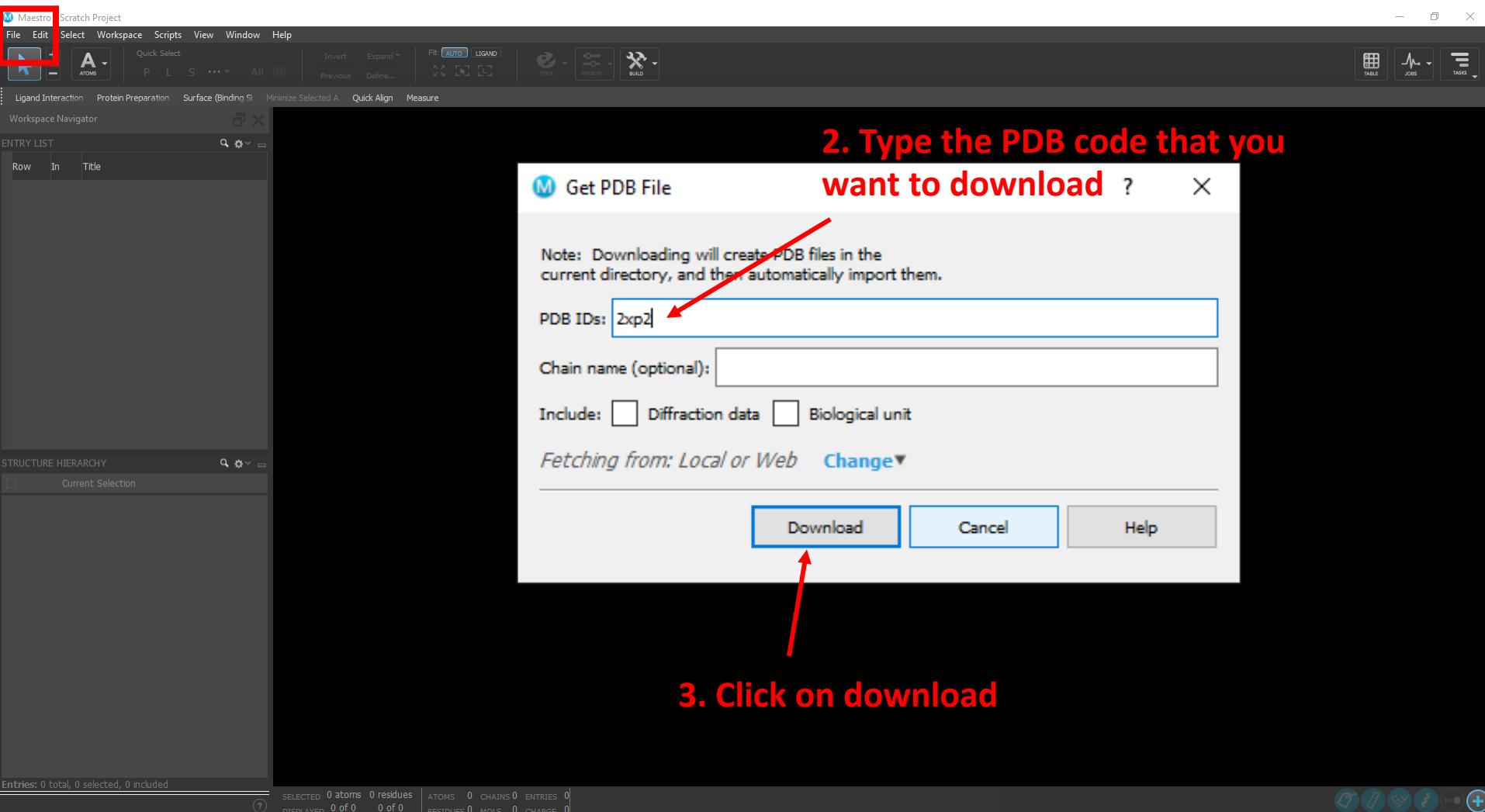


Load the PDB structure

1. Click on “File” -> “Get PDB...”

Change the directory:

File -> Change Working Directory



Visualize the protein

Maestro - Scratch Project

File Edit Select Workspace Scripts View Window Help

Quick Select Expand AUTO LIGAND Invert Previous Define... PREVIOUS PRESETS BUILD

Ligand Interaction Protein Preparation Surface (Binding Site) Minimize Selected A Quick Align Measure

Workspace Navigator

ENTRY LIST

Row	In	Title
1	●	2XP2

Title: 2XP2
PDB ID: 2XP2

STRUCTURE HIERARCHY

- Current Selection
- 2XP2
 - Ligands
 - A: SER 1136
 - A: PHE 1127
 - A: GLU 1129
 - A: ALA 1126
 - A: GLY 1133
 - A: GLN 1134
 - A: GLY 1128
 - A: VAL 1130
 - A: GLU 1132
 - A: VAL 1135

1/2

SELECTED 0 atoms 0 residues ATOMS 2459 CHAINS 1 ENTRIES 1
DISPLAYED 2459 of 2459 457 of 457 RESIDUES 457 MOLES 173 CHARGE -6

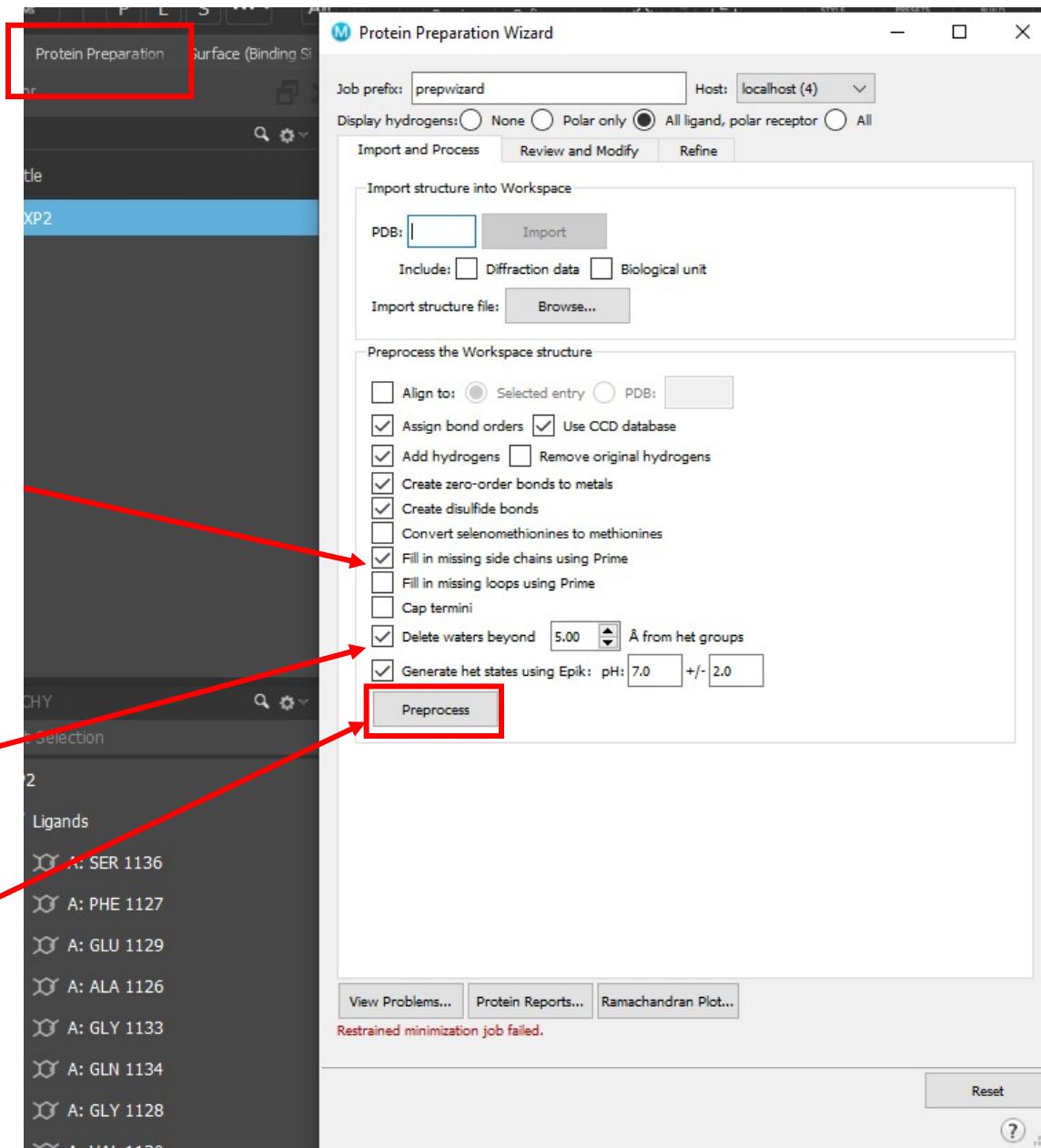
To rotate the protein -> hold and press the scroll button and move the mouse

To zoom in and out -> scroll

To translate -> right click and move the mouse

Protein Preparation

1. Click on “Protein Preparation” and this tab will open



2. Click on “Fill in missing side chains using Prime”

3. Click on “Delete waters beyond 5A from het groups”

4. Click on “Preprocess”

Job prefix: Host: ▾

Display hydrogens: None Polar only All ligand, polar receptor All

Import and Process **Review and Modify** **Refine** →

H-bond assignment

Sample water orientations
 Use crystal symmetry
 Minimize hydrogens of altered species
 Use PROPKA pH: 7.0 Label pKas
 Use simplified rules pH: Very Low Low Neutral High

Optimize Click on "Optimize" Interactive Optimizer...

Automatically optimize hydroxyl, Asp, Glu, Lys, Arg, Cys, His, Asn, Gln, Ser, Thr, Tyr, and Val.

Remove waters

Remove waters Beyond hets 3.0 Å
 With fewer than 3 H-bonds to non-waters

Restrained minimization

Converge heavy atoms to RMSD: Å
 Hydrogens only
 Force field: ▾
Minimize

View Problems... **Protein Reports...** **Ramachandran Plot...**

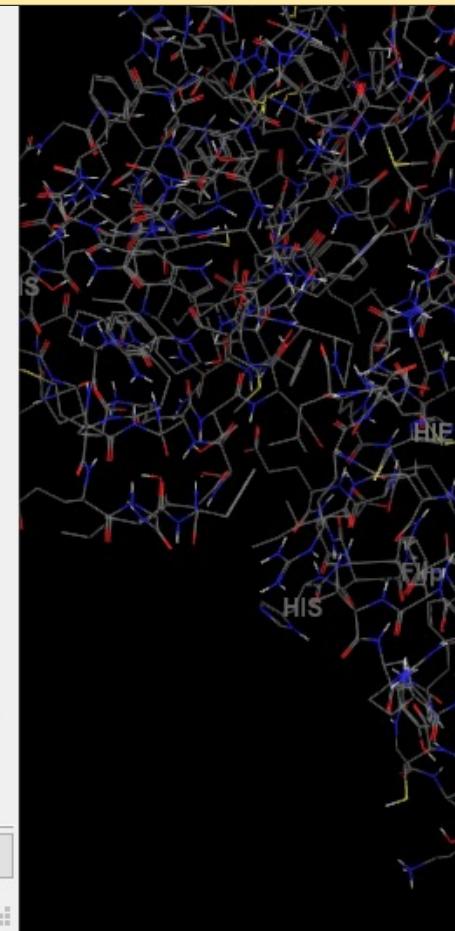
Optimize H-bond job incorporated.

Reset ?

Go to the “Refine” tab

Click on “Optimize”

Automatically optimize hydroxyl, Asn, Gln, and His states using ProtAssign



Job prefix: prepwizard Host: localhost (4)

Display hydrogens: None Polar only All ligand, polar receptor All

Import and Process Review and Modify Refine

H-bond assignment

Sample water orientations
 Use crystal symmetry
 Minimize hydrogens of altered species
 Use PROPKA pH: 7.0 Label pKas
 Use simplified rules pH: Very low Low Neutral High

Optimize Interactive Optimizer...

Remove waters

Remove waters Beyond hets 3.0 Å
 With fewer than 3 H-bonds to non-waters

Restrained minimization

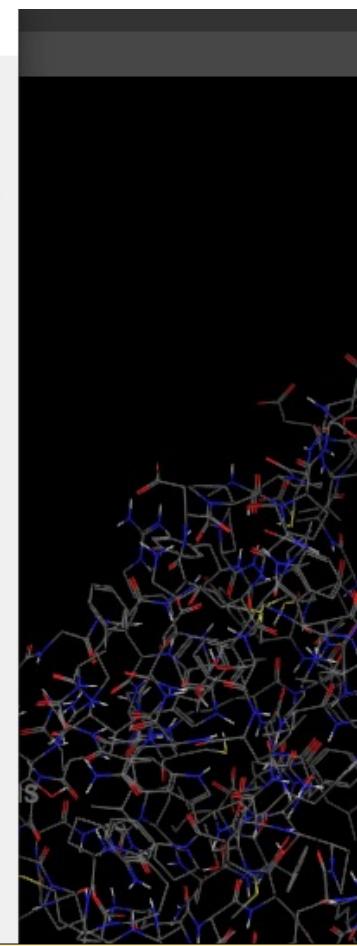
Converge heavy atoms to RMSD: 0.30 Å
 Hydrogens only
Force field: OPLS3e

Minimize

Click on “Minimize”

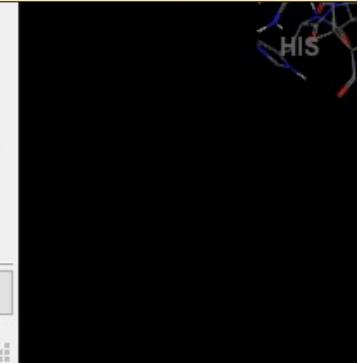
View Problems... Protein Reports... Ramachandran Plot... Optimize H-bond job incorporated.

Reset ?



Minimize

Run a restrained minimization job, with heavy atoms restrained (or frozen) and hydrogens unrestrained



Change ligand representation

Maestro - Scratch Project

File Edit Select Workspace Scripts View Window Help

LIGAND

ATOMS

Quick Select F L S All

Invert Expand Previous Define... Fit AUTO LIGAND

STYLE PRESETS BUILD

Ligand Interaction Protein Preparation Surface (Binding Site) Minimize Selected A Quick Align Measure

Workspace Navigator

Title: 2XP2 - minimized PDB ID: 2XP2

ENTRY LIST

Row	In	Title
1	○	2XP2
2	○	2XP2 - prep
3	○	2XP2 - hbond
4	●	2XP2 - minimized

STRUCTURE HIERARCHY

Current Selection 2XP2 - minimized

Entries: 4 total, 1 selected, 1 included

SELECTED 53 atoms 1 residue ATOMS 4598 CHAINS 1 ENTRIES 1
DISPLAYED 2827 of 4598 296 of 296 RESIDUES 296 MOLECS 12 CHARGE -5

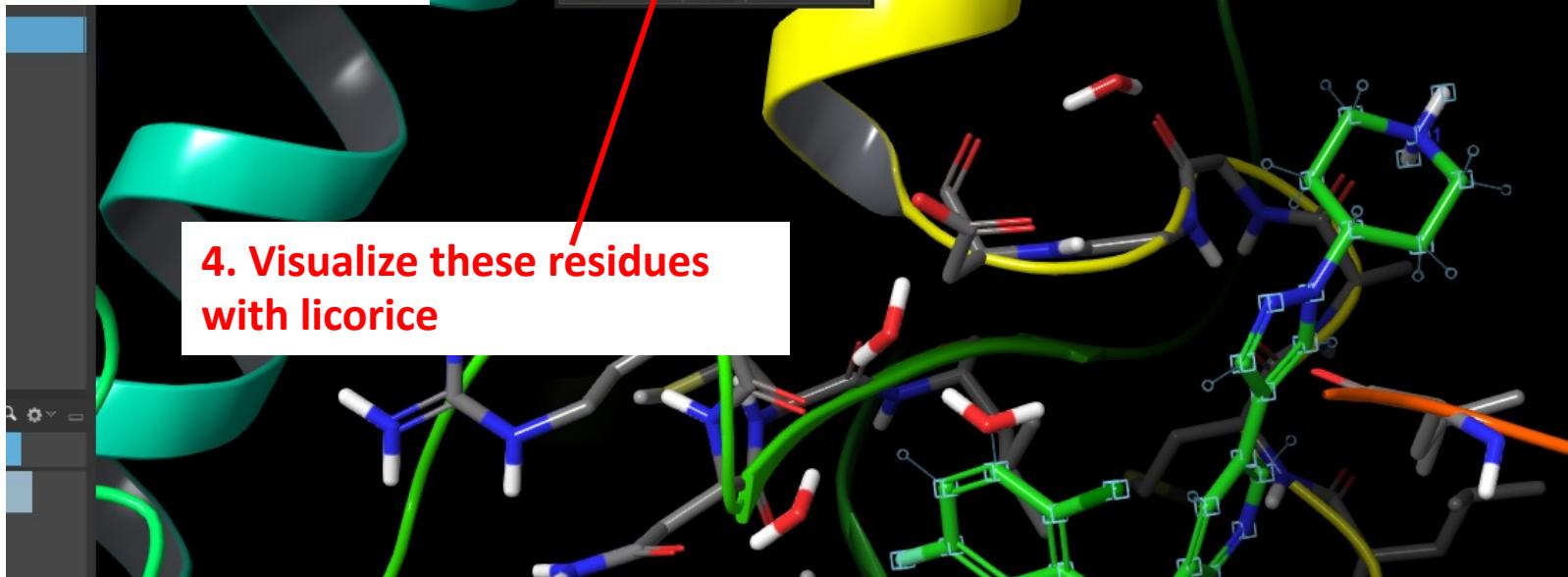
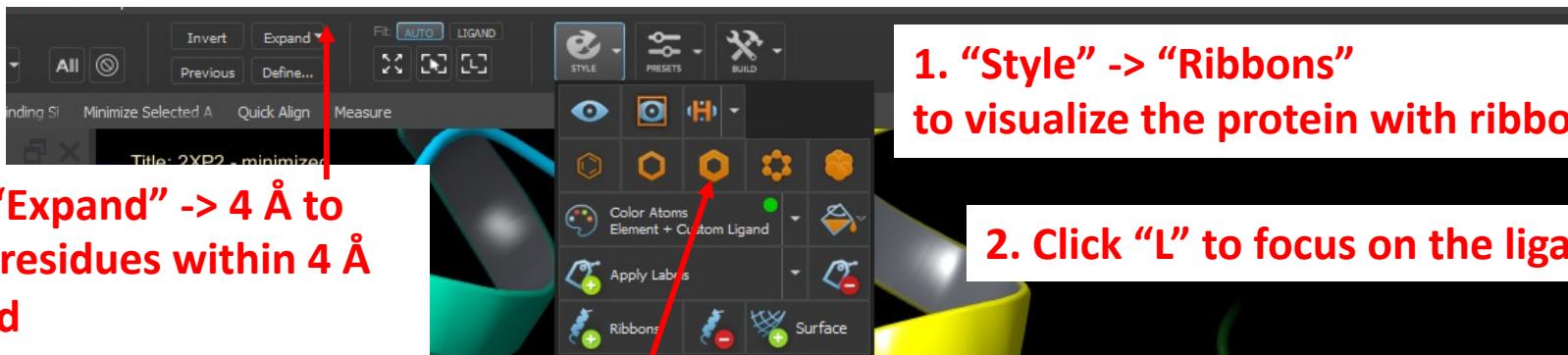
Select the ligand

And then

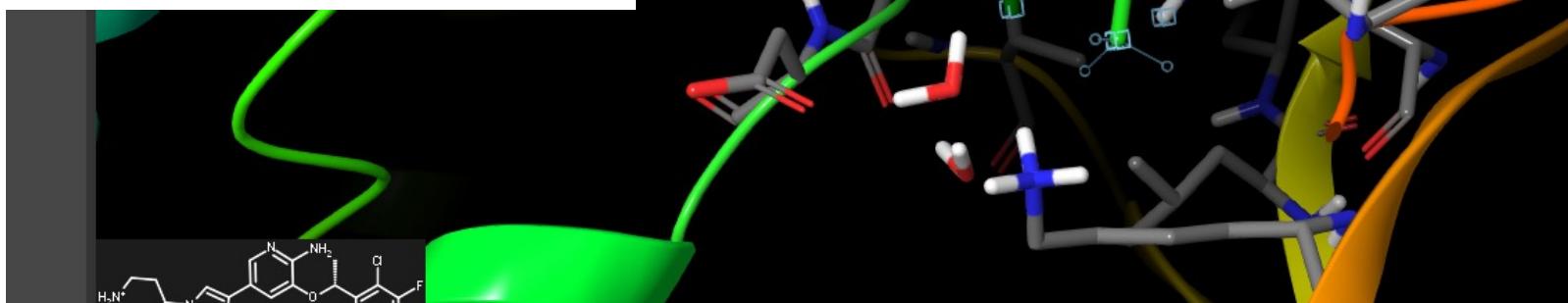
Press "L" on the keyboard to zoom in

The ligand is now visualized in licorice

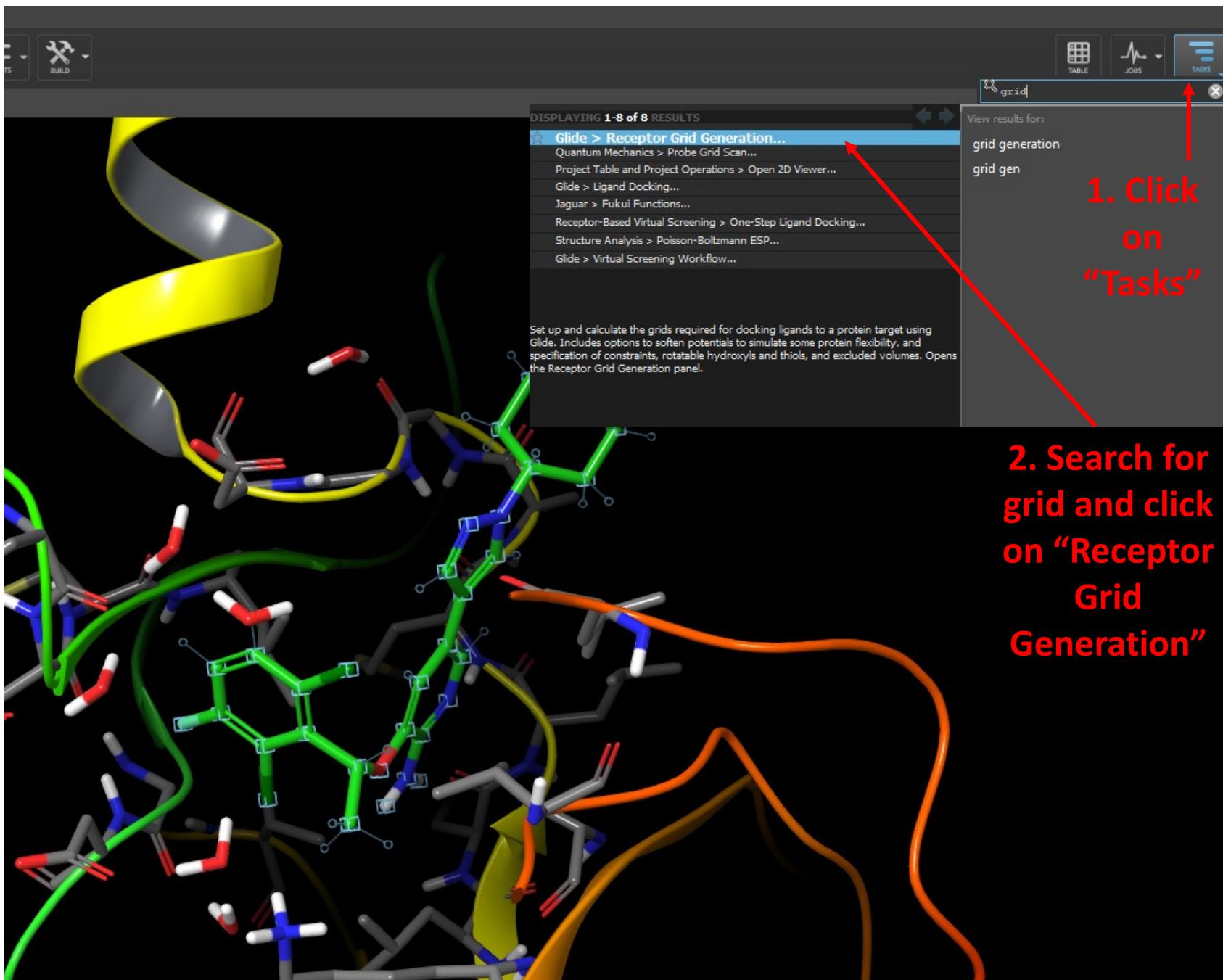
Display residues within 4 Å of the ligand



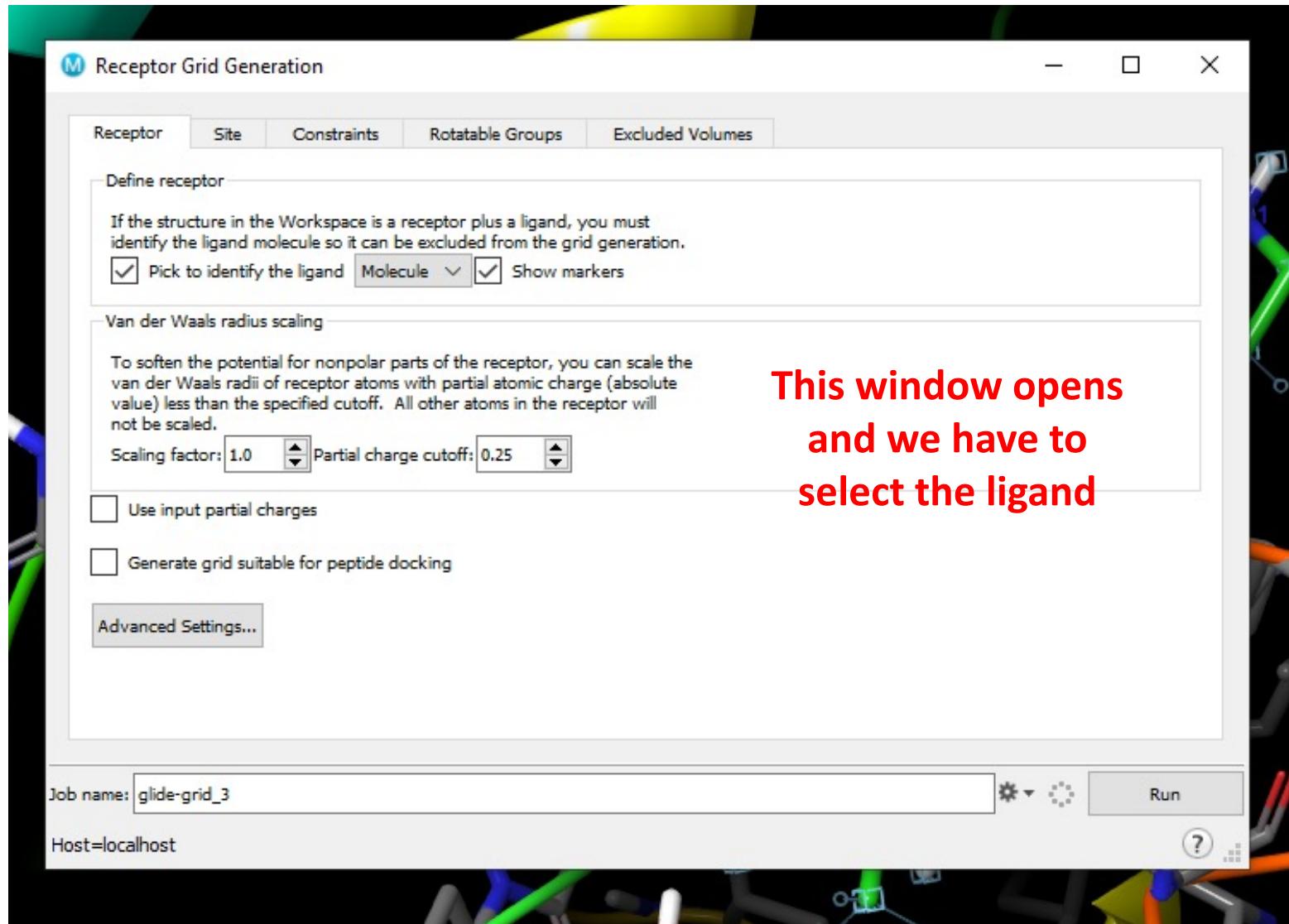
5. Check the Ligand interaction diagram



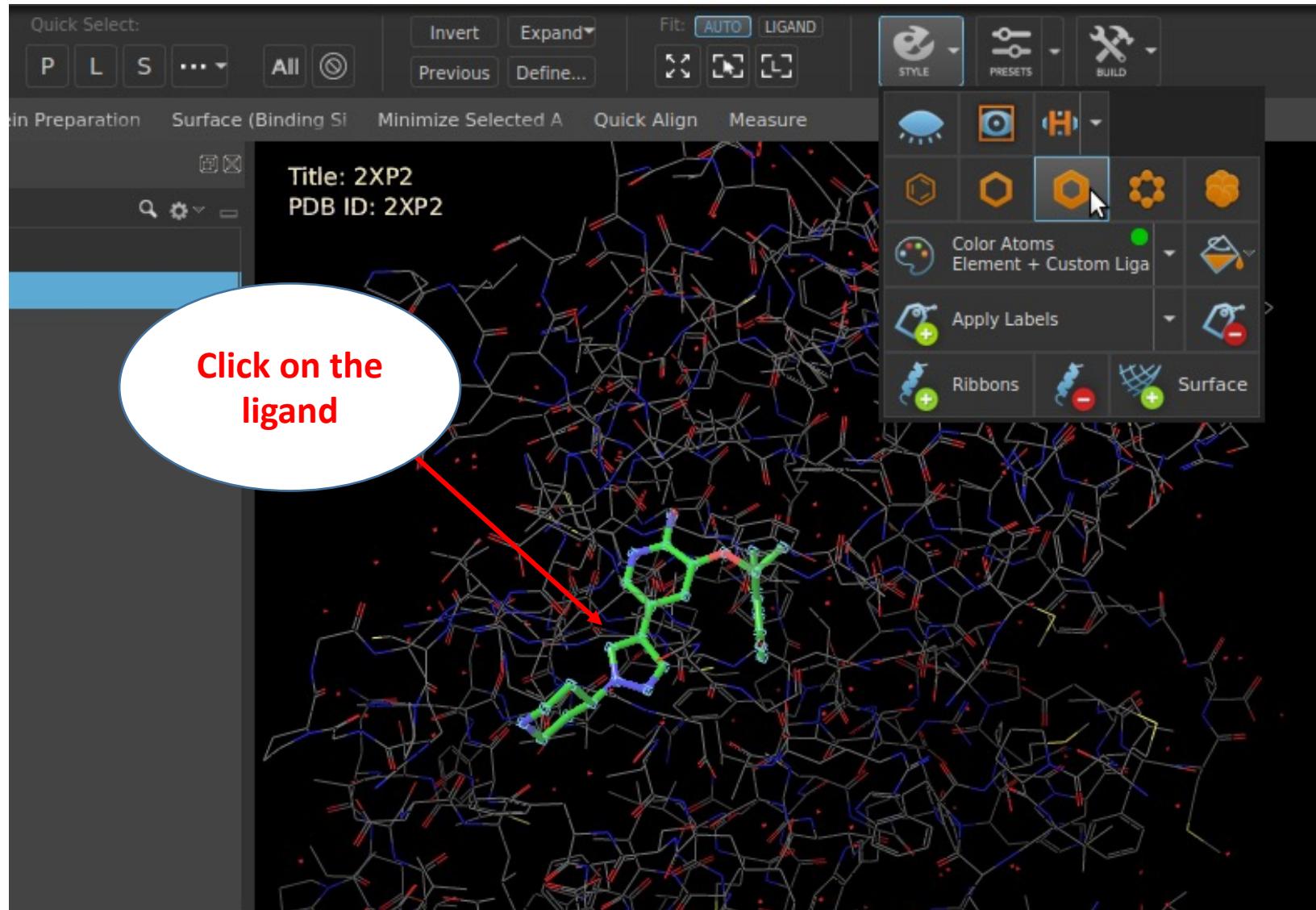
Maestro: Grid generation



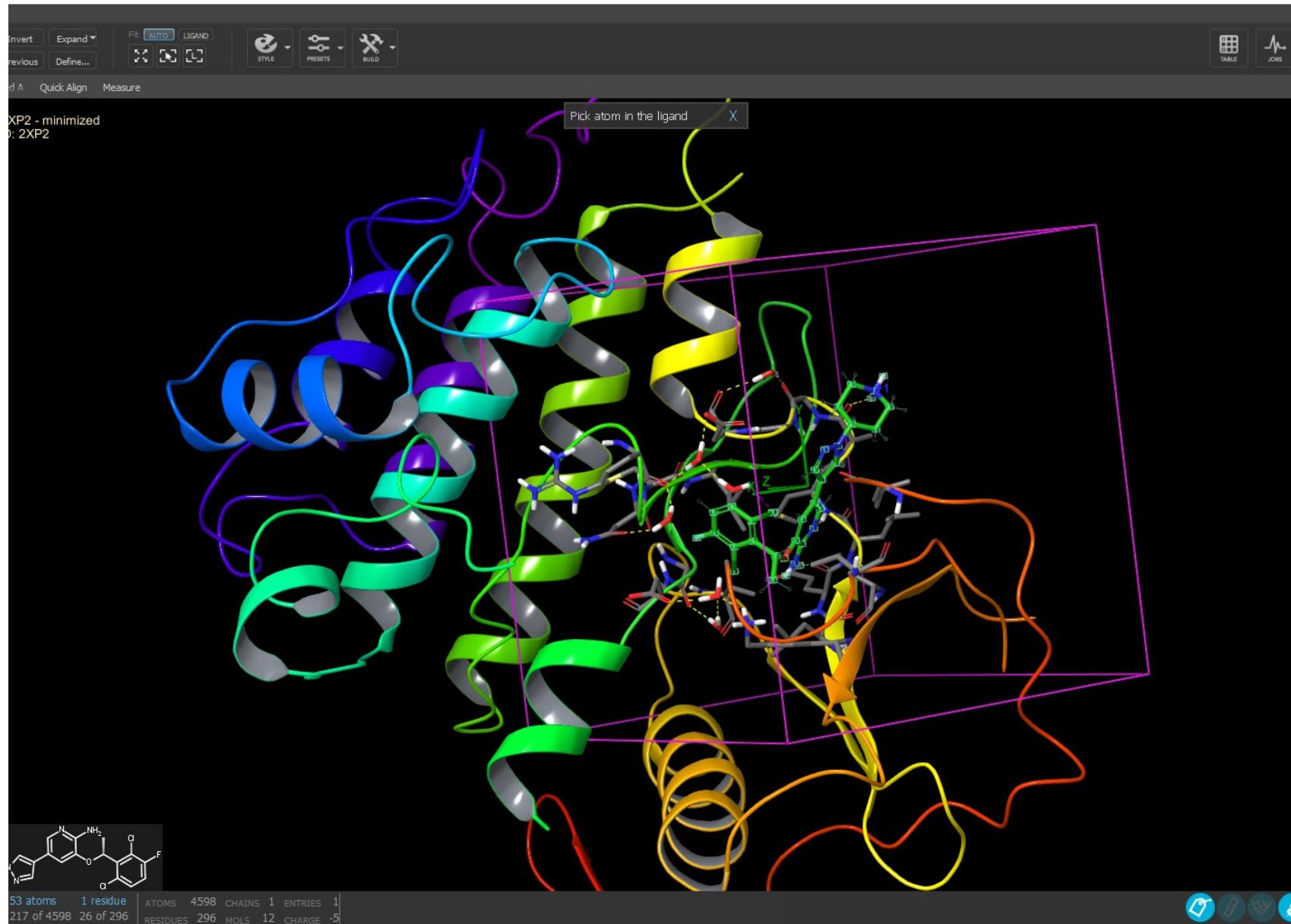
Maestro: Grid generation



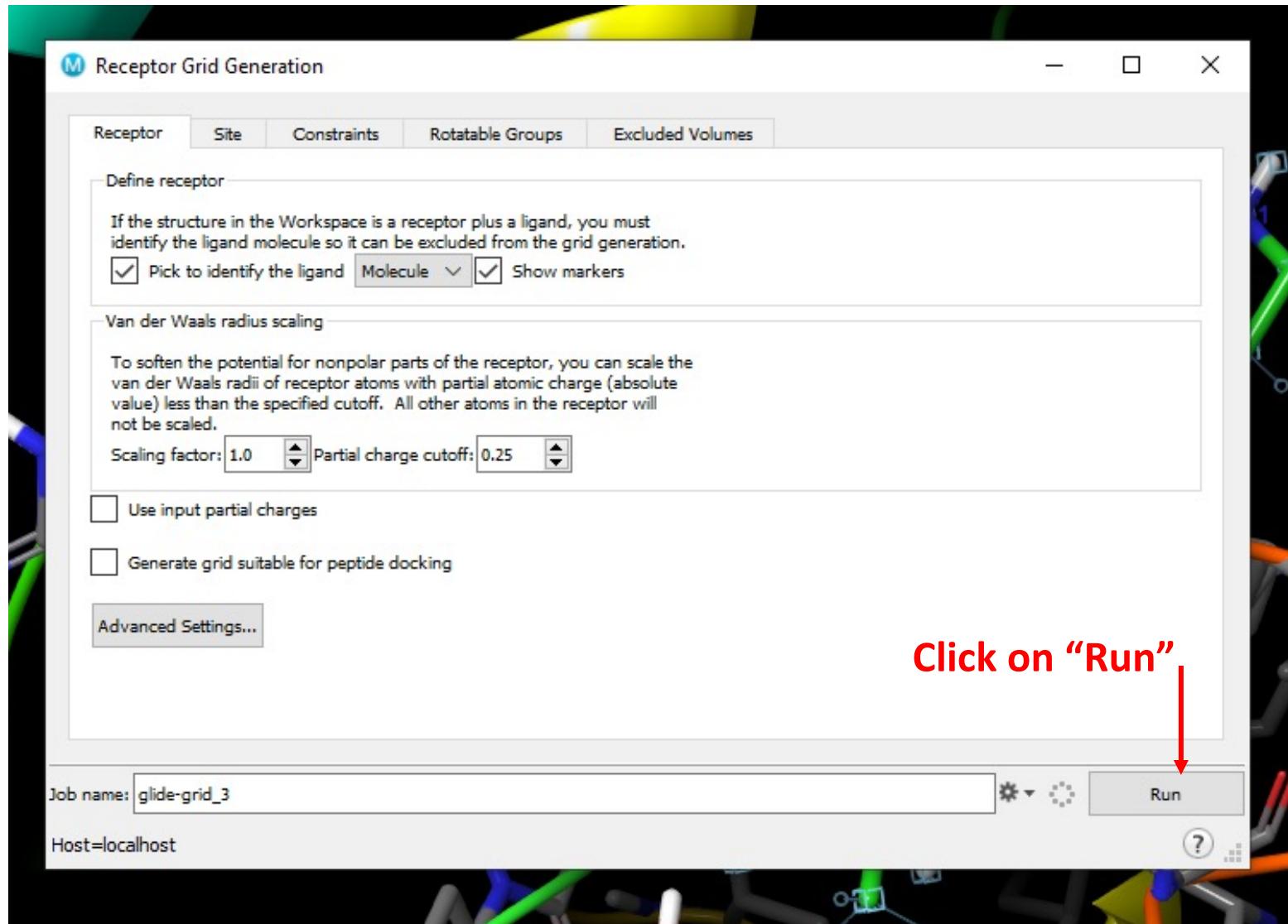
Select the ligand



Maestro: Grid generation



Maestro: Grid generation



Ligand docking

The screenshot shows a software interface for molecular docking. On the left, there is a 3D molecular model of a protein-ligand complex. The main window displays a list of tasks under the heading "DISPLAYING 1-10 of 20 RESULTS". The first item in the list is "Ligand Docking... Glide", which is highlighted with a blue background and has a cursor arrow pointing to it. To the right of the list is a "TASKS" panel. At the top of this panel is a search bar containing the text "docking". Below the search bar, the text "Search for 'do'" is displayed, followed by "Or use matching keywords (3):" and a list of three items: "dock", "docking" (which is also highlighted with a blue background), and "docking postprocessing". A red arrow points from the text "1. Click on 'Tasks'" to the "TASKS" button in the top right corner of the main window. Another red arrow points from the text "2. Search for docking and click on 'Ligand Docking'" to the "Ligand Docking..." entry in the task list.

DISPLAYING 1-10 of 20 RESULTS

Ligand Docking... Glide

Receptor Grid Generation... Glide

Induced Fit Docking...

Virtual Screening Workflow... Glide

Covalent Docking... Glide

One-Step Ligand Docking... Receptor-Based Virtual Screening

Lead Optimization Docking... Receptor-Based Virtual Screeni

Cross Docking... Receptor-Based Virtual Screening

QM-Polarized Ligand Docking... Glide

Protein-Protein Docking... Biologics

Dock ligands to a protein target (Glide), using pregenerated receptor grids. Includes settings for ligand sampling, pose filtering and post-processing; setting constraints to the receptor, a ligand core, or on ligand torsions; and using similarity or dissimilarity screening. Opens the Ligand Docking panel.

TABLE JOBS TASKS

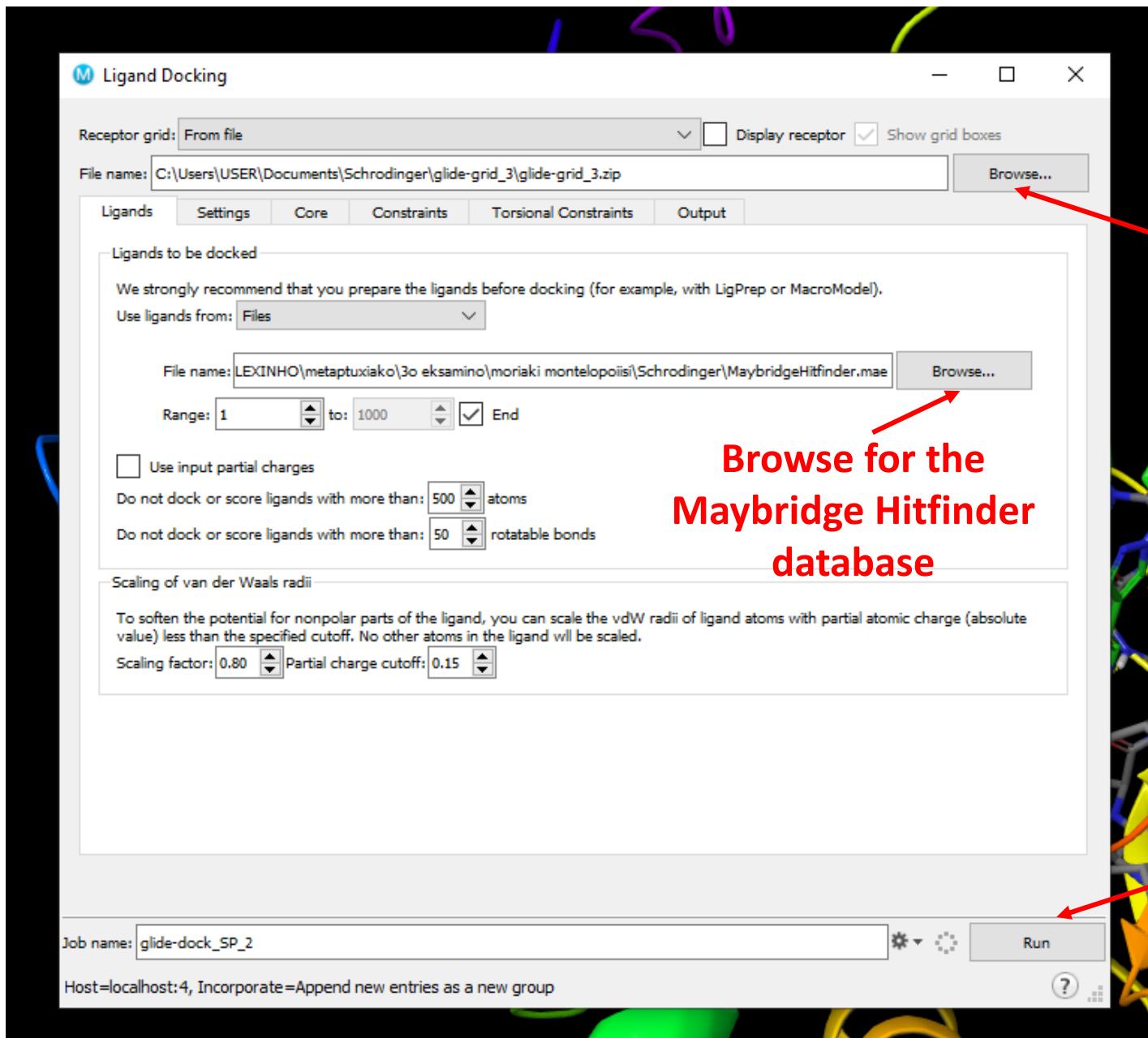
docking

Search for "do"
Or use matching keywords (3):
dock
docking
docking postprocessing

1. Click on "Tasks"

2. Search for docking and click on "Ligand Docking"

Maestro: Ligand Docking

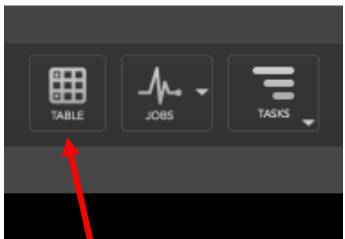


Browse for your grid file

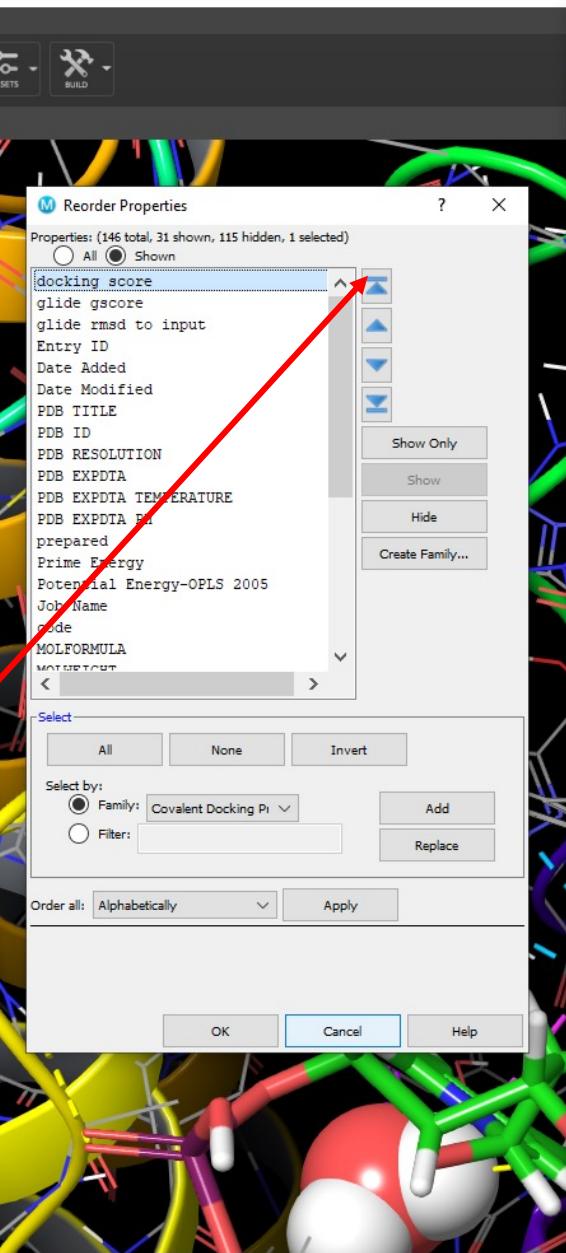
Browse for the Maybridge Hitfinder database

Click on "Run"

Ligand visualization



1. Open the Project table

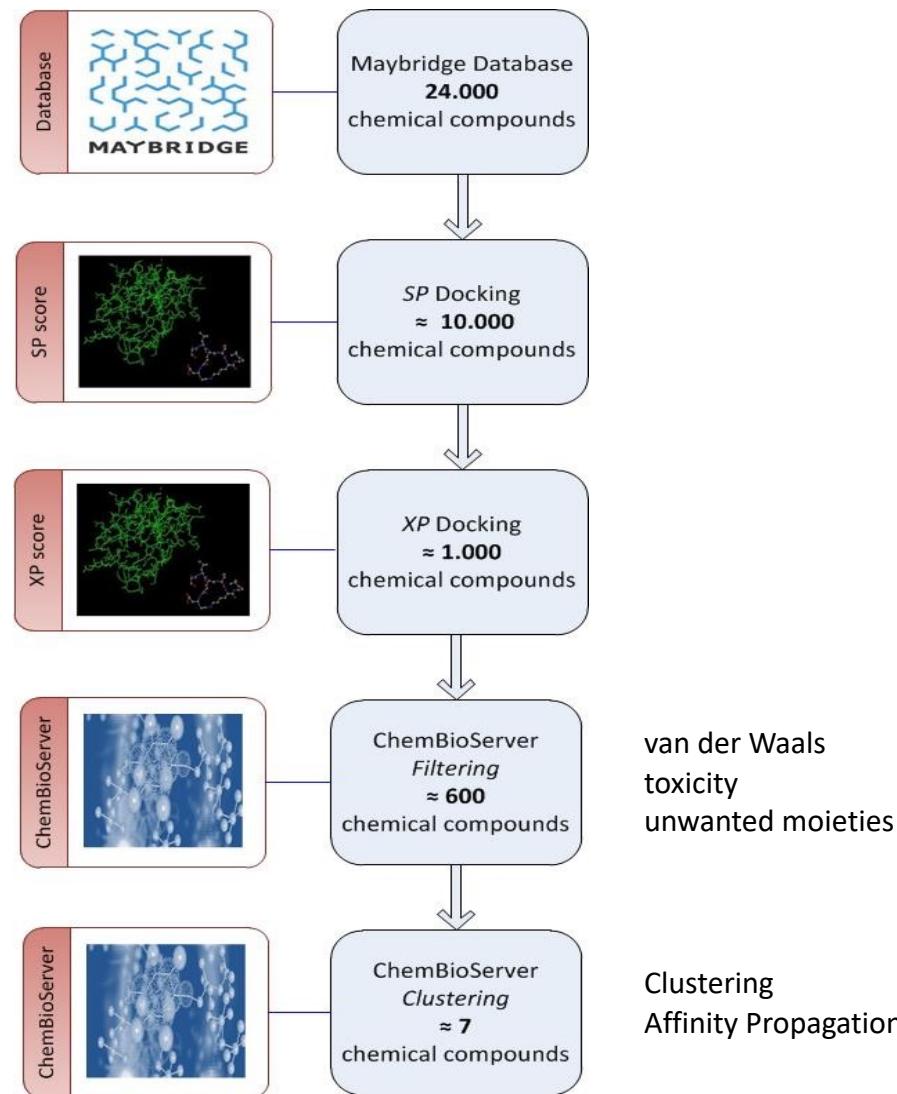


3. Select “docking score” and click on the up arrow to move selected properties on top of the list

2. Columns -> Reorder

Row	In	Title	Stars	glide
1		4X0T	★★★	
2	●	glide-dock_SP_3W9_maybridge_pv1 (24403)	★★★	
3		4X0T	★★★	
4		SPB 07799	★★★	
5		SPB 07799	★★★	
6		RJC 03499	★★★	
7		RJC 03355	★★★	
8		SPB 07799	★★★	
9		SPB 07799	★★★	
10		SPB 07799	★★★	
11		RH 01300	★★★	
12		SPB 07799	★★★	
13		SPB 07799	★★★	
14		SPB 07799	★★★	
15		RF 05209	★★★	
16		JFD 03457	★★★	
17		RJC 03499	★★★	
18		RH 02220	★★★	
19		RH 01230	★★★	
20		HTS 01523	★★★	
21		BTB 09392	★★★	
22		JFD 00399	★★★	
23		SPB 07799	★★★	
24		DSHS 00611	★★★	
25		HTS 00628	★★★	
26		CD 00167	★★★	
27		SPB 07799	★★★	
28		SPB 07799	★★★	
29		SPB 07799	★★★	
30		SPB 07799	★★★	
31		SPB 07799	★★★	
32		SPB 07799	★★★	

How are compounds selected for assaying?



Physicochemical property prediction with QikProp

Maestro - Scratch Project

Ligand Interaction Protein Preparation Surface (Binding Site) Minimize Selected A Quick Align Measure

ATOMS P L S All

Quick Select: Invert Expand Fit: AUTO LIGAND Previous Define... STYLE PRESETS BUILD

Workspace Navigator

Title: 2xp2 - hbond-opt PDB ID: 2XP2

ENTRY LIST

Row	In	Title
1	<input type="radio"/>	2xp2
2	<input type="radio"/>	2xp2 - preprocess...
3	<input type="radio"/>	2xp2 - minimized
4	<input type="radio"/>	2xp2 - hbond-opt
5	<input checked="" type="radio"/>	2xp2 - hbond-opt
6	<input type="radio"/>	sitemap_1_out1...
7	<input type="radio"/>	sitemap_1_sim... S
8	<input type="radio"/>	sitemap_1_sim... S
		sitemap_1_prot...

STRUCTURE HIERARCHY

Current Selection: 2xp2 - hbond-opt

DISPLAYING 1-3 of 3 RESULTS

Other Applications > QikProp...

ADME and Molecular Properties > Molecular Descriptors...

ADME and Molecular Properties > Ligand-Based ADME/Tox Predict...

Calculate ADME properties and 2D and 3D QSAR descriptors of small molecules. Opens the QikProp panel.

QikProp

Use structures from: Project Table (selected entries)

File name: Browse...

Fast mode

Identify the 5 most similar drug molecules

Job name: Run

QikProp: Host=localhost, Incorporate=Append new entries as a new

?