Simulation of Alanine Dipeptide in Implicit Solvent

In this exercises you will perform a **10 nsMD simulation of alanine dipeptide in implicit solvent** using Gromacs with the Amber99sb-ILDN force field and the GBSA solvent model.

General Notes:
Important things to consider if you set up an implicit solvent simulation:

I) **choice of forcefield:** ensure compatibility between the solvent model to use (GBSA in this case) with the forcefield (Amber99sb-ILDN, in our case).

II) **Structure file inspection:** each forcefield has a specific way in which the atom names are defined. Ensure the name of the atoms/residues in the PDB file agree with the ones in the forcefield files (forcefield.rtp, atomtype.dat). (The coordinates of alanine dipeptide below already have the atom names adapted to Amber's standard!).

III) **Three steps are required for implicit MD simulation using Gromacs:**
a) **Generate the topology file:**
gmx pdb2gmx -f ala2.pdb -ter -ignh -inter

IV) Select the force field Amber99sb-ILDN and None for the water model. It will automatically generate *conf.gro* and *topol.top* as output.

b) ***Energy minimization****:*
gmx grompp -f min-implicit.mdp -c conf.gro -p topol.top -o min.tpr
gmx mdrun -deffnm min -v >& min.out &

Note: there is **no need** to setup a box, add ions, or perform position restraint dynamics (equilibration) since implicit solvent MD utilizes a mean-field dielectric instead of actual atomic water particles for representing the solvent which implies there can be no clashes between water and the protein molecules.

c) ***Production run***:
gmx grompp -f md-implicit.mdp -c min.gro -p topol.top -o imd.tpr
gmx mdrun -deffnm imd -v >& imd.out &

Exercises:
All files, which you need, are provided on our website: http://www.strodel.info/teaching.php
For the following exercise, we will use our **computer cluster JUBIO and GROMACS 2016 (module load gromacs/2016)**. To copy something to **JUBIO** (for instance ala2.pdb), use the command on your computer (**not** in the **JUBIO** shell):
scp -r ala2.pdb biosimXX *@134.94.118.40:/home/biosimXY*

To copy the files from **JUBIO** to your computer, type the following command on your computer (**not** in the **JUBIO** shell; It will copy the files in your current directory!):
scp -r biosimXX@134.94.118.40*:/home/biosimXY/ala2.pdb .*

1) **Perform a 10 ns MD production run using *mdp* files *min-implicit.mdp* and *md-implicit.mdp*.**
Report the time needed for the simulation and compare with the time needed for the explicit-solvent MD run of alanine dipeptide.

2) **Analyze your simulation results**:
- Plot the free energy surface (FES) as a function of the Ramachandran angles Φ and Ψ.
- Identify the stable structures, name and show them. Mark them on the FES.
- Compare and describe your results to the FES obtained from the explicit-solvent MD simulation **in 5-8 sentences**.