Molecular Mechanics

Mostly From "A Guide to Using Chem3D"

Molecular mechanics is a non-quantum mechanical technique for calculating energies and some properties of molecules. Because of the way it treats the nuclei and electrons in the molecule, it is a comparatively fast computational method.

Molecular Mechanics Theory in Brief

Molecular mechanics describes the potential energy of a molecule in terms of a set of potential energy equations that are reminiscent of classical mechanics in physics. The potential energy equations to calculate the energy, the "atom types" that define different atoms in a molecule, and the parameters/constants used in the equations are known as a **force-field**.

Molecular mechanical methods are based on the following principles:

- Nuclei and electrons are lumped together and treated as unified atom-like particles typically treated as spheres.

- Bonds between particles are viewed as harmonic oscillators.

- Individual potential functions are used to describe the different interactions: bond stretching, angle bending, and torsional (bond twisting) energies, and through-space (non-bonded) interactions.

- Potential energy functions rely on empirically derived parameters (force constants, equilibrium values) that describe the interactions between sets of atoms as found for atoms in their "natural" or "ideal" state.

- The sum of interactions for a particular spatial distribution (conformation) of atoms is a measure of intramolecular strain that is relative to a hypothetical situation.

- Molecular mechanical energies have no meaning as absolute quantities. *They can only be used to compare relative steric energy (strain) between two or more conformations of the same molecule or for stereoisomers or for other molecules whose energies are calculated using identical parameters*.

The total potential energy of a molecular system is the sum of individual potential components. Simple molecular mechanics force fields include *bond stretching*, *angle bending*, *torsion*, and *van der Waals interactions* in their make-up. The sums extend over all bonds, bond angles, torsion angles, and non-bonded interactions in the molecule. Modern force fields add other terms

for greater accuracy. These properties are easiest to describe mathematically when atoms are considered as spheres of characteristic radii.

$$V = \sum V_{stretch} + \sum V_{bend} + \sum V_{torsion} + \sum V_{VDW} + ...$$
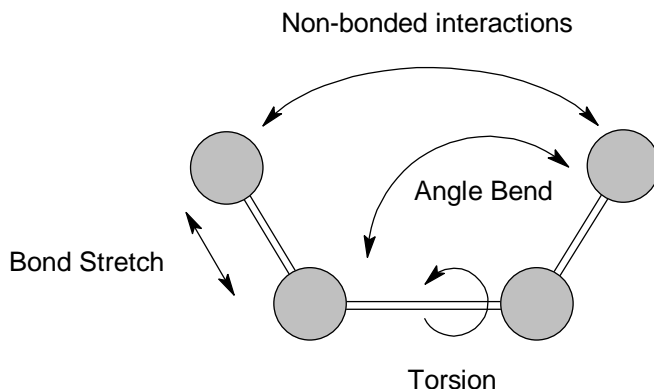
Molecular mechanics typically treats atoms as spheres, and bonds as springs. The mathematics of spring deformation (Hooke's Law, $F = -kx$) is used to describe the ability of bonds to stretch, bend, and twist. The potential energy, V, of a deformation is

$$V = -\int_{x1}^{x2} F(x)dx \qquad = \int_{x1}^{x2} (kx)dx$$
$$= 1/2kx^2$$

The simplest expressions for some of the individual potentials are shown below. Additional constants are added to these equations to refine the parameterization.

- **Bond Stretching**: bond stretching between directly bonded atoms (see previous example of Hooke's Law).

$$V_{stretch} = 1/2k_s(l-l_0)^2$$

k_s is the stretching force constant that is determined empirically. l is the actual bond length in the molecule and l_0 is the "natural" bond length. For example, if the strain-free bond length of a C_{sp3}-H bond is 1.10Å, then any deviation ($l-l_0$), either longer or shorter, will increase the energy of the molecule. The bond-stretching term is summed over all bonds in the molecule.

- **Angle Bending**: angle bending between atoms that are *geminal* to each other (bonded to the same central atom).

$$V_{bending} = 1/2 k_b (\theta - \theta_0)^2$$

K_b is the bending force constant that is determined empirically. θ is the actual bond angle in the molecule and θ_0 is the "natural" bond angle. If the optimal bond angle for H-Csp^2-Csp^3 is 122°, then any change in angle (θ-θ_0), either wider or narrower, will increase the energy of the molecule. The angle-bending term is summed over all bond angles in the molecule.

- **Torsion Energy**: torsional angle rotation between atoms that are *vicinal* (bonded to adjacent atoms) to each other.

$$V_{torsion} = 1/2 V_0 (1 + \cos n\omega)$$

Here, V_0 is the barrier to free rotation for the "natural" bond, *n* is the periodicity of the rotation (number of cycles in 360°), and ω is the torsion angle. The torsion term is summed over all rotating bonds in the molecule.
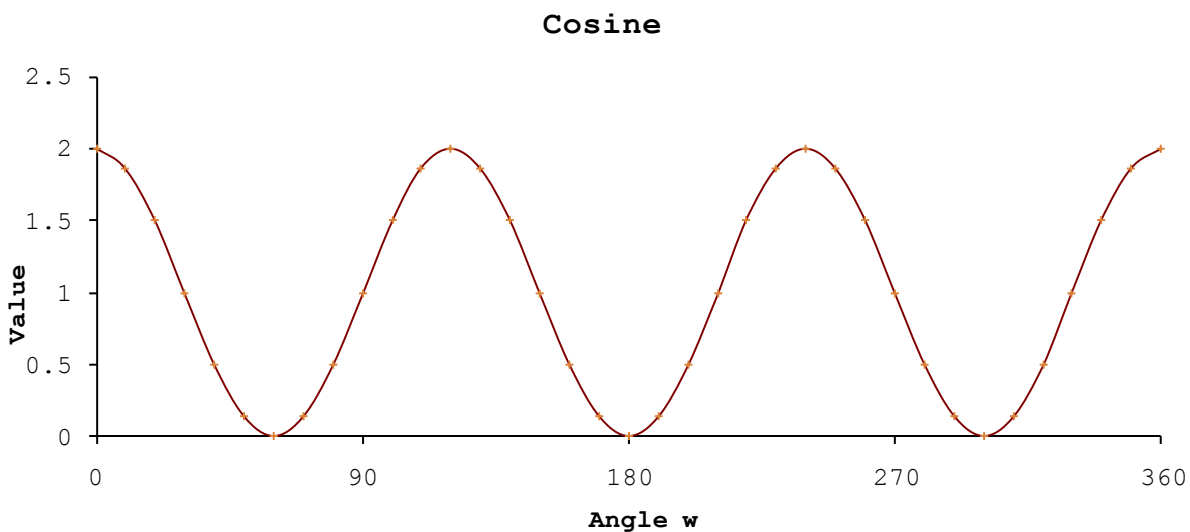
- **Non-bonded interactions**: atoms (greater than two bonds apart) interact through van der Waals attraction, steric repulsion, and electrostatic attraction/repulsion depending on their distance from each other. For two approaching non-bonded atoms, the interaction is attractive (London dispersion force) until the atoms get too close and start to repel each other (van der Waals repulsion/steric strain)

- **Dipole-Dipole interactions**: bond dipole moments can be used to represent electrostatic interactions in the molecule.

The reliability of a molecular mechanical force-field depends on the parameters and the potential energy functions used to describe the total energy of a model. Parameters must be optimized for a particular set of potential energy functions, and thus are not easily transferable to other force fields. Currently, force fields in inorganic and organometallic chemistry are not adequately formulated.

The sum of all these terms is called the *steric energy* of a molecule. Es is only a measure of intramolecular strain relative to a hypothetical situation. By itself, Es has no physical meaning. Because the force fields are parameterized from known bond energies, different parameters are used to calculate the strain energies of structural isomers. **Strain energy comparisons are valid only for stereoisomers and conformational isomers**. The molecules must have the same connectivity. Some examples of these isomers are *anti* and *gauche* butane, axial and equatorial methylcyclohexane, *cis* and *trans* 2-butene.