

MultiDock Screening Tool 3.2

A Graphic User Interface for AutoDock Vina 1.2.5

Software User Manual

About MultiDock:

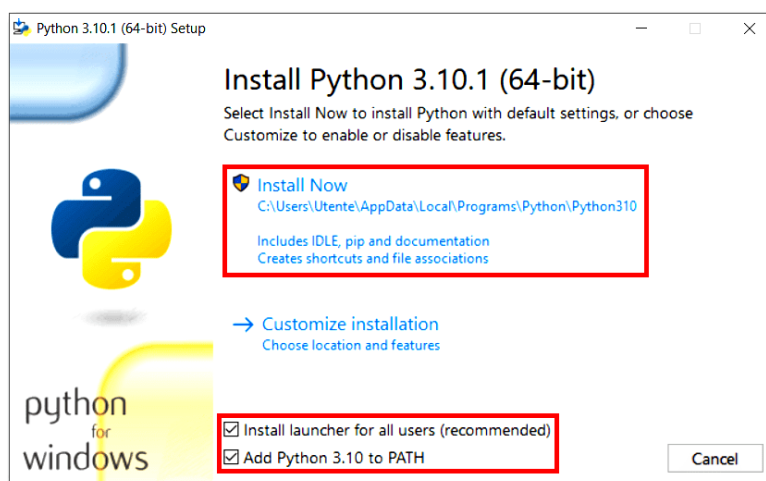
MultiDock is an easy to use graphic user interface for AutoDock Vina 1.2.5 version. It is built using Java programming language. It uses other softwares like Open babel for converting the molecules into sdf, mol and Smiles; ADFR suite for preparing the pdbqt files; Meeko python library for conversion of sdf files to ligand pdbqt files; Pymol for visualization of docking results.

Requirements for Windows/Linux Operating System:

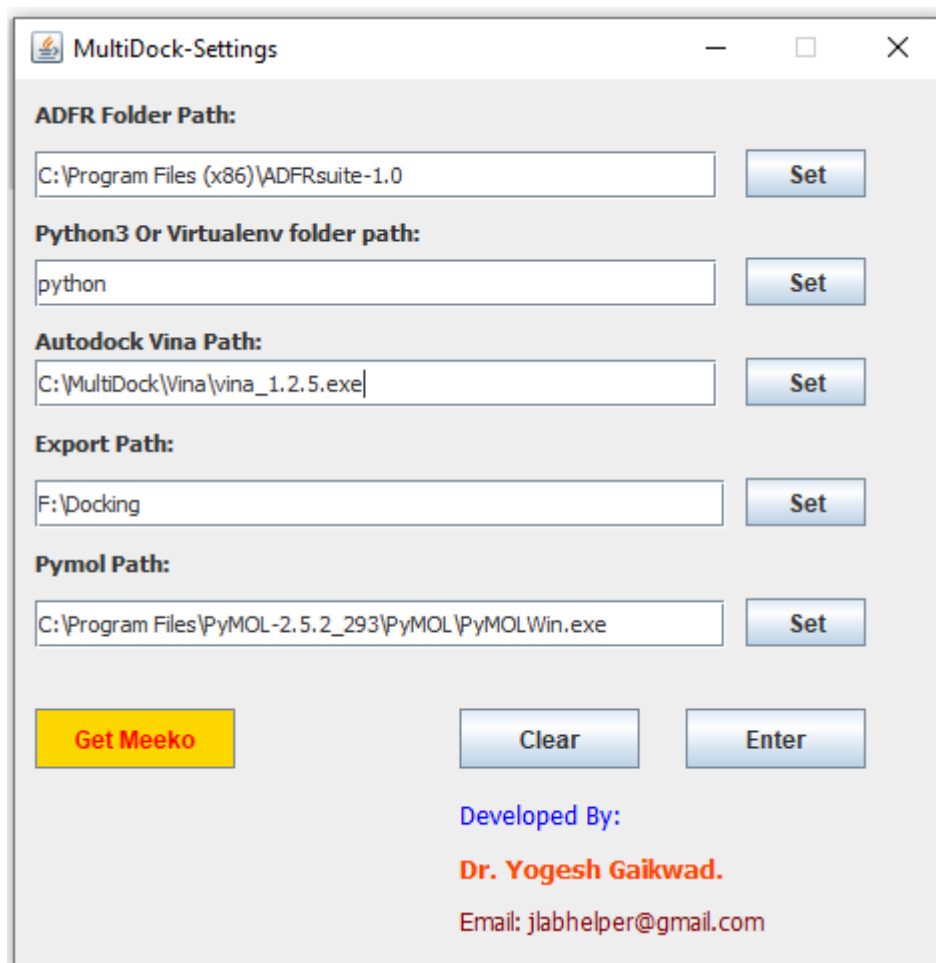
1. Java runtime environment (Version 22.0.2 or later)
2. ADFR Suite 1.0
3. AutoDock Vina version 1.2.5
4. Open babel
5. Pymol latest version for visualization
6. Python 3.10 or 3.11 for Rdkit and Meeko

Installations:

Install all the required softwares as per the instructions of respective software. Meeko library and other dependencies will be installed automatically by MultiDock 3.0. Precaution should be taken while installing Python 3.10 or 3.11, check add python 3.10/3.11 to PATH on Windows operating as per following image.



Settings on Windows computer:



Set the settings for ADFR path and Pymol as per above image. The export path is any folder where all result files you wish to be saved.

Important Settings for Python path:

The python path setting is most important and properly set. To determine the python path to be set run following commands in cmd.

```
C:\Windows\system32\cmd.exe

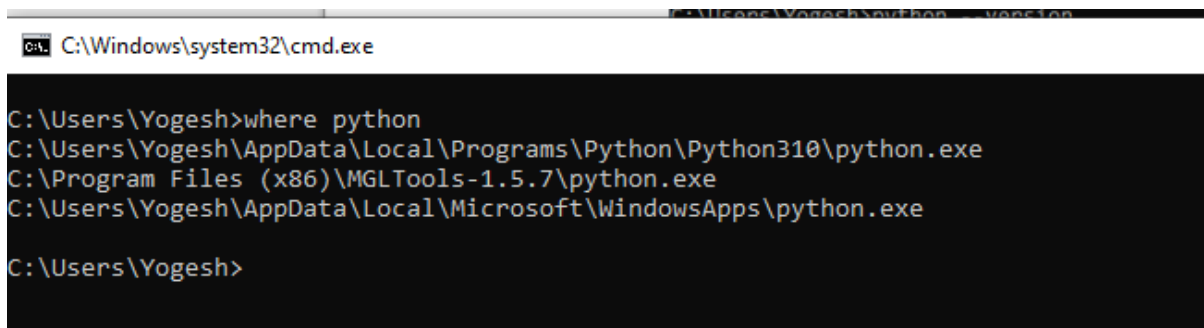
C:\Users\Yogesh>python --version
Python 3.10.5

C:\Users\Yogesh>
```

If on using command python --version the result shows the python version you have installed, which must be 3.10 or 3.11 you can set the python path in settings as **python** as shown in above image.

However, if the python version shown is 2.7 after using command **python --version** in cmd do the following:

Run command **where python** in cmd as follows



```
C:\Windows\system32\cmd.exe

C:\Users\Yogesh>where python
C:\Users\Yogesh\AppData\Local\Programs\Python\Python310\python.exe
C:\Program Files (x86)\MGLTools-1.5.7\python.exe
C:\Users\Yogesh\AppData\Local\Microsoft\WindowsApps\python.exe

C:\Users\Yogesh>
```

In result we can see path for python 3.10 or installed python version you have installed. In this case copy the path and add in settings as follows.



AutoDock Vina:

Download AutoDock Vina 1.2.5 and keep the .exe file in any folder and set the path. You can download the AutoDock Vina from official website.

Settings on Linux computer:



MultiDock-Settings

ADFR Folder Path:
/home/cognition/ADFRsuite-1.0 **Set**

Python3 Or Virtualenv folder path:
/home/cognition/MultiDock/Vina/pyenv **Set**

Autodock Vina Path:
vina **Set**

Export Path:
/home/cognition/Dockings **Set**

Pymol Path:
/home/cognition/Downloads/PyMOL-3.0.4/pymol/pymol **Set**

Get Meeko **Clear** **Enter**

Activate

Developed By:
Dr. Yogesh Gaikwad.
Email: jlabhelper@gmail.com

On linux computer install vina by command `sudo apt install vina` and set the AutoDock Vina path as 'vina'.

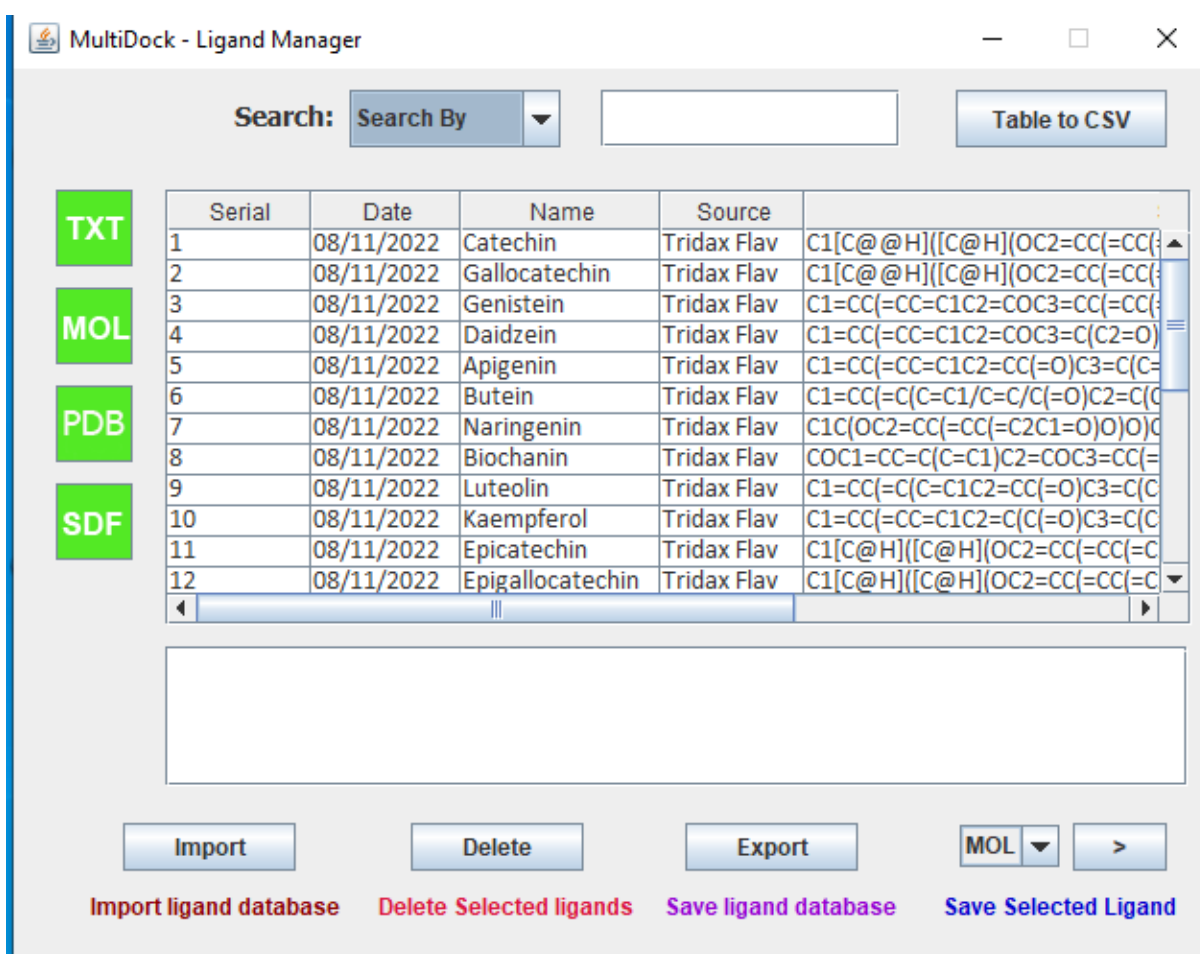
If the default python version is not python 3.10 or 3.11, it is preferable to use virtual environment for python version 3.10 or 3.11 and set the folder path. Other settings are same as on windows computer.

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.



MultiDock - Ligand Manager

Search: Search By Table to CSV

Serial	Date	Name	Source	SMILES
1	08/11/2022	Catechin	Tridax Flav	<chem>C1[C@@H]([C@H](OC2=CC(=CC(=C2)O)O)O)O</chem>
2	08/11/2022	Galocatechin	Tridax Flav	<chem>C1[C@@H]([C@H](OC2=CC(=CC(=C2)O)O)O)O</chem>
3	08/11/2022	Genistein	Tridax Flav	<chem>C1=CC(=CC=C1C2=COC3=CC(=CC(=C3)O)O)O</chem>
4	08/11/2022	Daidzein	Tridax Flav	<chem>C1=CC(=CC=C1C2=COC3=C(C2=O)C=CC3=O</chem>
5	08/11/2022	Apigenin	Tridax Flav	<chem>C1=CC(=CC=C1C2=CC(=O)C3=C(C2=O)C=CC3=O</chem>
6	08/11/2022	Butein	Tridax Flav	<chem>C1=CC(=C(C=C1/C=C/C(=O)C2=C(C(=C(C=C2)O)O)O)O)O</chem>
7	08/11/2022	Naringenin	Tridax Flav	<chem>C1C(OC2=CC(=CC(=C2C1=O)O)O)O</chem>
8	08/11/2022	Biochanin	Tridax Flav	<chem>COC1=CC=C(C=C1)C2=COC3=CC(=CC(=C3)O)O</chem>
9	08/11/2022	Luteolin	Tridax Flav	<chem>C1=CC(=C(C=C1C2=CC(=O)C3=C(C2=O)C=CC3=O)O)O</chem>
10	08/11/2022	Kaempferol	Tridax Flav	<chem>C1=CC(=CC=C1C2=C(C(=O)C3=C(C2=O)C=CC3=O)O)O</chem>
11	08/11/2022	Epicatechin	Tridax Flav	<chem>C1[C@H]([C@H](OC2=CC(=CC(=C2)O)O)O)O</chem>
12	08/11/2022	Epigallocatechin	Tridax Flav	<chem>C1[C@H]([C@H](OC2=CC(=CC(=C2)O)O)O)O</chem>

Import Delete Export MOL >

Import ligand database Delete Selected ligands Save ligand database Save Selected Ligand

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	<chem>COC1=C(C=CC(=C1)C=CC(=O)CC(=O)C=CC2=CC(=C(C=C2)O)OC)O</chem>			
3	Daidzein	Tridax Flav	<chem>C1=CC(=CC=C1C2=COC3=C(C2=O)C=CC(=C3)O)O</chem>			
4	Genistein	Tridax Flav	<chem>C1=CC(=CC=C1C2=COC3=CC(=CC(=C3C2=O)O)O)O</chem>			
5	Apigenin	Tridax Flav	<chem>C1=CC(=CC=C1C2=CC(=O)C3=C(C=C(C=C3O2)O)O)O</chem>			
5						
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.

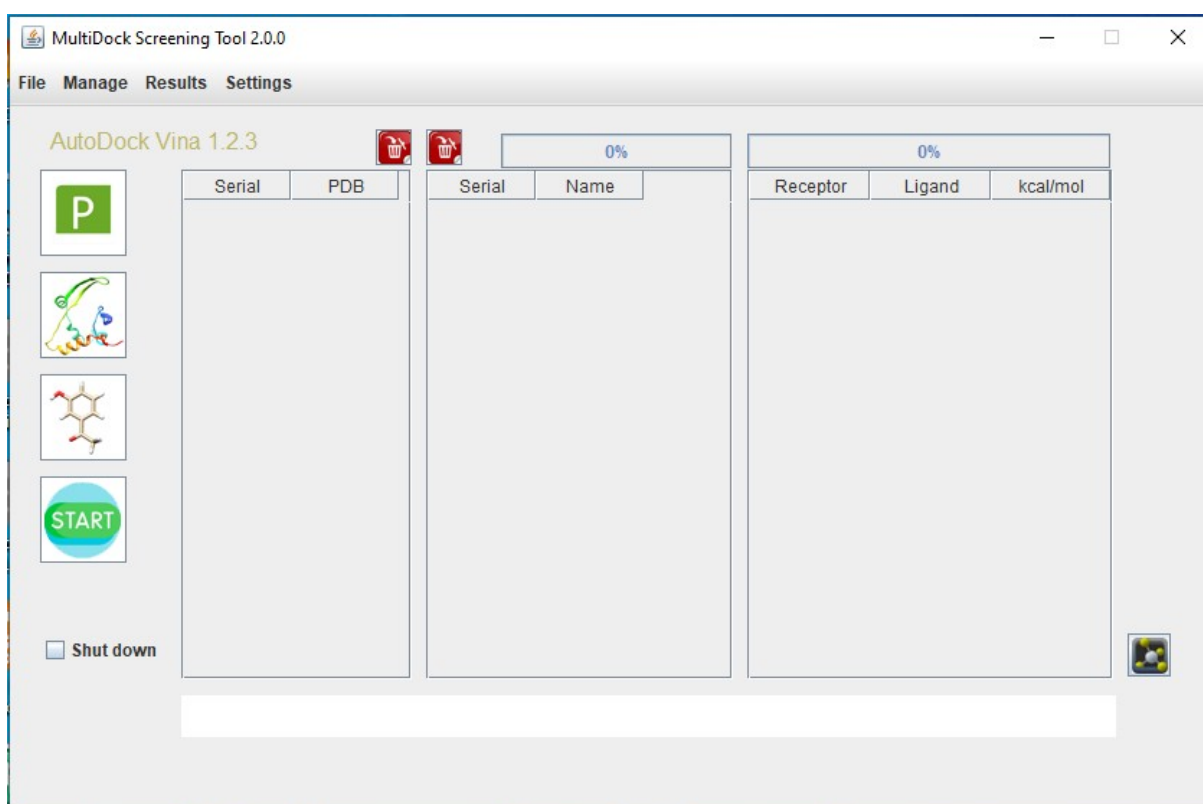
4. SDF files:

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

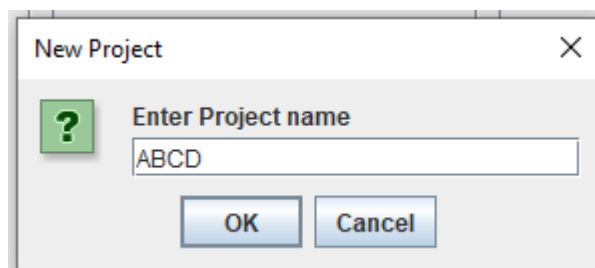
There are various docking options in MultiDock and accordingly you have to make setup.

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:

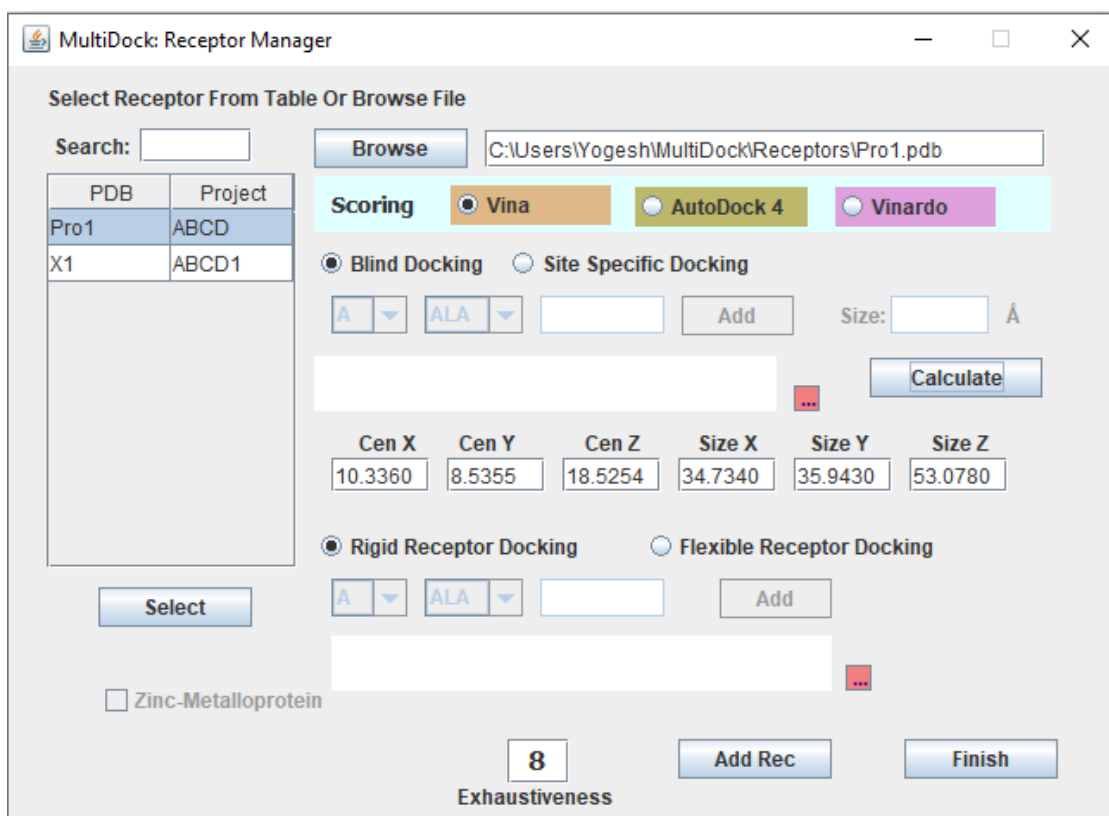
1. Open MultiDock and press Create a project the name of project should be unique.



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 the scoring function from Vina, AutoDock 4 and Vinardo.
2. 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.
3. Center X, Center Y, Center Z, Size X, Size Y and Size Z will be analyzed for entire protein/receptor.
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.

B) Site specific docking

1. Select the PDB file or browse.
2. Select the scoring function from Vina, AutoDock 4 and Vinardo.
3. 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.
4. 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.**

☐ Blind Docking ☒ Site Specific Docking

A ▼ TYR ▼ 37 Add Size: 5 Å

3o1f, TYR, A, 28; 3o1f, TYR, A, 37 Calculate

Cen X	Cen Y	Cen Z	Size X	Size Y	Size Z
-3.8811	-2.3229	-4.524	23.21	32.9	25.624

5. If you don't want to perform flexible docking, set exhaustiveness and press **Add Rec** button. A success message will be displayed.
6. If you want to add another receptor you can select the pdb or browse the and repeat the steps.
7. 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.

Cen X	Cen Y	Cen Z	Size X	Size Y	Size Z
-3.8811	-2.3229	-4.524	23.21	32.9	25.624

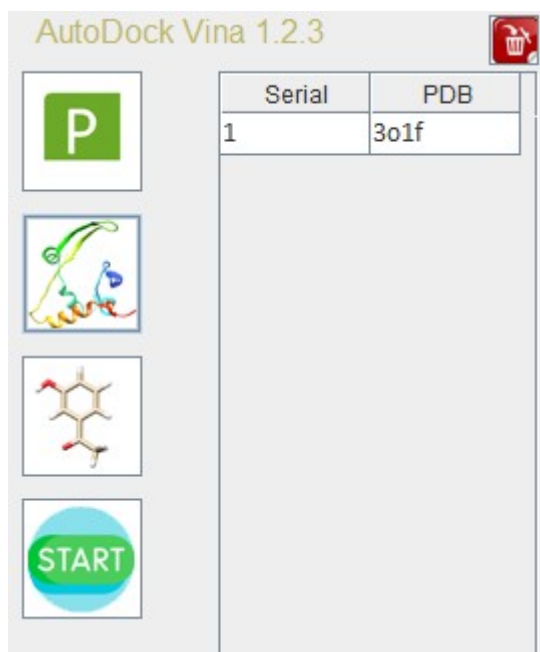
☐ Rigid Receptor Docking ☒ Flexible Receptor Docking

A ▼ TRP ▼ 37 Add

3o1f, A, TRP, 28; 3o1f, A, TRP, 37

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

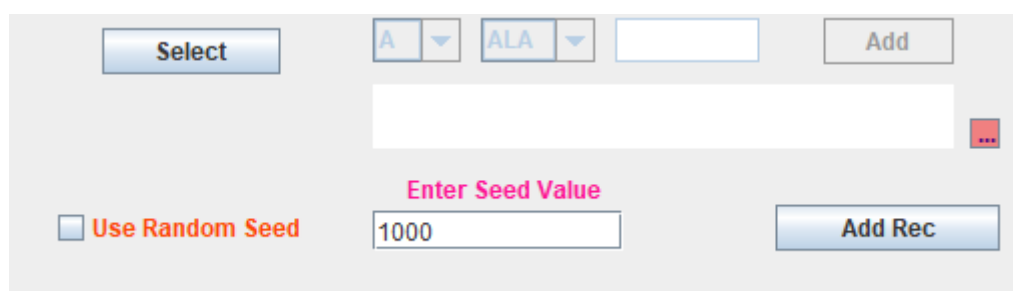
5. If you want to add another receptor you can select the pdb or browse the and repeat the steps.
6. Click the **Finish** button.



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

Set Random Seed manually:

In current version you can set the random seed value manually for reproducible results.



Ligand Selection and Fragmented or Multi-ligand Docking

Ligand selection:

Click on the ligand button on main 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.

MultiDock - Select Ligands for Docking

Search By ☐ Select All

Serial	Date	Name	Source	MolWt
1	23/12/2022	Catechin	Tridax Flav	290.268
2	23/12/2022	Gallocatechin	Tridax Flav	306.267
3	23/12/2022	Genistein	Tridax Flav	270.237
4	23/12/2022	Daidzein	Tridax Flav	254.237
5	23/12/2022	Apigenin	Tridax Flav	270.237
6	23/12/2022	Butein	Tridax Flav	272.253
7	23/12/2022	Naringenin	Tridax Flav	272.253
8	23/12/2022	Biochanin	Tridax Flav	284.263
9	23/12/2022	Luteolin	Tridax Flav	286.236
10	23/12/2022	Kaempferol	Tridax Flav	286.236
11	23/12/2022	Epicatechin	Tridax Flav	290.268

☐ Fragmented ligand docking (Max = 5) ☐ Combinations (Max = 10)

Main Frag. Any Group of 2

Add **Finish**

Note: Repeated selection of same ligand will be removed automatically

Search By

Search By

Date

Name

Source

MolWt <=

MolWt >=

MolWt <= 50 ☐ Select All

Serial	Date	Name	Source	MolWt
331	23/12/2022	CHEMBL116336	EMBL-Frag	26.0373
182	23/12/2022	CHEMBL183419	EMBL-Frag	27.0253
352	24/12/2022	CHEMBL2227836	EMBL-Frag	33.9976
65	23/12/2022	CHEMBL116902	EMBL-Frag	40.0639
80	23/12/2022	CHEMBL324784	EMBL-Frag	45.0406

0%

Serial	Name
331	CHEMBL116336
182	CHEMBL183419
352	CHEMBL2227836

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.

Serial	Date	Name	Source	MolWt
331	23/12/2022	CHEMBL116336	EMBL-Frag	26.0373
182	23/12/2022	CHEMBL183419	EMBL-Frag	27.0253
352	24/12/2022	CHEMBL2227836	EMBL-Frag	33.9976
65	23/12/2022	CHEMBL116902	EMBL-Frag	40.0639
80	23/12/2022	CHEMBL324784	EMBL-Frag	45.0406

☒ Fragmented ligand docking (Max = 5) ☐ Combinations (Max = 10)

Main Frag. Any ▼ Group of 2 ▼

0%	
Serial	
331,182,352	CHEMBL116336,CHEMBL183419,CHEMBL2227836

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.

Serial	Date	Name	Source	MolWt
331	23/12/2022	CHEMBL116336	EMBL-Frag	26.0373
182	23/12/2022	CHEMBL183419	EMBL-Frag	27.0253
352	24/12/2022	CHEMBL2227836	EMBL-Frag	33.9976
65	23/12/2022	CHEMBL116902	EMBL-Frag	40.0639
80	23/12/2022	CHEMBL324784	EMBL-Frag	45.0406

☐ Fragmented ligand docking (Max = 5) ☒ Combinations (Max = 10)

Main Frag. Any Group of 2 Total = 10

Serial	Date	Name	Source	MolWt
331	23/12/2022	CHEMBL116336	EMBL-Frag	26.0373
182	23/12/2022	CHEMBL183419	EMBL-Frag	27.0253
352	24/12/2022	CHEMBL2227836	EMBL-Frag	33.9976
65	23/12/2022	CHEMBL116902	EMBL-Frag	40.0639
80	23/12/2022	CHEMBL324784	EMBL-Frag	45.0406

☐ Fragmented ligand docking (Max = 5) ☒ Combinations (Max = 10)

Main Frag. Any Group of 4 Total = 5

	0%
Serial	Name
65,80	CHEMBL116902,CHEMBL324784
352,80	CHEMBL2227836,CHEMBL324784
352,65	CHEMBL2227836,CHEMBL116902
182,80	CHEMBL183419,CHEMBL324784
182,65	CHEMBL183419,CHEMBL116902
182,352	CHEMBL183419,CHEMBL2227836
331,80	CHEMBL116336,CHEMBL324784
331,65	CHEMBL116336,CHEMBL116902
331,352	CHEMBL116336,CHEMBL2227836
331,182	CHEMBL116336,CHEMBL183419

10 combinations when 2 at once from 5

	0%
Serial	Name
182,352,65,80	CHEMBL183419,CHEMBL2227836,CHEMBL116902,CHEMBL324784
331,352,65,80	CHEMBL116336,CHEMBL2227836,CHEMBL116902,CHEMBL324784
331,182,65,80	CHEMBL116336,CHEMBL183419,CHEMBL116902,CHEMBL324784
331,182,352,80	CHEMBL116336,CHEMBL183419,CHEMBL2227836,CHEMBL324784
331,182,352,65	CHEMBL116336,CHEMBL183419,CHEMBL2227836,CHEMBL116902

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.

Serial	Date	Name	Source	MolWt
331	23/12/2022	CHEMBL116336	EMBL-Frag	26.0373
182	23/12/2022	CHEMBL183419	EMBL-Frag	27.0253
352	24/12/2022	CHEMBL2227836	EMBL-Frag	33.9976
65	23/12/2022	CHEMBL116902	EMBL-Frag	40.0639
80	23/12/2022	CHEMBL324784	EMBL-Frag	45.0406

☐ Fragmented ligand docking (Max = 5)
 ☒ Combinations (Max = 10)

Main Frag. 80
 Group of 2
 Total = 4

0%

Serial	Name
65,80	CHEMBL116902,CHEMBL116902
352,80	CHEMBL2227836,CHEMBL2227836
182,80	CHEMBL183419,CHEMBL183419
331,80	CHEMBL116336,CHEMBL116336

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

In recent update there is another option to make combination of same ligand molecule. If the number of ligands is 2 there will be a pair of same ligand molecule.

☐ Fragmented ligand docking (Max = 5)
 ☒ Combinations (Max = 100)

Main Frag. Any
☐ Twin
 Group of 2
 Total = 3

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.

MultiDock Screening Tool 2.0.0

File Manage Results Settings

AutoDock Vina 1.2.3

☐ Shut down

Serial	PDB
1	3o1f

Serial	Name
65	CHEMBL116902
80	CHEMBL324784
65,80	CHEMBL116902,CHEMBL324784

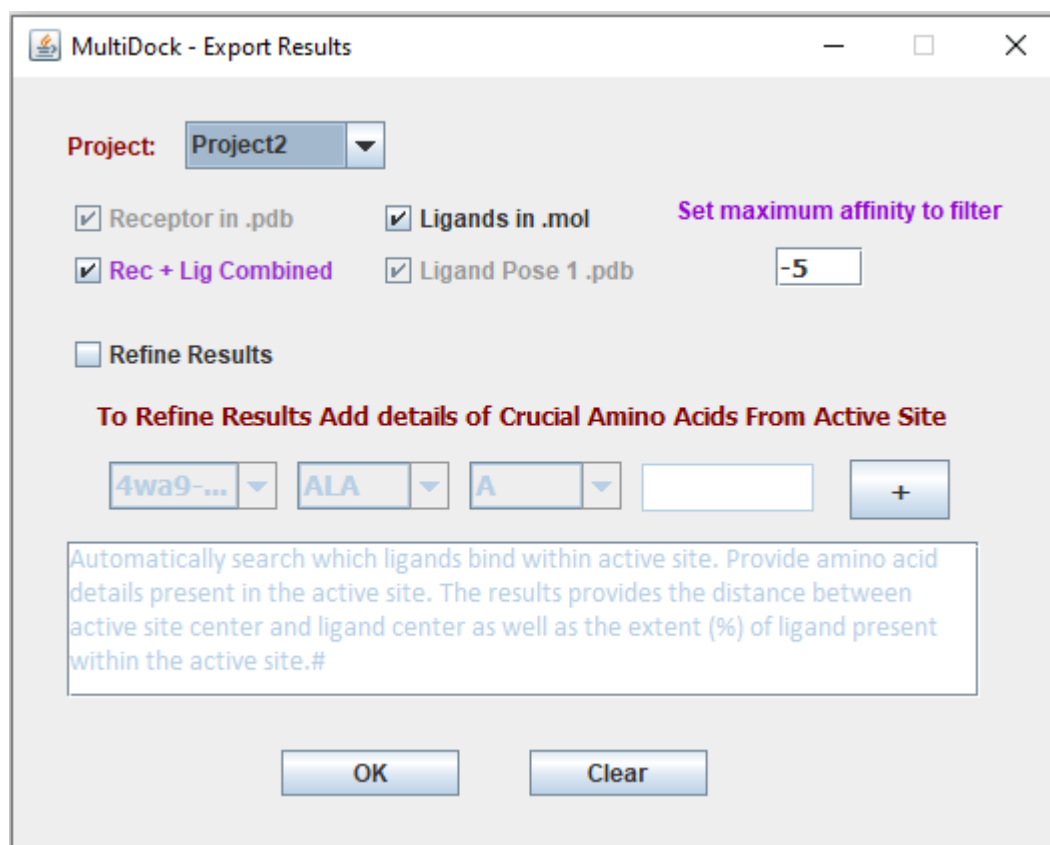
Receptor	Ligand	kcal/mol
----------	--------	----------

Project Name: ABCD Date: 24/12/2022 Status = Running..

Converting sdf to pdbqt..

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.

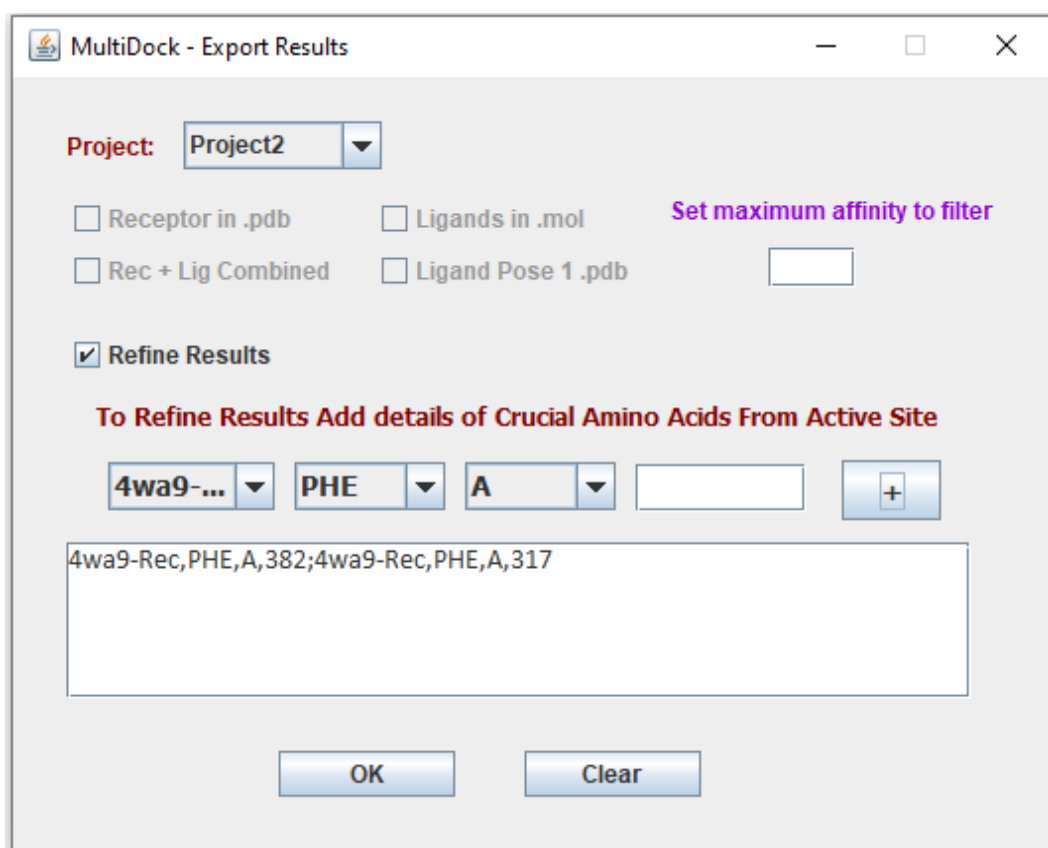
Refine the Blind Docking Results

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), K_i and the percentage of ligand inside the active site will be given. We can easily sort the ligands for further analysis.



MultiDock - Export Results

Project: Project2

☐ Receptor in .pdb ☐ Ligands in .mol **Set maximum affinity to filter**

☐ Rec + Lig Combined ☐ Ligand Pose 1 .pdb

☒ **Refine Results**

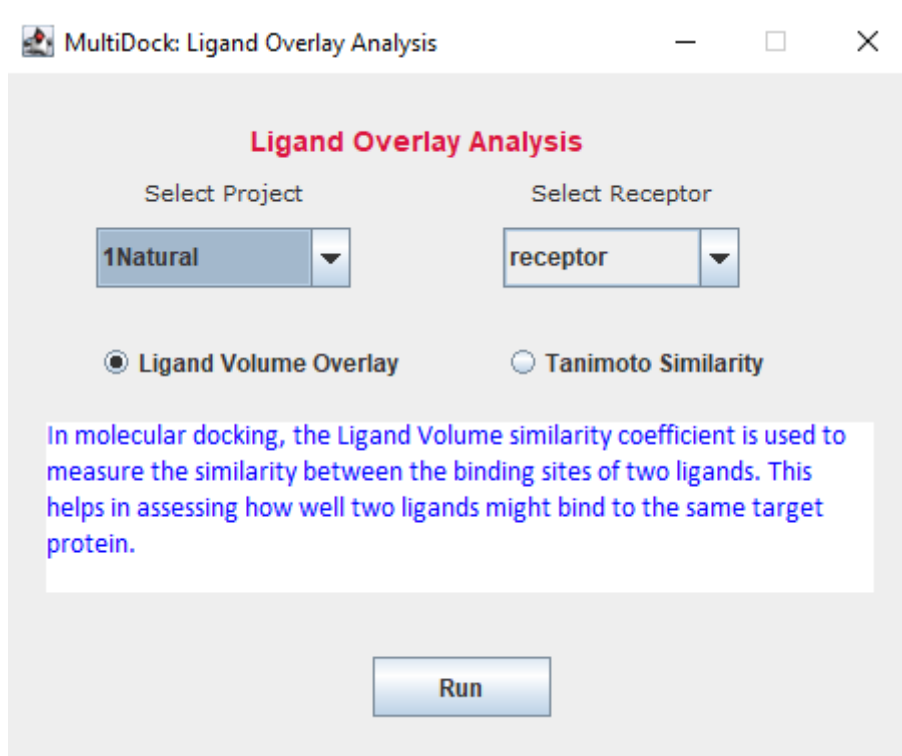
To Refine Results Add details of Crucial Amino Acids From Active Site

4wa9-... PHE A

4wa9-Rec,PHE,A,382;4wa9-Rec,PHE,A,317

Ligand Overlay Analysis

Tanimoto Ligand Overlay Analysis is a computational method used to assess the structural similarity between two or more molecular structures. The Tanimoto coefficient, a widely used metric in cheminformatics, quantifies the degree of overlap between molecular features such as functional groups, atomic positions, or pharmacophores.



Select the project, receptor and method of overlay analysis. Click on Run button. The analysis will be saved in export path folder.

There are two options in MultiDock to analyze the ligand overlay.

1. The simple ligand volume overlay to determine the similarity of positional volumes occupied by two ligands.
2. Tanimoto Similarity: More accurately determines and compare the atom overlays of two ligands.

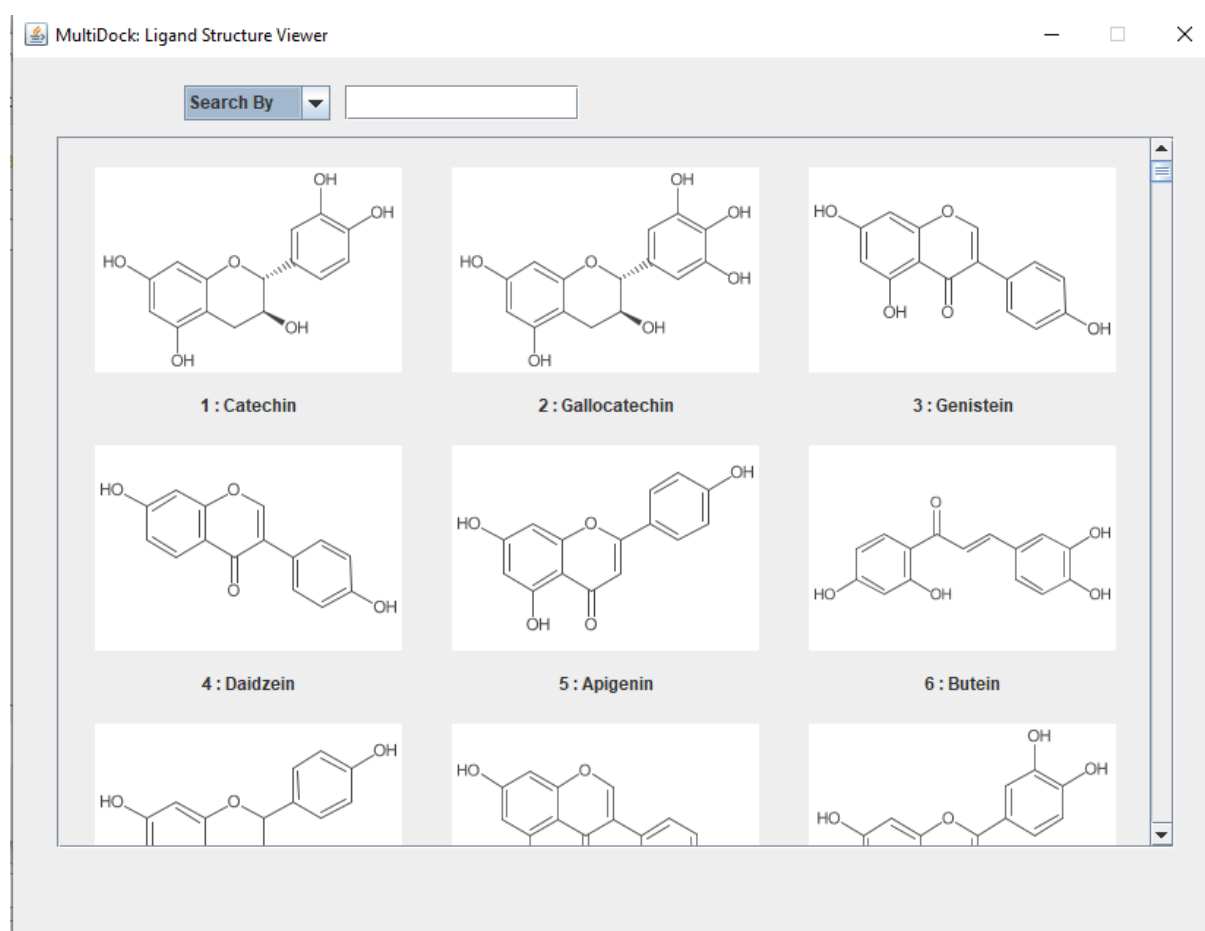
Ligand overlay result analysis:

The ligand overlay analysis shows coefficient and the values are between 0 and 1. More the coefficient more is the similarity between two ligand position. 0 indicate no overlay whereas 1 indicates 100% overlay.

	A	B	C	D	E	F	G	H
1	Overlay	Lig1	Coumestrol	Daidzein	Diosmetin	Diosmin	Galangin	Glabridin
2	Lig1	1	0.4286	0.3	0.1944	0.2321	0.4643	0.2941
3	Coumestrol	0.4286	1	0.3438	0.119	0.3036	0.5517	0.3333
4	Daidzein	0.3	0.3438	1	0.2432	0.2	0.4194	0.4242
5	Diosmetin	0.1944	0.119	0.2432	1	0.2881	0.1429	0.3421
6	Diosmin	0.2321	0.3036	0.2	0.2881	1	0.2542	0.2833
7	Galangin	0.4643	0.5517	0.4194	0.1429	0.2542	1	0.2895
8	Glabridin	0.2941	0.3333	0.4242	0.3421	0.2833	0.2895	1

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 database of multidock projects.

2. **Devlop:**

Contains all python files required for processing the files.

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:**

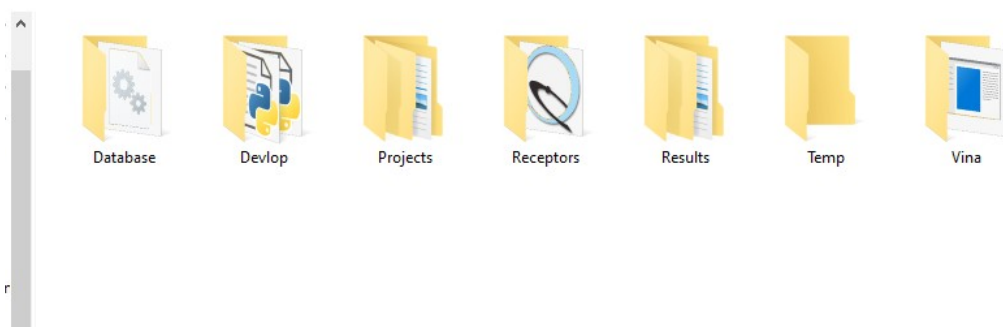
Contains all the project folders and in each folder there are files related to the results of the project.

6. **Temp:**

Contains all temporary files during project runs.

7. **Vina:**

It is not mandatory but you can keep the AutoDock Vina 1.2.5 .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.