Geometry optimizations

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Lab 2

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The challenge of conformers

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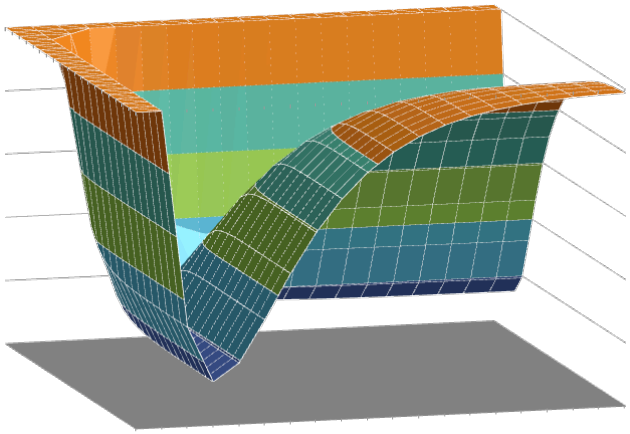
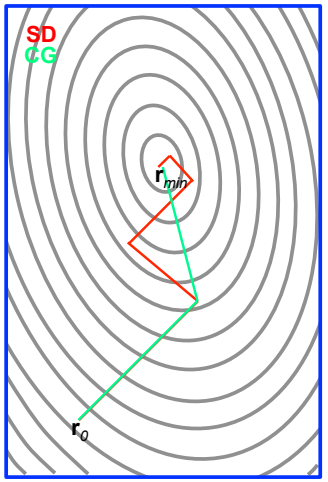
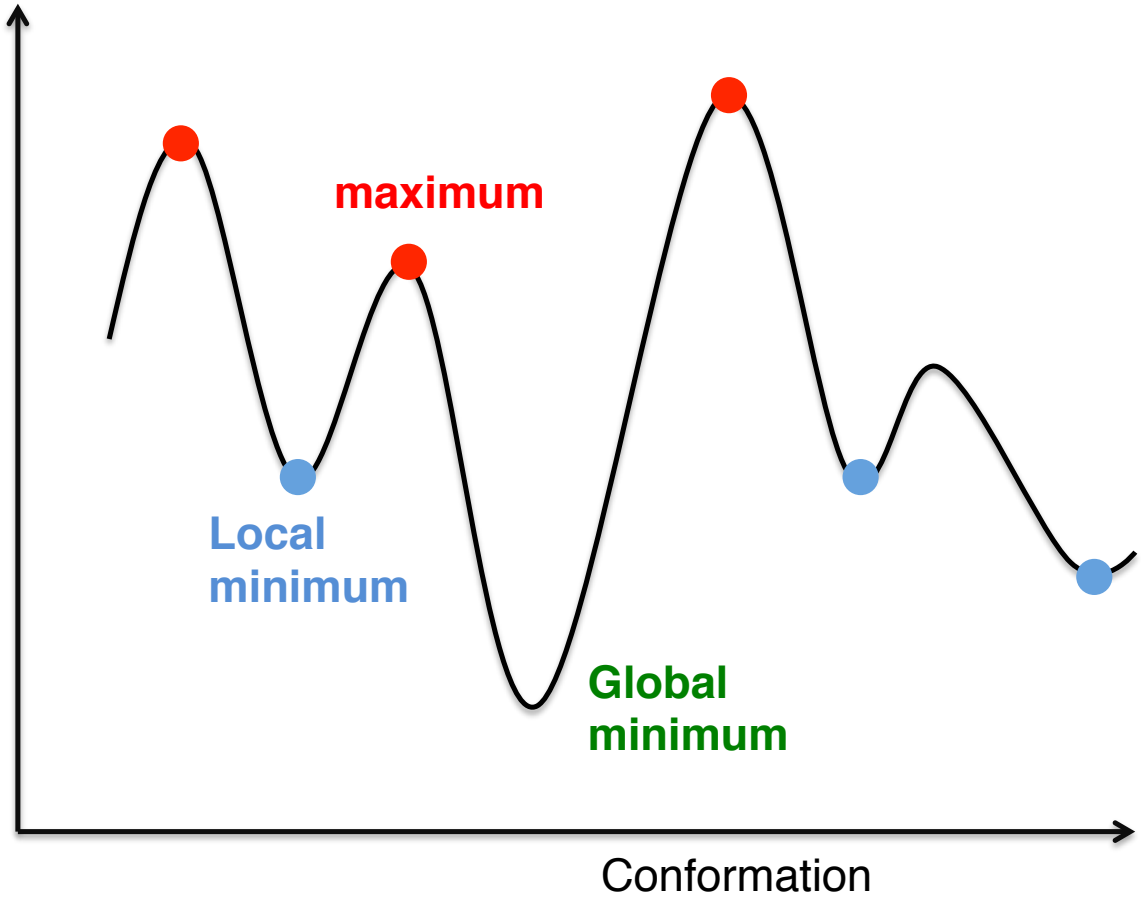
Today you will run optimizations/conformer searching for local minima and constrained optimizations to compute potential energy curves:







Optimization algorithms

Available in Avogadro:

- **Steepest descent:** always follow the gradient (*see T2 summary*).

- **Conjugate gradient:** use some history information – the direction is the weighted average of current and past gradient (*see T2 summary*).

Conformational sampling

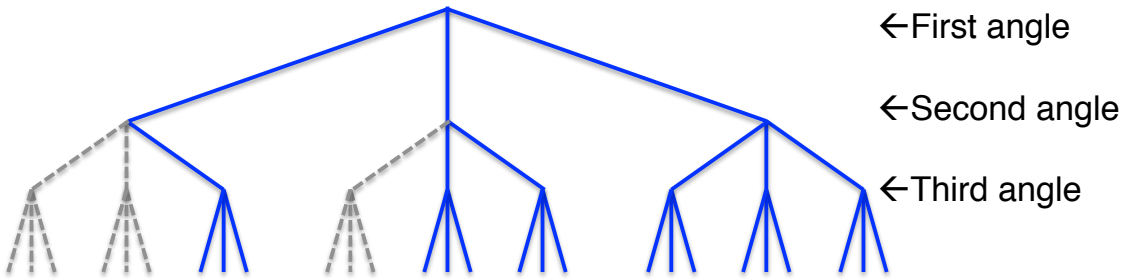
- Minimization techniques only find the nearest minimum – sometimes the *local* minimum instead of the *global* minimum.
- Number of minima grow exponentially with number of variables.

Multiple minima problem $CH_3(CH_2)_{n+1}CH_3$ with n rotatable bonds:

n	Conformers (3^n)	Time (1 conf/sec)
1	1	3 sec
5	243	4 min
10	59,049	16 hr
15	14,348,907	166 days

Systematic or grid search method is feasible only for small systems –iteratively vary rotations by fixed amount until all have been generated (works for 15-20 dihedral angles).

Can prune the search for torsions that always lead to clashing/high energy structures:



Also randomized searches, limiting the number of angles rotated, etc…
Outstanding challenge: conformer ranking sensitive to energy functional.

Conformational sampling

In Avogadro/OpenBabel:

- **Systematic searching** – iteratively vary rotations by fixed amount until all have been generated. This is hard to do when we have many rotatable bonds.

- **Genetic algorithm** – evolutionary algorithm (may not work in your Avogadro).

- **Random rotor**— Randomly generate guesses for the torsion and evaluate the energy.

- **Weighted rotor**—Stochastic: torsion angles are weighted based on relative energies of generated conformers (important for large number of rotatable bonds).

Dihedral barriers and the gauche effect

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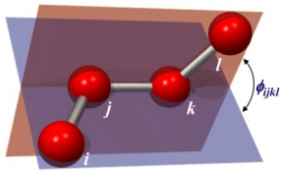
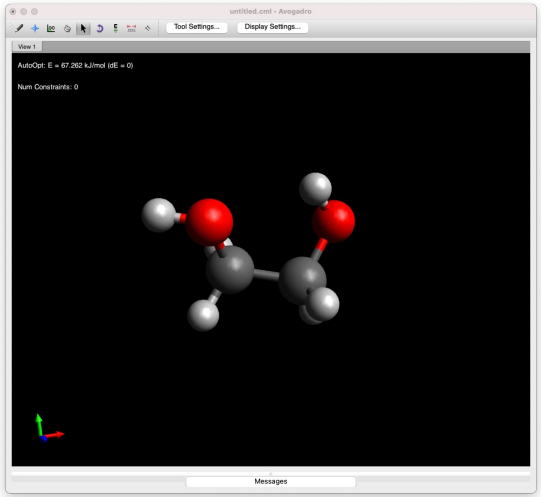
Dihedral scans and conformer searches of the torsional angles allow us to understand how force fields handle dihedrals and give us different relative energetics

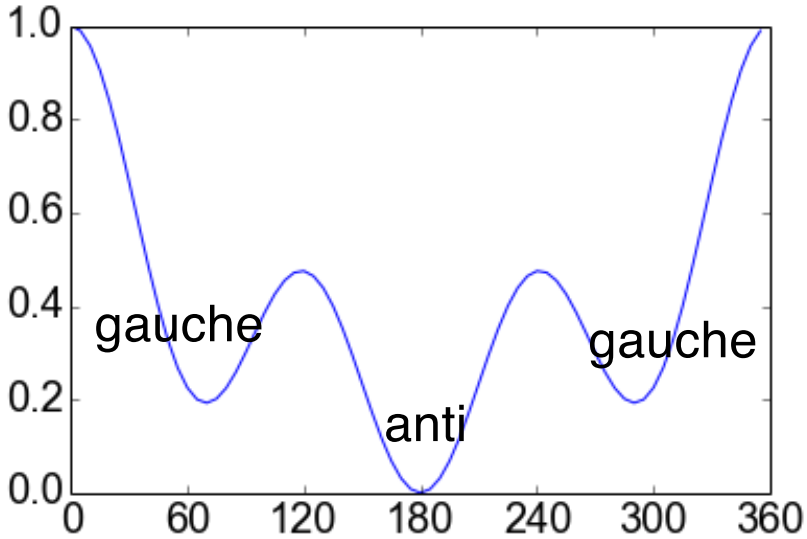
$$E_{\text{tors}} = \sum_{n=1} V_n \cos(n\omega)$$



The presence of hydrogen bonds can alter preferred minima: 1,2-ethanediol



The gauche effect refers to when the gauche-anti relative energetics are shifted



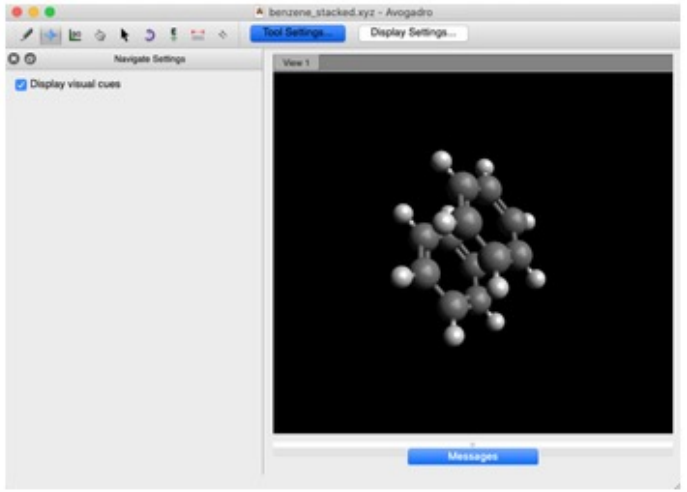
Lab 2

A. Study stacking interactions in two benzene molecules

B. Butane and 1,2-ethanediol conformer searching: predicting the gauche effect and hydrogen bonding.

C. Hydrogen bonds in more diverse molecules – remdesivir

D. Familiarizing yourself with linux commands, logging into Expanse, and running your first scripts



E_{int} = 2E(benzene)-E(benzene stack)
CCSD(T) E_{int} = 7.32 kJ/mol, d(C-C) = 3.90 Å
Experiment E_{int} = 8-12 kJ/mol