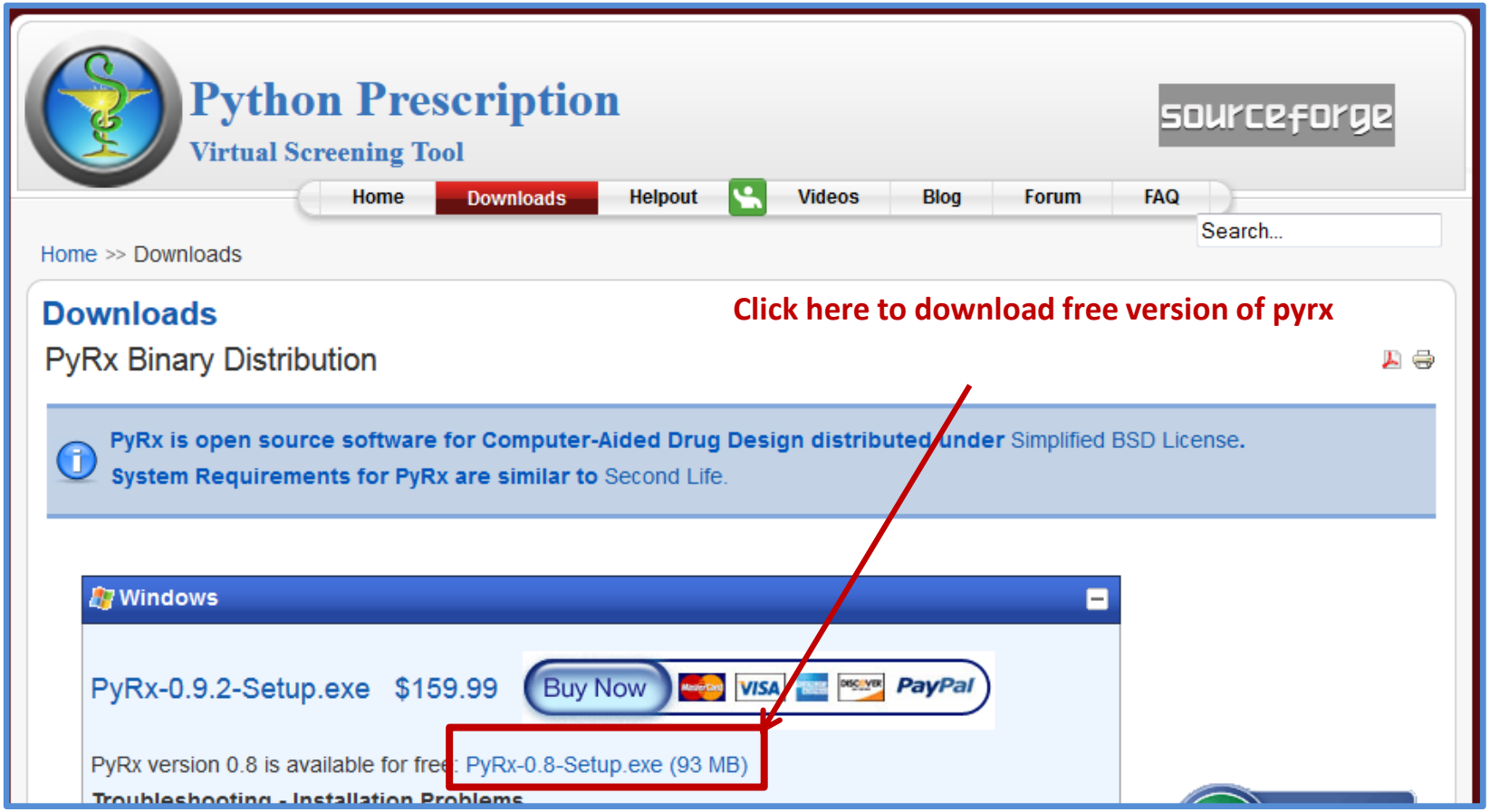
Protein-Ligand Docking with PyRx

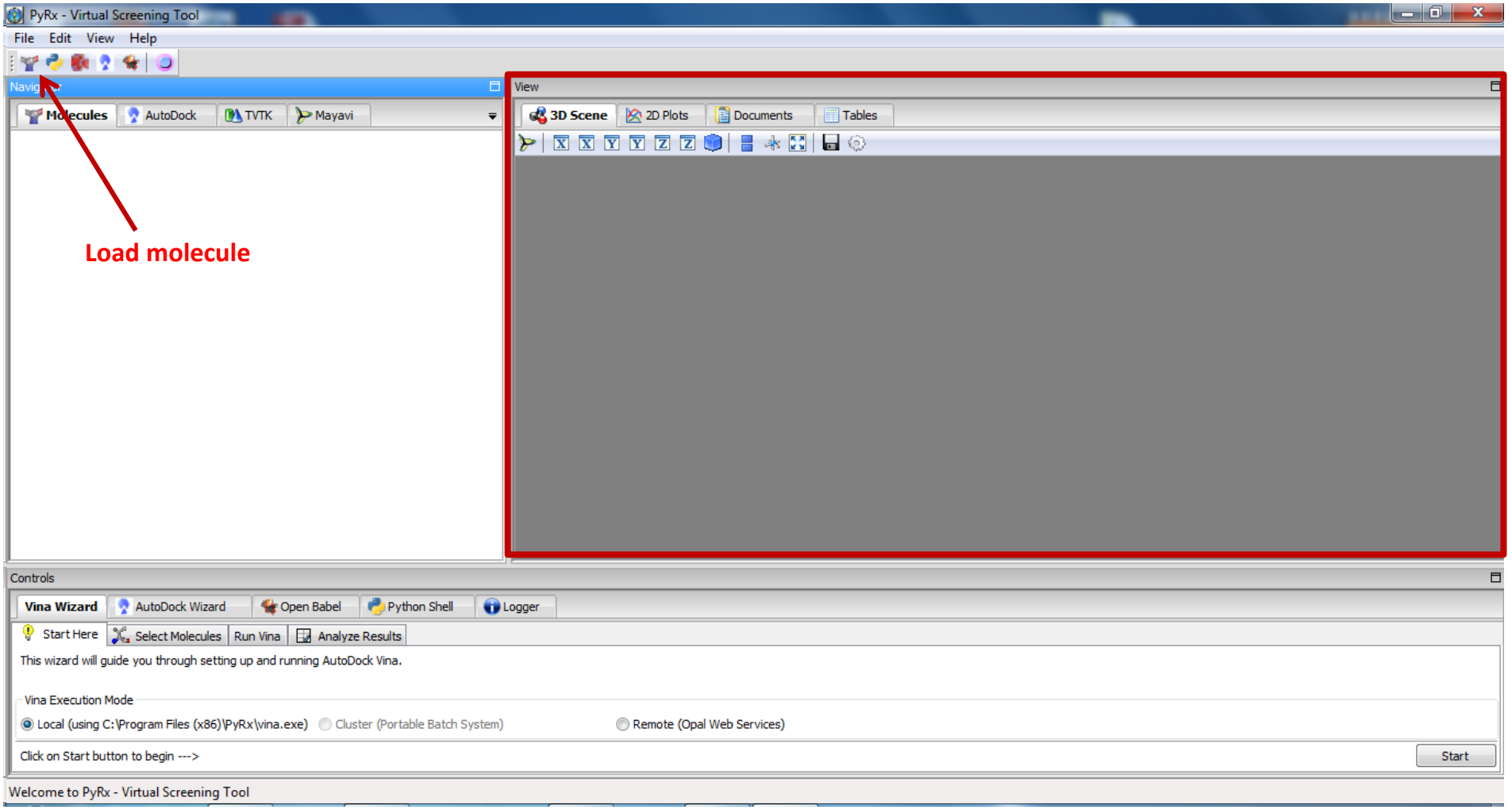
PyRx is an open source software to perform **virtual screening**. It is a combination of several softwares such as AutoDock Vina, AutoDock 4.2, Mayavi, Open Babel, etc. PyRx uses Vina and AutoDock 4.2 as docking softwares. In this tutorial we are going to use only Vina.

❑ Downloading PyRx :

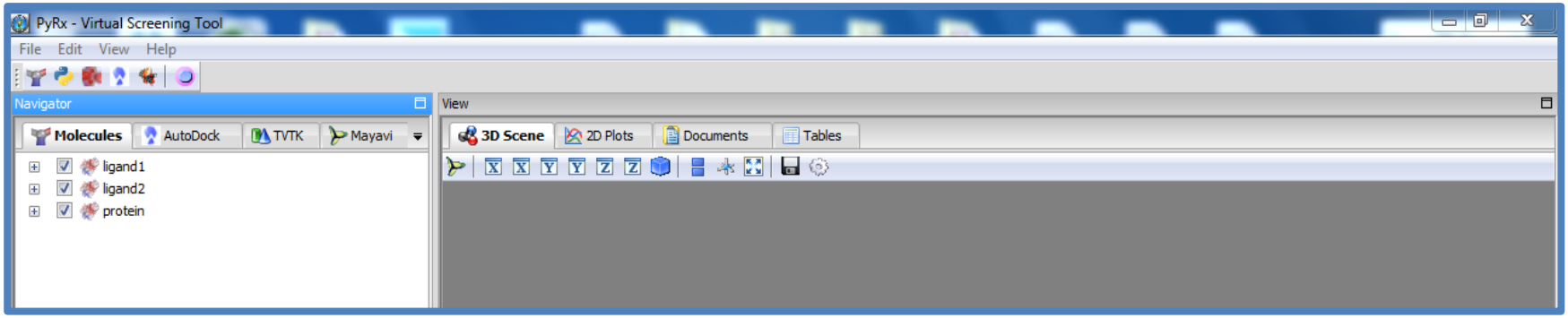
http://pyrx.sourceforge.net/downloads



❑ Loading molecules into PyRx workspace:



→ Use upper left button as shown in the figure to load your **protein** and **ligand (s)** into PyRx workspace.

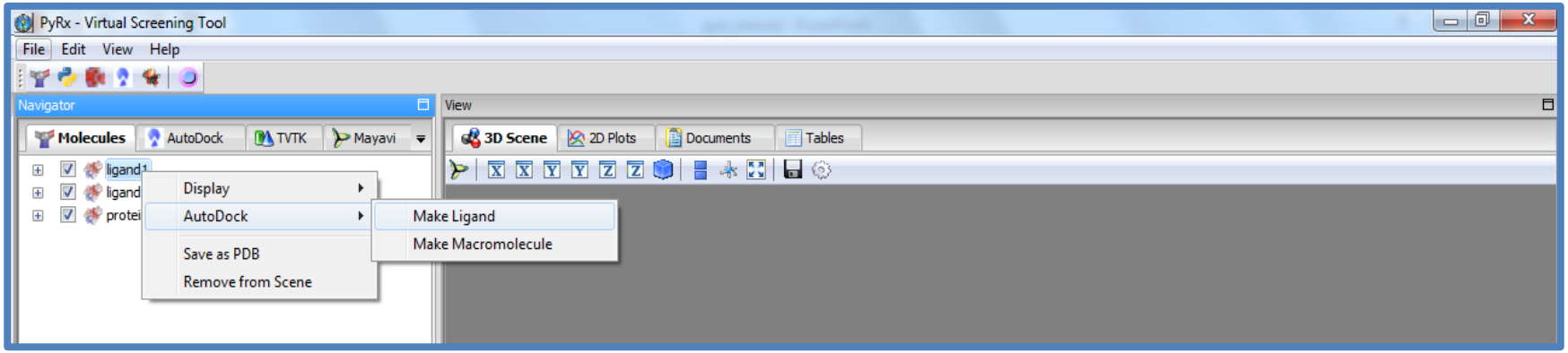


❑ Converting .pdb files to .pdbqt files (Vina input file format)

→ After successfully loading molecules in to the workspace, convert them into AutoDock input files (pdbqt files) as shown below.

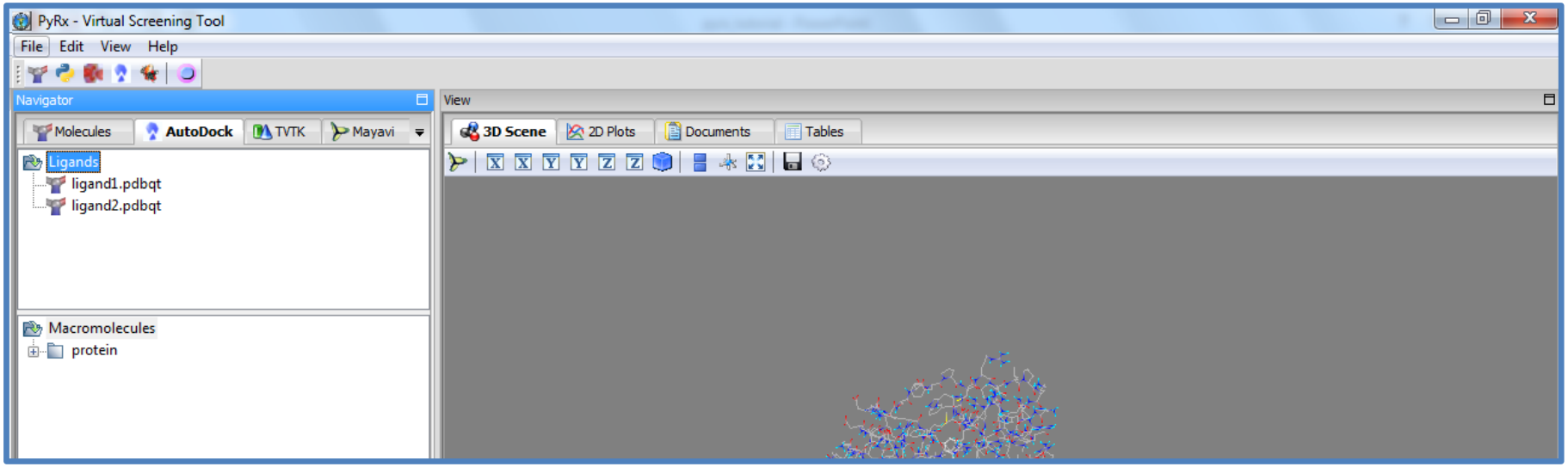
✓ Right click on **ligand(s)** > **AutoDock** > **Make ligand**

✓ Right click on **protein** > **AutoDock** > **Make Macromolecule**

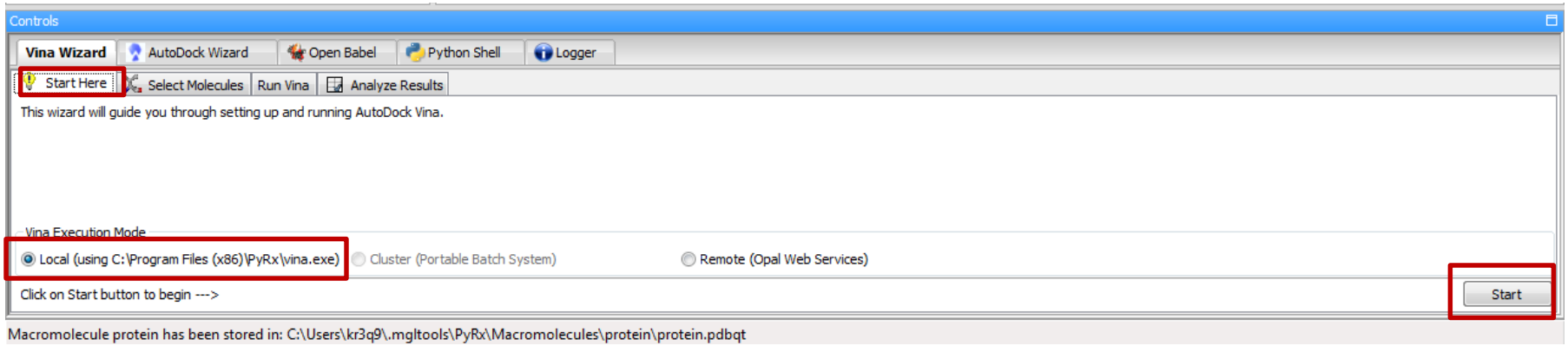


Note: AutoDock requires all it's input files in .pdbqt format (pdbqt file consists partial charges and atom types)

→ After converting pdb files into AutoDock input files (or .pdbqt files), you will see them under **AutoDock** tab as shown below (if you don't see any files, right click and refresh under AutoDock tab)

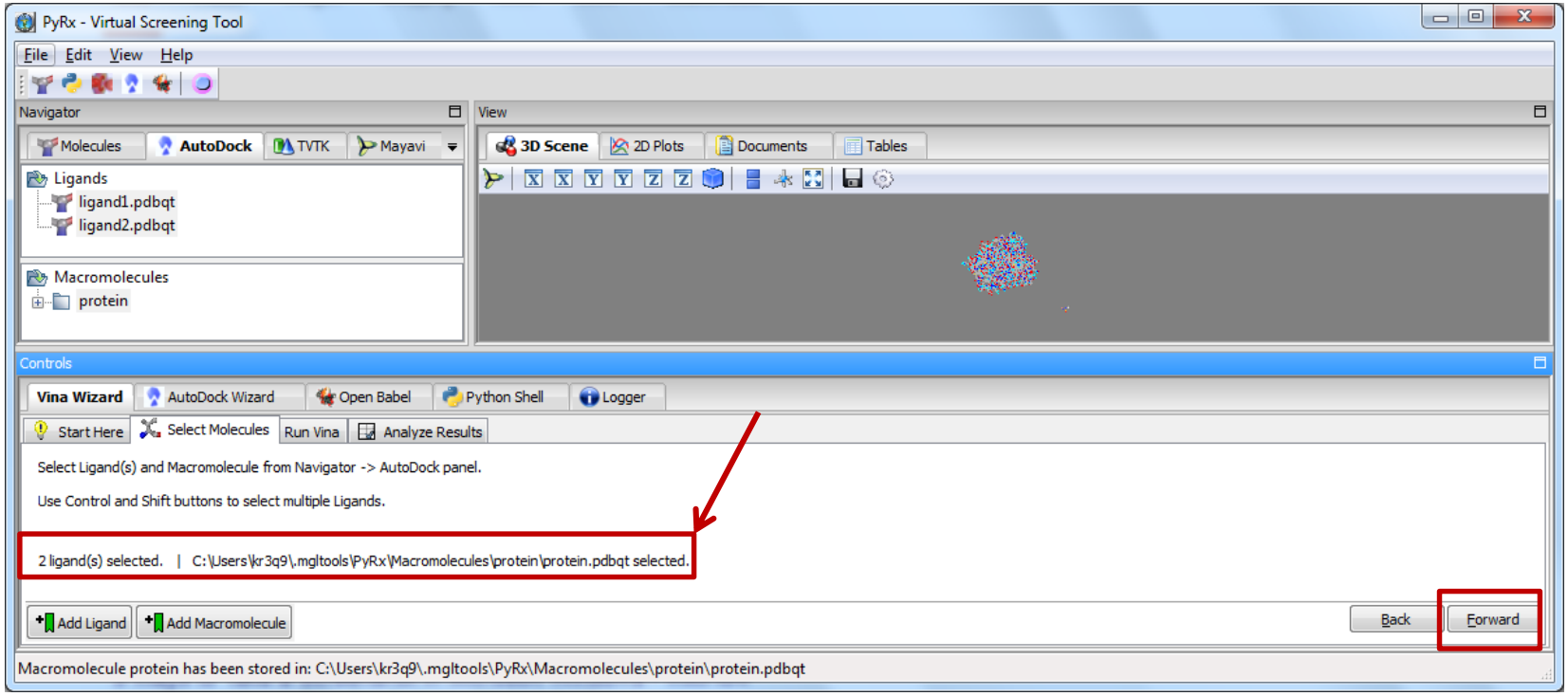


→ Now the protein and ligand(s) files are ready for docking.
→ Click on Start Here button under Vina Wizard.
→ Select Local button under Vina executioin Mode
→ Click Start button



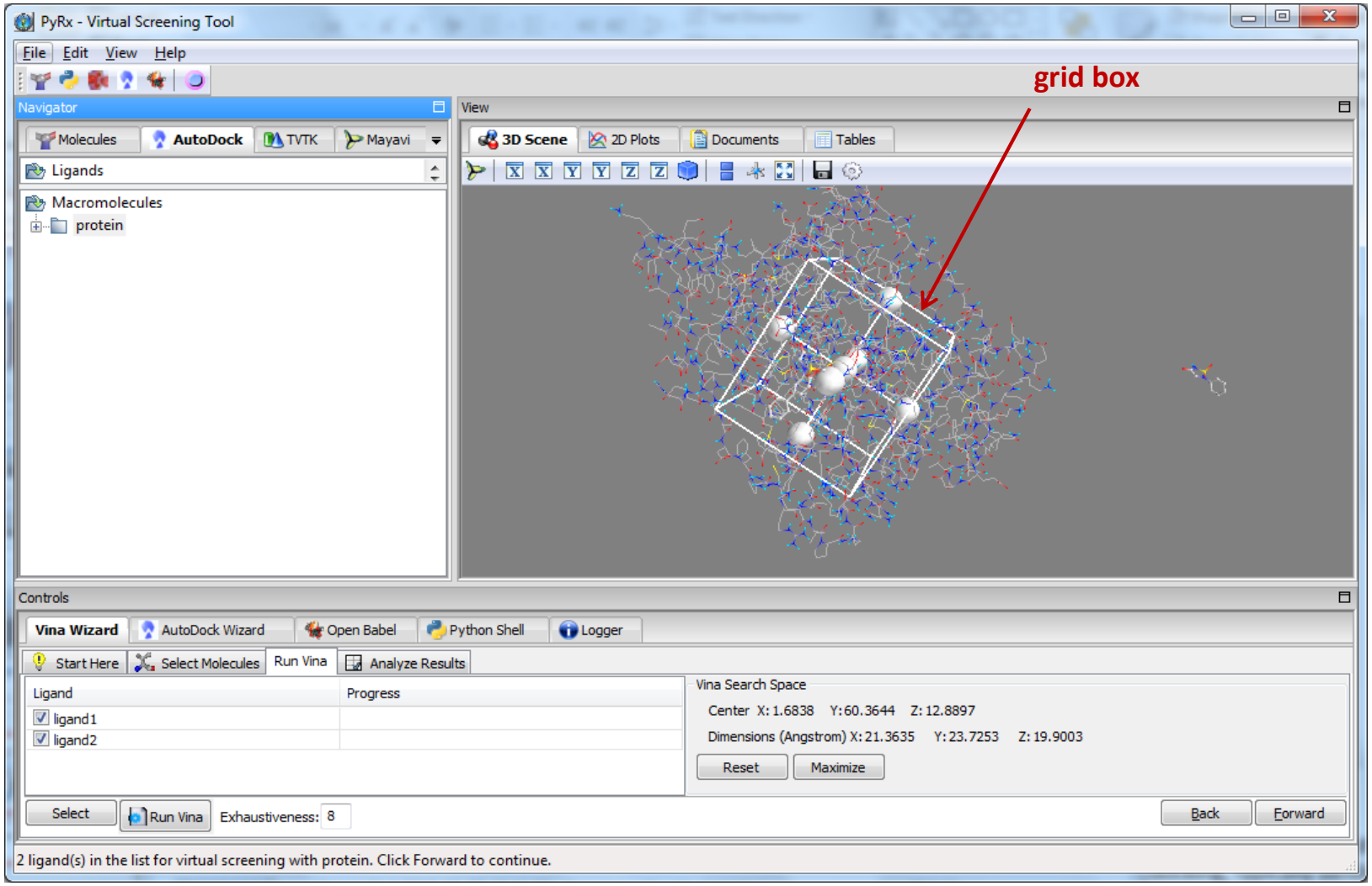
→ Select protein and ligand(s) by simply clicking on them. You will see a window like below (In the picture below we selected two ligand and one macromolecule).

→ Click Forward to **Run Vina** .



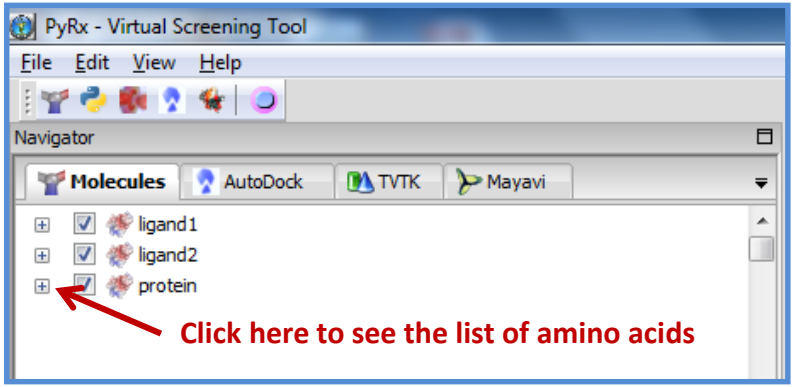
❑ Selecting Vina Search Space:

→ In this step you will see a **grid box** (white box with spherical handles) in the **3D scene** as shown below. This grid box allows you to select **search space** (Part of the protein, where we are going to perform docking, typically the binding site) in the protein.

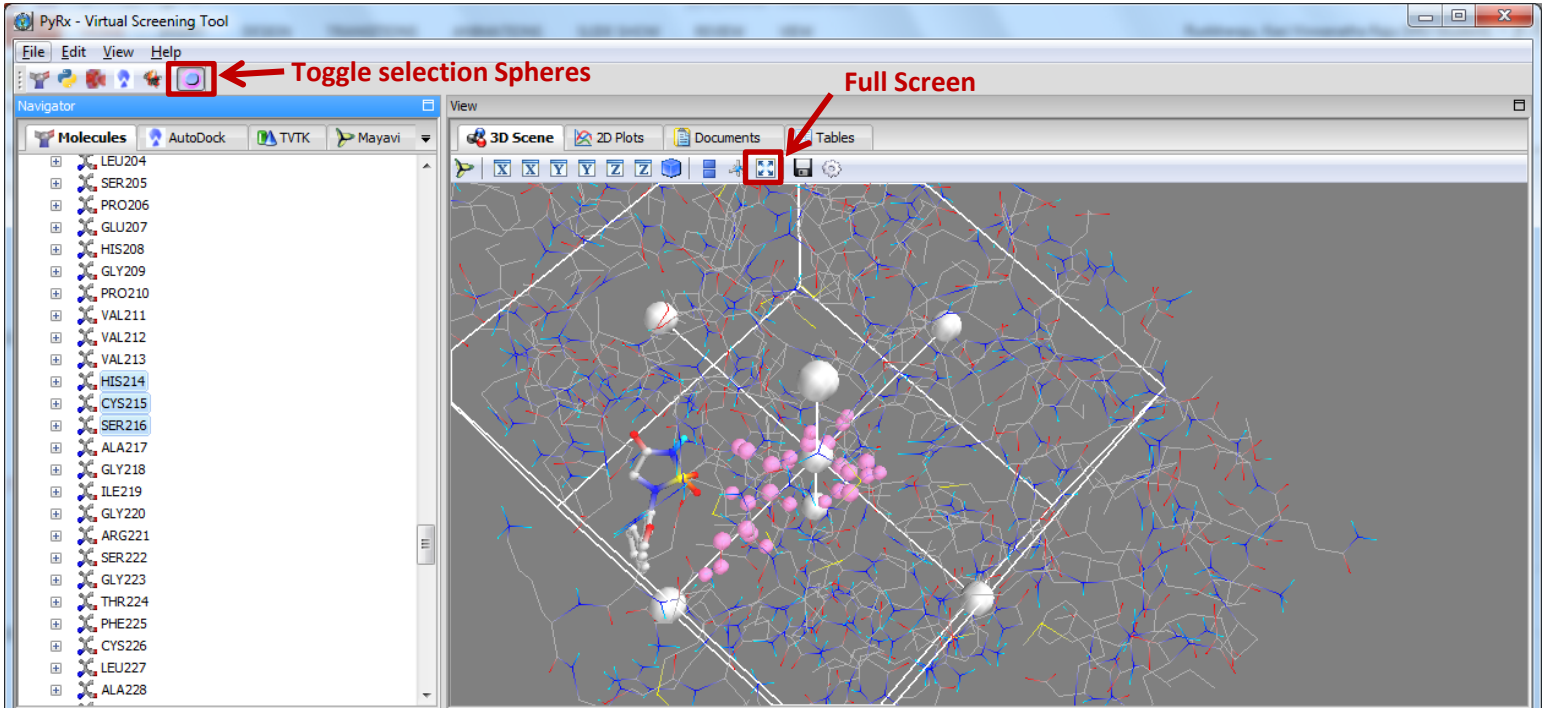


→ To help locating the **binding site** (or active site) we can use binding site amino acids (in this protein **HIS214, CYS215 and SER216** are active site amino acids).

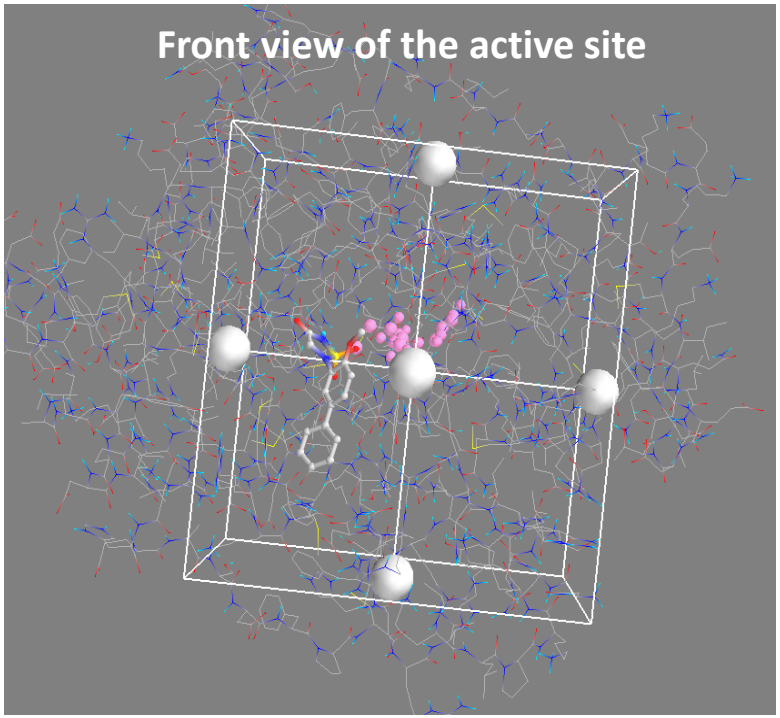
→ Click molecules button under Navigator panel, then click on **+** button located in front of protein tab.

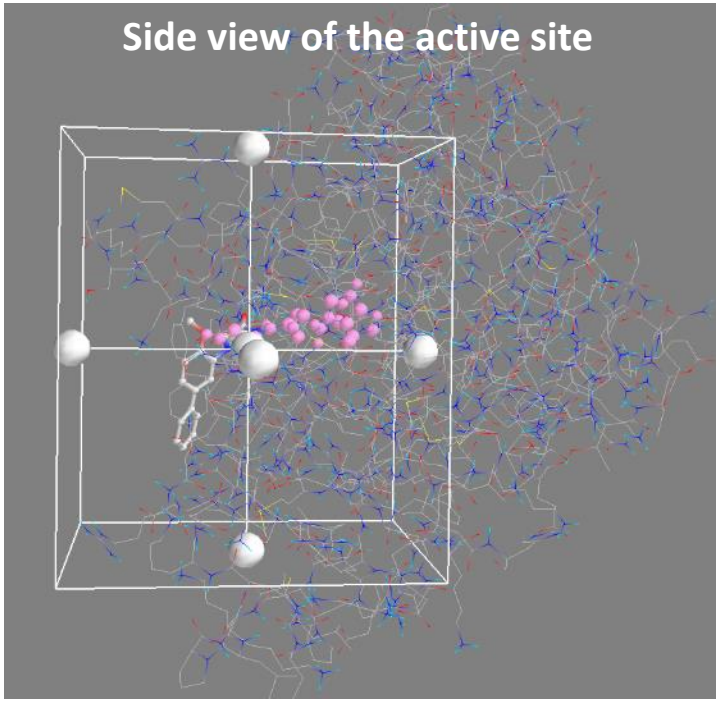


→ After selecting the amino acids (use **shift button** to select multiple amino acids) click on the **Toggle selection Spheres** button to see the selected amino acids as **pink spheres** .



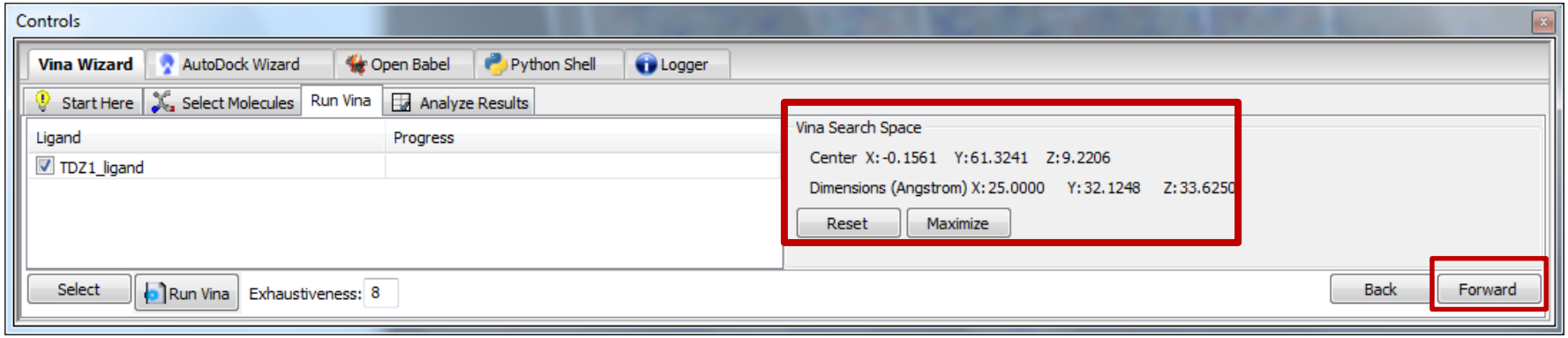
→ Now use the spherical handles of the grid box to select the search space as shown below.





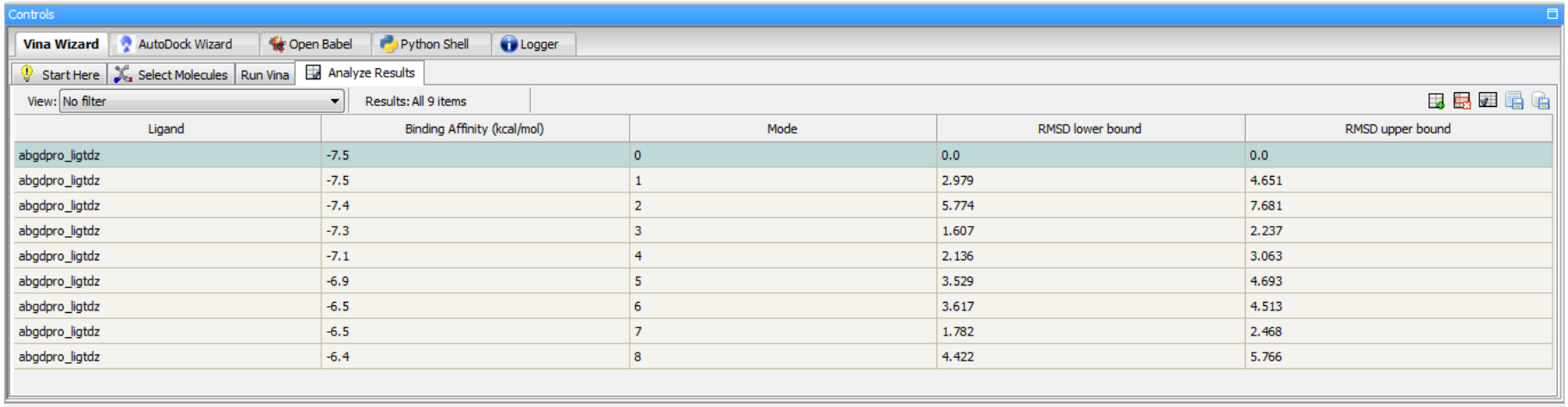
→ Make sure you select the grid box size big enough to allow the ligand to move freely in the search space.

→ **Use the search space (Vina search space) values close the ones mentioned in the picture below, to get better results.**



→ Click **forward** button to start Vina calculations.

→ Once the calculations are done, results will be populated as seen in the below table with the **Binding Affinity (kcal/mol)** values. More negative the binding affinity better the orientation of the ligand in the binding site.

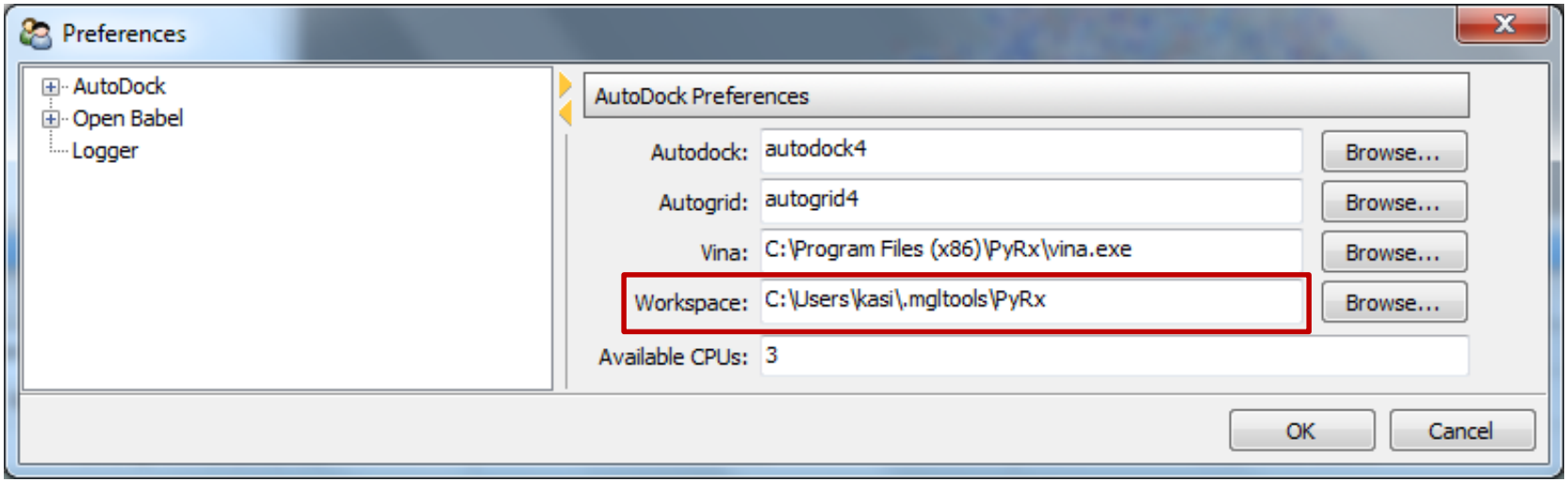


Ligand	Binding Affinity (kcal/mol)	Mode	RMSD lower bound	RMSD upper bound
abgdpro_ligtdz	-7.5	0	0.0	0.0
abgdpro_ligtdz	-7.5	1	2.979	4.651
abgdpro_ligtdz	-7.4	2	5.774	7.681
abgdpro_ligtdz	-7.3	3	1.607	2.237
abgdpro_ligtdz	-7.1	4	2.136	3.063
abgdpro_ligtdz	-6.9	5	3.529	4.693
abgdpro_ligtdz	-6.5	6	3.617	4.513
abgdpro_ligtdz	-6.5	7	1.782	2.468
abgdpro_ligtdz	-6.4	8	4.422	5.766

❑ Exporting Vina Results:

→ Results can be exported to other software programs like **UCSF Chimera or Pymol** for analysis.

→ Click on **Edit** > **Preferences**.
You will see a pop-up window like below. All your results will be saved in location specified as workspace.



→ Go to that location in my case it is *C:\Users\kasi\.mgltools\pyrx*, open **Macromolecules** file, all your results will be saved in **protein** folder (in my case the name is **protein**, but it varies if you choose some other name for your target protein)

→ The protein folder contains three files (protein.pdbqt, ligand1_out.pdbqt and conf.txt) If you use only one ligand for docking

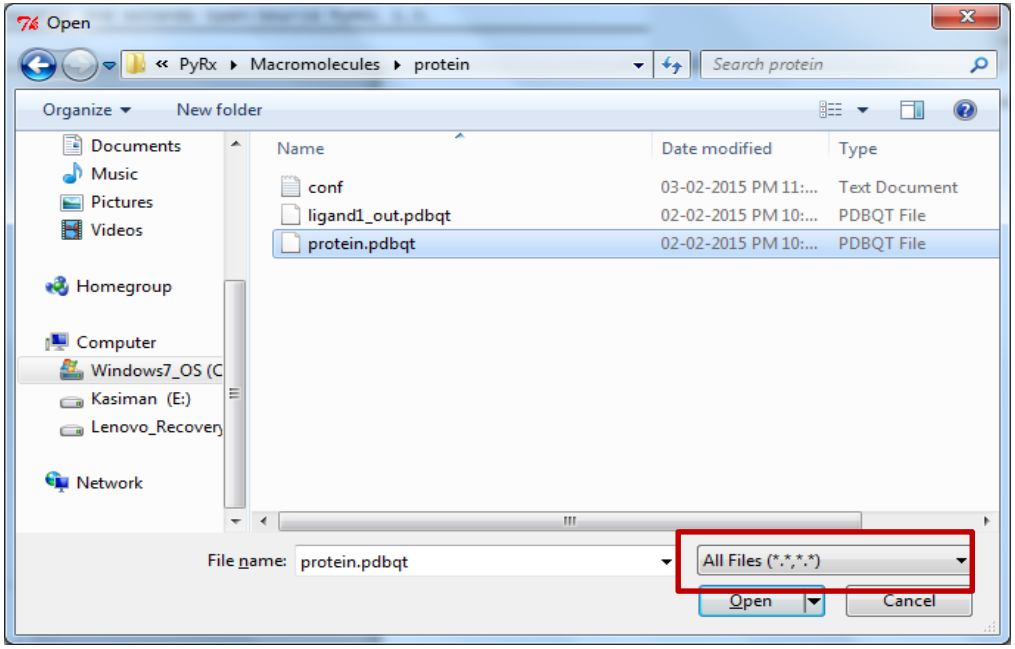
→ ligand1_out.pdbqt contains 8 or 9 best poses (or orientations) of the ligand1 and conf.txt file contains **search space** (or **grid box**) parameters.

→ **Save** this protein folder at your convenient location for further **analysis with Pymol**.

→ **You are done with PyRx**, now let's analyze the results by using **Pymol**.

❑ Analyzing Results with Pymol:

→ To open .pdbqt files in **Pymol** select **All Files(*.*,*.*)** in open pop-up window as shown below.



→ Open **protein.pdbqt** file followed by **ligand1_out.pdbqt** to analyze the results.


PyMOL Viewer
For Educational Use Only
all
protein.pdbqt
ligand1_out.pdbq
Click here to go to next pose
PyMOL>_

❑ Viewing protein-ligand interactions:

→ Select the ligand by using upper sequence bar and click on **sele A (action:) > find > Polar contacts > to any atoms.**