CHAPTER 2

Computational Methods
2.1.1 Molecular mechanics

Molecular mechanics is fundamentally different from 'first principles' and semi-empirical QM based methods, in that there is no attempt to solve the Schrödinger equation. There are no wave functions or molecular orbitals in molecular mechanics. In fact the electronic system is not treated explicitly (its effects of course are felt). Instead of blanketing the nuclei with a complicated electron density, in order to determine how much a geometric deformation increases or decreases the potential energy of a molecular system, the potential energy surface is determined from a set of very simple mathematical functions that are fit to reproduce experimental results. In this case, simplicity is a virtue because molecular mechanics methods can effectively treat large macromolecules such as proteins, involving tens of thousands of atoms.

Molecular mechanics treats molecules as a set of balls connected together by springs. Different bonds are represented with different kind of spring with a specific stiffness and equilibrium distance. Each bond and bond angle is assigned a potential function based on experimental bond distances and angles. These are added up and then minimized as the geometry is adjusted.

Hooke's law is assumed for the stretched bonds which results in a restoring force and a rise in energy of the system. In this way, each type of bond possesses a unique potential surface that is characteristic of the bond's natural length and strength. In general, this is also true for bond angles, bond torsions, strain energies and so on. Here the structure and energy of large molecules can be formulated in terms of empirical parameters derived from the elementary features of smaller, well known molecules. Together, the sum of all the energy terms for the bond stretches ($E_b$), angles ($E_\theta$), dihedrals ($E_\phi$), and non-bonded interactions ($E_{nb}$) of a molecule forms the potential energy surface.

$$E_T = \sum E_b + \sum E_\theta + \sum E_\phi + \sum E_{nb}$$ (2.2)
The functional forms of the various energy terms, and the parameters contained within them, make up what is called a force field. In order to provide reasonable agreement with experiment a force field is highly parameterized. The force fields are generally designed to treat specific classes of molecules since the parameters are different for different class of molecules. The most widely used force fields are the AMBER, CHARMM, DREIDING, UFF etc. Molecular mechanics methods are fast and used mainly for large molecules. The limitation of molecular mechanics methods is that the bond breaking and formation of covalent bonds cannot be treated and therefore some chemical systems cannot be simulated accurately.

The limitation of these methods is that we do not get electron density, vibrations, or other spectroscopic results from these methods.

2.2 Quantum Mechanical Methods

These differ mainly according to how, or if, “electron correlation” is treated. Electron correlation is the tendency of electrons to avoid each other, even within the same orbital. To describe completely the quantum-mechanical behaviour of a stationary system of \( N \) interacting electrons it is necessary to calculate its many-electron wavefunction. In principle this may be obtained from the time-independent Schrödinger equation. However, since the motion of each electron is coupled to that of the other electrons in the system, in practice the equation is not solvable analytically and approximations are needed.

The most direct way of determining the energetics and structure of a molecular system is to solve the quantum mechanical Schrödinger equation. This is a computationally demanding process and consequently only small molecular systems can be treated. The results, however, can be very accurate with experimental accuracy being attained in some cases. Other properties, such as transition state structures, reaction barriers and reaction profiles cannot be easily determined experimentally and are best calculated by computational...
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means. Quantum mechanical methods can also provide a detailed picture of the electronic structure of a molecular system, which can yield invaluable insights into the nature of the system.

The quantum mechanical methods which are further grouped into 'first principles' (or 'ab initio' methods) and semi-empirical approaches. The ab initio or "first principles" techniques are derived from the basic postulates of quantum mechanics and require little or no parameterization. The most widely used 'first principles' scheme is the ab initio Hartree-Fock method. Another quantum mechanical method known as density functional theory or DFT which is faster and generally more accurate than Hartree-Fock based methods. These methods are discussed latter in this chapter. The major disadvantage of these methods is that one can study the molecular systems with these methods for less than one hundred atoms due to high computational time required.

Another approach used to solve Schrödinger equation is the semiempirical methods which are much faster but less accurate than the ab initio methods. Semiempirical methods use precalculated orbital functions for different kinds of atoms. The most widely used semiempirical methods are the CNDO, INDO, MINDO, MDO, AM1, and PM3. With semiempirical methods many approximations are made in solving the Schrödinger equation that are designed to speed up the calculations. To make up for these approximations, many empirical parameters are introduced that have been fitted to experimental or ab initio results. The fitted parameters that are introduced give these methods the name "semi-empirical".

2.3 The Born-Oppenheimer Approximation used to solve the Schrödinger Equation

The many-particle Schrödinger equation is too difficult to solve. A widely used and accepted approximation to simplify this equation is the so-called Born-Oppenheimer (BO) approximation [12]. This approximation is based on the large difference in mass of the
electrons and nuclei. Since the nuclei are much heavier than the electrons their movement is much slower than that of the electrons. It states that, due to the difference in mass between the nuclei and the electrons, the movement of the particles of one kind can be described independently of the movement of the other. Therefore, the distribution of the electrons at a certain configuration of the nuclei can be calculated. The Schrödinger equation for the electronic system in principle has to be solved for all possible configurations of the nuclei. However, since the nuclei are very localized around their equilibrium positions in the body fixed frame we can consider them to be fixed at these positions. This reduces the problem to solving the electronic part of Eq. (2.1). This problem cannot be solved exactly for many-electron systems and in practice we need to make approximations by using perturbation theory or variational methods. Also the wavefunction describing the electrons has to be antisymmetric i.e. when two electrons are exchanged, the wavefunction has to change sign. The antisymmetry of the wavefunction can be achieved by building it from so-called Slater determinants. With BO approximations, solving the Schrödinger equation now involves finding the one-electron wavefunctions that give the most accurate total wavefunction. According to the variational principle, this is the wavefunction associated with the lowest energy.

The exact solution of the Schrödinger equation can be obtained only for few systems such as hydrogen atom. The BO approximation is the key approximations incorporated to solve the Schrödinger equation. Therefore, \( \Psi \) can be approximated as a product of electronic and nuclear wavefunctions.

\[
\Psi = \Psi_{\text{elec}} \Psi_{\text{nucl}} \tag{2.3}
\]

The electronic wavefunction, \( \Psi_{\text{elec}} \) can be obtained by assuming the electrons to be moving in a field of fixed nuclei and the nuclear wavefunction, \( \Psi_{\text{nucl}} \) can be obtained by assuming the nuclei to be moving in an average electronic field. Upon applying the Born-Oppenheimer
approximation to Eq. (2.1) the second term representing the kinetic energy of the nuclei can be removed from consideration of the electronic energy and the fifth term representing the repulsion between the nuclei becomes a constant. As a result, any constant added to an operator adds only to the operator eigenvalues but has no effect on the operator eigenfunctions. Therefore, Eq. (2.1) becomes

$$H_{el} = -\sum_{i=1}^{N} \frac{1}{2} v_{i}^{2} - \sum_{i=1}^{N} \sum_{A=1}^{M} \frac{Z_{A}}{r_{iA}} + \sum_{i=1}^{N} \sum_{j>i}^{N} \frac{1}{r_{ij}}$$  (2.4)

where $H_{el}$ is known as the electronic Hamiltonian, i.e. Hamiltonian describing the motion of $N$ electrons in a field of $M$ point charges.

Solution of the electronic Schrödinger equation,

$$H_{el} \Psi_{el} = E_{el} \Psi_{el}$$  (2.5)

gives the electronic wavefunction, $\Psi_{el}$ and the electronic energy $E_{el}$. The electronic wavefunction, describes the motion of the electrons or represents the molecular orbitals and the electronic energy, represents the energies of the molecular orbitals. The electronic wavefunction and electronic energy obtained by solving the electronic Schrödinger equation depends explicitly on the electronic coordinates and parametrically on the nuclear coordinates. Parametric dependence means that, for different arrangements of the nuclei, $\Psi_{el}$ is a different function of the electronic coordinates. The total energy of a system with fixed nuclei is given by

$$E_{tot} = E_{el} + \sum_{A=1}^{M} \sum_{B=1}^{M} \frac{Z_{A}Z_{B}}{R_{AB}} + \sum_{i} E_{b} + \sum_{i} E_{\theta} + \sum_{i} E_{\phi} + \sum_{i} E_{nb}$$  (2.6)

If one has solved the electronic problem, it is possible to solve for the motion of nuclei as well by using the same assumption as that used to solve the electronic problem. Since the electrons move much faster than the nuclei, it is a reasonable approximation to replace the electronic coordinates in Eq. (2.1) by their average values, averaged over the electronic wavefunction.
This then generates a nuclear Hamiltonian \( H_{\text{nuc}} \) for the motion of the nuclei in an average electronic field.

\[
H_{\text{nuc}} = \sum_{A=1}^{M} \frac{1}{2M_A} \left( -\sum_{i=1}^{N} \frac{1}{2} V_i^2 - \sum_{i=1}^{N} \sum_{A=1}^{M} \frac{Z_A}{r_{iA}} + \sum_{i=1}^{N} \sum_{j>i}^{N} \frac{1}{r_{ij}} \right) + \sum_{A=1}^{M} \sum_{B>A}^{M} \frac{Z_A Z_B}{R_{AB}} \tag{2.7}
\]

\[
H_{\text{nuc}} = -\sum_{A=1}^{M} \frac{1}{2M_A} \nabla_A^2 + E_{\text{elec}} + \sum_{A=1}^{M} \sum_{B>A}^{M} \frac{Z_A Z_B}{R_{AB}} \tag{2.8}
\]

\[
H_{\text{nuc}} = -\sum_{A=1}^{M} \frac{1}{2M_A} \nabla_A^2 + E_{\text{tot}} \tag{2.9}
\]

The total energy provides a potential for the nuclear motion. Therefore, the nuclei in the framework of the Born-Oppenheimer approximation move on a potential energy surface obtained by solving the electronic problem. Solving the nuclear Schrödinger equation,

\[
H_{\text{nuc}} \Psi_{\text{nuc}} = E \Psi_{\text{nuc}} \tag{2.10}
\]

gives the nuclear wavefunction \( \Psi_{\text{nuc}} \) which describes the rotation, vibration and translation of a molecule and the energy \( E \) which is a sum of the rotational, vibrational and translational energy of a molecule.

### 2.4 The Variation Method

The variational principle is the basis for the variational determination of a wavefunction. The variational principle states that the expectation value or average value of the energy for an approximate wave function always lies above or equal to the exact solution of the Schrödinger equation for the same Hamiltonian operator. This means that if we have a wave function that contains adjustable parameters and we adjust them to minimize the expectation value of the energy, then we are approaching the exact result. Assume the ground state energy of the system be with the corresponding wavefunction, and let \( \Psi \) be an arbitrary function, the expectation value of energy with the trial wavefunction \( \Psi \) can be expressed as

\[
E = \frac{\langle \Psi | H | \Psi \rangle}{\langle \Psi | \Psi \rangle} \tag{2.11}
\]
where the denominator is required for normalization. As stated above, according to the variation theorem for any $\Psi$ it is true that $E_0 \leq E$ and equality holds only if $\Psi = \Psi_0$. In order to find the ground-state energy of the system, we have to minimize Eq. (2.11). To achieve this, we have to select a set of known basis functions, express the trial wavefunction, $\Psi$, as a linear combination of these, and substitute the result into Eq. (2.11) and solve it to get a secular determinant and ultimately the trial wavefunction. A well known variation method is the Hartree-Fock method.

2.5 The Hartree-Fock Method

The conventional way of solving Schrödinger’s equation starts with Hartree-Fock (HF) theory. In this method, electron correlation (interaction between electrons with different spins) is not present explicitly. As electrons are Fermi particles, two electrons with the same spin cannot be present at the same time at the same position [13]. Two electrons with differing spin (one alpha, the other beta) can be present at the same time at the same place, but are less likely to do so due to electrostatic repulsion.

In HF model it is assumed that the total electronic wavefunction consists of only one single determinant and the electron-electron repulsion is included in an average way. This model neglects the Coulomb correlation between electrons. The Hartree-Fock (HF) or self-consistent field (SCF) calculation scheme is a self-consistent iterative variational procedure to calculate the Slater determinant (or the molecular orbitals) for which the expectation value of the electronic molecular Hamiltonian is minimum. This method does not include the effect of electron correlation.

The main idea of this approach is that each electron moves in a mean field generated by all other electrons and the external potential (e.g. the nuclear potential). This means that the potential in the Hamiltonian can be approximated by an effective single-particle potential. Consequently we can write the wave function as a Slater determinant of single-particle orbitals. We can then use the Rayleigh-Ritz variational theorem to minimize the expectation
value of the Hamiltonian with respect to this Slater determinant. This leads to the so-called
Hartree-Fock equations from which we can obtain the effective single-particle potential that
gives the lowest energy, the Hartree-Fock potential. Since this potential itself depends on the
single-particle orbitals of the Slater determinant, the problem has to be solved self-
consistently.

This assumption leads to the independent-particle model, which essentially reduces
the many-electron problem to the problem of solving a number of coupled single-electron
equations. The single-electron equations are solved in an iterative manner until a chosen level
of self-consistent accuracy is achieved. This primary approximation in the Hartree Fock
method is called the central field approximation. This means that the Coulombic electron-
electron repulsion is not specifically taken into account. However, its net effect is included in
the calculation. HF method is a variational calculation, meaning that the approximate
energies calculated are all equal to or greater than the exact energy. The energies are always
greater than the exact energy and approach a limiting value called the Hartree-Fock limit. The
Hartree-Fock limit has the best HF wave function and is reach with such a large and flexible
basis set. Basis sets are described in a separate section in this chapter.

The problem is that electrons are not paired up in the way that the Hartree-Fock
method supposes. Another limitation of HF calculations is that they do not include electron
correlation. The difference in energy between the exact result and the Hartree-Fock limit
energy is called the "correlation energy". The Hartree-Fock approximation is a fast and
reliable method for a wide range of atomic systems, but it is just a first approximation. There
are several calculation schemes developed to generate improved results. Any method which
goes beyond HF in attempting to treat this phenomenon properly is known as an electron
correlation method or a post-HF method. HF theory is very useful for providing initial, first-
level predictions for a wide range of problems and molecular systems.
The electron correlation is discussed in a separate section in this chapter.

The Hartree-Fock wave function is often used as a reference wave function in other post HF methods like, for example, the configuration interaction method, Møller plesset method etc.

2.6 The Perturbation Method

Perturbation theory works on the idea that if we know the answer to one problem we can work out an answer to a closely related problem. It is another method to find quantum mechanical wavefunctions [14]. It is especially suited to problems that are similar to model or ideal situations differing in only some small way, which is the perturbation. In perturbation theory, the Hamiltonian for any problem is partitioned into two or more parts. The first part is one for which the eigenfunctions and eigenvalues are known, while everything else represents the perturbation. This first part and the associated eigenfunctions and eigenvalues are distinguished in notation by a zero superscript. Assume the Schrödinger equation for the model system is written as

$$H^0 |\psi(0)\rangle = E^0 |\psi(0)\rangle \quad (2.12)$$

then the Schrödinger equation of the true system can be expressed as:

$$H|\Psi\rangle = E|\Psi\rangle$$

where $H = H^0 + \lambda V$

Here, $V$ is the potential representing the difference between the two systems and $\lambda$ is a dimensionless parameter, the *perturbation parameter*. If we can describe the true system as a small perturbation of the model, $\Psi$ and $E$ will not be very different from $\psi(0)$ and $E^0$, and both can be expressed using powers of $\lambda$:

$$\Psi = \psi(0) + \lambda \psi(1) + \lambda^2 \psi(2) + ... \quad \text{and} \quad E = E(0) + \lambda E(1) + \lambda^2 E(2) + ... \quad (2.13)$$

To simplify the mathematics, we choose the perturbed wavefunctions to be orthogonal. By inserting the proceeding two equations into Eq. $H|\Psi\rangle = E|\Psi\rangle$

$$(H^0 + \lambda V) (\psi(0) + \lambda \psi(1) + \lambda^2 \psi(2) + ...) = (E(0) + \lambda E(1) + \lambda^2 E(2) + ...) (\psi(0) + \lambda \psi(1) + \lambda^2 \psi(2) + ...)$$
Simplifying this equation and equating the coefficients of $\lambda$, $\lambda^2$, $\lambda^3$ etc. we get

$$H^0 \psi^{(0)} = E^{(0)} \psi^{(0)}$$

$$V \psi^{(0)} + H^0 \psi^{(1)} = E^{(1)} \psi^{(0)} + E^{(0)} \psi^{(1)}$$

$$V \psi^{(1)} + H^0 \psi^{(2)} = E^{(2)} \psi^{(0)} + E^{(1)} \psi^{(1)} + E^{(0)} \psi^{(2)}$$

and so on.

Depending on the power of $\lambda$ we truncate this expression. We refer to them as the first, second... etc. order of perturbation. First-order perturbation theory delivers $\psi^{(1)}$ and $E^{(1)}$, we obtain $\psi^{(2)}$ and $E^{(2)}$ at the second order and so on.

However an important question that arises is whether the perturbation series (Eq. 2.13) converges. In most practical cases, it does converge well (although it cannot be taken for granted). An important shortcoming of the perturbation theory is that it is not variational; i.e. perturbation theory does not provide an upper bound to the energy of the system. It is reasonable to expect, however, that by including the higher-energy terms, we may improve the quality of the results.

Another method which is developed to improve upon the HF wavefunction is the Møller-Plesset perturbation theory. In this approach, electron interaction is treated as a perturbation to the sum of one-electron Hamiltonians. If the perturbation correction to energy is truncated at the second, third, fourth or fifth order, the method is known as MP2, MP3, MP4 and MP5 respectively. Electron correlation is accounted for allowing one or more electrons to occupy higher-energy, unoccupied ("anti-bonding") MO's. This results in an energy correction that lowers the total energy because it lowers the electron-electron repulsion energy. The commonly-used MP2 method actually considers the effect of 2 electrons occupying anti-bonding orbitals. MP2 is more expensive than HF because more configurations must be calculated.

**Electron Correlation**
Because electrons repel each other according to Coulomb's law, there is a tendency for them to keep out of each other's way. In Hartree-Fock theory, this instantaneous electron-electron repulsion is replaced by the repulsion of each electron with an average electron charge cloud. This approximation introduces an error in the wavefunction and the energy. The error in energy is called the total correlation energy. The error in the total energy is about 1 ev per electron pair in a bond or lone pair. This correlation between the motion of electrons is referred to as "electron correlation". Thus, the HF method provides an inadequate treatment of the correlation between the motions of electrons within a molecular system, especially that arising between electrons of opposite spins. It however, accounts for the correlation between the motions of electrons of same spin. This correlation is termed as exchange correlation and is automatically taken into account by the antisymmetry requirement of the wavefunction.

The difference between HF energy and the exact (for a simplified non relativistic Hamiltonian) energy of a system is referred to as "correlation energy". Correlation energy is small compared to the total energy but it is of the same order of magnitude as the quantities of chemical interest. Any method which goes beyond SCF in attempting to treat electron correlation properly is known as an electron correlation method (despite the fact that HF theory does include some correlation effects) or a post-SCF method.

Most ab initio methods dealing with electron correlation are based on the HF reference wavefunction. Almost all the post-SCF methods, such as, configuration interaction (CI), coupled cluster (CC), multi-reference configuration interaction (MRCI), multi-configuration self-consistent field (MCSCF) and complete active space self-consistent field (CASSCF), use one of the following approaches to improve upon the HF wavefunction:

a) Optimizing only the coefficients of the Slater determinants.
b) Optimizing both the coefficients of the Slater determinants and the coefficients of
the one-electron wavefunctions forming the Slater determinant.

2.7 Density Functional Theory (DFT)

A different way to obtain the properties of many-electron systems without making any
explicit reference to the wave function was formulated in the 1960's by Hohenberg, Kohn
and Sham. This method called density-functional theory (DFT) has as fundamental quantity
the electron density. The DFT method is in principle based on two theorems derived and
proved by Hohenberg and Kohn in 1964. Hohenberg and Kohn showed in 1964 that the
external potential is a functional of the electron density. DFT describes the properties of the
ground state of a many-electron system solely by the electron density [15,16]. As a
consequence every ground-state property, and in particular the ground-state energy, is a
functional of the electron density. It has many advantages over the wavefunction based
methods. Whereas the complicated many-body wave function depends on three spatial
variables for each of the N electrons, the electron density is a collective variable which only
depends on three spatial variables, making the electron density a quantity that is easier to deal
with in practice. Furthermore, the electron density is also easier to deal with from a
conceptual point of view. That the ground-state properties of a many-electron system can be
obtained from the electron density alone is, however, not obvious. However, the Hohenberg-
Kohn theorems do not give the form of the functional dependence of the energy on the
density.

Energy of a molecule = $F[\text{electron density}]$, where electron density = $f(x,y,z)$

This theorem says that there exists a functional that will calculate molecular energy from
electron density. But it does not say what the functional is.

Shortly after, in 1965, Kohn and Sham formulated the idea that the electron density of
a system of interacting particles under the influence of some external potential can be
reproduced in a system of noninteracting particles under the influence of an effective potential, the so-called Kohn-Sham potential. According to the Hohenberg-Kohn theorem this Kohn-Sham potential is also a functional of the electron density. The Kohn-Sham formulation of DFT allows one to write the Schrödinger equation as a set of single-particle equations that together with the electron density can be solved in a self-consistent manner. Assuming that indeed such a Kohn-Sham system of noninteracting particles exists this theory is exact. The Kohn-Sham potential consists of the external potential, the Hartree potential, which is the average Coulomb potential generated by all the electrons, and the so-called exchange-correlation potential which contains all the remaining contributions. The latter potential is the functional derivative of the exchange-correlation energy with respect to the electron density. In practice we have to find approximations for the exchange-correlation energy and the corresponding potential.

DFT gives nearly the same accuracy as the second order Møller Plesset method (MP2), but with the (lower) computational cost of Hartree-Fock SCF. DFT methods account for electron correlation by estimating the interaction of an electron with the total electron density. DFT orbitals are also formed from basis functions like those used in SCF or MP2.

Kohn and Sham provided the first practical computational scheme, by postulating a reference system of noninteracting electrons, moving in an effective potential. This effective potential includes the external potential (of the nuclei) but also the Coulomb interaction of the electron density with itself and corrections to this averaged treatment of the electron-electron repulsion. These corrections are the exchange correlation, which originates from the fact that electrons are fermions and described by an antisymmetric wavefunction, and the Coulomb correlation, which is caused by the fact that electrons avoid each other due to their mutual electrostatic repulsion. The non-interacting reference system is then represented by a one-determinantal wavefunction, yielding the exact density of the interacting system and the
corresponding exact energy. This is computationally highly efficient, since one is not challenged by a multi-determinantal wavefunction. However, modelling the functional dependence of the exchange correlation energy on the electronic density is the problematic part of Kohn-Sham DFT.

The only problem with density functional methods is that the correct exchange and correlation functional form is not known and it is too complicated to be evaluated analytically. Therefore, numerical quadrature must be used which may lead to significant loss of precision. In practice $E_{xc}$ is divided into two parts, exchange $E_x$ and correlation $E_c$.

$$E_{xc} = E_x + E_c$$

There is no systematic way to improve the accuracy of a certain functional. Approximations have been developed, such as the local density approximation (LDA), or generalized gradient approximations (GGAs), hybrid functionals where different choices for the functional dependence of exchange and correlation parts on the density and different combinations thereof have lead to a wide range of available density functionals.

### 2.8 Exchange-Correlation Functionals

In order to apply the theory outlined in the previous section we need an approximations for the exchange-correlation functional $Exc[\rho]$. The first approximation that was widely used is the so-called local density approximation (LDA). The LDA approximates the true inhomogeneous system locally by a homogeneous electron gas. This is a very crude approximation and therefore one would expect that it will only work well in systems with a slowly varying density. However, it turns out that this simple approximation works rather well even in very inhomogeneous systems such as atoms and molecules. There are also some notable failures of the LDA. We will briefly discuss two of them. Since the exchange-correlation potential is proportional to the density it falls of exponentially at large distances from the nucleus instead of approaching zero as $-1/r$. This is the correct behaviour because at
large distance the electron sees the Coulomb potential of the positively charged ion that it has left behind which is equal to $-1/r$. At large distance the nuclear potential and the Hartree potential cancel each other and therefore the exchange-correlation potential must decay as $-1/r$. A second well-known failure of the LDA is the systematic underestimation of the band gap of semiconductors and insulators due to the absence of derivative discontinuities in the LDA. This means that the LDA exchange-correlation energy functional does not show a jump in its magnitude upon removal or addition of an infinitesimal fraction of the integer number of electrons.

Listed below are some of the commonly used exchange, correlation and hybrid functionals.

Exchange Functionals

- **Becke 88** - Becke's 1988 functional, which includes the Slater exchange along with corrections involving the gradient of the density [17].
- **PBE** - The 1996 functional of Perdew, Burke and Ernzerhof [26,27].

Correlation functionals

- **VWN**: Vosko, Wilk, and Nusair 1980 correlation functional(III) fitting the RPA solution to the uniform electron gas, often referred to as Local Spin Density (LSD) correlation [28].
- **VWNV(VWN5)**: Functional V from the 1980 paper which fits the Ceperly-Alder solution to the uniform electron gas [28].
• LYP: The correlation functional of Lee, Yang, and Parr which includes both local and non-local terms [29,30].
• PL (Perdew Local): The local (non-gradient corrected) functional of Perdew (1981) [31].
• P86 (Perdew 86): The gradient corrections of Perdew, along with his 1981 local correlation functional [32].
• B95 (Becke 95): Becke's $\tau$-dependent gradient-corrected correlation functional (defined as part of his one parameter hybrid functional [33].
• PBE: The 1996 gradient-corrected correlation functional of Perdew, Burke and Ernzerhof [26,27].

Hybrid functionals
• B3LYP: Becke Three Parameter Hybrid functionals. These functionals have the form devised by Becke in 1993 [34].
• B3P86 specifies the same functional with the non-local correlation provided by Perdew 86, and B3PW91 specifies this functional with the non-local correlation provided by Perdew/Wang 91.
• B1B95 - Becke One Parameter Hybrid functional [33].
• MPW1PW91 - uses modified Perdew-Wang exchange and Perdew-Wang 91 correlation [23].
• B98 - Becke's 1998 revisions to B97 [35, 36].
• B971 - Handy, Tozer and coworkers modification to B97 [37].
• B972 - Wilson, Bradley and Tozer's modification to B97 [38].
• PBE1PBE- hybrid functional of Perdew, Burke and Ernzerhof. This functional uses
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25% exchange and 75% correlation weighting [27].

- B1LYP – one parameter hybrid functional by Adamo and Barone [33-39].

DFT is now a leading method for electronic structure calculations in quantum chemistry fields, especially the Hybrid DFT. In many cases, it gives quite satisfactory results.

2.9 Time-dependent DFT

In 1984 Runge and Gross formulated the time-dependent extension of the Hohenberg-Kohn theorem. They showed that for two densities evolving from a common initial state and generated by two external potentials that differ by more than a purely time-dependent function and that both have a Taylor expansion around the initial time cannot be the same. Therefore, for a given initial state, the expectation value of any quantum mechanical operator is a unique functional of the density. One can then introduce a time-dependent Kohn-Sham system to obtain equations that can be solved in practice. This method is called time-dependent density-functional theory (TDDFT). However, TDDFT can only be used to describe systems that are under the influence of time-dependent fields that can be described by a time-dependent scalar potential.

2.10 Computational Modelling of Solvation

Most of chemical and biochemical reactions occur in solution, and the solvent can have a major effect on the position of chemical equilibrium and on reaction rates. While gas phase predictions are appropriate for many purposes, they are inadequate for describing the characteristics of many molecules in solution. Indeed the properties of molecules and transition states can differ considerably between the gas phase and solution. For example, electrostatic effects are often much less important for species placed in a solvent with high dielectric constant than they are in the gas phase.

Description of solvation requires the application of both quantum chemical and statistical mechanical techniques. Using quantum chemical techniques, one can accurately derive the
intermolecular forces of the system under consideration. Solvation can then be modeled using statistical mechanical techniques or molecular dynamics simulations.

Some of the important physical processes involved in solvation are as follows:

1) Intermolecular forces between pairs of molecules: The intermolecular forces are usually partitioned into electrostatic, polarization, dispersion and repulsion contributions.

2) Many-body effects: The effective force between pairs of molecules is influenced by the presence of neighbouring molecules. A simple example of this arises due to molecular Polarization; one molecule polarizes another, whose interaction with a third molecule is then affected.

Some of the commonly used solvation models are statistical models, Solvent/Solute Descriptor Models, molecular simulations, the supermolecule approach, and reaction field models. The most widely used models to study the solvation effects are the reaction field models. In the reaction field models, the solvent molecules are represented by a polarizable continuum of uniform dielectric constant \( \varepsilon \). The solute molecule is placed in a cavity in the solvent which becomes polarized. The induced solvent reaction field then interacts with the charge distribution of the solute. There are a variety of reaction field models available and they all differ in the way they define the cavity and the reaction field. The simplest reaction field model is the Onsager model in which the solute occupies a fixed spherical cavity of radius \( a_0 \) within the solvent field. The solute dipole induces a dipole in the solvent medium and the electric field applied by the solvent dipole in turn interacts with the solute dipole, resulting in net stabilization. One of the major drawbacks of this model is that systems having zero dipole moment will not exhibit any solvent effect.

Another popular reaction field model is the polarized continuum model (PCM), developed by Tomasi et al. [40]. In the PCM model, the cavity is defined as the union of a series of interlocking atomic spheres. The effect of polarization of the solvent is computed by
means of numerical integration rather than by an approximation to the analytical form used in
the Onsager model. The reaction field models described above do not provide a realistic
picture of solute-solvent interactions because of the assumption of a pre-defined shape such
as a sphere or a set of overlapping spheres for the solute cavity.

To overcome this shortcoming, isodensity surface models such as isodensity polarized
continuum model (IPCM) and self-consistent isodensity polarized continuum model
(SCIPCM) were developed. In the IPCM model, the cavity is defined as an isosurface of the
total electron density of the solute molecule. This isodensity is determined by an iterative
process in which an SCF cycle is performed and converged using the current isodensity
cavity. The resultant wavefunction is then used to compute an updated isodensity surface, and
the cycle is repeated until the cavity shape no longer changes upon completion of the SCF. A
cavity defined as an isosurface and the electron density are necessarily coupled. The SCIPCM
model was designed to take this effect fully into account. It includes the effect of solvation in
the solution of the SCF problem. This procedure solves for the electron density which
minimizes the energy including the solvation energy and which itself depends on the cavity
which in turn depends on the electron density. In other words, the effects of solvation are
folded into the iterative SCF computation rather than comprising an extra step afterwards.
SCIPCM model thus accounts for the full coupling between the cavity and the electron
density and includes coupling terms that IPCM neglects.

2.11 Basis Sets

A basis set is a mathematical function (basis function). The molecular orbitals \( \Psi_i \) in a
Hartree-Fock treatment are expressed as a linear combination of a pre-defined set of one-
electron functions or \( N \) nuclear-centered functions known as basis functions. Basis sets assign
a group of basis functions to each atom within a molecule to approximate its orbitals.
Molecular orbitals (MOs) are approximated as linear combinations of basis functions (the
basis set), which mathematically look like s, p, or d atomic orbitals. Each atom is assigned several (or many) basis functions. In turn, each basis set function is comprised of a number of gaussian functions called primitives. Calculations using large basis sets are more accurate because they are less restrictive on the location of the electrons. Such calculations are also more expensive because they require computing more integrals.

The basis functions are, more or less arbitrarily, chosen beforehand. Usually, the basis functions are located on the atoms involved. In essence, the solving of the Schrödinger equation consists of the finding of the set of coefficients that minimizes the energy of the electronic system. Important aspects determining the accuracy of the calculation are the size and the aptness of the basis set. One cannot increase the basis-set size infinitely: the computational cost increases rapidly with increasing basis-set size. Many basis sets have already been developed, each with its own advantages and disadvantages.

The following two types of basis functions are most widely used:

(1) Slater-type functions and (2) Gaussian-type functions.

The Slater-type orbitals (STOs) provide a very good representation of atomic orbitals because they possess a cusp at the nucleus. It is, however, very difficult to evaluate the two-electron integrals using STOs.

Gaussian-type functions (GTFs) lack the proper cusp behavior of the STOs as the distance between the nucleus and electrons approaches zero and they die off quickly at large distances. Even though the GTFs do not represent atomic orbitals as well as STOs, they are widely used because the evaluation of two-electron integrals is much easier using the GTFs.

Due to the ease of calculating two-electron integrals with GTFs, most ab initio electronic structure programs use GTFs rather than STFs as basis functions. In order to provide an improved description, the individual basis functions in a Gaussian basis set are often taken as a linear combination of GTFs. A brief description of various types of basis set is given below.
2.11.1 Minimal Basis Sets

A minimal basis set is the one which contains the minimum number of basis functions needed for each atom, while maintaining the overall spherical symmetry. Minimal basis set use fixed atomic-type orbitals. For instance, the “STO-KG” basis set is a minimal basis set which approximates the expansion of Slater-type atomic orbitals (STOs) by taking a linear combination of K gaussian functions. The commonly used STO-KG minimal basis set is STO-3G. The STO-3G basis set approximates the Slater-type atomic orbitals using three gaussian primitives.

2.11.2 Split Valence Basis Sets

Split-valence basis sets were developed by John Pople, 1998 Nobel Prize winner. The basis set nomenclature describes how the basis functions are constructed from the Gaussian primitives. For e.g. In 6-31G basis set, the first number (6) indicates the number of gaussian primitives used for core or inner electrons and the number of digits (two here, 3 and 1) indicates how many sub-orbitals each valence atomic orbital is split into. The values tell how many gaussian primitives make up each sub-orbital. Diffuse functions extend further out from the nucleus, and are necessary for modeling non-bonding or weakly-bonding systems.

A basis set obtained by doubling all the functions of a minimal basis set is referred to as a “double-zeta” basis set. An example of a double-zeta basis set is the Dunning-Huzinaga basis set (D95), in which all the molecular orbitals are formed by a linear combination of two different functions for each atomic orbital. A much simpler way of extending a basis set is to just double the valence functions of a minimal basis set. Such a basis set is known as a “split valence” basis set in general and a “double split valence” basis set in particular. The commonly used double split valence basis sets are 3-21G and 6-31G basis set. A 3-21G basis set is formed by taking a linear combination of three GTO’s to form the core orbitals and the valence orbitals are split into two parts, formed by taking a linear combination of two and one
GTO’s for the inner and outer parts respectively. A triple split valence basis set, such as 6-311G, is formed by splitting the valence orbitals into three parts.

2.11.3 Polarized Basis Set

Split valence basis sets allow orbitals to change size, but do not allow them to change shape. Polarized basis sets remove this limitation by adding orbitals with angular momentum beyond what is required for the ground state to the description of each atom. For example, polarized basis sets add \( p \) functions to hydrogen atoms, \( d \) functions to carbon atoms and \( f \) functions to transition metals. The most commonly used polarized basis set, 6-31G(d) (also represented as 6-31G*) is formed by adding \( d \) functions to all the heavy atoms. The other commonly used basis set, 6-31G(d,p) (also represented as 6-31G**) is formed from the 6-31G(d) basis set by adding \( p \) functions to hydrogen atoms. In a similar manner, the 6-31G(mdf, npd) basis set is formed from the 6-31G basis set by adding \( m \) sets of \( d \) functions and one set of \( f \) function to heavy atoms and \( n \) sets of \( p \) functions and one set of \( d \) function to hydrogen and helium. For cases where the description of hydrogen atoms is important, a set of \( p \) functions is usually added to hydrogen atoms.

2.11.4 Diffuse Basis Sets

Diffuse functions are larger-size versions of \( s \)-and \( p \)-type functions. They allow orbitals to occupy a larger region of space. Basis sets with diffuse functions are important for systems where electrons are relatively far from the nucleus: molecules with lone pairs, anions and other systems with significant negative charge, systems in their excited states, systems with low ionization potentials, description of absolute acidities, and so on. The 6-31+G(d) basis set is an example of a diffuse function basis set. It is formed from the 6-31G(d) basis set by incorporating a set of \( s \) and \( p \) diffuse functions to the heavy atoms. In general, a larger basis set, more accurately approximates the orbitals by imposing fewer restrictions on the location of electrons in space.
References: