CHAPTER I
A Review on Pharmaceutical Materials, Principles and Practice of Spectroscopic Techniques and Quantum Chemical Methods

1.1. Introduction

Spectroscopy is the interaction of electromagnetic radiation with matter. Absorption spectroscopy is most widespread and energy quanta from electromagnetic radiation are absorbed by the sample illuminated by the radiation. Depending upon the wavelength (frequency) of the electromagnetic radiation, transitions between different kinds of energy states are induced in the molecules of the sample. Spectroscopy consists in the recording of absorption changes as the frequency of the radiation is varied over a given range. A plot of absorption of energy versus frequency known as the spectrum usually shows a number of absorption bands whose characteristic position, intensity, width and shape yield important information. Spectroscopy is one of the important experimental techniques for determining the electronic structure of atoms and molecules. This introductory chapter is concerned with the pharmaceutical materials, applications of spectroscopy and a brief discussion about the quantum chemical methods. The experimental techniques of Fourier transform infrared, Fourier transform Raman and UV-Visible spectroscopy are discussed. Techniques involved in handling the samples are briefly explained.

1.2. Pharmaceutical materials

A pharmaceutical drug also referred to as a medicine or medication can be loosely defined as any chemical substance or product comprising such intended for use in the medical diagnosis, cure, treatment or prevention of disease. The word pharmaceutical comes from the Greek word Pharmakeia. The modern transliteration of Pharmakeia is Pharmacia. A drug is a substance which may have medicinal, intoxicating, performance enhancing or other effects when taken or put into a human body or the body of another animal and is not considered a food or exclusively a food. In pharmacology, a drug is “a chemical substance used in the treatment, cure, prevention or diagnosis of disease or used to otherwise enhance physical or mental well-being”. Drug is thought
to originate from Old French “drogue”, possibly deriving later into “droge-vate” from Middle Dutch meaning “dry barrels” referring to medicinal plants preserved in them. Medications can be classified in various ways, such as by chemical properties, mode or route of administration, biological system affected, or therapeutic effects. An elaborate and widely used classification system is the Anatomical Therapeutic Chemical Classification System (ATC system).

Without question, the drugs produced by the ethical pharmaceutical industry over the past century have irrevocably changed the fabric of society improving both the individual quality of life and life expectancy. Bacterial infections, polio, smallpox, tuberculosis and related diseases and gastric ulcers that were once life threatening have to a very major extent, become minor public health concerns although the emergence of bacterial resistance due to the overuse of antibiotics has begun to reverse this trend[1]. The increase in life expectancy resulting from drug therapy has also resulted in a shift in population demographics toward a healthier, elderly population. As a consequence diseases like cancer and neurodegenerative, degenerative and autoimmune diseases have become increasingly prevalent, resulting in the increase in health care needs and a greater consumption of the gross national product in providing health care. Drug regimes for birth control [2], compounds for erectile dysfunction [3] and new treatments for incontinence [4] are drugs that improve individual life choices and the quality of life. Similarly, HIV protease and reverse transcriptase inhibitors for the treatment of HIV infections in the space of a few years have changed a disease with a fatal prognosis to a potentially chronic one [5]. Cancer is also being viewed as a potentially chronic rather than fatal, disease with the potential for newer, non-cytotoxic approaches that include inhibitors of the angiogenic events supporting tumor growth and proliferation [6]. Despite progress to date, as the ethical pharmaceutical industry enters the 21st century, there remains an increasing need for novel, innovative therapeutic agents not only in areas that are historically well served like anti-infective, but also for the myriad
of diseases associated with aging for which there are generally no effective medications but considerable demand. This work deals with the study of molecular structure of chemotherapy, antiviral and anti-inflammatory drugs. Chemotherapy is the use of anticancer drugs to treat cancerous cells. Chemotherapy may be used alone for some types of cancer or in combination with other treatments such as radiation or surgery. Antiviral drugs are a class of medication used specifically for treating viral infections. Like antibiotics for bacteria, specific antivirals are used for specific viruses. Anti-inflammatory drug inhibits or suppresses most inflammatory responses of an allergic, bacterial, traumatic or anaphylactic origin, as well as being immunosuppressant.

1.3. Vibrational and UV-Visible spectroscopy

Vibrational spectroscopy deals with changes in the vibrational energy levels in molecules. This term covers the two common techniques, infra-red (IR) and Raman spectroscopy. They require very small quantities and can be used in the examination of samples in all phases of matter [7-14]. Both IR and Raman spectroscopy deal with the interaction of vibrational energy levels in molecules with photons of light. It is found that those photons which excite molecular vibrations are in the infra-red region of electromagnetic radiation. That means photons with considerably less energy than visible light. These interactions are useful to chemists because they can be used to diagnose chemical structure. The application of vibrational spectroscopy depends on the type of compound being investigated. Photons on colliding with molecules undergo inelastic scattering and have frequencies lower and higher than the incident frequency, which is known as raman scattering. Raman spectroscopy, which has developed along with infrared spectroscopy, deals with the study of vibrational spectra of molecule. Raman spectrum is due to the change in polarisability of the molecule during vibrations. For a complete vibrational analysis, both methods should be necessarily used [15-18]. Vibrational spectroscopy gives a dynamical picture of the molecule, while X-ray diffraction method gives a static picture. With the introduction of Fourier transform infrared spectrometers and
lasers as source for recording Raman spectra, vibrational spectroscopy has become an effective tool for the elucidation of molecular structure [19, 20]. It has very wide applications since the technique for instance be applied to solids as crystals or powder, liquids, solutions, melt, gases, films and adsorbed species. It is a valuable tool for the elucidation of molecular structure. It also provides important information about the intra molecular forces acting between the atoms in a molecule, the intermolecular forces in condensed phase and the nature of the chemical bond. Other applications include the identification of functional groups or compound identification, determination of strength of chemical bond and the calculation of thermodynamical properties. It may be pointed out here that the goal of high resolution molecular spectroscopy is the determination of molecular geometry and potential energy function. Vibrational spectra can be utilized directly and simply as molecular ‘finger prints’ to characterize and identify the molecule.

1.3.1. Infrared Spectroscopy

Infrared spectroscopy is one of the most powerful analytical techniques, which offers the possibility of molecular confirmation. The most advantage of infrared spectroscopy over the other usual methods of structural analysis is that it provides useful information about the structure of the molecules quickly without tiresome evaluation methods.

The infrared region of the electromagnetic spectrum lies between the red end of the visible spectrum and the beginning of the microwave region. Conventional infrared spectroscopy is concerned with mid infrared range extending from approximately 4000-400 cm\(^{-1}\). Each functional group absorbs characteristic frequencies of infrared radiation uniquely and hence the infrared spectrum is a finger print of the chemical groups [21-24]. An infrared spectrum originated from molecular vibrations causes a change in the dipole moment of the molecule. Such a spectrum, therefore, reflects the structure of the molecule, especially the masses of the constituent atoms and the intermolecular forces acting between them, as well as the intermolecular forces operating in crystalline state.
With most forms of spectroscopy the spectrum is a plot of the absorbance of the sample against wavelength but in infrared the transmittance is plotted against wavenumber. An infrared spectrum has characteristically four main features namely (i) the number of bands present (ii) the wavenumber position (iii) shape of the bands and (iv) the intensities of the bands. The infrared region of the spectrum encompasses radiation with wave numbers ranging from about 12,800 to 10 cm\(^{-1}\) or wavelengths from 0.78 to 1000 μm. From instrumentation and application point of view, the infrared region has been subdivided into near IR region (overtone region), mid IR region (vibration rotation region) and far IR region (rotation region). When a molecule absorbs infrared radiation the usual vibrational transitions is from ground state to the first excited state, producing bands of fundamental frequencies. In addition to this other transition can also occur, although not common, giving rise to weaker bands than the fundamentals and are called as overtones. If two fundamental vibrations are simultaneously excited, then these are called combination bands. The actual position of a band in infrared spectrum depends on the force constant that binds the atoms. The various bands can be interpreted according to the characteristic functional groups present in the compound [25].

1.3.1.1. Molecular vibrations

The complex vibrations of a molecule are the superposition of relatively simple vibrations called the normal modes of vibration. Each normal mode of vibration has a fixed frequency. It is easy to calculate the expected number of normal modes for a molecule made up of \( N \) atoms. A molecule consisting of \( N \) atoms has a total of \( 3N \) degrees of freedom, corresponding to the Cartesian coordinates of each atom in the molecule. In a nonlinear molecule, 3 of these degrees are rotational and 3 are translational and the remaining corresponds to fundamental vibrations; in a linear molecule, 2 degrees are rotational and 3 are translational.

\[ X \rightarrow \Delta \nu \rightarrow Y \]

\[ X \rightarrow \Delta \nu \rightarrow Y \]
For linear molecule of N atoms: normal modes $= 3N - 5(3\text{ translations} + 2\text{ rotations})$
For Nonlinear molecule of N atoms: normal modes = 3N – 6(3 translations + 3 rotations)

A diatomic molecule has only one stretching vibration, while polyatomic molecules have stretching as well as deformation vibrations. All motions other than stretching vibrations are termed as deformation modes. The number of stretching vibrations is equal to the number of valence bonds in the molecule and the remaining vibrations are deformation modes. The deformation modes may be further classified as bending, rocking, wagging or torsional modes etc. Each vibration may be described in terms of internal coordinates defined as increments in bond length, bond angle or dihedral angle.

a. Bond stretching

It denotes an increment in the bond length of a diatomic group during a vibration (Fig.1.1 (a)). The displacement vectors are along the bond and are defined by the coordinate Δυ. The symbol υ is used to indicate the stretching frequency.

b. Angle deformation

It represents a change in the interbond angle and the displacement vectors at the terminal atoms are perpendicular to the bond (Fig.1.1 (b)). The coordinate Δα defines the bending vibration.

c. Rocking

Here the –XY₂ moiety moves as a whole with respect to another atom say Z as shown by the displacement vectors in Fig. 1.1 (c). Rocking vibration is denoted by the symbol ρ.

d. Wagging
Fig.1.1.(d). Wagging vibration

Fig.1.1. (e). An Out-of-plane bending vibration

Fig.1.1.(f). Twisting or Torsional vibration
A change in the angle between a bond and plane or the folding of a plane about a line through it defines a wagging mode (Fig.1.1. (d)). It is usually denoted by the symbol $\omega$. The wagging vibration could also be defined in terms of out of plane bending mode.

e. Out of plane deformation

The movement of an atom out of the molecular skeleton constitutes as out of plane bending vibration (Fig.1.1.(e)). The coordinates, which defines the out of plane bending is denoted by $\pi$.

f. Twisting and torsion

Twisting of the part of a molecule about an axis is visualized (Fig.1.1.(f)). It could be represented by change in the dihedral angle between two planes as in the wagging vibration but the movement of the terminal atoms here is in the opposite direction with respect to each other. It is usually denoted by $\tau$.

1.3.2. Group theory and molecular vibrations

Knowledge of the point group symmetry of a molecule and application of group theory concept is useful in the classification of the normal vibrations, determination of their normal vibrations and determination of their spectral activity. Molecule of different symmetries has qualitatively different spectra [7, 26-28].

A very important property of the normal vibrations is that they transform according to the irreducible representation of the molecular point group. Because of their relationship with the normal coordinates, the vibrational wave function associated with the vibrational energy levels also behaves in the same way. Hence, the normal coordinates and the vibrational wave functions can be classified according to their symmetry properties.

1.3.3. Fourier Transform Infra-red (FT-IR)

Fourier transform spectroscopy simultaneously exposes a sample to the entire range of IR frequencies. Frequencies not absorbed by the sample constitute the “sample beam”, which reaches
Fig. 1.2. Michelson interferometer

Fig. 1.3. Simplified diagram of Fourier transform infrared spectrometer
the detector at 100% transmittance. As this takes place, another beam of IR radiation reaches the detector. This “reference beam” has not passed through the sample. The sample beam and the reference beam are allowed to interfere with each other as they reach the detector and the resulting data is used to construct an interferogram. This interferogram is converted to a normal spectrum by performing a Fourier transformation. Once data has been collected by the spectrometer, it is sent to the computer as an interferogram. The computer determines the frequency and intensity of each component wave of the interferogram, by performing a Fourier transform of the data. These frequencies and intensities make up the peaks of an IR spectrum.

1.3.3.1. Michelson interferometer

Interferometer is an important part of FT-IR spectrometer. It consists of two perpendicular mirrors as shown in Fig.1.2. One of them is a stationary mirror while the other one is a movable mirror that can be displaced perpendicularly towards the fixed mirror at a constant velocity. Between the two mirrors, there is a beam splitter placed at 45° from the identical position of the movable mirror. When a parallel beam of radiation from the source is passed on to the mirrors through the beam splitter, the beam splitter divides the beam and transmits half of the incoming radiation to the fixed mirror and the other half to the movable mirror.

1.3.3.2. FT-IR Instrumentation

The IFS 66v/S is a flexible vacuum FT-IR spectrometer whose spectral range may be expanded from far-IR to the near UV. The working and schematic diagram of FT-IR spectrometer has been given below in Fig. 1.3. The FT-IR spectra of the sample were recorded in the wavelength region of 4000 – 400 cm\(^{-1}\). This spectrometer consists of an Interferometer between source (Globar) and sample compartment. The working of Interferometer has been explained above. The sample compartment is located between the interferometer and the detector. The radiation from the interferometer incident on the sample, then it goes to the detector. The
compound in the present work is solid. So, the KBR pellet method was used for recording spectrum. The sample was then pelletized with KBr and the signals were recorded.

1.3.3.3. Sample handling techniques

Sample handling is considered as an important technique in infrared spectroscopy. There are various methods of sample preparation to enable almost any type of sample to be examined. Some significant problems arise when trying to construct sample containers for vibrational spectrometry, because every material has some vibrational absorption. The material of choice for IR spectroscopy is a solid potassium bromide plate. Such plates are used in a number of ways. Polyethylene pellets are used for recording the far IR spectra.

a. Solids

Solids are sampled in a wide variety of ways. If the sample is soluble, it may be dissolved and handled as for a liquid. Solid samples for which no solvent is suitable can be prepared for analysis by incorporating them into a pressed pellet of alkali halide, usually potassium bromide. Sample is mixed with a weighed amount of powdered potassium bromide and the mixture is admitted to a pressure of several tones in a dye, to produce a highly transparent plate or disc which can be inserted into the spectrophotometer. The use of KBr eliminated the problems of additional bands due to mulling agent. KBr does not absorb infrared light in the region 2.5 – 15 μm and a complete spectrum of the sample is obtained. Solid samples have also been examined in the form of a thin layer deposited by sublimation or solvent evaporation on the surface of a salt plate. Another method, called mulling has also been developed, in which the powdered sample is mixed to form a paste with little heavy paraffin oil. The mull is sandwiched between salt plates for measurement. Mulls are formed by grinding 2 to 5 mg of finely powdered sample in the presence of one or two drops of heavy hydrocarbon oil called Nujol [29-34].

b. Liquids
In most instances the spectra of liquids are measured in either a demountable type cell or in fixed thickness or sealed cells. The spectra of pure samples can be measured as very thin films squeezed between two alkali halide windows of a demountable cell. This technique can produce a film of thickness 0.01 mm or less. This method is most useful for qualitative work only because the sample thickness cannot be controlled. Liquid cells consist of two alkali halide windows usually NaCl or KBr, separated by a spacer of suitable thickness made of Teflon or lead which limits the volume of the cell [29-34].

C. Gases

Absorption spectra of gases can be measured in a wide variety of gas cells ranging from a few centimeters to several meters that can be directly placed in the path of the infrared beam. The end walls of the cell are usually made of sodium chloride which is transparent to infrared. The low frequency vibrational changes in the gaseous phase often split the high frequency vibrational bands[35].

d. Solvents

Solvents of good infrared transparency over a convenient frequency range are available and the spectra of the sample dissolved in carbon tetrachloride and carbon disulphide provide the complete range. Chloroform is considered to be an important solvent and is frequently used because it shows absorptions though it is less symmetric molecule than carbon tetrachloride and carbon disulphide.

1.3.3.4. Advantages of Fourier Transform Infrared Technique

The main advantages of FT spectroscopy are the greater ease and speed of measurement. The entire spectrum can be recorded within few seconds using sophisticated computers. Recent developments in FT Infrared spectrometers have thus led to higher resolution, total wavelength coverage, higher accuracy in frequency and intensity measurements. It can also be used in the characterization of all kinds of samples. In FT method, all the source energy passes through the
instrument and the resolving power is constant over the entire spectrum. The signal to noise ratio is also improved [36]. The smoothening of peaks and the vertical and horizontal expansion of selective region is also possible.

1.3.4. Theory of Raman Effect

Raman spectroscopy is an optical analysis technique based on an effect discovered by Chandrasekhara Venkata Raman. Raman was a self-made scientist who was known for his outrageous ideas, simple experimental design and in-depth observations. An interest in optical phenomena led him to demonstrate in 1921 that the scattering of light is responsible for the colour of the ocean rather than sky reflection or absorption as previously thought [37]. Then in 1928 he discovered the inelastic scattering of light, or Raman Effect, which won him the Nobel Prize two years later [38]. These experiments used a narrow band photographic filter to produce a monochromatic light source from sunlight, a “crossed” filter to block scattered light and the human eye as a detector. Raman and his co-worker Krishnan found that when a benzene sample was irradiated by this intense monochromatic light source, light of a different frequency passed through the “crossed” filter. Since these early days of crude instrumentation, Raman spectroscopy has gradually developed to become a well-established scientific tool. The effect was subject to intensive research in the first decade after its discovery. However, during the Second World War it became overshadowed by the infrared spectroscopy, a technique that was enhanced by the development of sensitive detectors and advances in electronics. The popularity of Raman spectroscopy was not restored until the invention of the laser in the early 1960s and has grown steadily since. In recent years, instrumentation has progressed with the availability of durable and affordable lasers and increasing accessibility of high-powered computer technology. Nowadays Raman spectroscopy is widely used to analyze materials well beyond the capabilities of other methods, with the ability to obtain a detailed account of the physical and chemical makeup of a material at the molecular level. The fundamental process of the Raman Effect is the transfer of
Fig. 1.4. Energy Level Diagram
energy between light and matter. Raman spectroscopy employs this effect by measuring the scattering of light from molecules in different vibrational states of a material and the consequent energy exchange between the incoming light and the molecules [39]. When a beam of monochromatic electromagnetic radiation impinges on a material, it can be either scattered or absorbed (Fig. 1.4). If light is scattered from an atom or molecule within the material, most photons are elastically scattered. This is known as Rayleigh scattering, in which the scattered photons have the same energy $E$ as the incident photons given by

$$E = h\nu_0$$

(1.11)

where $h$ is Plank’s constant and $\nu_0$ is the frequency of the incident light. However, a small fraction of scattered light (approximately 1 in every billion photons) undergoes what is known as inelastic or Raman scattering. In this case light is scattered from molecules with frequencies of oscillation that vary from the frequency of the incident photons. It is this difference in frequency, or energy between the incoming and outgoing light that is the measurable quantity used as the basis of Raman spectroscopy.

1.3.4.1. Stokes and Anti-stokes Raman Scattering

The Raman Effect comprises of two distinct types of scattering, known as Stokes and anti-Stokes scattering (Fig.1.4). The most likely to occur is Stokes scattering, in which the incident light interacts with a molecule that absorbs energy from it. This molecule is excited from its ground state to the “virtual state” and then relaxes back down to finish in a vibrational excited state. In this case photons are scattered that are lower in energy and frequency than the incoming photons and therefore longer in wavelength. Anti-Stokes scattering is the less probable and weaker effect, which occurs when light interacts with a molecule that is already in a vibrational excited state. After being excited up to the “virtual state” this molecule falls down to the ground state, causing the incident photons to gain energy and scatter at a higher frequency and shorter wavelength.
A classical treatment of Raman scattering demonstrates the occurrence of these two effects mathematically [40]. The electric field strength \(E\) of the incoming electromagnetic radiation is given by

\[
E = E_0 \cos(2\pi \nu_0 t)
\]

(1.12)

where \(t\) is time, \(E_0\) is the vibrational amplitude of the electric field and \(\nu_0\) is the frequency of the radiation. When this light interacts with a molecule, it induces an electric dipole moment

\[
P = \alpha E = \alpha E_0 \cos(2\pi \nu_0 t)
\]

(1.13)

where \(\alpha\) is known as polarisability. Molecular polarisability can be interpreted as the deformability of the electron cloud by the external electric field. In general, \(\alpha\) is a tensor that depends on \(E\). However, for simplicity the tensor properties of polarisability are neglected here.

The above oscillatory dipole moment allows scattering to occur, as the molecule moves to an excited state. The charge distribution in the material is then vibrating with a frequency \(\nu\) and nuclear displacement

\[
q = q_0 \cos (2\pi \nu t)
\]

(1.14)

where \(q_0\) is the vibrational amplitude. These oscillations may induce a change in the polarisability of the molecule. When \(q\) is small, polarisability varies linearly with displacement and can be approximated by a Taylor series expansion of \(\alpha\) resulting in

\[
\alpha = \alpha_0 + \left[ \frac{\partial \alpha}{\partial q} \right]_0 q_0 + \ldots
\]

(1.15)

where \(\alpha_0\) is the polarisability at equilibrium and produces elastic scattering, whilst \((\partial \alpha/\partial q)_0\) is the rate of change of \(\alpha\) with respect to \(q\) at this point and is the origin of inelastic scattering.

Combining the previous three equations, making substitutions and simplifying gives

\[
P = \alpha E_0 \cos(2\pi \nu_0 t) + \frac{1}{2} \left[ \frac{\partial \alpha}{\partial q} \right]_0 q_0 E_0 \left[ \cos\{2\pi(\nu_0 - \nu)t\} + \cos\{2\pi(\nu_0 + \nu)t\} \right]
\]

(1.16)

The result is an expression consisting of two terms. The first term represents the outgoing light that remains unchanged from when it enters the material, possessing the frequency of the incident
Fig. 1.5. Schematic representation of Raman Scattering
light $\nu_0$. This is Rayleigh scattering. The second term represents the inelastically scattered light and contains two frequency shifts $(\nu_0 - \nu)$ and $(\nu_0 + \nu)$ arising from Stokes and anti-Stokes Raman scattering respectively.

The key to using Raman scattering to investigate the physiochemical makeup of a material is the change in photon energy between the incident and scattered light, measured as the shifts in frequency derived previously. As shown in Fig. 1.5, light exits a material at a number of different energies that are shifted from the original energy of the incoming photons $E$. In this case the more probable Stokes scattering is demonstrated, in which there is a loss in energy and therefore a decrease in frequency. These different energy changes, $\Delta E_i$ etc, correspond to light scattering from molecules being excited to a number of distinct vibrational energy levels. The frequency shifts corresponding to these different molecular vibrational modes, $(\nu_0 - \nu_1)$ etc, are displayed as a spectrum of peaks. The position and intensity of each peak relates to a specific type of molecular vibration such as the stretching, bending, torsion or deformation of a bond, combining to form a spectrum that represents the chemical fingerprint of a material.

The Stokes and anti-Stokes Raman bands are much weaker than the Rayleigh line and occur symmetrically on either side of it, corresponding to the same amount of energy lost and gained respectively by the incident photons. The Boltzmann distribution indicates that within a system at thermal equilibrium, the lower energy state is more populated than the higher energy state. For a material, this translates to a larger number of molecules in lower energy states than in higher energy states. Therefore in a Raman spectrum the bands relating to Stokes scattering are more intense than those corresponding to anti-Stokes scattering. These peaks have a magnitude of light intensity, or counts, and are usually displayed as a Raman shift $\tilde{\nu}$. This parameter is common to vibrational spectroscopy. It is essentially wavenumber with units of cm$^{-1}$ and is related to wavelength $\lambda$ and frequency $\nu$ via
Fig. 1.6. Simplified diagram of FT- Raman Spectrometer
\[ \tilde{\nu} = \frac{\nu}{c} = \frac{1}{\lambda} \]  

(1.17)

where \( c \) is the speed of light. In Raman spectroscopy, the unit of wavenumber is used simply for convenience. If wavelength or frequency were used, the position of peaks in a spectrum would be determined by the wavelength of the excitation light that they originated from. Instead spectra are displayed in Raman shifts from the Rayleigh peak, which is always set to 0 cm\(^{-1}\). This means that the positions of peaks for a particular material are independent of the excitation wavelength. Experimentally, a Raman shift can be determined from

\[ \tilde{\nu} (\text{cm}^{-1}) = 10^7[(1/\lambda_0)-(1/\lambda_R)] \]  

(1.18)

where \( \lambda_0 \) and \( \lambda_R \) are the laser wavelength and Raman scattering wavelength respectively, both in nanometers.

1.3.4.2. FT-Raman measurements

FT-Raman spectra of the samples were recorded using the Bruker RFS 100/S spectrophotometer that uses 1064 nm laser excitation and provides a 4 cm\(^{-1}\) resolution (Fig. 1.6). The solid sample was taken in sample holder and was subjected to laser irradiation. The orientation of the sample holder was adjusted to obtain maximum amplitude.

1.3.4.3. Excitation laser

The FT-Raman spectrometers currently available use Nd: YAG lasers operating at nm. The laser output is filtered by nm band pass filter to remove spontaneous emission, and then directed to the sample. Some spectrometers have a provision for 180\(^{\circ}\) geometry or 90\(^{\circ}\). Since an interferometer has a large aperture than the slit of the dispersive/CCD system, it is not always necessary to focus the laser on to a small spot. For this reason, the beam steering mirror (or prism M3) is placed to the right of the collection lens. An optical focusing lens, that may be easily removed and placed in the laser beam path, is used. An unfocused or weakly focused laser is advantageous in FT-Raman because it lowers
the power density at the sample and relaxes the tolerance on alignment of laser, collection optics and sample.

1.3.4.4. Collection optics

The collected light can be coupled directly with parallel path of the interferometer, but it usually passes through an aperture. This aperture called jacquinot stop and it permits control of the degree of collimation in the interferometer and excludes severely of axis light.

1.3.4.5. Interferometers

Interferometers were developed for FT-IR and adapted for FT-Raman with minimal change. The FT-Raman accessory consists of a laser, sample chamber, filter and detector that are added to a stand-alone FT-IR spectrometer. The schematic representation of Interferometers is shown in Fig.1.2.

1.3.4.6. Laser Rejection Filters

The laser rejection filter serves the essential function of reducing the strong elastically scattered laser relative to the weak Raman scattering. The noise in FT-Raman spectrum is proportional to the square root of the average intensity of light across entire spectrum. The laser rejection filters are variations of the holographic notch filters, which enhance the possibility of observing low frequency shifts of the order 85cm\(^{-1}\).

1.3.4.7. Detectors

Currently available detectors for the 1100 to 1700nm wavelength range appropriate to FT-Raman are low band gap semiconductors, particularly germanium (Ge) and indium gallium arsenide (InGaAs). The parameters used to specify the efficiency and performance of the detector is the dark signal and quantum efficiency. These parameters critically affect the detector performance.

1.3.4.8. Sample handling techniques

Sample handling techniques for Raman spectroscopic measurements is simpler than for
infrared spectroscopy because glass can be used for windows, lenses and other optical components instead of the more fragile and atmospherically less stable crystalline halides. In addition, the laser source is easily focused on slit. Consequently very small samples can be investigated. In fact, a common sample holder for non-absorbing liquid sample is an glass melting-point capillary.

a. Liquid Samples

The spectrum of a liquid can be recorded as neat or in solution. Ordinarily about 0.3 ml of a liquid may be required. The sample could be taken in glass or silica containers or capillaries. The spectra can be measured directly from the reaction vessel. Water is a good solvent for recording the Raman spectra. Water absorbs strongly in the infrared but it is a poor Raman scatterer. Raman spectroscopy is thus a valuable tool for studying water soluble biological materials.

b. Solid samples

The Raman spectra of solids as polycrystalline material or as a single crystal can be recorded. No medium such as null, KBr or solvent is needed. A few milligrams of the solid samples are required. Solid can be packed into capillary tubes as a powder. The crystal can be mounted in a goniometer on a glass or silica fiber. The spectra can be measured for different orientation of the crystal. For single crystals, the Raman spectrum varies depending on the direction of the crystal axis, when polarized light is used as incident radiation. Raman spectra of adsorbed species can be recorded at different temperatures and pressures.

c. Gas samples

The Raman spectra of gases are generally weaker than those of liquids or solids and hence may require cells of larger path length. The gas may be filled in a glass or silica tube of 1 to 2 cm diameter. If the resolving power of the instrument is good and if the molecule has sufficiently low
moment of inertia, the rotational fine structure may be observed on either side of the Rayleigh line. Generally a broadband contour may be observed.

The main advantage of Raman spectroscopy is that it may be used for a wide variety of sizes and forms of the sample. Samples in gas, liquid and solid states can be examined easily.

1.3.4.9. Advantages and disadvantages

Raman spectroscopy has long been used in many areas of physics, chemistry and materials science [41]. However, more recent applications of the technique have been in biological and medical research, both in vitro and in vivo [42, 43]. Raman spectroscopy offers many benefits to work in these fields:

(1) It is non-invasive, requiring no labelling or other preparation of the sample;

(2) As long as suitable laser wavelengths, powers and exposure times are used, it does not cause significant damage to biological cells and tissue;

(3) It can be used under a wide range of conditions such as varying temperature or pressure;

(4) Typical "background" species such as carbon dioxide and water do not significantly interfere with spectra, as they have weak Raman scattering;

(5) It allows the investigation of samples in physiological conditions, therefore lengthening the time period for measurements and making it possible to experiment in real-time.

For any application, the lack of sample preparation needed prior to analysis with Raman spectroscopy is one of the greatest advantages of the technique. This allows it to be a very rapid analytical technique, leading to high quality data in very short periods of time. Furthermore, Raman scattering originates from the surface of a sample (typically no deeper than several hundred microns), so there is no concern with sample thickness, size or shape.

Raman spectroscopy can be used for a variety of purposes. The technique is often used as a qualitative or identification tool, as it provides exceptional chemical specificity. A Raman spectrum
contains a wealth of analytical information and no two molecules will give the same one. Raman spectroscopy also has a greater sensitivity to chemical functional groups not seen strongly by other similar methods. The selection rules governing the technique require a change in the polarisability of a molecule in order to be Raman-active, a condition that is unique to Raman spectroscopy. In addition, the intensity of scattered light is related to the amount of material present, allowing Raman spectroscopy to be used in quantitative applications.

As with any scientific technique, Raman spectroscopy also has its limitations. The most significant disadvantage of Raman spectroscopy is the interference it suffers from fluorescence. This phenomenon originates from different mechanisms to Raman scattering; however, they can occur together. Fluorescence is broad and more intense than Raman scattering, often overwhelming it. There are ways to avoid such interferences, as discussed in the following chapter, but the potential for fluorescence must always be considered during applications of Raman spectroscopy. Other disadvantages of Raman spectroscopy include equipment cost and the sensitivity of the technique. The Raman Effect is very weak, therefore efficient collection and detection of scattering requires sensitive and highly optimized instrumentation.

1.3.5. Ultraviolet-Visible spectroscopy

1.3.5.1. Basic principles

Ultraviolet (UV) and visible radiation comprise only a small part of the electromagnetic spectrum, which includes such other forms of radiation as radio, infrared (IR), cosmic and X rays. The energy associated with electromagnetic radiation is defined by the following equation:

\[ E = h \nu \]  

where \( E \) is energy (in joules), \( h \) is Planck’s constant \( (6.62 \times 10^{-34} \text{ Js}) \), and \( \nu \) is frequency (in seconds). Electromagnetic radiation can be considered a combination of alternating electric and magnetic fields that travel through space with a wave motion. Because radiation acts as a wave, it
can be classified in terms of either wavelength or frequency, which is related by the following equation:

\[ \nu = \frac{c}{\lambda} \quad (1.20) \]

where \( \nu \) is frequency (in seconds), \( c \) is the speed of light \((3 \times 10^8 \text{ ms}^{-1})\), and \( \lambda \) is wavelength (in meters). In UV-visible spectroscopy, wavelength usually is expressed in nanometers \((1 \text{ nm} = 10^{-9} \text{ m})\). It follows from the above equations that radiation with shorter wavelength has higher energy. In UV-visible spectroscopy, the low-wavelength UV light has the highest energy. In some cases, this energy is sufficient to cause unwanted photochemical reactions when measuring sample spectra.

1.3.5.2. Origin of UV-Visible spectra

When radiation interacts with matter, a number of processes can occur, including reflection, scattering, absorbance, fluorescence/phosphorescence (absorption and reemission) and photochemical reaction (absorbance and bond breaking). In general, when measuring UV-visible spectra, we want only absorbance to occur. Because light is a form of energy, absorption of light by matter causes the energy content of the molecules (or atoms) to increase. The total potential energy of a molecule generally is represented as the sum of its electronic, vibrational and rotational energies:

\[ E_{\text{total}} = E_{\text{electronic}} + E_{\text{vibrational}} + E_{\text{rotational}} \quad (1.21) \]

The amount of energy a molecule possesses in each form is not a continuum but a series of discrete levels or states. The differences in energy among the different states are in the order:

\[ E_{\text{electronic}} > E_{\text{vibrational}} > E_{\text{rotational}} \]

In some molecules and atoms, photons of UV and visible light have enough energy to cause transitions between the different electronic energy levels. The wavelength of light absorbed is that having the energy required to move an electron from a lower energy level to a higher energy level.
1.3.5.3. Origin of the absorptions

Fig.1.7. Electron transitions in ultraviolet/visible spectroscopy
Valence electrons can generally be found in one of three types of electron orbital:

1. Single or σ bonding orbitals
2. double or triple bonds (π bonding orbitals) and
3. non-bonding orbitals (lone pair electrons)

Sigma bonding orbitals tend to be lower in energy than π bonding orbitals, which in turn are lower in energy than non-bonding orbitals. When electromagnetic radiation of the correct frequency is absorbed, a transition occurs from one of these orbitals to an empty orbital, usually an antibonding orbital, σ* or π*.

The exact energy difference between the orbitals depends on the atoms present and the nature of the bonding system. Most of the transitions from bonding orbitals are of too high a frequency (too short a wavelength) to measure easily, so most of the absorptions observed involve only π→ σ*, n→ σ* and n → π* transitions (Fig.1.7).

1.3.5.4. Absorption laws

Beer’s law tells us that absorption is proportional to the number of absorbing molecules – ie. to the concentration of absorbing molecules (this is only true for dilute solutions) – and Lambert’s law tells us that the fraction of radiation absorbed is independent of the intensity of the radiation. Combining these two laws, we can derive the Beer-Lambert Law:

\[ \log_{10} \left( \frac{I_0}{I} \right) = \varepsilon l c \]  \hspace{1cm} (1.22)

where \( I_0 \) = the intensity of the radiation

\( I \) = the intensity of the transmitted radiation

\( \varepsilon \) = a constant for each absorbing material, known as the molar absorption coefficient

\( l \) = the path length of the absorbing solution in cm

\( c \) = the concentration of the absorbing species in mol dm\(^{-3}\).
Fig. 1.8. Simplified diagram of UV-visible Spectrometer
The value of $\log_{10} (I_0/I)$ is known as the absorbance of the solution and can be read directly from the spectrum as ‘absorbance units’. The wavelength at which maximum absorption occurs is represented by $\lambda_{\text{max}}$. The values of both $\varepsilon$ and $\lambda_{\text{max}}$ are strongly influenced by the nature of the solvent, and for organic compounds, by the degree of substitution and conjugation.

1.3.5.5. Instrumentation

Because only small number of absorbing molecules is required, it is convenient to have the sample in solution. In conventional spectrometers electromagnetic radiation is passed through the sample which is held in a small square-section cell (usually 1cm wide internally). Radiation across the whole of the ultraviolet/visible range is scanned over a period of approximately 30 s, and radiation of the same frequency and intensity is simultaneously passed through a reference cell containing only the solvent. Photocells then detect the radiation transmitted and the spectrometer records the absorption by comparing the difference between the intensity of the radiation passing through the sample and the reference cells (Fig.1.8.). In the latest spectrometers radiation across the whole range is monitored simultaneously.

A hydrogen or deuterium discharge lamp covers the ultraviolet range, and a tungsten filament (usually a tungsten/halogen lamp) covers the visible range. The radiation is separated according to its frequency /wavelength by a diffraction grating followed by a narrow slit. The slit ensures that the radiation is of a very narrow waveband – i.e. it is monochromatic.

The cells in the spectrometer must be made of pure silica for ultraviolet spectra because soda glass absorbs below 365 nm, and pyrex glass below 320 nm. Detection of the radiation passing through the sample or reference cell can be achieved by either a photomultiplier or a photodiode, which converts photons of radiation into tiny electrical currents; or a semiconducting cell (that emits electrons when radiation is incident on it) followed by an electron multiplier similar to those used in mass spectrometers. The spectrum is produced by comparing the currents generated by the sample and the reference beams. Modern instruments are self-calibrating, though
the accuracy of the calibration can be checked if necessary. Wavelength checks are made by passing the sample beam through glass samples (containing holmium oxide) that have precise absorption peaks, and the absorption is calibrated by passing the sample beam through either a series of filters, each with a specific and known absorption, or a series of standard solutions.

1.3.5.6. UV-Visible spectroscopy in the study of pharmaceutical drugs

UV-Visible spectroscopy is one of the main methods in the field of drug research. It is a bench tool in almost all the research and development laboratories dedicated to drug design and research. It is also a powerful tool in the analysis of drugs and their metabolites in blood samples. Methods based on light absorption, measured after chemical reactions are extensively applied for the determination of active substances in bulk drugs. UV-Visible spectroscopic techniques are applied to test the stability of pharmaceutical products provided it is made sufficiently selective for upgraded material or decomposition products. UV-Visible spectroscopy is applied to control the quality of drugs in production units. This method of spectroscopy can be used as an ancillary technique in attacking majorituy of the analytical problems in pharmaceutical research together with the conventional methods.

1.3.6. Recent trends in spectroscopy

FT-IR and FT-Raman spectroscopy combined with ab initio/DFT is becoming a powerful tool for vibrational assignment and structure and property study of complex molecules[44-51], nano structures[52], hyperpolarizabilities[53], hydrogen bonding[54] and thermodynamic modeling[55].

Field-emission scanning electron microscopy (FE-SEM), energy dispersive X-ray micro analysis (EOX), combined with micro Raman and Fourier transform infrared (FT-IR) spectroscopy, provided a vast amount of information concerning the raw materials present in the pigments, organic binder, plasters and mortars of the wall painting[56]. Prinsloo and Colomban[57] analyzed oblate seed beads excavated in South Africa by Raman microscopy and
supportive techniques in order to determine the glass technology and pigments used to produce the beads. Raman spectroscopy has been used for the study of the exceptional ivory stock of an archaeological discovery of great importance for the history of wood working tools by Long et al.[58]. In a paper published by Edwards et al.[59] reported the examples of the analytical capability of Raman spectroscopy using long wavelength excitation in the near infrared spectral region for the characterization of archaeological resins from Egyptian dynastic and pre-dynastic period artifacts are used to illustrate the advantages and limitations of the techniques.

Mebendazole is a broad spectrum anthelminthic drug, which exhibits three crystalline forms: polymorphs A, B and C. Ayala et al.[60] have made a vibrational investigation on this active pharmaceutical ingredient in order to characterize its polymorphs. The kinetics of the pseudopolymorphic transitions of niclosamide crystals were monitored by using Raman spectroscopy [61]. In this study, the anhydrate and hydrate forms of niclosamide crystals were quantified, primarily due to its high sensitivity to the strong intermolecular interactions present in these systems. Recently, the so-called spatial offset Raman spectroscopy (SORS), which is capable of reaching depths well beyond those accessible with conventional confocal Raman microscopy, has been developed by Matousek et al.[62]. This technique enables the probing of the internal constituency of turbid media with high chemical specificity, as for example, required in the analysis of pharmaceutical tablets for the identification of the presence of undesired polymorphs. In a continuing work, Eliasson and Matousek[63] have demonstrated the feasibility of enhancing signals in SORS using a dielectric band pass filter. The method is shown to lead to the enhancement of both the surface and subsurface Raman layer signal improving the signal to noise ratio of Raman spectra from the deep areas of samples, thus enhancing the technique’s sensitivity and penetration depth. A proof of principle study for an analysis of seized drugs using a portable Raman spectroscopic instrument was performed [64], who demonstrated the viability
of Raman spectroscopy for the rapid identification of illicit substances in their containers in an airtight environment.

1.4. Quantum Chemical Calculations

1.4.1. Computational Chemistry

The term theoretical chemistry may be defined as the mathematical description of chemistry. The term computational chemistry is generally used when a mathematical method is sufficiently well developed that it can be automated for implementation on a computer. Computational chemistry is the branch of theoretical chemistry whose major goals are to create efficient computer programs that calculate the properties of molecules (such as total energy, dipole moment, vibrational frequencies) and to apply these programs to concrete chemical objects. In theoretical chemistry, chemists and physicists together develop algorithms and computer programs to allow precise predictions of atomic and molecular properties and/or reaction paths for chemical reactions. Computational chemists in contrast mostly “simply” use existing computer programs and methodologies and apply these to specific chemical questions.

Computational chemistry may be defined as the application of mathematical and theoretical principles to the solution of chemical problems. Molecular modelling, a subset of computational chemistry, concentrates on predicting the behaviour of individual molecules within a chemical system. The most accurate molecular model use ab initio or ‘first principles’ electronic structure methods, based upon the principles of quantum mechanics, and are generally very computer-intensive. However, due to advances in computer storage capacity and processor performance, molecular modeling has been a rapidly evolving and expanding field, to the point that it is now possible to solve relevant problems in an acceptable amount of time.

The types of predictions possible for molecules and reactions include [65]:

- Heats of formation
➢ Bond and reaction energies
➢ Molecular energies and structures (thermo chemical stability)
➢ Energies and structures of transition states (activation energies)
➢ Reaction pathways, kinetics and mechanisms
➢ Charge distribution in molecules (reactive sites)
➢ Substituent effects
➢ Electron affinities and ionisation potentials
➢ Vibrational frequencies (IR and Raman spectra)
➢ Electronic transitions (UV/Visible spectra)
➢ Magnetic shielding effects (NMR spectra)

This work presents a review of computational chemistry techniques, focusing on electronic structure methods. Electronic structure methods, particularly ab initio calculations, are capable of consistent predictions with high accuracy over a wide range of systems – a critical prerequisite for the successful modeling of Pharmaceutical materials.

The programs used in computational chemistry are based on many different quantum-chemical methods that solve the molecular Schrodinger equation. The ultimate goal of most quantum chemical approaches is the “approximate” solution of the Schrodinger equation. Several methods have been developed and implemented in computational programs to solve the Schrodinger equation. The methods that do not include empirical or semi-empirical parameters in their equations are called ab initio methods. The most popular classes of ab initio methods are: Hartree-Fock, Moller-Plesset perturbation theory, configuration interaction, coupled cluster, reduced density matrices and density functional theory. Each class contains several methods that use different variants of the corresponding class, typically geared either to calculating a specific molecular property, or, to application to a special set of molecules. The abundance of these
approaches shows that there is no single method suitable for all purposes. Computational chemistry can be used to carry out the following:

- Molecular energy and structures
- Energies and structure of transition states
- Molecular orbital
- IR and Raman spectra
- NMR properties
- Performing geometry optimizations. Geometry optimization depends primarily on the gradient of the energy (the first derivative of the energy with respect to atomic positions).
- Computing the vibrational frequencies of a molecule resulting from inter atomic motion within the molecule. Frequencies depend on second derivative of the energy with respect to atomic structure. Frequency calculations are not possible or practical for all computational chemistry methods.

1.4.2. Computational chemistry methods

All molecular modeling techniques can be classified under three general categories: ab initio electronic structure calculations, semi-empirical methods and molecular mechanics. Ab initio or ‘first principles’ electronic structure methods are based upon quantum mechanics and therefore provide the most accurate and consistent predictions for quantum chemical systems. However ab initio methods are extremely computer intensive. Semi-empirical methods are also founded upon quantum mechanics, but speed computation by replacing some explicit calculations with approximations based upon experimental data. Molecular mechanics techniques are purely empirical methods based on the principles of classical physics and as such are computationally fast. Molecular mechanics methods
completely neglect explicit treatment of electronic structure, and are therefore severely limited in scope.

1.4.2.1. Ab initio methods

Ab initio quantum chemistry methods are computational chemistry methods based on quantum chemistry [66]. The term ab initio was first used in quantum chemistry by Robert Parr and coworkers, including David Craig in a semiempirical study on the excited states of benzene [67].

Of the three, ab initio molecular orbital methods are the most accurate and consistent because they provide the best mathematical approximation to the actual system. The term ab initio implies that the computations are based solely on the laws of quantum mechanics, the masses and charges of electrons and atomic nuclei, and the values of fundamental physical constants, such as the speed of light \( c = 2.998 \times 10^8 \) m/s or Planck’s constant \( h = 6.626 \times 10^{-34} \) Js, and contain no approximations. Molecular orbital methods solve Schrödinger’s equation for the chemical system using a basis set of functions that satisfy a series of rigorous mathematical approximations. Molecular properties can be assessed from a user specified input (single point energy calculation or SPE), or the molecule can be allowed to relax to a minimum energy configuration (geometry optimization).

Ab initio molecular orbital computations can provide accurate quantitative predictions of chemical properties for a wide range of molecular systems. However, they place a considerable demand on computer resources. The choice of theoretical method and basis set determine the duration of the calculation; thus, a sophisticated method and a large basis set will provide more accurate results, but will also require more computer resources.

1.4.2.2. Semi-empirical methods

Semi-empirical methods increase the speed of computation by using approximations of ab initio techniques (e.g., by limiting choices of molecular orbitals or considering only valence
electrons) which have been fitted to experimental data (for instance, structures and formation energies of organic molecules). Until recently, the size of many energetic molecules placed them beyond the scope of ab initio calculations, so preliminary theoretical studies were performed using semi-empirical techniques. However, semi-empirical methods have been calibrated to typical organic or biological systems and tend to be inaccurate for problems involving hydrogen-bonding, chemical transitions or nitrated compounds \[68,69\].

Several semi-empirical methods are available and appear in commercially available computational chemistry software packages such as HyperChem and Chem3D. Some of the more common semi-empirical methods can be grouped according to their treatment of electron-electron interactions 1.4.2.3. Molecular mechanics

Molecular mechanics (MM) is often the only feasible means with which to model very large and non-symmetric chemical systems such as proteins or polymers. Molecular mechanics is a purely empirical method that neglects explicit treatment of electrons, relying instead upon the laws of classical physics to predict the chemical properties of molecules. As a result, MM calculations cannot deal with problems such as bond breaking or formation, where electronic or quantum effects dominate. Furthermore, MM models are wholly system-dependent; MM energy predictions tend to be meaningless as absolute quantities, and are generally useful only for comparative studies. Despite these shortcomings, MM bridges the gap between quantum and continuum mechanics, and has been used quite extensively to study ‘mesoscopic’ effects in energetic materials. Applications include modelling reaction and dissociation on classical potential energy surfaces, studies of equilibrium crystal properties (e.g., density, packing, specific heats), dynamic investigations of shock interactions with crystals and defects and simulating detonation in molecular crystals.

The basic assumptions of typical molecular mechanics methods are listed below.
Each atom (i.e., electrons and nucleus) is represented as one particle with a characteristic mass.

A chemical bond is represented as a ‘spring,’ with a characteristic force constant determined by the potential energy of interaction between the two participating atoms. Potential energy functions can describe intramolecular bond stretching, bending and torsion, or intermolecular phenomena such as electrostatic interactions or van der Waals forces.

The potential energy functions rely on empirically derived parameters obtained from experiments or from other calculations.

Current molecular mechanics models are characterised by the set of potential energy functions used to describe the chemical forces. These force fields depend upon:

- Atomic displacements (i.e., bond lengths)
- Atom types, that is, the characteristics of an element within a specific chemical context (e.g., a carbonyl carbon versus a methyl carbon) and
- One or more parameter sets relating atom types and bond characteristics to empirical data.

1.4.3. Ab initio molecular orbital theory

1.4.3.1. The physico-chemical model

The basis of electronic structure methods is the assumption that all chemistry can be described in terms of the interactions between electronic charges within molecules. Hence, chemical bonds can be loosely defined as a redistribution of electronic charge that stabilises the molecule with respect to a collection of its (isolated) constituent atoms.

Relative stabilities are expressed in terms of the total energy of the system, which is defined by a differential equation,

\[ \hat{H} = \hat{T} + \hat{V} \]  \hspace{1cm} (1.23)
where the Hamiltonian operator representing the sum of kinetic (T) and potential (V) energies.

In quantum mechanical systems, the kinetic energy of a particle is

\[ T = \frac{-\hbar^2}{2m} \nabla^2 \]  

(1.24)

where \( m \) is the mass of the particle, \( \hbar \) is Planck’s constant (\( \hbar = 1.055 \times 10^{-34} \text{ J} \cdot \text{s} \)) and

\[ \nabla^2 = \frac{\partial^2}{\partial x^2} + \frac{\partial^2}{\partial y^2} + \frac{\partial^2}{\partial z^2} \]  

(1.25)

For electrostatic systems, the potential energy is generally expressed in terms of pairwise interactions between charged particles.

\[ V = \frac{q_1 q_2}{4\pi \varepsilon_0 \left| r_2 - r_1 \right|} \]  

(1.26)

where \( \varepsilon_0 \) is the permittivity of free space (\( \varepsilon_0 = 8.854 \times 10^{-12} \text{ C}^2/\text{N} \cdot \text{m}^2 \)), and \( \left| r_2 - r_1 \right| \) is the distance between charges \( q_1 \) and \( q_2 \).

### 1.4.3.2. The molecular Hamiltonian

Under the basic assumption of electronic structure methods, a molecule is a collection of charged quantum particles. The molecular Hamiltonian has the form of Eq. 1.23, however the kinetic energy is now a summation over all the particles in the molecule

\[ H = \sum_i \frac{-\hbar^2}{2m_i} \nabla_i^2 + \sum_{ij} \frac{q_i q_j}{4\pi \varepsilon_0 \left| r_i - r_j \right|} \]  

(1.27)

and the potential energy is the Coulomb interaction between each pair of charged particles (electron-nucleus attraction, nucleus-nucleus repulsion and electron-electron repulsion):

\[ V = \sum_j \sum_{k<j} \frac{q_j q_k}{4\pi \varepsilon_0 \left| r_k - r_j \right|} \]  

(1.28)

For electrons, \( q = -e \) (\( e = 1.602 \times 10^{-19} \text{ C} \)), and for nuclei of atomic number \( Z \), \( q = +Ze \)

### 1.4.3.3. Hartree-Fock theory

#### 1.4.3.3.1. The Schrödinger equation
The quantum mechanical description of chemical bonds is given by a space- and time- dependent probability distribution: the molecular wavefunction $\psi_{mol(t)}$. The molecular wavefunction is defined by the Schrödinger equation

$$\hat{H}_{mol}\psi_{mol}(t) = i\hbar \frac{\partial \psi_{mol}(t)}{\partial t} \quad (1.29)$$

If the potential energy operator is time-independent, then the solution obtained by separation of variables, leads to the molecular wavefunction

$$\psi_{mol}(t) = \psi_{mol}e^{-iE_{mol}t/\hbar} \quad (1.30)$$

where $\psi_{mol}$ satisfies the time-independent Schrödinger equation

$$\hat{H}_{mol}\psi_{mol} = E_{mol}\psi_{mol} \quad (1.31)$$

and $E_{mol}$ is the total energy of the molecule. Solutions of the time-independent Schrödinger equation represent various stationary states of the molecule (corresponding to stable or meta-stable electronic configurations). The set of wavefunctions $\psi$ which satisfy Eq.1.31 are its eigen functions and the energies of the molecule, $E_{mol}$ in each stationary state are its eigen values. The stationary state with the lowest energy is called the 'ground state'.

1.4.3.3.2. Antisymmetry and electron spin

Standard electronic structure methods assume that the molecular wavefunction describing several electrons can be written as a product of single-electron wavefunctions called ‘orbitals’, that is, for a molecule containing n electrons,

$$\psi_{mol}(1,2,...,n) = \psi(1)\psi(2)\ldots\psi(n) \quad (1.32)$$

Electrons possess an intrinsic angular momentum or ‘spin’ with a value of $\pm\frac{1}{2}$. A half-integer spin quantum number implies that electrons are antisymmetric with respect to exchange – in other words, a wavefunction describing a pair of electrons i and j must change sign when the electrons are interchanged:
The simplest antisymmetric combination of molecular orbitals (MOs) is a matrix determinant.

A HF wavefunction is constructed by assigning electrons to molecular orbitals \( \phi(r) \) in pairs of opposite spin and then forming a determinant using two spin functions \( \alpha \) and \( \beta \), where

\[
\begin{align*}
\alpha(\uparrow) &= 1 & \alpha(\downarrow) &= 0 \\
\beta(\uparrow) &= 0 & \beta(\uparrow) &= 1
\end{align*}
\]

For two electrons \( i \) and \( j \) the total wavefunction takes the form:

\[
\Psi (i,j) = \phi(r) \begin{vmatrix}
\alpha(i) & \beta(i) \\
\alpha(j) & \beta(j)
\end{vmatrix}
\]

with a determinant

\[
\Psi (i,j) = \frac{\phi(r)}{\sqrt{2}} [\alpha(i)\beta(j) - \beta(i)\alpha(j)]
\]

which satisfies the antisymmetrisation condition of Eq.1.32. For a molecule containing \( n \) electrons, the wavefunction is referred to as a ‘Slater determinant’ and takes the form:

\[
\psi = \begin{vmatrix}
\phi_1(1)\alpha(1) & \phi_1(1)\beta(1) & \phi_2(1)\alpha(1) & \phi_2(1)\beta(1) & \cdots & \phi_{n/2}(1)\alpha(1) & \phi_{n/2}(1)\beta(1) \\
\phi_1(n)\alpha(n) & \phi_1(n)\beta(n) & \phi_2(n)\alpha(n) & \phi_2(n)\beta(n) & \cdots & \phi_{n/2}(n)\alpha(n) & \phi_{n/2}(n)\beta(n)
\end{vmatrix}
\]

1.4.3.3.3. Ab inito essentials

For systems of more than two interacting particles, the Schrodinger equation cannot be solved exactly. Therefore, all ab initio calculations for many body systems (e.g. molecules) involve some level of approximation and indeed, some level of empirical parameterization. Nevertheless, ab initio methods for molecular calculations must satisfy a set of stringent criteria:

1. Solutions must be well defined and specified by both the structure and the electronic states of the molecule.

2. The Potential energy of the molecule must vary smoothly and continuously with respect to
displacements of the atomic nuclei.

3. The model must contain no bias (e.g., assuming a chemical bond exists between two atoms).

4. The model must be ‘size consistent’ – that is, solutions and their associated errors must scale in proportion to the size of the molecule.

5. The model must be ‘variational’ – that is, approximate solutions must provide an upper bound to the true energy of the system. Consequently, the approximate solution having the lowest energy represents the closest fit to the true wavefunction, within the constraints of the method.

1.4.3.3.4. Born-Oppenheimer approximation

Electrons in molecules are much lighter than nuclei, and therefore generally have much higher velocities. Hence, under most circumstances, once can assume that electrons respond instantaneously to nuclear displacements. In practice, this means that the molecular Hamiltonian can be written assuming the nuclear positions are fixed (i.e., neglecting nuclear kinetic energy terms):

\[ \hat{H}_{\text{mol}} = \hat{T}_{\text{elec}} + V = \frac{-\hbar^2}{2m_e} \sum_i^{\text{electrons}} \nabla_i^2 + \frac{1}{4\pi\varepsilon_0} \sum j \sum_{k>j} q_j q_k \frac{1}{|r_k - r_j|} \]  

(1.37)

Most ab initio calculations solve only the electronic part of the molecular wavefunction, and therefore cannot account for systems where the electronic states are strongly coupled to nuclear vibrations.

1.4.3.3.5. Single particle approximation

Standard electronic structure methods approximate the total wavefunction of a many electron system as the product of single electron wavefunctions. This is the essence of Hartree-Fock theory, which describes each electron in a molecule as moving in the average electric field generated by the other electrons and nuclei. As a single particle theory, HF theory systematically overestimates molecular energies because it neglects the correlated motion of electrons resulting from Coulomb interactions.
1.4.3.3.6. **Linear combination of atomic orbitals (LCAO)**

Although there is no exact analytical solution to the time-independent molecular Schrodinger equation for systems containing more than one electron, approximate solutions can be obtained using standard numerical techniques. The approach of all ab initio techniques is to build the total wavefunction from a ‘basis’ set of mathematical functions capable of reproducing critical properties of the system. An individual molecular orbital may then be expressed as

$$\phi_i(r) = \sum_{\mu=1}^{N} c_{\mu i} \chi_\mu(r) \quad (1.38)$$

where $\chi_\mu(r)$ are the basis functions and the coefficients $c_{\mu i}$ are adjustable parameters. For a molecular wavefunction, the electronic orbitals of the constituent atoms form a natural set of basis functions. These atomic orbitals can in turn be represented by different types of mathematical functions. A highly accurate set of atomic orbitals (Slater type orbitals or STO) are based on hydrogenic wavefunctions having the form

$$\chi_{STO}(r) \sim Ce^{-\alpha r} \quad (1.39)$$

Exponential functions are not well suited to numerical manipulation, so most electronic structure calculations approximate STOs with a linear combination of Gaussian-type functions

$$\chi_{STO}(r) \sim \chi_\mu = \sum_\nu d_{\mu \nu} e^{-\alpha_\nu r^2} \quad (1.40)$$

Where $d_{\mu \nu}$ and $\alpha_\nu$ are adjustable parameters. Gaussian-type functions provide reasonable approximations of STOs, except at very small or very large electron-nucleus separations. Linear combinations of ‘primitive’ gaussian functions are referred to as ‘contracted’ Gaussians. Gaussian software offer a choice of basis sets containing contracted gaussians optimized to reproduce the chemistry of a large range of molecular systems.

**1.4.4. Density functional theory**
A technique that has gained considerable ground in recent years to become one of the most widely used techniques for the calculation of molecular structure is density functional theory (DFT). Its advantage include less demanding computational effort, less computer time and better agreement with the experimental values than is obtained from Hartree-Fock procedures. The central focus of DFT is the electron density, \( \rho \), rather than the wavefunction \( \psi \). The ‘functional’ part of the name comes from the fact that the energy of the molecule is a function of the electron density, written \( E[\rho] \), and the electron density is itself a function of position, \( \rho(r) \), and in mathematics a function of a function is called as functional.

1.4.4.1. The Kohn-Sham approach

Density functional theory [70-72] is based on the Hohenberg-Kohn theorem[73], which states that the total energy of a system in its ground state is a functional of that system’s electronic density, \( \rho(r) \), and that any density, \( \rho'(r) \), other than the true density will necessarily lead to a higher energy. Therefore, the Hohenberg-Kohn theorem introduces an alternative approach to perform exact, variational, abinitio electronic structure calculations. In conventional ab initio methodology, Schrodinger’s equation \( E\psi = H\psi \) must be solved. Meanwhile, DFT requires only that we minimize the energy functional, \( E[\rho(r)] \). The conceptual simplification thus offered cannot be overstated. Unfortunately, the exact nature of the energy functional is not known and the total energy of a system cannot be simply output when a trial density, \( \rho'(r) \), is given as input. Therefore, we must turn to approximate DFT methods, and though we will not have a wavefunction, we will have to make use of one – electron Kohn-Sham molecular orbitals, which rather closely resemble molecular orbitals from the well known Hartree-Fock(HF) method.

Early applications of DFT tended to be within the physic community, concentrating on systems where the HF approximation is a particularly poor starting point [74]. Therefore, the vast majority of the applications were on metallic systems, because a single determinantal approach is notoriously bad in such cases. Since DFT works with the density, and
not the wavefunction, systems that would require a great number of electronic configurations to be well described by conventional \textit{ab} \textit{initio} approaches are in principle neither harder nor more expensive, for DFT than the systems that are well described by a single configuration. Correlation effects, absent within the HF approximation, are also built into the approximate energy functional used in modern DFT applications. Therefore, DFT methods are in principle able to treat the entire periodic table with unvarying ease and accuracy.

Though the Hohenberg-Kohn Theorem clearly established that one could, in principle, work directly with the density in \textit{ab} \textit{initio} calculations, it was the subsequent work of Kohn and Sham (KS)\cite{64} that offered a practical approach to perform DFT calculations. In the KS approach, the unknown Hohenberg-Kohn energy functional, $E[\rho(r)]$, is partitioned in the following manner\cite{74}

$$E[\rho(r)] = U[\rho(r)] + T[\rho(r)] + E_{XC}[\rho(r)]$$

In this partitioning scheme, $U[\rho(r)]$ is simply the classical electrostatic energy, the sum of the electron-nucleus attractions and the electron-electron repulsions\cite{74}.

$$U[\rho(r)] = \left( \sum_A \int \frac{-Z_A \rho(r)}{|r-R_A|} \, dr \right) + \frac{1}{2} \iint \frac{\rho(r)\rho(r')}{|r-r'|} \, dr \, dr'$$

The next term, $T[\rho(r)]$, is defined as the kinetic energy of a system of non interacting electrons with the same density $\rho(r)$, as that of the real system of interacting electrons being studied. This may seem to introduce a severe error. However, this is not the case, because the final term $E_{XC}[\rho(r)]$ is made to contain, in addition to the exchange and correlation (XC) contributions to the energy, the difference between $T[\rho(r)]$ and the true electronic kinetic energy of the system.

Following KS, $\rho(r)$ of an N-electron system (with $N_\alpha$ spin up electrons and $N_\beta$ spin down electrons) is expressed as the sum of the square moduli of single occupied, orthonormal Kohn-Sham molecular orbitals\cite{74}.
\[ \rho(r) = \rho^\alpha(r) + \rho^\beta(r) = \sum_i^{N_e} |\psi_i^\alpha(r)|^2 + \sum_i^{N_e} |\psi_i^\beta(r)|^2 \]  \hspace{1cm} (1.43)

Having done this, \( T[\rho(r)] \) can now be defined as

\[ T[\rho(r)] = \sum_{\sigma=\alpha,\beta} \sum_i N_{\sigma} \int \psi_i^\sigma(r) \frac{-\nabla^2}{2} \psi_i^\sigma(r) \, dr \]  \hspace{1cm} (1.44)

One should note that \( T[\rho(r)] \) is not a true density functional, because the KS orbitals are required. Alternate forms of \( T[\rho(r)] \) that depend only on the electronic density and do not require KS orbitals have been proposed [70]. However, they are too imprecise to be of any practical use in chemistry.

Finally, recalling the fact that the energy functional is minimized by the true ground state density \( \rho(r) \), the energy functional \( E[\rho(r)] \) must be stationary with respect to any arbitrary variation in either of the spin densities [74] i.e.,

\[ \frac{\delta E[\rho(r)]}{\delta \rho^\sigma(r)} = 0 \]  \hspace{1cm} (1.45)

This condition yields the one – electron KS equations

\[ \left\{ \frac{-\nabla^2}{2} \sum_A \frac{Z_A}{|r - R_A|} + \int \frac{\rho(r)}{|r - r'|} \, dr' + \frac{\delta E_{XC}[\rho(r)]}{\delta \rho^\sigma(r)} \right\} \psi_i^\sigma(r) = \epsilon_i \psi_i^\sigma(r) \]  \hspace{1cm} (1.46)

\[ \sigma = \beta \alpha \]  \hspace{1cm} (1.47)

Thus, a scheme for performing practical DFT calculation emerges. With an initial guess at the total spin densities, \( \rho^\sigma(r) \) and \( \rho^\beta(r) \), the KS equations are constructed and solved, and the resulting set of KS-orbitals, \( \psi_i^\sigma(r) \) are then used to generate new guesses at \( \rho^\sigma(r) \) and \( \rho^\beta(r) \). This procedure is repeated until self-consistency is achieved, that is, the same densities and KS orbitals are generated.

In this preceding discussion, we avoided to deal with the precise nature of the XC energy functional \( E_{XC}[\rho(r)] \) and the XC potentials, which are the functional derivatives of \( E_{XC}[\rho(r)] \) with respect to \( \rho^\sigma(r) \) and \( \rho^\beta(r) \);
\[ \nu_{XC}^{\alpha} = \frac{\delta E_{XC}[\rho(r)]}{\delta \rho^\alpha(r)} \]  
\[ \nu_{XC}^{\beta} = \frac{\delta E_{XC}[\rho(r)]}{\delta \rho^\beta(r)} \]  

If the true XC energy functional, \( E_{XC} [\rho(r)] \), were known, this scheme would yield the true ground state density and in turn, exact values for all ground state properties. Unfortunately, the precise nature of \( E_{XC} [\rho(r)] \) is not known, and at the first glance, it may seem that we are no further along to performing practical DFT calculations then when we had only the Hohenberg-Kohn theorem and an unknown total energy functional \( E_{XC} [\rho(r)] \) can, perhaps surprisingly to some, yield fairly accurate results. The KS approach is therefore of great practical importance and has become the cornerstone of all modern DFT applications.

### 1.4.5. Basis set

A basis set is a mathematical description of the orbital within a system (which in turn combines to approximate the total electronic wave function) used to perform the theoretical calculations. The molecular orbitals which arise in the slater determinant are usually expanded in the form of linear combination of a finite set of one-electron functions known as basis functions. Larger the basis sets, more accurately approximate the orbital by imposing fewer restrictions on the locations of the electrons in space. In the true quantum mechanical picture, electron has finite probability of existing anywhere in space.

Standard basis sets for electronic structure calculations use linear combinations of Gaussian functions to form the orbital. Gaussian offers a wide range of pre-defined basis sets, which may be classified by the number of basis functions that they contain. Basis sets assign a group of basis functions to each atom within a molecule to approximate its orbital. These basis functions themselves are composed of a linear combination of Gaussian functions referred as “contracted functions” and the component Gaussian functions are referred as primitives. A basis function consisting of a single Gaussian function is termed as uncontracted function.
1.4.5.1. Minimal basis sets

The most common minimal basis set is STO-nG, where n is an integer. This n value represents the number of Gaussian primitive functions comprising a single basis function. In these basis sets, the same number of Gaussian primitives comprises core and valence orbitals. Minimal basis sets typically give rough results that are insufficient for research-quality publication, but are much cheaper than their larger counterparts. Commonly used minimal basis sets of this type are:

- STO-3G
- STO-4G
- STO-6G
- STO-3G* - Polarized version of STO-3G

1.4.5.2. Split-valence basis sets

During most molecular bonding, it is the valence electrons which principally take part in the bonding. In recognition of this fact, it is common to represent valence orbitals by more than one basis function. Basis sets in which there are multiple basis functions corresponding to each valence atomic orbital are called valence double, triple, quadruple-zeta, and so on, basis sets. Since the different orbitals of the split have different spatial extents, the combination allows the electron density to adjust its spatial extent appropriate to the particular molecular environment. Minimum basis sets are fixed and are unable to adjust to different molecular environments.

The notation for the split-valence basis sets arising from the group of John-pople is typically X-YZg. In this case, X represents the number of primitive Gaussians comprising each core atomic orbital basis function. The Y and Z indicate that the valence orbitals are composed of two basis functions each, the first one composed of a linear combination of Y primitive Gaussian functions, the other composed of a linear combination of Z primitive Gaussian functions. In this case, the presence of two numbers after the hyphens implies that this basis set is a split-valence
double-zeta basis set. Split-valence triple- and quadruple-zeta basis sets are also used, denoted as \( X_{YZWg} \), \( X_{YZWVg} \), etc. Here is a list of commonly used split-valence basis sets of this type:

- 3-21G
- 3-21G\(^*\) - Polarized
- 3-21+G - Diffuse functions
- 3-21+G\(^*\) - With polarization and diffuse functions
- 4-21G
- 4-31G
- 6-21G
- 6-31G
- 6-31G\(^*\)
- 6-31+G
- 6-31+G\(^*\)
- 6-31G(3df, 3pd)
- 6-311G
- 6-311G\(^*\)
- 6-311+G\(^*\)

Basis sets in which there are multiple basis functions corresponding to each atomic orbital, including both valence orbitals and core orbitals or just the valence orbitals, are called double, triple or quadruple-zeta basis sets.

Commonly used multiple zeta basis sets are:

- \( \text{cc-pVDZ} \) - Double-zeta
- \( \text{cc-pVTZ} \) - Triple-zeta
- \( \text{cc-pVQZ} \) - Quadruple-zeta
- \( \text{cc-pV5Z} \) - Quintuple-zeta, etc.
- aug-cc-pVDZ, etc. - Augmented versions of the preceding basis sets with added diffuse functions.
- TZVPP- Triple –zeta
- QZVPP-Quadruple-zeta

The 'cc-p' stands for ‘correlation-consistent polarized’ and the ‘V’ indicate they are valence-only basis sets. They include successively larger shells of polarization (correlating) functions ($d, f, g$, etc.). More recently these 'correlation-consistent polarized' basis sets have become widely used and are the current state of the art for correlated or Post- Hartree-Fock calculations.

1.4.5.3. Polarised basis sets

Polarisation functions can be added to basis sets to allow for non-uniform displacement of charge away from atomic nuclei, thereby improving descriptions of chemical bonding. Polarisation functions describe orbitals of higher angular momentum quantum number than those required for the isolated atom (e.g.,p-type functions for H and He, and d-type functions for atoms with Z>2), and are added to the valence electron shells. For example, the 6-31G (d) basis set is constructed by adding six d-type Gaussian primitives to the 6-31G description of each non-hydrogen atom. The 6-31G (d,p) is identical to 6-31G(d) for heavy atoms, but adds a set of Gaussian p type functions to hydrogen and helium atoms. The addition of p-orbitals to hydrogen is particularly important in systems where hydrogen is a bridging atom.

1.4.5.4. Diffuse basis sets

Species with significant electron density far removed from the nuclear centres(e.g., anions, lone pairs and excited states) require diffuse functions to account for the outermost weakly bound electrons. Diffuse basis sets are recommended for calculations of electron affinities, proton affinities, inversion barriers and bond angles in anions. The addition of diffuse s- and p- type Gaussian functions to non-hydrogen atoms is denoted by a plus sign as in 3-21G. Further addition of diffuse functions to both hydrogen and larger atoms is indicated by a double plus.
1.4.5.5. High angular momentum basis sets

Basis sets with multiple polarization functions are now practical for many systems and although not generally required for Hartree-Fock calculations, are useful for describing the interactions between electrons in electron correlation methods. Examples of high angular momentum basis sets include:

6-31G (2d) – two d-functions are added to heavy atoms;

6-311G (2df, pd) - besides the (311) valence functions, two d functions and one f function are added to heavy atoms, and p and d functions to hydrogen;

6-311G (3df, 2df, p) - three d functions and one f function are added to atoms with Z>11, 2 d functions and one f functions to first-row atoms (Li to Ne) and one p function to hydrogen;

High angular momentum basis sets augmented with diffuse functions represent the most sophisticated basis sets available. The most accurate ab initio studies of energetic materials would be produced by reasonable sophisticated polarized split-valence basis sets augmented with high angular momentum and diffuse atomic orbitals. However, the size of the optimum basis set, especially when used with electron correlation methods will ultimately be determined by the size of the energetic molecule, the amount computing power available, and the time allotted for the studies.

1.5. Computational details

1.5.1. GAUSSIAN

GAUSSIAN is a computational chemistry software program. It is a general purpose electronic structure package capable of predicting many properties of atoms, molecules and reactive systems. The Gaussian package was first written by John pople and the name originates from Pople’s use of Gaussian orbital to speed calculations over those using Slater-type orbital.

Capabilities of Gaussian are:

- Determine most stable (optimum) molecular geometry and energy.
- Define a potential energy surface by stepping through a range of values for a geometry coordinate, such as bond distance or torsion angle.

- Predict IR, Raman, UV, NMR, and other spectra

- Optimize transition states

- Solvate molecules using the ‘polarized continuum (PCM)’ or other models.

- Special tools for optimizing transition metal complexes, and other molecules containing large atoms.

- “ONIOM” technique for defining layers within one molecule where higher and lower accuracy methods can be applied.

- Model surfaces using a 2D periodic boundary condition (PBC) method, or crystals using 3D PBC.

1.5.2. Gauss view

Gaussview is a graphical user interface (GUI) designed to be used with Gaussian to make calculation preparation and output analysis easier, quicker and more efficient. With the help of Gaussview, one can prepare input for submission to Gaussian and to examine graphically the output that Gaussian produces. Gaussview incorporates an excellent molecule builder. One can use it to rapidly sketch in molecules and examine them in three dimensions. Molecules can be built by atom, ring, group, amino acid and nucleoside. Gaussview can graphically display a variety of Gaussian calculation results, including the following:

- Molecular orbitals

- Atomic charges

- Surfaces from the electron density, electrostatic potential, NMR shielding density and other properties. Surfaces may be displayed in solid, translucent and wire mesh modes.

- Surfaces can be colored by a separate property.

- Animation of the normal modes corresponding to vibrational frequencies.
Animation of the steps in geometry optimizations, potential energy surface scans, intrinsic reaction coordinate (IRC) paths and molecular dynamics trajectories from BOMD and ADMP calculations.

1.6. Normal Coordinate Analysis

Normal coordinate analysis provides information concerning the nature of vibrations. Accurate assignment is the basis for using characteristic frequencies of various functional groups. Detailed analysis of data obtained by normal coordinate analysis (NCA) has traditionally been based on the symmetry of the equilibrium structure. The optical activity and characteristics of the normal vibration can be deduced from the constructed symmetry coordinates [75, 76]. Recent advances in computing have a tremendous impact on analysis of vibrational spectroscopy. Vibrational modeling of polymers has traditionally involved use of a NCA based on Wilson’s GF matrices and force constants transferred from small molecules [77]. Refinements in force field are often required to better fit the polymer system. Such analyses can only involve the specific chain conformation generated with well-established bond lengths and valence and torsional angles. The generation of structures consistent with helical parameters obtained from diffraction data usually tests the structural parameters.

A requisite for accurate NCA analysis is the availability of a reliable force field. In general only intramolecular potential energies are needed. The Cartesian coordinate is most convenient to define all individual atoms in space. It is, however, most natural to consider the potential energy of the molecule in terms of bond, valence angles and torsion angles, commonly referred to as internal coordinates. All force constants are defined in this coordinate system. The relationship between the two sets of coordinates is easily established [75]. With few exceptions, such as polyethylene and trans-1, 4- polybutadienes explicit evidence of optically active intermolecular vibrations is unavailable [78]. Therefore, interchain interactions are seldom considered, even though well defined interatomic potentials can easily be incorporated. As the numbers of force
constants (both diagonal and off-diagonal coupling) are much larger than the number of observations, few are determined with certainty. In both intra and intermolecular interactions, the force fields are transferred from those established for small molecules.

Normal coordinate analysis is now-a-days commonly employed as an aid in the interpretation of the vibrational spectra of large molecules. In order to get meaningful results, knowledge of the vibrational force field is necessary. Since the number of force constants grows quadratically with the number of atoms, one has to employ many approximations in the calculation of harmonic force field even for moderately large molecules.

Gwinn [79] developed a program for NCA analysis using mass weighted Cartesian coordinates, which eliminates the redundancy problems arising when internal valence coordinates, are used, as in the GF-method. Gwinn’s methods have subsequently been improved [80, 81]. MOLVIB is based on the same fundamental idea, but differs from the above mentioned programs in many respects. This program has been described by Sundius. MOLVIB is FORTRAN program for the calculation of harmonic force fields and vibrational modes of molecules, up to 50 atoms. This expresses the infrared and Raman intensities in the same units as the Gaussian program.

1.7. Geometry Optimization

Generally structural changes within the molecule produce differences in its energy and other properties. Its PES specifies the way the energy of a molecular system varies with small changes in is structure. PES is the mathematical relation linking molecular structure and energy. The minimum which corresponds to the lowest point in some limited region on the PES is called local minimum. But global minimum is the lowest energy point anywhere on the PES. The point, which is maximum in one direction and minimum in other direction, is called saddle point. Saddle point corresponds to the transition structure between two equilibrium structures. The minimum specifies the equilibrium structure of the molecular system with different minima corresponding
to different conformations. After finding the energy and gradient in some number of cycle, finally optimization gets completed when it has converged.
References


[71] F. Jenson, Introduction to Computational Chemistry, Wiley and Sons, Baffins Lane, United Kingdom, 1999.


