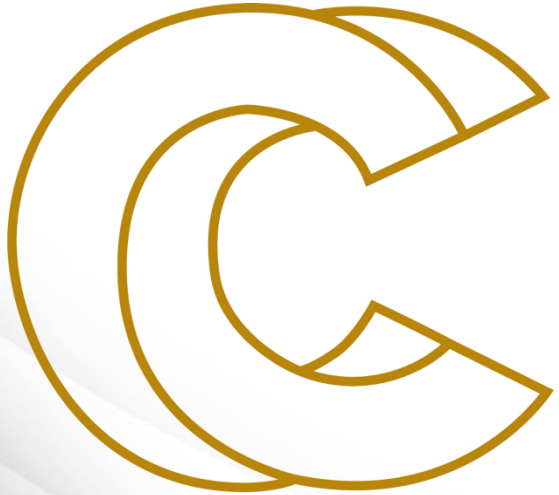

EURO 4SEE

MM/GB(P)SA free energy calculations using various programs

Assoc.Prof Sefer BADAY
Istanbul Technical University, Informatics Institute

ncc@ulakbim.gov.tr

Lesson 1: MM/PBSA calculation using CaFE

General Information about CaFE

- CaFE is a VMD plugin that supports MM/PBSA and LIE energy calculations
- Amber and NAMD Simulation trajectories are supported.
- Uses NAMD to calculate energy values

Workflow for MM/PBSA

Before

- Topology file generation
- Conformational Sampling by MD simulation

Preparation by Cafe

- Post Processing the trajectory file
- Removing water molecules etc.
- Creating complex, receptor and ligand protein structure files

Calculations

- Calculating the gas-phase energy
- Calculating the PB energy by solving solving the Poisson–Boltzmann (PB) equation
- Calculate the SASA term

END

- Obtaining DeltaG values for binding for each frame

What programs do you need?

General Information about CaFE

- VMD program: Typically this is already installed in HPC centers.
- CaFE plugin
- NAMD
- APBS or Delphi

How to install Cafe Plugin

- Download the cafe program: https://github.com/HuiLiuCode/CaFE_Plugin
- Upload the folder into a path in your account on UHEM
- Rename the src folder into cafe1.0

```
[sbaday@altay:~/programs/CaFE_Plugin-master ]$ ls
LICENSE  README.rst  cafe1.0  doc  examples  image  patch
```

- Then create text file named .vmdrc in your home directory and write the following code in it:
- set auto_path [linsert $auto_path 0 {/ari/users/sbaday/programs/CaFE_Plugin-master}]
- Note that you should change the path of the CaFE_Plugin-master folder according to path in your account.

How to install APBS

- You can download pre-compiled binary files APBS-3.4.1.Linux.zip from the following link
- https://github.com/Electrostatics/apbs/releases
- But you need to register first to download the binary files
- https://server.poissonboltzmann.org/
- Once you downloaded the folder you can upload into your account.

Cafe input file

Mmpbsa.vmd

```
package require cafe 1.0

mmpbsa -top       com.psf \
       -trj       protein_500.dcd \
       -out       result.log \
       -par       ./toppar/par_all36m_prot.prm \
       -par       ./toppar/par_all36_na.prm \
       -com       "segname PROA or segname PROB or segname PROC or segname PROD or segname PROE" \
       -rec       "segname PROA or segname PROB or segname PROC or segname PROD " \
       -lig       "segname PROE" \
       -debug     2 \
       -first     0 \
       -last      -1 \
       -stride    1 \
       -mm        1 \
       -pb        2 \
       -pb_exe    apbs \
       -pb_bndcon 4 \
       -pb_rad    mparse \
       -pb_bcfl   mdh \
       -sa        1 \
       -sa_rad    mparse \
       -pb_chgm   spl2 \
       -sa        1 \
       -sa_rad    mparse \
       -sa_gamma  0.00542 \
       -sa_beta   0.92 \

quit
```

Give path for all necessary parameter files

Check all parameters especially for dielectric constant

Slurm file

- Load necessary modules
- Vmd –dispdev text command allows us to run vmd script on the command line

```
#SBATCH --output=slurm-%j.out
#SBATCH --error=slurm-%j.err


source ~/.bashrc
module load VMD/vmd-1.9.3.textmode-with-egl
module load ek-moduller-easybuild
module load NAMD/2.14-foss-2020a-mpi

export LD_LIBRARY_PATH=/ari/users/sbaday/programs/APBS-3.0.0.Linux/lib:$LD_LIBRARY_PATH
export PATH=/ari/users/sbaday/programs/APBS-3.0.0.Linux/bin:$PATH


vmd -dispdev text -e mmpbsa.vmd > mmpbsa_out.log
```

Output log file

Title	Frames	Mean	SD
Complex:			
Elec:	528	-17167.2686	115.5958
Vdw:	528	-4444.1349	61.3031
PB:	528	-16465.5005	184.0288
SA:	528	280.1833	2.1868
Gas:	528	-21611.4035	129.4984
Sol:	528	-16185.3172	183.0330
Pol:	528	-33632.7692	90.2774
Npol:	528	-4163.9516	61.9812
Total:	528	-37796.7208	97.6713
Receptor:			
Elec:	528	-17209.3168	116.9939
Vdw:	528	-4391.6769	61.2329
PB:	528	-16306.9694	183.0492
SA:	528	281.9521	2.1434
Gas:	528	-21600.9937	130.8541
Sol:	528	-16025.0173	182.1754
Pol:	528	-33516.2862	88.5659
Npol:	528	-4109.7248	61.8430
Total:	528	-37626.0110	98.0176
Ligand:			
Elec:	528	99.2389	2.9150
Vdw:	528	10.7170	3.2397
PB:	528	-256.8475	5.1927
SA:	528	6.7715	0.1630
Gas:	528	109.9559	4.3913
Sol:	528	-250.0760	5.1068
Pol:	528	-157.6086	3.5879
Npol:	528	17.4885	3.2752
Total:	528	-140.1201	4.5112
Delta:			
Elec:	528	-57.1907	18.3937
Vdw:	528	-63.1750	5.4287
PB:	528	98.3164	29.3337
SA:	528	-8.5403	0.2601
Gas:	528	-120.3657	19.1978
Sol:	528	89.7760	29.3317
Pol:	528	41.1257	13.1765
Npol:	528	-71.7153	5.5005
Total:	528	-30.5896	12.5441

* All energy values are in kcal/mol

Next lecture

We will see how we can run MM/GB(P)SA calculations using AmberTools

References

https://github.com/HuiLiuCode/CaFE_Plugin

https://github.com/HuiLiuCode/CaFE_Plugin/blob/master/doc/manual.pdf

Liu, Hui, and Tingjun Hou. "CaFE: a tool for binding affinity prediction using end-point free energy methods." *Bioinformatics* 32, no. 14 (2016): 2216-2218.

APBS can be downloaded from https://www.poissonboltzmann.org/

EURO 4SEE

Thanks!

Co-funded by
the European Union

EuroHPC
Joint Undertaking

This project has received funding from the European High-Performance Computing Joint Undertaking (JU) under grant agreement No 101191697. The JU receives support from the Digital Europe Programme and Germany, Türkiye, Republic of North Macedonia, Montenegro, Serbia, Bosnia and Herzegovina.