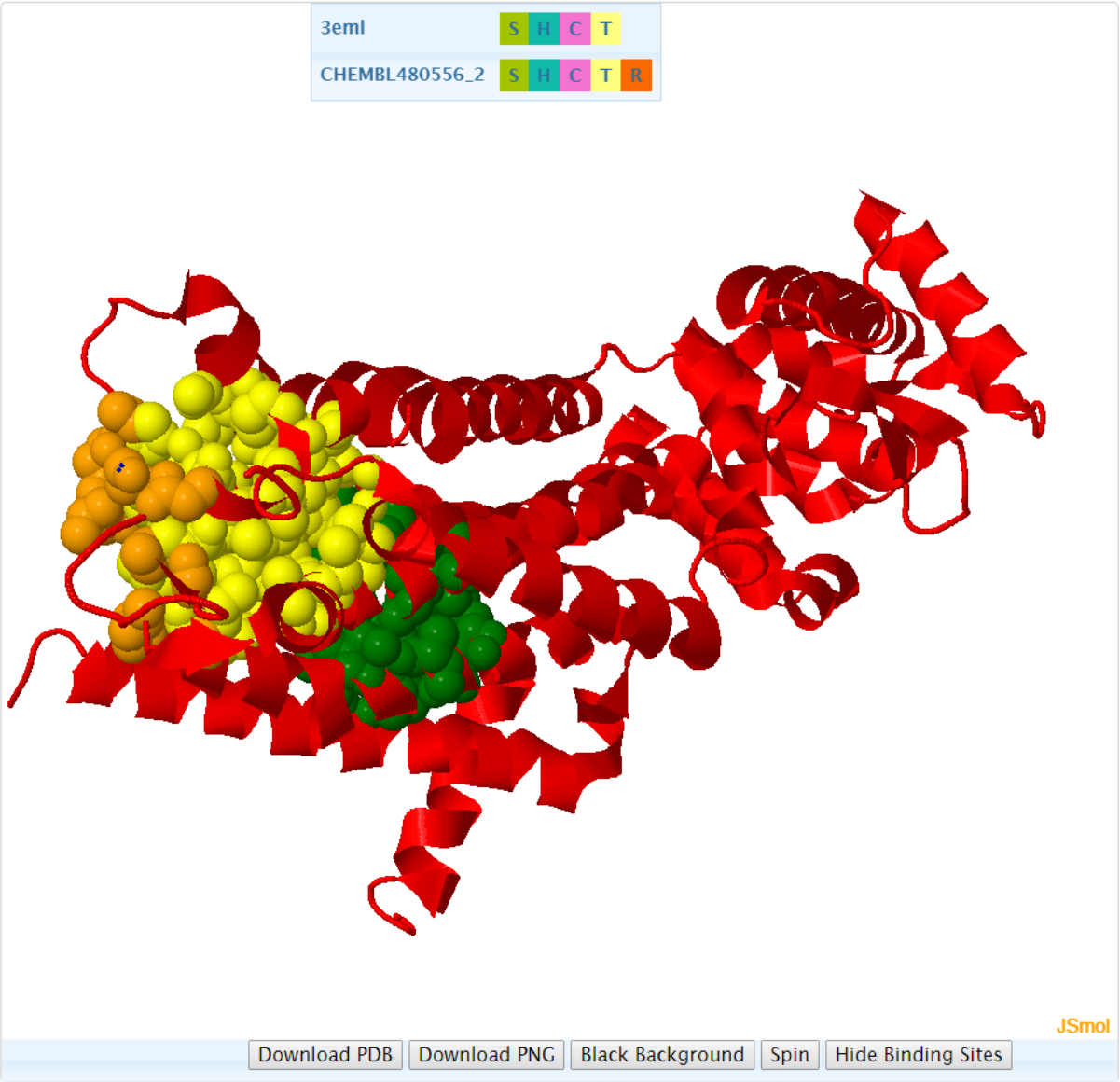


Figure 15: Shown binding sites

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.

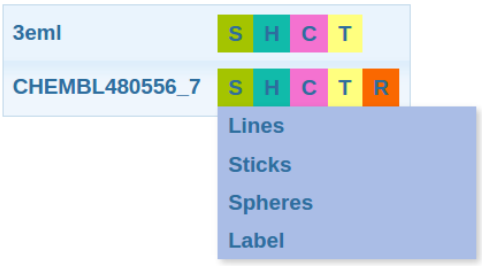


Figure 16: Menu: Show

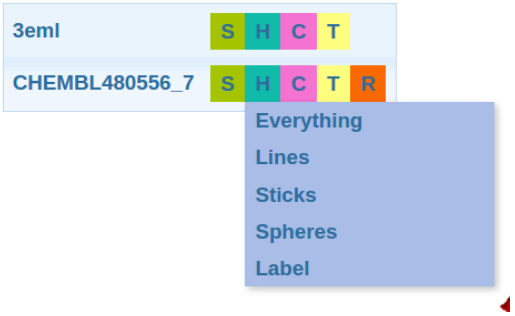


Figure 17: Menu: Hide

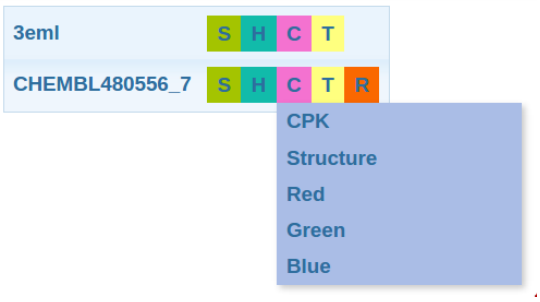


Figure 18: Menu: Color

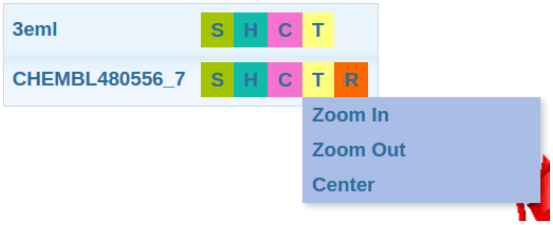


Figure 19: Menu: Tools

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

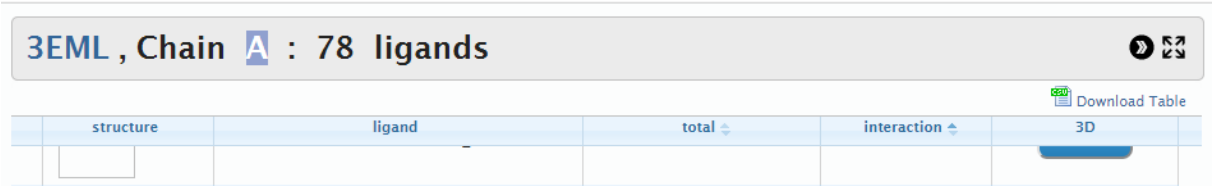
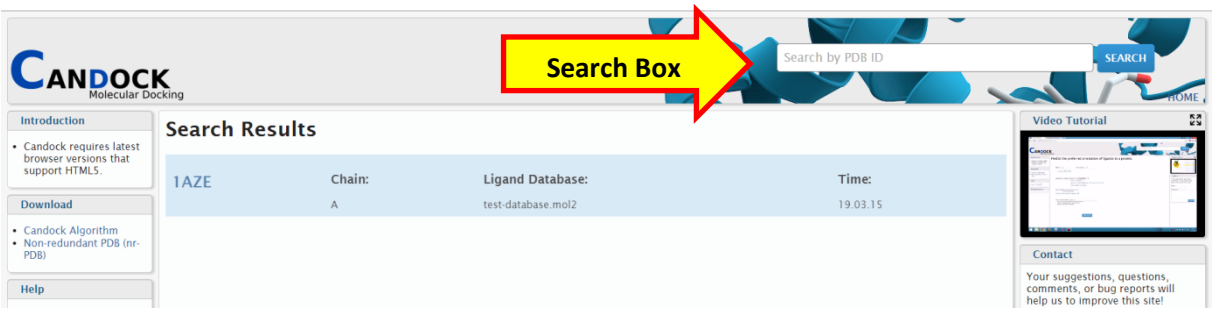


Figure 20: Table Control

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



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.