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

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1. Introduction

In this tutorial, the MolAICal (https://doi.org/10.1093/bib/bbaa161) is used to calculate the MM/GBSA between ligand N3 and SARS-CoV-2 Mpro based on molecular dynamical (MD) simulated results by NAMD. This tutorial is just a demo. To save running and storage space, only 25 frames of MD simulated trajectories of SARS-CoV-2 Mpro in complex with N3 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

3.1. 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 like the command "atomselect" of VMD software such as "atomselect top protein or resname LIG". 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 in Linux operating system as below:

#> namd2 +p3 complex.conf >& complex.log &

Where the symbol "&" assigns the command to run in the background on the Linux operating system. If NAMD runs on Windows operating system, the symbol "&" must be omitted. For instance:
#> namd2 +p3 complex.conf > complex.log

3.2. 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 in the similar way of "complex.conf"

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

3.3. 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 in the similar way of "complex.conf"

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

3.4. 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:
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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