Computational Inorganic Chemistry: An Introduction

Rebecca M. Jones

Austin Peay State University

jonesr@apsu.edu

Outline

- Introduction
- Computational Methods Overview
  - Ab initio
  - Semi-empirical
  - DFT
  - Molecular mechanics
  - QM/MM
- A recent literature example
- Visualizing vibrational modes

Introduction

- Imagine studying a molecule on the level of each electron.
  - What happens to the electrons on atom A when a bond is broken?
  - What do molecular vibrations actually look like?
  - What is the best geometry for an unknown intermediate?
  - How does a protein structure change with temperature?
- Computational chemistry and molecular modeling provide a means to address these questions

Introduction

- Computational chemistry
  - a subset of theoretical chemistry
  - uses mathematics and fundamental laws of physics to study processes, molecules, etc. of chemical interest
    - e.g. the optimized geometry of ethanol and all its vibrational modes can be calculated and visually displayed in a matter of seconds
  - is quickly becoming a common tool that complements experimentation
- Useful applications have only become practical within the last few decades with the advent of faster processors and expanded memory in computers.

Considering expense

- Various characteristics of molecular structure add expense to a calculation
- A cheap calculation will finsh quickly with little computer resources.
- An expensive calculation requires more computer power, memory, and time.
  - Modeling proteins are generally very expensive because the molecules are so large
  - Transition metal complexes are also generally expensive because of the presence of d electrons
  - Models can be constructed to minimize expense
    - Considering only the protein acitve site
    - Converting large ligands to smaller ones (– PR_3 to –PH_3)

Computational Methods Overview

- There are many different methods of modeling molecules in a computer
- Each method has strengths and weaknesses depending upon the system you are interested in studying
- Computational Methods
  - Ab initio (quantum methods)
  - Semi-empirical
  - DFT
  - Molecular mechanics
  - QM/MM

Quantum Methods

- Quantum mechanics originated in the 1920s.
  - Goal: to calculate all chemical interactions, thereby making experiments almost obsolete (Dirac)
- Hartree performed first reliable calculations in the 1930s, using a hand calculator and applying the Self Consistent Field (SCF) method.
- Although computational power has increased considerably since Hartree, the exact solution of the Schrödinger equation [1926] still has only been found for one-electron systems.
- Various approximations have enabled solutions to be obtained by multiple iterations.

Ab initio

- Means “from the beginning”
- Implies going back to the basics of what dictates molecular structure and movement, namely quantum mechanics
- Solutions have no reference to experimental data- they are reached solely by application of quantum theory.
- Goal is to find solutions to Schrodinger’s equation for a multi-electron system using SCF (self-consistent field) or Hartree-fock (HF) method

Basic Hartree-Fock

- All electrons in an atom except one (call it Fred) form a cloud of electric charge thru which Fred moves.
- The electron cloud has a certain charge density which is a function of which AOs those electrons are in.
- The interaction between Fred and the cloud is calculated, the Schrödinger equation is solved, and improved AOs are obtained.
- These improved AOs replace the initial guess and are used to calculated a new charge density.
- These iterations are repeated until they converge (a certain mathematical threshold is reached).

Applied Hartree Fock

- For molecules, MOs are used instead of AOs. To construct these MOs, linear combinations of the atomic orbitals (LCAOs) are used.
- Solving the integrals of these atomic functions is quite cumbersome
  - Ab initio programs use sets of functions to describe the solutions to these integrals - groups of these functions make up basis sets.

Basis Sets

- A basis set for a given calculation is defined by the number and functional form of the AOs used to construct the MOs; there are different types of basis sets
  - Minimal: comprised of AOs up to and including valence shell of atoms in the molecule (smallest STO-3G)
  - Extended: employs AOs lying outside the valence shell in additional to the minimal basis set (like 6-31G*, adds empty orbitals like p orbitals to hydrogen and d to oxygen)

Application of Ab initio

- Ab initio calculations can be performed on both closed and open shell systems
  - Closed shell: all electrons are paired, use what is called restricted Hartree Fock (RHF)
    - Each wavefunction solution is for 2 electrons occupying the same orbital
  - Open shell: at least one electron is unpaired and Unrestricted Hartree Fock (UHF) must be used;
    - A different wavefunction is calculated for every electron in the system

Application of Ab initio

- Symmetry can be used to reduce the computational expense (by eliminating integrals that are equal to zero.
  - This is only useful when the molecule is small enough to have symmetry higher than C1
- Expense of computing an ab initio calculation is α N^4 where N is the number of basis functions (or AOs)
  - As the molecule gets larger, the expense gets very large quickly

Ab initio

- Advantages
  - very accurate
  - many excellent basis sets have been developed
- Disadvantages
  - computationally expensive, especially on large systems
  - generally not suitable for larger molecules without high symmetry

Semi-Empirical Methods

- Semiempirical Methods are simplified versions of Hartree-Fock theory using empirical (=derived from experimental data) corrections in order to improve performance.
- Basically, a number of assumptions are made to cut back on the computational time; however, this also cuts back on the accuracy of the result.
- Some typical assumptions
  - Only consider valence electrons; treat inner electrons as a “hard core”, ignore any effect they may have on the valence MOs.
  - Assume zero-differential overlap: implies electrons can only have density on one atom

Semi-Empirical Methods

- The details of these assumptions and how the resulting integrals are “parameterized” is what makes the different semi-empirical methods unique
- These methods are usually referred to through acronyms encoding some of the underlying theoretical assumptions.
- Most frequently used methods
  - MNDO (Modified Neglect of Differential Overlap)
  - AM1 (Austin Model 1)
  - PM3 (Parametric Model number 3)

Semi-Empirical Methods

- Advantages
  - Faster than ab initio, able to handle larger molecules more efficiently
  - Good first attack on organic compounds
- Disadvantages:
  - often not appropriate for transition metals (especially if using a minimal basis set), the approximations can be quite detrimental to understanding redox chemistry

Density Functional Theory

- DFT is based upon the proof by Hohenberg and Kohn that the energy of the electronic ground state is determined solely from the electron density
  - There is a 1:1 relationship between the electron density of a system and its energy
- In general, instead of solving for wavefunctions via SCF, the electron density is solved for and related to energy.
  - This change in perspective does not remove accuracy (like semi-empirical methods) or involve any assumptions;
- An *ab initio* method

Density Functional Theory

- The solution of the integrals involved in DFT requires much less time compared to ab initio
- As a result, DFT can be applied to large systems such as coordination compounds, organometallic, inorganic, and biological systems.
- Advantages
  - DFT is faster than ab initio and more accurate than semi-empirical, can handle larger systems
- Disadvantages
  - Large systems (>50 atoms) are still very computationally expensive even using super-computers or clusters

Molecular Mechanics

- Based upon the classical physical description of the molecule
- Force field: a simple equation which describe the energetic expense of changing geometry
- Molecular description
  - Atom characteritics (radii, charge, mass, etc.)
  - Atom preferences (preferred bond lengths and angles)
  - Constraints (prevent calculation from making moves that are too expensive, e.g. keep a planar molecule from distorting out of the plane)
- AMBER, CHARMm, tripos

Molecular Mechanics

- In molecular dynamics, calculations simulate the motion of each atom in a molecular system at a fixed energy, fixed temperature, or with controlled temperature changes.
- Advantages
  - Very useful in studying protein structure
  - Less expensive than quantum methods
  - Easier to use on large systems
- Disadvantages
  - Cannot be used for compounds or atoms where no empirical data is known to develop good force fields
  - Many chemical processes do no obey Newton’s laws!

QM/MM

- Quantum Mechanical/Molecular Mechanical Calculations
- Exploits accuracy of quantum methods and cheap MM approximations for large molecules (e.g. enzymes)
- QM
  - Semiempircal (MNDO, AM1)
  - *Ab initio*
  - Density Functional Methods
  - MOPAC
- MM
  - CHARMM, AMBER, or GROMOS

QM/MM Basics

- A small reactive part of the system is treated quantum mechanically (i.e., by an electronic structure method)
  - this allows the electronic rearrangements involved in a chemical reaction, for example, during bond breaking and making, to be modelled.
- The large nonreactive part is described molecular mechanically.
- The two regions are allowed and able to interact.
- The combination of the efficiency and speed of the MM force field with the versatility and range of applicability of the QM method allows reactions in large systems to be studied.

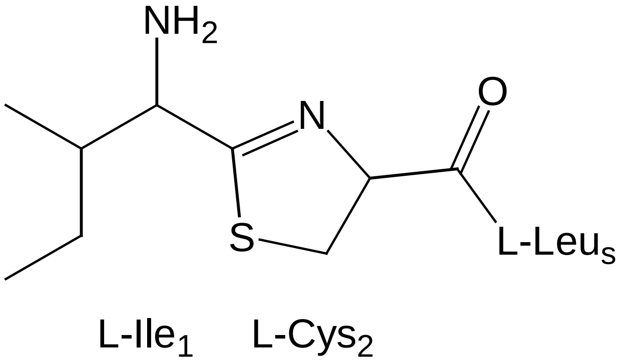
QM/MM

- Advantages
  - Good approach to modelling enzyme-catalyzed reactions
  - Provides accuracy while minimizing expense
- Disadvantages
  - Interaction between QM and MM sections can be problematic
  - Decisions must be made regarding how much of the molecule you solve with the QM approach and how much you can afford to look at from the MM approach

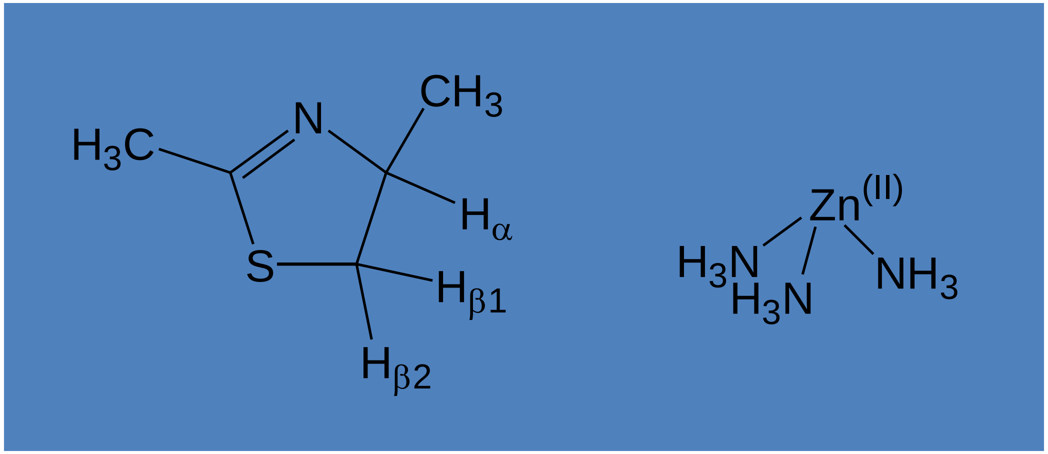
A literature example

- Drabløs et al., *J. of Computational Chemistry*, Vol. 21, No. 1, p1-7.
- Bacitracin A is a small 10 a.a. long peptide that binds zinc(II)
- The structure of zinc-free Bacitracin is known, but no x-ray structure has been determined for the zinc-bound enzyme
- Spectroscopic data (EXAFS and NMR) are inconclusive regarding where the Zn atom is bound, to N or S?
    - Drabløs modeled the active site using ab initio methods (Cadpac and Dalton)

A literature example



Bacitracin A Active Site

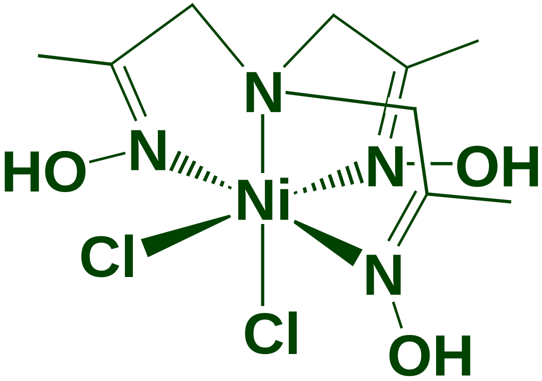


Model System

- Results showed lowest energy configuration has Zn^{2+} bound to N
- Calculations also suggested a reinterpretation of the NMR data and proposed resolution of the discrepancy

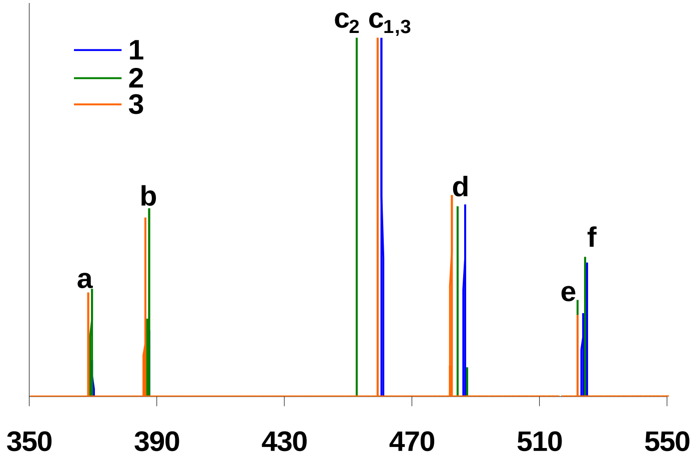
Pursuing catalytic Ni-O_2 reactions

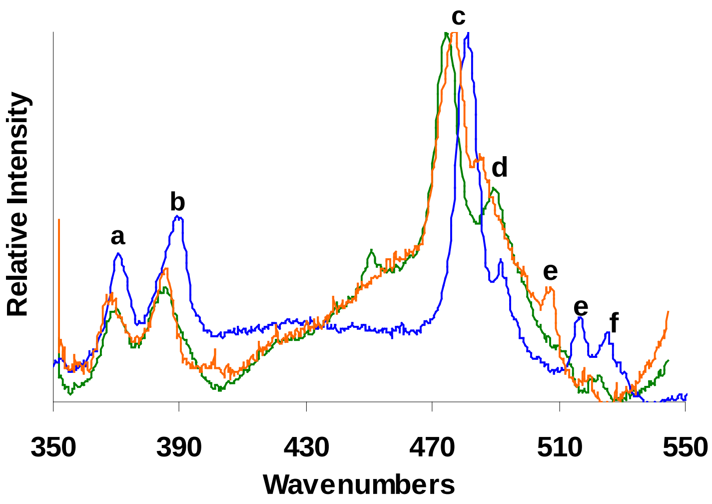
- The oxygen reactive Ni complexes and O_2 adduct(s) developed by the Baldwin group are not yet fully characterized
  - Various spectroscopic handles are available
  - A complementary approach is computational molecular modeling
- A theoretical model has been developed using the well characterized precursor to the O_2 active species, Ni(TRISOXH_3)Cl_2



- Complexes with ^{15}N isotope substituted TRISOXH_3 were used to assign 28 normal vibrational modes

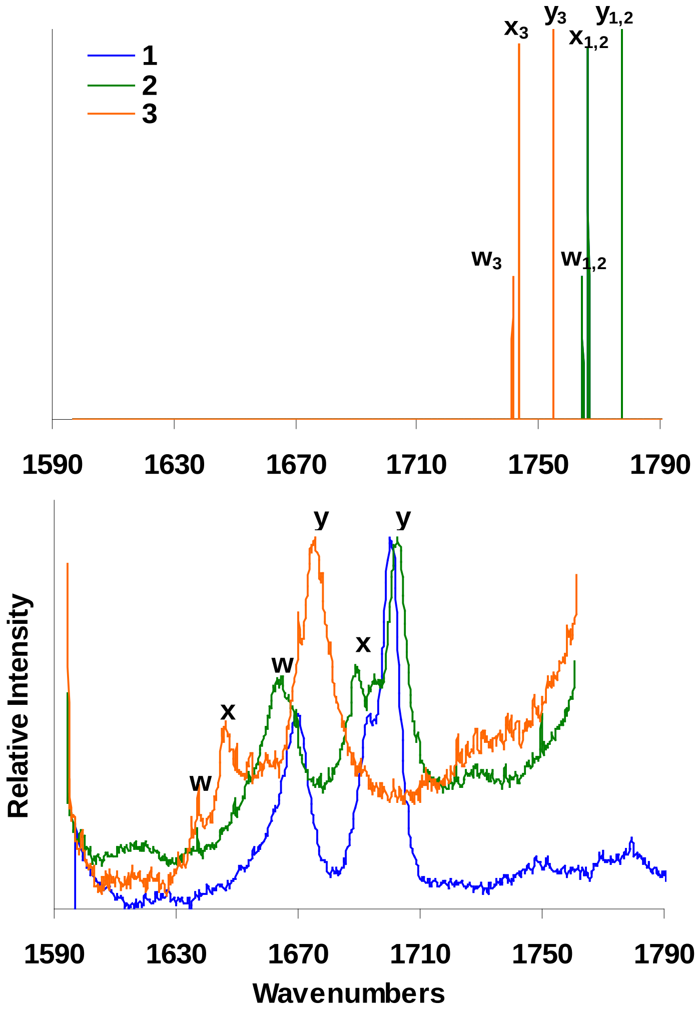
Visualizing vibrational modes



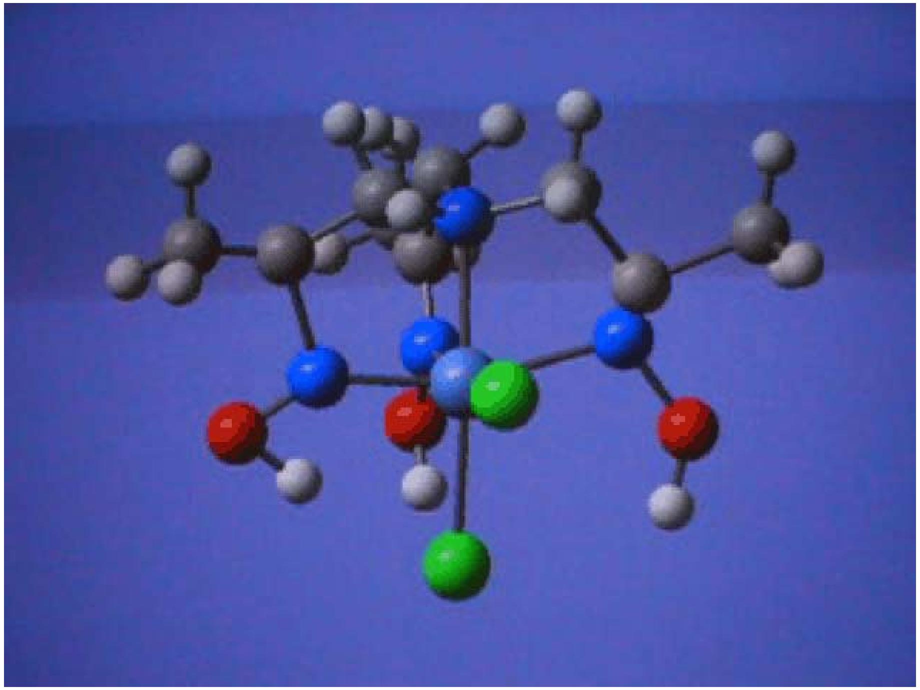


- Ni(TRISOXH$_3$)Cl$_2$ Raman spectra
- Mode C is assigned as the principle Ni-N1 stretch

Visualizing vibrational modes



- Ni(TRISOXH_3)Cl_2 Raman spectra
- Mode W, X, Y are assigned as C=N stretches.



References

- James B. Foresman and AEleen Frisch, *Exploring Chemistry with Electronic Structure Methods, 2nd Edition,* Gaussian, 1996.
- Frank Jensen, *Introduction to Computational Chemistry*, New York, John Wiley and Sons, 2001.
- Drabløs et al., *J. of Computational Chemistry*, Vol. 21, No. 1, p1-7.
- “Theoretical, structural, and spectroscopic studies of a series of $Ni^{II}(TRISOXH_3)X_2$ complexes.” Rebecca M. Jones, Michael J. Goldcamp, Jeanette A. Krause, Michael J. Baldwin, *Polyhedron*, 2006, **25**, 3145–3158.
- “Development of a computational model of Nickel(II)$TRISOXH_3Cl_2$ with comparison to X-ray crystallography and vibrational spectroscopy”, Rebecca M. Jones and Michael J. Baldwin, *Journal of Physical Chemistry A*., 2004, 108(16), 3537-3544.