Free energy of CIT and CRN

1. Build solute and water box

gmx editconf -f water\_martini3.gro -o water\_newbox.gro -box 11.84 11.84 23.68 -center 5.92 5.92 5.92

gmx editconf -f cg\_cit.gro -o cit\_new.gro -box 11.84 11.84 23.68 -center 5.92 5.92 5.92

gmx solvate -cp cit\_new.gro -cs water\_newbox.gro -o cit\_water.gro

2. Build Octanol box

------------------------**creat OCOS BOX**-----------------------------

**a. indexer.py**

#!/usr/bin/env python

nmols = 1138 # Number of molecules

atspermol = 9 # AA atoms per molecule

beadspermol = 3 # CG beads per molecule

firstbead = 3 # AA atoms in the first bead

secondbead = 3 # AA atoms in the second bead

atsperbead = 3 # AA atoms per CG bead

lastbead = 3 # AA atoms in the last bead

outname = "mapping.ndx" # Output filename

with open(outname,'w') as NDX:

for mol in range(nmols):

for bead in range(beadspermol):

# The number of atoms (nats) might depend on whether it's a first,

# last, or middle bead. NDXs are 1-based

if bead==0:

nats = firstbead

startat = 1

elif bead==beadspermol-1:

nats = secondbead

startat = atspermol-secondbead+1

elif bead==beadspermol-1:

nats = lastbead

startat = atspermol-secondbead-lastbead+1

else:

nats = atsperbead

startat = (bead-1)\*atsperbead + firstbead + 1

startat += mol\*atspermol

ats = range(startat, startat + nats)

ats = " ".join(map(str, ats))

NDX.write("[ mol%dbead%d ]\n%s\n" % (mol+1,bead+1, ats))

**b.** *seq 0 3413 | gmx traj -f octanolnoh.gro -s octanolnoh.gro -oxt cg\_octanol.gro -n mapping.ndx -com -ng 3414*

**#creat octanol box (size *11.84 11.84 11.84)***

*gmx solvate -cp cg\_octanol.gro -cs cg\_octanol.gro -o octanol\_newbox.gro -box 11.84 11.84 11.84*

***#octanol minimization***

***edit*** *octanol.top index.ndx*

*[ molecules ]*

*OCO 5229*

*gmx grompp -f minimization.mdp -c octanol\_newbox.gro -p octanol.top -o oct\_minim.tpr -maxwarn 1*

*gmx mdrun -deffnm oct\_minim -v*

***#octanol equilibration***

***edit*** *oct\_equil.mdp*

*gmx grompp -f equilibration.mdp -c oct\_minim.gro -p octanol.top -o oct\_equil.tpr -maxwarn 1*

*gmx mdrun -deffnm oct\_equil -v*

***#extend octanol box with same dimensions of CIT\_water (11.84 11.84 23.68)***

*gmx editconf -f oct\_equil.gro -o octanol\_new.gro -box 11.84 11.84 23.68 -center 5.92 5.92 17.76*

---------------------------------------------------------------------

***#assemble two box***

gmx solvate -cp cit\_water.gro -cs octanol\_new.gro -o Cit\_Solv.gro

*>* ***gmx make\_ndx -f Cit****\_Solv.gro* ***-o system.ndx***

*name 2(2kda) ProDrug*

***3(W) | 4(WF) | 5(ION) | 6 (OCO) ------- Solvent***

***3(W) | 4(WF) | 5(ION) ------------ WATER***

***# Biphase minimization***

*gmx grompp -f minimization.mdp -c* ***Cit****\_Solv.gro -p system.top -o minimization.tpr -n system.ndx -maxwarn 1*

*gmx mdrun -deffnm minimization -v*

***# position restraint***

*gmx genrestr -f minimization.gro -n system.ndx -o* ***cit****\_res.itp -fc 100000 100000 100000*

***edit system.top***

*; Ligand position restraints*

*#ifdef POSRES\_* ***Cit***

*#include "****cit****\_res.itp"*

*#endif*

***edit equilibration.mdp***

*define = -DSTRONG\_POSRES*

***edit : 2kda\_mapped.itp***

[ position\_restraints ]

; i funct fcx fcy fcz

1 1 100000 100000 100000

2 1 100000 100000 100000

3 1 100000 100000 100000

***# Biphase equilibration***

*gmx grompp -f* ***equilibration****.mdp -c minimization.gro -p system.top -o* ***equilibration****.tpr -n system.ndx -r minimization.gro -maxwarn 1*

*gmx mdrun -deffnm* ***equilibration*** *-v*

***Umbrella sampling***

***#define the em.mdp, em2.mdp, eq.mdp file.***

*Add restraint conformation and pull code*

***; Bond parameters***

*continuation = no ; continuing from NPT*

*constraints =* ***none***

*constraint-algorithm = lincs*

***; pressure***

*Pcoupl = parrinello-rahman*

*Pcoupltype =* ***semiisotropic*** *; semiisotropic*

*tau-p = 12.0*

*compressibility =* ***4e-5 4e-5*** *;3e-4*

*ref-p =* ***1.0 1.0*** *;1.0*

***; Pull code***

*pull = yes*

*pull\_ncoords = 1 ; only one reaction coordinate*

*pull\_ngroups = 2 ; two groups defining one reaction coordinate*

*pull\_group1\_name = WATER*

*pull\_group2\_name = ProDrug*

*pull\_coord1\_type = umbrella ; harmonic potential*

*pull\_coord1\_geometry = distance ; simple distance increase*

*pull\_coord1\_dim = N N Y*

*pull\_coord1\_groups = 1 2*

***pull\_coord1\_start = no ; define initial COM distance > 0***

*pull-coord1-init = 0.0*

***pull\_coord1\_rate = 0,0 ; 0.01 nm per ps = 10 nm per ns***

*pull\_coord1\_k = 1000 ; kJ mol^-1 nm^-2*

***pull-pbc-ref-prev-step-com = yes***

***pull-group1-pbcatom = 6495***

***#pull.mdp#***

*> gmx grompp -f pull.mdp -c ../equilibration.gro -p ../../Parameters/system.top -o pull.tpr -n ../system.ndx*

*> gmx mdrun -nt 1 -deffnm pull -v &> pullrun.log*

**#em.mdp#**

*> gmx grompp -f em.mdp -c pull.gro -p ../../Parameters/system.top -o em.tpr -n ../system.ndx*

*> gmx mdrun -nt 1 -deffnm em -v &> emrun.log*

**#em2.mdp#**

*> gmx grompp -f em2.mdp -c em.gro -p ../../Parameters/system.top -o em2.tpr -n ../system.ndx*

*> gmx mdrun -nt 1 -deffnm em2 -v &> em2run.log*

***#eq.mdp#***

*> gmx grompp -f eq.mdp -c em2.gro -p ../../Parameters/system.top -o eq.tpr -n ../system.ndx*

*> gmx mdrun -nt 1 -deffnm eq -v -px eq\_x -pf eq\_f &> eqrun.log*

*gmx grompp -f pull.mdp -c ../equilibration.gro -p ../../Parameters/system.top -o pull.tpr -n ../system.ndx*

*gmx mdrun -nt 1 -deffnm pull -v &> pullrun.log*

*gmx grompp -f em.mdp -c pull.gro -p ../../Parameters/system.top -o em.tpr -n ../system.ndx*

*gmx mdrun -nt 1 -deffnm em -v &> emrun.log*

*gmx grompp -f em2.mdp -c em.gro -p ../../Parameters/system.top -o em2.tpr -n ../system.ndx*

*gmx mdrun -nt 1 -deffnm em2 -v &> em2run.log*

*gmx grompp -f eq.mdp -c em2.gro -p ../../Parameters/system.top -o eq.tpr -n ../system.ndx*

*gmx mdrun -nt 1 -deffnm eq -v -px eq\_x -pf eq\_f &> eqrun.log*

***Production***

*gmx grompp -f md.mdp -c ../../Initial/$window/eq.gro -p ../../Parameters/system.top -o md.tpr -n ../../Initial/system.ndx*

*gmx mdrun -nt 2 -deffnm md -v -px md\_x -pf md\_f -cpi md.cpt &> mdrun.log*

***Analysis***

***ls -d ../Production/\*/md.tpr > tpr-files.dat***

***ls -d ../Production/\*/md\_x.xvg > pullx-files.dat***

***gmx wham -ix pullx-files.dat -it tpr-files.dat -bsres -bins 200 -temp 300 -unit kJ -b 100 -nBootstrap 100 -zprof0 0.0 -min 0 -max 12***