

Molecular Modeling



Outline

- Molecular Modeling Overview
 - Techniques
 - Historical approach (Hartree-Fock)
 - Molecular Mechanics
 - Semiempirical
 - Density Functional Theory
 - Tools
 - ChemSketch and WebMO
 - A Few Applications

Modeling of Molecules

- Computers require a mathematical representation of chemical reality to solve
- Historically: Based on approximate solutions to the Schrödinger Equation (Hartree-Fock approach)

$$H\Psi = E\Psi$$

- Computationally expensive
- Energies obtained often have poor agreement with known, experimental values
- Better ways to model were sought

One Approach

- Molecular Mechanics
 - Apply classical physics to molecules
 - No electrons, orbitals, wavefunctions, etc.
 - Bonds are springs that obey Hooke's Law
 - Bond angles and dihedral angles are also mathematically treated as springs
 - Charge interactions: Coulomb's Law
 - Other interactions (van der Waals, Hydrogen bonding, etc.) have simple mathematical constructs

Molecular Mechanics - continued

- Geometry Optimization
 - Move the atoms until the forces on them are ≈ 0
 - All springs at equilibrium positions
- Many parameters required
 - Force constants for all springs, etc.
 - Programs often focus on a type of molecule to reduce the number of parameters needed
- Overall, or “steric” energy
 - Add up all the contributions
 - Bonds, angles, electrostatic, vdW, H-bonding,...

Molecular Mechanics: Pros and Cons

- Computationally inexpensive
 - Can do large molecules
- Gives good geometries
 - Starting point for other calculation types
- Energies reported not externally referenced
 - Can't compare different molecules' results
- Lack of parameters
 - Don't have parameters for all situations
- No electrons or orbitals
 - Can't study reactions, transition states, etc.

Molecular Mechanics: Uses

- Our main use
 - After drawing a structure:
 - Used to clean things up
 - Geometry is changed (optimized)
 - More realistic bond lengths and angles are applied to your depiction
 - Structure prepared for further calculations
 - Beware! Use your chemical intuition!!
 - Sometimes a **maximum energy** structure is returned!
 - Example: Eclipsed ethane instead of staggered

Importance of Structure

- Optimized (lowest energy) structures are required to calculate various properties
 - Under typical experimental (wet lab) conditions, a molecule will be in its lowest energy conformation
 - To directly compare computed and experimental properties, our virtual molecules must have the correct geometry
- **ALWAYS optimize the geometry before calculating some molecular property**

Semiempirical Techniques

- Historically, the Hartree-Fock approach gave energies that didn't match experiment
 - Computationally expensive
 - To give better agreement with experiment, certain aspects were parameterized (exp. values used), and other aspects were ignored
 - Distance cut-offs to reduce number of terms
 - Only consider valence electrons
 - Usually parameterized to give good geometries and energies

- Molecular Orbital PACkage
 - Various types: AM1, PM3, MINDO/3, PM6, and RM1
 - Vary in the parameters used
 - AM1 and PM3 widely used in many programs
 - Typically expect **qualitative** results
 - Trends will be in the right direction
 - Quantities will vary from experimental results
 - Solution phase parameters are available
 - Much experimental work done in solution

Semiempirical: Pros and Cons

- Low computational expense
 - Medium-sized molecules in a reasonable time
- Good qualitative results (semiquantitative?)
- Solution phase parameters available
- Parameters not available for all atoms
 - Some programs will continue on regardless!
- Only calculate properties method was parameterized for (ground state energy, geometry)
- Molecule/parameter set similarity

Use of Semiempirical Methods

- Great for many educational uses
 - Interactive calculations – quick feedback
 - Trends match what is expected
 - Qualitative results often O.K.
- Key molecular modeling question:
→ **What do I want to know, how accurately do I need to know it, and how long am I willing to wait?**
 - Answer will dictate the method you choose

Density Functional Theory (DFT)

- Hartree-Fock approach tries to find the best wavefunction (Ψ) for the molecule
 - Wavefunctions are difficult to deal with
- DFT looks at the energy in terms of the electron density (ρ), instead of Ψ
 - Mathematically, it is easier to deal with electron density than with wavefunctions
- DFT is often the most cost-effective method to achieve a given level of quantitative accuracy

Density Functional Theory - continued

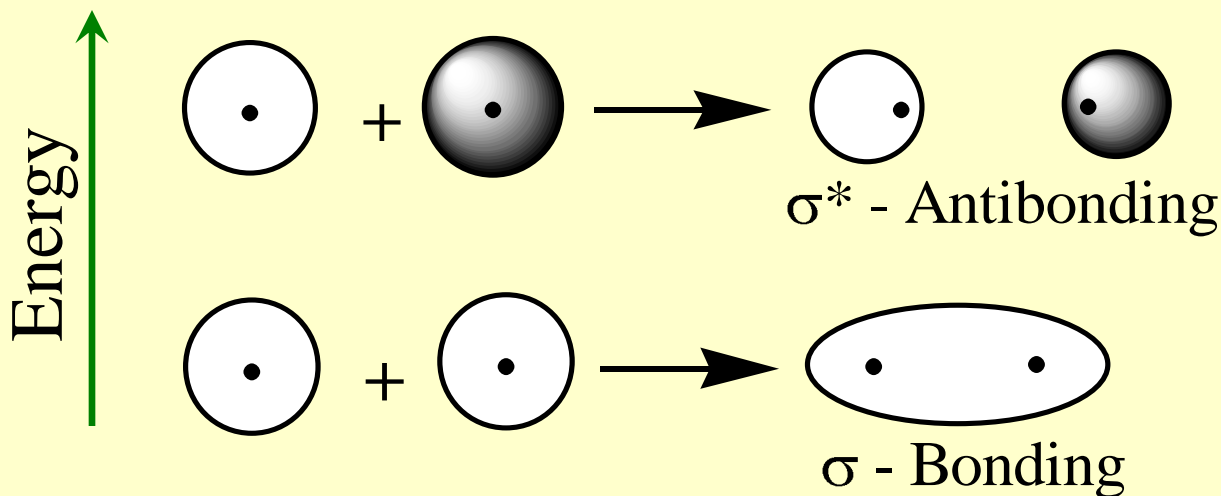
- As with the Hartree-Fock approach, the DFT process is computationally expensive
 - Quantitative accuracy is greater
- Always a balance between quantitative accuracy and computational expense
 - DFT adjusts the electron density to find the lowest energy for a molecule
 - The electron density is adjusted using basis functions, which represent the atomic orbitals

Basis Functions

- LCAO
 - Linear Combination of Atomic Orbitals
 - Key approximation made in quantum mechanics
 - Atomic orbitals are mathematically represented by a set of basis functions which proscribe the angular shape and radial extent of the AOs around the nucleus of each atom
 - The basis functions are combined together (linear combination) to construct the molecular orbitals

Example: H₂ Molecular Orbitals

- Linear combination of two *1s* atomic orbitals
 - Produces two molecular orbitals (MOs)
 - One is bonding (σ), one is antibonding (σ^*)



- More accurate mathematical descriptions of AOs lead to better MOs, which lead to better calculated quantitative results

DFT Basis Set Choice

- WebMO has three built-in basis set choices
 - Basic: 3-21G
 - Routine: 6-31G(d)
 - Accurate: 6-311+G(d,p)
- In general, quantitative accuracy will increase with a larger basis set, and so will the computational cost
 - Comp. time scales $\sim N^3$, here N is the number of basis functions

DFT: Pros and Cons

- Good quantitative accuracy
- Better results than Hartree Fock method
- Main method used by many researchers
- Computational expense is high
 - Still acceptable for small molecules
- More accurate quantitative results require larger basis sets
 - Computational expense grows quickly
 - What do I want to know, how accurately do I need to know it, how long am I willing to wait?

Tools

- ChemSketch
 - Good for drawing/visualizing molecules in 3D
 - Can import into WebMO as .mol files
 - Does basic molecular mechanics calculations

- WebMO
 - Can also draw/visualize molecules
 - Does molecular mechanics, semiempirical, and DFT calculations, and others
 - Many possible applications

Applications

- Viewing molecules
 - Rotate, translate, zoom
- Measure bond distances and angles (VSEPR)
- Visualize dipole moments (Intermolec. forces)
- Find atomic partial charges
- View atomic and molecular orbitals
- View electron density, electrostatic potential, electrophilic/nucleophilic susceptibilities
- Scan bond lengths or angles and calculate the energy changes
 - Bond lengths and energies

Exercises

- Practice with ChemSketch and WebMO
 - Starting exercises assume no knowledge; give click-by-click instruction
 - Later ones assume you know the basics
- Tomorrow afternoon
 - Additional exercises (spectroscopy, parallel)
 - CCCE site :
www.computationalscience.org/ccce
 - WebMO Curriculum ideas at:
www.webmo.net/curriculum/index.html