Chemistry & Computers

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COMPUTATIONAL CHEMISTRY

Computational chemistry uses result of theoretical chemistry incorporated into efficient computer programmed to calculate structure and properties of molecule.

It calculate the properties of molecule such as structure, relative energy, charge distribution, dipole moment, vibrational frequency, reactivity and other spectroscopic quantity.

Computational chemistry range from highly accurate (*Ab initio* method to less accurate (semiemiprical) to very approximate (molecular mechanics).

Advantage of Computational Chemistry

1) It allows the medicinal chemist for use the computational power of computer for measurement of

- Mol. geometry
- electron density
- electrostatic potentional
- conformational analysis
- different types of energies.

2) Determination of structure of ligand and target through X-ray crystallography and NMR spectroscopy.

3) Docking of ligand in rececpter active sites and exact measerment of geometric and energetic favor ability of such interaction.

4) Comparssion of various ligands throgth various parameters.

What does Computational Chemistry Calculate?

✓ Energy, Structure and Properties

- What is the energy for a given geometry?
- How does energy vary when geometry changes?
- Which geometries are stable?
- How do atoms rearranges to form new molecules?
- How do stucture, energy, and properties change over time?

✓ Examples

- Ionization energy (HOMO energy).
- Electron affinity (LUMO energy).
- Proton affinity.
- Electronic excitation energy (UV-Vis spectra).
- NMR chemical shifts and coupling constants.
- Reaction path and barrier height.
- Reaction rate.

Molecular modeling method

The three dimensional shape of both ligand and target site may be determined by X-ray crystallography or computational method.

The most common computational methods are based on either molecular or quantum mechanics.

Both this approaches produce equation for total energy of the structure.

Computational method

- There are two main types method depending on the starting point theory.

- Classical method :-

  Are those method use Newton mechanics to model molecular system.

- Quantum chemistry method:-

  Which makes use of Quantum mechanics to model the molecular system. This method used different type of approximation to solve Schrödinger's Equation.

- **Classical Methods**
  1. Molecular Mechanics
  2. Molecular Dynamics.

- **Quantum Mechanics Methods**
  1. Semi empirical Methods.
  2. *Ab initio* Methods.
  3. Density functional Theory.

Molecular Mechanics

- Molecular mechanics programs use equations based on classical physics to calculate force fields.
- Atoms treated as spheres, bonds as springs and electron are ignored.
- It assume that the total potential energy (E_{total}) of molecule is given by sum of all the energies of attractive and repulsive forces between atom in structure.

Molecular Dynamics

- Molecular dynamics is a molecular mechanics program designed to mimic the movement of atoms within a molecule.
- Molecular dynamics can be carried out o a molecule to generate different conformation which on energy minimization, give a range of stable conformation. Alternatively bonds can be rotated in a stepwise process to generate different conformation.
- Molecular dynamics can also be used to find minimum energy structures and conformational analysis.

Quantum mechanics

- Quantum mechanics is based on arrangement of electrons of molecule and interaction of those electron with electron and nuclei of other molecule.
- It based on the realization that electron and all material exhibit wavelike properties.
- The Quantum mechanics based on finding solution to Schrödinger wave equation.

Schrödinger's Equation

- The Schrödinger equation is the basis of quantum mechanics and gives a complete description of the electronic structure of a molecule. If the equation could be fully solved all information of a molecule could be determined.

$$H\psi = E\psi$$

Where

H=Hamiltonian operator

Ψ =wave fuction

E =Energy system

To solve schrodinger equation was found to difficult. Hydrogen-total energy of hydrogen (E) can be described as the sum of kinetic energy and potential energy of its two component i.e. proton and electron.

Quantum Mechanics Method

1. *Ab inito* method
2. Semiemperical method
3. Density functional theory

Ab Initio method

- *Ab initio* translated from Latin means from "first principles".
- This refers to the fact that no experimental data is used and computations are based on quantum mechanics.
- It derived directly from theoretical principle.

Choice of Method

The method of calculation based on what calculation needs to done and size of molecule.

Molecular mechanics useful for

- Energy minimization
- Identifying stable conformation
- Energy calculation for specific conformations
- Studying molecular motion
- Studying different conformation.

Quantum mechanics method are suitable for calculating,

- Molecular orbital energies
- Heat formation for specific conformation
- Dipole moment
- Bond dissociation energy
- Transition-state geometries and energies

❑ Computational approach in cheminformatics and bioinformatics

- Computational Approaches in Cheminformatics and Bioinformatics covers:
- Data sources available for modelling and prediction purposes.
- Developments of conventional Quantitative Structure-Activity Relationships (QSAR).
- Computational tools for manipulating chemical and biological data.
- Novel ways of probing the interactions between small molecules and proteins.
- The invaluable applications for drug discovery, cellular and molecular biology, enzymology, and metabolism make computational approaches in Cheminformatics and Bioinformatics the essential guidebook for evolving drug discovery research and alleviating the issue of chemical control and manipulation of various systems.

Thank you