Computational Methods Summary

Types of Energy Models (QM or MM)

1. Molecular mechanics (MM)
   - Useful for initial calculations on small organics, can do any size up through proteins.
   - Uses classical ball-and-spring laws where each force constant, ideal bond length, angle and dihedral angle are empirical parameters. Through-space electrostatic and VDW interactions are also added.
   - Empirical parameters mean that method is only useful if you have parameters (a force field) closely matching every type of linkage in your system.
   - Programs available here: Macromodel, AMBER, NAMD, Desmond, Gromacs, more……

2. Hartree-Fock (QM)
   - Mainly used as a starting point for high-level ab initio calculations or mixed with DFT (see 3).
   - Approximate solution of the Schrödinger equation neglecting instantaneous electron-electron interactions (correlation) unless corrections are applied.
   - Energy and orbital coefficients solved for by an iterative self consistent field (SCF) method.
   - High-level calculations (configuration interaction, coupled cluster, G3, etc.) can correct for correlation and achieve chemical accuracy but only possible for small numbers of atoms, very time consuming.
   - Programs available here: Gaussian, Jaguar, QChem, Gamess, NWChem, more ……

3. Density functional theory (QM)
   - Appropriate for systems up to ca. 100 atoms (sometimes larger), best choice for most organometallics
   - Based on an equation analogous to the Schrödinger equation where energy is a functional of electron density, not the true wavefunction. Iterative SCF procedure is similar to that of HF.
   - Implicitly includes electron correlation, so much more accurate than HF, but behavior is sometimes unpredictable because the electronic density functional cannot be derived ab initio.
   - Myriad functionals designed (parameterized) based on certain principles. The most popular one is B3-LYP which includes some HF exchange (hybrid DFT). B3LYP has very good performance for organic molecules, but may not suitable for metal complexes and structures with non-covalent interactions.
     Some recently developed functionals are ωB97X-D, M06, HSE06, BMK, TPSSh, etc…
   - Programs available here: Gaussian, Jaguar, QChem, Gamess, NWChem, more……

Basis Sets (for QM calculations only)
- The set of atomic orbitals whose coefficients are optimized in SCF.
- Each orbital usually represented by a linear combination of Gaussian functions.
- The number of Slate-type orbital (STO) determines the size of a basis set. The bigger the basis set, the better the results, but for DFT not much gain beyond triple-zeta level (three STO).
- 6-31G is a popular double-zeta level split-valance basis set. It uses 6 Gaussian functions to describe inner shell orbitals, while 3 and 1 Gaussian functions for the 1st and the 2nd valance STO, respectively.
- Polarization functions (**) or (d,p) after G) add d functions to p shells (carbon, phosphorus, etc.) and p functions to hydrogen. Must use at least d functions on p shells (one *) for acceptable results!
- Diffuse functions (++ before G) add next-principal-quantum-number shell. In DFT, normally only useful for anions, excited states or sometimes late transition metals.
- Effective core potentials (ECP) replace core electrons with a potential felt by valence electrons, simplifies calculation of heavy atoms. The relativistic effect of core electrons can be included in the ECP. Normally needed for atoms heavier than 1st-row transition metals.
- If you have metals/heavy atoms, start with LANL2DZ but then see our page for suggestions about better basis sets: http://glab.chem.berkeley.edu/glab/faqs/ gauss_custombasis.html
QM Output:
- Can include orbital energies/pictures, excitation energies, partial charges, dipole and multipole moments, polarizabilities, NMR shielding and coupling constants, etc.

Common Types of Geometry Algorithms
1. Molecular energy (calculates energy of input geometry – no geometry change)
   - Can be used on a previously optimized geometry
     - MM: Energy is relative to a hypothetical unstrained system.
     - QM: SCF energy, relative to a separated collection of electrons and nuclei.
   - Add up energies of species on each side of a balanced chemical equation and calculate reaction energy (Make sure the total number of basis functions are the same in the whole reaction).

2. Geometry optimization (also called minimization)
   - Finds local minimum: the bottom of whichever potential energy well in which a molecule is drawn.
   - Iterative process, with the molecular energy calculated between each optimization cycle.
   - Can optimize all coordinates or constrain one or more coordinates.
   - Default convergence criteria are arbitrarily set, you might allow looser or need tighter criteria.

3. Coordinate Scan
   - Can be used to manually adjust a distance, angle or torsion systematically. Commonly used for searching torsions (dihedral drive) or as a manual method to locate transition states (TS).

4. Conformational searching
   - Best methods randomly sample potential energy surface to find global minimum-energy structure.
   - Nearly always confined to MM methods due to number of structures generated/minimized.
   - For flexible organic species, perform conformational search before QM geometry optimization.

5. Transition state searching
   - Needed to model chemical kinetics, locates an energy maximum along a reaction coordinate while minimizing energy w.r.t. all other coordinates for a reaction mechanism study.
   - Normally used with QM methods, locating correct TS in the reaction pathway is much more difficult to be successfully achieved than optimization for intermediates.
   - A converged TS must have exactly one imaginary vibrational frequency.
   - Perform intrinsic reaction coordinate (IRC) calculation for a TS and confirm reactant and product.

6. Vibrational frequencies
   - Normally used with QM methods, calculates the molecular vibrational frequencies and sometimes IR and/or Raman intensities.
   - Also calculates zero-point energies (ZPE), thermal enthalpies and thermal Gibbs free energies which should be added to SCF energies when studying reaction kinetics or thermodynamics.
   - A true minimum has all real-valued frequencies, a transition state has exactly one imaginary frequency.

7. Molecular dynamics
   - Applicable to MM (up to macromolecules) and sometimes QM methods (very small systems).
   - Models molecular motion over time, response to forces acting on molecule.
   - Will eventually sample all accessible conformations at a given temperature, if the simulation is run long enough (this can be very long and in some cases impractical).
   - For large systems (proteins, DNA, etc.) more useful than conformational searching.
   - Takes into account that reaction trajectories do not always follow the exact minimum-energy path.