Recommended workflow for equilibrium molecular dynamics simulations with Gromacs 5.1 of surfactants adsorbed at the vacuum/water interface

VI-SEEM application Mol_Surf

The first step of the construction of a typical model system is geometry optimization of an isolated surfactant molecule by a quantum chemical method or an appropriate force field. The second step is replication of the molecule on the nodes of a regular 2D square lattice (for example, the software package VMD [http://www.ks.uiuc.edu/Research/vmd/] can be used) so that the final spacing of the certain number of molecules in total corresponds to a predefined area/surfactant. The commands used in VMD are the following:

```
1) set mol [mol new Molecule.gro type gro waitfor all]
2) set newmol [::TopoTools::replicatemol $mol X Y Z ]
3) animate write pdb replicated.pdb $newmol
```

where `Molecule.gro` is a Gromcs file containing the Cartesian coordinates of an isolated optimized molecule, the notations X, Y, and Z should be replaced by integer values corresponding to the number of surfactants in this direction. Since we study only monolayers Z=1 always but X and Y can be different values depending on the requirements for the area per molecule and model size. These surfactants are then rotated by 180° and translated along z (the axis coinciding with the long molecular axis) at a certain distance (measured between the sulfur atoms of the heads, denoted by Z_{tr} below) to obtain a mirror monolayer. Both monolayers are constructed in separate files for the opposite Z-directions and after that the files are concatenated. The following sequence of commands is used:

```
4) gmx editconf –f replicated.gro –translate 0 0 Ztr –o
   monolayer1.gro
5) gmx editconf –f replicated.gro –rotate 180 0 0 –o
   monolayer2.gro
6) gmx editconf –f monolayer2.gro –translate 0 0 Ztr –o
   monolayer2-surface.gro
7) cat monolayer1.gro monolayer2-surface.gro > surfactants.gro
```

After that water molecules are added to fill the gap between the surfactant heads and to fully solvate them. Then, counterions are randomly placed in the water to neutralize the negatively charged surfactants. If necessary, e.g., to mimic certain ionic strength, another type of ions are placed randomly again. Here are the commands for solvation and addition of ions:

```
8)  gmx solvate –cp surfactants.gro –cs –o surfactants_water.gro
9)  gmx grompp –f min.mdp –p surfactants-water.top –c surfactants-
    water.gro –n system.ndx –o ions.tpr
10) gmx genion –s ions.tpr –np 'counterions-number' –o
    surfactants-water-ions.gro
```

After step 10, the file surfactants-water.top should be corrected to reflect the increased number of ions and correspondingly reduced number of water molecules – one water molecule is replaced by one ion in the above procedure.

General remark on file types: The *.mdp files contain commands, keywords, and parameters for the calculation, while *.top files represent the description of the model system contents and call the particular force field used to compute energies and some files (*.itp) containing the topology and some force field parameters for the surfactants. Some sample files are enclosed to this workflow. Please consult the manual of Gromacs for further details.

It is recommended that periodic boundary conditions are applied in the three directions throughout the simulations but along z (the axis normal to the interface) vacuum is added to discontinue the periodicity in this direction.

The force field CHARMM36 [Pastor, R. W., MacKerell, A. D., Jr., J. Phys. Chem. Lett. 2011, 2, 1526–1532] is used for all ions and the model TIP3P [Jorgensen, W. L.; Chandrasekhar, J.; Madura, J. D.; Impey, R. W.; Klein, M. L., J. Chem. Phys. 1983, 79, 926−935] is employed for the water molecules. The following computational procedure is applied to all studied systems: energy minimization of the initial configuration (min.mdp), heating to the desired simulation temperature (heat.mdp), relaxation for several ns, depending on the model system size and specifics (relax.mdp), and production runs (prod.mdp). For each step, an input tpr file is generated by using the following command:

```
grompp –f *.mdp –p surfactants-water.top –c *.gro –o *.tpr
(Optional for specific atom selections present in the system: –n
*.ndx)
```

After that the simulation is run in serial interactive mode:

```
mdrun –v –s *.tpr –deffnm name-of-outputs
```

For a **parallel job** submitted to the HPC facility Avitohol, a sample script for the PBS queueing system is enclosed (queue_script.pbs).

Recommended main settings for atomistic MD (might be changed according to the specifics of the problem):

Leap-frog [M. P. Allen, D. J. Tildesley, Computer Simulation of Liquids, Clarendon Press, Oxford, 1987] to integrate the equations of motion with a time step of 2 fs. All MD simulations in NVT ensemble to comply with the selected surface concentration. Constant temperature maintained with the V-rescale thermostat with coupling constant of 0.1 ps. The Lennard-Jones potential truncated at 12 Å with a switch function turned on at 10 Å. The electrostatic interactions evaluated in the monopole approximation with the method PME [(a) Darden, T.; York, D.; Pedersen, L. J. Chem. Phys. 1993, 98, 10089-10092; (b) Essmann, U.;

Perera, L.; Berkowitz, M. L.; Darden, T.; Lee, H.; Pedersen, L. G. J. Chem. Phys. 1995, 103, 8577-8593; (c) Toukmaji, A.; Sagui, C.; Board, J.; Darden, T. J. Chem. Phys. 2000, 113, 10913-10927] with cutoff for the direct part of the sum of 12 Å with a switch function initiated at 10 Å.

Equilibration of the systems should be verified by monitoring the evolution of the total energy and temperature, and of the temperatures of the separate components (surfactants, water, and ions). All these parameters should fluctuate around constant average values during the production runs, which confirm that thermodynamic equilibrium has been attained. The obtained trajectories may then be analyzed statistically to extract desired properties.