

There are two set of executables, together with required input files, included in this demo. One set is in the folder 'SVD', the other set is in the folder 'biasMD'.

1. Singular value decomposition of a generalized work functional matrix. This set of files are in the folder 'SVD'.

* Input file: `./data/IC_GWF.dat`. This file contains a 623 x 623 matrix that is the generalized work functional calculated from the energy relaxation trajectories of HIV protease bound to DRV.

* Executable: `SVD.py`

* Output file: `./result/U.dat`. It is a text file that contains a 623 x 623 matrix in double-precision. Each column is a singular coordinate of HIV protease bound to DRV.

* Command line to run the executable:

```
$ python3 SVD.py
```

** Note: In order to run the command line above, NumPy module needs to be installed on your computer. The typical run time for this command is less than 10 seconds.

2. Generating RC-uncovered trajectories along SCs of HIV protease. This set of files are in the folder 'biasMD'.

* Input files: Files contained in folder `./md_data` and its sub-folders. They include files for initial conditions for MD simulations, force field files for GROMACS, and files for visualizing the trajectories generated by the executables in UCSF Chimera.

* Executables: File `'gmx_d'` is the executable of custom GROMACS codes generated on Intel Xeon x86-64 CPU with Centos 7 Linux operating system. File `'runMD.sh'` is the script file to run the executable.

* Output files: In the command line below, if the first argument is '0', the output file is `'MA-CA.trr'` in the destination folder you specified. This file is a GROMACS trajectory file for an RC-uncovered trajectory along `u_0` of HIV protease bound to MA/CA peptide. If the first argument is '1', the output file is `'DRV.trr'` in the destination folder you specified. This file is a GROMACS trajectory file for an RC-uncovered trajectory along `u_0` of HIV protease bound to DRV. Each trajectory contains only protein and ligand atoms, while the water atoms are neglected to minimize the file size. Each trajectory is 100 ps in duration, saved at 0.5 ps interval.

* Command line to run the executable:

1) To generate an RC-uncovered trajectory along u_0 of HIV protease bound to MA/CA peptide, use the following command line:

```
$ ./runMD.sh 0 <trajectory : folder>
```

where <trajectory : folder> is the destination folder to store the GROMACS trajectory generated by the executable.

2) To generate an RC-uncovered trajectory along u_0 of HIV protease bound to DRV, use the following command line:

```
$ ./runMD.sh 1 <trajectory : folder>
```

** Estimated simulation time: On an HPC computing node with Intel Xeon CPU (16 cores, 2.60 GHz, 128 GB memory), a simulation of 100 ps requires around 1 hour 30 minutes.

* Steps to visualize the trajectory files generated above in UCSF Chimera.

a) Open a Chimera window. In this window, click: Tools —> MD/Ensemble Analysis —> MD movie. A panel titled 'Get Ensemble Info' will show up.

b) There are three boxes in this panel.

In the 'Trajectory format' box, select 'GROMACS'.

In the 'Run input (.tpr)' box, type in: './md_data/DRV.tpr', or click 'Browse' button and select this file from the corresponding folder.

In the 'Trajectory (.trr or .xtc)' box, type in: '<trajectory : folder>/DRV.trr', or click 'Browse' button and select this file from folder <trajectory : folder> specified above.

c) Press 'OK' button at the bottom of the panel, and the system and the trajectory 'DRV.trr' will load into the Chimera window.

The steps above are for visualizing the RC-uncover trajectory for HIV protease bound to DRV. To visualize the trajectory for HIV protease bound to MA/CA peptide, follow the same steps but replace 'DRV.tpr' and 'DRV.trr' by 'MA-CA.tpr' and 'MA-CA.trr'.