



4. Empirical Force Field Models: Molecular Mechanics (Leach)

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4.1. Introduction

- QM deals with electrons in a system
 - there are some semi-empirical schemes.
- Force field methods is known as **molecular mechanics**
 - ignore electronic motions
 - calculate the energy of a system as a function of the nuclear position only.
 - used to perform calculations on the systems containing significant numbers of atoms.
- Why molecular mechanics work?
 - Born-Oppenheimer approximation — energy as a function of the nuclear coordinates
- Molecular mechanics is based on the simple model of interactions within a system with angles and the rotations about single bonds.
- Transferability is a key attribute of force field, enables a set of parameters developed and tested on small number of cases to be applied to wider range of problems.

4.1.1. A Simple Molecular Mechanics Force Field



Force field contains terms to describe the 4 component picture of intra- and inter- molecular forces within the system.

- Energetic penalties are associated with deviations of bonds and angles away from their 'equilibrium' values.
- There is a potential energy function that explains how the energy changes as bonds are rotated
- Force field contains terms that describe the interaction between non-bonded parts of the system.

$$U(r^N) = \sum_{bonds} \frac{k_i}{2} (l_i - l_{i,0})^2 + \sum_{angles} \frac{k_i}{2} (\theta_i - \theta_{i,0})^2 + \sum_{torsions} \frac{V_n}{2} (1 + \cos(n\omega - \gamma)) + \sum_{i=1}^N \sum_{j=1}^N \left(4\epsilon_{ij} \left[\left(\frac{\sigma_{ij}}{r_{ij}} \right)^{12} - \left(\frac{\sigma_{ij}}{r_{ij}} \right)^6 \right] \right)$$

- Potential Energy function — function of the positions r_N of N particles
- First term — bonded interactions; modelled by harmonic potential; increase in energy as bond length deviates from reference value.
- second term — bonded interactions; modelled by harmonic potential; increase in energy as bond angle deviates from reference value.
- third term — bonded interactions; modelled by torsional potential; increase in energy as bond rotates from reference value.
- forth term — nonbonded interactions; modelled using Coulomb potential term for electrostatic interactions and Lennard-Jones potential for van der Waals.
- 4 key contribution to molecular mechanics force field
 - Bond stretching
 - Angle bending
 - Torsional terms
 - Non-bonded interactions

4.2. Some General Features of Molecular Mechanics Force Fields

- Need to define the constants
- Some parts of the force field can be considered standalone (bond and angle terms)
- But force field is considered one entity and not divide it into its individual component, interdependent.
- Transferability — same set of parameters can be used to model a series of related molecules. (for example, n-alkanes.)
 - Transferability of the functional form and parameters is an important feature of force field
- Only develop FF for small molecule system if particular accuracy is required.
- Force field is empirical — no ‘correct’ form for a force field
- Important to remember, there is always better force fields.
- Often a compromise between accuracy and computational efficiency.
 - most accurate function form may often be unsatisfactory for efficient computation.
 - As computational power increase, can incorporate more sophisticated model.
- Atom type — key concept in force fields.
 - In QM calculations, necessary to specify: atomic numbers of nuclei present; geometry of system; overall charge; spin multiplicity
 - In force field, necessary to specify: info about hybridization state; local environment.
 - for example, reference angle for tetrahedral C is 109.5° .
 - trigonal planar is 120° .

4.3. Bond Stretching

- The true bond stretching is not really harmonic but more like Morse potential
 - but it is not useful in molecular mechanics force fields because it is not amenable to efficient computations and it requires 3 parameters.
 - Not a problem because the effects seen in Morse potential to harmonic is very small.
- Force between bonded atoms are very strong
- Consider energy is required for bond to deviate significantly from its equilibrium value.
- High order is needed to model Morse curve. So harmonic is good enough.

4.4. Angle Bending

- harmonic potential
- less energy to bend angle than to stretch bonds

4.5. Torsional Terms

- bond-stretching and angle bending are the hard degrees of freedom and a substantial amount of energy is needed to deform them.

4.8. Introduction to Non-bonded Interactions

- Two groups: electrostatic interactions and van der Waals.

4.9. Electrostatic Interactions

- *Partial charges* — charges restricted to nuclear centers
- electrostatic interaction between two groups are calculated as sum of interactions between pairs of point charges using Coulomb's law.

$$V = \sum_{i=1}^{N_A} \sum_{j=1}^{N_B} \frac{q_i q_j}{4\pi\epsilon_0 r_{ij}} \quad (4.19)$$

- N(A) and N(B) are numbers of point charges in the two molecules
- Central multiple expansion — calculate electrostatic intermolecular interaction by treating a molecule as single entity
 - based upon electric moments or multipoles

4.9.5. Deriving Charge Models for Large Systems

- Impractical to perform QM calculations on a molecule with so many atoms, so it must be broken into fragments of a suitable size.
 - For example, to obtain partial atomic charges for amino acids, calculation on 'dipeptide' fragments, which is more akin to the environment within a protein than in an isolated amino acid.
- Charge sets obtained from electrostatic potential fitting is dependent upon the basis set used to drive the wavefunction.
 - Charges don't always improve if a larger basis set is used.
 - 5-31G* basis set is generally considered to give reasonable results for calculation relevant to the condensed phases.
 - Sometimes, can scale down to lower basis set or lower level of theory (semi-empirical) to get comparable results.
- A complicating factor is that the charges obtained from electrostatic potential fitting can depend on the conformation being inputted in the QM calculation.
 - To get around, get each charge weighted based on Boltzmann distribution.
 - Charges can vary continuously with the conformation.

4.9.6. Rapid Methods for Calculating Atomic Charges

- Gasteiger-Marsili approach uses the concept of partial equalisation of *orbital electronegativity*.
- Electronegativity is the power of an atom to attract electron
- Mulliken define electronegativity is the average of ionization potential I_A and its electron affinity E_A .

$$\chi_A = \frac{1}{2}(I_A + E_A)$$

- Rappe and Goddard's method of charge equilibration meth
 - employed in 'Universal Force Field' — calculating charge distributions over a wide range of molecules.
 - charge are dependent upon the molecular geometry

- uses a series expansion of energy of an isolated atom in terms of the charge.

4.9.10. Polarization

- So far, mainly the focus is on ‘permanent’ features of charge distribution.
- Polarization- electrostatic interactions arises from changes in charge distribution of a molecule or atom caused by external field.
 - Effect of the external electric field is to induce dipole in the molecule.

$$\mu_{ind} = \alpha E$$

- μ is induced dipole moment proportional to the electric field, with the constant of proportionality being the polarizability α
- For isolated atoms, polarizability is isotropic
 - does not depend on orientation
- Interaction between dipole and induced dipole is independent of disorienting effect of thermal motions
- Important note is that dipole induced on a molecule (A) will affect the charge distribution of another molecule.

4.10 Van der waals interaction

- Electrostatics cannot account for all the non-bonded interactions in a system.
- Energy increases as the separation decreases further.

4.10.1 Dispersive Interactions

- An instantaneous dipole in a molecule can in turn induce a dipole in neighboring atoms, giving rise to an attractive effect.
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4.10.2. The Repulsive Contribution

4.10.3. Modelling Van der Waals Interactions

- Lennard-Jones 12-6 function

$$\nu(r) = 4\epsilon \left[\left(\frac{\sigma}{r} \right)^{12} - \left(\frac{\sigma}{r} \right)^6 \right] \quad (4.63)$$

Interactions between two atoms.

Has two adjustable parameters: collision diameter, sigma and well depth, epsilon.

4.10.4. Van der Waals Interactions in Polyatomic Systems

- Interaction energy depend not only upon their separation but also their relative orientation and conformations.
- To calculate LJ interaction energy between two C-O molecules using two-site model would require van der waal parameters for carbon-carbon interactions and O-O interaction but also C-O interactions
- System containing N different types of atoms would require
- The charge-charge contribution to the potential energy is due to all pairs of charges in the central simulation box can be written:
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