

# Computational Chemistry

*Mostly From "A Guide to Using Chem3D"*

Computational chemistry extends beyond the traditional boundaries separating chemistry from physics, biology, and computer science. It allows the exploration of molecules through the use of a computer in cases when an actual laboratory investigation may be inappropriate, impractical, or impossible. As an adjunct to experimental chemistry, its significance continues to be enhanced by explosive increases in computer speed and power.

Aspects of computational chemistry include:

- Molecular modeling.
- Computational methods.
- Computer-Aided Molecular Design (CAMD).
- Chemical databases.
- Organic synthesis design.

While a number of different definitions have been proposed, the definition of computational chemistry offered by Lipkowitz and Boyd as "those aspects of chemical research that are expedited or rendered practical by computers" is perhaps the most inclusive.

## *Computational Methods Overview*

Computational chemistry methods encompass a variety of mathematical methods which fall into two broad categories: **molecular mechanics** and **quantum mechanics**. Molecular mechanics applies the laws of classical physics to molecular nuclei without explicit consideration of electrons. Quantum mechanics relies on the Schrödinger equation to describe a molecule with explicit treatment of electronic structure. Generally, quantum mechanical methods can be subdivided into two classes: *ab initio* and semiempirical, making a total of three generally accepted method classes. An individual computational method may also be referred to as a "theory". Only MM2 is available in Chem3D Pro ver. 10, the software that is used in the class. The trial version of Chem3D Ultra includes all methods.

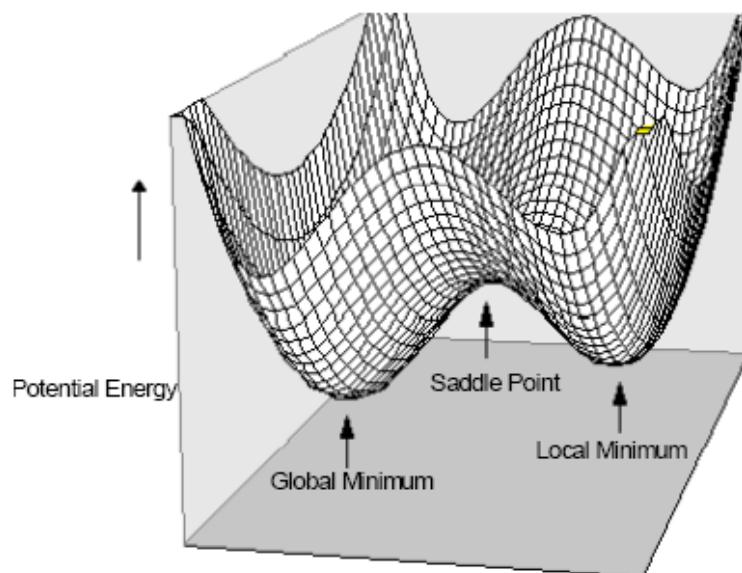
Computational methods calculate the **potential energy surface** (PES) of a molecule. While the methods differ in the way the surface is calculated, and in the molecular properties that can be derived from the energy surface, they generally perform the following basic types of calculations:

- *Single point energy calculation*—which is the energy of a given spatial arrangement of the atoms in a model, or more precisely, the value of the PES for a given set of atomic coordinates.
- *Geometry optimization*—which is a systematic modification of the atomic coordinates of a model resulting in a 3-dimensional arrangement of atoms in the model representing an energy minimum (a stable molecular geometry to be found without crossing a conformational energy barrier). This is also called *Energy Minimization*.
- *Property calculation*—which predicts certain physical and chemical properties, such as charge, dipole moment and heat of formation.

### **Potential Energy Surfaces**

A potential energy surface (PES) is a plot of the mathematical relationship between the molecular structure and its energy. It can describe:

- either a molecule or ensemble of molecules having constant atom composition,
- a system where a chemical reaction occurs,
- relative energies for conformers.



All the minima on a potential energy surface of a molecule represent stable stationary points where the forces on atoms sum to zero. The **global minimum** represents the most stable conformation; the **local minima**, less stable conformations; and the **saddle points** represent transition conformations between minima.

Using the conformations of *n*-butane as an example, the global minimum is the anti conformer, local minima are the gauche conformers, and the saddle points are the eclipsed conformations.

### **Single Point Energy Calculations**

Single point energy calculations can be used to calculate properties of the current geometry of a model. The values of these properties are dependent on where the model currently lies on the potential surface. Further:

- A single point energy calculation at a *global minimum* provides information about the model in its *most stable* conformation.
- A single point calculation at a *local minimum* provides information about the model in *one of many* stable conformations.
- A single point calculation at a *saddle point* provides information about a *transition state* of the model.
- A single point energy calculation at any other point on the potential energy surface provides information about that particular geometry, not a stable conformation or transition state.

### ***Geometry Optimization (Energy Minimization)***

Geometry optimization is a technique used for locating a stable conformation of a model. As a general rule, this should be performed before performing additional computations or analyses of a model. Locating global and local energy minima is often accomplished through energy minimization; locating a saddle point is referred to as optimizing to a transition state.

The ability of a geometry optimization to converge to a minimum will depend on the starting geometry, the potential energy function used, and the settings for a minimum acceptable gradient between steps (convergence criteria).

Geometry optimizations are iterative and begin at some starting geometry. First, the single point energy calculation is performed on the starting geometry. Then the coordinates for some subset of atoms are changed and another single point energy calculation is performed to determine the energy of that new conformation. The first or second derivative of the energy (depending on the method) with respect to the atomic coordinates then determines how large and in what direction the next increment of geometry change should be. Then the change is made.

Following the incremental change, the energy and energy derivatives are again determined and the process continues until convergence is achieved, at which point the minimization process terminates.

The starting geometry of the model will determine which minimum is reached. For example, starting at **(b)**, minimization will result in geometry **(a)**, which is the **global minimum**. However, starting at **(d)** will lead to geometry **(f)**, which is a **local minimum**. The proximity to a minimum, but not a particular minimum, can be controlled by specifying a minimum gradient that should be reached. Geometry **(f)**, rather than geometry **(e)**, can be reached by decreasing the value of the gradient where the calculation ends.

