MM/GBSA tutorials for SARS-CoV-2 Mpro in complex with inhibitor N3 by MolAICal and NAMD

Qifeng Bai
Email: molaical@yeah.net
Homepage: https://molaical.github.io
School of Basic Medical Sciences
Lanzhou University
Lanzhou, Gansu 730000, P. R. China

1. Introduction

In this tutorial, we introduce the MM/GBSA calculations of SARS-CoV-2 Mpro based on molecular dynamical (MD) simulated results by NAMD and MolAICal. This tutorial is just a demo. To save running and storage space, only 25 frames of MD simulated trajectories of SARS-CoV-2 Mpro are selected for this tutorial.

2. Materials

2.1. Software requirement

1) MolAICal : https://molaical.github.io
2) NAMD: https://www.ks.uiuc.edu/Research/namd/

2.2. Example files

1) All the necessary tutorial files are downloaded from:
https://github.com/MolAICal/tutorials/tree/master/004-MMGBSA

3. Procedure

Go to the tutorial directory:
#> cd 004-MMGBSA

1. Extracting trajectory of protein in complex with ligand

#> vmd -dispdev text -psf "mpro.psf" -e stripDCD.vmd -args protein,or,resname,LIG "mpro.dcd" "complex" mpro.psf mpro.pdb

-args: it is the usage liking “atomselect” of VMD software such as "atomselect top protein". Here, comma "," represents blank space " ".

It will generate complex.psf, complex.pdb and complex.dcd. Turning on the parameters of “GBIS” and “sasa”. Open “complex.conf” and modify the appropriate parameters of red fonts as below:

---

structure complex.psf
coordinates complex.pdb
outputName complex

paraTypeCharmm on
parameters par_all36_prot.prm
parameters par_all36_cgenff.prm
parameters ligand.str
parameters toppar_water_ions.str

coorfile open dcd complex.dcd

Our tutorial is run by CPU. You can run it on GPU. Running NAMD command as below:
#> namd2 +p3 complex.conf >& complex.log &

2. Extracting trajectory of protein only.
#> vmd -dispdev text -psf "mpro.psf" -e stripDCD.vmd -args protein "mpro.dcd" "protein" mpro.psf mpro.pdb

It will generate protein.psf, protein.pdb and protein.dcd. Open "protein.conf" and modify the appropriate parameters liking "complex.conf"

Our tutorial is run by CPU. You can run it on GPU. Running NAMD command as below:
#> namd2 +p3 protein.conf >& protein.log &

3. Extracting trajectory of ligand only.
#> vmd -dispdev text -psf "mpro.psf" -e stripDCD.vmd -args resname,LIG "mpro.dcd" "ligand" mpro.psf mpro.pdb

It will generate ligand.psf, ligand.pdb and ligand.dcd. Open "ligand.conf" and modify the appropriate parameters liking "complex.conf"

Our tutorial is run by CPU. You can run it on GPU. Running NAMD command as below:
#> namd2 +p3 ligand.conf >& ligand.log &

4. Calculating MM/GBSA by MolAICal
#> molaical.exe -mmgbsa -c complex.log -r protein.log -l ligand.log

The output contains the binding free energy ΔG as below:
---
delta E(internal): -4.0000007572871255E-6
delta E(electrostatic) + deltaG(sol): 7.702936000001536
delta E(VDW) + deltaG(sol): -44.43611599999989
delta G binding: -36.73318399999911
