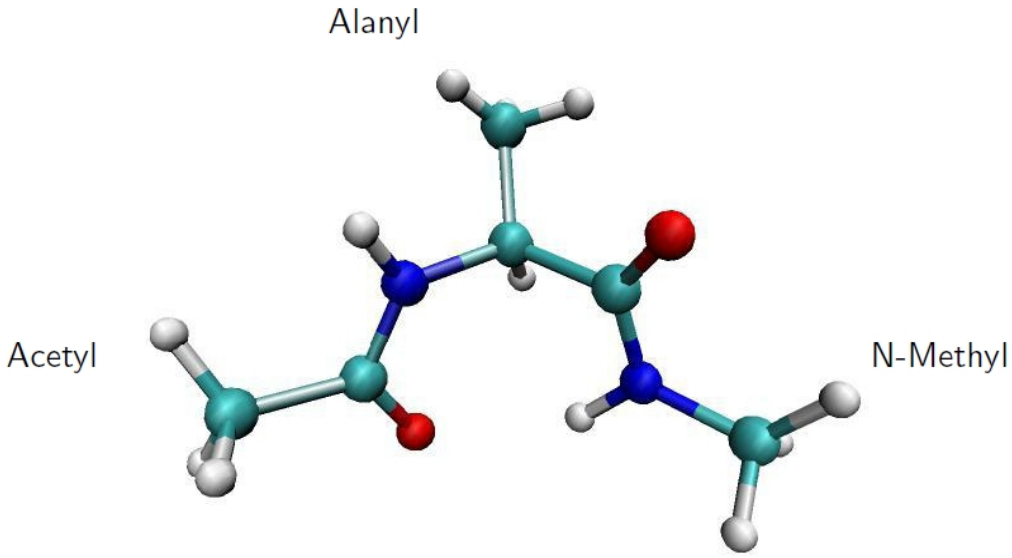
Protocol: Simulation of Alanine Dipeptide



In this exercises you will perform a **10 ns MD** simulation with **Gromacs** using the **Amber99sb-ILDN** force field with the **TIP3P** water model. **Check your setup after each preparation step by looking at the system using VMD.**

Attention: Follow the exercises and include the complete **Gromacs commands** for each step in your protocol!

Task - Perform all steps and answer the questions in the following steps

1) Prepare the starting structure *input.pdb* with *gmx pdb2gmx*.

2) Set up the simulation box with *gmx editconf* as a *dodecahedron* with a distance of *1.25 nm* between the molecule and the box edges.

3) Perform energy minimization of the molecule in vacuum. For the em.mdp file, use the settings proposed on em.mpd of our MD tutorial but use a maximum force of *100 kJ/mol/nm (emtol=100)*.

- Include your *.mdp file* in your answers.
- How many minimization steps were performed?
- Report the initial and final energy and force.

4) Solvate the molecule with *gmx solvate*.

- How many water molecules were added?

5) Add NaCl to the system at a concentration of 0.15 M with *gmx grompp* and *gmx genion*.

- How many Na^+ and Cl^- ions were added?

6) Perform an energy minimization of the whole system using a maximum force of 100 kJ/mol/nm (*emtol=100*) and a maximal number of 1000 steps (*nsteps=1000*).

- Include your .mdp file in your answers.
- Show the simulation box showing the peptide with CPK, water with Lines and ions as VDW. Use a white background.
- Report the initial and final energy and force.

7) Perform a 50-ps MD equilibration with positional restraints for the peptide.

Collect simulation data every 1.0 ps.

To study the effect of the influence of the thermostat, repeat this step with *different thermostats* (always start from the system obtained in step 6).

- Perform the equilibration with *tcoupl=no*, *tcoupl=berendsen*, *tcoupl=nose-hoover* and t*coupl=v-rescale*. Report your choice of *tau_t* for each thermostat. Show the complete *.mdp* file for one of the thermostats.
- How long does each MD simulation take?
- Describe and compare the potential energies and temperatures as a function of time for the thermostats **in few sentences**.

8) Perform a 10 ns MD simulation with *tcoupl=nose-hoover* using the structure from 7) which was prepared with t*coupl=v-rescale*.

Collect simulation data every 2.0 ps.

Hint: The simulation will take about 2–3 hours!

9) Analyze your obtained simulation:

- Create the Ramachandran plot.
- Plot the free energy surface (FES) as a function of the Ramachandran angles Φ and Ψ.
  Compare the Ramachandran plot and free energy surface.
- Identify the stable structures, name and show them. Mark them on the FES.
  Would you expect other stable structures as well?
- Analyze the transitions between the stable structures by plotting Φ and Ψ against time for 500 ps of the simulation.*
  Which transitions can you observe?
  What is the estimated time scale for the various transitions?
  Please, describe all answers **in few sentences**.

* **Help - Exmaple:**

```
~$ gnuplot
gnuplot> set datafile commentschars "#!%@"
gnuplot> set xlabel 'frame (2 ps)'
gnuplot> set ylabel 'phi (deg)'
gnuplot> plot [4750:5000] 'rama.xvg' using 1 with line notitle
gnuplot> set ylabel 'psi (deg)'
gnuplot> plot [4750:5000] 'rama.xvg' using 2 with line notitle
```