KinomeRun – Integrative kinome screening and comparative interaction fingerprint analysis Pipeline

Operating Manual

by

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PREREQUISITES TO RUN KinomeRun:

KinomeRun GUI run in python3

Linux Operating system 64 bit with bash shell

GNU parallel (/usr/local/bin)
Link to download and installation of GNU Parallel (http://ftp.gnu.org/gnu/parallel/)

Autodock Vina (http://vina.scripps.edu/download.html**)**

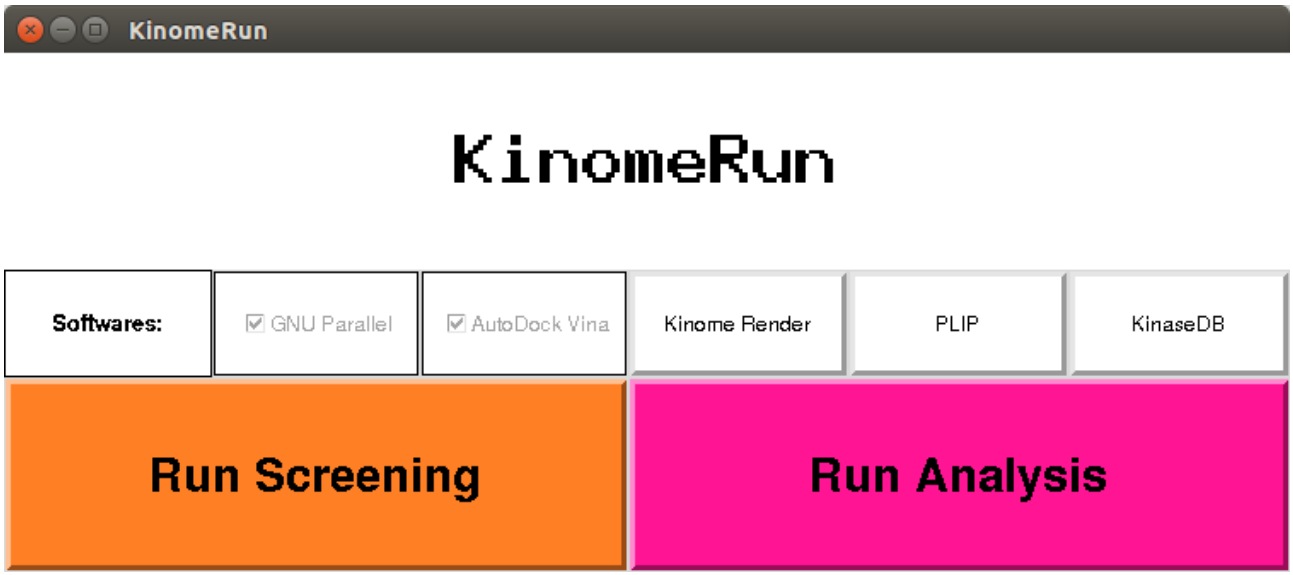
- ✓ vina (/usr/local/bin)
- ✓ vina_split (/usr/local/bin)

Protein-Ligand Interaction Profiler (PLIP) (https://github.com/ssalentin/plip**)**
KinomeRender (http://biophys.umontreal.ca/nrg/resources.html**)**
Kinome Dataset (https://drive.google.com/file/d/18iR8jMFPw9XzM2DtLff7rFmigfSVyRzh/view**)**

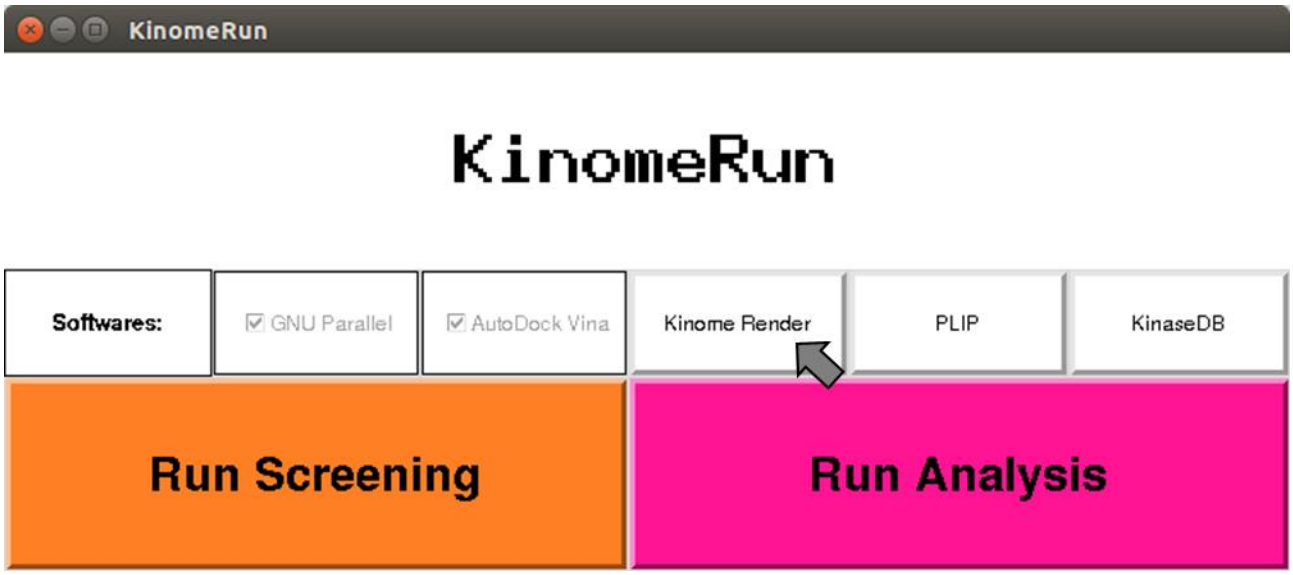
Video Tutorial available at:
https://www.youtube.com/playlist?list=PLuIaEFtMVgQ7v__WigQH9ilGVxrfI1LKs

Software configuration:

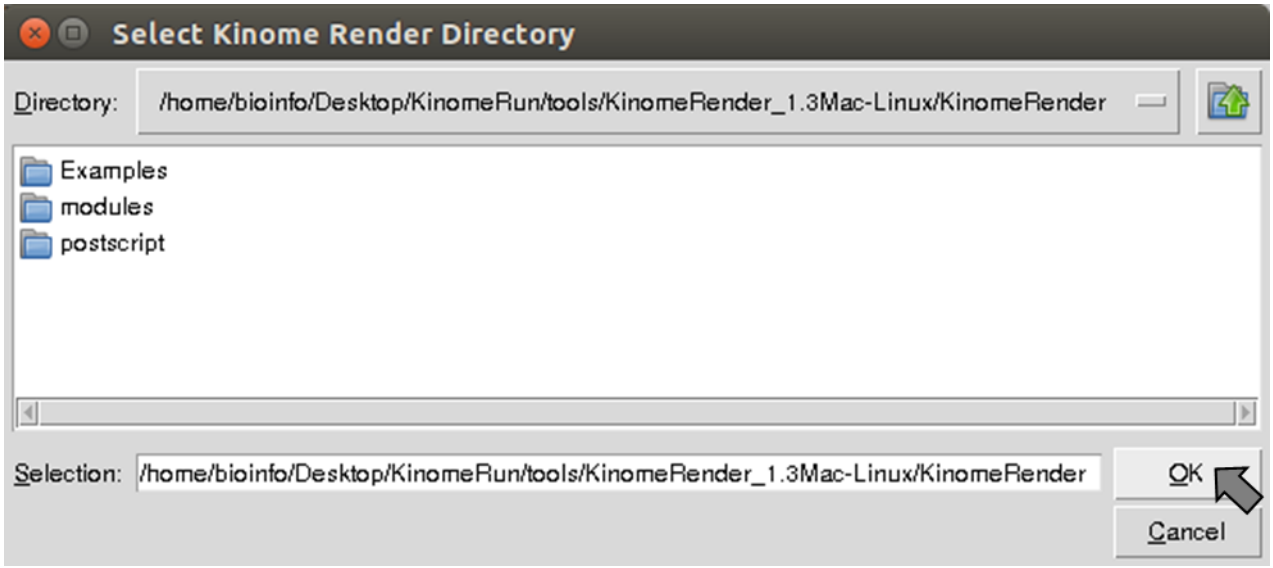
1. On execution of KinomeRun, The list of software's configured properly will appear along with a as tick in the checkbox. If you want to configure the tools. For example: PLIP



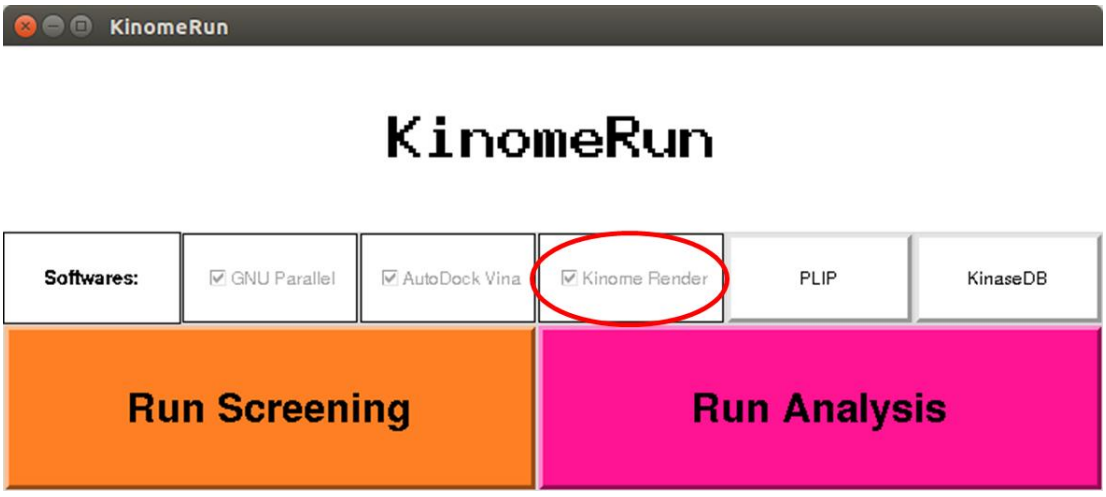
2. Click the KinomeRender button



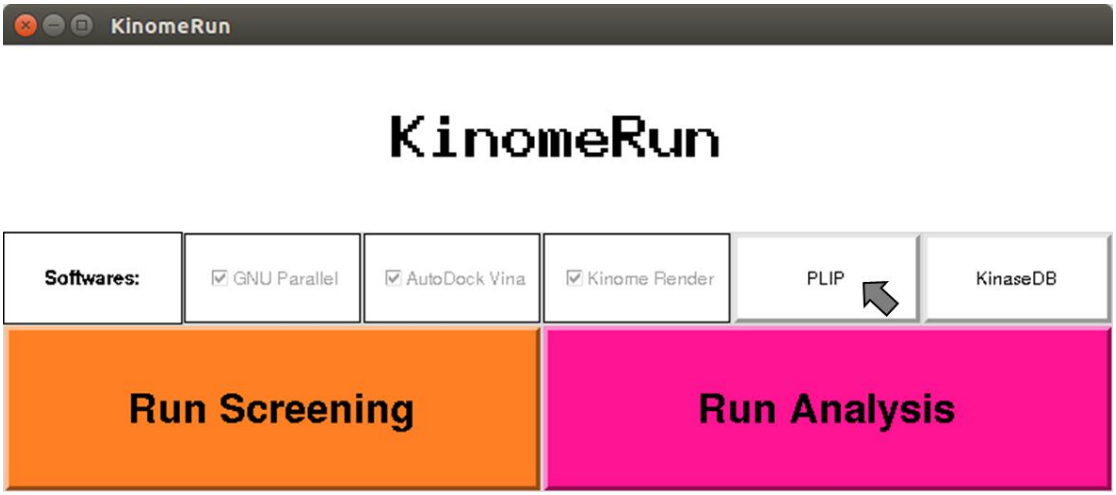
3. Change to the respective directory of where KinomeRender executable was extracted and just click ok.

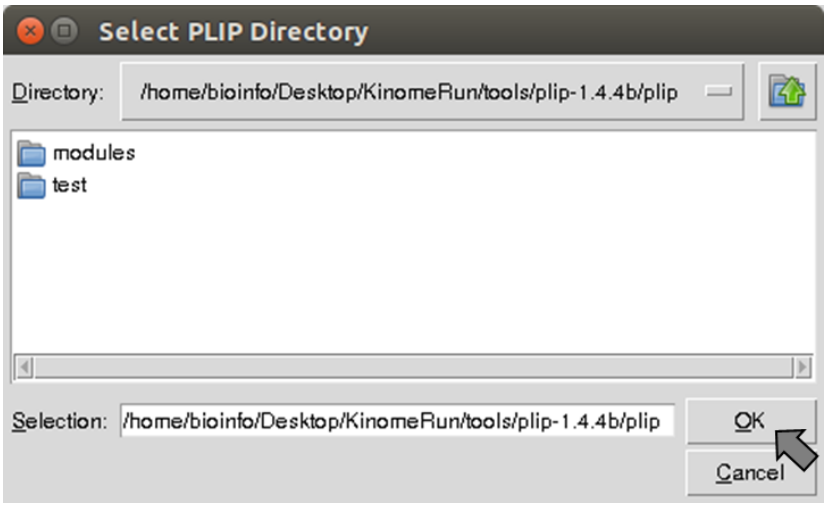


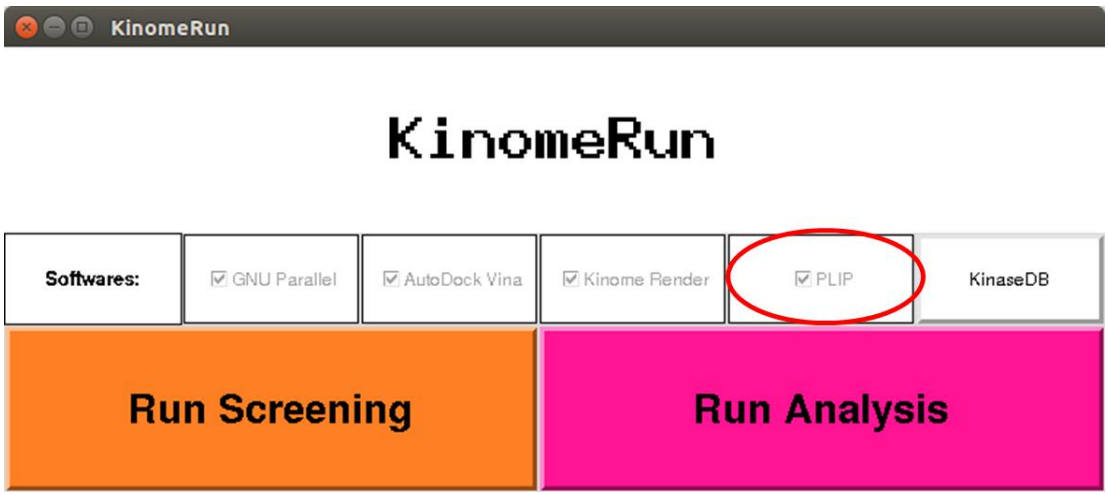
4. If the correct path is provided, the button will be changed to checkbox with a tick mark.

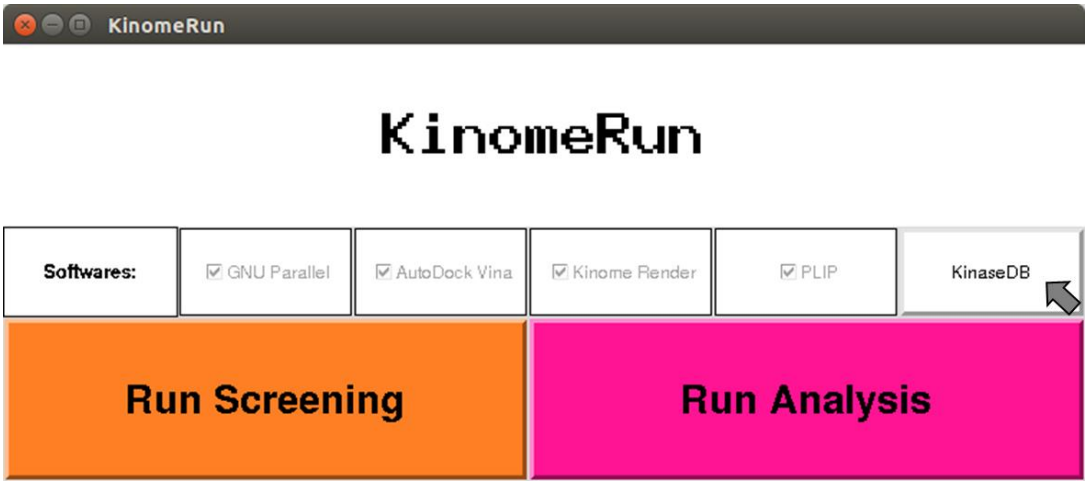


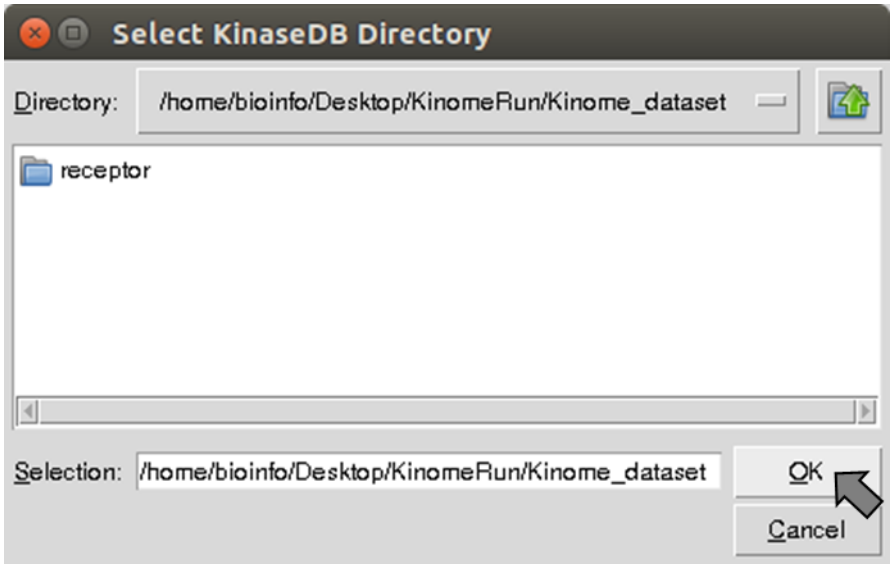
5. Same procedure can be followed for configuring other tools also. Ex: PLIP, KinaseDB.

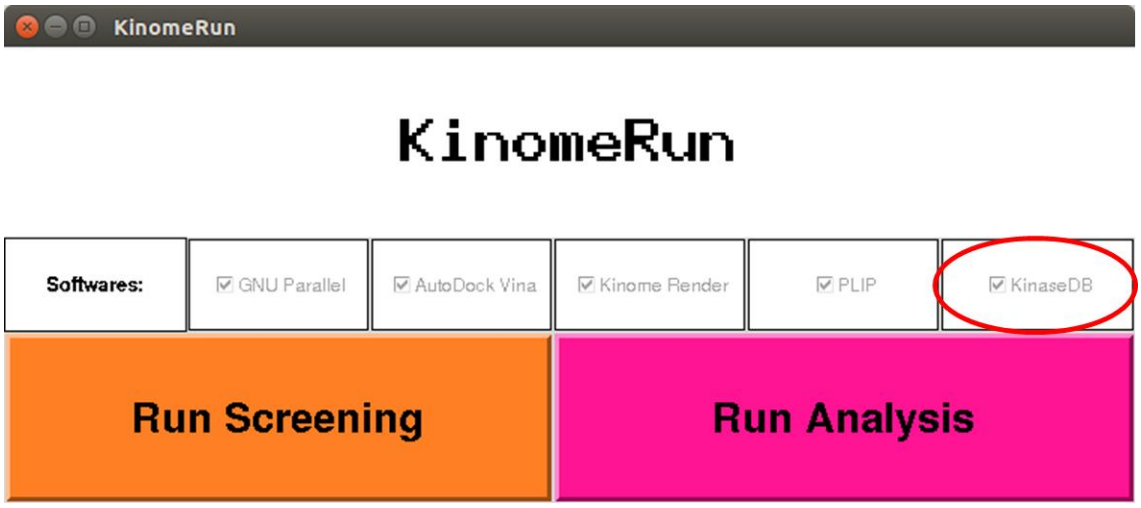




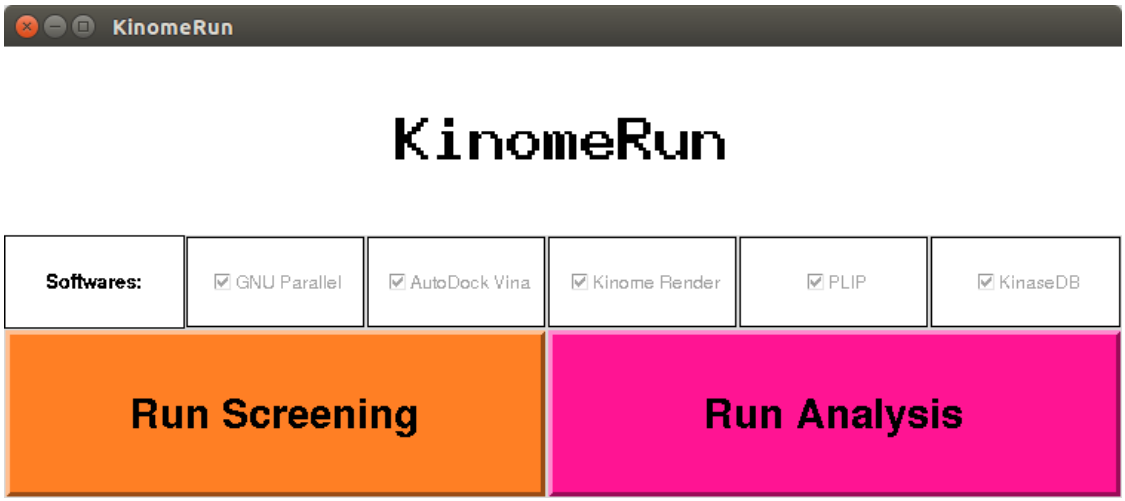



KinomeRun
KinomeRun
Softwares:
GNU Parallel
AutoDock Vina
Kinome Render
PLIP
KinaseDB
Run Screening
Run Analysis


Select KinaseDB Directory
Directory:
/home/bioinfo/Desktop/KinomeRun/Kinome_dataset
receptor
Selection:
/home/bioinfo/Desktop/KinomeRun/Kinome_dataset
OK
Cancel


KinomeRun
KinomeRun
Softwares:
GNU Parallel
AutoDock Vina
Kinome Render
PLIP
KinaseDB
Run Screening
Run Analysis

6. config.ini file will be created in the current directory which contains all the path information for the tools which will be used when starting the script next onwards without need of configuring each and every time and you can check the check box ticked for confirmation also.



config.ini

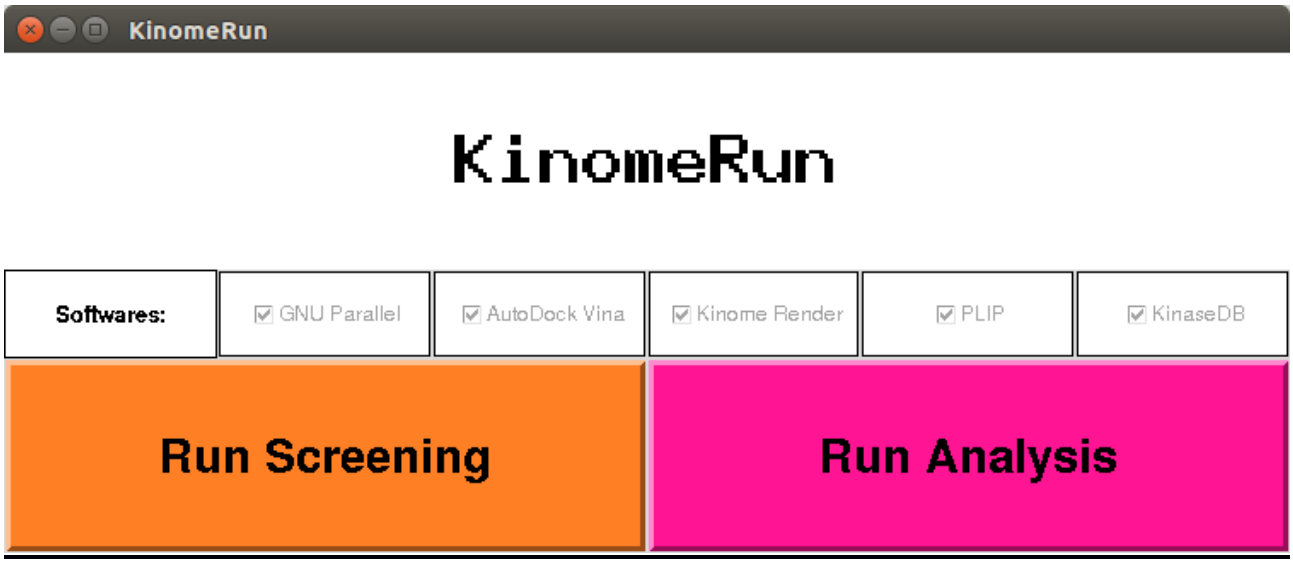
KinomeRun-v1.0.py × config.ini ×

```
1 [softwares]
2 KINOMERENDER = /home/bioinfo/Desktop/KinomeRun/tools/KinomeRender_1.3Mac-Linux/KinomeRender
3 PLIP = /home/bioinfo/Desktop/KinomeRun/tools/plip-1.4.4b/plip
4 KINASE_DB = /home/bioinfo/Desktop/KinomeRun/Kinome_dataset
```

OPERATING INSTRUCTIONS:

Kinome Screening:

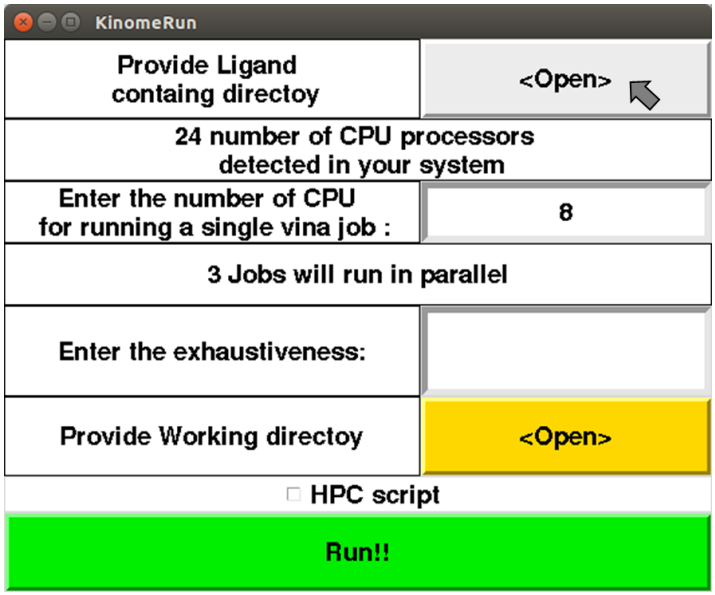
1. After ensuring the proper installation of software, Run the python script KinomeRun-v1.0.py in the terminal

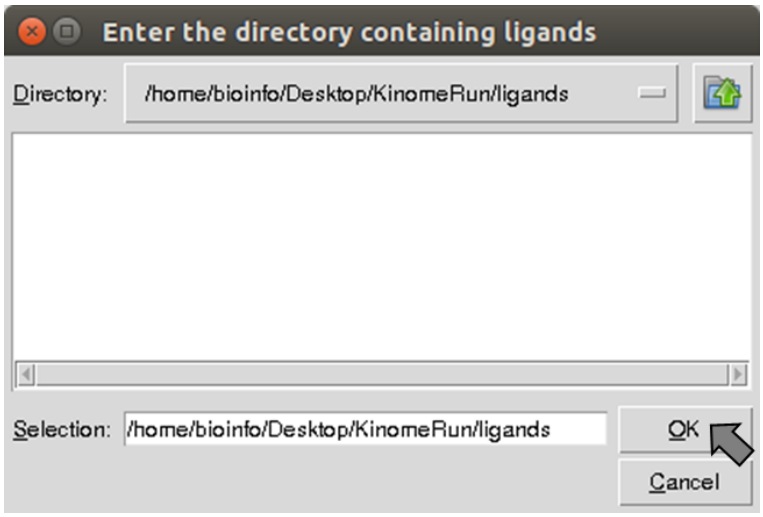


2. Select the Run Screening button

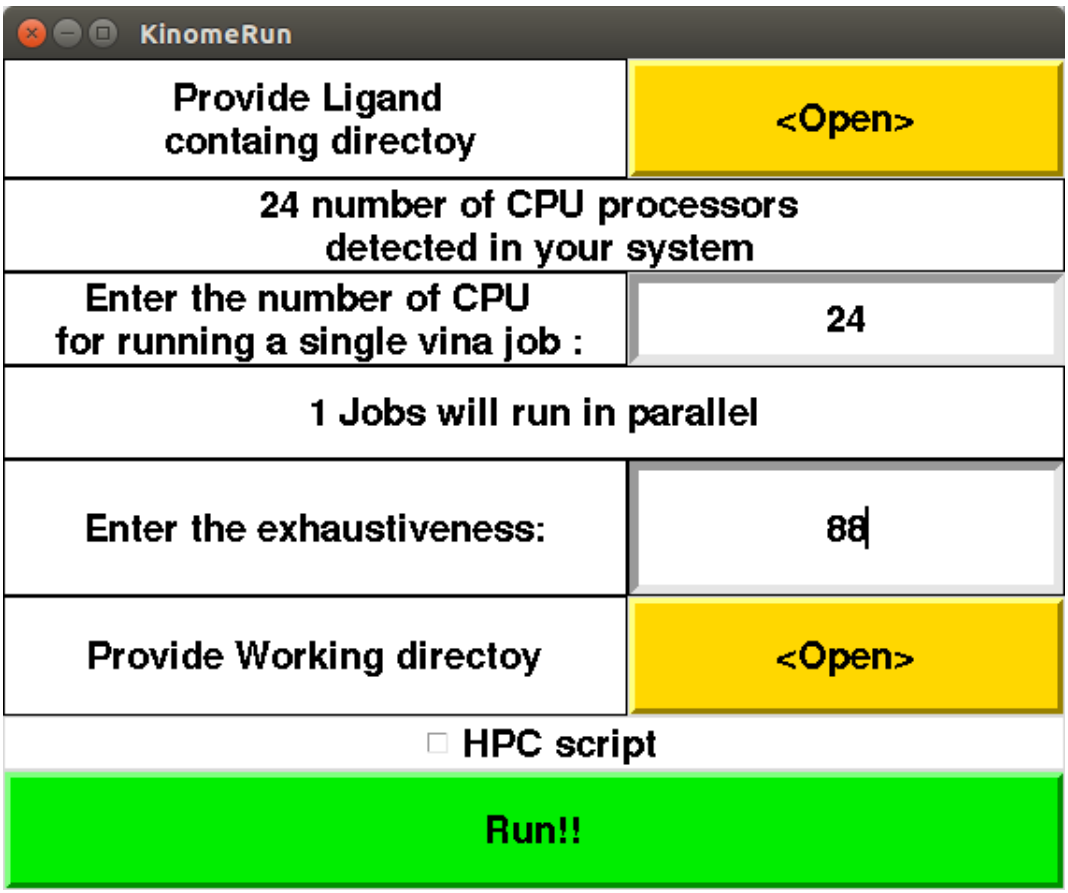
3. Pop-Up window will prompt from getting input for the kinome screening.

4. Select the open button to provide directory containing ligands to be screened in .pdbqt format.

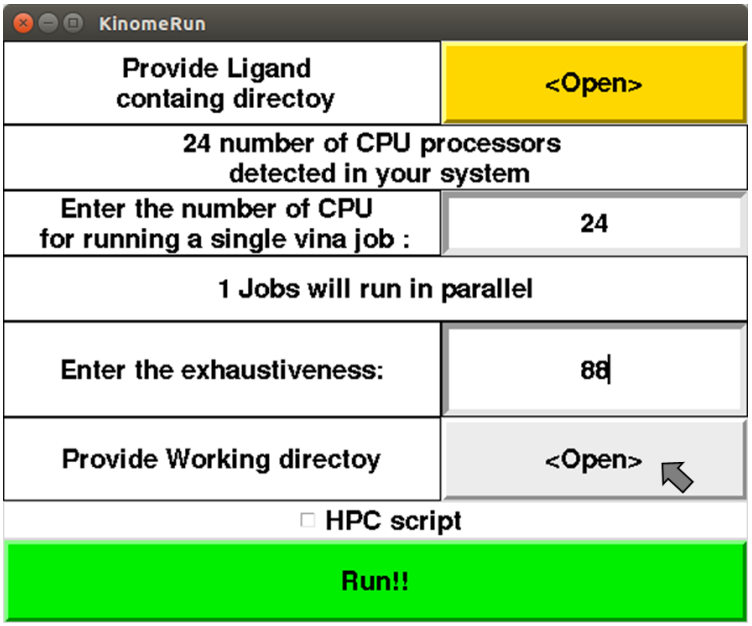




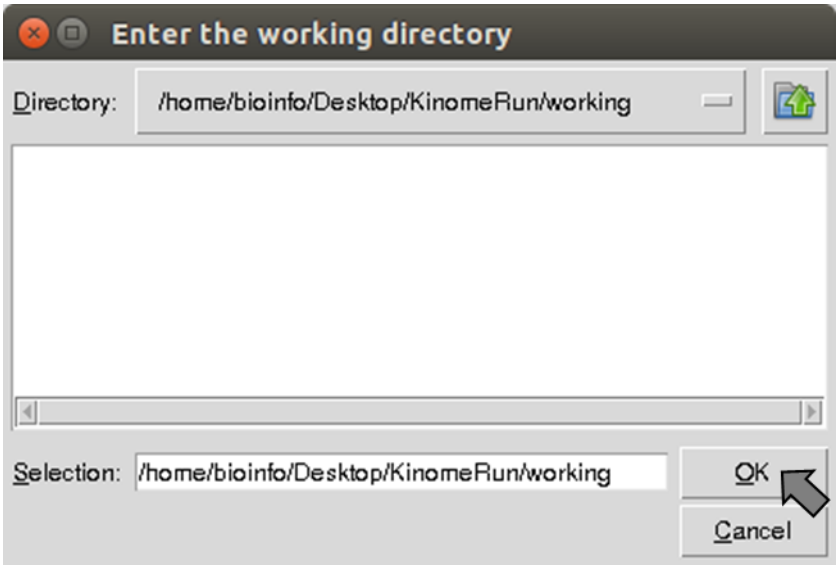
5. Enter the number of CPU's to be taken for running single vina job and exhaustiveness value.



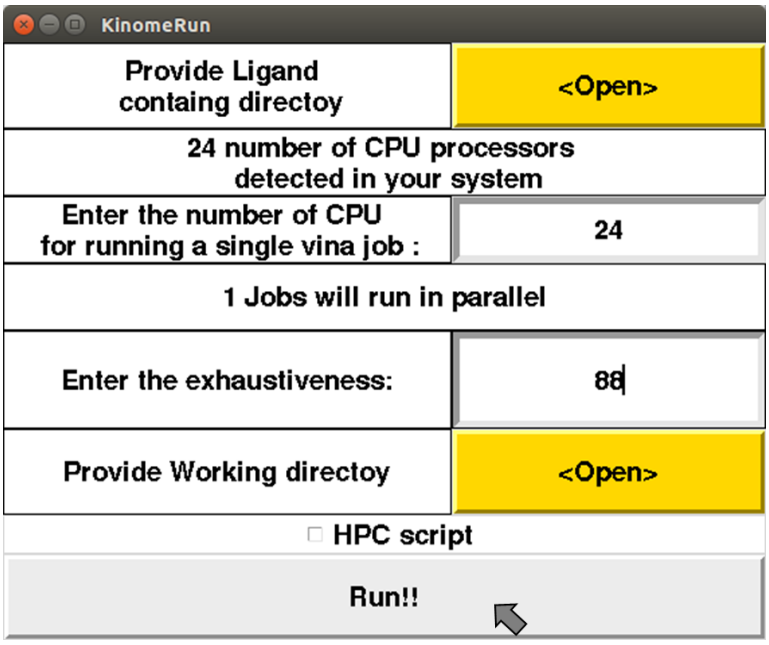
6. Provide the path to working directory



KinomeRun



7. After providing all the inputs click Run!! Button.



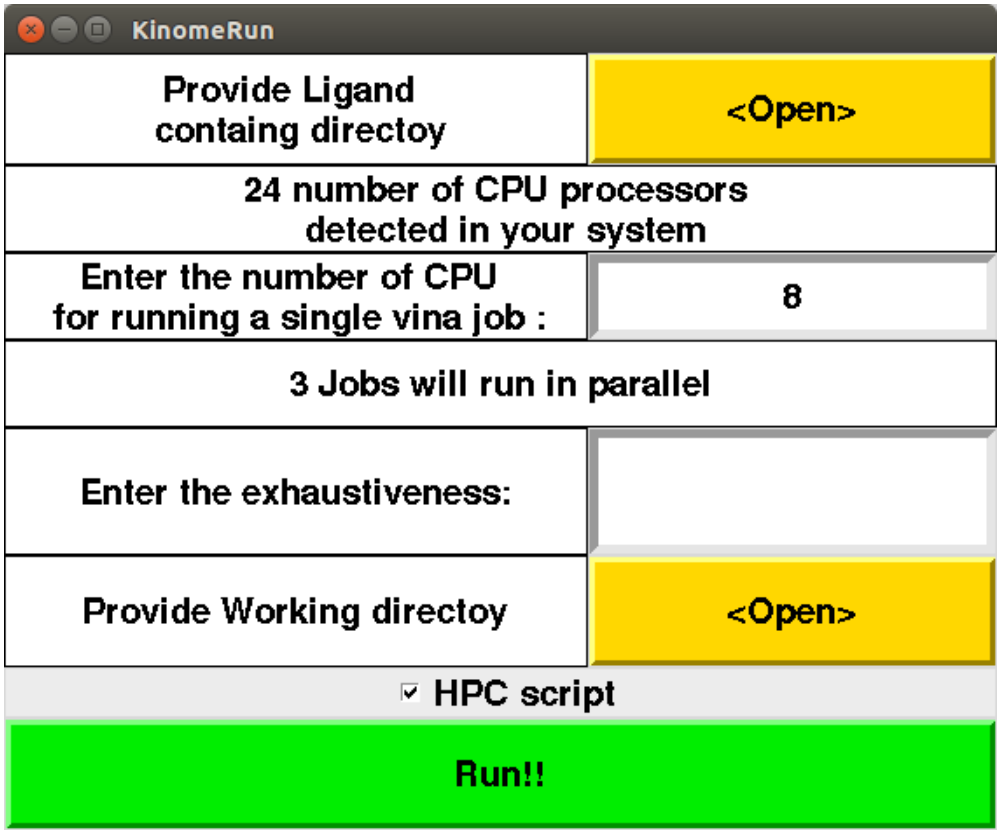
8. The KinomeRun.bash script will be generated in the working directory based on the input provided. The bash script can be run in the terminal by typing bash KinomeRun.bash from the working directory which will perform functions of the provided input and the results will be stored in the working directory.

9. After the kinome screening finishes there will the master file available in the working/ligand_name_dir/Results/ligand_name.txt. This file is the master file which contains the target structure name with pose information, docking energy, total number of interaction, residue number, pocket number and followed by types of interaction presence or absence. This file needed to be provided as input for customized filteration.

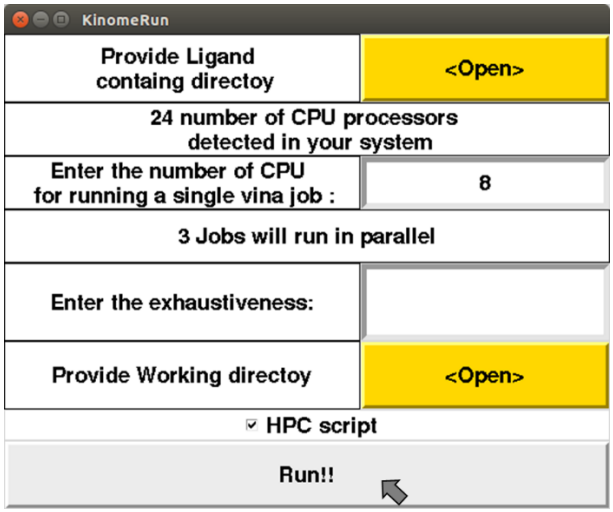
For running KinomeRun in HPC remote servers:

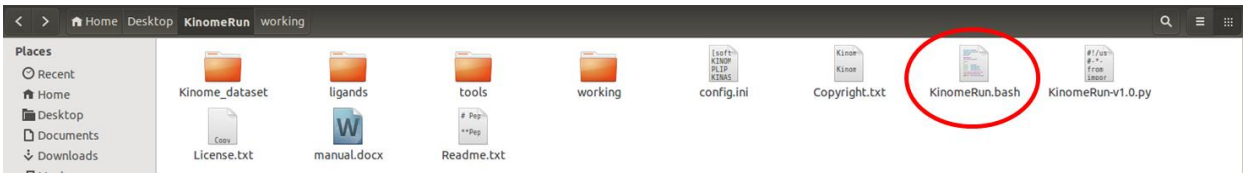
1. If you want to run the KinomeRun in HPC. Click Run screening button.

2. Click the HPC check box below near the Run button. Don't provide any other information.



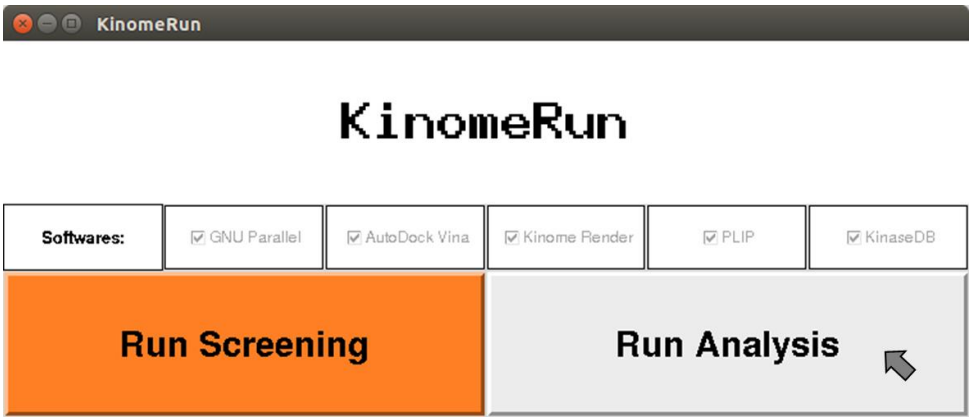
3. Hit Run!! Button. This will generate KinomeRun.bash script in the directory where the KinomeRun-v1.0py is opened. The user needs to manually enter the directory path of LIGAND, WORKING, PLIP, number of jobs to run single vina job, number of jobs to run in parallel, exhaustiveness value etc., and submit the command as follows: bash KinomeRun.bash &>>log.txt



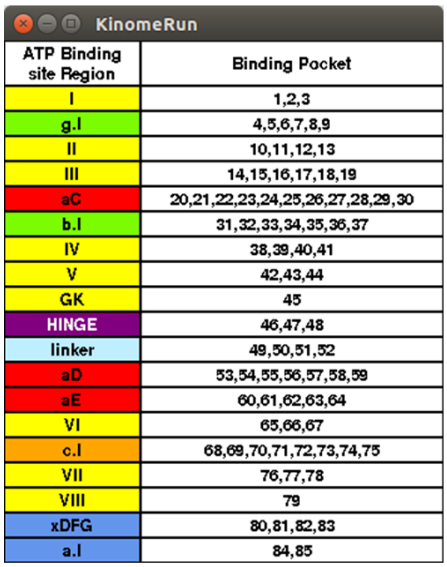


For Customized filteration

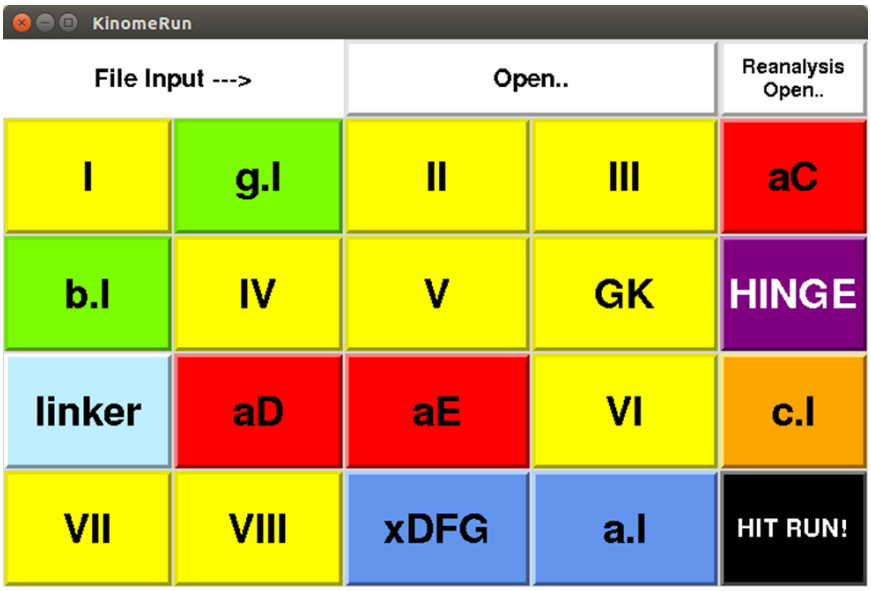
1. For performing the customized filteration click Run analysis button.



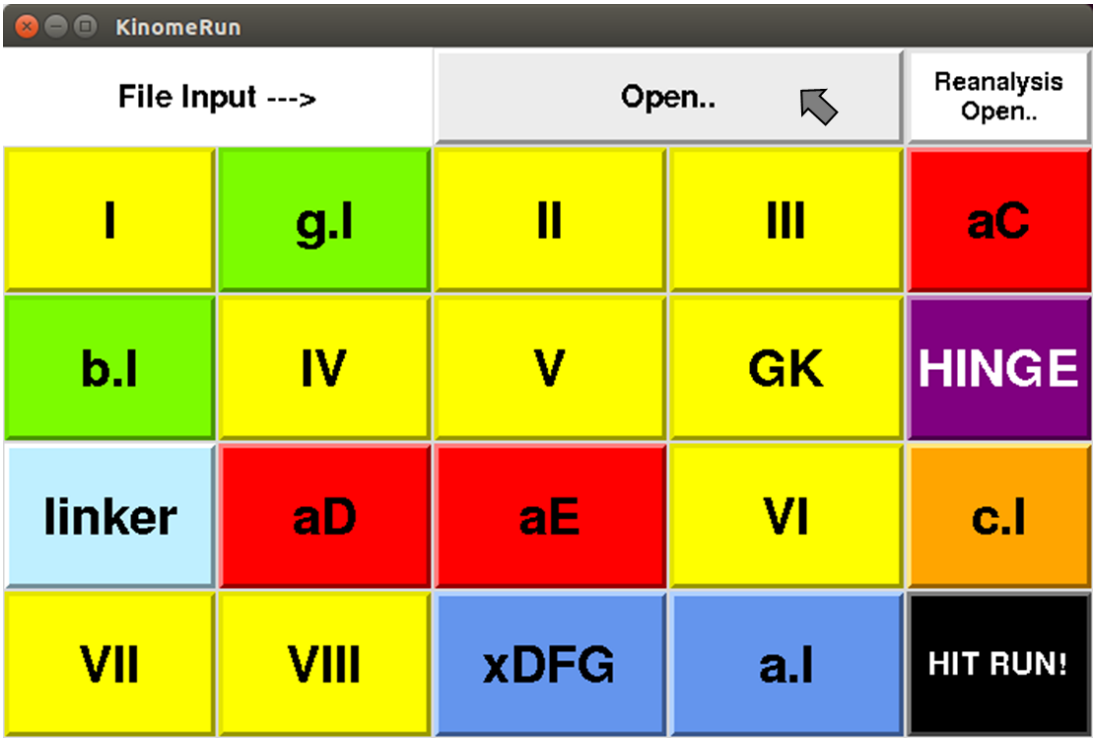
2. Two windows will be pop-up. The smaller window will contain the ATP binding site regions and their binding pocket number for reference. Another window will contain buttons with ATP binding region which need to be used for providing input to the user.

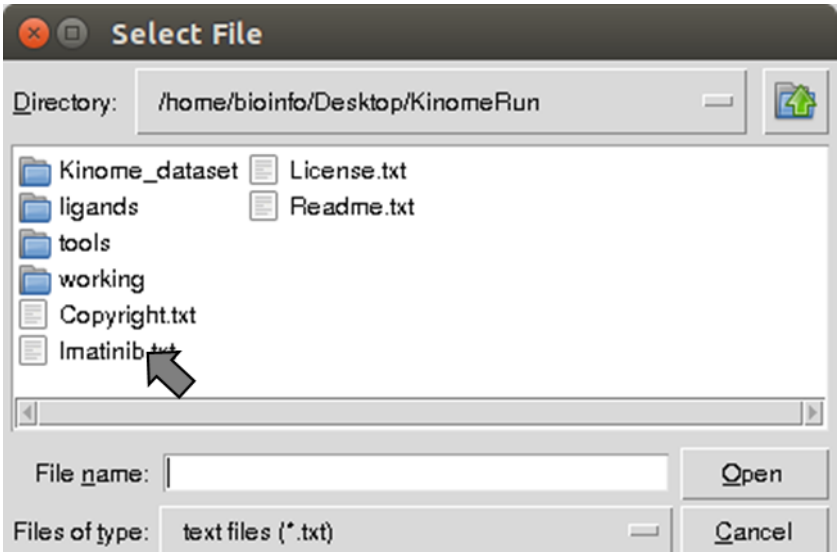


ATP Binding site Region	Binding Pocket
I	1,2,3
g.I	4,5,6,7,8,9
II	10,11,12,13
III	14,15,16,17,18,19
aC	20,21,22,23,24,25,26,27,28,29,30
b.I	31,32,33,34,35,36,37
IV	38,39,40,41
V	42,43,44
GK	45
HINGE	46,47,48
linker	49,50,51,52
aD	53,54,55,56,57,58,59
aE	60,61,62,63,64
VI	65,66,67
c.I	68,69,70,71,72,73,74,75
VII	76,77,78
VIII	79
xDFG	80,81,82,83
a.I	84,85

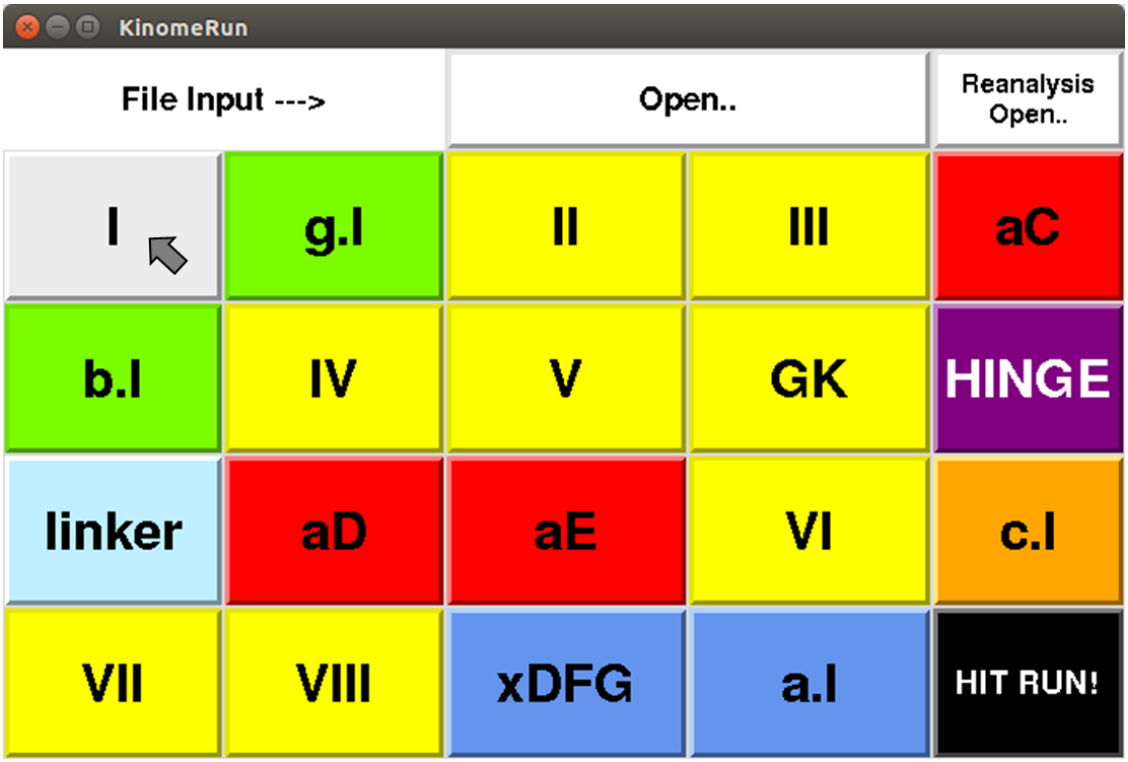


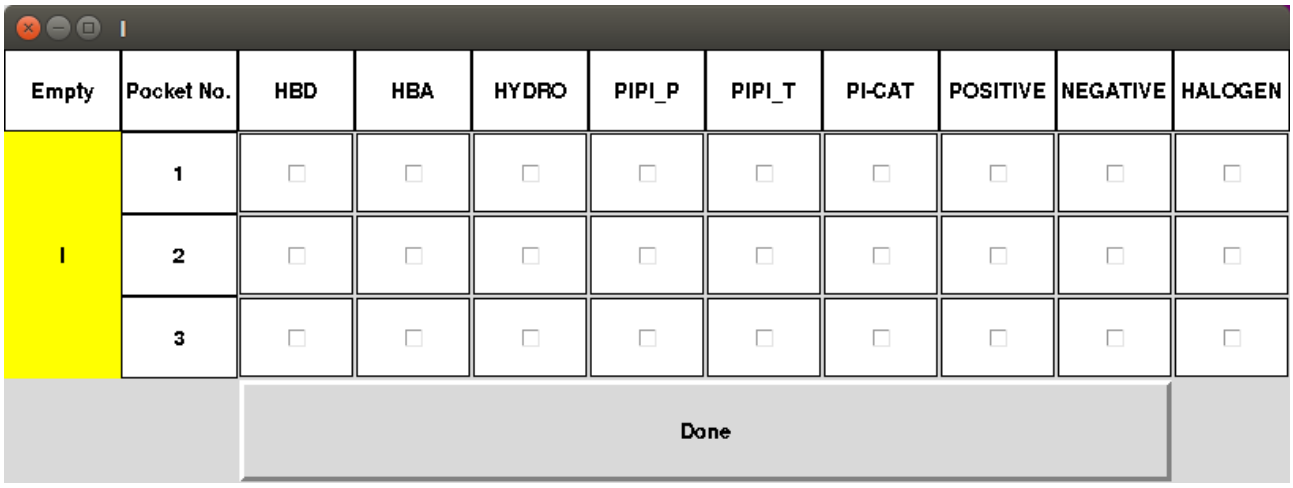
3. Click Open button and provide the master file obtained from KinomeRun screening.



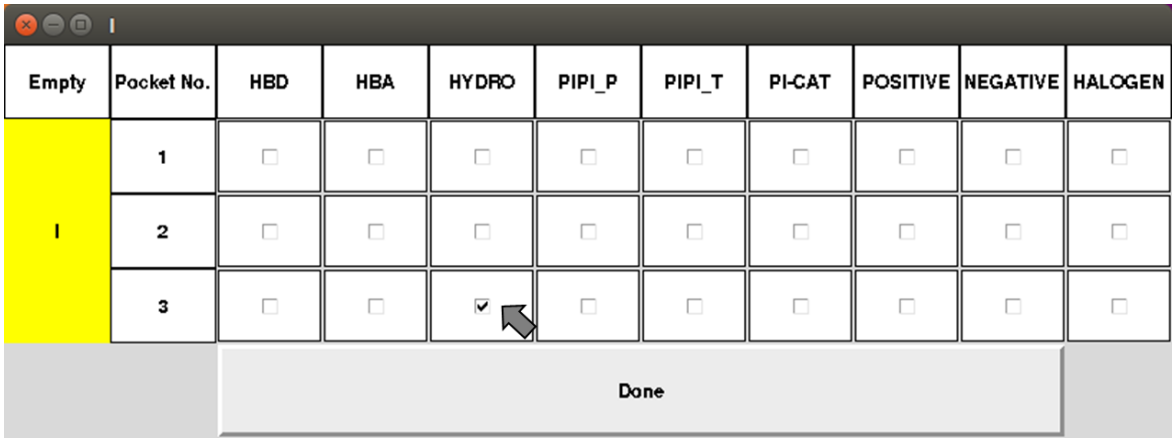


4. The filteration criteria need to be provided. For selecting the hydrophobic interaction at pocket number 3. Select the I button. Which will pop-up new window with binding pocket residue number and the checkbox of interaction types inputs.

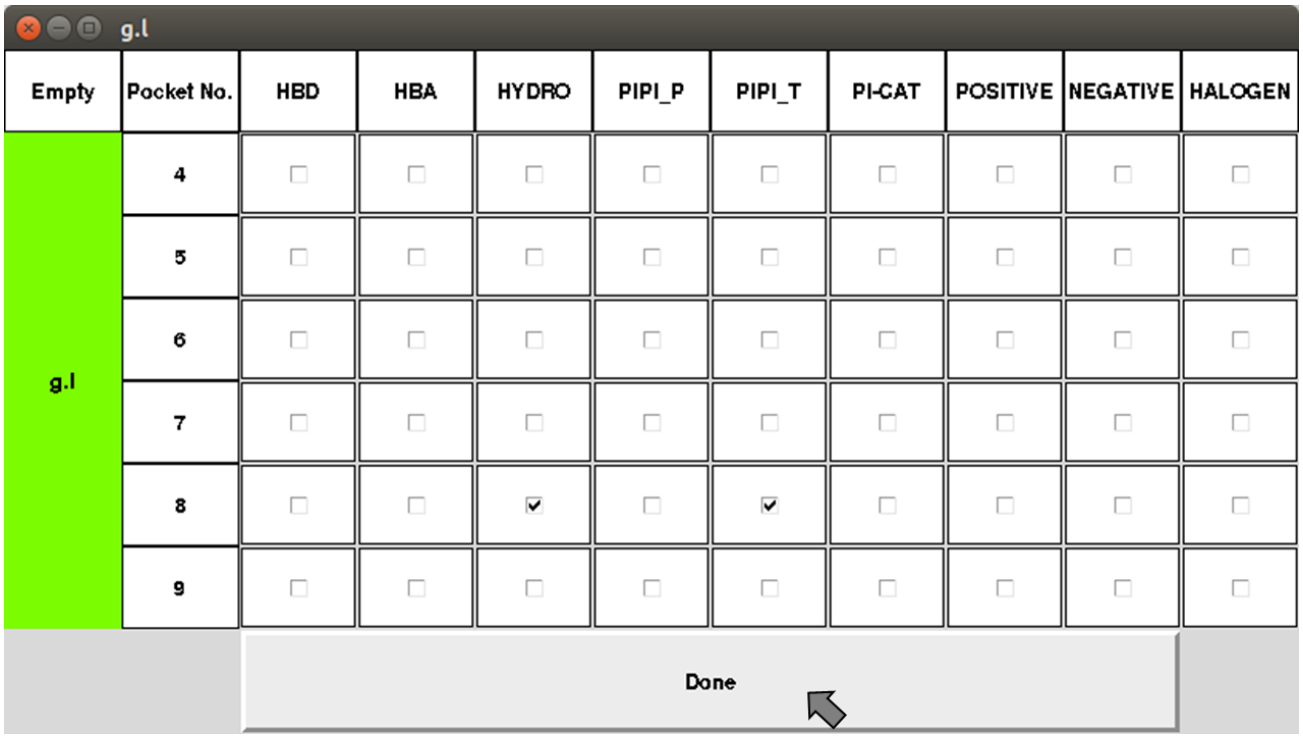


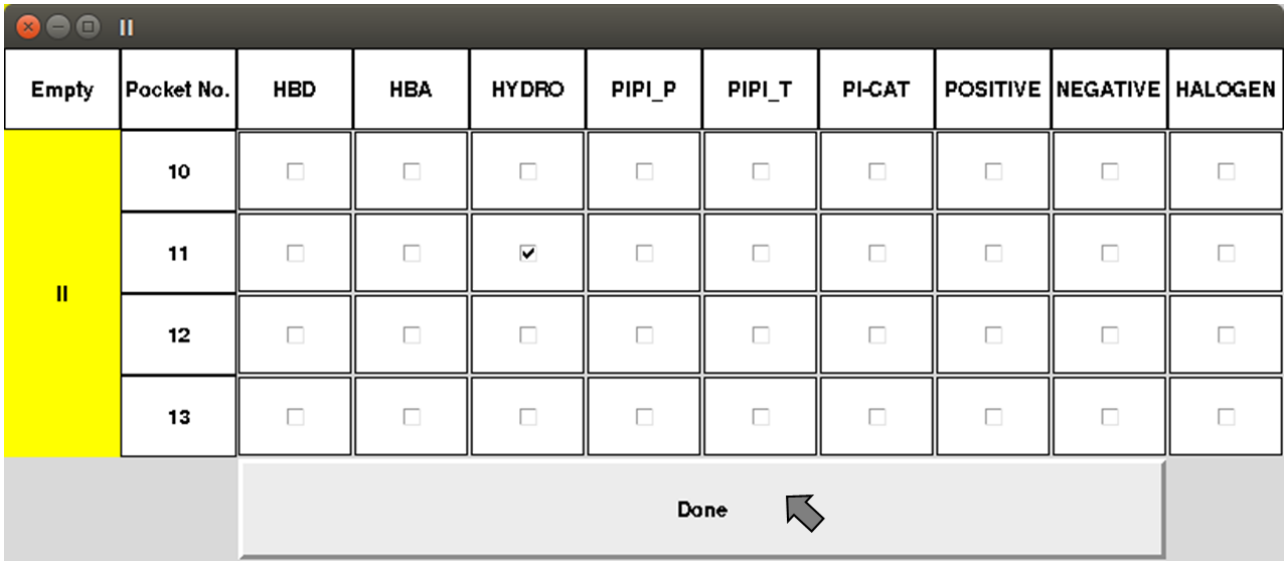


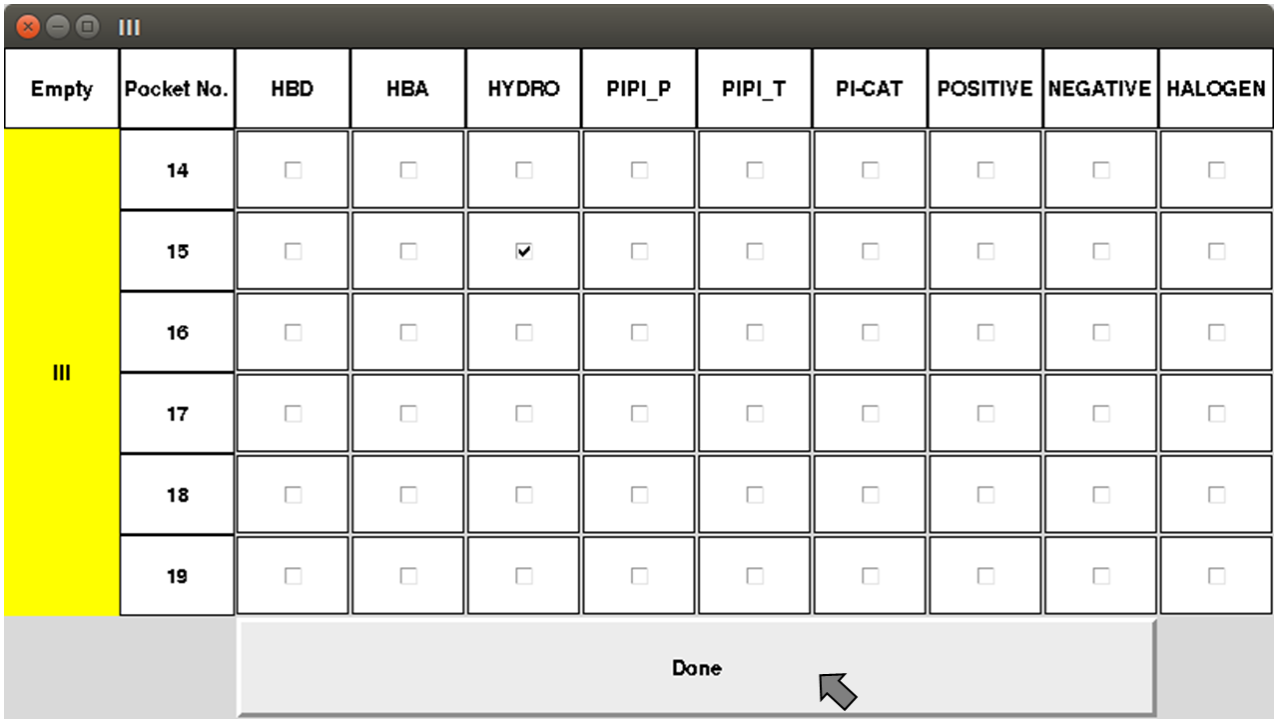
5. Select the Hydro check box for pocket no.3 and click done.

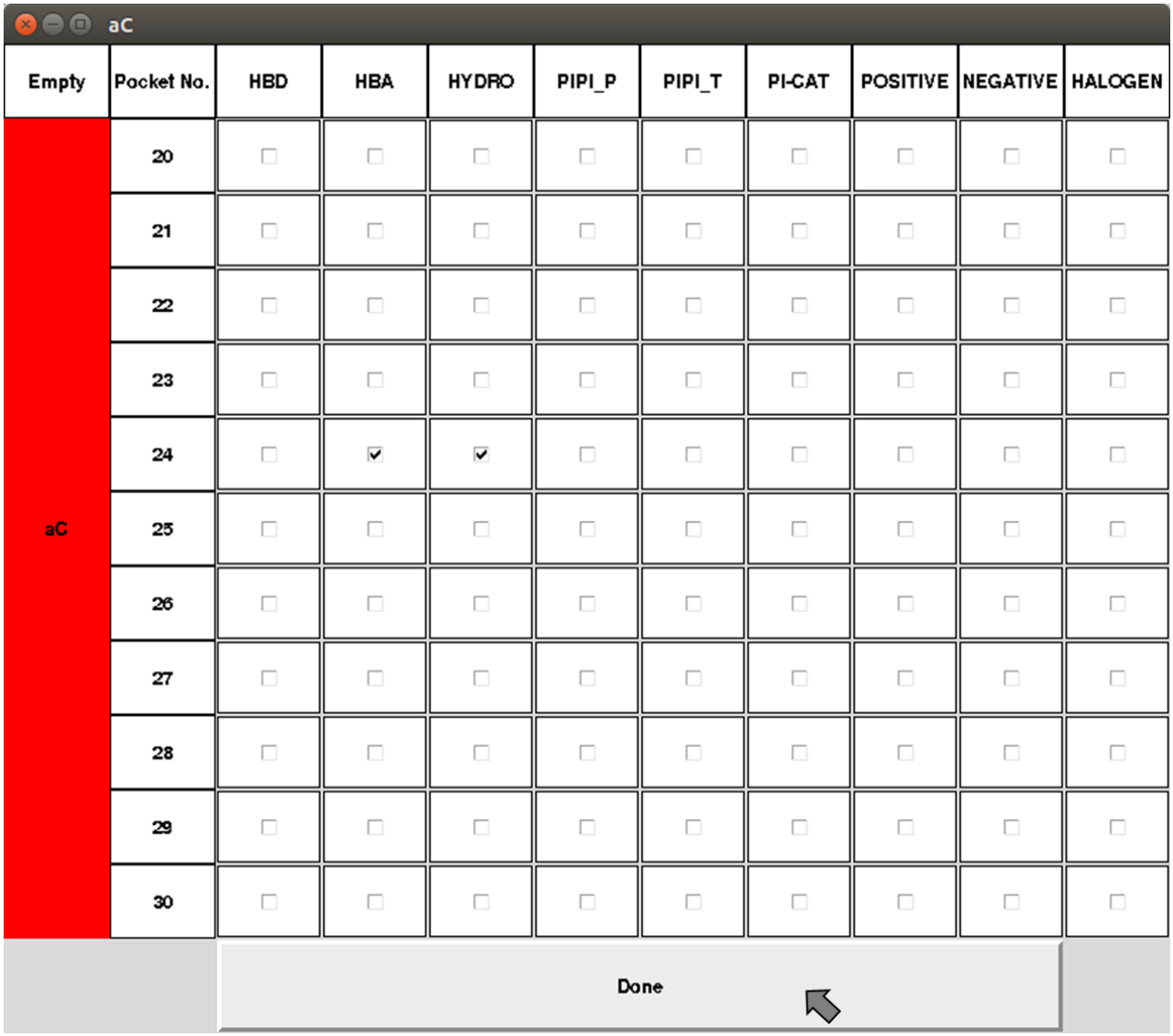


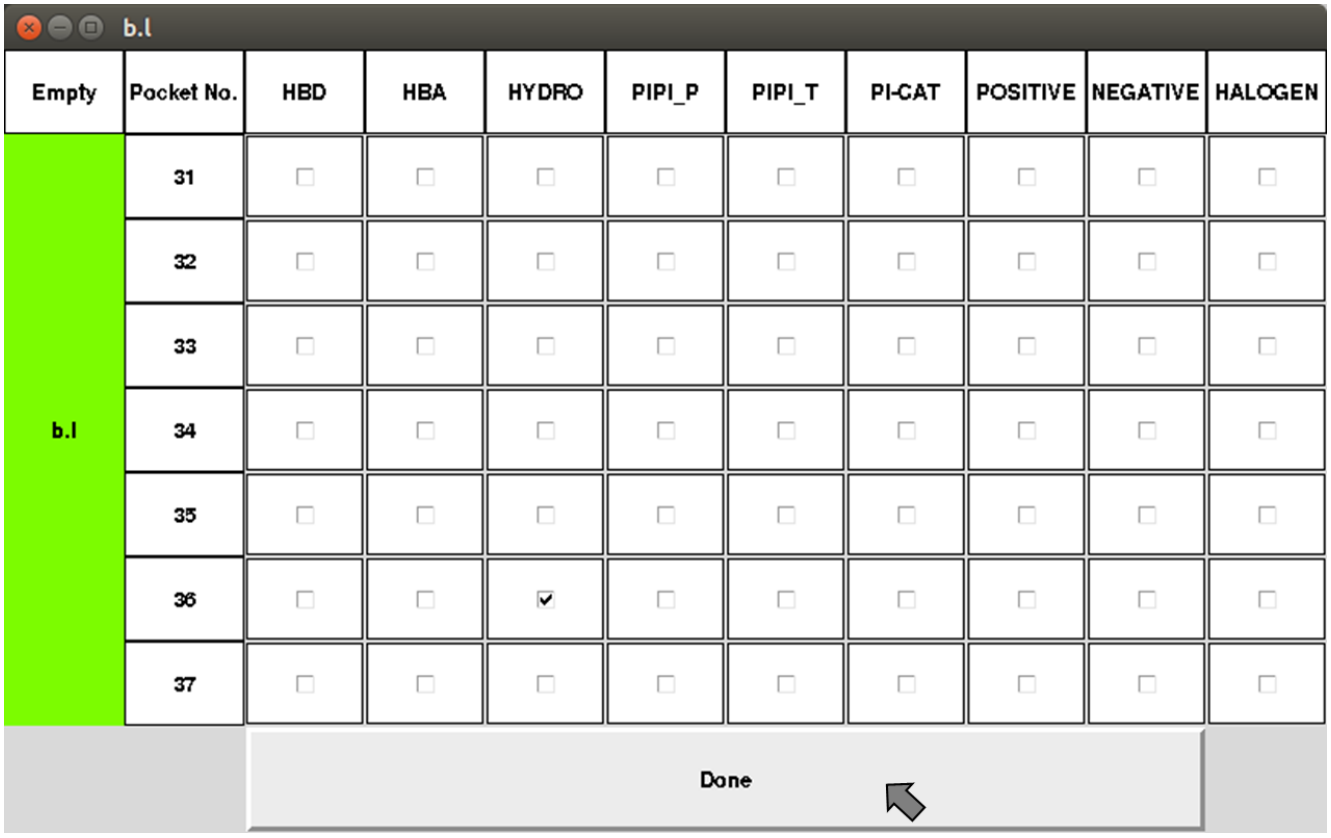
6. Provide other input filteration parameters also.

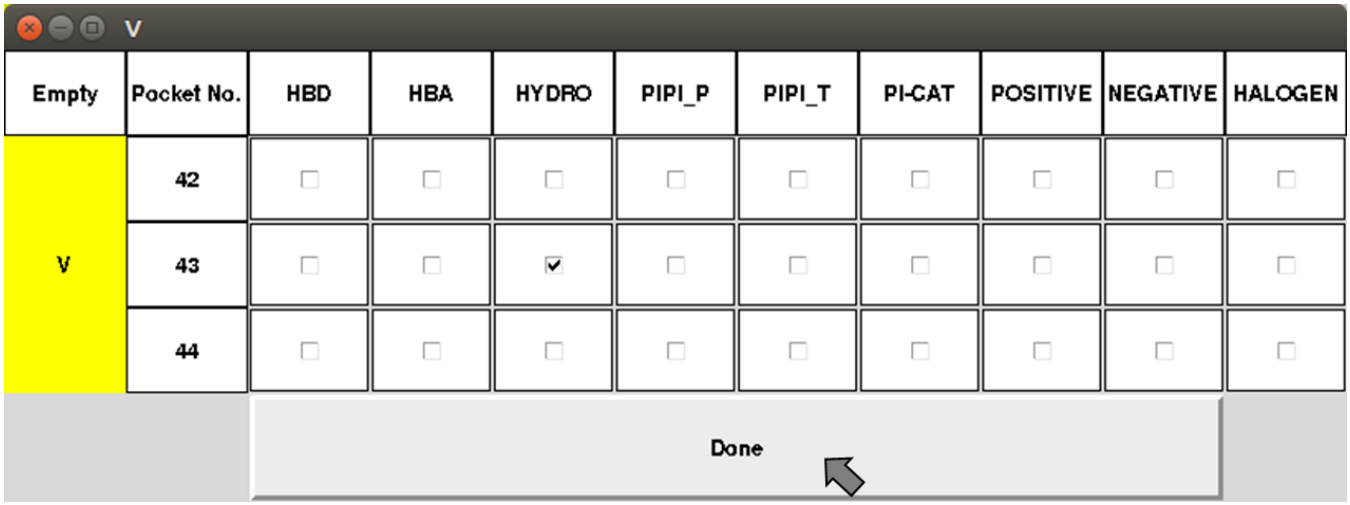


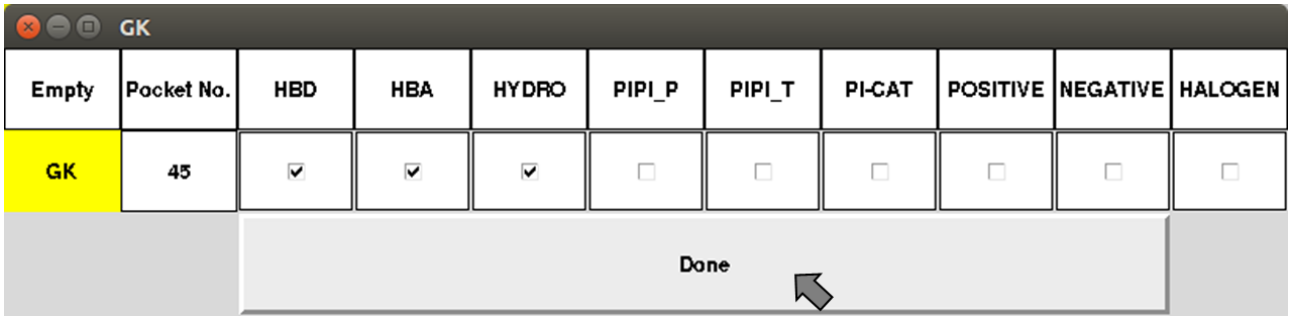


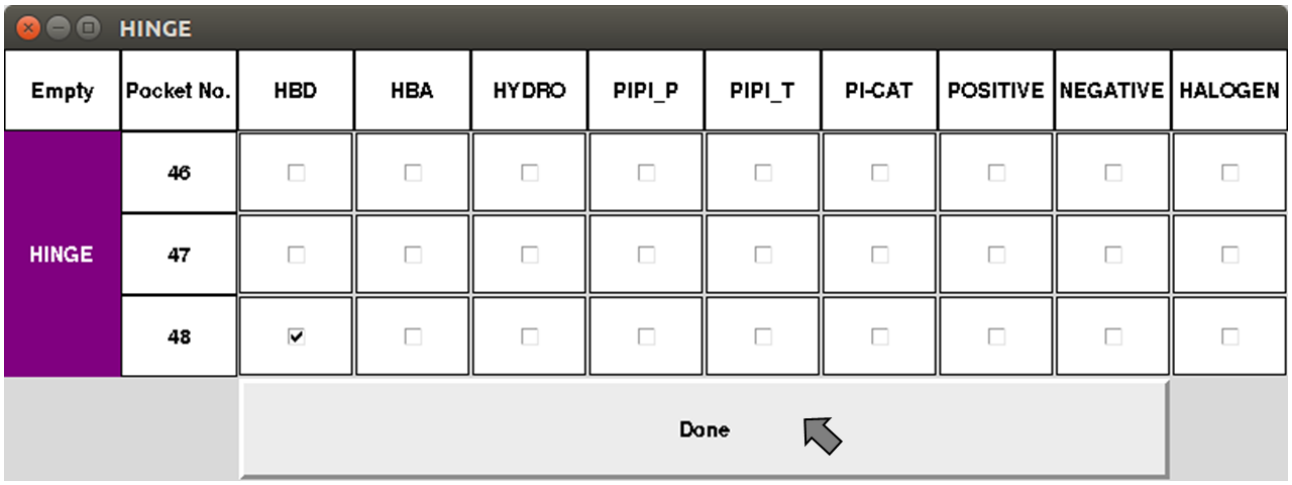

III
Empty
Pocket No.
HBD
HBA
HYDRO
PIPI_P
PIPI_T
PI-CAT
POSITIVE
NEGATIVE
HALOGEN
III
14
15
16
17
18
19
Done

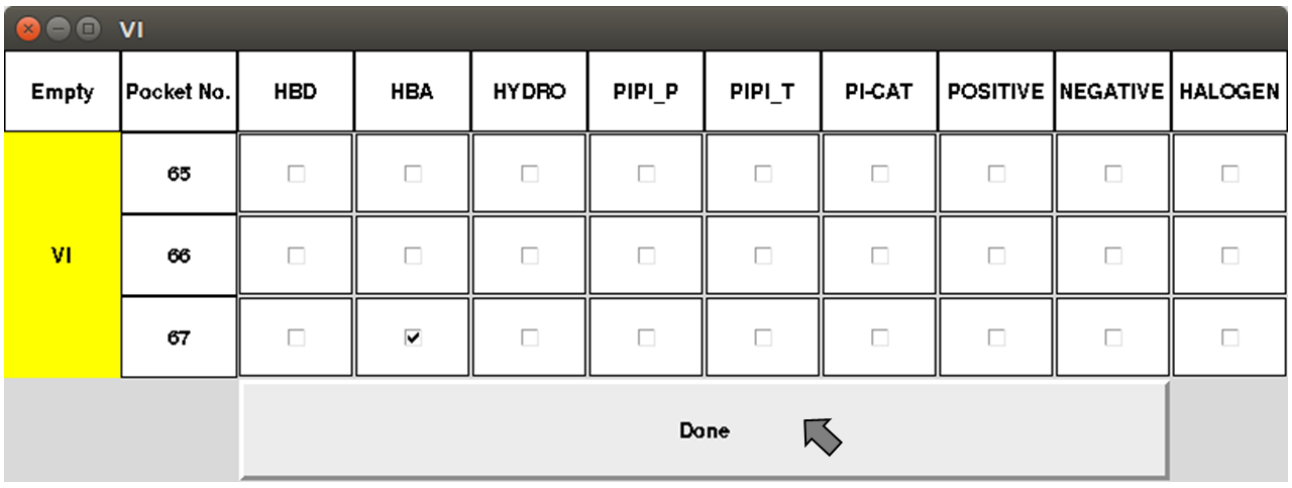

aC
Empty
Pocket No.
HBD
HBA
HYDRO
PIPI_P
PIPI_T
PI-CAT
POSITIVE
NEGATIVE
HALOGEN
aC
20
21
22
23
24
25
26
27
28
29
30
Done


b.l
Empty
Pocket No.
HBD
HBA
HYDRO
PIPI_P
PIPI_T
PI-CAT
POSITIVE
NEGATIVE
HALOGEN
b.l
31
32
33
34
35
36
37
Done


V
Empty
Pocket No.
HBD
HBA
HYDRO
PIPI_P
PIPI_T
PI-CAT
POSITIVE
NEGATIVE
HALOGEN
V
42
43
44
Done


GK
Empty
Packet No.
HBD
HBA
HYDRO
PIPI_P
PIPI_T
PI-CAT
POSITIVE
NEGATIVE
HALOGEN
GK
45
Done


HINGE
Empty
Packet No.
HBD
HBA
HYDRO
PIPI_P
PIPI_T
PI-CAT
POSITIVE
NEGATIVE
HALOGEN
HINGE
46
47
48
Done


VI
Empty
Packet No.
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HBA
HYDRO
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PIPI_T
PI-CAT
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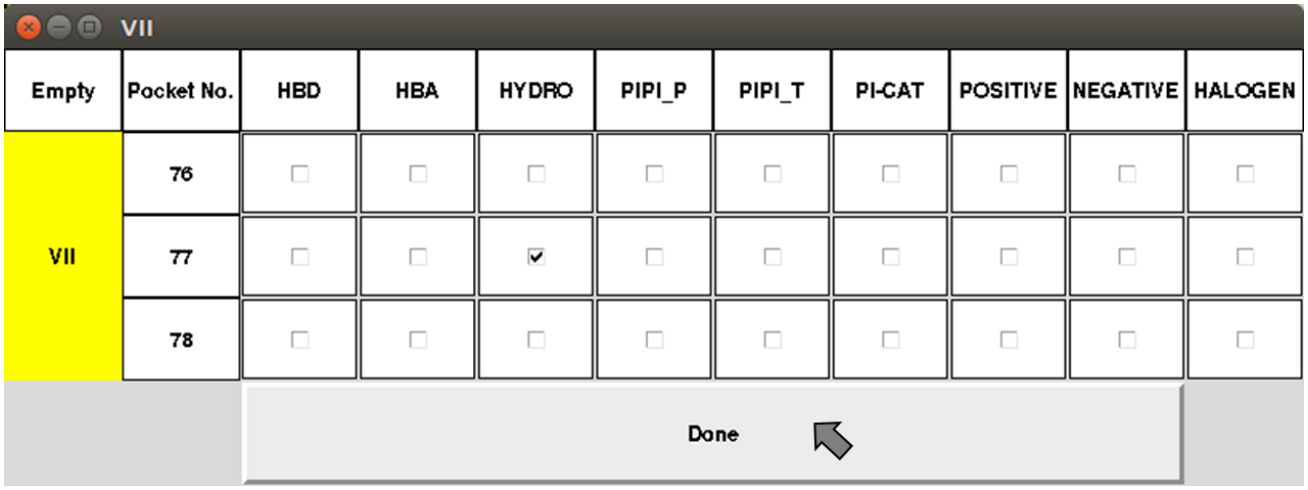
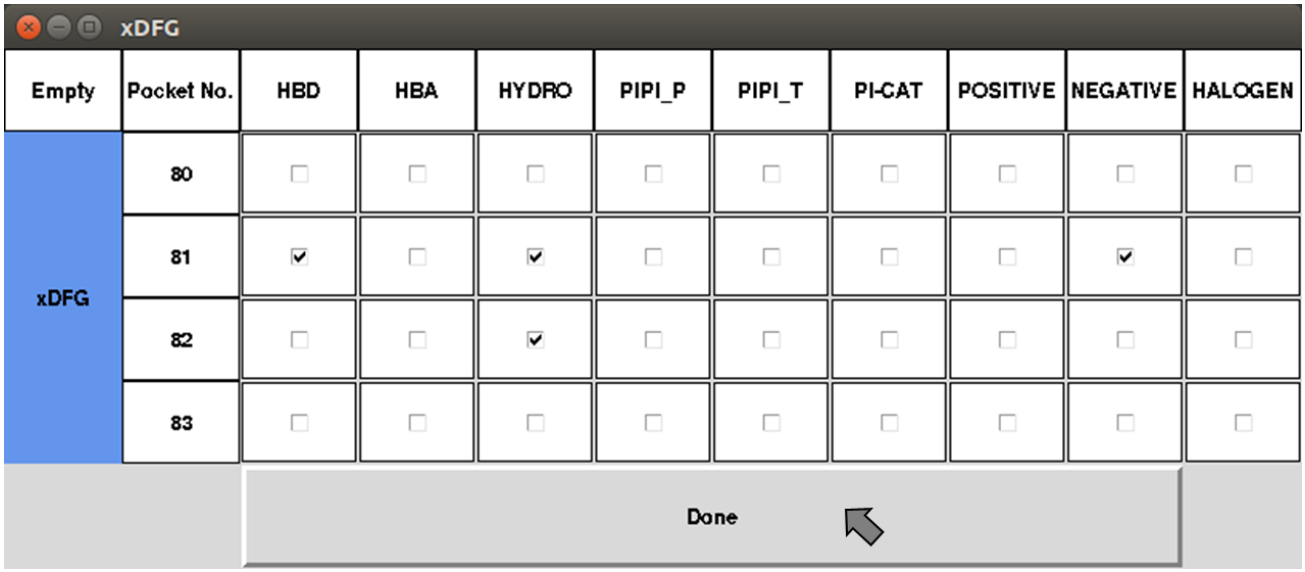
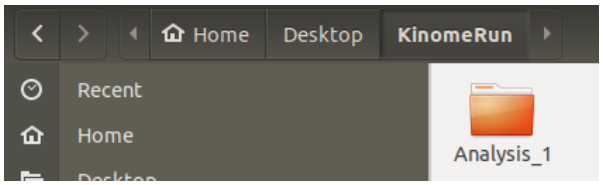
NEGATIVE
HALOGEN
VI
65
66
67
Done


VII
Empty
Pocket No.
HBD
HBA
HYDRO
PIPI_P
PIPI_T
PI-CAT
POSITIVE
NEGATIVE
HALOGEN
VII
76
77
78
Done


xDFG
Empty
Pocket No.
HBD
HBA
HYDRO
PIPI_P
PIPI_T
PI-CAT
POSITIVE
NEGATIVE
HALOGEN
xDFG
80
81
82
83
Done


Home
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KinomeRun
Recent
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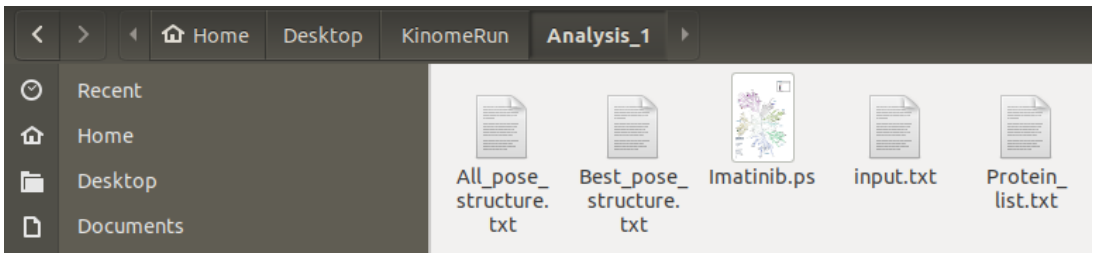
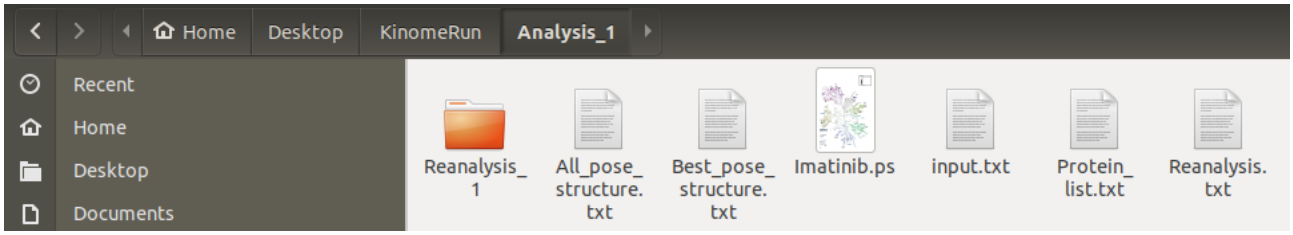
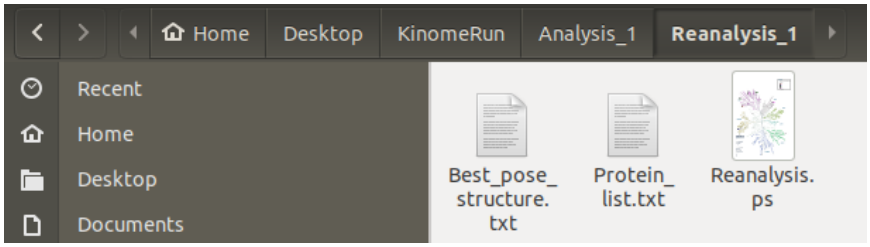
Analysis_1


Home
Desktop
KinomeRun
Analysis_1
Recent
Home
Desktop
Documents
All_pose_structure.txt
Best_pose_structure.txt
Imatinib.ps
input.txt
Protein_list.txt

KinomeRun

7. The user can filter based on the presence of specific interaction in the All_pose_structure.txt using excel/awk command and provide the new file as input for reanalysis button.





Text File information:

Input.txt:

The inputs provided by the user for customized filteration

All_pose_structure.txt:

All poses of the targets docked with ligand containing atleast one of the input interaction pattern. The information in file column-wise are as follows: target structure name, pose number, Kinase family name, Mutation, DFG conformation, αC conformation, Vina binding energy, Total number of interaction, number of input interaction pattern and followed by the options provided. 1: Hydrogen bond donor, 2: Hydrogen bond acceptor, 3: Hydrophobic, 4.π-π stacking: P-type, 5. π-π stacking: T-type, 6. π-cation interaction, 7. Positive: ionic interaction with residue positive side chain, 8. Negative: ionic interaction with residue negative side chain and 9: Halogen interaction.

Best_pose_strucure.txt:

Best pose among the rest poses for each structure is selected based on the pose with highest number of input interaction patterns. If there are more than one poses with highest number of interaction pattern for a structure then the best pose is selected based on the pose with lowest binding energy and higher total number of interaction. Information in the file is similar to that contained in the All_pose_structure.txt file.

Protein_list.txt:

Best protein representative is selected based on the similar criteria used for best_pose_structure.txt, in which only one structure representative among the different structure for that protein is selected

and filtered. The text file contain protein name in the first column, pose information is removed and rest information of the text file are similar to that present in the All_pose_structure.txt