

This folder contains the source codes for generating RC-uncovered trajectories using our custom codes in GROMACS and the input files necessary for obtaining RC-uncovered trajectories along u\_0 of HIV protease bound to MA/CA peptide and u\_0 of HIV protease bound to DRV.

**1. Input files:** Files in folder ./md-data and its sub-folders.

**2. Source codes:** Files in folder ./gromacs-2019.2-code.

**3. Installation instructions.** To install the custom code, please follow the steps listed below.

1). Download GROMACS 2019.2 from GROMACS website: (<https://manual.gromacs.org/2019.2/download.html>).

2). unzip the download file gromacs-2019.2.tar.gz

```
$ tar -zyxf gromacs-2019.2.tar.gz
```

3). After unzipping, there will be a folder './gromacs-2019.2' in your current folder. Copy the following file/folder to this folder.

```
$ cp -r gromacs-2019.2-code ./gromacs-2019.2
$ cp cptofolder.sh ./gromacs-2019.2
$ cp install_GMX2019.2.sh ./gromacs-2019.2
$ cp -r md_data ./gromacs-2019.2
$ cp runMD.sh ./gromacs-2019.2
```

4). Replace the official GROMACS codes by the custom codes we provided using command line:

```
$ cd gromacs-2019.2
$ ./cptofolder.sh
```

5). Install GROMACS with our custom codes using command line:

```
$ ./install_GMX2019.2.sh
```

6). After installation completes, a new executable file of GROMACS with our custom code is generated:

```
./buildinstallpath/bin/gmx_d
```

**4. Command line to run the executable generated above:**

a) 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 : path>
```

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

b) To generate an RC-uncovered trajectory along u\_0 of HIV protease bound to DRV, use the following command line:

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

\* 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.

**5. Output files.** In the command line above, 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.

**6. Installation requirements.** The installation procedure above was test installed on Intel Xeon x86-64 CPU with Centos 7 Linux operating system. The installation process should take about 3 minutes. 'CMake 3.13.3' and 'GCC compiler 8.2.0' were used for compilation. Our custom codes do not have dependencies. For dependencies related to GROMACS installation, please refer to GROMACS 2019.2 tutorial for detailed instructions.

## 7. 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'.