Protein Model with Polarizability and Transferability (*proMPT*) Gromacs Tutorial for Amyloid Beta (Aβ) in Triethylamine Mesylate ([TEA][Ms])

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* For the original paper, please see: Pei-Yin Lee, and Silvina Matysiak. *Manuscript in preparation. 2023.*
* Python3 and Gromacs 2019.4 are used.

[Create topology for Aβ]

Use "*create_indent.py*" to generate a CG conformation as an extended strand for A**β** peptide. File needed to provide: "*seq.txt*". A file named "*protein.gro*" will be generated and this is our CG protein topology for A**β**.

[Create force field parameter files]

1. File "*fixedff_abeta_D23-9_cationpi2.itp*" is the force field file that is derived from *ProMPT*. Additional parametrization were done to adjust the *ad-hoc* non-bonded interaction parameters related to [TEA][Ms].
2. Use "*genitp_md.py*" to generate the itp file for A**β**. File needed to provide: "*seq.txt*". A file named "*output.itp*" will be generated as the itp file for A**β**. 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. Here the second to last column should be 6 (double-well) and the last column should be 10 (the force constant).
3. Files "*water.em.itp*"/"*water.md.itp*" are from MARTINI for water.
4. File "tea_D3.itp" is the force field for [TEA] cation and file "mesylate.itp" is the file for [Ms] anion.

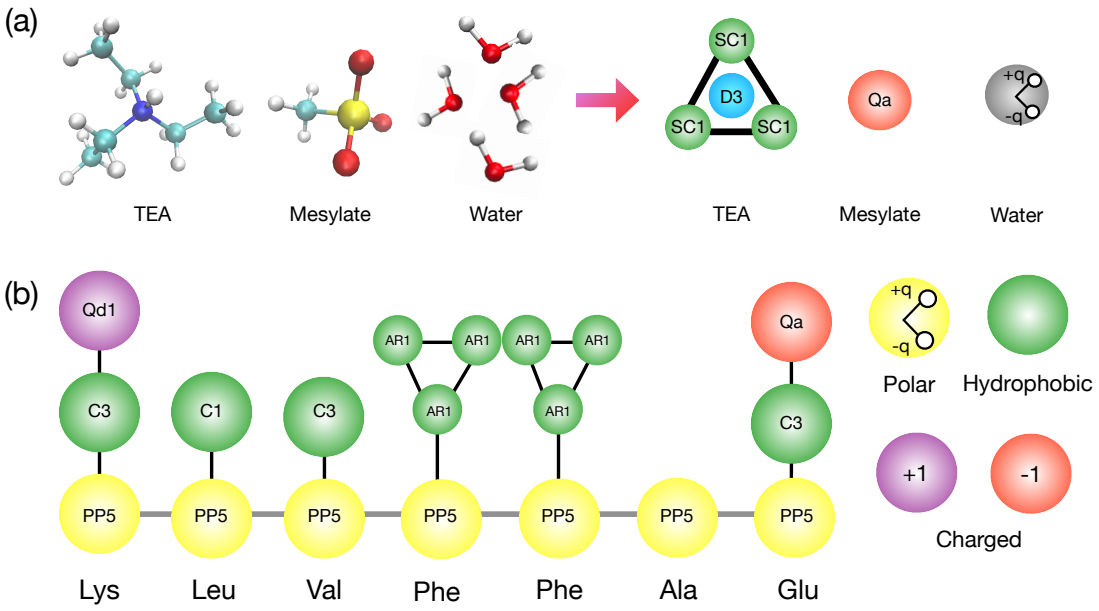

Figure: The CG mapping scheme for (a) [TEA][Ms] and (b) A$\beta_{16\text{-}22}$ peptide. On the left side of (a) shows the atomistic scheme for the IL and water, where nitrogen is in blue, carbon is in cyan, hydrogen is in white, sulfur is in yellow, and oxygen is in red. On the right side of (a) is the CG scheme for the IL where the bead types are marked.

[Construct the simulation system for 8 Aβ peptides in 10 wt% [TEA][Ms] to study Aβ aggregation in ionic liquid]

1. Create a box that has 8 Aβ peptides being randomly placed:

gmx_mpi insert-molecules -ci protein.gro -o box1.gro -nmol 8 -box 7.5 7.5 7.5

2. Add [TEA] cations:

gmx_mpi insert-molecules -f box1.gro -ci tea.gro -o box2.gro -nmol 101

3. Add [Ms] anions:

gmx_mpi insert-molecules -f box2.gro -ci mesylate.gro -o box3.gro -nmol 101

4. Solvate water:

gmx_mpi solvate -cp box3.gro -cs water_001.npt.gro -o ready.gro -p newprotein.top -maxsol 2500

*Here the "*water_001.npt.gro*" is taken from MARTINI.

*Note that the number of cations, anions, and water depend on the size of the box. Just make sure that the concentration of [TEA][Ms] is 10 wt% (or any desired concentration). In addition, the water molecules used here is coarse-grained, so there is a 1 to 4 mapping to the atomistic water molecules. When calculating the needed CG water molecules, this should be taken into consideration.

[Energy minimization]

1. Generate the tpr file for energy minimization: gmx_mpi grompp -f em.mdp -c ready.gro -p newprotein.top -o em.tpr
2. Run simulation:

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. Generate the tpr file for NPT equilibration: gmx_mpi grompp -f npt_posres_befion.mdp -p newprotein.top -c em.gro -o npt.tpr -maxwarn 1 -r em.gro -r em.gro.

3. Run simulation:

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. Generate the tpr file for MD production run: gmx_mpi grompp -f md.mdp -p newprotein.top -c npteq.gro -o md.tpr
3. Run simulation: mpirun gmx_mpi mdrun -s md.tpr -cpi npt_eq.cpt -tableb ./table_a/table_a*.xvg ./table_d*.xvg -deffnm md