

Protein-Protein Docking Pipeline Tutorial

CS384R, CAM395T, BME383J, Fall 2010

1 Introduction

This document outlines how to carry out different steps of a docking experiment using TexMol. TexMol offers both a visual interface and a command line interface for docking, reranking and input preparation. TexMol acts as a frontend to a docking server running on the PRISM2 cluster.

The following functions are supported-

1. F2d file generation: Includes generation of atomic charges and radii, identification of protein skin regions
2. Quad file generation: Includes generation of molecular surfaces and quadrature point computation
3. Docking
4. Re-ranking

Section 2 describes the command line interface and Section 3 describes the visual interface.

Refer to the parameter documentation and the handout titled ‘Protein Docking Pipeline Tutorial’ for details about the steps and the files.

2 Using the command line

Submitting jobs using the command line is a good option for batch processing, specially during the parameter learning.

2.1 F2d Generation

To produce f2d files from pdbs, the following command need to be executed.

```
./TexMol -f2dgen <>.inp
```

The input file (which must have a .inp extension) contains exactly three lines.

```
staticMoleculePDB <>.pdb  
movingMoleculePDB <>.pdb  
resolution <int>
```

staticMoleculePDB and *movingMoleculePDB* specify the pdb file of the receptor and the ligand respectively. *resolution* specifies the size of the grid used and should be 64, 128 or 256.

After completion, the pqr and f2d files are stored.

2.2 Quad file generation

To produce quad files from pdbs, the following command need to be executed.

```
./TexMol -qudgen <>.inp
```

The input file format is the same as f2d generation. After completion, the pqr, rawn (surface) and quad files are stored.

2.3 Docking

The following command submits a docking job to the server.

```
./TexMol -dock <>.inp
```

Each row of the input file is a 'key value' pair as before, where the key is the name of a parameter of F2Dock. Refer to the parameter list handout for parameter names, default values and acceptable ranges. Note that all parameters with a default value are optional.

2.4 Re-Ranking Solutions

The following command submits a reranking job to the server.

```
./TexMol -rerank <>.inp
```

Each row of the input file is a 'key value' pair as before, where the key is the name of a parameter of Reranking. Refer to the parameter list handout for parameter names, default values and acceptable ranges. Note that all parameters with a default value are optional.

3 Visual interface

The UIs can be used to select parameters/files, submit jobs, monitor their progress and save the resulting output (done automatically when they are ready).

Note that it is still under development and there might be small problems.

3.1 Job Management

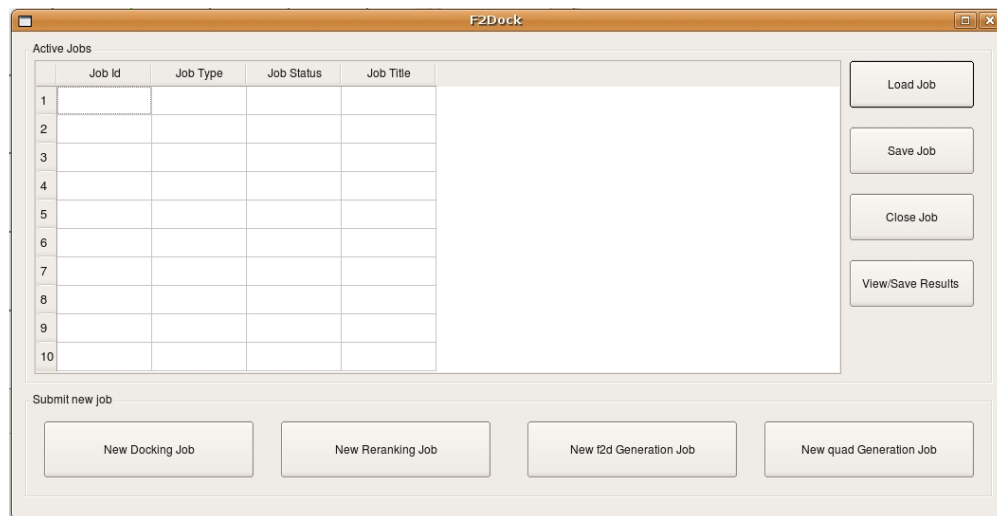


Figure 1: Job management

The main window of the F2Dock Client has options to create new docking/reranking and pqr/f2d/rawn/quad file generations, save created jobs, load previously saved jobs and viewing available results.

Once successfully created and submitted to the server, a job shows up on the list and its status is set to 'Submitted'. The client polls the server in the background for all incomplete jobs and updates the status

to ‘running’ when the job exits the queue on the server and actually starts executing. The status changes to ‘complete’ when the execution ends. Once it is completed, the client automatically retrieves all required files/outputs from the server, stores them and changes the job status to ‘available’. The results can now be viewed/used.

Jobs can be saved anytime irrespective of the state and loaded in the future. Closing a job would save it and remove it from the list. [Note: there are a few minor glitches at the present in the load/save. But it is still usable.]

Note that, the client generates the .inp files required for each type of jobs based on the parameters selected by the users using the job submission UIs (to be detailed in the next 4 subsections). These .inp files as well as the files required for saving jobs are named ‘Jobtitle.extension’ and are saved in the current directory.

3.2 F2d Generation

Figure 2: F2d Generation

The user can select two pdb files (receptor and ligand) and a resolution (fine = 256x256x256, medium = 128x128x128 and coarse = 64x64x64), and choose to save the generated f2d and/or pqr files.

There are no known bugs in this UI.

3.3 Quad Generation

This UI is very similar to F2d Generation. The only difference is that the users now have a option to save the generated quad and/or rawn files.

There are no known bugs in this UI.

3.4 Docking

Figure 3 show the first tab of the docking UI. Only the basic and essential options are exposed here. The users can select two pdbs and submit it immediately with default values for other parameters. Intermediate input files (pqr, f2d, rawn, quad) are autogenerated on the server. But, if the user intends to use the same pdb files for multiple docking jobs, then it is better to generate the intermediate files once and use them later to reduce the computation time. In Figure 4, the third and fourth tabs are shown- which can be used to pass and save intermediate files respectively.

Note that, if an rmsd file is passed, f2dock can compute and report the rmsd values and identify the number of hits on its own.

Figure 3: Basic Options for docking

All the other parameters on Figure 3 and Figure 5 are explained in the parameter documentation. Note that sometimes it becomes tedious to select/change the values of parameters one by one. So, there is also an option to upload a user-defined .inp file directly.

There are no known bugs in this UI.

3.5 Reranking

The UI for reranking is pretty similar to docking.

There are no known bugs in this UI. But the server is having trouble running GB-rerank at the moment.

3.6 Results

Once the results are available, they are displayed in the UI shown in Figure 8. The table on the left lists all the results by mentioning the rank, score and rmsd (if available). If it was a reranking job, then the new rank and new score are also shown.

On the right panel, the summary of the result is displayed. It reports the number of hits in different ranges, the best hit, the topranked hit and the time.

Individual results can be selected from the list on the left to see details about that result. These details are displayed in the tab shown in Figure 9. The details include breakdown of the scores of different scoring terms and filters and the transformation. The selected result can be stored as a transformed pdb of the ligand. This is useful if the user is interested in doing further informatics like binding affinity calculations, area/volume estimation etc.

In the near future, this UI would also provide interface details for each individual result.

Also coming soon is the option of interactive rendering of the resulting configuration. The users can select the type of visualization they need and the selected result (receptor+transformed ligand) is displayed

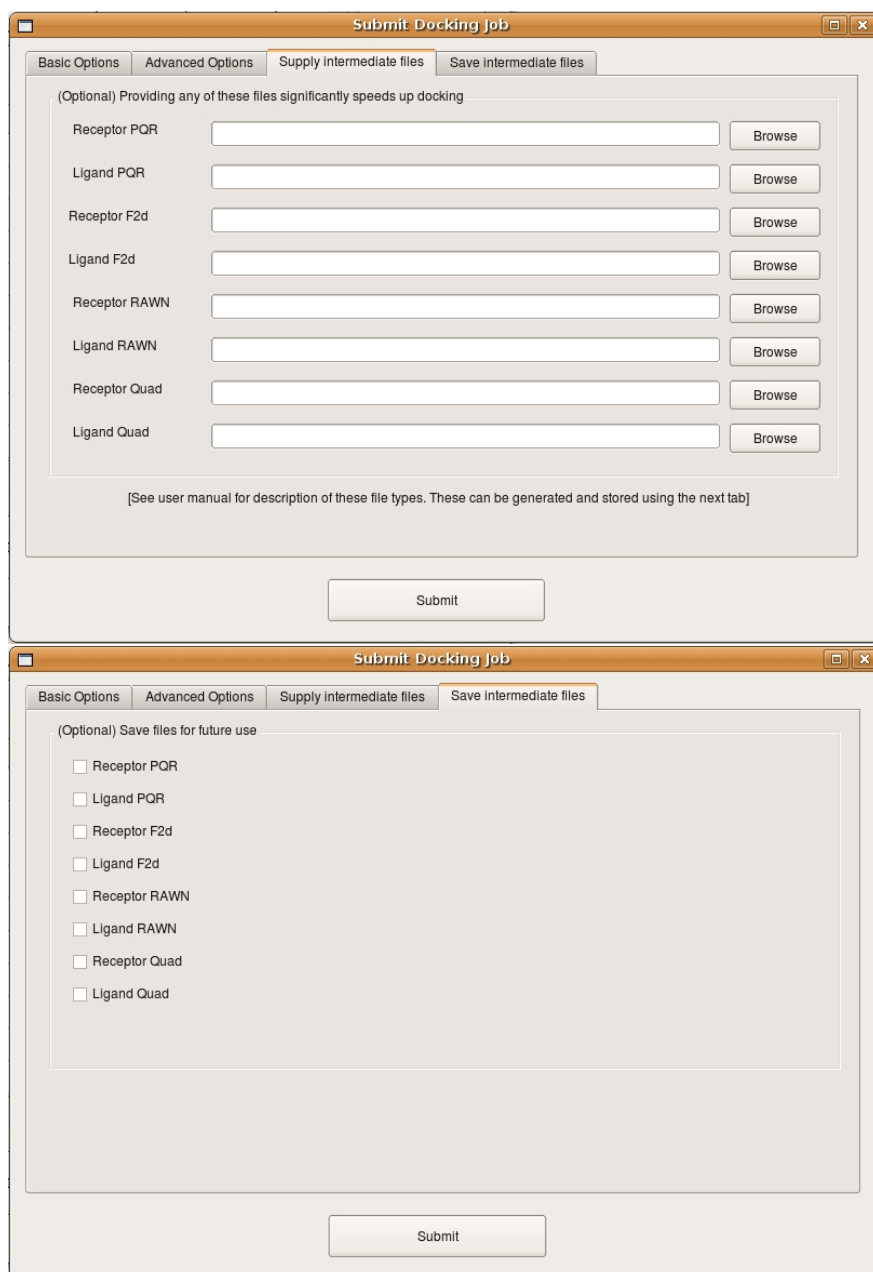


Figure 4: Intermediate file management. Top: passing intermediate files to the server. Bottom: choosing to store intermediate files so that they can be used in later docking runs

on the main window of TexMol.

Submit Docking Job

Basic Options **Advanced Options** Supply intermediate files Save intermediate files

Search Space Parameters

Grid Spacing: 1.2

Rotational Sampling: 4

of peaks per rotation: 1

Filters

☒ Apply Clash Filter

☒ Apply Lennard Jones Filter

☒ Apply Pseudo Gsol Filter

☐ Apply Dispersion Filter

☐ Apply Basic Reranking

Weights

Skin-skin overlap weight: 0.7

Skin-core overlap weight: -0.2

Core-core overlap weight: 17

Electrostatic weight: 0.86

Hydrophobicity weight: 8.5

Hydrogen bonding weight: 0

Simple Charge Compl. weight: 2

Reset to default

Docking input file *

* [Can be used to specify any parameters, as well as to override the ones listed above.
But must not include any file paths]

Figure 5: Advanced Options for docking

Submit Reranking Job

Basic Options

Advanced Options

Supply intermediate files

Save intermediate files

Job Title

[Used for autogenerating names of temporary files (No spaces allowed)]

Receptor PDB

Browse

Ligand PDB

Browse

F2Dock Output

Browse

How many docking outputs should be reranked?

2000

Submit

Submit Reranking Job

Basic Options

Advanced Options

Supply intermediate files

Save intermediate files

Weights

Solvation Energy (Polar) Weight

-1

Solvation Energy (Non- Polar) Weight

0.005

On-the-fly Docking Score Weight (*)

0.5

Approximation Error

Born Radii (%) Error Bound

0.7

Polarization Energy (%) Error Bound

0

(*) F2Dock uses shape complementarity, coulombic and hydrophobicity terms by default

Reset to default

Submit

Figure 6: Basic and advanced options for reranking

Submit Reranking Job

Basic Options Advanced Options **Supply intermediate files** Save intermediate files

(Optional) Providing these files significantly speeds up reranking

Receptor PQR

Ligand PQR

Receptor RAWN

Ligand RAWN

Receptor QUAD

Ligand QUAD

[See user manual for description of these file types. These can be generated and stored using the next tab]

Submit Reranking Job

Basic Options Advanced Options **Save intermediate files** Supply intermediate files

(Optional) Save files for future use

☐ Receptor PQR

☐ Ligand PQR

☐ Receptor RAWN

☐ Ligand RAWN

☐ Receptor QUAD

☐ Ligand QUAD

Figure 7: Intermediate file management

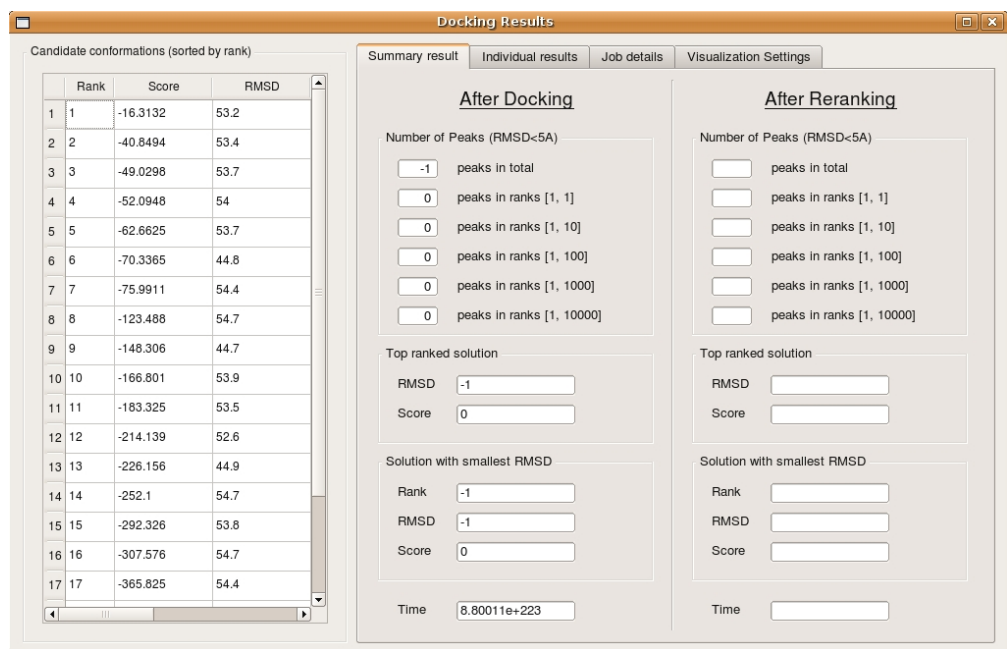


Figure 8: Summary of docking result

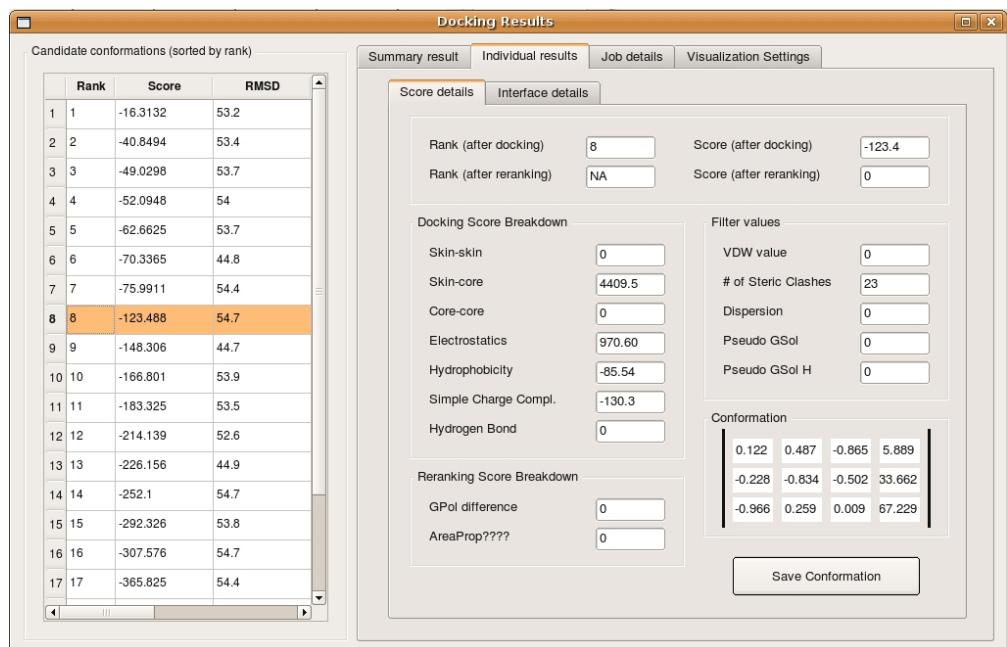


Figure 9: Details of individual results