Force Field Parameterization of a Small Molecule

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- Initially developed in the research group of Prof. Martin Karplus
- Mainly focus on biomolecules (proteins, DNA and carbohydrates)
- Currently being expanded to include materials.
- Compatible with many MD codes: NAMD, LAMMPS and GROMACS
- Requires two types of files: a topology file (top_all36*) and parameter file (par_all36*)

$$V(r^N) = \sum_{i,j}^{VdW} \epsilon_{ij} * \left[\left(\frac{\sigma_{ij}}{r_{ij}} \right)^{12} - \left(\frac{\sigma_{ij}}{r_{ij}} \right)^{6} \right] + \sum_{i,j}^{electrostatics} \frac{q_i q_j}{4\pi\epsilon_0 r_{ij}}$$

$$+ \sum_{i}^{bonds} k_b^i (r_i - r_i^{min})^2 + \sum_{j}^{angles} k_\theta^j (\theta_j - \theta_j^{min})^2 + \sum_{m}^{dihedrals} k_\delta^m (1 + cos(n\phi - \delta)) + \sum_{l}^{impropers} k_\psi^l (\psi_l - \psi_l^{min})^2$$

BONDS

atomtype1	atomtype2	fc	r_min
CG1N1	CG2R61	345.00	1.4350

ANGLES

atomtype1	atomtype2	atomtype3	fc	theta_min
CG2R61	CG1N1	NG1T1	40.00	180.00

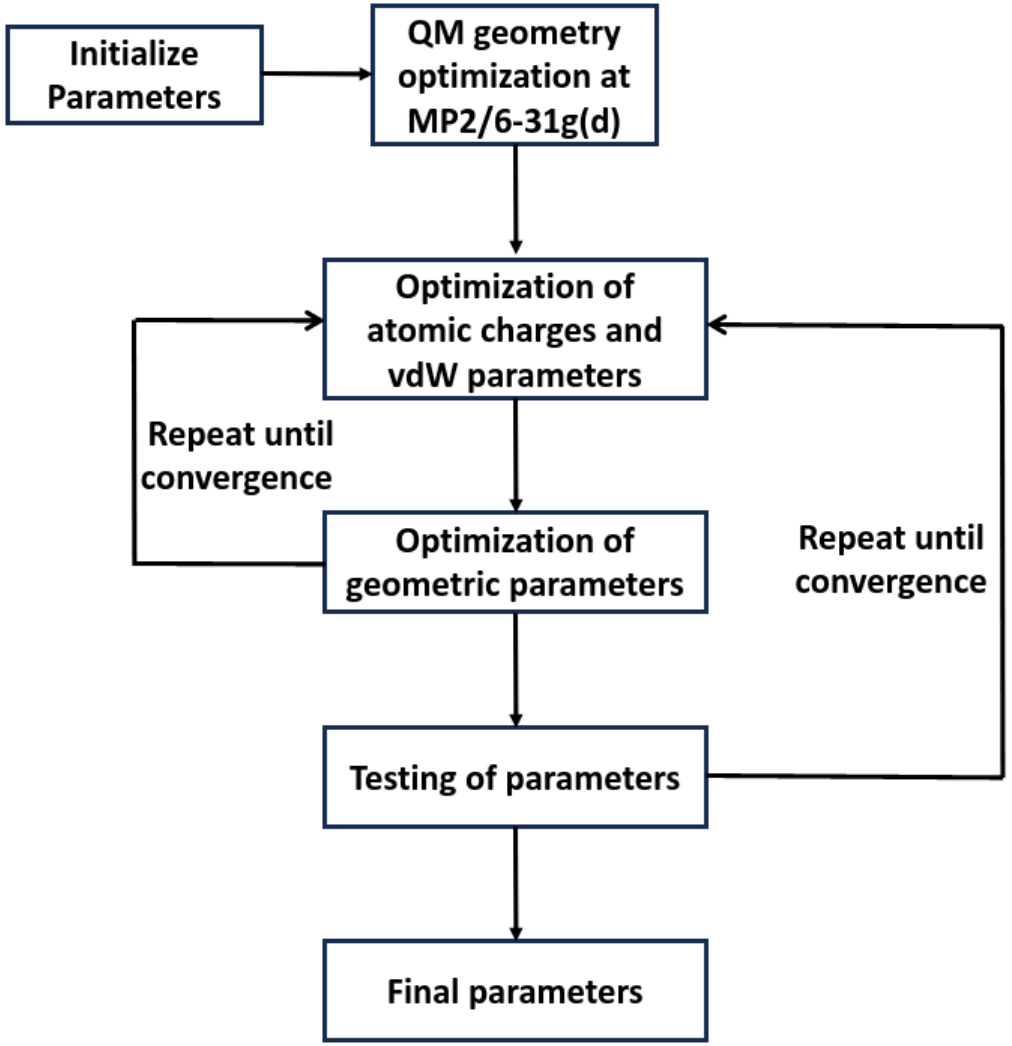
DIHEDRALS

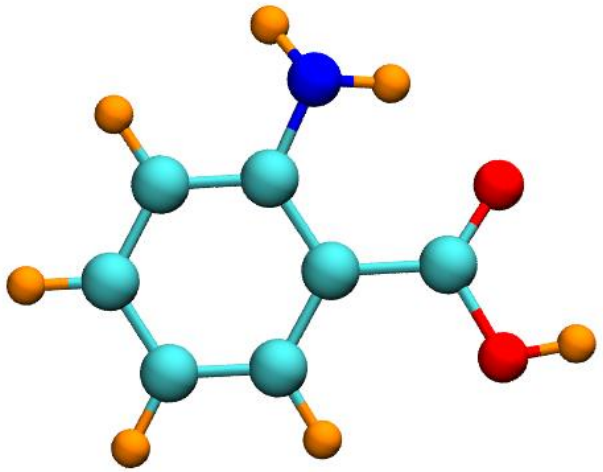
atomtype1	atomtype2	atomtype3	atomtype4	fc	n	phi_min
CG2R53	CG251O	CG25C1	CG2R53	6.4000	2	180.00

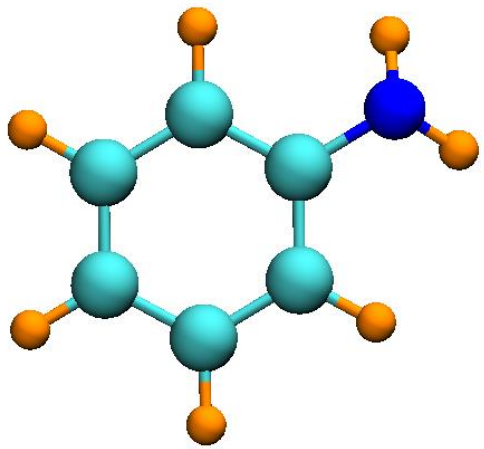
Force constants for bonds > Force constants for angles > Force constants for dihedrals

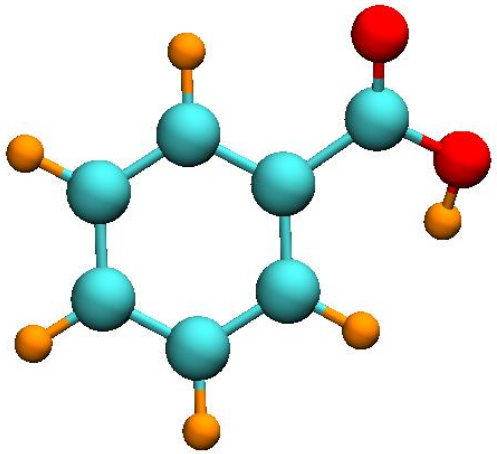
Why??

Conformational transitions in biomolecules are controlled by dihedral torsions


Initialize Parameters
QM geometry optimization at MP2/6-31g(d)
Optimization of atomic charges and vdW parameters
Repeat until convergence
Optimization of geometric parameters
Repeat until convergence
Testing of parameters
Final parameters







Building the Molecule

- Copy files from /ocean/projects/see220002p/shared/charmm_tutorials
- Change directory to mm_files
- Modify step1_build.inp according to instructions (edit breakpoints)
- Obtain the correct crd, psf and pdb files.

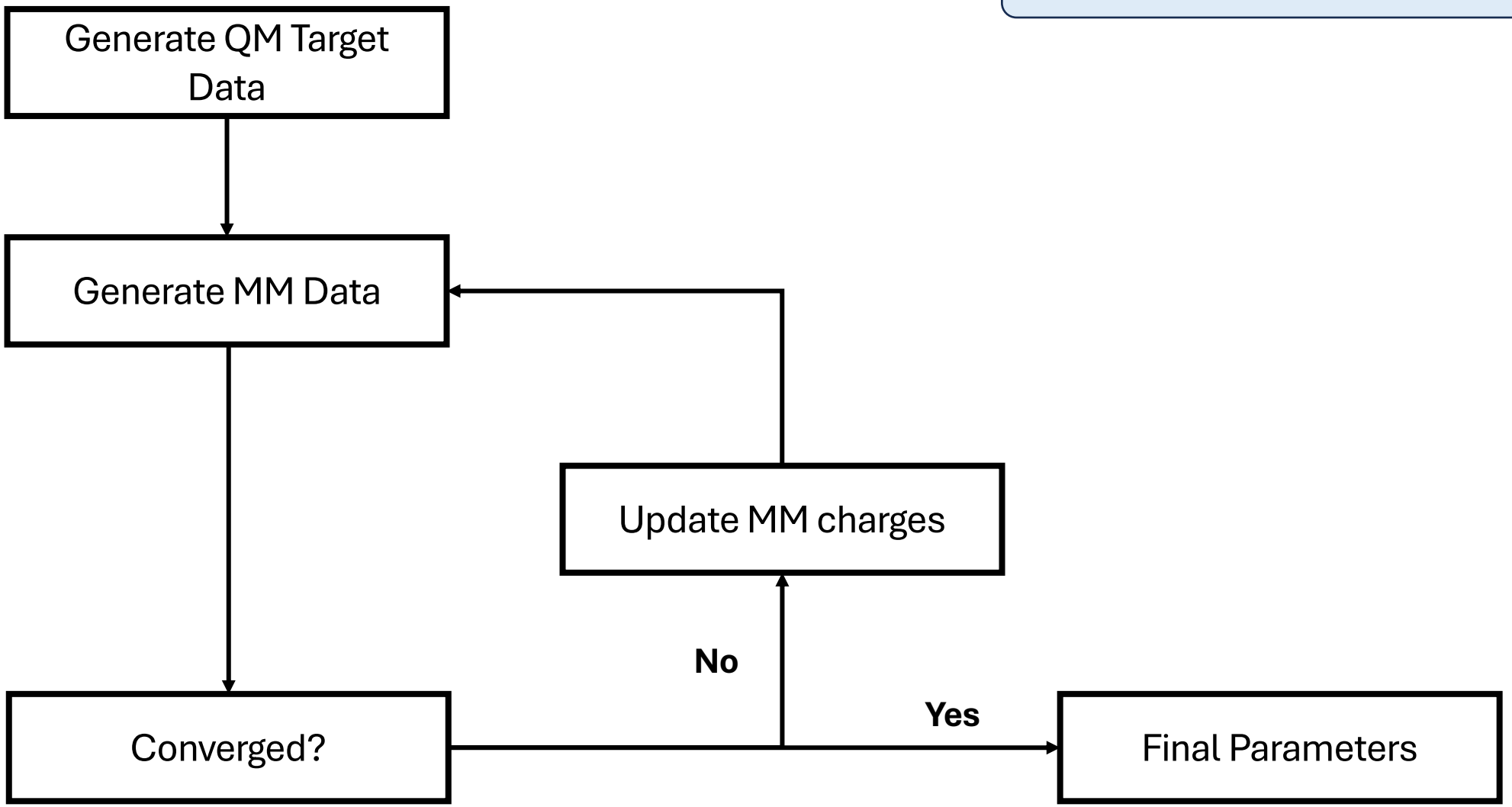
Optimizing Partial Charges

- Modify step2_water.inp according to instructions (edit breakpoints)
- Compare the MM energies with QM energies (provided in qm_files/water)
- Rerun step2_water.inp after modifying partial charges in mol.str file
- Obtain convergence

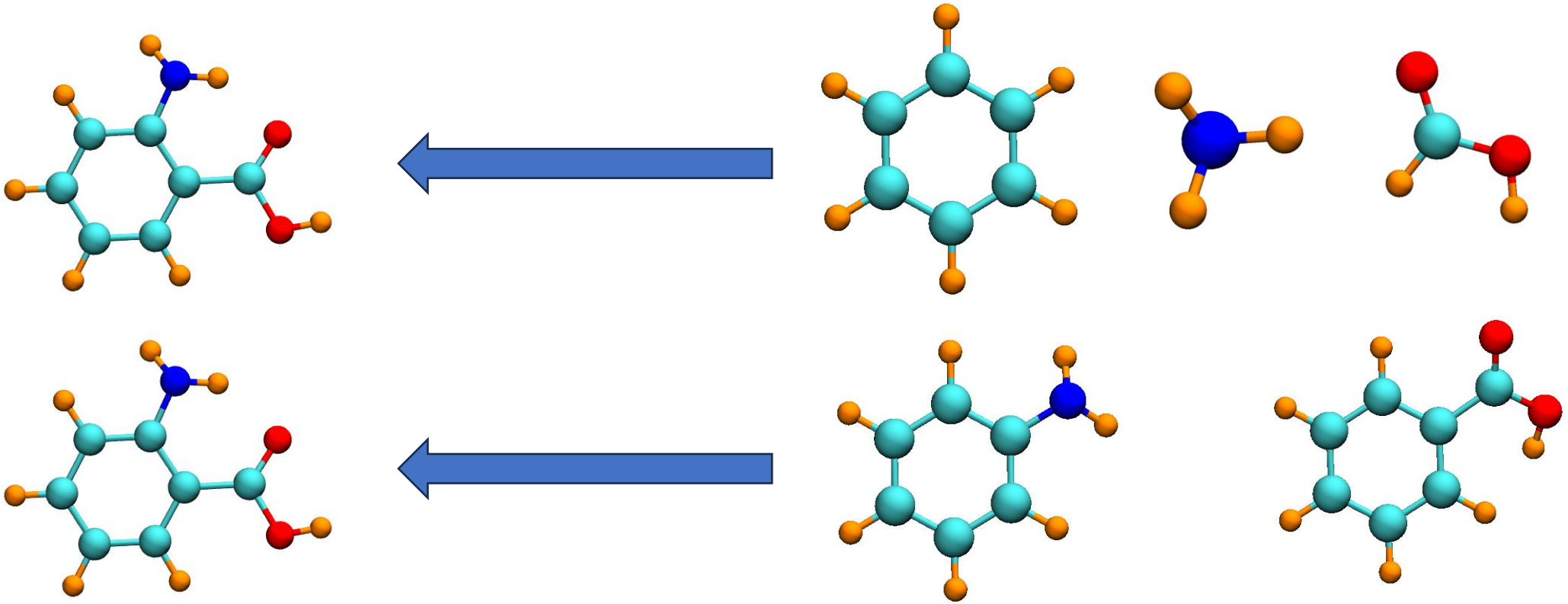
Optimizing Dihedrals

- Modify step3_dihe.inp according to instructions.
- Prepare input files for lsfit according to instructions.
- Run lsfitpar according to instructions.
- Modify mol.str file and rerun step3_dihe.inp
- Obtain convergence.

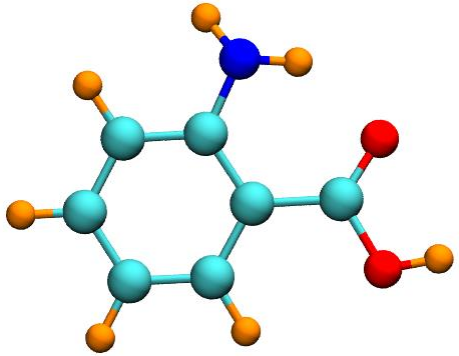
Fitting Partial Charges

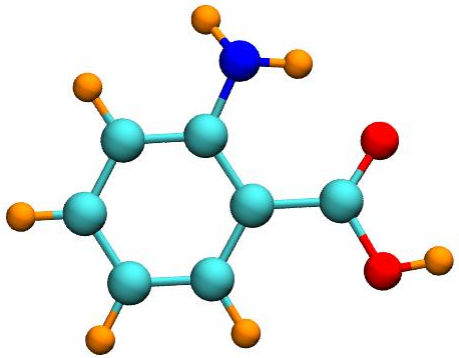


- The parameters are transferred based on chemical similarity from the CHARMM parameter library.
- Each transfer is then assigned a penalty depending on how close are the chemical environments in the target and source molecules.

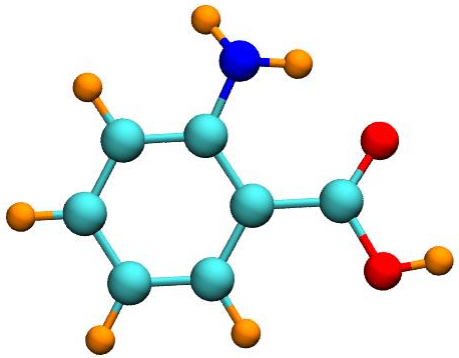


Fitting Bonded Parameters





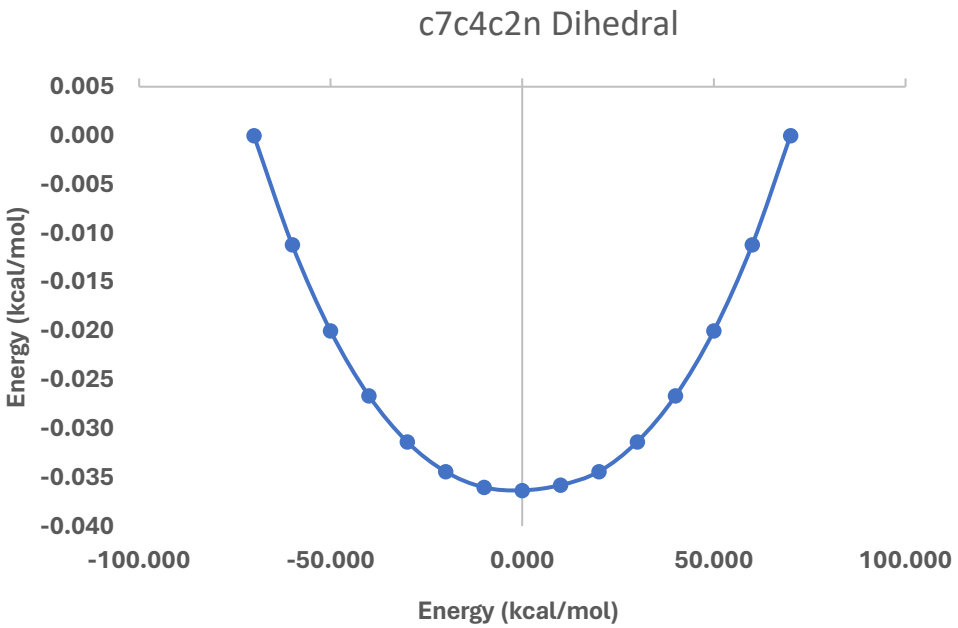
MM minimized Geometry

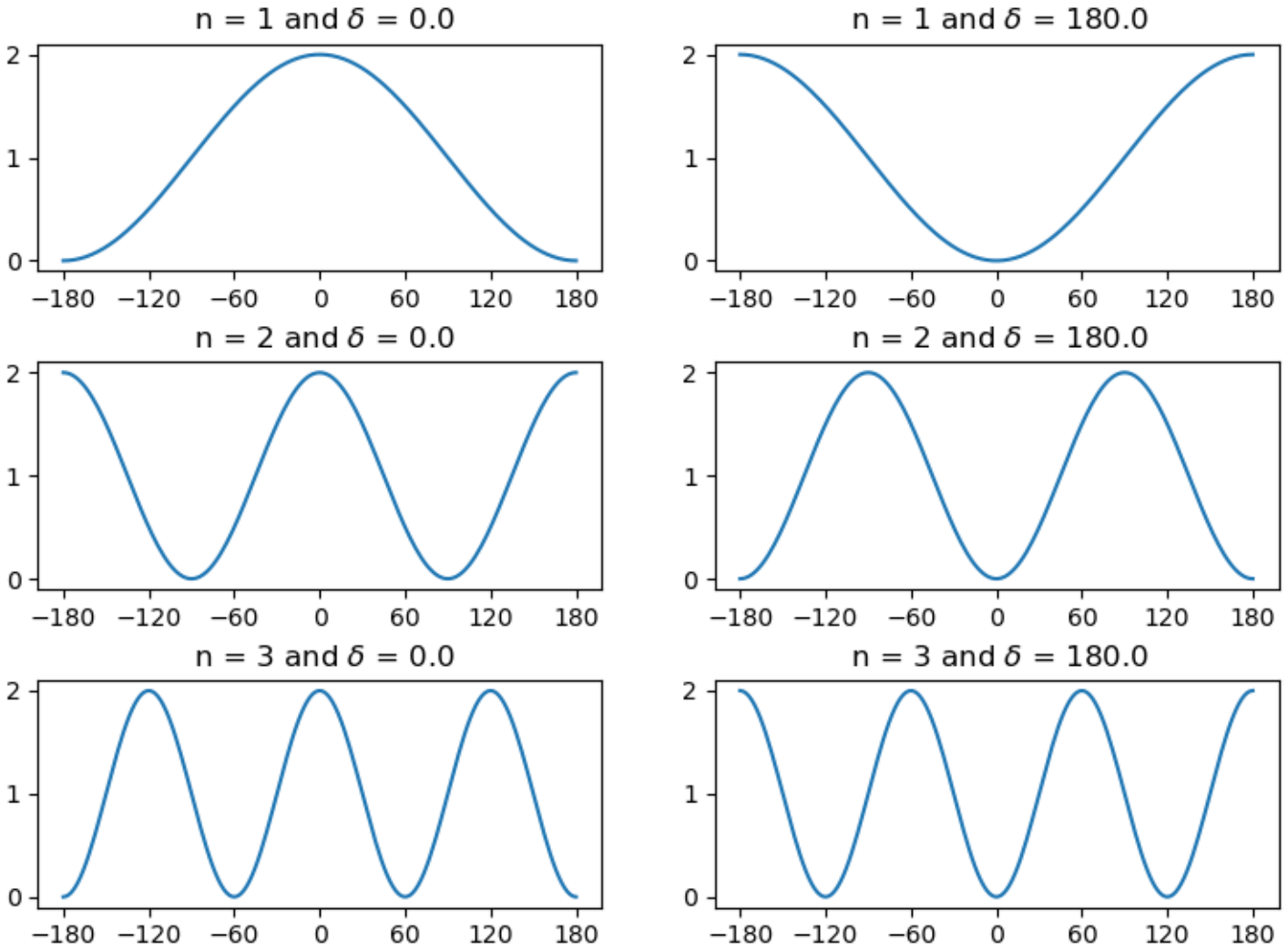


Initial Guess from Transferred Parameters

QM optimized Geometry

Check convergence


c7c4c2n Dihedral
0.005
0.000
-0.005
-0.010
-0.015
-0.020
-0.025
-0.030
-0.035
-0.040
Energy (kcal/mol)
-100.000
-50.000
0.000
50.000
100.000
Energy (kcal/mol)


n = 1 and δ = 0.0
n = 1 and δ = 180.0
n = 2 and δ = 0.0
n = 2 and δ = 180.0
n = 3 and δ = 0.0
n = 3 and δ = 180.0
2
1
0
−180 −120 −60 0 60 120 180

Generate QM Target Data

Generate MM0 Target Data

Run lsfit to get new dihedral parameters

Update multiplicity and (or) delta

Transfer and test the parameters

Converged

No

Yes

Final Parameters