Protein Model with Polarizability and Transferability (*proMPT*)
Gromacs Tutorial for Mini-Protein Trp-cage

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* For the original paper, please see: Sahoo, Abhilash, Pei-Yin Lee, and Silvina Matysiak. "Transferable and Polarizable Coarse Grained Model for Proteins— ProMPT." *Journal of Chemical Theory and Computation* 18, no. 8 (2022): 5046-5055.
* Python3 and Gromacs 2019.4 are used.

[Create topology for protein]
Either (1) a structure converted from PDB or (2) an extended structure can be used as the initial protein conformation.

1. [Converted topology from PDB] Use "*aa2cg.py*" to generate a CG conformation for the protein from the its PDB conformation. Files needed to provide: "*martinize_3.py*" (use MARTINI script to convert PDB file to a CG topology with only main beads and no dummies), "*1l2y.pdb*" (PDB file for Trp-cage), "*trial.gro*", and "*EG.gro*". A file named "*CG.gro*" will be created and this is our final CG protein topology.
2. [Random coil] Use "*create_indent.py*" to generate a CG conformation as an extended strand. Files needed to provide: "*seq.txt*". A file named "*protein.gro*" will be generated and this is our final CG protein topology.

[Create force field parameter files]
1. Use "*genff_proMPT.py*" to generate a system-specific CG force field. This force field file is system-specific because we take into account the cation-pi effects within the protein. Cation-pi effects are only effective when a positively charged residue and an aromatic residue are at least two residues away, and therefore it is sequence dependent. Files needed to provide: "*seq.txt*" (specify the protein sequence), "*martini_v2.P.itp*" (take parameters from MARTINI2.P). A file named "*proMPTff.itp*" will be generated and this will be our general force field.
2. Use "*genitp_md.py*" to generate the itp file for protein. Files needed to provide: "*seq.txt*" and "*1l2y.pdb*". A file named "*output.itp*" will be generated as the itp file for protein. Here we need to manually modify the table number for the backbone dihedral potential according to the desired secondary structure. In the [dihedral] section, the second to last value is the table number for the backbone dihedral. 1 is for alpha helix, 2 for 3-10 helix, 4 for beta-sheet, and 6 for double-well (same preference for alpha helix and beta sheet). Currently only alpha helix, 3-10 helix, and beta sheet automation based on the pdb file is implemented. We recommend to check the [dihedral] section before running simulations to make sure the assigned secondary structure is desired.
3. "*martini_v2.0_ions.itp*" and "*water.em.itp*"/"*water.md.itp*" are from MARTINI.

[Construct protein in a water box]

1. Create a protein in a box where the protein is at the center and the cubic box length is 1 nm larger than both sides of protein:
gmx_mpi editconf -f protein.gro -o box1.gro -c -d 1.0 -bt cubic
2. Solvate water:
gmx_mpi solvate -cp box1.gro -cs water_001.npt.gro -o box2.gro -p newprotein.top
Here the "*water_001.npt.gro*" is taken from MARTINI.
3. Add ions:
gmx_mpi grompp -f ions.mdp -c box2.gro -p newprotein.top -o ions.tpr
gmx_mpi genion -s ions.tpr -o ready.gro -p newprotein.top -nname CL -nn 1 (select group PW to be replaced)

[Energy minimization]

1. gmx_mpi grompp -f em.mdp -c ready.gro -p newprotein.top -o em.tpr
2. gmx_mpi mdrun -s em.tpr -c em.gro -tableb ./table_a/* ./table_d* -v Here the angular potential and the dihedral potential files need to be provided

[NPT equilibration]

1. First need to change "*water.em.itp*" to "*water.md.itp*" in "*newprotein.top*".
2. gmx_mpi grompp -f npt_posres_befion.mdp -p newprotein.top -c em.gro -o npt.tpr -maxwarn 1 -r em.gro

2. mpirun gmx_mpi mdrun -s npt.tpr -cpi state.cpt -tableb . /table_a/table_a*.xvg ./table_d*.xvg -deffnm npt_eq

[MD production run]

1. An NVT ensemble is used here, but an NPT ensemble can also be used. The simulation temperature is set at 350K, but it does not correspond to the real world 350K.
2. gmx_mpi grompp -f md.mdp -p newprotein.top -c npteq.gro -o md.tpr
3. mpirun gmx_mpi mdrun -s md.tpr -cpi npt_eq.cpt -tableb ./table_a/table_a*.xvg ./table_d*.xvg -deffnm md