User's manual Multi Docking

Multi Dock was developed using c# programming language and Visual Studio Community edition. C# is a simple, modern, object-oriented, and type-safe programming language. The visual interface was done in Windows Forms.

This computational program runs the docking on AutoDock Vina [1] and uses PDB database (https://www.rcsb.org/) to search for the targets.

I. Steps to use the program

In this section it will be presented the steps involved in docking process with one ligand and many proteins using Multi Docking program. Before starting, the workspace path must be set (Figure 1), which means that all the information you work with will be found in that specific folder. Also, one can select the workspace for the MGL-Tools [2] and AutoDock Vina. Once these are set the Multi Docking process can start.

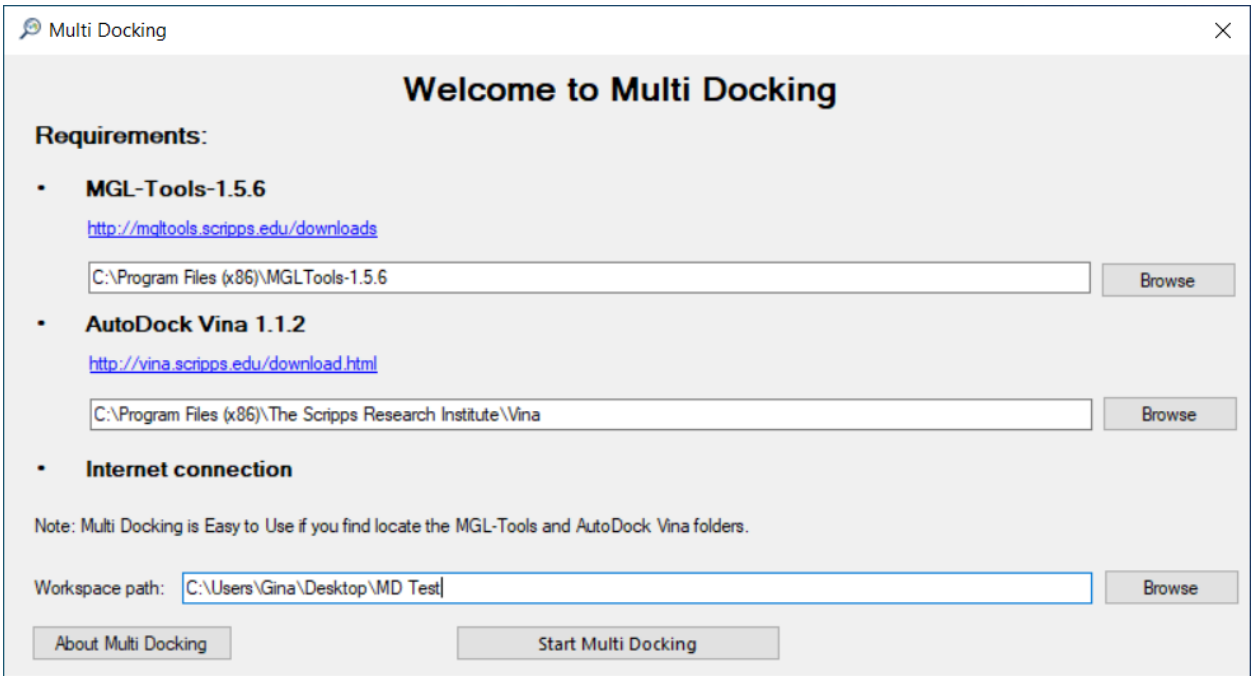

Figure 1. Select the working path

After that, a window with different working tabs will appear showing: Search Targets, Prepare Targets, Targets to PDBQT, Run Multi Docking, Export Results, Help. These will be described in the next paragraphs (Figure 2). Navigating from one tab to another is done manually after an active process is finished.

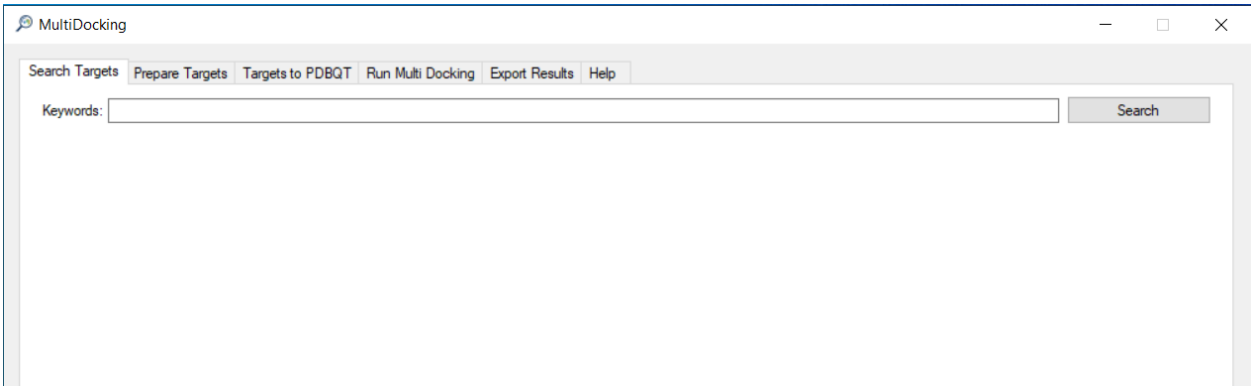

Figure 2. Working tabs

II.A. Search for targets

The process can be initiated from the first tab “Search Targets” were in the input field the targets could be found after the keywords (see Fig. 2). These are defined as digits, numbers, words, or a combination of them. Once written and the button “search” pressed, a list of PDB IDs will be displayed. You can select all, none or whatever you want or maybe change the download path before saving it. Automatically, a folder “downloadPdb” will be created to save all targets in the same place (Figure 3). Once the preferences are fixed, the button “Start Download” must be pressed.

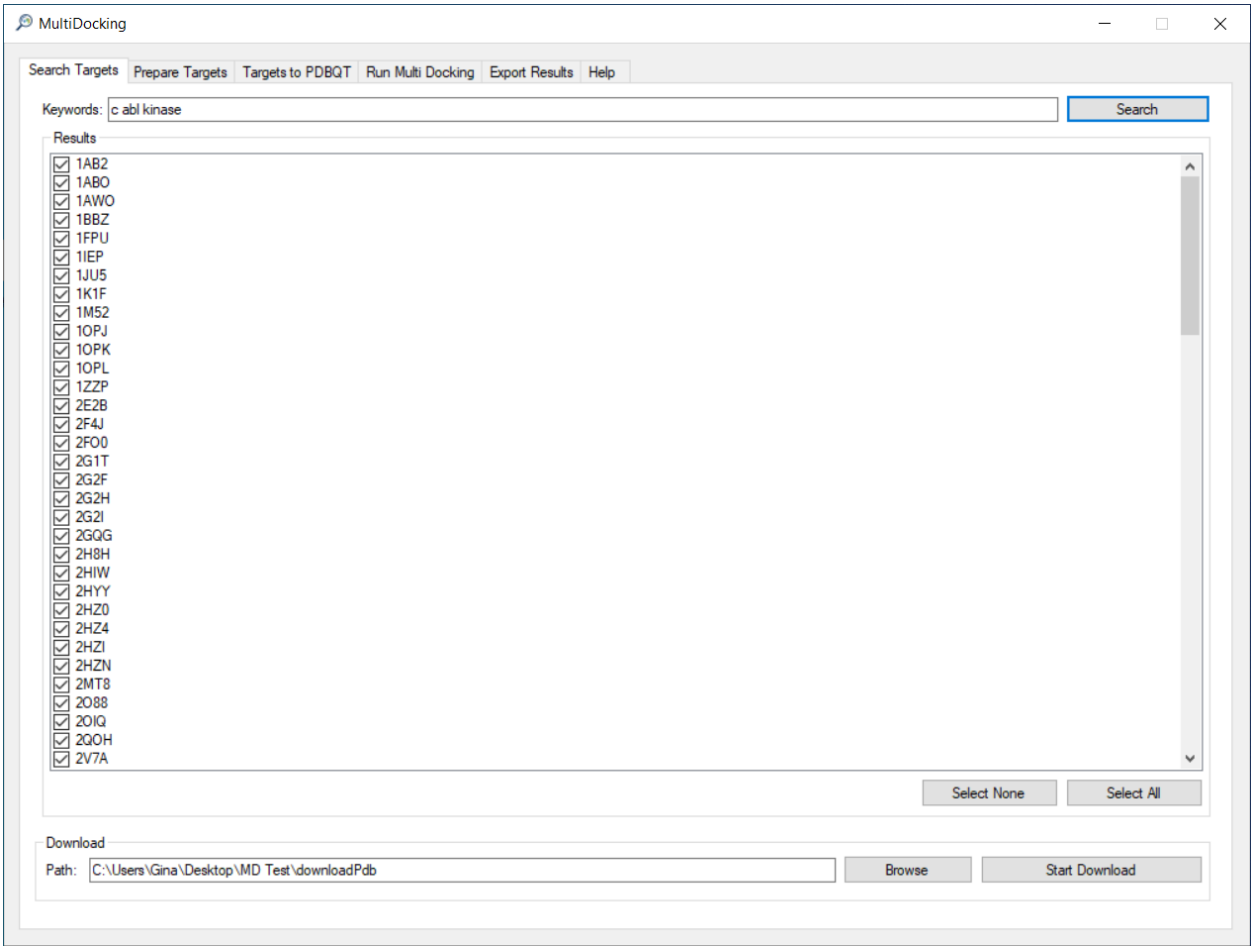

Figure 3. Search Targets tab

II.B. Prepare Targets

In the next working tab called “Prepare Targets” the targets saved above must be loaded again. There is also the possibility to select all, none or any specific target from the list (Figure 4). And, the most important, if there is any ligand crystallized with it can be removed in this step and after saved in the same (recommended) or other path, according to preferences. Before running the multi docking process, the format for targets must be “.pdbqt”. In this way, in the next tab “Targets to PDBQT”, the proteins loaded can be converted to PDBQT, when a folder “proteinsPdbqt” will be created. In this tab is specified the path for python MGL-Tools 1.5.6 and prepare_receptor4.py. Once, the preferred settings are done, the button “Convert to Pdbqt” can be pressed.

II.C. Select your ligand

After preparing the targets, the ligand must be loaded. In the tab “Run Multi Docking” the ligand path can be selected. It must be in the PDBQT format. If not, it can be converted before using different programs like Open Babel [3], Mercury [4], Discovery Studio [5], etc. If the ligand

structure is not from a database, it must be specified that ligand should be in a 3D format, with all hydrogens added, the root detected and the torsions chosen. It happens for the crystallographic files not to have hydrogens added, so it must be done manually. All these steps could be done with AutoDock Tools (ADT) [6].

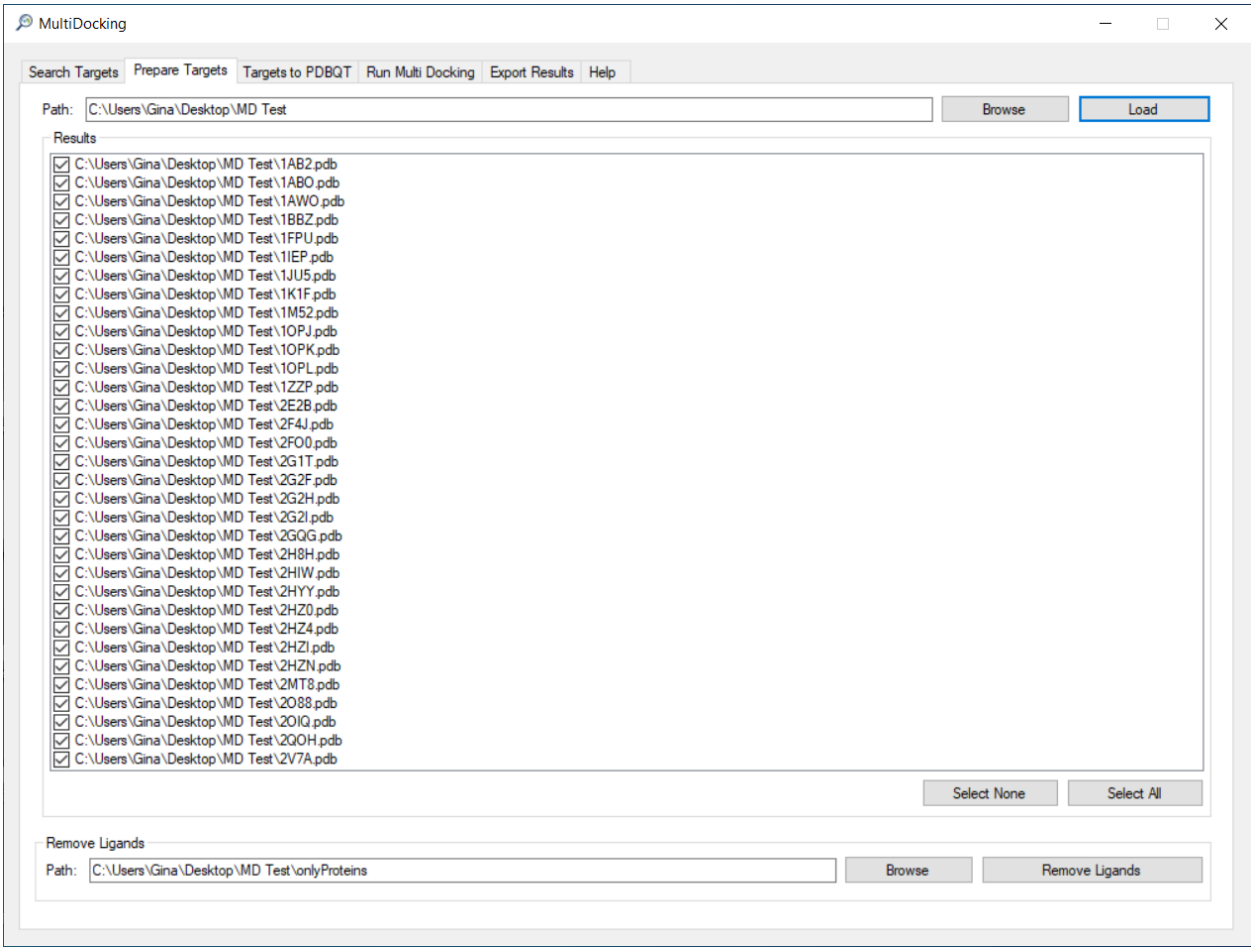

Figure 4. Prepare targets

II.D. Run Multi Docking process

To run multi docking process, the tab with the same name must be selected (Figure 5). In this window, the path for Vina and Results must be selected. Also, the docking process parameters can be set: *Docking num_modes*, *Docking exhaustiveness*, *Number of docking runs*. If it happens for the target to be in a dimer form, the docking process could be done only on a monomer by checking the box "First mer". After all the steps have been done as preferred, the button "Run Multi Docking" must be pressed and a small window will show the time and the progress bar.

To optimize the docking process, some parameters are needed to adjust the search for the most realistic results.

- *num_modes* - is a parameter that sets a maximum number for the possible binding modes to be generated.

- *exhaustiveness* - taking into account the characteristics of a complex protein-ligand, for the beginning, the docking process will try random conformations. With this parameter increased by the researcher, the process time for search will be longer and it will eliminate more possibilities of not identifying the smallest binding energy.
- *docking runs* - this parameter refers to the number of initiations of the docking process. As we know, AutoDock Vina uses a genetic probabilistic algorithm which has a seed number to start the docking process. Because of this, AutoDock Vina might output different results for the same docking runs with exactly the same configuration. Hence, we can run the docking multiple times with this parameter set.
- *first mer* - it refers to a target that has a dimer form, with this parameter set, the docking runs will be made only on one monomer.

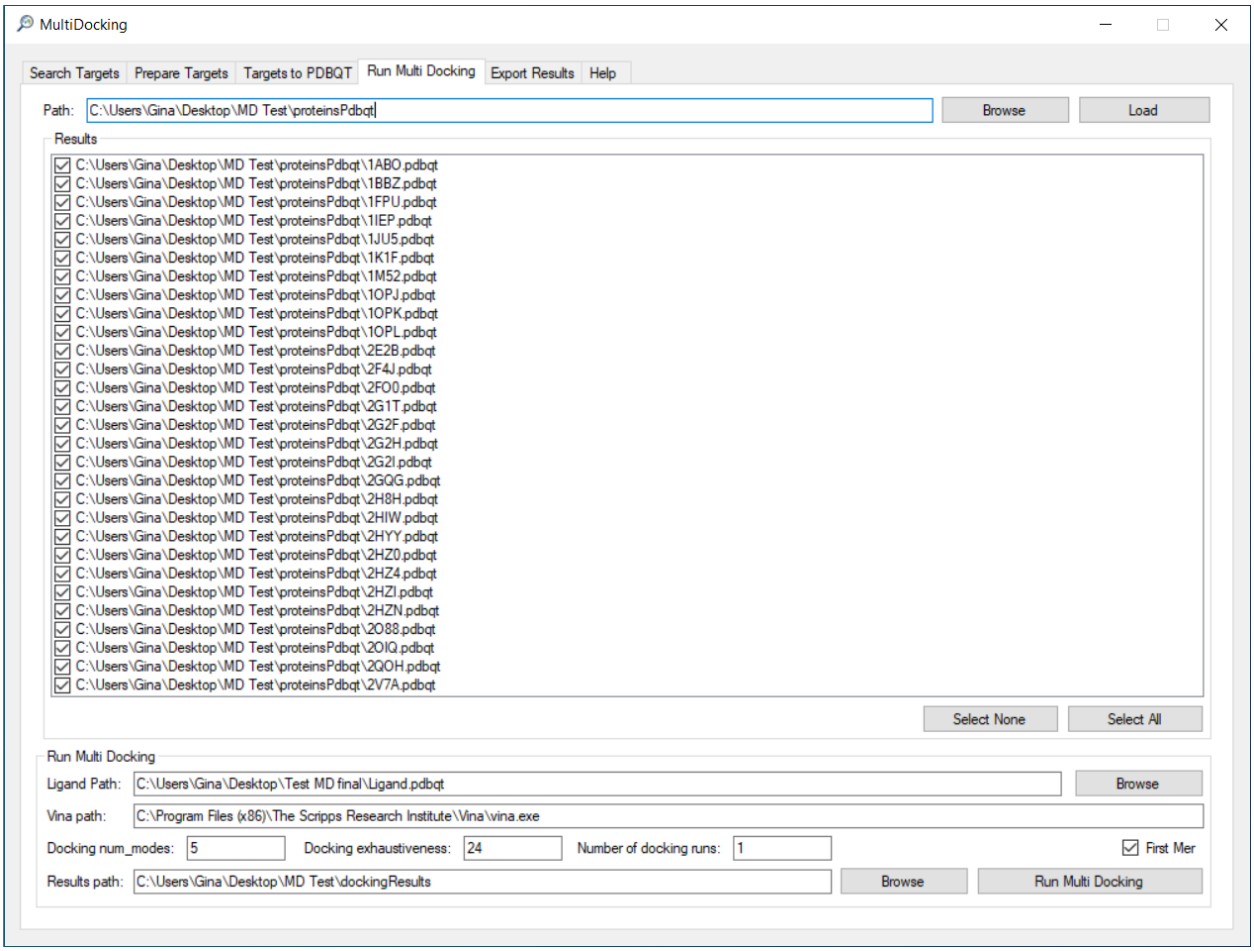

Figure 5. Run Multi Docking bar

II.E. See results

From the tab "Export Results" one can load the .txt format of them, select all or some of them and after Export to xlsx. In order to proceed with it, the Microsoft Excel [7] must be installed or one can chose to export the results in .cvs file. Note that once you exit the Multi Docking program

without exporting the results to xlsx/cvs, there is no problem because these can be reloaded again whenever needed by selecting the folder that contains the docking results. These will be presented in the processing order but also, can be rearranged as preferred.

References

[1] O. Trott and A. J. Olson, "AutoDock Vina: Improving the Speed and Accuracy of Docking with a New Scoring Function, Efficient Optimization and Multithreading," *J. Comput. Chem.*, no. 31, pp. 455–461, 2010.

[2] "http://mgltools.scripps.edu/downloads." .

[3] N. M. O. Boyle, M. Banck, C. A. James, C. Morley, T. Vandermeersch, and G. R. Hutchison, "Open Babel: An open chemical toolbox," *J. Cheminform.*, vol. 33, no. 3, pp. 1–14, 2011.

[4] E. P. Clare F. Macrae, Paul R. Edgington, Patrick McCabe and M. T. and J. van de S. Greg P. Shields, Robin Taylor, "Mercury: visualization and analysis of crystal structures," *J. Appl. Crystallogr.*, vol. 39, pp. 453–457, 2006.

[5] Ref. Dassault Systèmes BIOVIA, "Discovery Studio Modeling Environment." 2017.

[6] R. Huey, G. M. Morris, and S. Forli, "Using AutoDock 4 and AutoDock Vina with AutoDockTools: A Tutorial," *Scripps Res. Inst. Mol. Graph. Lab.*, pp. 1–32, 2012.

[7] M. Corporation, "Microsoft Excel." 2018.