

Preparing an MD simulation

the procedures – briefly

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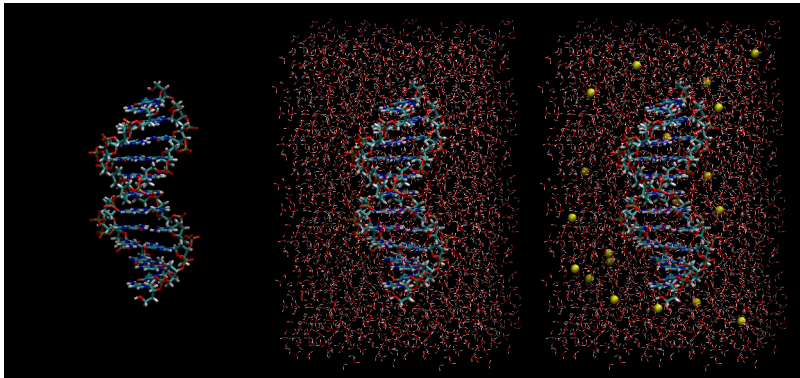
- ① build the initial structure
- ② bring the system into thermodynamic equilibrium
- ③ perform the productive simulation
- ④ analyze the trajectory

Tools to build the structure

- do it yourself
- specific programs within simulation packages
- 'universal' visualization programs – VMD, Molden, Pymol
- databases of biomolecular systems – PDB, NDB
- specialized web services – Make-NA
- tools to create periodic box and hydrate system

Tools to build the structure

build the solute, solvate it and add counterions



Why equilibrate?

- the initial structure may have high potential energy – dangerous – remove ‘close contacts’
- often, static structure available – velocities missing
- often, structure resolved at different conditions (xtal)
- structure of solvent artificially regular – entropy wrong

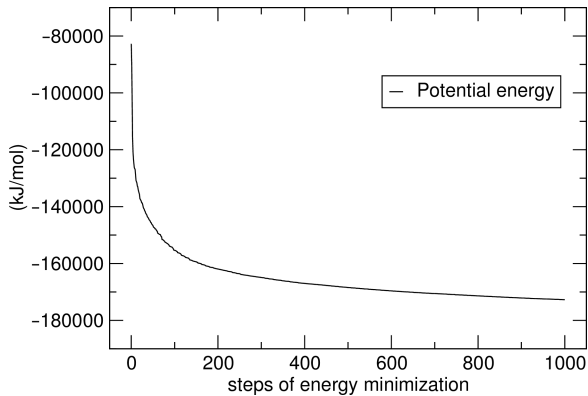
How to equilibrate

- 1 short energy minimization – remove ‘bad contacts’

Short energy minimization

```
integrator          = steep
nsteps             = 1000
pbc                = xyz
nstlist            = 10      ; update pairlist
;
coulombtype         = PME
vdwtype            = Cut-off
rlist              = 1.0     ; nm
rvdw               = 1.0     ; nm: cut-off for vdw
rcoulomb           = 1.0     ; nm
;
constraints         = hbonds
```

Short energy minimization



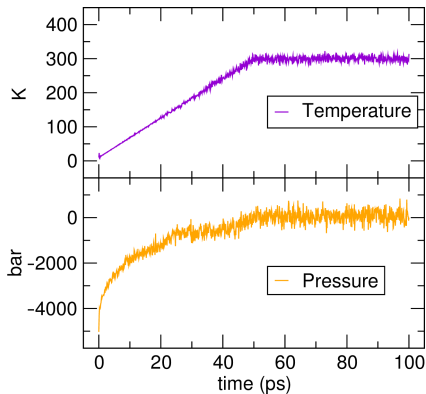
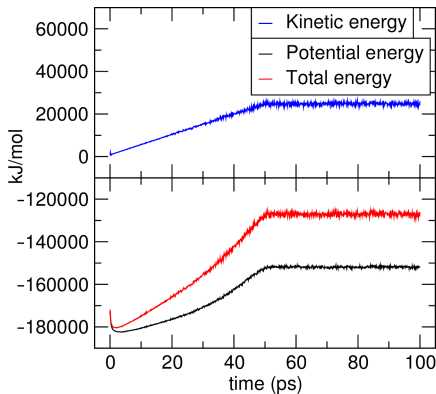
How to equilibrate

- ① short energy minimization – remove ‘bad contacts’
- ② assignment of velocities – randomly, at some (low) T
- ③ thermalization – heating the system up to the desired T , possibly gradually, with a thermostat – NVT simulation

Thermalization

```
integrator      = md
pbc             = xyz
dt             = 0.002    ; ps
nsteps         = 50000
nstlist        = 10       ; update pairlist
coulombtype     = PME
vdwtype        = Cut-off
rlist          = 1.0      ; nm
rvdw           = 1.0      ; nm
rcoulomb       = 1.0      ; nm
;
gen_vel        = yes
gen_temp       = 10.      ; K
constraints     = hbonds
;
tcoupl         = nose-hoover
tc_grps        = System
tau_t          = 0.5      ; ps
ref_t          = 300.     ; K
;
annealing      = single
annealing_npoints = 3
annealing_time = 0. 50. 100. ; ps
annealing_temp = 10. 300. 300. ; K
```

Thermalization



last 40 ps: $T = 300 \pm 7$ K, $p = 64 \pm 266$ bar

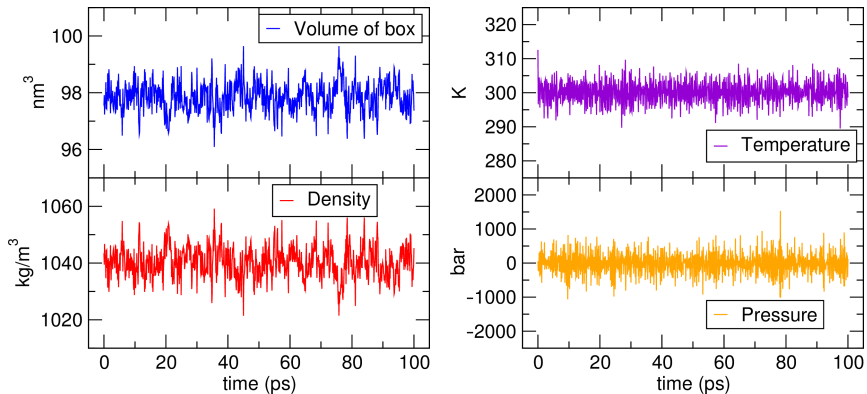
How to equilibrate

- ① short energy minimization – remove ‘bad contacts’
- ② assignment of velocities – randomly, at some (low) T
- ③ thermalization – heating the system up to the desired T , possibly gradually, with a thermostat – NVT simulation
- ④ simulation with the same setup as the production
– probably NPT, with appropriate thermostat and barostat

Equilibration

```
integrator      = md
pbc             = xyz
dt             = 0.002
nsteps         = 50000
nstlist        = 10           ; update pairlist
coulombtype     = PME
vdwtype        = Cut-off
rlist          = 1.0          ; nm
rvdw           = 1.0          ; nm
rcoulomb        = 1.0          ; nm
;
gen_vel         = no
constraints     = hbonds
;
tcoupl         = nose-hoover
tc_grps        = System
tau_t          = 0.5          ; ps
ref_t          = 300.         ; K
;
pcoupl         = parrinello-rahman
tau_p          = 0.5          ; ps
ref_p          = 1.0          ; bar
compressibility = 4.5e-5       ; 1/bar
```

Equilibration



last 40 ps: $T = 300 \pm 3$ K, $p = -11 \pm 331$ bar

What comes then?

Productive simulation

- easy 😊

Analysis of the trajectory

- let us see. . .