Force Field Parameter Development

Typical Functional Form

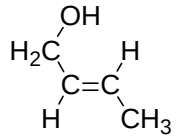
- Sum of energy terms
  - Bonded terms
    - V = k_s (r - r_0)^2
    - E = k (θ - θ_0)^2
    - Eω = Vn (1 + s cos nω)
  - Nonbonded terms

$$V_{VDW} = e\left[\left(\frac{r_0}{r}\right)^{12} - 2\left(\frac{r_0}{r}\right)^{6}\right] \qquad V = \frac{q_1 q_2}{Dr}$$

$$V = \frac{m_i m_j}{Dr_{ij}^{3}}\left(\cos x - 3\cos a_i \cos a_j\right)$$

Quiz

- Given the molecule below, describe the number and types of experimentally-derived parameters that would be needed to describe bonding interactions in a molecular mechanics calculation using a typical forcefield – DEFINE APPROPRIATE ATOM TYPES!



Determine the Force Field Goal

- Force field parameterization involves fitting calculated values to reference values through optimization of parameters
- The nature of the reference data (geometric, energetic, spectroscopic, etc.) determines situations in which the force field will be successful

Collect the Reference Data - I

- Experimental (examples)
  - Geometries
    - Crystallography: Bond distances, angles, torsions
    - Microwave spectroscopy: Bond distances
    - NMR: Angles, torsions
    - Molecular volumes
  - Energies
    - NMR: Relative conformational differences
    - IR: Bond stretching frequencies (energies)
    - Heats of vaporization

Experimental Bond Distances

- r_e: equilibrium bond distance - bottom of energy well
- r_{av}: average distance (slightly longer than r_e)
- r_a : thermal average, from electron diffraction radial distribution function
- r_g : derived from r_a (~0.002 Å longer) averaged over all molecular vibrations
- r_α: distance between mean atom positions at a given T
- r_α°: r_α extrapolated to 0 K
- r_o: directly obtained from microwave
- r_s: directly obtained from microwave
- r_z: microwave result with vibrational correction (should agree with r_α°

Experimental Bond Distances

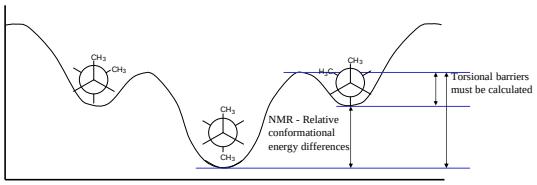
- Electron Diffraction
  - Thermal average of occupied states
  - Gives r_a, r_g, r_α, r_α°
- Microwave
  - Values for the state examined
  - Gives r_o, r_s, r_z
- Molecular Mechanics
  - Usually parameterized to give room-temperature vibrationally-averaged structures: r_α
  - Comparable to x-ray or electron diffraction (usually)
  - NOT comparable to *Ab Initio* (which gives r_e)!

Collect the Reference Data - II

- Ab initio
  - Equilibrium geometry – from optimized structures
  - Force constants – by single-point calculations on non-equilibrium structures
  - Atomic partial charges – by fitting to the molecular electrostatic potential
  - Energies – directly from the calculations

A Note on Reference Data

- Torsional barriers:
  - Rarely available from experimental data



Parameterization

- Trial and Error
  - Challenging due to number of parameters to be simultaneously optimized
  - Also challenging due to incomplete separability of parameters
- Least squares fitting
- Genetic algorithm (Cundari Group parameterization of semi-empirical methods for transition metals)

Expanding Forcefields

- Most common situation – you need parameters for a functional group that isn't represented in the forcefield that suits the remainder of your system
- Your best guide in this case is to follow the procedure outlined in the initial publication of the forcefield

Separability of Parameters

- 'Hard' parameters
  - Bond lengths, angles and torsions often come directly from experimental data
  - They are often the same (or nearly the same) from force field to force field
  - Changes in these parameters don't often influence the best choice of other parameters
- 'Soft' parameters
  - Non-bonded parameters (electrostatic & VDW)
  - Changes in one often requires changes in others

Reading

- First Edition: Section 3.17
- Second Edition: Section 4.18
- READ the paper describing the development of whatever force field you are using for your project (and reference it in your written work)