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 decribes 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.

| Load Job |
|-------------------------|
| Load Job |
| |
| Save Job |
| |
| Close Job |
| |
| |
| View/Save Results |
| |
| |
| |
| |
| |
| New quad Generation Job |
| |
| |

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

| | Submit pqr and f2d generation job | |
|---|--|----|
| Job Title | [Used for autogenerating names of temporary files (No spaces allowed)] | |
| Receptor PDB | Brow | se |
| Ligand PDB | Brow | se |
| Resolution | Fine 🔷 | |
| Save Only f2d | | |
| Save Both f2d and p | ıqr | |
| | Submit | |

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.

| | Submit Docking 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 | |
| Complex type | Unknown (Re)sets parameters to default values] | |
| # of Solutions | 2000 | |
| # of Rotations | 20000 | |
| RMSD Atoms (Optional) | Browse | |
| ✓ Unbound? | | |
| Perform Rerank | | |
| | | |
| | Submit | |

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

| | Submit Docking Job | |
|-------------------------------|---|--|
| Basic Options Advanced 0 | Options Supply Intermediate files Save Intermediate files | |
| (Optional) Providing any o | f these files significantly speeds up docking | |
| Receptor PQR | Browse | |
| Ligand PQR | Browse | |
| Receptor F2d | Browse | |
| Ligand F2d | | |
| Becentor BAWN | | |
| neceptor name | Browse | |
| Ligand RAWN | Browse | |
| Receptor Quad | Browse | |
| Ligand Quad | Browse | |
| | Submit Docking Job | |
| Basic Options Advanced | Options Supply intermediate files Save intermediate files | |
| (Optional) Save files for ful | ture use | |
| Receptor PQR | | |
| Ligand PQR | | |
| Receptor F2d | | |
| Receptor RAWN | | |
| Ligand RAWN | | |
| Receptor Quad | | |
| Ligand Quad | | |
| | | |
| | | |
| | | |
| | | |
| | Submit | |

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 Do | cking job | | | | |
|--------------------|------------------------|---|--|-------------------------|-------|---|--|
| Basic Options | Advanced Options | Supply intermediate files | Save intermediat | e files | | | |
| Search Spac | ce Parameters | | Weights | | | | |
| Grid Spa | acing | 1.2 | Skin-skin ov | verlap weight | 0.7 | | |
| Rotation | al Sampling | 4 \$ | Skin-core o | verlap weight | -0.2 | | |
| # of peak | ks per rotation | 1 | Core-core o | verlap weight | 17 | | |
| | | | Electrostatio | c weight | 0.86 | | |
| Filters | | | Hydrophobi | city weight | 8.5 | | |
| Apply Clash Filter | | | Hydrogen bonding weight 0 | | | | |
| V Appl | y Lennard Jones Filter | | rge Compl. weight | 2 | | | |
| ✓ Appl | y Pseudo Gsol Filter | | | | | | |
| Appl | y Dispersion Filter | | | | | | |
| Appl | y Basic Reranking | | | Reset to defau | llt | | |
| Docking in | nout file * | | | | | | |
| Dooking in | | | | | Brows | 8 | |
| | * [Can be us | ed to specify any parameters, But must not inc | as well as to overri lude any file paths] | de the ones listed aboy | ve. | | |
| | | | | | | _ | |
| | | Sub | omit | | | | |

Figure 5: Advanced Options for docking

| | | | Submit Rer | anking Job | | |
|---|---|---|---|--|--------|---|
| Basic Options | Advanced Op | ptions S | Supply intermediate files | Save intermediate files | | |
| Job Title | | [U | Jsed for autogenerating r | ames of temporary files (No spaces allowed)] | | |
| Receptor | PDB | | | | Browse | |
| Ligand PI | рв | | | | Browse |] |
| F2Dock C | utput | | | | Browse | |
| How man | y docking outpu | ts should be | e reranked? | 2000 | | |
| | | | | | | |
| | | | Su | Ibmit | | |
| | | | Submit Rer | anking Job | | |
| Basic Options | Advanced Op | ptions S | Submit Ren Supply intermediate files | anking Job Save intermediate files | | |
| Basic Options Weights | Advanced Op | ptions | Submit Rer Supply intermediate files | anking Job Save intermediate files Approximation Error | | |
| Basic Options Weights Solvation | Advanced Of Energy (Polar) 1 | ptions S Weight | Submit Rer Supply intermediate files | anking Job Save intermediate files Approximation Error Born Radii (%) Error Bound | 0.7 | |
| Basic Options Weights Solvation Solvation | Advanced Of Energy (Polar) I Energy (Non- P | ptions S Weight olar) Weigh | Submit Ren Supply intermediate files | anking Job Save intermediate files Approximation Error Born Radii (%) Error Bound Polarization Energy (%) Error Bound | 0.7 |) |
| Basic Options Weights Solvation Solvation On-the-fly | Advanced Of Energy (Polar) 1 Energy (Non- P Docking Score | ptions S Weight olar) Weigh Weight (*) | Submit Ren Supply intermediate files 1 0.005 0.5 | anking Job Save intermediate files Approximation Error Born Radii (%) Error Bound Polarization Energy (%) Error Bound | 0.7 |) |
| Basic Options Weights Solvation Solvation On-the-fly (*) F2Doc | Advanced Of Energy (Polar) I Energy (Non- P Docking Score k uses shape co | ptions S Weight olar) Weigh Weight (*) | Submit Ren Supply intermediate files -1 at 0.005 0.5 | anking Job Save intermediate files Approximation Error Born Radii (%) Error Bound Polarization Energy (%) Error Bound | 0.7 | |
| Basic Options Weights Solvation Solvation On-the-fly (*) F2Doc | Advanced Op Energy (Polar) \ Energy (Non- P Docking Score k uses shape co | ptions S Weight olar) Weigh Weight (*) implementa | Submit Ren supply intermediate files -1 -1 -1 -1 -1 -1 -1 -1 -1 -1 -1 -1 -1 | anking Job Save Intermediate files Approximation Error Born Radii (%) Error Bound Polarization Energy (%) Error Bound polarization Energy (%) Error Bound | 0.7 |) |
| Basic Options Weights Solvation Solvation On-the-fly (*) F2Doc | Advanced Op Energy (Polar) 1 Energy (Non- P Docking Score k uses shape co | ptions S Weight olar) Weigh Weight (*) | Submit Rer Supply Intermediate files Int 0.005 0.5 urlty, coulombic and hydro Reset | anking Job Save intermediate files Approximation Error Born Radii (%) Error Bound Polarization Energy (%) Error Bound pophobicity terms by default | 0.7 | |

Figure 6: Basic and advanced options for reranking

| | | | | Submit R | eran | nking Jo | ob | | | | | | |
|--|---|--|--------------|-------------------|-------------------|-------------------------------|---------------|----------|--|---|-------|------|--|
| Basic Options | Advanced | Options | Supply | intermediate file | S | Save inte | ermedia | te files | | | | | |
| (Optional) P | roviding these | e files signi | ificantly sp | beeds up rerank | ing | | | | | | | | |
| Receptor | PQR | | | | | | | | | | Brows | e | |
| Ligand P | QR | | | | | | | | | | Brows | ie i | |
| Receptor | RAWN | | | | | | | | | | | | |
| 1100000101 | | | | | | | | | | | Brows | e | |
| Ligand RA | AWN | | | | | | | | | | Brows | e | |
| Receptor | QUAD | | | | | | | | | | Brows | e | |
| Ligand Ql | UAD | | | | | | | | | | Brows | e | |
| | | | | | Subm | nit | | | | | | | |
| Basic Options | Advanced | Options | Supply i | Submit R | Subm eran | nit Iking Jo Save inte | ob ermedia | te files | | _ | | | |
| Basic Options | Advanced ave files for fu | Options | Supply i | Submit R | Subm eran s | nit Iking Jo Save inte | ob ermedia | te files | | | | | |
| Basic Options (Optional) S | Advanced ave files for fu | Options | Supply i | Submit R | Subm eran s | nit Iking Jo Save inte | ob ermedia | te files | | | | | |
| Basic Options (Optional) S Recep | Advanced ave files for fu otor PQR d PQR | Options Iture use | Supply i | Submit R | subm s | nit Iking Jo | ob ermedia | te files | | | | | |
| Basic Options (Optional) S Recep Ligand | Advanced ave files for fu otor PQR d PQR otor RAWN | Options ture use | Supply i | Submit R | subm eran s | nit Iking Ja | ob ermedia | te files | | | | | |
| Basic Options (Optional) S Recep Ligand Ligand | Advanced ave files for fu otor PQR d PQR otor RAWN d RAWN | Options | Supply i | Submit R | subm eran | nit Iking Jo | ob ermedia | te files | | | | | |
| Basic Options (Optional) S Recep Ligand Recep Ligand Recep | Advanced ave files for fu otor PQR d PQR otor RAWN d RAWN d RAWN | Options during the second seco | Supply i | Submit R | eran s | nit Isking ja Save inte | ob ermedia | te files | | | | [| |
| Basic Options (Optional) S Recep Ligand Recep Ligand Recep Ligand | Advanced ave files for fu otor PQR d PQR otor RAWN d RAWN otor QUAD d QUAD | Options | Supply | Submit R | eran s | nit Iking ja | ob ermedia | te files | | | | | |
| Basic Options (Optional) S Recep Ligand Recep Ligand Recep Ligand | Advanced ave files for fu otor PQR d PQR otor RAWN d RAWN otor QUAD d QUAD | Options | Supply I | Submit R | subm s | nit aking ja Save inte | ob ermedia | te files | | | | | |
| Basic Options (Optional) S Recep Ligand Recep Ligand Recep | Advanced ave files for fu otor PQR d PQR otor RAWN d RAWN otor QUAD d QUAD | Options ture use | Supply I | Submit R | subm s | nit Iking jo | ob ermedia | te files | | | | | |
| Basic Options (Optional) S Basic Optional) S Basic Ligand Recep Ligand Recep Ligand | Advanced ave files for fu otor PQR d PQR otor RAWN d RAWN otor QUAD d QUAD | Options ture use | Supply I | Submit R | subm s | nit sking ja Save inte | ermedia | te files | | | | | |
| Basic Options (Optional) S Recep Ligand Recep Ligand Recep | Advanced ave files for fu otor PQR d PQR otor RAWN d RAWN otor QUAD d QUAD | Options ture use | Supply | Submit R | Subm eran s | nit Iking ja Save inte | ermedia | te files | | | | | |

Figure 7: Intermediate file management

| uiu | ale com | onnations (sone | u by fallk) | Summary result | Individual results | Job details | Visualization Settings |
|-----|---------|-----------------|-------------|----------------|-------------------------|-------------|-----------------------------|
| | Rank | Score | RMSD | | After Decking | | After Perapking |
| 1 | 1 | -16.3132 | 53.2 | - | Aller Docking | | Aller heraliking |
| 2 | 2 | -40.8494 | 53.4 | Number of Pe | eaks (RMSD<5A) | | Number of Peaks (RMSD<5A) |
| 3 | 3 | -49.0298 | 53.7 | -1 # | beaks in total | | peaks in total |
| 4 | 4 | -52.0948 | 54 | 0 \$ | beaks in ranks [1, 1] | | peaks in ranks [1, 1] |
| 5 | 5 | -62.6625 | 53.7 | 0 F | beaks in ranks [1, 10] | | peaks in ranks [1, 10] |
| 6 | 6 | -70.3365 | 44.8 | F | beaks in ranks [1, 100] | | peaks in ranks [1, 100] |
| 7 | 7 | -75.9911 | 54.4 | F | beaks in ranks [1, 1000 | 9 | peaks in ranks [1, 1000] |
| 8 | 8 | -123.488 | 54.7 | t | beaks in ranks [1, 1000 | 0] | peaks in ranks [1, 10000] |
| 9 | 9 | -148.306 | 44.7 | Top ranked s | olution | | Top ranked solution |
| 10 | 10 | -166.801 | 53.9 | RMSD | -1 | | RMSD |
| 11 | 11 | -183.325 | 53.5 | Score | 0 | | Score |
| 12 | 12 | -214.139 | 52.6 | | | | |
| 13 | 13 | -226.156 | 44.9 | Solution with | smallest RMSD | | Solution with smallest RMSD |
| 14 | 14 | -252.1 | 54.7 | Rank | -1 | | Rank |
| 15 | 15 | -292.326 | 53.8 | RMSD | -1 | | RMSD |
| 16 | 16 | -307.576 | 54.7 | Score | 0 | | Score |
| 17 | 17 | -365.825 | 54.4 | | | | |

Figure 8: Summary of docking result

| inan | uale con | onnations (some | tu by fallk) | \$ | Summary result | Individual results | Job details | Visualization Se | ettings | | |
|------|----------|-----------------|--------------|----|----------------|--------------------|-------------|------------------|----------|-----------|--------|
| | Rank | Score | RMSD | | Score details | Interface detai | Is | | | | |
| 1 | 1 | -16.3132 | 53.2 | | | | | | | | |
| 2 | 2 | -40.8494 | 53.4 | | Rank (afte | er docking) | 8 | Score (after do | cking) | -1 | 23.4 |
| 3 | 3 | -49.0298 | 53.7 | | Rank (afte | er reranking) | NA | Score (after re | ranking) | 0 | |
| 4 | 4 | -52.0948 | 54 | | | | | | | | |
| 5 | 5 | -62.6625 | 53.7 | | Docking Sc | ore Breakdown | | Filter values | 5 | | |
| 6 | 6 | -70.3365 | 44.8 | | Skin-skin | | 0 | VDW valu | le | 0 | |
| 7 | 7 | -75.9911 | 54.4 | = | Skin-core | | 4409.5 | # of Steri | c Clashe | s 2 | 3 |
| 8 | 8 | -123.488 | 54.7 | | Core-core | | 0 | Dispersio | n | 0 | |
| 9 | 9 | -148.306 | 44.7 | | Electrosta | atics | 970.60 | Pseudo G | Sol | 0 | |
| 10 | 10 | -166.801 | 53.9 | | Hydropho | bicity | -85.54 | Pseudo G | Sol H | 0 | |
| 11 | 11 | -183.325 | 53.5 | | Simple Ch | narge Compl. | -130.3 | Oraclassia | | | |
| 12 | 12 | -214.139 | 52.6 | | Hydrogen | Bond | 0 | Contormatic | | | |
| 13 | 13 | -226.156 | 44.9 | | Boronking 6 | aara Brookdown | | 0.122 | 0.487 | -0.865 | 5.889 |
| 14 | 14 | -252.1 | 54.7 | | neranking s | SCOLE DIGREGOMU | | -0.228 | -0.834 | -0.502 | 33.662 |
| 15 | 15 | -292.326 | 53.8 | | GPOLOITE | erence | 0 | -0.966 | 0.259 | 0.009 | 67.229 |
| 16 | 16 | -307.576 | 54.7 | | AreaProp | m | 0 | | | | |
| 17 | 17 | -365.825 | 54.4 | | | | | 5 | Save Cor | nformatio | n |

Figure 9: Details of individual results