
بسم الله الرحمن الرحيم

Introduction to Computational Chemistry

Lecture # 01

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Key Concepts

- In this lecture we ‘ll learn:
- Computational Chemistry
- Common Computational Investigations
- Quantum Mechanics
- Tools of Computational Chemistry

Theoretical & Computational Chemistry

- "All Theoretical Chemistry is really Physics; and all Theoretical Chemists know it".

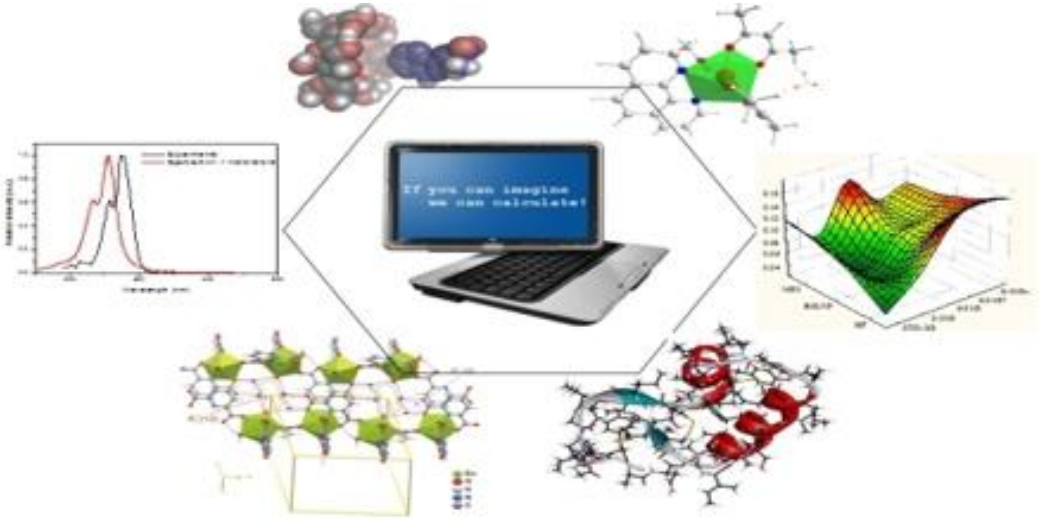
Richard Feynman

- However,

"*There is a difference between knowing the rules of chess and being able to play*"

Computational Chemistry

- Computational chemistry (also called molecular modelling; the two terms mean about the same thing) is a set of techniques for investigating chemical problems on a computer rather than using chemicals.
- It uses the results of theoretical chemistry, incorporated into efficient computer programs, to calculate the structures and properties of molecules.



Common Computational Investigations

- Questions commonly investigated computationally are:

✓ Molecular geometry: the shapes of molecules – bond lengths, angles and dihedrals.

✓ Energies of molecules and transition states: this tells us which isomer is favored at equilibrium, and (from transition state and reactant energies) how fast a reaction should go.

✓ Chemical reactivity: for example, knowing where the electrons are concentrated (nucleophilic sites) and where they want to go (electrophilic sites) enables us to predict where various kinds of reagents will attack a molecule.

✓ IR, UV and NMR spectra: these can be calculated, and if the molecule is unknown, someone trying to make it knows what to look for.

Quantum Mechanics

- The domain of physics that describes how electrons and protons interact is Quantum Mechanics.[1]

$$\hat{H}\Psi(\tau) = \mathcal{E}\Psi(\tau) \quad \hat{H} = \sum_{a=1}^{M}\sum_{b<a}^{M}\frac{Z_a \cdot Z_b}{r_{ab}} - \sum_{i=1}^{N}\sum_{a=1}^{M}\frac{Z_a}{r_{ia}} + \sum_{i=1}^{N}\sum_{j<i}^{N}\frac{1}{r_{ij}} - \sum_{i=1}^{N}\frac{1}{2}\nabla_i^2 - \sum_{a=1}^{M}\frac{1}{2m_a}\nabla_a^2$$

- Models that solve the Schrödinger Equation are called *ab initio* (from the beginning). This is the realm of Quantum Chemistry.

- [1] (Note: There is more than one "Quantum Theory" and some problems in Chemistry require to go beyond the Schrödinger Equation. For example, the Dirac Equation for systems with heavy atoms to include the effects of Special Relativity Theory or Quantum Electrodynamics for highly accurate descriptions).

Tools of Computational Chemistry

- Computational chemists have a selection of methods at their disposal. The main tools available belong to five broad classes:

✓ Molecular mechanics

✓ *Ab initio* calculations

✓ Semi empirical methods

✓ Density Functional Theory

✓ Molecular Dynamics

Molecular Mechanics

- Molecular mechanics is based on a model of a molecule as a collection of balls (atoms) held together by springs (bonds).
- By knowing the spring lengths, their angles, and how much energy it takes to stretch and bend the springs, we can calculate the energy of a given collection of balls and springs, i.e., of a given molecule.
- Geometry is changed until the lowest energy is found enables us to do a geometry optimization.
- Molecular mechanics is fast: a fairly large molecule like a steroid (e.g., cholesterol, $C_{27}H_{46}O$) can be optimized in seconds on a good personal computer.

Ab initio Calculations

- *Ab Initio* calculations (*ab initio*, Latin: “from the start”, i.e., from first principles”) are based on the Schrödinger equation.
- This is one of the fundamental equations of modern physics and describes, among other things, how the electrons in a molecule behave.
- The *ab initio* method solves the Schrödinger equation for a molecule and gives us an energy and *wavefunction*.
- The *wavefunction* is a mathematical function that can be used to calculate the electron distribution (and, in theory at least, anything else about the molecule).

Ab initio Calculations

- *The underlying physical laws necessary for the mathematical theory of a large part of physics and the whole of chemistry are thus completely known, and the difficulty is only that that the exact application of these laws leads to equations much too complicated to be solvable.* – **P.A.M. Dirac**
- The challenge in computational chemistry is to simplify the calculation enough to be solvable, but still accurate enough to predict the desired physical quantity.
- There is an enormous toolbox of theoretical methods available, and it will take skill and creativity to solve real-world problems.

Semiempirical Calculations

- Semiempirical calculations are, like *ab initio*, based on the Schrödinger equation.
- Here, more approximations are made in solving it, and the very complicated integrals that must be calculated in the *ab initio* method are not actually evaluated.
- Instead, the program draws on a kind of library of integrals that was compiled by finding the best fit of some calculated entity like geometry or energy (heat of formation) to the experimental values.
- This plugging of experimental values into a mathematical procedure to get the best calculated values is called *parameterization*.

Semiempirical Calculations

- It is the mixing of theory and experiment that makes the method "*semiempirical*".
- It is based on the Schrödinger equation, but parameterized with experimental values (*empirical* means experimental).
- Semiempirical calculations are slower than molecular mechanics but much faster than *ab initio* calculations.
- Semiempirical calculations take roughly 100 times as long as molecular mechanics calculations, and *ab initio* calculations take roughly 100–1,000 times as long as semiempirical.

Density Functional Theory Calculations

- Density functional calculations (DFT calculations) are, like *ab initio* and semiempirical calculations, based on the Schrödinger equation.
- However, unlike the other two methods, DFT does not calculate a conventional wavefunction, but rather derives the electron distribution (*electron density function*) directly.
- A *functional* is a mathematical entity related to a function.
- Density functional calculations are usually faster than *ab initio*, but slower than semiempirical.

Different Density Functionals

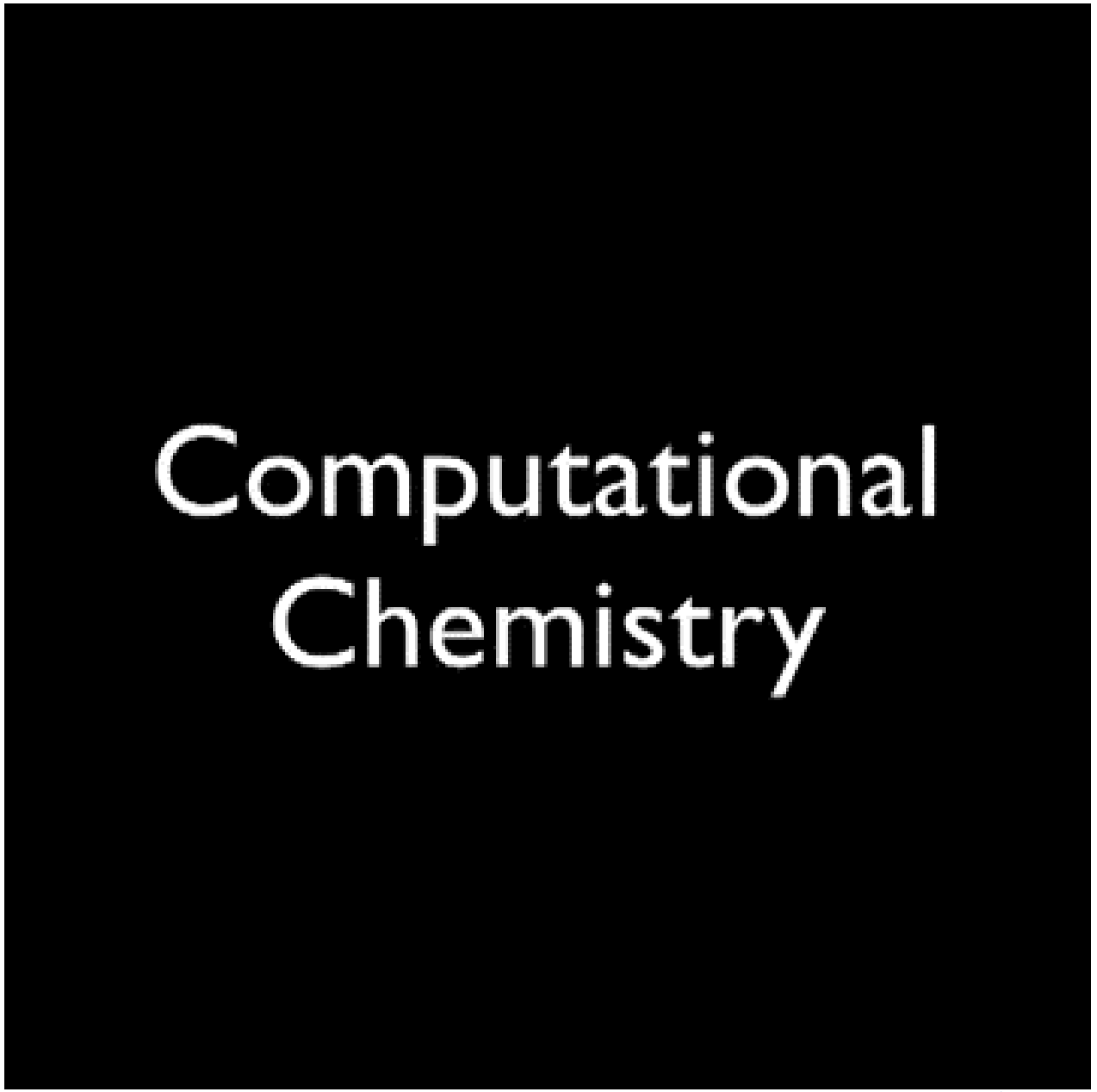
Exchange	Pure	Hybrid		Range separated hybrid	Long range correction
HFS	VSXC	B3LYP	X3LYP	HSEH1PE	LC-wPBE
XAlpha	HCTH	B3P86	BMK	OHSE2PBE	CAM-B3LYP
HFB	HCTH93	B3PW91	M06-HF	OHSE1PBE	wB97XD
	HCTH147	B1B95	M06-2X	wB97XD	
	B97D3	mPW1PW91	PBEh1PBE	wB97	
	M06L	PBE1PBE		wB97X	
		mPW1PBE		M11	

Molecular Dynamics Simulations

- Molecular dynamics calculations apply the laws of motion to molecules.
- Thus, one can simulate the motion of an enzyme as it changes shape on binding to a substrate, or the motion of a swarm of water molecules around a molecule of solute.
- Quantum mechanical molecular dynamics also allows actual chemical reactions to be simulated.

Tools of Computational Chemistry

- Very large biological molecules are studied mainly with molecular mechanics.
- Novel molecules, with unusual structures, are best investigated with *ab initio* or possibly DFT calculations.


Computational
Chemistry

Important Software

- MS Word (Word Processor)
- Endnote (Referencing Software)
- ChemDraw (To Draw Chemical Structures)
- Dropbox
- GaussView
- Gaussian