

Classical Molecular Mechanics

In classical molecular mechanics approaches we effectively treat molecules as sets of spheres bound together by 'springs'. The spheres may correspond directly to atoms, to molecular fragments or to anything else we care to include in our system (and this defines their mass). The 'springs' are of different types and strengths chosen to represent the different interactions between the spheres. In this way it is really the 'springs' that contain the chemical information in the system.

The parameters for the 'springs' or *interaction potentials* are determined by fitting to results from experiments or *ab initio* calculations. These are essentially empirical methods although it is an implicit assumption that the interaction potentials are transferable between systems as they capture some of the basic 'chemical nature' of the entities that they are describing. A collection of constants defining the spheres and interaction potentials is referred to as a *force field*.

Force Fields

The force field allows us to calculate the potential energy of the system and is generally based on a pairwise sum over all the different sphere pairs present in the system. For example, the Amber force field has the following expression:

$$V = \sum_{\text{bonds}} k_r (r - r_0)^2 + \sum_{\text{angles}} k_{\theta_0} (\theta - \theta_0)^2 + \sum_{\text{dihedrals}} v_n [1 + \cos(n\phi - \gamma)] \\ + \sum_{\text{non-bonded pairs}} \left[\frac{A}{r^{12}} - \frac{B}{r^6} + \frac{q_1 q_2}{r} \right]$$

The first term defines the potential for bonded pairs; the second the potential for pairs separated by a bonded angle; the third for pairs separated by a bonded dihedral angle and the final term defines a term for non-bonded pairs (made up of a diffusive interaction and a Coulombic term).

Force fields have been determined for different classes of molecules including small organic molecules, biopolymers, solid-state oxides and inorganic molecules. Examples of commonly employed force fields include Amber (for biopolymers), MM3 (for single organic molecules) and OPLS-AA (for organic molecules in the condensed phase.)

Advantages

Classical molecular mechanics techniques are based on simple mathematical formulae and allow us to investigate systems that are out of reach for more extensive quantum mechanical treatments. We can study systems of up to 10^6 particles with relative ease. This allows us to treat biopolymers, liquids and extract information about the bulk properties of the system.

Calculations are conceptually easy to understand and we have total flexibility in defining the interactions between components.

Disadvantages

In order to perform classical molecular mechanics calculations we must have all of the parameters for the force field available. To have all the parameters available for all the molecules we might like to study would rather unlikely. To see why this is so we can consider an idealized case:

The elements that appear most often in typical molecules are a subset of the Periodic Table that includes everything up through Krypton (atomic number 36). Leaving out the Noble Gases (He, Ne, Ar, and Kr) we shall assume that each of the remaining 32 elements could form a bond with every other element and that each element can also form a bond with another atom of the same type. With 32 elements we would have:

$$32(32 + 1)/2 = 528$$

We would need 528 parameters to handle all of the single bonds between these 32 elements. We may also have multiple bonds between elements. One way to look at this is to consider different atom hybridizations (sp^3 , sp^2 , sp) for single, double, and triple bonds between each of our 32 elements. Now we have 96 different element types, which would lead to:

$$96(96 + 1)/2 = 4656$$

We would also need to know the equilibrium bond lengths for each of these bonds, giving a total of 9312 parameters. If we include other things we need to know, such as values for every possible bond angle, various dihedral angle force constants, values for van der Waals forces, atomic charge values for electrostatic interactions for every possible bond type, etc., we would need something on the order of 10^7 parameters! And recall we left out the other ~70 elements of the Periodic Table in our estimate.

In addition to this force field problem it can also be more problematic setting up these calculations than the (supposedly more complex) electronic structure calculations.

It goes without saying that we also lose the ability to investigate any *electronic* properties of the system as we have discarded all the information on the detailed electronic structure.

Applications

- Condensed phase systems and biomolecules.
- Calculation and relative stability of structures.
- Vibrational analysis.
- Time evolution of system – dynamics.
- Drug docking.
- Modelling of configuration space – bulk properties.

Software Available on the EaStCHEM RCF

- **DL_POLY** – Flexible and fast classical molecular dynamics program. You can specify any force field and simulate large systems. No real analysis tools included so you have to write your own. You must also specify the force field yourself.
- **Amber** – Molecular modelling suite written specifically for simulating biological molecules. Can perform many types of calculation including: structure optimization, molecular dynamics and vibrational analysis. Includes a wide range of tools for analysing the results and setting up the calculations.
- **Gaussian** – Able to perform molecular mechanics calculations on single molecules. Includes molecular dynamics and structure optimization.