Sample Input Files for MD Simulations Using Gromacs:

1. Topology File:

```
[ defaults ]
; nbfunc  comb-rule gen-pairs fudgeLJ        fudgeQQ
1         2         no        1               1
;nbfunc=1 for LJ; 2 for LB rule and 3 for geometric mixing rule.

[ atomtypes ]
; name  at_no    mass    charge    ptype   sigma    epsilon ;SPC/E
 U        92     238.0289   2.5     A      0.295       0.530
 Ou       8    15.99940    -0.25    A      0.383       0.057
 Ow       8    15.99940    -0.8476  A   3.165492e-01 0.650299455
 Hw       1    1.00800      0.4238  A         0        0

[ nonbond_params ]
; i   j    func sigma(c6)      eps(c12) ;SPC/E water model
U    Ow   1    0.306          0.587
U    Hw   1    0              0
Ou   Ow   1    0.350          0.192
Ou   Hw   1    0              0

[ moleculetype ]
; molname nrexcl
ION       2

[ atoms ]
; id at type        res nr    residu name    at name  cg nr charge
1    Ou        1    UO2       Ou1  1    -0.25
2    U         1    UO2       U    1     2.5
3    Ou        1    UO2       Ou2  1    -0.25


[ bonds ]
; i     j       funct   length  force.c.
1       2       1       0.1761   622300.0   ; By Vlad, from B3LYP
2       3       1       0.1761   622300.0

[ angles ]
```

```
; i     j       k       funct   angle   force.c.
1       2       3       1        180.000   198  ; By Vlad, from B3LYP

[ moleculetype ]
; molname nrexcl
SOL       2

[ atoms ]
;   nr   type  resnr residue  atom   cgnr     charge       mass
#ifndef HEAVY_H
     1      Ow      1    SOL     OW      1    -0.8476   15.99940
     2      Hw      1    SOL    HW1      1     0.4238    1.00800
     3      Hw      1    SOL    HW2      1     0.4238    1.00800
#else
     1      Ow      1    SOL     OW      1    -0.8476    9.95140
     2      Hw      1    SOL    HW1      1     0.4238    4.03200
     3      Hw      1    SOL    HW2      1     0.4238    4.03200
#endif

#ifndef FLEXIBLE
[ settles ]
; OW funct     doh  dhh
1    1    0.1  0.16330

[ exclusions ]
1    2    3
2    1    3
3    1    2
#else
[ bonds ]
; i  j    funct     length    force.c.
1    2    1    0.1  345000    0.1     345000
1    3    1    0.1  345000    0.1     345000

[ angles ]
; i  j    k    funct     angle     force.c.
2    1    3    1    109.47    383  109.47    383
#endif

[ system ]
Uranyl ion in water
```

```
[ molecules ]
ION          1
SOL          1000
```

2. Partial initial sample .gro file:

```
Uranyl ion in water
 3003
    1ION    Ou1    1   1.250   1.250   1.426
    1ION      U    2   1.250   1.250   1.250
    1ION    Ou2    3   1.250   1.250   1.074
    2SOL     OW    4   0.569   1.275   1.165
    2SOL    HW1    5   0.476   1.268   1.128
    2SOL    HW2    6   0.580   1.364   1.209
    3SOL     OW    7   1.555   1.511   0.703
    3SOL    HW1    8   1.498   1.495   0.784
    3SOL    HW2    9   1.496   1.521   0.623
    4SOL     OW   10   1.743   0.618   0.856
    4SOL    HW1   11   1.776   0.712   0.856
    4SOL    HW2   12   1.794   0.564   0.922
    5SOL     OW   13   1.135   0.703   0.717
    5SOL    HW1   14   1.192   0.781   0.692
    5SOL    HW2   15   1.075   0.729   0.793
      .
      .  (used genbox (included in Gromacs package) command to solvate the simulation box)
      .
  999SOL     OW 2995   2.945   2.846   1.949
  999SOL    HW1 2996   2.922   2.899   1.867
  999SOL    HW2 2997   3.026   2.790   1.930
 1000SOL     OW 2998   1.941   3.102   2.515
 1000SOL    HW1 2999   1.940   3.055   2.603
 1000SOL    HW2 3000   2.023   3.074   2.464
 1001SOL     OW 3001   2.290   2.286   2.382
 1001SOL    HW1 3002   2.320   2.214   2.320
 1001SOL    HW2 3003   2.251   2.246   2.465
   3.12000   3.12000   3.12000
```

3. MDP file for production run, for properties calculations other than hydration free energy (we are not including files for initial energy minimization and equilibration, as they will be trivial for reproducing our results):

```
integrator  = md
dt          = 0.002
tinit       = 0
nsteps      = 75000000
nstcomm     = 10
pbc           = xyz

constraint_algorithm    = lincs
continuation            = yes
nstxout                  = 0
nstvout                  = 50000
nstfout                  = 0
nstlog                   = 5000
nstenergy                = 5000
nstxtcout                = 20
;Such small frequency of saving trajectories is not necessary to
;reproduce results in this paper.
xtc-precision            = 1000
nstlist                 = 5
ns_type                 = grid
rlist                    = 1.48
coulombtype              = PME_switch
rcoulomb_switch          = 1.1
rcoulomb                 = 1.2
vdw-type                 = switch
rvdw-switch              = 1.1
rvdw                     = 1.2
lincs_order             = 9
DispCorr    = EnerPres          ; account for cut-off vdW scheme

; PME electrostatics parameters
fourierspacing  = 0.12
fourier_nx      = 0
fourier_ny      = 0
fourier_nz      = 0
pme_order       = 6
ewald_rtol      = 1e-6
```

```
optimize_fft    = yes

tcoupl      = nose-hoover
tc-grps     = System
tau_t       = 6           ; time constant, in ps
ref_t       = 298.15

pcoupl              = no
gen_vel             = no
```

4. For hydration free energy calculations.

Sample MDP file for production run (we are not including files for initial energy minimization and equilibration, as they will be trivial for reproducing our results):

Note: We used different MDP files for hydration free energy calculations of one ion. First, the ion was in totally decoupled state with water solvents, then it was made coupled from none to van der Waals coupled state (by changing `init_lambda` from 0 to 1). After this, ion was coupled from van der Waals coupled state to a fully coupled state: VDW+electrostatic interactions (again, by changing `init_lambda` from 0 to 1). `g_bar`, included in Gromacs package, was used twice to calculate the free energies of the two processes. The two numbers were added to get the final hydration free energies.

We used `init_lambda` as {0, 0.05, 0.10, … , 0.95, 1.0}, and correspondingly varied `foreign_lambda`. For e.g., for `init_lambda = 0.4`, `foreign_lambda = 0.35 0.45` was used; for `init_lambda = 0.7`, `foreign_lambda = 0.65 0.75` was used; and so on. For `init_lambda = 0.0`, `foreign_lambda = 0.05` was used; for `init_lambda = 1`, `foreign_lambda = 0.95` was used.

Sample MDP file for changing from no interaction to only VDW interactions between ion and water molecules:

```
integrator              = sd       ; Langevin dynamics
tinit                   = 0
dt                      = 0.002
nsteps                  = 1000000
comm_mode               = Linear
nstcomm                 = 10
lincs_order             =9

nstxout                 = 10000
nstvout                 = 20000
```

```
nstfout                  = 20000
nstlog                   = 2000
nstenergy                = 2000
nstxtcout                = 0
xtc-precision            = 1000

nstlist                  = 5 ;default: 10
ns_type                  = grid
pbc                      = xyz

rlist                    = 1.45
coulombtype              = PME-Switch
rcoulomb                 = 1.2
rcoulomb-switch          = 1.1
vdw-type                 = switch
rvdw                     = 1.2
rvdw-switch              = 1.1

DispCorr                  = EnerPres
; Spacing for the PME/PPPM FFT grid
fourierspacing           = 0.12
pme_order                = 6
ewald_rtol               = 1e-06
epsilon_surface          = 0
ewald_geometry           = 3d
optimize_fft             = yes

; tcoupl is implicitly handled by the sd integrator
tc_grps                  = system
tau_t                    = 2.0
ref_t                    = 298.15

Pcoupl                   = Parrinello-Rahman
tau_p                    = 2
compressibility          = 4.5e-05
ref_p                    = 1

gen_vel                  = no
continuation             = yes

; Sample input for free energy control, from no interaction to VDW
```

```
interactions.
free_energy              = yes
init_lambda              = 0.30 ;change this from 0 to 1
delta_lambda             = 0
foreign_lambda   = 0.25 0.35 ;change this according to init_lambda
sc-alpha                 = 0.5
sc-power                 = 1.0
sc-sigma                 = 0.3
couple-moltype           = ION  ; name of moleculetype to decouple
couple-lambda0           = none ; no interaction between ION and SOLs
couple-lambda1           = vdw  ; only vdw interaction
couple-intramol          = no
nstdhdl                  = 100
```

Part of sample MDP file for changing VDW only interaction to full (VDW+electrostatic) interactions between ion and water molecules:

```
;Copy rest of the missing part from above file.
;Sample input for free energy control, from VDW only interaction to
full (VDW+electrostatic) interactions:
free_energy              = yes
init_lambda              = 0.85 ;change this from 0 to 1
delta_lambda             = 0
foreign_lambda      = 0.80 0.90 ;change this according to init_lambda
sc-alpha                 = 0.0
sc-power                 = 1.0
sc-sigma                 = 0.0
couple-moltype           = ION     ; name of moleculetype to decouple
couple-lambda0           = vdw      ; vdw interactions
couple-lambda1           = vdw-q     ; vdw and charge interactions
couple-intramol          = no
nstdhdl                  = 100
```