MultiDock 2.0

A Graphic User Interface for AutoDock Vina 1.2.3

Software User Manual

About MultiDock:

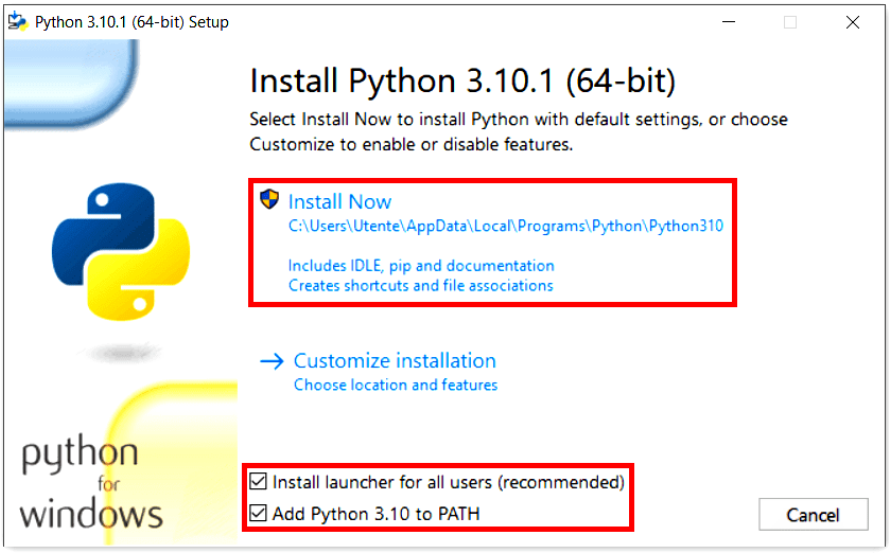
MultiDock is an easy to use graphic user interface for AutoDock Vina 1.2.3 version. It is built using Java programming language. It uses other softwares like Open babel for converting the molecules into sdf, mol and Smiles; MGL tools or ADFR suite for preparing the pdbqt files; Meeko python library for conversion of sdf files to ligand pdbqt files; Pymol for visualization of docking results.

Requirements:

1. Java runtime environment
2. MGL Tools 1.5.7 or ADFR Suite 1.0
3. Open babel 2.4.1
4. Pymol latest version for visualization
5. Python 3.10 or later for Meeko

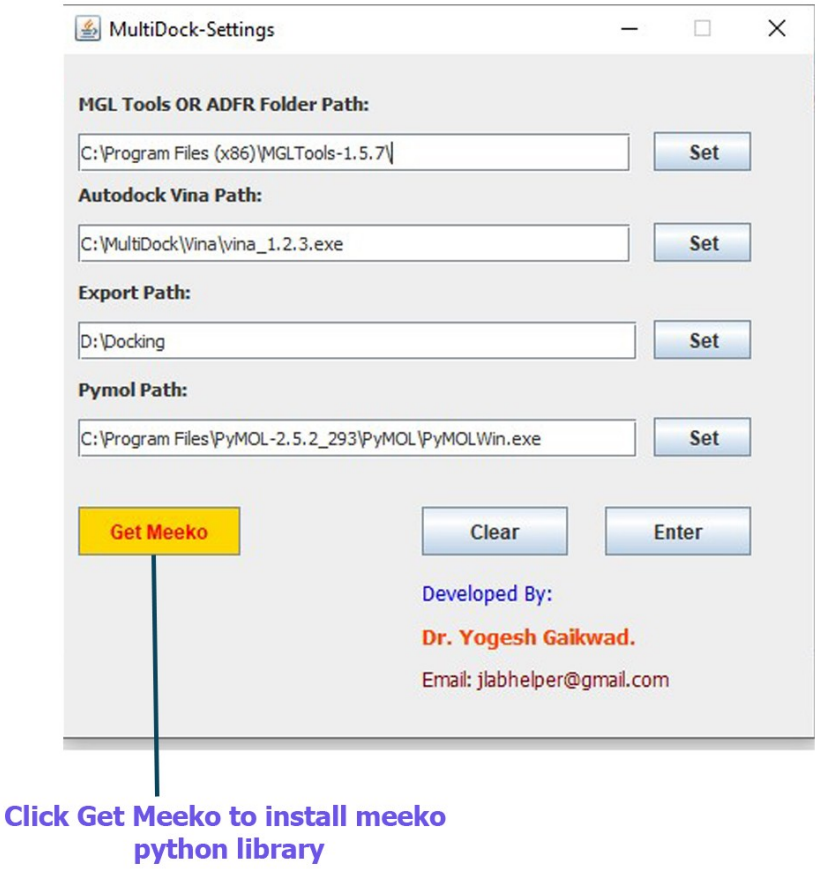
Installations:

Install all the required softwares as per the instructions of respective software. Meeko library and other dependencies will be installed automatically by MultiDock 2.0. Precaution should be taken while installing Python 3.10, check add python 3.10 to PATH as per following image.



Activation and Settings of MultiDock:

The MultiDock software should be activated by specific license key for a computer. Go to settings tab of multidock and click Activate button, in a new window you can find a specific local id of your computer copy and send the local id while purchasing a license key to jlabhelper@gmail.com. Once the software is activated you can make other settings. Set the paths as per the image and click Enter button. Finally install meeko and other dependencies by pressing Get Meeko button. A new window will open click on install and wait for the completion. Once the Meeko is installed there is no need to install it again.



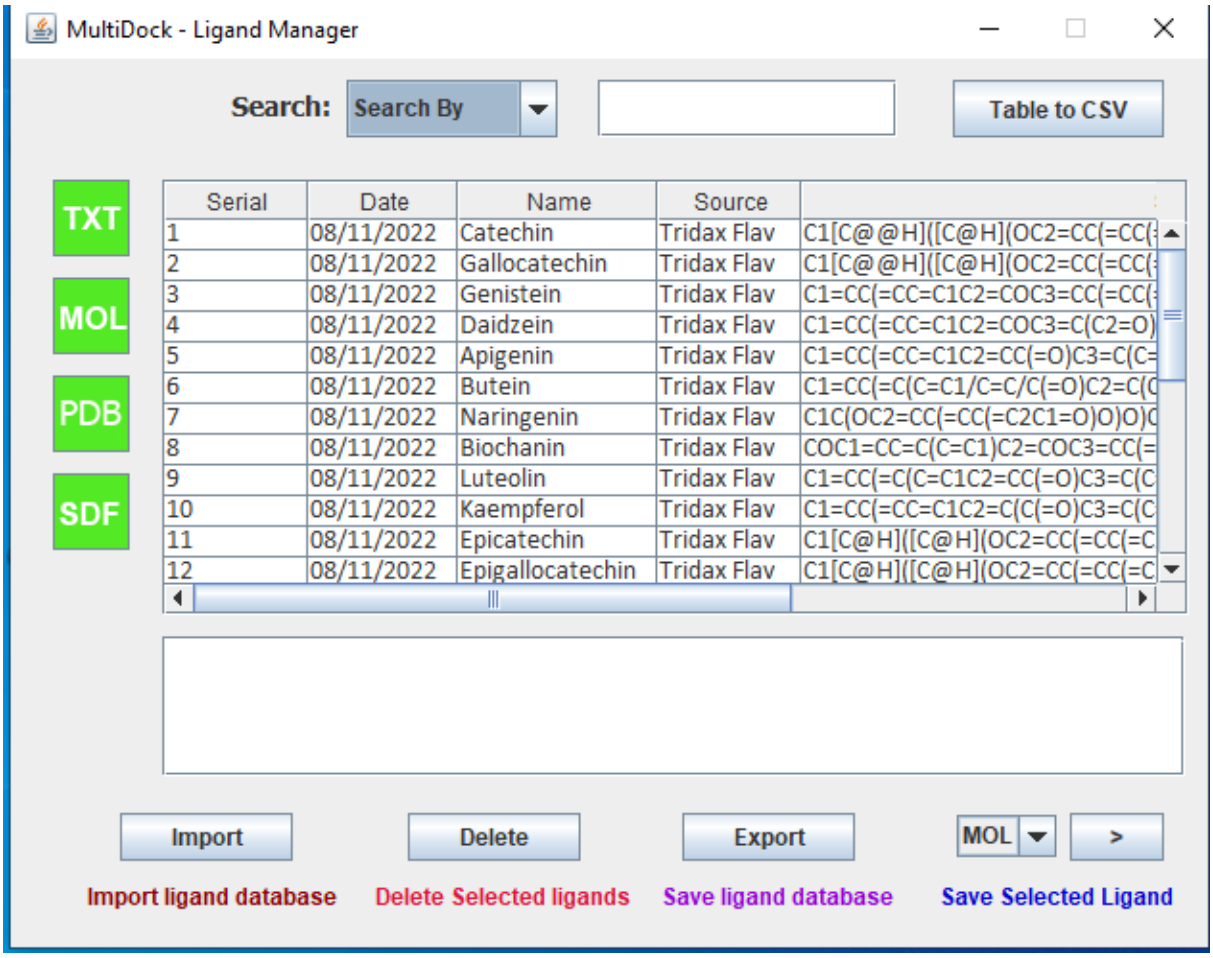
Click Get Meeko to install meeko python library

Ligand Database Management:

Ligands can be added in the database by various ways like,

1. Tab Delimited Text (TXT) file
2. Mol files
3. Small PDB file
4. SDF files

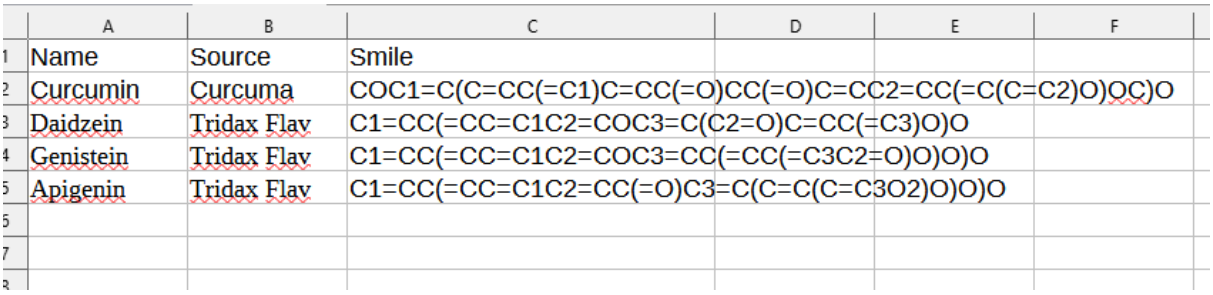
You can share the ligand database from others by importing or export your database in .ligdb format and save it for future of share to your colleagues. The ligand database table can be saved in CSV format.



To save the structures in .mol/.pdb/.sdf format select the rows and press > button. The structures will be saved in molecules folder.

1. TXT file:

The TXT file should be made in Microsoft Excel or any other spreadsheet application. There should be three columns viz Name, Source and Smile as follows.



	A	B	C	D	E	F
1	Name	Source	Smile			
2	Curcumin	Curcuma	COC1=C(C=CC(=C1)C=CC(=O)CC(=O)C=CC2=CC(=C(C=C2)O)OC)O			
3	Daidzein	Tridax Flav	C1=CC(=CC=C1C2=COC3=C(C2=O)C=CC(=C3)O)O			
4	Genistein	Tridax Flav	C1=CC(=CC=C1C2=COC3=CC(=CC(=C3C2=O)O)O)O			
5	Apigenin	Tridax Flav	C1=CC(=CC=C1C2=CC(=O)C3=C(C=C(C=C3O2)O)O)O			
6						
7						
8						

Save the excel file in Tab Delimited Text file format. The first row should be as per the picture shown or blank. The name of ligand/compound should be unique. To enter the TXT file click on the TXT button and navigate the saved TXT file. Be patient while entering large number of ligands in the database. The ligands are added at the speed of about two to three molecules per second depending on the system. (*Name should be unique otherwise it will not be entered in database*.)

2. MOL file:

Select the structures saved in .mol format. You can select multiple files at once. The name of the file will be saved in database as name of compound.

3. PDB file:

Select the .pdb files, here the pdb file should be perfectly of ligand. Do not select large files.

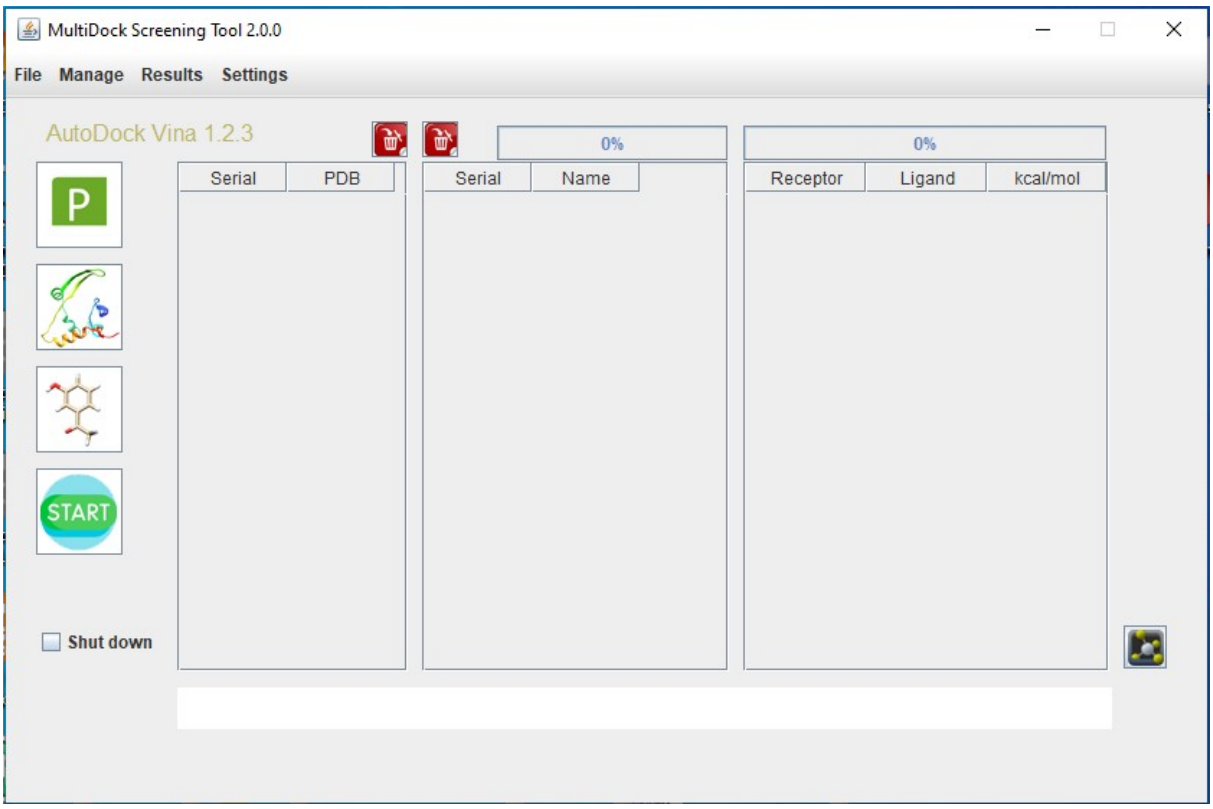
4. SDF files:

Select the structures saved in .sdf format. You can select multiple files at once. If there are multiple structures in the file they will be added automatically.

Setup and Performing Docking

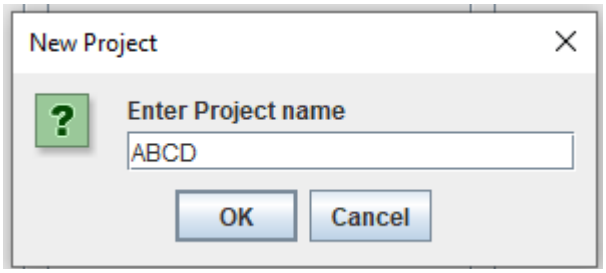
There are various docking options in MultiDock and accordingly you have to make setup.

1. *Blind docking* – entire protein will be explored for docking poses and affinity.
2. *Specific Site docking* – a specific cavity or active site is selected for docking.
3. *Rigid receptor docking* – all amino acids are kept rigid.
4. *Flexible receptor docking* – Some amino acid side chains from active site or docking site are kept flexible.
5. *Fragmented ligand or multi-ligand docking* – multiple ligand fragments can be docked simultaneously.
6. *Reverse docking* – a ligand docked with multiple proteins.



Steps:

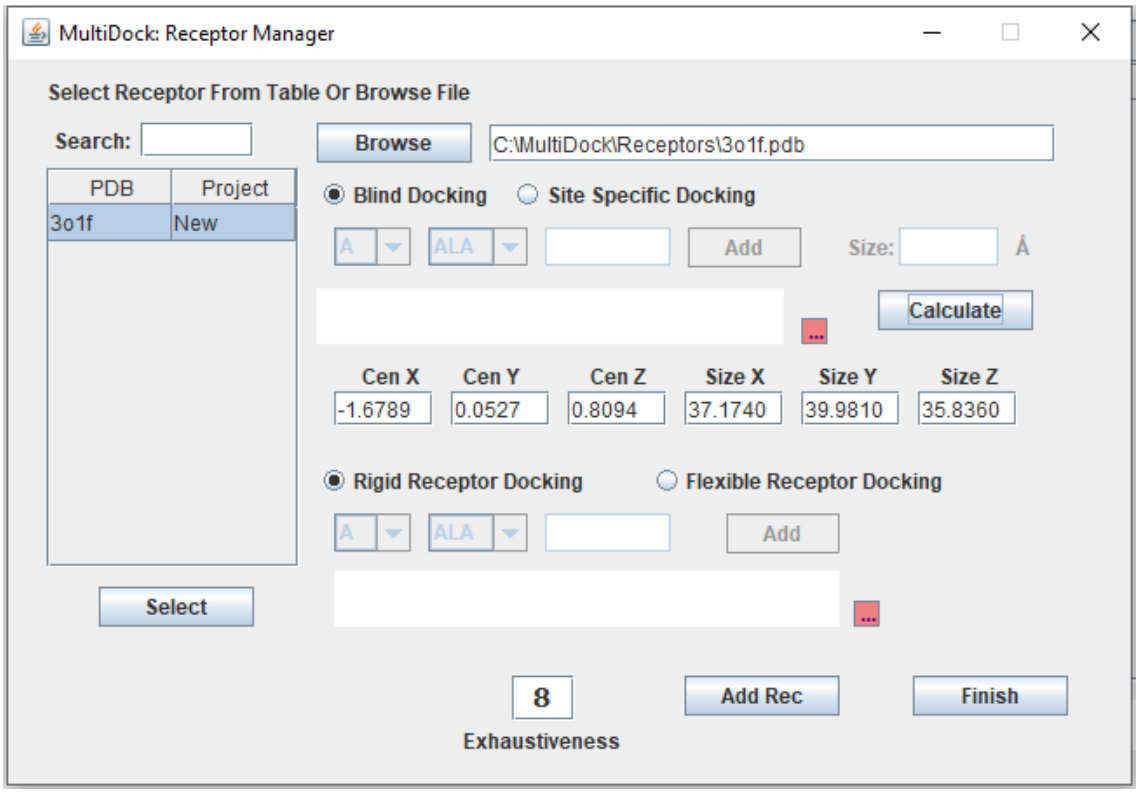
1. Open MultiDock and press Create a project the name of project should be unique.



2. Once the project is created click the Receptor button. A receptor manage window will open.
3. Setup the receptor as per the docking protocol to follow.

A) **Blind Docking:**

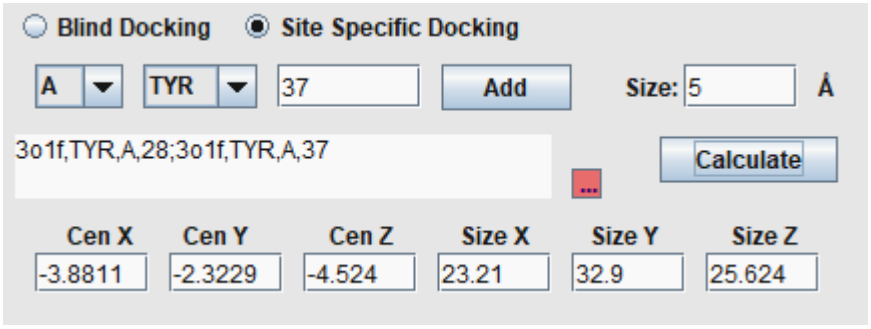
Browse your receptor pdb file or you can select the pdb of previous projects by selecting row and clicking Select button.



1. Select Blind Docking radio button and click Calculate button. The pdb file will be processed, firstly the polar hydrogens will be added and then it will be converted to pdbqt file.
2. Center X, Center Y, Center Z, Size X, Size Y and Size Z will be analyzed for entire protein/receptor.
3. If you don't want to perform flexible docking, set exhaustiveness and press Add Rec button. A success message will be displayed.
4. If you want to add another receptor you can select the pdb or browse the and repeat the steps.
5. Click the Finish button.

B) Site specific docking

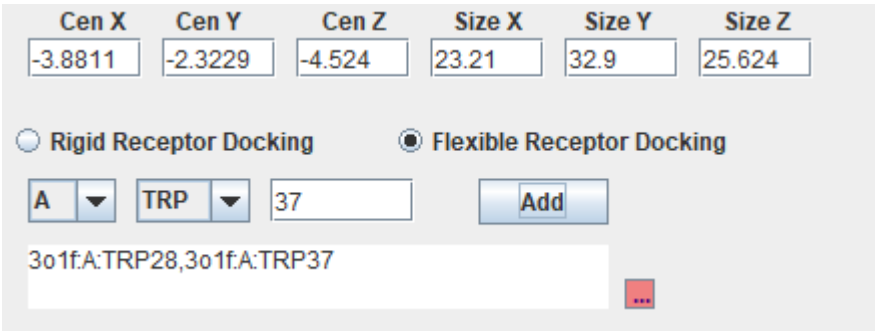
1. Select the PDB file or browse.
2. To set the site specific amino acids select the chain, amino acid residue and add the number of residue; click the Add button. You can add single or preferably multiple residues. You can reset the selection by small red … button near the text area.
3. Set the site specific amino acids as shown in following image. Here example is shown in which the site where you want to dock has two amino acids TYR28 and TYR37 therefore those are selected. Size is set 5Å as it will be added to the distance between the selected amino acids. The values of the Size X, Size Y and Size Z can be changed as per the size of grid box you want. **OR if you know the center_x, center_y, center_z, size_x, size_y and size_z you can just select the select the option Blind docking and edit the values in respective text box after pressing Calculate button.**



4. If you don't want to perform flexible docking, set exhaustiveness and press Add Rec button. A success message will be displayed.
5. If you want to add another receptor you can select the pdb or browse the and repeat the steps.
6. Click the Finish button.

C) Flexible receptor docking:

1. Once the center and sizes (grid box) are calculated you can chose Rigid Receptor docking or flexible receptor docking.
2. To perform flexible receptor docking you must give the residues to keep flexible. In following image two tyrosine amino acids are set flexible.
3. To set the flexible amino acids select the chain, amino acid residue and add the number of residue; click the Add button. You can add single or multiple residues present within the grid box. You can reset the selection by small red button near the text area.



4. Set exhaustiveness and press Add Rec button. A success message will be displayed.

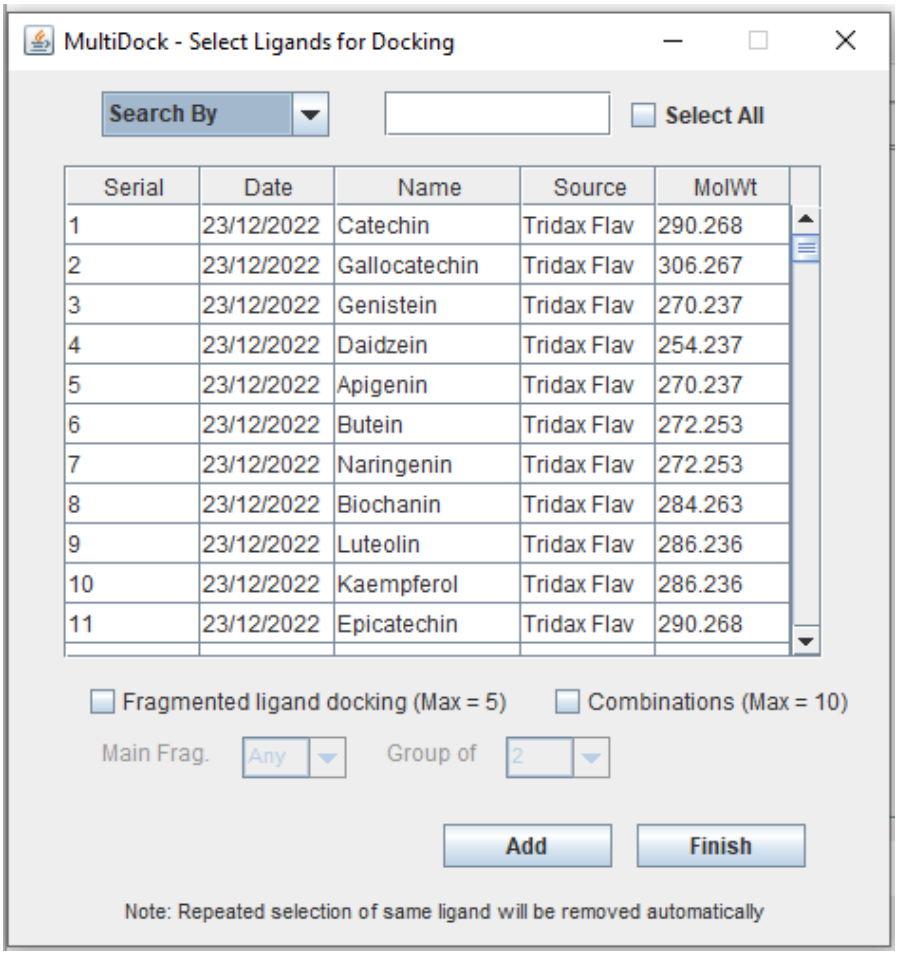
5. If you want to add another receptor you can select the pdb or browse the and repeat the steps.
6. Click the Finish button.

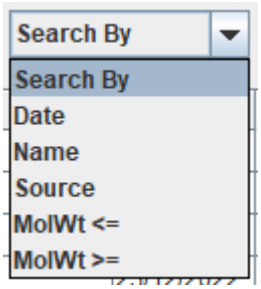
The selected protein receptors should appear in the Receptor table as in above image.

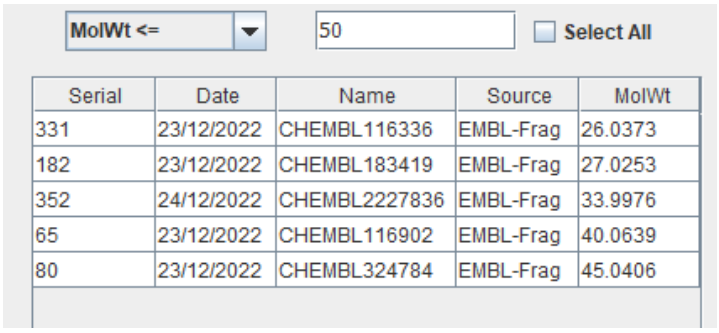
Ligand Selection and Fragmented or Multi-ligand Docking

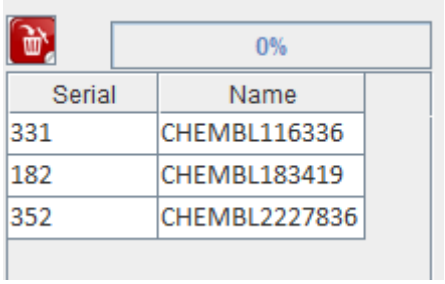
Ligand selection:

Click on the ligand button on manin window of multidock software. A ligand selection window will appear. Select the table rows and click Add button. You can select many rows and click Add many times repeated selections will be removed automatically. You can search the ligands by Date, Name, Source and molecular weights more than or less than. Click the Finish button ligands will be added for docking.







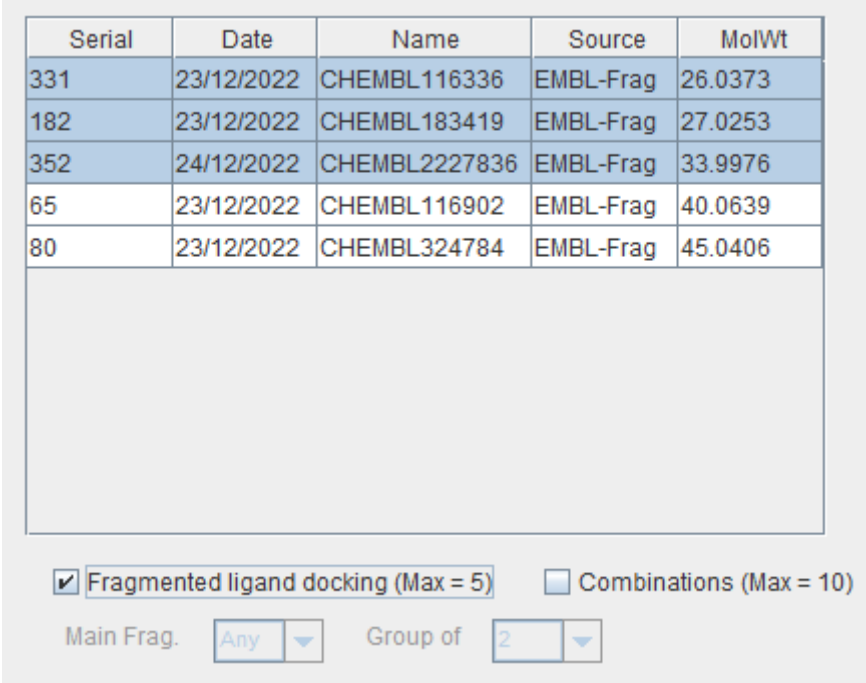


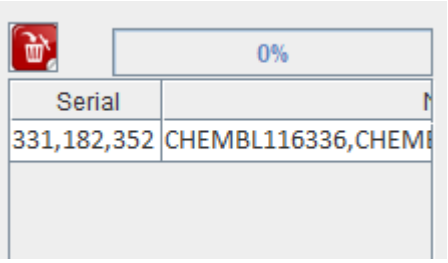
Ligands added in main window

Fragmented Ligand Docking or Multi-ligand docking:

Fragmented or multi-ligand means the selected fragments of ligands will be docked simultaneously. In multidock there are two ways to select the fragments.

1. Direct fragments: Select two to five ligands and check the fragmented ligand docking. Click Add button and then Finish button. All the selected ligands will be added at in single docking shown below. You can multiple group of fragmented ligands.

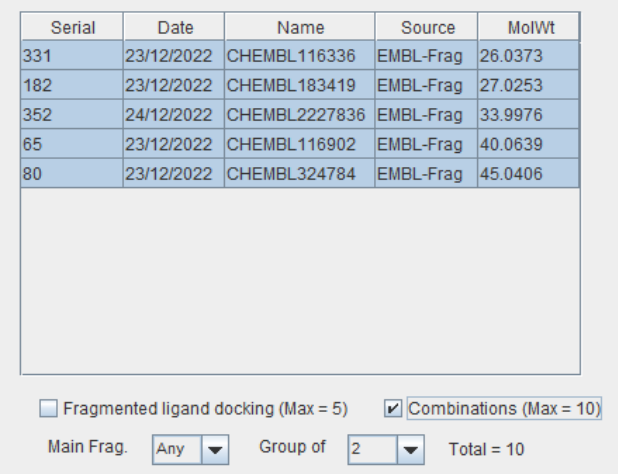


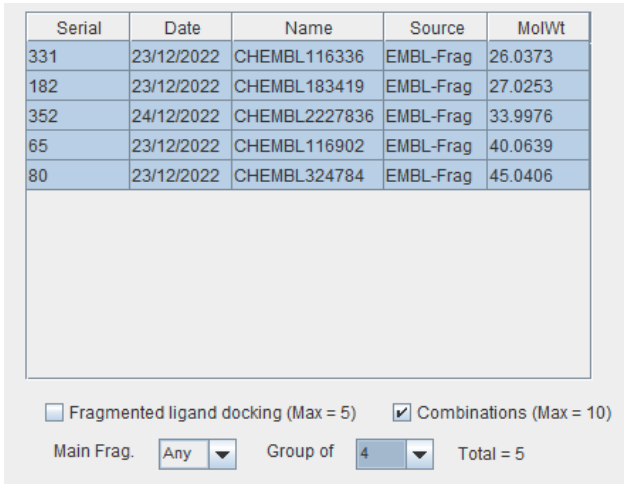


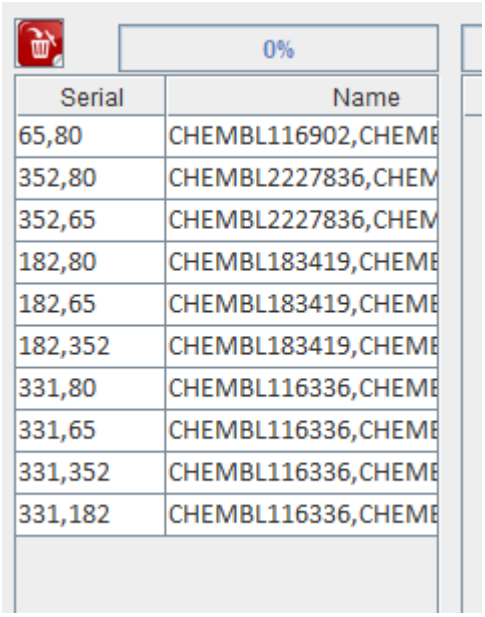
Fragments added in main window

2. Combinations of fragments:

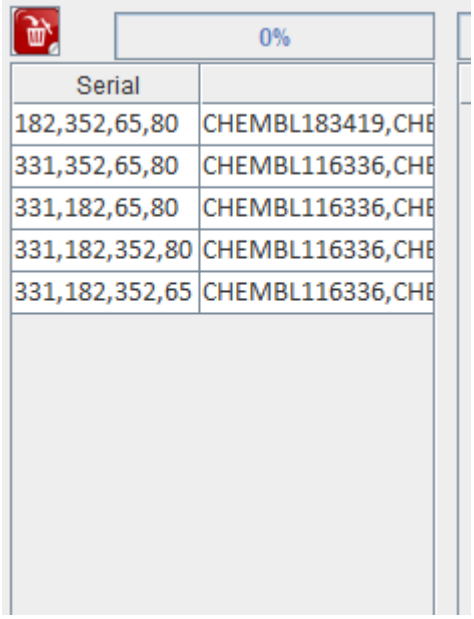
Combinations of fragments can be added for docking. For this option you can select more than three but less than ten fragments from the table. Here in the example below 5 fragments are selected and 2 taken at once will give total 10 combinations. Likewise 4 taken at once will result in 5 combinations. This will be true when no main fragment selected.





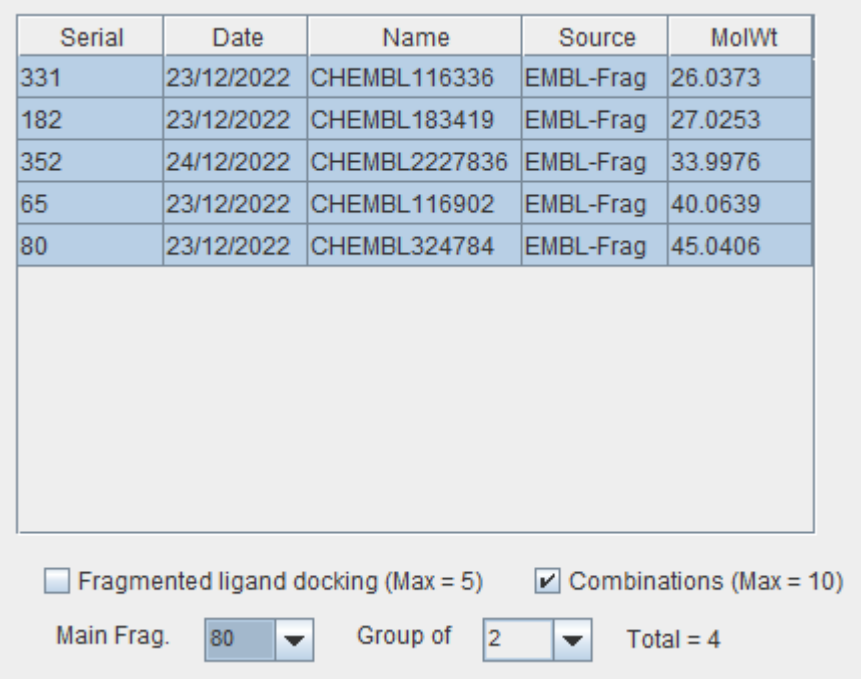


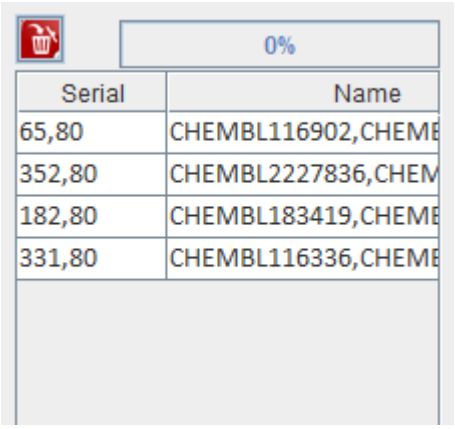
10 combinations when 2 at once from 5



5 combinations when 4 at once from 5

When selected one of the fragment as main the combinations are made but only containing the main fragment. For example shown below fragment 80 is selected as main fragment as a result only 4 combinations are possible.

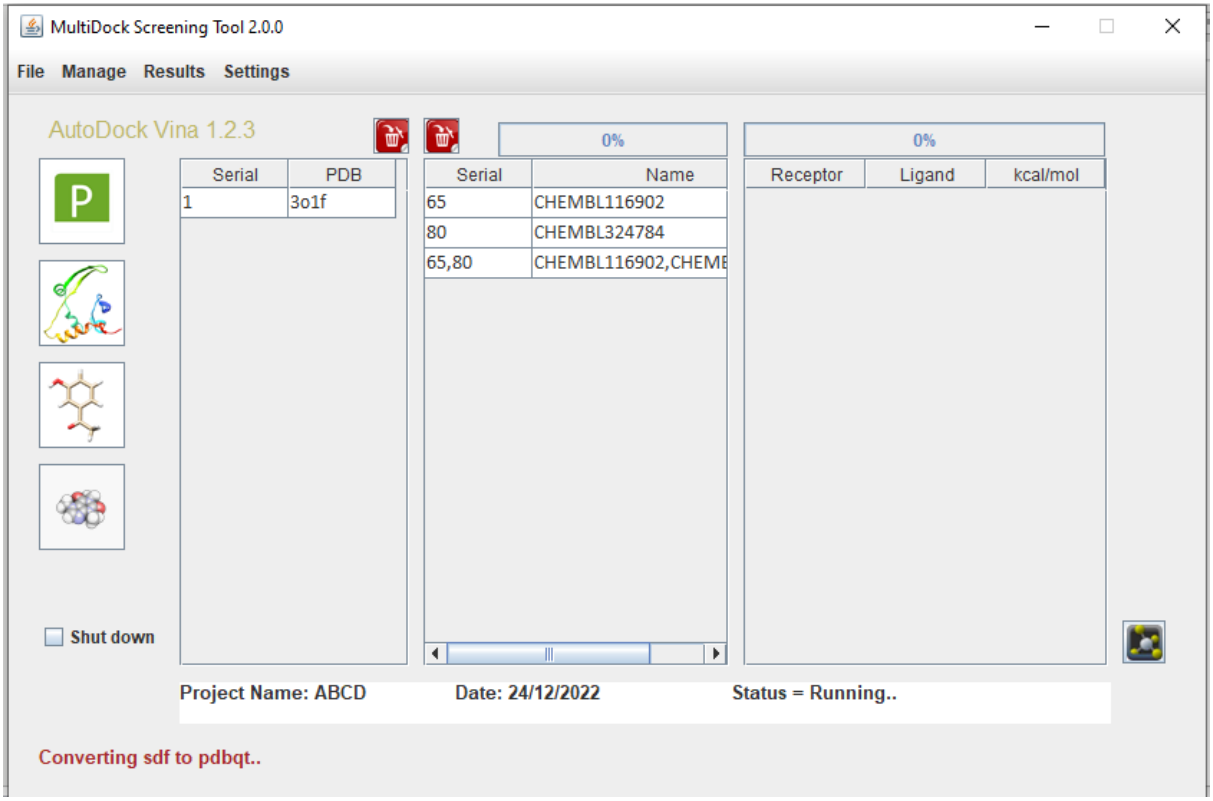




Fragment 80 is selected as main and 2 at once out of 5.

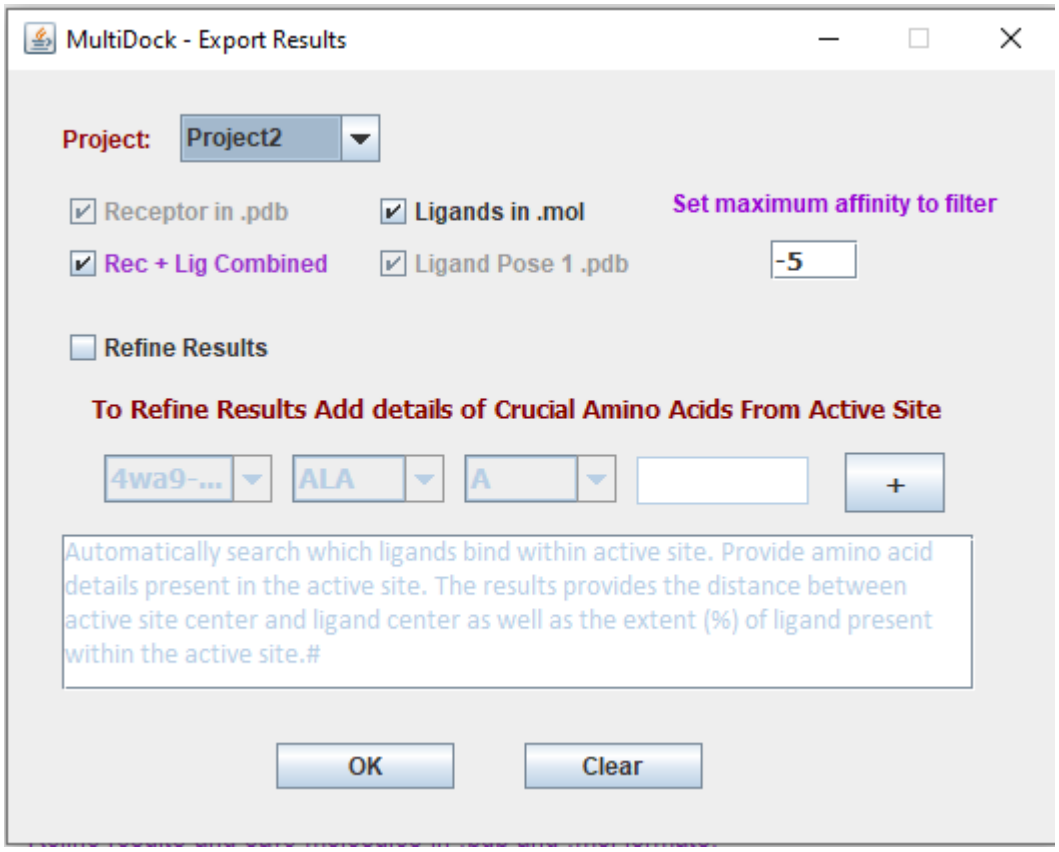
Start Docking

Once the selection of receptor and ligand is completed click on start button. You can check Shut down to shut down computer after completion of project. To visualize the docking results select a result row and click pymol viewer button. Remember that conversion of ligand SDF to pdbqt by mk_prepare_ligand.py takes more time than prepare_ligand.py.



Exporting The Result Files

You can export the result structures like receptor-ligand complex or pdb files. You have to select the project first and select checkbox of the required formats. You can limit the results by limiting the binding energy. For example if there is one protein and 10 ligands in a project and you set limit -7.0 only the ligands with kcal/mol less than -7.0 will be saved or exported. To save all result files keep the value 0. Click Ok button to export or save files. Wait for the process to finish.



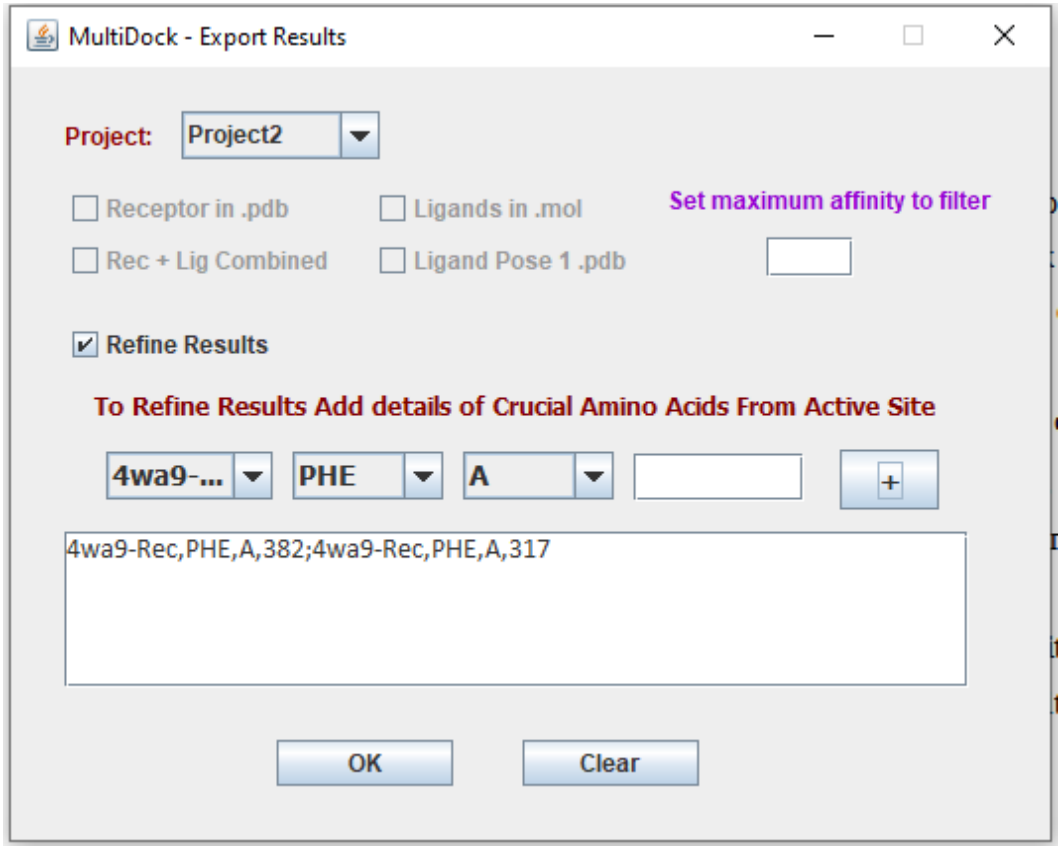
Here the project, file formats to be saved or exported and maximum affinity to filter is set to -5. Only those results will be considered which have affinity less than -5.

Refine the Blind Docking Results

If you have docked one or many receptor with a large of number ligands in blind docking mode, it will be very difficult task to check each and every ligand whether it binds in the active site of the receptor. In such cases you can use refine result function.

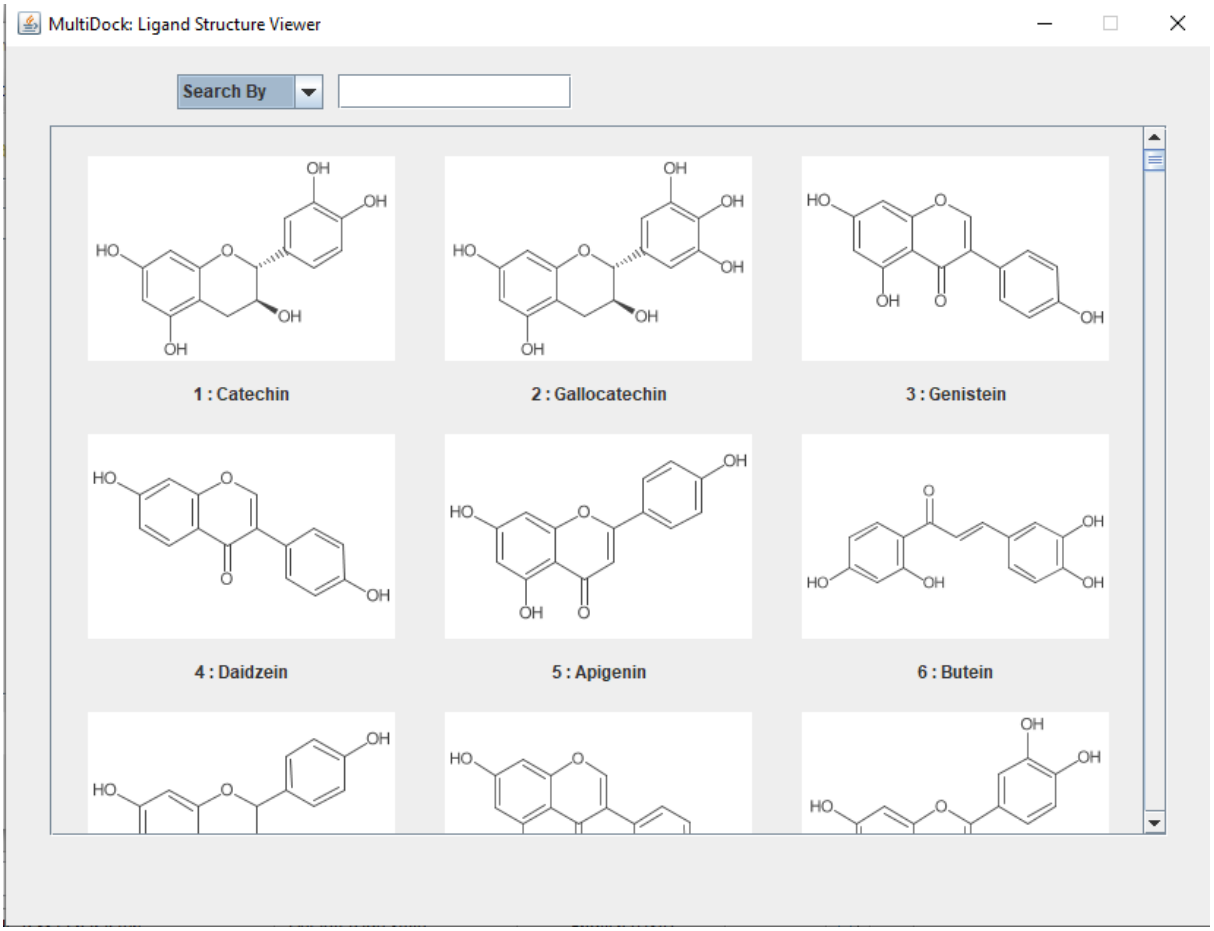
Select the project, protein and some active site amino acid, chain and residue number as shown below. Click + button to add the residues. Once the selection is complete click on Ok button, within a few seconds refined result table will appear.

In refine results the distance between ligand and active site, ligand efficiency (LE), Ki and the percentage of ligand inside the active site will be given. We can easily sort the ligands for further analysis.



Ligand Structure Viewer

In the main window of MultiDock go to Manage menu and select Structure viewer to see the ligand structures of your database. You can search the ligands in various ways.



Folder and File Structure of MultiDock

The folder and file structure of multidock is as following image. There are seven folders.

1. **Database:**

   Contains SQLite database of multidock.

2. **Devlop:**

   Contains all python files required by multidock.

3. **Projects:**

   Contains all the project folders and in each folder there are files related to the project.

4. **Receptors:**

   Contains all pdb files used as receptor for handling in future.

5. **Results:**

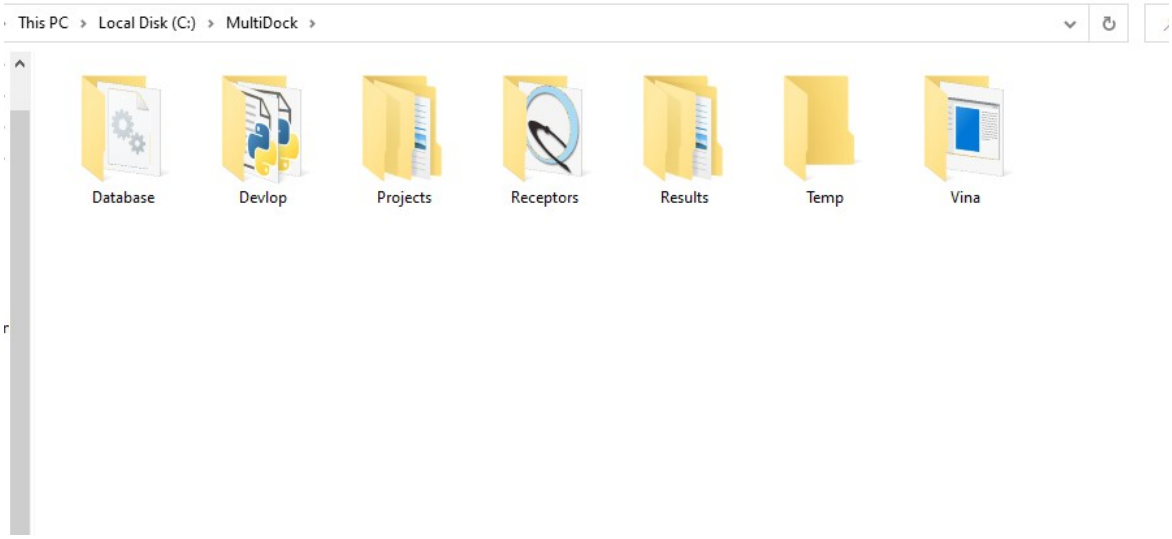
   Contains all the project folders and in each folder there are files related to the results of the project.

6. **Temp:**

   Contains all temporary files during project runs.

7. **Vina:**

   It is not mandatory but you can keep the AutoDock Vina 1.2.3 .exe file in this folder and Set the path in the settings.



Important Note

If you are going to format your computer you should backup all the folders and restore it in future to keep your whole data as it is.

Keep visiting the Github repository to check for new updates weekly. You can suggest new functionalities, report bugs and express opinions through email to jlabhelper@gmail.com.