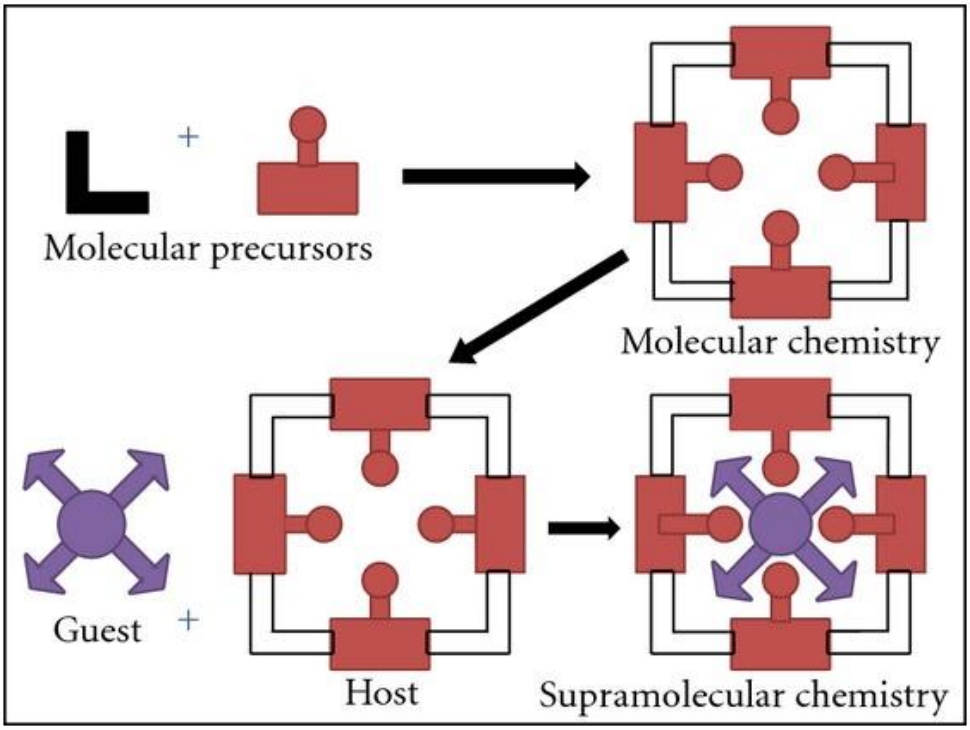
CHAPTER: II

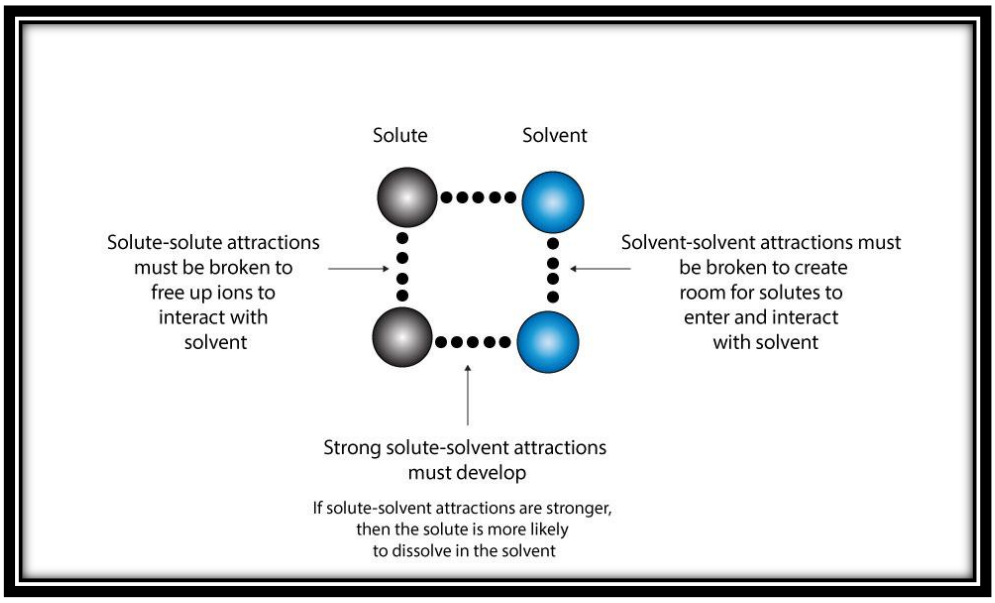
General Introduction (Review of the Earlier works)



II. (1) Molecular Interactions (Noncovalent Interactions) in the Solution

Molecular Interactions are attractive or repulsive forces shown *between molecules* in addition to between non-bonded atoms. Molecular interactions are significant in diverse fields of protein folding, drug design, material science, sensors, nanotechnology, separations, and origin of life. [1] Molecular interactions are also identified as noncovalent interactions or intermolecular interactions. Molecular interactions are not the real bonds that hold atoms together *within molecules*, whereas a molecule is a set of atoms that associates tightly enough that it does not detach or lose its structure when it interacts with its environment. Whilst the overall physicochemical properties of the molecule can have a major influence it

probable that specificity might be driven by optimisation of strength and geometry of specific molecular interactions. An intermolecular force in a solution controls their thermodynamic properties and the understanding of the solvation thermodynamics is essential to the characterization and interpretation of any process carried out in the liquid phase. The object of this introductory chapter is to call attention to the significance of solvents and the study made on assorted interaction prevailing in liquid systems by studying their thermodynamic and transport properties.



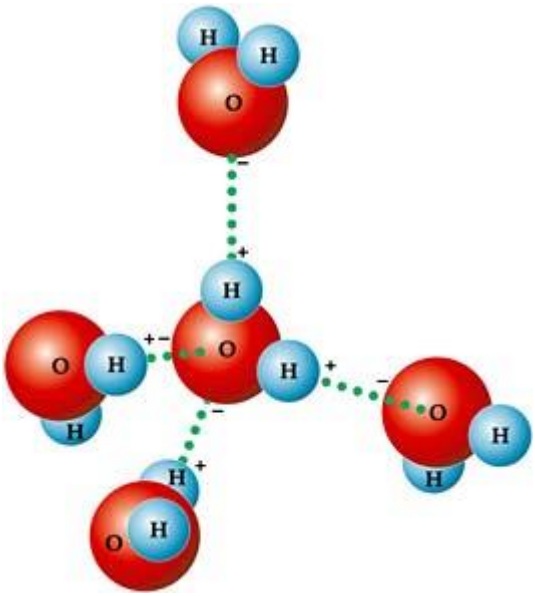
To understand transport properties of electrolytes/solutes along with thermodynamic and theoretical ones to characterize molecular interactions in solutions Ion-Solvent/Solute-Solvent, Ion-Ion/Solute-Solute and Solvent-Solvent Interaction in terms of Thermodynamic parameters are being prescribed as supporting key points. [2]

- ***Assorted interactions are discussed as follows:***

* *Anatomy of a hydrogen bonding*

A hydrogen bond is a favorable interaction between atoms with basic lone pair of electrons (a Lewis Base), a hydrogen atom that has been partially stripped of its electrons as it is

covalently bound to an electronegative atom (N, O, or S). These bonds can occur between molecules in a system (intermolecularly), or within different parts of a single molecule (intramolecularly). The hydrogen bond (5 to 30 kJ/mole) is stronger than the van der Waals interaction, but weaker than covalent or ionic bonds. This type of bond occurs in both inorganic molecules such as water, ammonia and organic molecules such as DNA. Certain substances such as H_2O, HF, NH_3 form hydrogen bonds, and the formation of which affects properties (i.e., m.p, b.p, solubility) of substance. Other compounds containing OH and NH_2 groups also form the hydrogen bonds. Molecules of several organic compounds such as alcohols, acids, amines, and amino acids contain these groups, and thus hydrogen bonding plays an important role in biological science. So it can be said that the Hydrogen bond is a ubiquitous element of the recognition in imperative biological systems as studied in the various investigations.

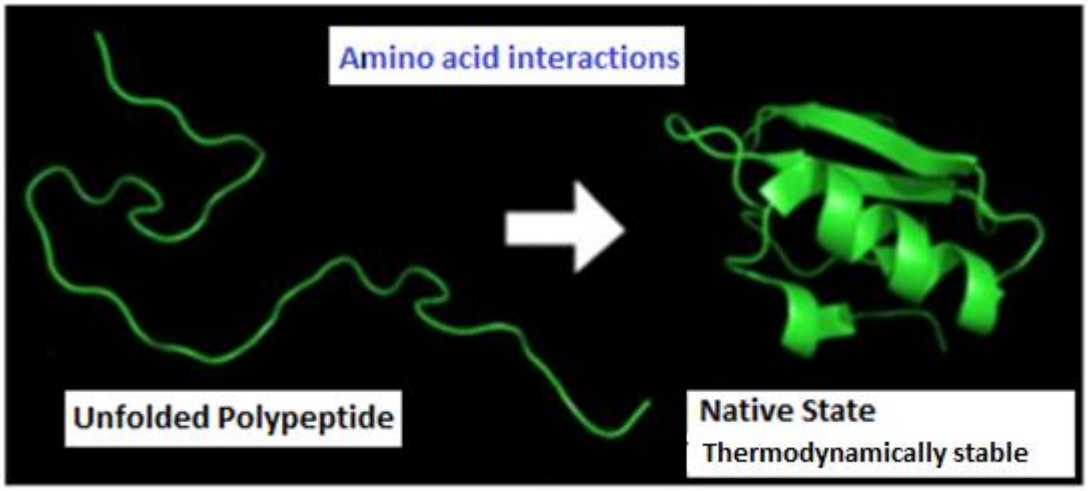


* *Hydrophobic Interactions (Folding and assembly of imperative biological macromolecules)*

The “Hydrophobic effect “refers to the idea that energetically protein folding is driven by two factors: - Hydrophobic side-chains prefer to "get away" from water, whilst hydrophilic side-chains prefer to interact with the water. Whilst this is extended to interaction of guest molecules with the binding situate; the classic concept of hydrophobic effect is as follows: A

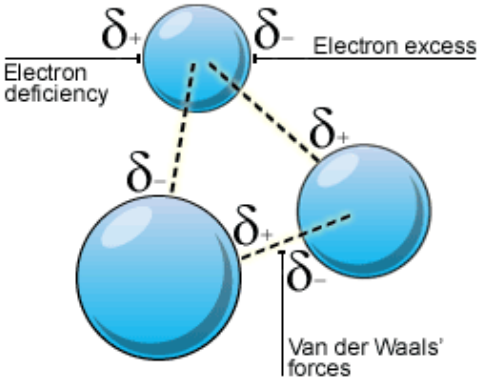
hydrophobic guest disrupts the configuration of bulk water and decreases entropy as of stronger bonding and ordering of water molecules in the region of the solute.

In sphere of biological systems proteins fold into globular structures known as native states. These native states and assemblies are stabilized via molecular interactions of enormous number and complexities. Native states are weakened by their low conformational entropy. The prime groups of studied amino acids have nonpolar side chains. When associated together by a series of peptide bonds, amino acids outline a polypeptide, an additional word for protein.The polypeptide will subsequently fold into a particular conformation depending on the interactions linking its amino acid side chains. Accordingly the aggregated protein forms large assemblies has also been evaluated.

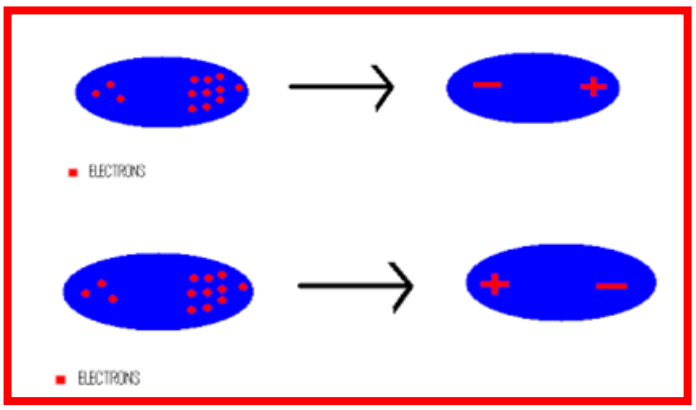


* *Note on Van der Waals interactions*

Van der Waals interactions are forces are driven through induced electrical interactions connecting two or more atoms or molecules that are very close to each other. Van der Waals interaction is weakest of all intermolecular attractions between molecules. However, with a lot of Van der Waals forces interacting between two objects, interaction can be extremely strong. Explicit information about various types of Vander Waals interactions are mentioned in the thesis.

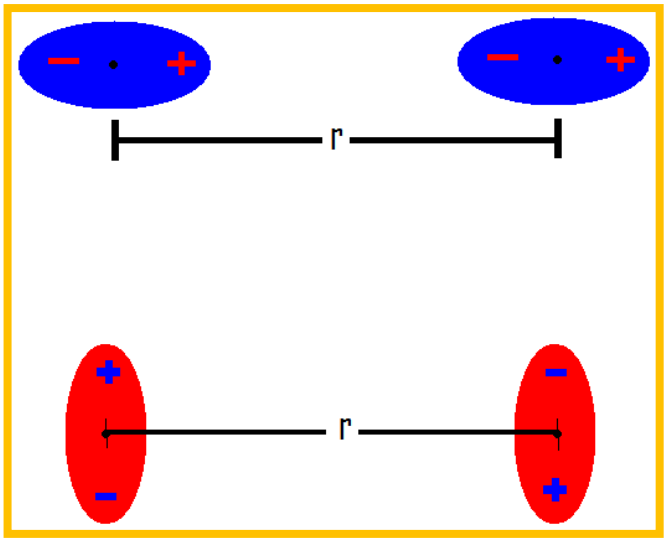


Causes of the aforesaid interaction arise from Quantum mechanics. Two important aspects of Quantum Mechanics strongly suggest that the electrons are constantly are moving in an atom, so dipoles are probable of occurring. A specific dipole is defined as molecules or atoms by means of equal and opposite electrical charges separated by means of a small distance. There occur two types of fluctuations.

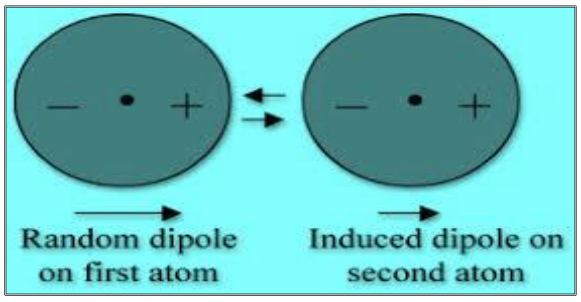


Further these fluctuations are responsible to show various types of interactions, depicted as follows:

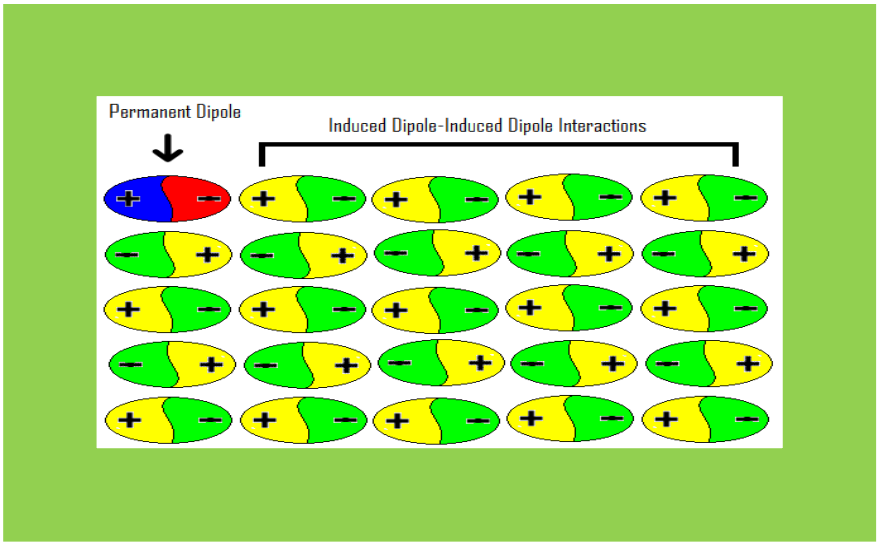
- ***Dipole-Dipole Interaction:*** arise stuck between molecules that have permanent dipoles; these molecules are furthermore referred to as polar molecules. The figure below shows the electrostatic interaction connecting two dipoles.



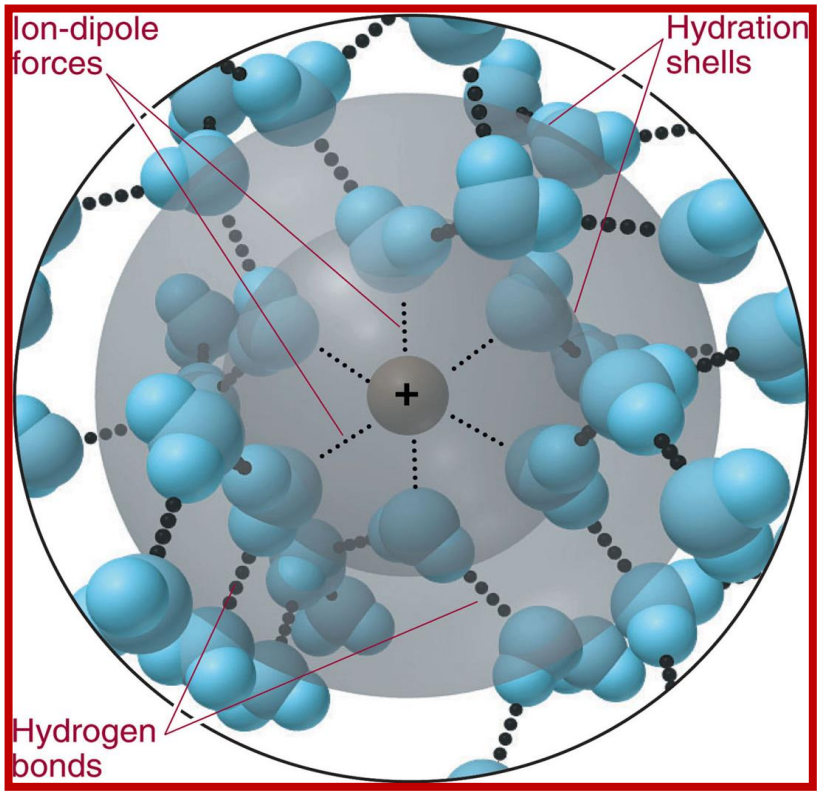
- ***Induced Dipoles:*** An induced dipole moment is a temporary condition during which neutral nonpolar atoms undergoes separation of charges due to the environment. Whilst an instantaneous dipole atom approaches a neighboring atom, it causes atom to moreover produce dipoles. Then the neighboring atom is considered to have an induced dipole moment.



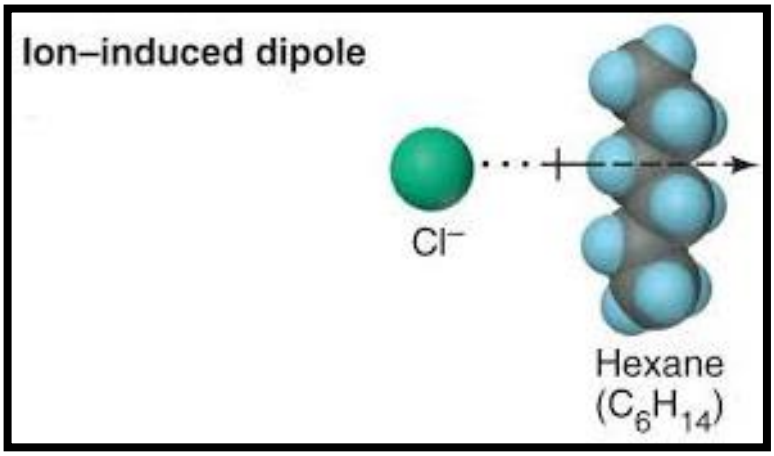
- ***Dispersion forces or Spontaneous -Dipole-Induced -Dipole Interaction:*** in addition recognized as London forces. They are large networks of intermolecular forces between nonpolar and non-charged molecules, atoms. Molecules having induced dipoles may also induce neighboring molecules to have dipole moments, so a large network of induced dipole-induced dipole interactions may exist. The picture below illustrates a network of induced dipole-induced dipole interactions.



- ***Ion-Dipole Interactions:*** electrostatic interaction that results between a charged ion and a molecule that has a dipole. It is an attractive force that is generally found in solutions, especially ionic compounds dissolved in polar liquids. A cation can attract partially negative end of a neutral polar molecule, while an anion attracts the positive end of a polar molecule in solutions. Ion-dipole attractions become **stronger** as charge on the ion increases or as the magnitude of the dipole of the polar molecule increases. These aforesaid interactions can be exceptionally significant factors in many chemical situations.



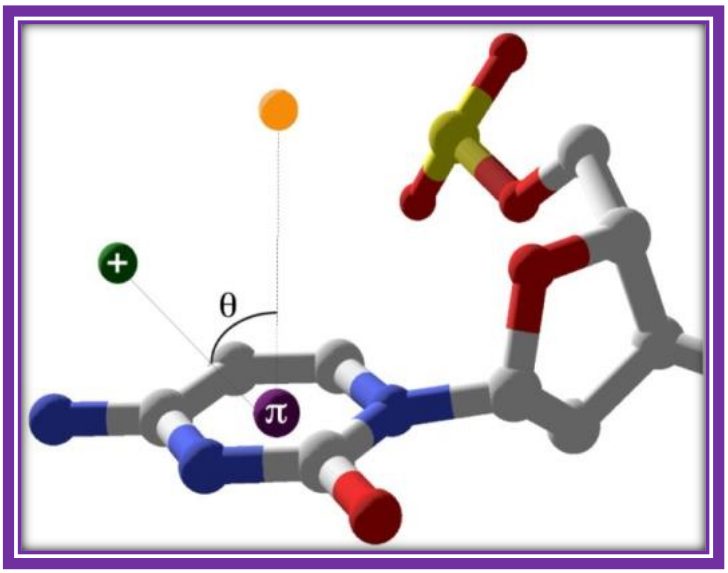
- ***Ion - Induced Dipole Interactions:*** The charges on the ions as well as charge separation in polar molecules elucidate fairly strong interactions amid them, with very strong ion - ion interactions, weaker ion - dipole interactions, and considerably weaker dipole-dipole interactions. Even in a non-polar molecule, though, the valence electrons are moving around and there will occasionally be instances when more are on one side of the molecule than on the other.



* Π-*stacking*

Aromatic based interactions are intermolecular forces concerning electron rich molecules so as long been known. They are problematical to revise, however aromatic interactions offer great potential in drug design, structural biology, conformational analysis and asymmetric catalysis. Though interrelated, the various aromatic interactions vary drastically in their strength, physical nature, and specificity. These types of interactions are being analyzed in the thesis. Thus it useful to consider them individually as listed:

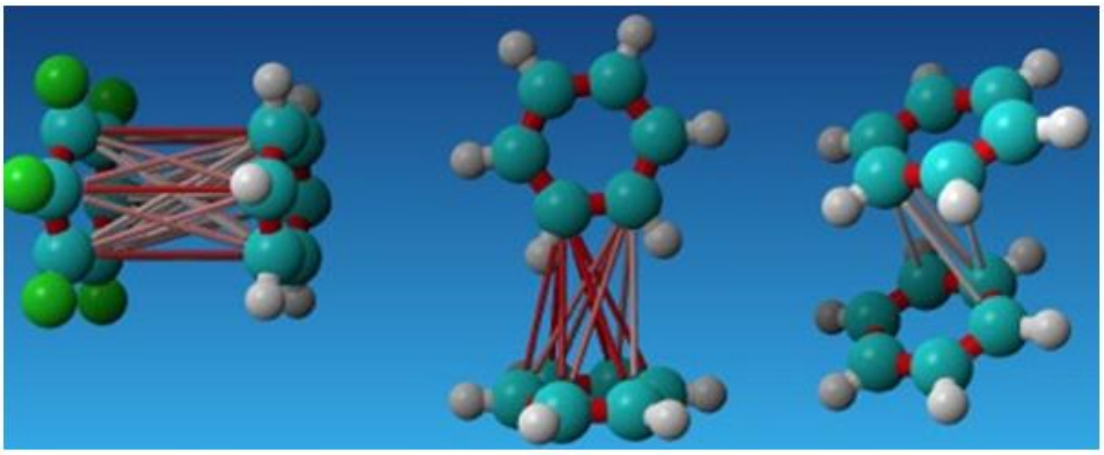
- ***The Cation Π Interactions or Cation-Aryl Interactions:*** arises from the electrostatic interaction of a cation with the face a Π system in a solution.



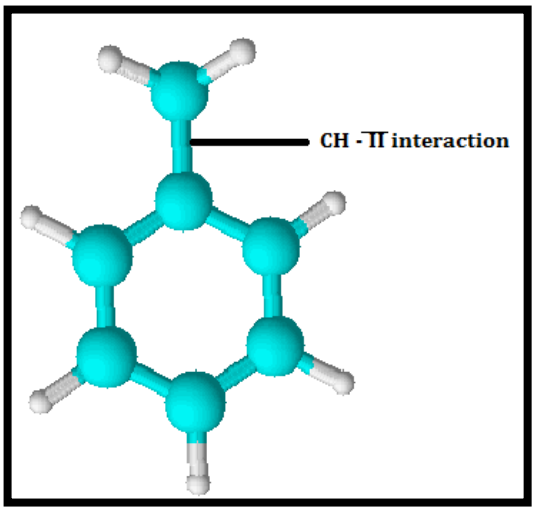
Survey of protein database shows that cation-Π stabilization is a most important facet of protein structure and enzyme catalysis. It is now considered as important as hydrogen bonding, ion pairing, and hydrophobic effects in determining protein structures.

In vision of the review works of Dougherty [3], investigated that cation Π energies for the alkali metals in aqueous solution computationally finds that the trend is very different than it was in the gas phase. Cation Π is strong and specific even across a range of solvents, whereas most other intermolecular forces are sharply attenuated in polar media, and the nature of the interaction and its energetics are very well understood.

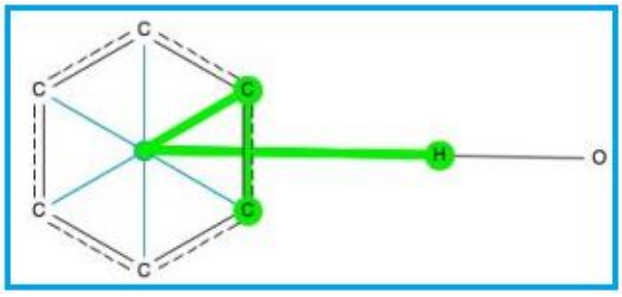
- ***Aryl-Aryl Interactions or Π-Π Interactions:*** Interactions amid aromatics rings be well documented, 60% of the aromatic residues are involved in aryl-aryl interactions. It refers to attractive, noncovalent interactions between aromatic rings, since they have Π bonds. These interactions are imperative in nucleobase stacking within DNA and RNA molecules stabilization, protein folding, and template-directed synthesis, materials science, and molecular recognition, drug intercalation and widely in supramolecular chemistry. [4]



- ***The CH - π Interaction:*** gives rise to interaction geometries where the CH bond lies directly in line with a p orbital on the ring.

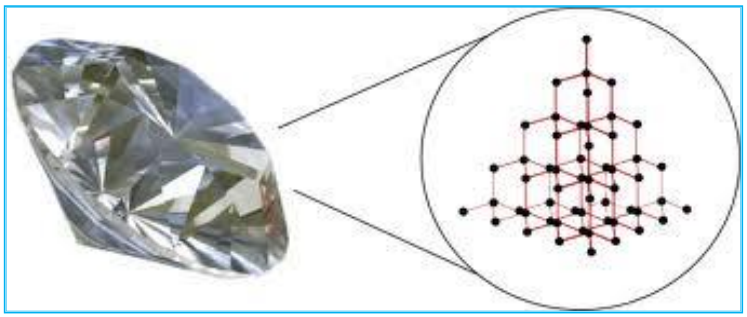


- ***OH and NH Bonding to Aromatics:*** Alcohols, amides and amines all bind to aromatic rings. [5]

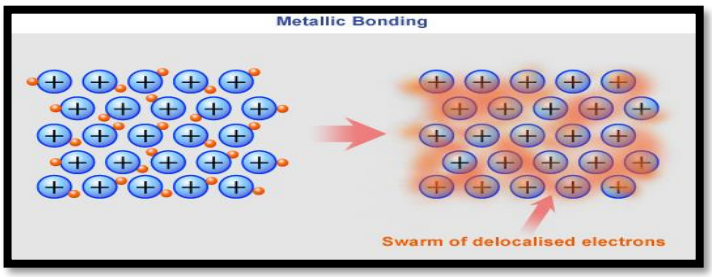


Covalent bonding: it is intramolecular force that exists rather than intermolecular force. It is mentioned here, as some solids are formed due to covalent

bonding. For example, in diamond, silicon, quartz etc., in these all atoms the entire crystal is linked together by means of covalent bonding. These all solids are hard, brittle, have high melting points and holds atoms tighter than ionic attraction.



Metallic bonding: Forces between atoms in metallic solids belong to one more category. Valence electrons in metals are widespread and not restricted to certain atoms or bonds. Rather run freely in the entire solid, providing good conductivity for heat and electric energy. These behaviors of electrons provide special properties such as ductility and mechanical strength to metals.



The majority of reactions happening in solutions are of chemical or biological in nature. It was presumed before that the solvent only provides an inert medium for chemical reactions. The significance of *"ion-solvent interactions"* was realized after intensive studies in aqueous, non-aqueous and mixed solvents. Intermolecular forces are also vital in determining the solubility of a matter. "*Like*" intermolecular forces for solute and solvent will build the solute soluble in the solvent system. In this regard ΔH_{soln} is either negative or positive. Furthermore, solubility of the matter is affected by

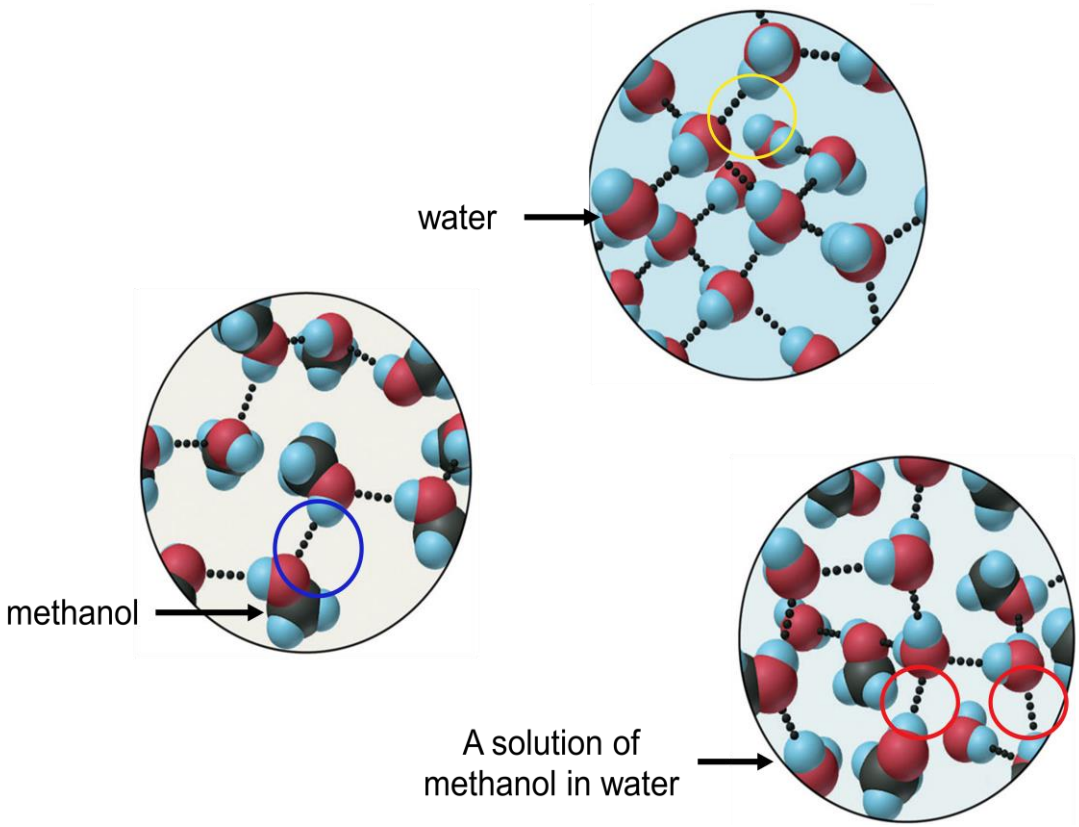
(a) Energy of attraction (due Ion-dipole force) that affects the solubility.

(b) Lattice energy (energy holding the ions together in the lattice structure).

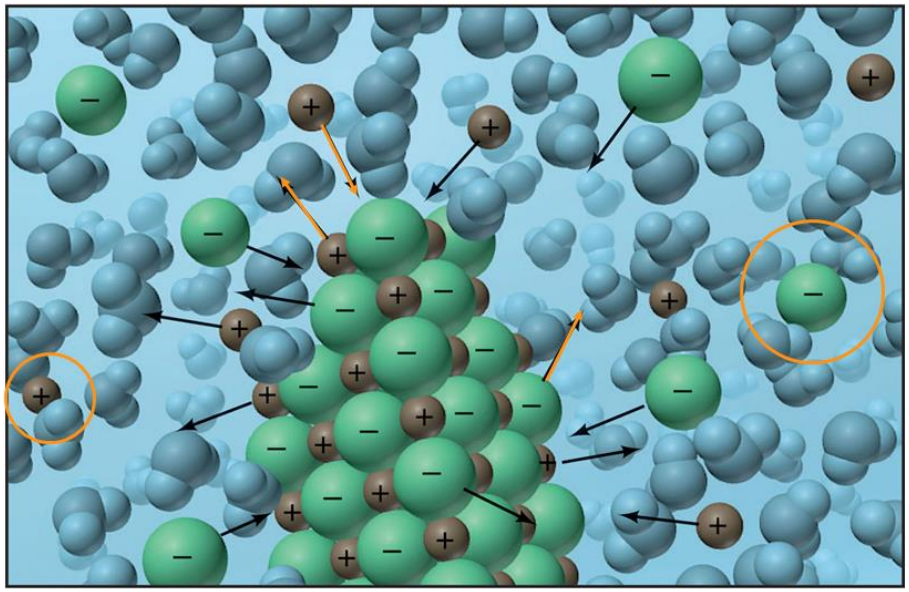
(c) Charge on the ions: larger charge means higher lattice energy.

(d) Size of the ion: large ions stand for smaller lattice energy.

Like dissolves like: solubility of methanol in water.



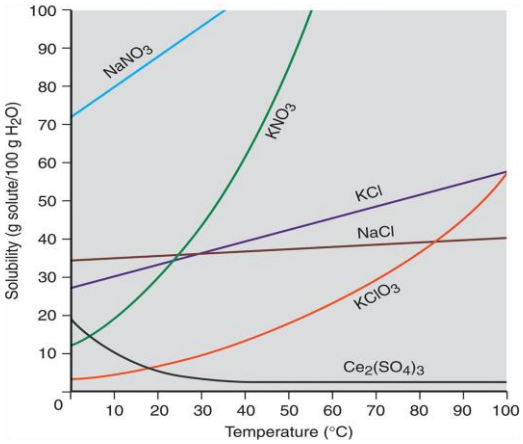
Equilibrium in a saturated solution.



solute (undissolved) ⇌ solute (dissolved)

Sodium acetate crystallizing from a supersaturated solution.

The relation between solubility and temperature for several ionic compounds.



II. (2) *Interactions in the Solution media*

There are three types of interactions in the solution media:

f. ***Solute-solvent/ion-solvent interactions***: ΔH is negative since bonds are created between them.

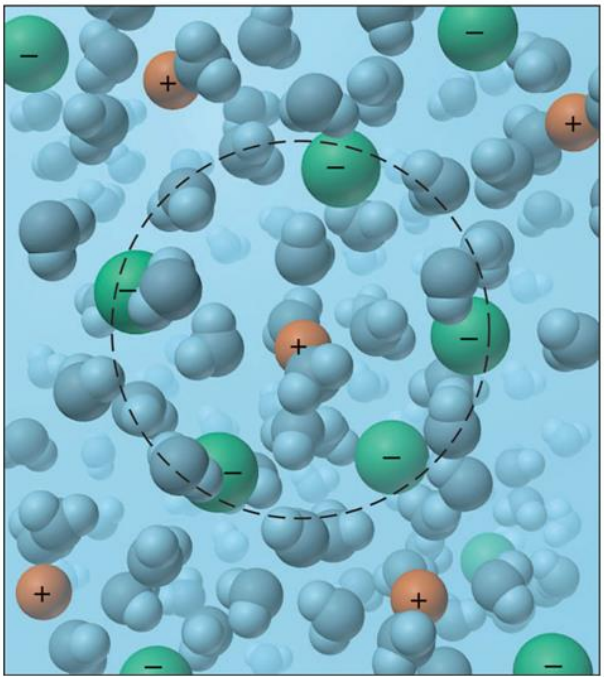
g. ***Solute-solute/ion-ion interactions***: energy required to break intermolecular bonds between the solute molecules in the solution.

h. ***Solvent-solvent interactions***: energy required to break weak bonds between solvent molecules in the solution.

For liquid systems, the macroscopic properties are usually well known, whereas the microscopic structure is rarely studied. The liquid phase is characterized by local order and long-range disorder, and to study processes in liquids, it is therefore valuable to use techniques that probe the local surrounding of the constituent particles. The same is also true

for solvation processes: a local probe is a key to obtain insight into the physical and chemical processes going on.

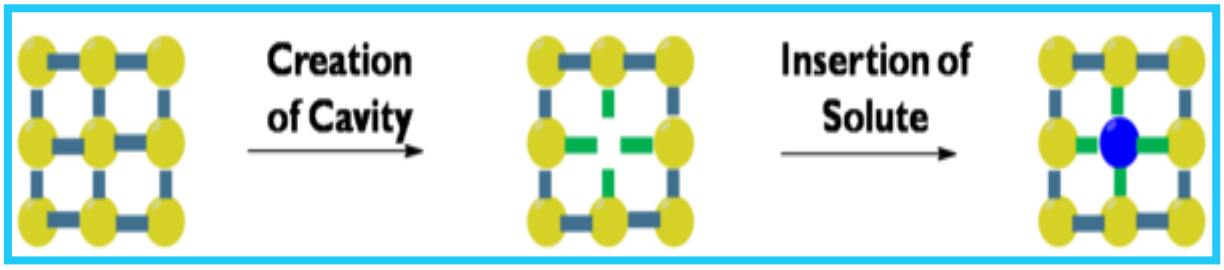
An ionic atmosphere model for nonideal behavior of electrolyte solutions.



- ***The Solvation energy and thermodynamic considerations***

The Solvation progression will be thermodynamically favored only if the overall Gibbs energy of the solution is decreased, compared to the Gibbs energy of the separated solvent and solute (solid or gas or liquid). This means that change in enthalpy minus change in entropy (multiplied by the absolute temperature) is a negative value, or that Gibbs energy of the system also decreases gradually. It is important to remember, however, that a negative Gibbs energy indicates a spontaneous process but does not supply information about the rate of dissolution. Solvation involves multiple steps processes with different energy consequences. First, a cavity should form in the solvent to make space for a solute. This is equally entropically and enthalpically unfavorable, as solvent ordering increases and solvent-solvent interactions decreases. Stronger interactions amongst solvent molecules lead to a greater enthalpic penalty for the cavity formation. Next, a particle of solute has to get separated from the bulk. This is enthalpically adverse as solute-solute interactions decreases, when the solute particle enters the cavity; resulting solute- solvent interactions are

enthalpically favorable. Finally, as solute mixes into solvent system, and there is an entropy gain.



A negative enthalpy of solution evaluates that the solute is less soluble at high temperatures. The sum of the enthalpy and entropy changes throughout various steps is called the solvation energy. Enthalpy of solvation helps to explain why solvation occurs with some ionic lattices not with others.

Heats of solution and solution cycles

1. *Solute particles separate from each other* - endothermic

solute (aggregated) + heat ⟶ solute (separated) $\Delta H_{solute} > 0$

2. *Solvent particles separate from each other* - endothermic

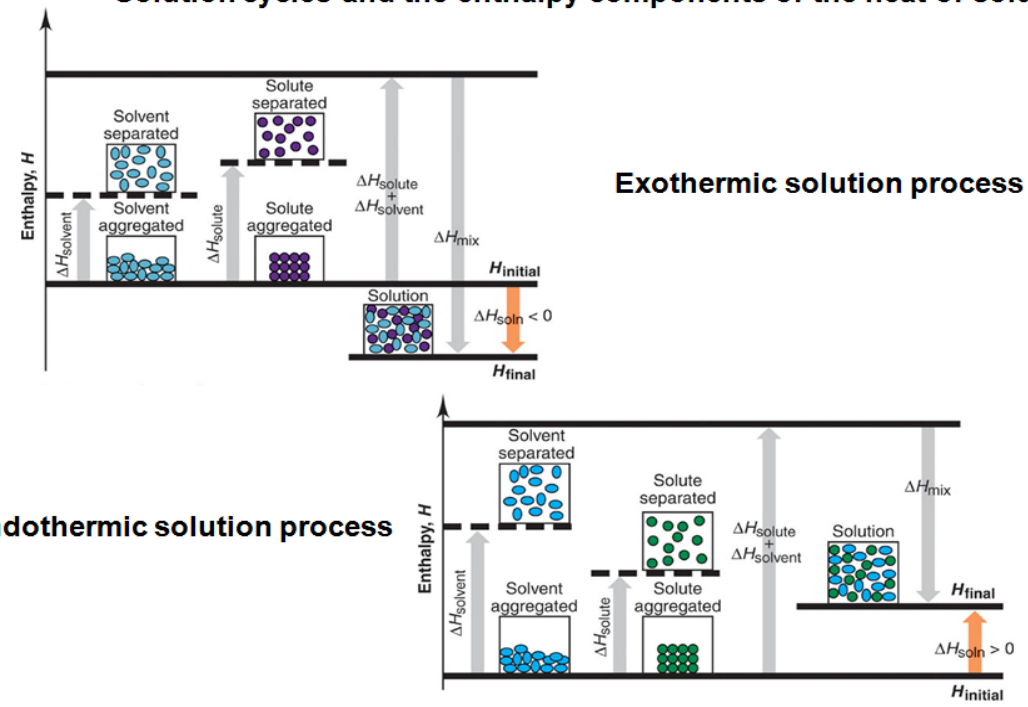
solvent (aggregated) + heat ⟶ solvent (separated) $\Delta H_{solvent} > 0$

3. *Solute and solvent particles mix* - exothermic

solute (separated) + solvent (separated) ⟶ solution + heat $\Delta H_{mix} < 0$

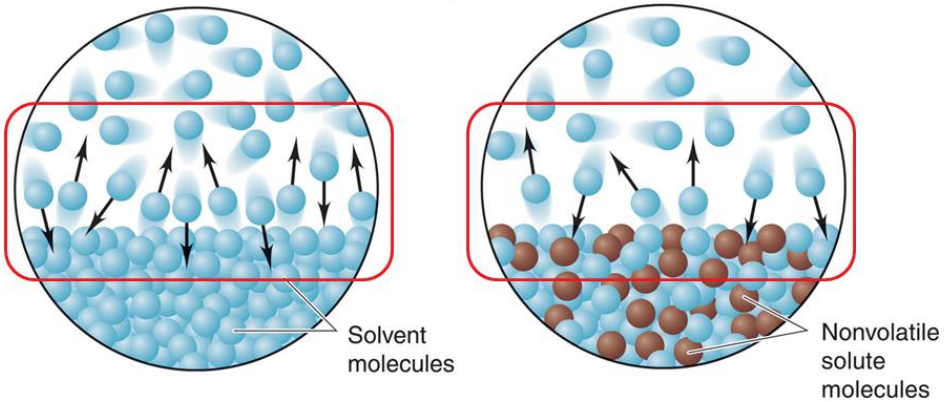
$$\Delta H_{soln} = \Delta H_{solute} + \Delta H_{solvent} + \Delta H_{mix}$$

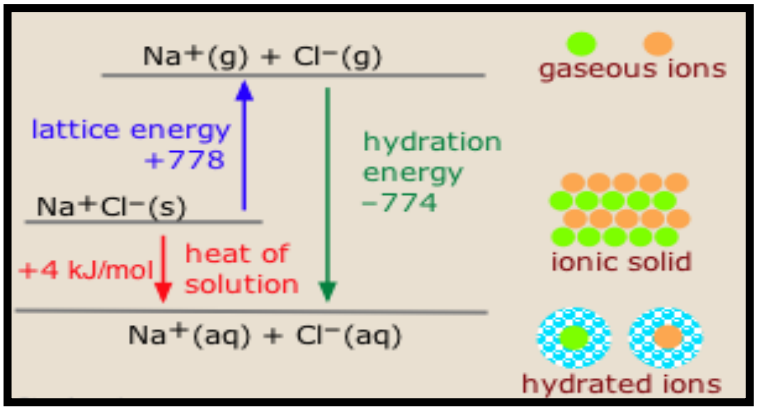
Solution cycles and the enthalpy components of the heat of solution.



When salt is dissolved in water, the ions of the salt dissociate from each other in the solution and associate with the dipole of the water molecules. This result in a solution known as an "*electrolyte*". These facts meant forces can be attractive or repulsive depending on whether like or unlike charges are closer together in the solvation media. On average, dipoles in a liquid orient themselves to form attractive interactions with their neighbours, but thermal motion create some prompt configurations unfavorable.

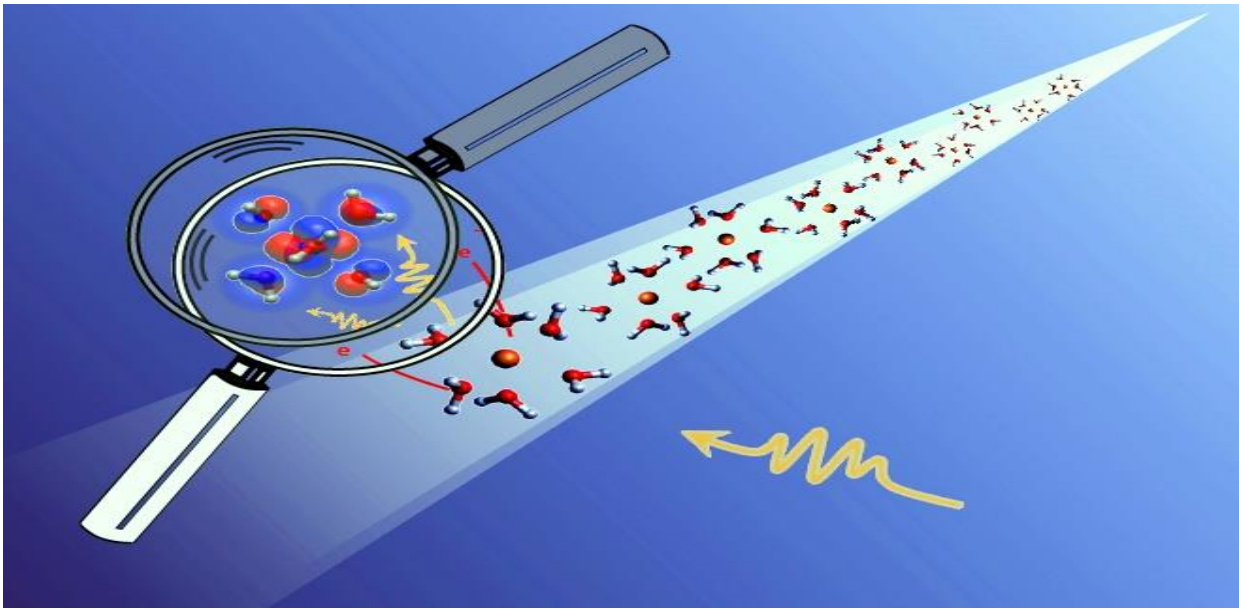
The effect of a solute on the vapor pressure of a solution.





Therefore, if a salt crystal is positioned in water, the polar water molecules are attracted to ions on the crystal surfaces. The water molecules steadily surround and isolate the surface ions. The ions therefore become hydrated. They gradually move away from the crystal into solution media. This separation of ions from each other is known as dissociation. The surrounding of solute particles by solvent particles is known as solvation. When the ions are dissociated, each ionic species in the solution media acts as though it were present alone. Therefore, a solution of sodium chloride acts as a solution of sodium ions and chloride ions.

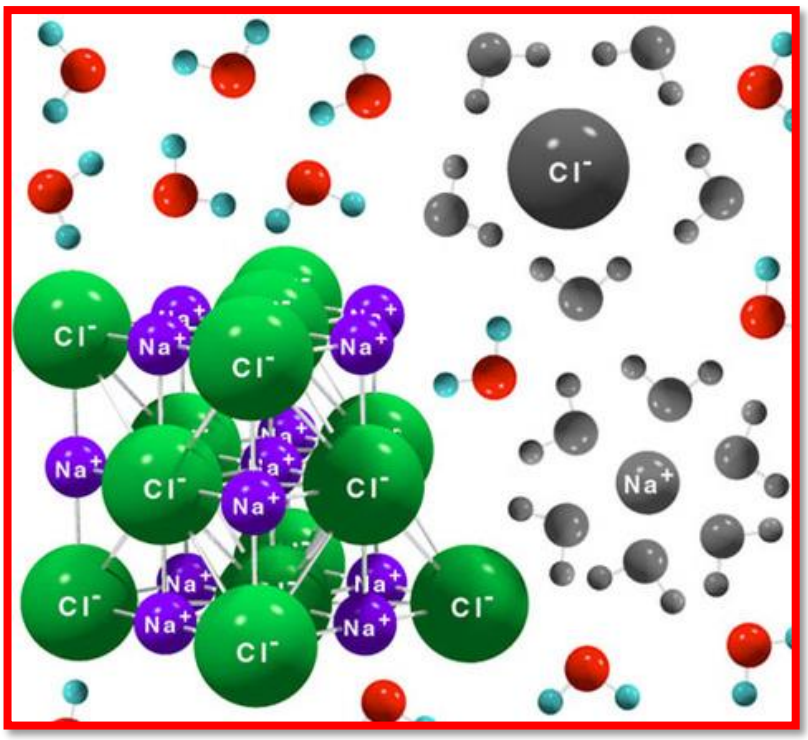
The determination of thermodynamic, transport, optical, morphological and biological properties of different electrolytes in various solvents would thus afford an important step in this direction. Naturally, in the expansion of theories, dealing with electrolyte solutions, much interest has been devoted to ion-solvent interactions which are the controlling forces in infinitely dilute solutions where ion-ion interactions are absent. It is possible by separating these functions into ionic contributions to verify the contributions due to cations and anions in the solute-solvent interactions. Thus "*ion-solvent interactions show a very important role to know the physico-chemical properties of solutions*". One of the causes for intricacies in solution chemistry is structure of the solvent molecule is not known properly with certainty. The introduction of a solute also modifies the solvent structure to an doubtful magnitude whereas the solute molecule is also modified and the interplay of forces like solute-solute, solute-solvent and solvent-solvent interactions become predominant though the isolated picture of any of the forces is still not known totally to the solution chemist. The problems of ion-solvent interactions which are closely similar to ionic solvations can be studied from diverse angles using almost all the available physico-chemical techniques.



a) Ion-Solvent Interaction

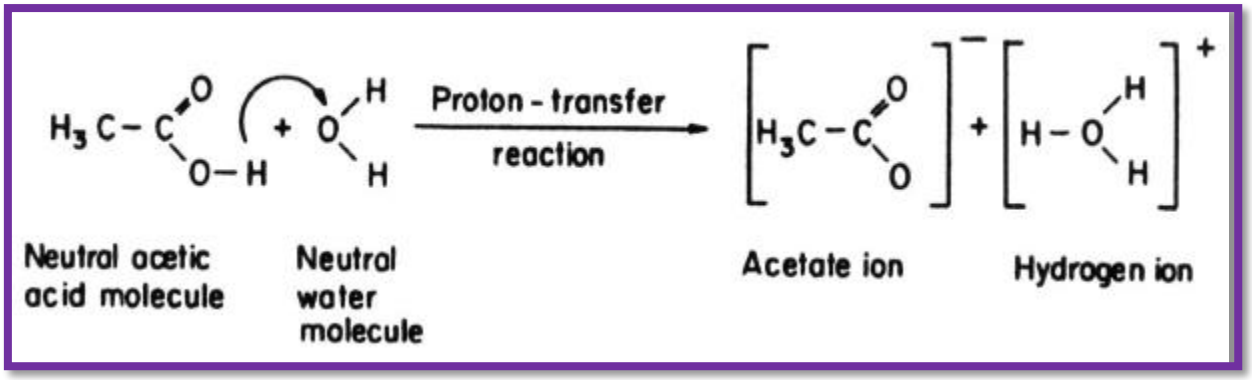
Solutions which conducts electricity consisting of (solute + solvent). Electrolytes may be defined as a class of compounds, which, upon dissolution in a polar solvent, dissociate at least partially into ions. [5, 6]

NaCl is an ionic compound consisting of Na^+ and Cl^- ions joined collectively via ionic bonds in a crystal lattice. When solid NaCl is put in contact with water, the solvent molecules rapidly attack the lattice, disrupt and break the ionic bonds and thereby generate hydrated ions $Na^+(aq)$ and $Cl^-(aq)$ as outlined schematically below.[7, 8]



Two distinct ways is formed by the mobile ions in solution to create ionically conducting phases that make up the solution side of an electrode–solution system.

A different condition pertains for acetic acid. In this case a specific reaction between the solute and solvent, a proton transfer reaction, results in the generation of acetate $CH_3CO_2^-$ and hydronium ions. A proton is transferred from the organic acid (a proton donor) to a water molecule (a proton acceptor) outlined beneath. This is a case of *Bronsted-Lowry acid/base reaction*. Typically the degree of dissociation is ca. 10^{-3}. [9, 10]

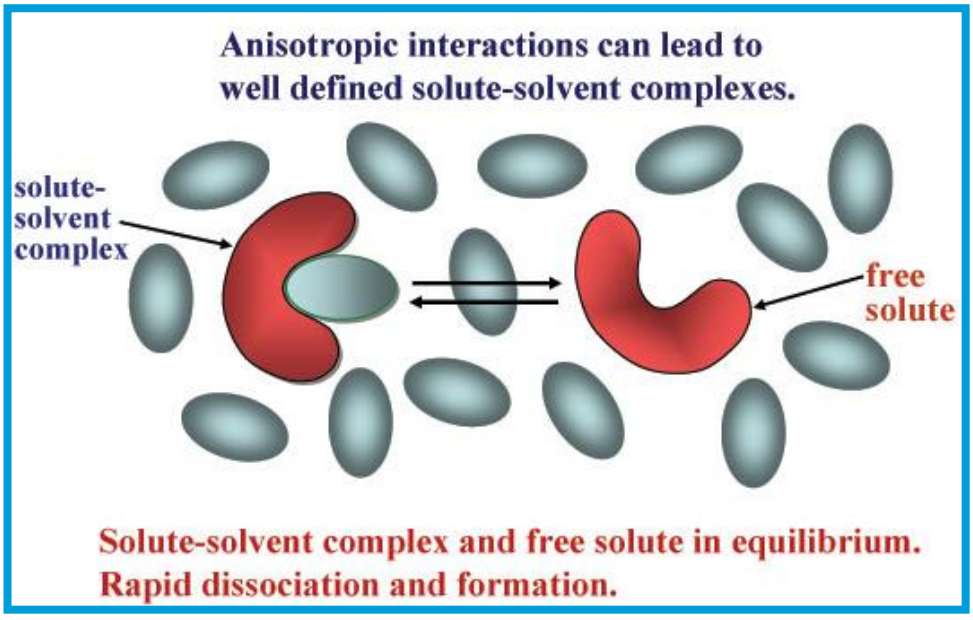


Ion-Solvent/Solute-Solvent interactions play a vital role in solution phase chemistry. These interactions not only stabilize intermediate states by solvation of the corresponding valence charge distributions, but modify energy barriers thereby altering transition states, and allow

for the ultrafast solvent dynamics. Solute- Solvent interactions are thus frequently vital in determining ground-states and steering chemical reaction mechanisms in solution-phase chemistry.

We seek to comprehend the role of solvation and solvation dynamics upon external perturbations through excitation of electronic and vibrational degrees of freedom. While extended collective motions of solvent molecules and their corresponding spectral density are useful in understanding the influence of solvation (dynamics) on the solute's constituents during chemical reactions.[11, 12]

Both, vibrational and core-level transitions extend over length scales from functional groups to individual atoms, making them tremendous spectroscopic probes of solute-solvent interactions. So, it can be said that Ions orient dipoles; spherically symmetrical electric field of the concerned ion may well tear solvent dipoles out of the solvent lattice and orient them with appropriate charged end in the direction of central ion. Thus, screening the ion as a point charge and the solvent molecules as electric dipoles, ion-dipole forces become the principal source of ion-solvent interactions. While vibrational transitions can basically be associated with structural dynamics, core-level transitions report on valence electronic distributions as well structural parameters such as bond lengths and geometries. [13, 14]



The majority of reactions happening in solutions are chemical or biological in nature. It was presumed previously that the solvent only provides an inert medium for chemical reactions.

The significance of ion-solvent interactions was realized following extensive studies in aqueous, non-aqueous and mixed solvents.

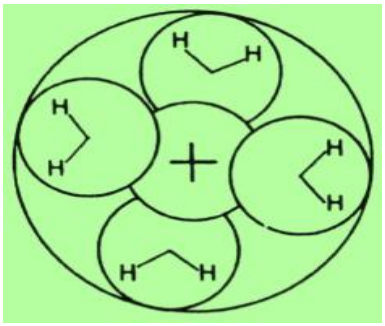
The role of solvent is so immense that million fold rate changes take place in some reactions simply by changing the reaction medium. Human body is composed of 65 to 70% water, which acts as a lubricant, as an aid to digestion and more specifically as a stabilizing factor to the double helix conformations of DNA. The solvent governs movement and energy of the reacting species to such a level that a reaction undergoes a several-million fold change in rate when the solvent is changed. [15, 16]

As water is the "*universal solvent*" in nature and has major importance to chemistry, biology, agriculture, geology, etc., water has been extensively used in kinetic and equilibrium studies. But still our knowledge of molecular interactions in water is extremely limited in a particular boundary.

Moreover, the uniqueness of water as a solvent has been questioned and it has been realized that the studies of other solvent media like non aqueous and mixed solvents would be of helpful in understanding diverse molecular interactions and a host of complicated phenomena. Varieties of organic solvents have been classified on the basis of dielectric constants, organic group types, acid base properties, or association through hydrogen bonding donor-acceptor properties hard and soft acid-base principles etc. As a result, the different solvents show a wide change in properties, ultimately influencing their thermo physical, thermodynamic, transport qualitatively and quantitatively, in presence of electrolytes and non-electrolytes in these solvents. Henceforth, in the development of theories of electrolytic solutions, much awareness has been devoted to the controlling forces *'ion-solvent interactions'* in infinitely dilute solutions wherein ion-ion interactions are almost absent. By sorting out these functions into ionic contributions, it is possible to determine the contributions of cations and anions in the ion-solvent interactions. One of the major causes for the intricacies in solution chemistry is the uncertainty about the structure of the solvent molecules in solution. The introduction of a solute modifies the solvent structure to an uncertain magnitude, the solvent molecule and the interplay of forces like solute-solute, solute-solvent also modify the solute molecule and solvent-solvent interactions becomes predominant, though the isolated picture of any of the forces is still incomplete to the solution chemist.[17]

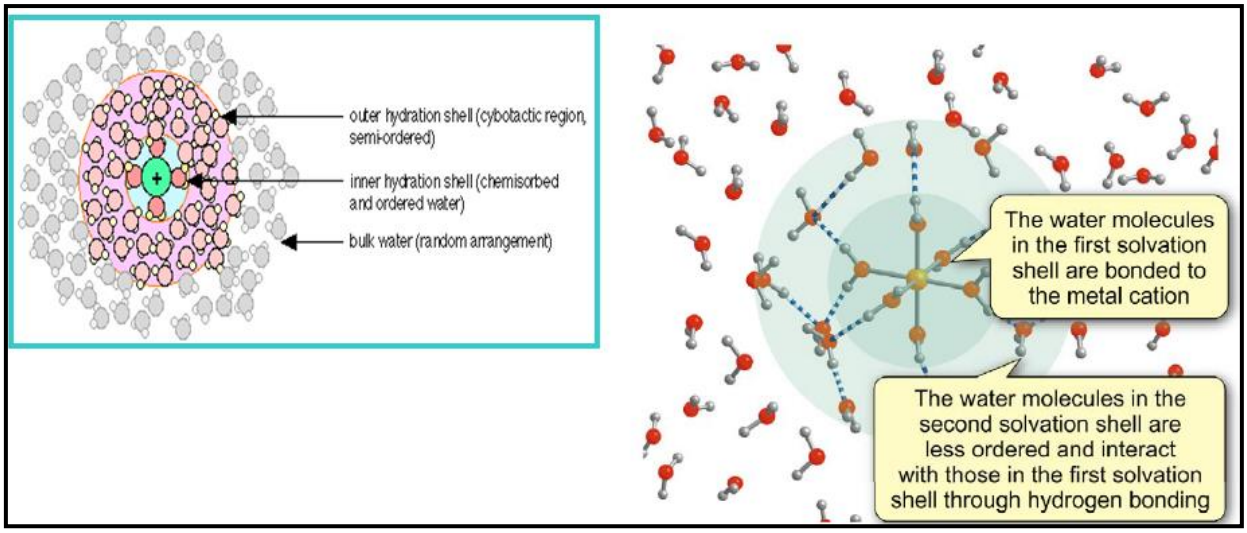
♣ *How does the presence of an Ion affect the structure of neighboring water?*

The aim here is to take a microscopic vision of an ion inside a solvent. The central consideration is that the ions get oriented as dipoles. The spherically symmetrical electric field of the ion may tear water dipoles out of the water lattice and craft them like a point (like compass needles oriented toward a magnetic pole) with the appropriate charged end toward the central ion. Hence screening the ion by considering it as a point charge and the solvent molecules as electric dipoles, one obtains a picture of ion–dipole forces as the principal source of ion–solvent interactions.



♣ *How does the presence of an Ion affect Structure of neighboring water?*

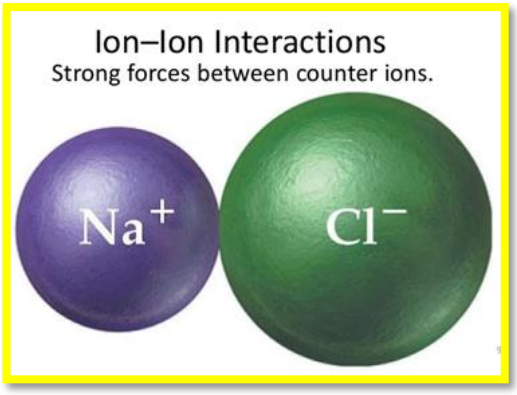
Owing to the action of ion–dipole forces, a number of water molecules in the immediate vicinity of the ion may be trapped and oriented in the ionic field. Such water molecules cease to connect with the water molecules that remain part of the network characteristic of water. They are immobilized except in a distance as the ion moves, in which case the sheath of immobilized, water molecules moves with the ion. The ion and its water sheath then become a distinct kinetic entity. Thus, the depiction of a hydrated ion is one of an ion enveloped by a solvent sheath of oriented, immobilized water molecules.



The spectral solvent shifts or the chemical shifts can establish the qualitative and quantitative nature of ion-solvent interactions. But still qualitative or quantitative apportioning of the ion-solvent interactions into the variety of possible factors is still an uphill task. It is thus apparent that the real understanding of the ion-solvent interaction is a difficult task. The aspect embraces a wide range of topics but we concentrated only on the measurement of transport properties like viscosity, conductance etc; physicochemical, thermodynamic properties as apparent or partial molar volumes, apparent molar adiabatic compressibility, and spectral properties as FT-IR spectroscopy, U.V, Fluorescence, NMR, SEM, HRTEM and HRMS etc. [18]

6) Ion-Ion Interaction

When an ion looks out upon its surroundings, it sees not only solvent dipoles but also other ions in the solvent sphere. The mutual interaction between these ions constitutes a vital part of the picture of an electrolytic solution. Ion-solvent interactions are only a part of the story of an ion related to its atmosphere. The surrounding of an ion sees only other ions, no solvent molecules. [19, 20]



Why are ion-ion interactions in solution important?

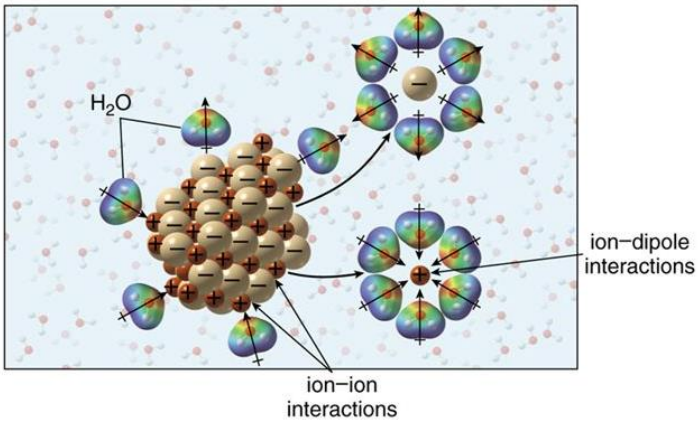
Because, as will be revealed from various experimental data [21, 22], they affect the equilibrium properties of ionic solutions, and also because they interfere with the drift of ions, for instance, under an externally applied electric field. [23]

Now, the degree to which these interactions influence properties of solutions will depend on the mean distance of the ions, i.e., on the way how densely the solution is populated with ions, because the interionic fields are distance dependent. This ionic population density will in turn depend on the nature of the electrolyte, i.e., on the extent to which the electrolyte gives rise to ions in solution. Thus ionic compounds contain oppositely charged particles held together by extremely strong electrostatic interactions. These ionic interactions are much stronger than the intermolecular forces present between covalent molecules. It is comparable to Coulomb's law, which states that the energy of interaction between two ions is directly proportional to the product of the charges of the two ions and inversely proportional to the distance between them. [24]

- **To dissolve an ionic compound, the strong ion-ion interactions must be replaced by many weaker ion-dipole interactions.**

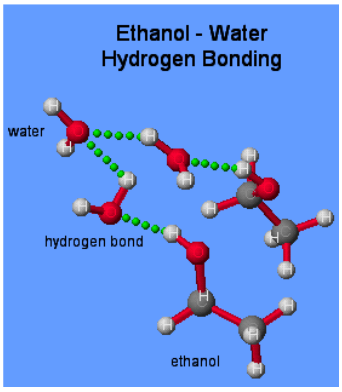
Dissolving an ionic compound in H_2O

- When an ionic solid is dissolved in H_2O, the ion–ion interactions are replaced by ion–dipole interactions. Though these forces are weaker, there are so many of them that they compensate for the stronger ionic bonds.



c.) Solvent-Solvent Interactions (Theory of Mixed Solvents)

Solubility provides a suitable parameter for studying the solvation interaction. Solvent–solvent interaction plays a major role in the overall solvation process. [25] Mixed binary solvents provide systems where it is possible to vary the solvent–solvent interaction and as such, study in these media is likely to throw light on the role of such type of interactions on the solvation process. Solvation in mixed binary aqueous solvents shows non-ideal behaviour and solvent–solvent interaction play a key role in determining solubility. As the use of mixed and non-aqueous solvents are increasingly in chromatography, solvent extraction, elucidation of reaction mechanism, preparing high density batteries, etc. a number of molecular theories, based on either the radial distribution function or the choice of suitable physical model, have been developed for mixed solvents.[26]



L. Jones and Devonshire [27] were first to evaluate thermodynamic functions for a single fluid in conditions of interchange energy parameters and used *"Free volume" or "Cell model"*.

Prigogine and Garikian[28] extended the aforesaid approach to solvent mixtures. *Prigogine and Bellemans*[29] further investigated a two *fluid version of the cell model* and found that while excess molar volume (V^E) was negative for mixtures with molecules of almost same size. It was large positive for mixtures with molecules having minute difference in their molecular sizes.

Treszczanowiczet.al. [30] recommended that V^E is the result of numerous contributions from several opposing effects. These may be divided arbitrarily into three types, viz., physical, chemical and structural effects. Physical contributions contribute a positive term to V^E and the chemical or specific intermolecular interactions effects volume decrease and contribute negative values to V^E. The structural contributions are mostly negative values and arise from several effects, particularly from interstitial accommodation and changes in the free volume. The actual volume change would therefore depend on the relative strength of these effects totally. On the other hand, it is generally assumed that when V^E is negative, viscosity deviation ($\Delta\eta$) may be positive and vice-versa. This assumption is not a real, as evidence behind it is proved from some studies. [31, 32]

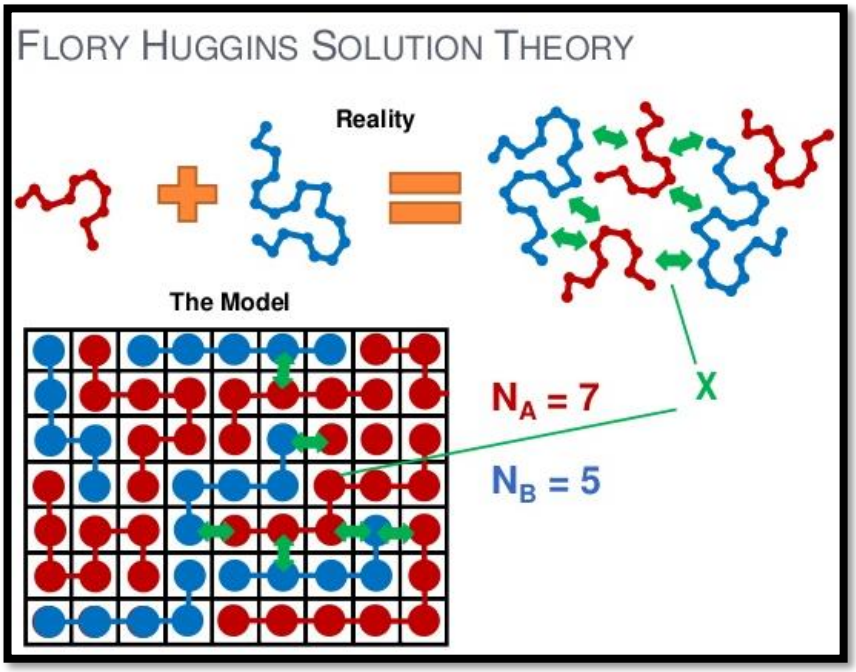
Rastogi et al. [33] recommended the experimental excess property is a combination of an interaction and non-interaction part. The non-interaction part in the form of size effect can be comparable to the interaction part which may be sufficient to reverse the trend set by the latter.

Pitzer[34], *L. Huggins*[35] introduced a new approach in their *theory of conformal solutions*. Using a simple perturbation approach, showed that the properties of mixtures could be obtained from the knowledge of intermolecular forces, thermo physical and thermodynamic properties of the pure components.

Rowlinson et al. [36-38] reformulated the *average rules for Vander Waal's mixtures* and their calculated values were in much improved agreement with the experimental values even when *one fluid theory* was applied.

The more current independent effort is the *perturbation theory* of *Baker and Henderson*. [39]

A more successful approach is due to *Flory* who used certain features of *cell theory* [40, 42] and also developed a *statistical theory* for predicting the excess properties of binary mixtures by using the equation of state and the properties of pure components along with a few adjustable parameters. This theory is applicable to mixtures containing molecules of dissimilar shapes and sizes.



Patterson and Dilamas[43] combined both *Prigogine and Flory* theories to a joined one for rationalizing various contributions of free volume, internal pressure, etc. to the excess thermodynamic properties.

Heintz[44-46] *and coworkers* suggested a theoretical model based on a statistical mechanical derivation and accounts for self-association, cross association in hydrogen bonded solvent mixtures, which is termed as *Extended Real Associated Solution model (ERAS)*. It combines the effect of association with non-associative intermolecular interaction occurring in various solvent mixtures based on equation of state developed originally by *Flory*. Subsequently ERAS model has been successfully applied by many workers [47-49] to describe excess thermodynamic properties of alkanol-amine mixtures. *A new symmetrical reformation on the Extended Real Association* (ERAS) model has been described in the literature [50] which explained the *symmetrical-ERAS (S-ERAS) model* and made it possible to describe excess molar enthalpies and excess molar volumes of binary mixtures containing very similar compounds described by extremely small mixing functions. [51]

Gepert et al. [52] applied *symmetrical-ERAS (S-ERAS)* [53] model for studying some binary systems containing alcohols.

II. *(3) The Specific techniques used in conducting Experiments*

♣ *Densitometry*

As a consequence, densitometry preceded and accompanied the birth and development of the thermodynamic theory. One of the well-recognized approaches to the study of molecular interactions in fluids is the use of thermodynamic techniques. Thermodynamic properties are commonly suitable parameters for interpreting solute-solvent and solute-solute interactions in the solution phase. The physicochemical properties of liquid mixtures have attracted much attention from both theoretical and engineering applications point of view. As the mixed and non-aqueous solvents are progressively more used in chromatography, solvent extraction, in the elucidation of reaction mechanism, in preparing high density batteries, etc. a number of molecular theories, based on either the radial distribution function or the choice of suitable physical model, have been developed for mixed solvents.

Volumetric and densitometry techniques are complementary, as volume determinations can give precise density values and vice versa, but often it is easier to assess accurately only one of the properties. The volumetric information including 'Density' is used as a function of weight, volume and mole fraction and excess volumes of mixing.

Thermodynamic properties of pure substances (molar volumes) and substances in solution (partial molar volumes) can be deduced from either of these techniques. Fundamental properties such as enthalpy, entropy and Gibbs free energy represent the macroscopic state of the system as an average of numerous microscopic states at a specified temperature and pressure. An interpretation of these macroscopic properties in terms of molecular phenomenon is in general difficult to study. Sometimes higher derivatives of these properties can be interpreted more specifically in terms of molecular interactions. The volumetric information possibly will be of immense importance in this regard. Various concepts concerning molecular processes in solutions like electrostriction, [53] hydrophobic hydration,[54] micellization[55] and co-sphere overlap all through solute-solvent interactions[56, 57] have been derived and interpreted starting

from the partial molar volume data of many compounds. Other quantities such as hydration or hydrodynamic volumes are usually evaluated by non-thermodynamic properties and assumptions, or by calculations based on structural observations. For example mesoscopic systems (for instance, globular proteins in aqueous solution) some interesting observations suggest that the specific volumes are the result of an average among domains whose local densities range from 0.6 kgL^{-1} to 3.0 or 3.5 kgL^{-1}. Further the definition of domain volumes, as well as the definition of whole volume of a macromolecule in initiate contact with solvent, suffers a certain degree of arbitrariness.

♣ *Apparent and Partial Molar Volumes*

The molar volume of a pure substance can be derived using density data. In complex multi-component systems such as solutions, it is easier to explain a system in terms of the intrinsic or molal properties rather than the extensive properties. Any extensive property of a system can be calculated by the summation of the respective partial molal properties if all components have a known concentration. Although the additive definition of partial molal properties is convenient, direct measurement of these solution properties are difficult, as interactions with other species contribute to partial molal properties. However, the volume contributed to a solvent by the addition of one mole of an ion is difficult to decide. This is so because, upon entry into the solvent, the ions change the volume of the solution due to a breakage of the solvent structure near the ions and the compression of the solvent under the influence of the ion's electric field, i.e., electrostriction. Electrostriction is a general phenomenon and whenever there are electric fields of the order of 10^9-10^{10} V m^{-1}, the compression of ions and molecules is expected to be significant. The effective volume of an ion in solution system, the partial molar volume, can be determined from a directly obtainable quantity-apparent molar volume (ϕ_V). The apparent molar volumes, (ϕ_V), of the solutes can be calculated by means of the following relation. [57, 58]

$$\phi_V = \frac{M}{\rho_0} - \frac{1000(\rho - \rho_0)}{c\rho_0} \quad (1)$$

Where M is the molar mass of the solute, c is molarity of the solution; $\rho_o$and ρ are the densities of solvent and the solution respectively. Partial molar volumes, ϕ_{2v} can be obtained from the equation :[59]

$$\phi_{2V} = \phi_V + \frac{(1000 - c\phi_V)}{2000 + c^{3/2}\left(\partial\phi_V / \partial\sqrt{c}\right)} c^{1/2}\left(\partial\phi_V / \partial\sqrt{c}\right) \quad (2)$$

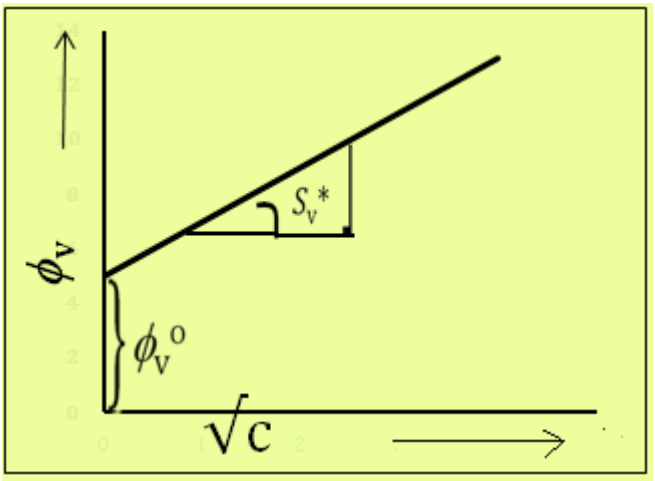
The extrapolation of apparent molar volume of electrolyte to infinite dilution and expression of the concentration dependence of the apparent molar volume have been made by four major equations over a period of years – the *Masson equation* ,[59] *the Redlich-Meyer equation* ,[60] *the Owen-Brinkley equation*,[61] *and the Pitzer equation* .[34, 32] Masson found that the apparent molar volume of electrolyte, ϕ_V , vary with square root of the molar concentration by the linear equation:

$$\phi_V = \phi_V^0 + S_V^* \sqrt{c} \quad (3)$$

ϕ_V^o = the limiting apparent molar volume at infinite dilution, indicates **ion-solvent interaction**

S_V*= the experimental slope, signifies the **ion-ion interaction**

Where, ϕ_V^0 is the apparent molar volume (equal to the partial molar volume) at infinite dilution and S_V^* is the experimental slope. The greater part of ϕ_V data in water [62] and nearly all ϕ_V data in non-aqueous solvents [63-67] have been extrapolated to infinite dilution through the utilization of equation (3).



A diagrammatic representation for the explanation of molal volume

The temperature dependence of ϕ_V^0 or various investigated electrolytes in various solvents can be articulated by the general equations follows:

$$\phi_V^0 = a_0 + a_1 T + a_2 T^2 \quad (4)$$

Where a_0, a_1 and a_2 are the coefficients of a particular electrolyte and *T* is the temperature in Kelvin.

The limiting apparent molar expansibilities (ϕ_E^0) can be calculated by the following equation:

$$\phi_E^0 = \left(\delta\phi_V^0/\delta T\right)_P = a_1 + 2a_2 T \quad (5)$$

The limiting apparent molar expansibilities (ϕ_E^0) change in magnitude with the change of temperature. During the past few years, different workers emphasized that S_V^* is not the sole criterion for determining structure-making or breaking tendency of any solute. *Helper* [68] developed a technique of examining the sign of $\left(\delta\phi_E^0/\delta T\right)_P$ for the solute in terms of long–range structure-making and breaking capacity of the electrolytes in the mixed solvent systems. The general thermodynamic expression used is as follows:

$$\left(\delta\phi_E^0/\delta T\right)_P = \left(\delta^2\phi_V^0/\delta T^2\right)_P = 2a_2 \quad (6)$$

If the sign of $\left(\delta\phi_E^0/\delta T\right)_P$ is positive or small negative the electrolyte is a **structure maker** and when the sign of $\left(\delta\phi_E^0/\delta T\right)_P$ is negative, it is a **structure breaker**. *Redlich and Meyer* [60, 61] have shown that an equation (3) cannot be any more than a limiting law where for a given solvent and temperature, the slope S_v^* should depend only upon the valence type. They suggested the equation:

$$\phi_v = \phi_v^0 + S_v\sqrt{c} + b_v c \quad (7)$$

$$\text{Where } S_v = Kw^{3/2} \quad (8)$$

S_V is the theoretical slope, based on molar concentration, including the valence factor where

$$w = 0.5\sum_{i}^{j} Y_i Z_i^2 \quad (9)$$

$$\text{And } K = N^2 e^2 \left(\frac{8\pi}{1000 \in^3 RT}\right)^{1/2} \left[\left(\frac{\partial \ln \in}{\partial p}\right)_T - \frac{\beta}{3}\right] \qquad (10)$$

In equation (10), K is the compressibility of the solvent and the other terms having their usual significance.

Redlich-Meyer's extrapolation equation [60, 61] adequately represents the concentration dependence of many 1:1 and 2:1 electrolytes in dilute solutions; however, studies [60-71] on some 2:1, 3:1 and 4:1 electrolytes show deviations from this equation. Thus, for polyvalent electrolytes, the more complete *Owen-Brinkley equation* [61] can be used to aid the extrapolation to infinite dilution and to adequately represent the concentration dependency of ϕ_V. The *Owen-Brinkley equation* [61] which includes the ion-size parameter in (cm), is prearranged as:

$$\phi_V = \phi_V^0 + S_V \tau(\kappa a)\sqrt{c} + 0.5 w_V \theta(\kappa a) c + 0.5 K_V c \quad (11)$$

Where symbols have usual significance. However, this equation is not extensively used for non-aqueous solutions.

Recently, the *Pitzer formalism* [34] has been used by *Pogue and Atkinson* [71, 73] to fit the apparent molal volume data. The *Pitzer equation* [34] for the apparent molar volume of a single salt $[M\gamma_M M\gamma_X]$ is

$$\phi_V = \phi_V^0 + V\left|Z_M Z_X\right| A_V \left|2bIn\left(I + bI^{\frac{1}{2}}\right) + 2\gamma_M \gamma_X RT\left[mB_{MX}^2 + m^2\left(\gamma_M \gamma_X\right)^{\frac{1}{2}} C_{MX}^V\right]\right. \quad (12)$$

Where symbols have their usual significance.

♣ *Ionic Limiting Partial Molar Volumes*

The individual partial ionic volumes give information relevant to the general question of the structure near the ion, i.e., its solvation. The calculation of ionic limiting partial molar volumes

in organic solvents is, however, a hard one. At present, however, most of the existing ionic limiting partial molar volumes in organic solvents were obtained by the application of methods initially developed for aqueous solutions to non-aqueous electrolyte solutions. In the last few years, the way suggested by *Conway et al.* [74] has been used more frequently. These authors used the procedure to determine the limiting partial molar volumes of anion for a series of homologous tetraalkylammonium chlorides, bromides and iodides in aqueous solution. They plotted the limiting partial molar volume $\phi^0_{v\,R_4NX}$, for a series of these salts with a halide ion in general as a function of the formula weight of the cation, $M_{R4N}{}^+$and obtained straight-lines for every series. Therefore, they proposed the following equation:

$$\phi^0_{v\,R_4NX} = bM_{R_4N^+} + \phi^0_{v\,X^-} \quad (13)$$

The extrapolation to zero cationic formula weight gave limiting partial molar volumes of the halide ions $\phi^0_{V\,X^-}$.

Uosaki et al. [75] used this process for the separation of some literature values and of their own $\phi^0_{V\,R_4NX}$ values into ionic contributions in organic electrolyte solutions. *Krumgalz* [76] applied the equivalent technique to a large number of partial molar volume data for non-aqueous electrolyte solutions in a wide temperature range.

♣ *Excess molar volumes*

The excess molar volumes, V^E are calculated from molar masses M_i and densities of pure liquids and mixtures according to the following equation [77-78]

$$V^E = \sum_{i=1}^{n} x_i M_i \left(\frac{1}{\rho} - \frac{1}{\rho_i}\right) \quad (14)$$

Where ρ_i and ρ are density of the i^{th} component and density of the solution mixture respectively. V^E is resultant of contributions from several opposing effects. These may be further divided arbitrarily into three types, namely, chemical, physical and structural. Physical contributions, are nonspecific interactions among real species present in mixture, contribute a positive term to V^E. The chemical or specific intermolecular

interactions result in a volume decrease, so contributing negative V^E values. The structural contributions are usually negative and arise from several effects, particularly from interstitial accommodation and changes of free volume. [17] These phenomena are therefore results of difference in energies of interaction between molecules being in solutions and packing effects. Disruption of the ordered structure of pure component during formation of the mixture leads to a positive effect observed on excess volume while an order formation in mixture leads to negative contribution in the solution.

♣ *Viscometric studies*

As fundamental and imperative properties of liquids, viscosity and volume could also provide a lot of information on the structures and molecular interactions of liquid mixtures. Viscosity and volume are diverse types of properties of one liquid, and there is a certain relationship between them. So by measuring and studying them together, relatively more realistic and comprehensive information could be expected to be gained. The relationship among them could also be studied. Viscometric information comprises 'Viscosity' act as a function of composition on basis of weight, volume and mole fraction; comparison of experimental viscosities with those designed with several equations and excess Gibbs free energy of viscous flow. Viscosity, one of the most assorted transport properties is used for the determination of ion-solvent interactions and studied extensively.[79-80] Viscosity is not a thermodynamic quantity, but viscosity of an electrolytic solution along with the thermodynamic property, $\phi_{v,2}^0$, i.e., the partial molar volume, gives a bundle of information and insight regarding ion-solvent interactions and nature of structures in the electrolytic solutions.

♣ *Viscosity of pure liquids and liquid mixtures*

Since the molecular motion in liquids is controlled by the influence of the neighboring molecules, transport of momentum in liquids takes place, in sharp contrast with gases at ordinary pressures, not by real movement of molecules but by intense influence of intermolecular force fields. It is this aspect of the mechanism of momentum transfer which forms the basis of assorted procedures for predicting the variations in the viscosity of liquids and liquid mixtures.

♣ Early Theoretical Considerations on Liquid Viscosity

The theoretical development of liquid viscosity in early stages has been reviewed by *Andrade* [81] *and Frenkel.* [82] By considering the forces of collision to be the only important factor and assuming that at the melting point, the frequency of vibration is equal to that in the solid state, one-third of the molecules are vibrating along each of the three directions normal to one another. *Andrade* [81] formulated equations which checked well against data on monatomic metals at the melting point. *Frenkel* [82] considered the molecules of a liquid to be spheres moving with an average velocity with regard to the surrounding medium by using *Stokes' law and Einstein's relation* [83] for self-diffusion-coefficient, arrived at a complicated expression for liquid viscosity with only limited applicability. Further assumed the momentum transfer to take place by the irregular Brownian movement of the holes which were linked to clusters in a gas and thus, in equivalence with the gas theory of viscosity and with assumption of the equipartition law of energy, showed that for liquids:

$$\eta = 0.915 \frac{RT}{V} \left(\frac{m}{\sigma} \right) e^{\frac{A}{RT}} \quad (15)$$

Where η, V and m are viscosity, volume and mass, respectively, T is the temperature, R is the universal gas constant, σ is the surface tension and A is the work function at the melting point in the solution medium. He compared his theory with experiment as well as with the theories of *Andrade* [82] *and Ewell and Eyring* [85] *Auluck, De and Kothari* [86] further modified the theory and successfully explained the variations of viscosity with pressure. A critical review of these simple theories and their abilities to elucidate momentum transport in liquids is given by *Eisenschitz.* [87]

♣ The Cell Lattice Theory and Liquid Viscosity

A model interrelated to in the literature by various names such as cell, lattice, cage, free volume or one particle model was introduced by *Lennard-Jones* [88] and *Devonshire*

[89] and further expanded by *Pople*. [90] *Eisenschitz* employing this model developed a theory based on viscosity by considering the motion of the representative molecules to be *Brownian* and their distribution according to the *Smoluchowski equation*. Even by means of certain assumptions, the final expression showed shortcomings most of which were later overcome in a subsequent publication. [91]

♣ *Statistical and Mechanical approach to Liquid Viscosity*

The distribution functions for the liquid molecules were obtained on the basis of statistical mechanical theory mostly by the efforts of *Kirkwood*, [92, 93] *Mayer and Montroll*, [94] *Mayer*, [95] *Born and Green* [96] considerations on the basis of the general kinetic theory led *Born and Green* to build up a viscosity equation which provided explanation for several empirical equations [80-83] proposed for liquid viscosity. In this connection to the theoretical contributions of Kirkwood *and coworker* [84, 98-105] *Zwanzig et al.*, [105] *Rice and coworkers*, [106-109] *Longuet-Higgins and Valleau* [110] and *Davis and Coworkers* are noteworthy. [111, 112]

♣ *Principle of Corresponding States and Liquid Viscosity*

The principle of the corresponding states has been useful to liquids in the same way as to gases [113] the basic assumption being that the intermolecular potential among two molecules is a universal function of the reduced intermolecular separation. This assumption is a good approximation for spherically symmetric mono atomic non-polar molecules in solution. Intended for complex molecules, the principle becomes increasingly crude. In general, more parameters are introduced in the corresponding state correlations on somewhat empirical grounds in the expectation that such modification in some way would compensates the shortcomings of the above stated assumption. In this correlation the studies by *Rogers and Brickwedde, Boon and Thomaes, Boon, Legros and Thomaes, and Hollman and Hijmans* are worth mentioning. [114-119]

♣ *The Reaction Rate Theory for Viscous Flow*

Considering viscous flow as a chemical reaction in which a molecule moving in a plane intermittently acquires the activation energy necessary to sleep over the potential barrier to the next equilibrium position in the same plane. *Eyring* showed that the viscosity of the liquid in a solution medium is given by:

$$\eta = \frac{\lambda_i h F_n}{\kappa \lambda^2 \lambda_2 \lambda_3 F_a^*} \exp \frac{\Delta E_{act}}{kT} \quad (16)$$

Where λ is the average distance between the equilibrium positions in the direction of motion, λ_1 is the perpendicular distance between two neighboring layers of molecules in relative motion, λ_2 is the distance between neighboring molecules in the same direction and λ_3 is the distance from molecule to molecule in the plane normal to the path of motion. The transmission coefficient (κ) is the measure of the chance that a molecule having once crossed the potential barrier will react and notrecross in the reverse direction, F_n is the partition function of normal molecules, F_a^* that of the activated molecule with a degree of freedom corresponding to flow, ΔE_{act} is the energy of activation for flow process, h is Planck's constant and k is Boltzmann constant in the flow process. *Ewell and Eyring* argued that for a molecule to flow into a hole, it is not indispensable that the latter be of the same size as the molecule. Consequently they assume that ΔE_{act} is a function of ΔE_{vap} for viscous flow because ΔE_{vap} is the energy necessary to make a hole in the liquid of the size of a molecule. Utilizing the initiative and certain additional relations finally gets [82, 120]

$$\eta = \frac{N_A h (2\pi m k T)^{\frac{1}{2}}}{Vh} \frac{bRTV^{\frac{1}{3}}}{N_A^{\frac{1}{3}} \Delta E_{Vap}} \exp \frac{\Delta E_{Vap}}{nRT} \quad (17)$$

Where n and b are constants. It was found that the theory could reproduce the trend in temperature dependence of η but the computed values are larger than the observed values by a factor of 2 or 3 for most liquids. *Kincaid, Eyring and Stearn* have summarized all the working relations. [121, 122]

♣ *The significant structure theory and Liquid Viscosity*

Eyring and coworkers [123-126] enhanced the "holes in solid" model theory to picture the liquid state by identifying three significant structures. In brief, a molecule has solid like properties for the little time it vibrates about an equilibrium position and then it assumes instantly the gas like behavior on jumping into the neighboring vacancy. The above idea of significant structures leads to the following relation for the viscosity of liquid. [128]

$$\eta = \frac{V_s}{V}\eta_S + \frac{V - V_s}{V}\eta_g \quad (18)$$

Where V_S is the molar volume of the solid at the melting point, V is the molar volume of the liquid at the temperature of interest while η_S and η_g are the viscosity contributions from the solid-like and gas-like degrees of freedom, correspondingly. The terms for η_S and η_g are given by *Carlson, Eyring and Ree*. *Eyring and Ree* have discussed in detail the evaluation of η_S from the reaction rate theory of *Eyring* assuming that a solid molecule can jump into all neighbouring empty sites. The expression for η_S takes the following form [131]

$$\eta_S = \frac{N_A h}{Z\kappa}\cdot\frac{V}{V_S}\cdot\frac{6}{2^{\frac{1}{2}}}\cdot\frac{1}{V - V_S}\cdot\frac{1}{1 - e^{\frac{\theta}{T}}}exp\frac{\acute{a}E_S V_S}{(V - V_S)RT} \quad (19)$$

Where N_A is Avogadro's number, Z is the number of nearest neighbors, ϑ is the Einstein characteristic temperature, E_S is the energy of sublimation and a' is proportionality constant. On the other hand, the term η_g is obtained from the kinetic theory of gases by the relation: [131]

$$\eta_g = \frac{2}{3d^2}\left(\frac{mkT}{\pi^3}\right)^{\frac{1}{2}} \quad (20)$$

Where d is the molecular diameter and m is the molecular mass.

♣ *Viscosity of electronic solutions*

The viscosity relationships of electrolytic solutions are highly complicated and difficult to clarify because ion-ion and ion-solvent interactions are occurring in the solution and separation of the related forces is a difficult task. But, from careful analysis, vivid and

valid conclusions can be drawn regarding structure and nature of the solvation of the particular system. As viscosity is a measure of the friction between adjacent, relatively moving parallel planes of the liquid, something that increases or decreases the interaction between the planes will raise or lower the friction and thus, increase or decrease the viscosity. If large spheres are positioned in the liquid, the planes will be keyed together in increasing the viscosity. Similarly, increase in average degree of hydrogen bonding between the planes will increase friction between the planes, thereby viscosity. An ion with a large rigid co-sphere for a structure-promoting ion will behave as a rigid sphere placed in the liquid and raise the inter-planar friction. Similarly, an ion increasing the degree of hydrogen bonding or the degree of correlation among the adjacent solvent molecules will increase the viscosity of the solution. On the other hand, ions destroying correlation would decrease the viscosity. In 1905, *Grüneisen* performed the first methodical measurement of viscosities of a number of electrolytic solutions over a wide range of concentrations. He elucidated non-linearity and negative curvature in viscosity concentration curves irrespective of low or high concentrations. In 1929, *Jones and Dole* recommended an empirical equation quantitatively correlating the relative viscosities of the electrolytes with molar concentrations (c): [132, 133]

$$\frac{\eta}{\eta_o} = \eta_r = 1 + A\sqrt{c} + Bc \qquad (21)$$

The above equation can be rearranged as:

$$\frac{\eta_r - 1}{\sqrt{c}} = A + B\sqrt{c} \qquad (22)$$

Where A *and* B are constants definite to ion-ion and ion-solvent interactions. The equation is valid equally to aqueous and non-aqueous solvent systems where there is no ionic association and has been used comprehensively. The term $A\sqrt{c}$, formerly ascribed to *Grüneisen effect*, arose from the long-range coulombic forces linking the ions. The connotation of the phrase had since then been realized due to the development *Debye-Hückel theory of inter-ionic attractions* in 1923. The A -coefficient depends on the ion-ion interactions and can be designed from *interionic attraction theory* and is given by *Falkenhagen Vernon equation*: [134-137]

$$A_{Theo} = \frac{0.2577\Lambda_o}{\eta_o(\varepsilon T)^{0.5}\lambda_+^o\lambda_-^o}\left[1-0.6863\left(\frac{\lambda_+^o\lambda_-^o}{\Lambda_o}\right)^2\right] \quad (23)$$

Where symbols contain their usual significance. In accurate work on aqueous solutions, A -coefficient has been obtained by fitting η_r to equation and compared with the values calculated from the equation, agreement was on average excellent. The accuracy achieved with partially aqueous solutions was however of poorer quality. A-coefficient should be calculated from conductivity measurements. *Crudden et al.* suggested that if association of the ions occurs to form an ion pair, the viscosity should be analyzed by the equation: [138-140]

$$\frac{\eta_r - 1 - A\sqrt{\alpha c}}{\alpha c} = B_i + B_P\left(\frac{1-\alpha}{\alpha}\right) (24)$$

Where A, B_i and B_P are characteristic constants, determines degree of dissociation of ion pair. Thus, a plot of (η_r-1-A$\sqrt{\alpha}$c/αc) against $(1-\alpha)/\alpha$, when extrapolated to $(1-\alpha)/\alpha = 0$ gave the intercept value of B_i. However, for the majority of the electrolytic solutions both aqueous and nonaqueous, the equation is valid up to 0.1 (M) within experimental errors. At higher concentrations the extended part of the equation, involving an additional coefficient D, originally used by *Kaminsky*, has been used by several workers and is given below: [141-144]

$$\frac{\eta}{\eta_o} = \eta_r = 1 + A\sqrt{c} + Bc + Dc^2 \quad (25)$$

The coefficient D can't be evaluated appropriately and the significance of the constant is also not always meaningful and therefore, equation is used by the most of the workers.

The plots of [$(\eta/\eta_o$ -1)/$\sqrt{}$c against $\sqrt{}$c] for the electrolytes ought to provide the value of A-coefficient. But sometimes, the values appear to be negative or considerably scatter and also show deviation from linearity.[142-147] Thus, as a substitute of determining A-coefficient from the plots or by the least square method, the A-coefficient is generally calculated using *Falkenhagen-Vernon equation*. [22, 23] A-coefficient must have the value zero for non-electrolytes. According to Jones and Dole, the A-coefficient probably

represents the *stiffening effect* on the solution of electric forces between ions, which tend to uphold a space-lattice structure. [133] The ***B*-coefficient may be either positive or negative and it is in fact the ion-solvent interaction parameter**. Therefore it is conditioned by ions and solvent which can't be calculated a priori. The B–coefficients in Jones Dole are obtained as slopes of straight lines via least square method and intercepts equal to A values.

The factors influencing $\mathcal{B}$ - coefficients are listed below as: [148, 149]

(1) Effect of ionic solvation along with action of field of ion in producing long-range order in solvent molecules, increases η or B -value.

(2) The demolition of three dimensional structures of solvent molecules (i.e., structure breaking effect or depolymeriation effect) decreases with η values.

(3) High molal volume and low dielectric constant, which yield high B-values for analogous solvents.

(4) Reduced B-values are obtained when the primary solution of ions is sterically hindered in high molal volume solvents or if either ion of a binary electrolyte can't be specifically solvated.

♣ *Viscosities at higher concentration*

For routine work using aqueous solutions it had been found that the viscosity at high concentrations (1M to saturation) can be represented by the empirical formula suggested by *Andrade*:

$$\eta = Aexp^{\frac{b}{T}} \qquad (26)$$

The several alternative formulations have been proposed for representing the results of viscosity measurements in the high concentration range. An equation suggested by *Angell* based on an extension of *free volume theory of transport phenomena in liquids* and fused salts to ionic solutions are mainly noteworthy. [150-158]

The equation is:

$$\frac{1}{\eta} = A\exp\left[-\frac{K_1}{N_o - N}\right] \qquad (27)$$

Where N represents the concentration of the salt in eqv.litre^{-1}, A and K_1 are constants supposed to be independent of salt composition and N_o is hypothetical concentration at which the arrangement becomes glass. The equation was recast by *Majumder et al.* introducing the limiting condition i.e., $N \rightarrow 0$, $\eta \rightarrow \eta_o$; which is viscosity of the pure solvent system. Thus, we have: [158-160]

$$\ln \eta/\eta_o = \ln \eta_{Rel} = \frac{K_1 N}{N_o(N_o - N)} \qquad (28)$$

Equation (28) shows a straight line passing through origin for the plot of $ln\eta_{Rel}$ vs. $N/(N_o\text{-}N)$ if a suitable choice for N_o is made. *Majumder et al.* proved the equation (28) by using literature data as well as their own experimental data. Best choice for N_o and K_1 was chosen by a trial and error methods. Set of K_1 and N_o producing minimum deviations among η_{Rel}^{Exp} and η_{Rel}^{Theo} was accepted. Therefore in dilute solutions, $N << N_o$ and we have:

$$\eta_{Rel} = \exp\left(\frac{K_1 N}{N_o^2}\right) \cong 1 + \frac{K_1 N}{N_o^2} \qquad (29)$$

Equation (29) is nothing but the *Jones-Dole equation* with the ion-solvent interaction term represented as $B=K_1/N_o^2$.The arrangement between B-values determined in this way and using *Jones-Dole equation* has been found to be good for several electrolytes.

Further, the equation (28) can also be written in the form: [153]

$$\frac{N}{ln\eta_{Rel}} = \frac{N_0^2}{K_1} - \left(\frac{N_0}{K_1}\right) N \qquad (30)$$

It directly resembles the *Vand's equation* for fluidity (reciprocal for viscosity):

$$\frac{2.5c}{2.3 \log \eta_{Rel}} = \frac{1}{V_h} - Qc \qquad (31)$$

Where c is molar concentration of the solute molecule and V_h is effective rigid molar volume of the salt and Q is the interaction constant.

♣ *Division of B-Coefficient into ionic values*

The viscosities B –coefficients in solution system have been determined by a large number of workers in aqueous, mixed and non-aqueous solvents. [161-191] However, the *B* -coefficients as determined experimentally using the *Jones-Dole equation*, does not provide any impression regarding ion-solvent interactions unless there is some way to identify the separate contribution of cations and anions to the total solute-solvent interaction. The division of B -values into ionic components is quite arbitrary and based on a few assumptions, the validity of which may be questioned. The subsequent methods have been used for division of B – values in ionic components:

(1) *Cox and Wolfenden* carried out the division on conjecture that B_{ion} values of Li^+ and IO_3^- in $LiIO_3$ are proportional to the ionic volumes which are proportional to third power of ionic mobility's. The method of *Gurney* and also of *Kaminsky* [143] is based on: [192, 193]

$$B_{K^+} = B_{Cl^-} \text{ (in water)} \quad (32)$$

The argument in favor of this assignment is based on the fact that the *B* -coefficients for KCl is extremely minute and that the motilities' of K^+ and Cl^- are very comparable over temperature range 288.15 – 318.15 K. This assignment is supported from other thermodynamic properties. *Nightingle*, however chosen RbCl or CsCl to KCl from mobility considerations. [194]

(2) The scheme suggested by *Desnoyers and Perron* is based [144] on the assumption that the Et_4N^+ ion in water is neither structure breaker nor a structure maker. Thus, they suggested it is possible to apply with a high degree of accuracy in Einstein's equation, [195]

$$B = 0.0025\overline{V_o} \quad (33)$$

and have an accurate value of the partial molar volume of ion, V_o, it is likely to calculate the value of 0.359 for $B_{Et_4N^+}$ in water at 298.15 K. Recently, *Sacco et al.* proposed "reference electrolytic" technique for division of *B* -values.[196]

Consequently, for tetra phenyl phosphonium tetra phenyl borate in water, we have:

$$B_{BPh_4^-} = B_{PPh_4^+} + B_{BPh_4PPh_4}/2 \quad (34)$$

$B_{BPh_4PPh_4}$ (Scarcely soluble in water) has been obtained by the aforesaid method:

$$B_{\mathrm{BPh_4PPh_4}} = B_{\mathrm{NaBPh_4}} + B_{\mathrm{PPh_4Br}} - B_{\mathrm{NaBr}} \qquad (35)$$

The values are in good agreement with those obtained by other methods. The criterion adopted for separation of *B*-coefficients in nonaqueous solvents differs from those usually used in aqueous solution. On the other hand, the methods are based on the equality of equivalent conductances of counter ions at infinite dilutions.

(a) *Criss and Mastroianni* assumed $B_{K^+} = B_{Cl^-}$ in ethanol solution based on equal mobilities of ions. They also adopted $B^{25}_{\mathrm{Me_4N^+}} = 0.25$ as the initial value for acetonitrile solutions.

(b) For acetonitrile solutions, *Tuan and Fuoss* proposed the equality, as they thought that these ions have similar mobilities. However, *Springer et al.*, $\lambda^o_{25}(Bu_4N^+) = 61.4$ and $\lambda^o_{25}(Ph_4B^-) = 58.3$ in acetonitrile solutions. [197, 198]

$$B_{\mathrm{Bu_4N^+}} = B_{\mathrm{Ph_4B^-}} \qquad (36)$$

(c) *Gopal and Rastogi* resolved *B* -coefficient in N-methyl propionamide solutions assuming that $B_{\mathrm{Et_4N^+}} = B_{\mathrm{I^-}}$ at all temperatures.

(d) In Dimethyl sulphoxide, division of *B* -coefficients carried out by *Yao and Be union* assuming: [147]

$$B_{[(\mathrm{i-pe})_3\mathrm{BuN^+}]} = B_{\mathrm{Ph_4B^-}} = 1/2B_{[(\mathrm{i-pe})_3\mathrm{BuNPh_4B}]} \qquad (37)$$

at every temperatures.

Extensive use of this technique has been made by a variety of authors for dimethyl sulphoxide, sulpholane, hexamethyl phosphotriamide and ethylene carbonate solutions. [199] The aforesaid means, though, have been strongly criticized by *Krumgalz*. According to him, any method of resolution based on the equality of equivalent conductances for certain ions suffers from disadvantage that it is impossible to choose any two ions for which $\lambda_o^+ = \lambda_o^-$ in all solvents at all temperatures. Thus, though $\lambda_K^+ = \lambda_{Cl}^-$ at 298.15 K in methanol, but is not so in ethanol or in any further solvents. In addition, if the mobilities of some ions are even equal

at infinite dilution, but it is not necessarily true at moderate concentrations for which the *B*-coefficient values are designed. Further, according to him, equality of dimensions of $(i-pe)_3 BuN^+$ or $(i-Am)_3 BuN^+$ and Ph_4B^- does not necessarily involve the equality of *B* -coefficients of these ions and they are likely to be solvent and ion-structure dependent. *Krumgalz* has recently proposed a method for the resolution of *B*-coefficients. The method is based on the fact that large tetra alkyl ammonium cations are not solvated in organic solvents (in the normal sense involving significant electrostatic interaction). Thus, ionic *B* -values for large tetra alkyl ammonium ions, R_4N^+ (where R > Bu) inorganic solvents are proportional to their ionic dimensions. So, we have: [200-203]

$$B_{R_4NX} = a + br^3 R_4N^+ \qquad (38)$$

$a=B_{X^-}$ *B* and *b* is a constant dependent on temperature, solvent nature.

The extrapolation of the plot of B_{R_4NX}(R > Pr or Bu) against r^3 to R_4N to zero cation dimension gives directly B_{X^-} in the proper solvent and thus *B* -ion values can be calculated.

B -ion values can also be calculated from the equations:

$$B_{R_4N^+} - B_{R_4'N^+} = B_{R_4NX} - B_{R_4'NX} \qquad (39)$$

$$\frac{B_{R_4N^+}}{B_{R_4'N^+}} = \frac{r^3_{R_4N^+}}{r^3_{R_4'N^+}} \qquad (40)$$

The radii of tetra alkyl ammonium ions have been planned from the conductometric data. [204] *Gill and Sharma* used Bu_4NBPh_4 as reference electrolyte. The method of resolution is based on hypothesis, like *Krumgalz*, that Bu_4N^+ and Ph_4B^-ions with large R-groups are not solvated in non-aqueous solvents and their dimensions in such solvents are constant. The ionic radii of Bu_4N^+ (5.00Å) and Ph_4B (5.35 Å) were found to remain constant in different non-aqueous and mixed non-aqueous solvents by *Gill and co-workers*. They proposed the equations: [182]

$$\frac{B_{Ph_4B^-}}{B_{Bu_4N^+}} = \frac{r^3_{Ph_4B^-}}{r^3_{Bu_4N^+}} = \left(\frac{5.35}{5.00}\right)^3 \qquad (41)$$

$$B_{Bu_4NBPh_4} = B_{Bu_4N^+} + B_{Ph_4B^-} \qquad (42)$$

The scheme requires only the *B* - values of Bu_4NBPh_4 and is equally applicable to mixed non-aqueous solvents. The *B* - ion values obtained by this technique agree well with

those reported by Sacco *et al.* in different organic solvents using the assumption as given below:

$$B_{[(i-Am)_3Bu_4N^+]} = B_{Ph_4B^-} = 1/2B_{Bu_4NBPh_4} \quad (43)$$

Recently, *Lawrence and Sacco* used tetrabutylammonium tetrabutylborate (Bu_4NBBu_4) as reference electrolyte because the cation and anion in every case are symmetrical in shape and have almost equal Vander Waal's volume. Thus, we have:

$$\frac{B_{Bu_4N^+}}{B_{Bu_4B^-}} = \frac{V_{W(Bu_4N^+)}}{V_{W(Bu_4B^-)}} \quad (44)$$

$$B_{Bu_4N^+} = \frac{B_{Bu_4NBPh_4}}{[1 + V_{W(Bu_4B^-)}/V_{W(Bu_4N^+)}]} \quad (45)$$

A similar division can be made for Ph_4PBPh_4 system.

Recently, *Lawrence et al.* made viscometric dimensions of tetraalkyl (from propyl to heptyl) ammonium bromides in DMSO and HMPT. [182-185]

B-coefficients $B_{R_4NBr} = B_{Br^-} + a[f_x R_4N^+]$ were plotted as functions of Vander Waal's volumes. The B_{Br^-} values thus obtained were compared with accurately determined B_{Br^-} value by means of Bu_4NBBu_4 and Ph_4PBPh_4 as reference salts. They concluded that the 'reference salt' manner is the best available method for division into ionic contributions.

Jenkins and Pritchett [205] suggested a least square analytical technique to examine additivity relationship for combined ion thermodynamics data, to effect apportioning into single-ion components for alkali metal halide salts by employing *Fajan's competition principle* and 'volcano plots' of *Morris* . The principle was extended to derive absolute single ion *B*-coefficients for the alkali metals and halides in water. They also observed $B_{Cs^+} = B_{I^-}$ suggested by *Krumgalz* to be more reliable than $B_{K^+} = B_{Cl^-}$ in aqueous solutions. However, we require more data to test the validity of this technique. [202-207]

It is apparent that almost all these procedure are based on certain approximations and anomalous results may arise unless proper mathematical theory is developed to calculate *B* -values.

♣ *Temperature dependence of B – ion values*

Regularity in behaviour of $B_{\pm}$ and $dB_{\pm}/dT$ has been observed together in aqueous and non-aqueous solvents and valuable generalizations have been made by *Kaminsky*. He observed that (i) within a group of periodic table B -ion values decrease as the crystal ionic radii increase, (ii) within a group of periodic system, temperature co-efficient of B_{Ion} values enlarge as ionic radius. The results can be summarized as follow:

(a) A and $dA/dT > 0$ (46)

(b) $B_{Ion} < 0$ and $dB_{Ion}/dT > 0$ (47)

characteristic of the structure breaking ions.

(c) $B_{Ion} > 0$ and $dB_{Ion}/dT < 0$ (48)

characteristic of the structure making ions.

An ion when surrounded by a solvent sheath, properties of the solvent system in the solvational layer may be dissimilar from those present in the bulk arrangement. This is well reflected in *'Co-sphere'* model of *Gurney*, A, B, C *Zones of Frank and Wen* and hydrated radius of Nightingle. [194, 208, 209]

Stokes and Mills gave an analysis [200] of viscosity records incorporating the basic ideas presented before. The viscosity of a dilute electrolyte solution has been equated to viscosity of the solvent (η_o) plus the viscosity changes ensuing from the competition between various effects occurring in the ionic neighborhood. Thus, the *Jones-Dole equation:*

$$\eta = \eta_o + \eta^* + \eta^E + \eta^A + \eta^D = \eta_o + \eta(A\sqrt{c} + Bc) \qquad (49)$$

Where η^*, the positive increment in viscosity is caused by coulombic interaction. Thus,

$$\eta^E + \eta^A + \eta^D = \eta_o Bc \qquad (50)$$

B -coefficient can thus be interpreted in terms of competitive viscosity effects. Following *Stokes, Mills and Krumgalz* we can write:

$$B_{Ion} = B_{Ion}^{Einst} + B_{Ion}^{Orient} + B_{Ion}^{Str} + B_{Ion}^{Reinf} \quad (51)$$

whereas according to scientists *Lawrence and Sacco* :

$$B_{Ion} = B_W + B_{Solv} + B_{Shape} + B_{Ord} + B_{Discord} \quad (52)$$

$B_{Ion}^{Einst}$is the positive increment arising from the obstruction to the viscous flow of solvent caused by shape and size of ions (the term corresponds to η^E or B_{Shape}). $B_{Ion}^{Orient}$is the positive increment arising from the alignment or structure building action of the electric field of the ion on the dipoles of solvent molecules (the term corresponds toη^Aor B_{Ord}). B_{Ion}^{Str} is the negative increment related to destruction of the solvent structure in the region of ionic co-sphere arising from the opposing tendencies of ion to orientate the molecules round itself centrosymetrically and solvent to maintain its own structure (this corresponds to η^Dor B_{Disord}). B_{Ion}^{Reinf} is the positive increment accustomed by the effect of'reinforcement of the water structure' by large tetraalkylammonium ions owing to hydrophobic hydration. The phenomenon is inherent in intrinsic water structure and absent in organic solvents. B_W and B_{Solv} account for viscosity increase and endorsed to the Vander Waals volume and volume of the solvation of ions. Thus, small and highly charged cations like Li^+ and Mg^{2+} form a firmly attached primary solvation sheath in the region of these ions (B_{Ion}^{Orient} or η^E positive). At ordinary temperature, alignment of solvent molecules around the inner layer also causes increase in B_{Ion}^{Orient} (η^A), B_{Ion}^{Orient} (η^D)is minute for these ions. Thus, B_{Ion} will be large, positive as $B_{Ion}^{Einst} + B_{Ion}^{Orient} > B_{Ion}^{Str}$ However, B_{Ion}^{Einst} and B_{Ion}^{Orient} would be small for ions of greatest crystal radii (within a group) like Cs^+ or I^- because of small surface charge densities resulting in weak orienting and structure forming effect. B_{Ion}^{Str} would be large due to structural disorder in the immediate neighbourhood of ion due to competition between the ionic field and the bulk configuration. Accordingly, $B_{Ion}^{Einst} + B_{Ion}^{Orient} < B_{Ion}^{Str}$ and B_{Ion} is negative. Ions of

intermediate dimension (e.g., K^+ and Cl^-) have a close balance of viscous forces in their vicinity, *i.e.*, $B_{Ion}^{Einst} + B_{Ion}^{Orient} = B_{Ion}^{Str}$ so that *B* is almost close to zero.

Large molecular ions like tetraalkylammonium ions have large B_{Ion}^{Einst} on account of large size but B_{Ion}^{Orient} and B_{Ion}^{Str} would be small, *i.e.*, $B_{Ion}^{Einst} + B_{Ion}^{Orient} \gg B_{Ion}^{Str}$ would be positive and large values. The value would be further reinforced in water arising from B_{Ion}^{Reinf} as a result of hydrophobic hydrations.

The increase in temperature will have no consequence on B_{Ion}^{Einst}. But the orientation of solvent molecules in the secondary layer will be decreased owing to increase in thermal motion leading to decrease in B_{Ion}^{Str}. B_{Ion}^{Orient} will decrease slowly with temperature as there will be less competition between the ionic field and reduced solvent arrangement. The positive or negative temperature co-efficient will thus depend on the transformation of the relative magnitudes of B_{Ion}^{Orient} and B_{Ion}^{Str}.

In case of structure-making ions, the ions are firmly surrounded by a primary solvation sheath and secondary solvation zone will be considerably be ordered leading to an increase in B_{Ion} and concomitant decrease in entropy of solvation along with mobility of ions. Structure breaking ions, are not solvated to a great extent and the secondary solvation zone will be tangled leading to a decrease in B_{Ion} values and increase in entropy of solvation and mobility of ions. Moreover, the temperature induced change in viscosity of ions (or entropy of solvation or mobility of ions) would be more marked in case of smaller ions than in case of the larger ions. So, there is a connection between viscosity, entropy of solvation and temperature dependent mobility of ions. Thus, ionic *B*-coefficient and entropy of solvation of ions have rightly been used as probes of ion-solvent interactions and as a direct signal of structure making and structure breaking character of ions. The linear plot of ionic *B*-coefficients adjacent to the ratios of mobility, viscosity products at two temperatures (a more sensitive variable than ionic mobility) by $Gurney$ clearly express a close relation between ionic *B*-coefficients and ionic mobilities. $Gurney$ demonstrated a clear correlation between molar entropy of solution values with *B* -coefficient of salts. The ionic *B*-values demonstrate a linear relationship with partial molar ionic entropies or partial molar entropies of hydration $(\overline{S}_h^o)$ as:[206, 207]

$$\bar{S}_h^o = \bar{S}_{aq}^o - \bar{S}_g^o \qquad (53)$$

Where, $\bar{S}_{aq}^o = \bar{S}_{ref}^o + \Delta S^o, \bar{S}_g^o$, is calculated summation of translational and rotational entropies of the gaseous ions. *Gurney* obtained a single linear plot between ionic entropies and ionic *B*-coefficients for all monoatomic ions by equating entropy of the hydrogen ion (S_{H+}^o) to –5.5 cal.mol^{-1}deg^{-1}. *Asmus* used the entropy of hydration to correlate ionic *B* values and *Nightingale* showed that a single linear relationship could be obtained with it for equally monoatomic and polyatomic ions. [208-210] The correlation was utilized by *Abraham et al.* to assign single ion *B*-coefficients so that a design of ΔS_e^o the electrostatic entropy of solvation or $\Delta S_{I,II}{}^o$ the entropic contributions of first and second solvation layers of ions against *B* points (taken from the works of *Nightingale*) for both cations and anions lie on the identical curve. There are exceptional linear correlations between $\Delta S_e{}^o$ and $\Delta S_I{}^o$ and single ion *B* -coefficients.[211-213] Together entropy criteria ($\Delta S_e{}^o$ and $\Delta S_{I,II}{}^o$) and *B* -ion values designate that in water the ions Li^+, Na^+, Ag^+ and F^- are not structure makers, and ions Rb^+, Cs^+, Cl^-, Br^-, I^- and ClO_4^- are structure breakers, K^+ is a border line case.

♣ *Thermodynamics of Viscous Flow*

Assuming viscous flow as a rate process, the viscosity (η) is represented from *Eyring's* approaches as: [214]

$$\eta = Ae^{\frac{E_{vis}}{RT}} = \left(\frac{hN_A}{V}\right)e^{\frac{\Delta G^*}{RT}} = \left(\frac{hN_A}{V}\right)e^{\left(\frac{\Delta H^*}{RT} - \frac{\Delta s}{R}\right)} \qquad (54)$$

Where E_{vis} = experimental entropy of activation determined from a plot of ln η against 1/T. ΔG^*, ΔH^* and ΔS^* are free energy, enthalpy and entropy of activation, correspondingly.

Nightingale and Benck dealt in the problem in a dissimilar way and calculated the thermodynamics of viscous flow of salts in aqueous solution with the help of *Jones-Dole equation* (neglecting the *A c* term). [215]

Thus, we have:

$$R\left[\frac{dln\eta}{d(1/T)}\right] = r\left[\frac{dln\eta_o}{d(1/T)}\right] + \frac{R}{(1+Bc)}.\frac{d(1+Bc)}{d(1/T)} \quad (55)$$

$$\Delta E^{\neq}_{\eta(Soln)} = \Delta E^{\neq}_{\eta_o(Solv)} + \Delta E^{\neq}_{V} \quad (56)$$

$\Delta E^{\neq}_{V}$ can be interpreted as the increase or decrease of the activation energies for viscous flow of the pure solvents caused by presence of ions, i.e., effective influence of the ions upon the viscous flow of the solvent molecules. *Feakins et al.* have suggested an alternative formulation rooted in the transition state treatment of relative viscosity of electrolytic solution. They together suggested the following expression: [216]

$$B = \frac{\left(\phi^0_{V,2} - \phi^0_{V,1}\right)}{1000} + \phi^0_{v,2}\frac{\left(\Delta\mu_2^{0\neq} - \Delta\mu_1^{0\neq}\right)}{1000RT} \quad (57)$$

Where $\phi^0_{v,1}$ and $\phi^0_{v,2}$ are partial molar volumes of solvent and solute correspondingly and $\Delta\mu_2^{o\neq}$ is the contribution per mole of solute to free energy of activation for viscous flow of solution. $\Delta\mu_1^{o\neq}$ is free energy of activation for viscous flow per mole of the solvent which is given by:

$$\Delta\mu_1^{0\neq} = \Delta G_1^{0\neq} = RT\ln(\eta_0\phi^0_{v,1}/hN_A) \quad (58)$$

Further, if *B* is known at assorted temperatures, we can calculate entropy and enthalpy of activation of viscous flow respectively from the following equations as given below:

$$\frac{d(\Delta\mu_2^{o\neq})}{dT} = -\Delta S_2^{o\neq} \quad (59)$$

$$\Delta H_2^{o\neq} = \Delta\mu_2^{o\neq} + T\Delta S_2^{o\neq} \quad (60)$$

♣ *Effects of Shape and Size*

Stokes and Mills have dealt with the aspect of shape and size widely. Ions in solution can be regarded to be rigid spheres suspended in continuum. The hydrodynamic treatment accessible by *Einstein* leads to the equation: [195]

$$\frac{\eta}{\eta_0} = 1 + 2.5\phi \qquad (61)$$

where ϕ is volume fraction occupied by the particles. Modifications of the equation have been proposed by (i) *Sinha* on the basis of departures from spherical shape and (ii) *Vand* on the basis of dependence of flow patterns around neighboring particles at higher concentrations. However, in view of different aspects of the problem, spherical shapes have been assumed for electrolytes having hydrated ions of large effective size (particularly polyvalent monatomic cations). Thus, from equation (61): [217]

$$2.5\phi = A\sqrt{c} + Bc \qquad (62)$$

Since $A\sqrt{c}$ term can be neglected in comparison with *Bc* and ϕ = c$\phi_{v,1}^0$

where $\phi_{v,1}^0$ is partial molar volume of the ion, we obtain:

$$2.5\phi_{v,1}^0 = B \qquad (63)$$

In ideal case, the *B* -coefficient is a linear function of partial molar volume of solute, $\phi_{v,1}^0$ with slope 2.5. Therefore, $B_{\pm}$ can be equated to:

$$B_{\pm} = 2.5\phi_{\pm}^0 = \frac{2.5\times 4}{3}\frac{\left(\pi R_{\pm}^3 N\right)}{1000} \qquad (64)$$

Assuming the ions behave like rigid spheres with an effective radius, $R_{\pm}$ moving in a continuum. $R_{\pm}$, calculated by means of equation (64) should be close to crystallographic radii or corrected *Stoke's* radii if the ions are scarcely solvated and act as spherical entities. But, in general, $R_{\pm}$ values of the ions are elevated than the crystallographic radii representing appreciable solvation.

The number n_b of solvent molecules bound to the ion in primary solvation case can be simply calculated by comparing the *Jones-Dole equation* with the *Einstein's equation*:

$$B_{\pm} = \frac{2.5}{1000\left(\phi_i + n_b\phi_s\right)} \qquad (65)$$

Where ϕ_i is molar volume of the base ion and ϕ_s, is molar volume of the solvent. Equation (65) has been used by a number of workers to revise the nature of solvation and solvation number.

♣ *Viscosity of Non-Electrolytic Solutions*

The equations of *Vand, Thomas* and *Moulik* proposed mainly to account for the viscosity of concentrated solutions of bigger spherical particles have been also found to correlate the mixture viscosities of usual non electrolytes. These equations are: [218-222]

Vand equation: $$\ln \eta_r = \frac{\alpha}{1-Q} = \frac{2.5V_h c}{1-QV_h c} \quad (66)$$

Thomas equation: $$\eta_r = 1 + 2.5V_h + 10.05cV_h^2 c \quad (67)$$

Moulik equation: $$\eta^2 = I + Mc^2 \quad (68)$$

where η_r is relative viscosity, a is constant depending on axial ratios of particles, Q is interaction constant, V_h is molar volume of the solute including rigidly held solvent molecules due to hydration, c is molar concentration of the solutes; I and M are constants. The viscosity equation proposed by *Eyring and coworkers* for pure liquids on the basis of pure significant liquid structures theory, can be even extended to calculate the viscosity of mixed liquids. The final expression for liquid mixtures takes the following form:

$$\eta_m = \frac{6N_A h}{\sqrt{2} r_m (V_m - V_{Sm})}\left[\sum_i^n \left\{1 - \exp\left(\frac{-\theta_i}{T}\right)\right\}^{-x_i}\right] \exp\left[\frac{a_m E_{Sm} V_{Sm}}{RT(V_m - V_{Sm})}\right] + \frac{V_m - V_{Sm}}{V_m}\left[\sum_i^n \frac{2}{3d_i^2}\left(\frac{m_i kT}{\pi^3}\right)^{\frac{1}{2}} x_i\right] \quad (69)$$

Where n values is 2 for binary and 3 for ternary liquid mixtures. The mixture parameters, r_m, E_{Sm}, V_m, V_{Sm} and a_m were calculated from corresponding pure component parameters by using the following relations : [223-229]

$$r_m = \sum_i^n x_i^2 r_i + \sum_{i \neq j} 2x_i x_j r_{ij} \quad (70)$$

$$E_{Sm} = \sum_i^n x_i^2 E_{Si} + \sum_{i \neq j} 2x_i x_j E_{Sij} \quad (71)$$

$$V_m = \sum_i^n x_i V_i V_{Sm} = \sum_i^n x_i V_{Si} a_m = \sum_i^n x_i a_i \quad (72)$$

$$r_{ij} = (r_i r_j)^{\frac{1}{2}} \text{and} \quad E_{Sij} = (E_{Si} E_{Sj})^{\frac{1}{2}} \quad (73)$$

$$\theta = \frac{h}{\kappa 2\pi} \left(\frac{b}{m}\right)^{\frac{1}{2}} \quad (74)$$

$$b = 2Z\varepsilon \left[22.106 \left(\frac{N_A \sigma^2}{V_S}\right)^4 - 10.559 \left(\frac{N_A \sigma^3}{V_S}\right)^2\right] \frac{1}{\sqrt{2}\sigma^2} \left(\frac{N_A \sigma^3}{V_S}\right)^{\frac{2}{3}} \quad (75)$$

Here σ and ε are *Lennard-Jones* potential parameters and other symbols have their usual significance.

For interpolation and limited extrapolation purposes, the viscosities of ternary mixture can be correlated to a high degree of accuracy in conditions of binary contribution by the following equations.

$$\eta_m = \sum_i^3 x_i \eta_i + x_1 x_2 [A_{12} + B_{12}(x_1 - x_2) + C_{12}(x_1 - x_2)^2] + x_2 x_3 [A_{23} + B_{23}(x_2 - x_3) + C_{23}(x_2 - x_3)^2] + x_3 x_1 [A_{31} + B_{31}(x_1 - x_2) + C_{31}(x_1 - x_2)^2] \quad (76a)$$

The correlation of ternary solution is modified to the following form:

$$\eta_m = \sum_i^3 x_i\eta_i + x_1x_2[A_{12} + B_{12}(x_1 - x_2) + C_{12}(x_1 - x_2)^2] + x_2x_3\,[A_{23} + B_{23}(x_2 - x_3) + C_{23}(x_2 - x_3)^2] + x_3x_1[A_{31} + B_{31}(x_1 - x_2) + C_{31}(x_1 - x_2)^2] + A^*_{123}x_1x_2x_3 \quad (76b)$$

However, an improved result may be obtained using the following relation:

$$\eta_m = \sum_i^3 x_i\eta_i + x_1x_2[A_{12} + B_{12}(x_1 - x_2) + C_{12}(x_1 - x_2)^2] + x_2x_3\,[A_{23} + B_{23}(x_2 - x_3) + C_{23}(x_2 - x_3)^2] + x_3x_1[A_{31} + B_{31}(x_1 - x_2) + C_{31}(x_1 - x_2)^2] + x_1x_2x_3[A_{123} + B_{123}x_1^2(x_2 - x_3)^2 + C_{123}x_1^3(x_2 - x_3)^3] \quad (76c)$$

Where A_{12}, B_{12}, C_{12}, A_{23}, B_{23}, C_{23}, A_{31}, B_{31} and C_{31}, are constants for binary mixtures; A_{123}, B_{123} and C_{123} are constants for ternaries; and other symbols have their standard significance.

♣ *Viscosity Deviation*

Viscosity of liquid mixtures provide information for elucidation of the fundamental behavior of liquid mixtures, aid in correlation of mixture viscosities with those of pure components, and may afford a basis for the selection of physicochemical methods of analysis. Quantitatively, as per the absolute reaction rates theory, the deviations in viscosities $\Delta\eta$, from ideal mixture can be designed as: [230]

$$\Delta\eta = \eta - \sum_{i=1}^{j}(x_i\eta_i) \quad (77)$$

Where η is dynamic viscosities of the mixture, $x_i\eta_i$ are the mole fractions, viscosity of ith component in the mixture respectively.

♣ Gibbs Excess Energy of Activation For Viscous Flow

Quantitatively, the Gibbs excess energy of activation for viscous flow ΔG^E can be calculated as:

$$\Delta G^E = RT\left[\ln \eta V - \sum_{i=1}^{j}(x_i \ln \eta_i V_i)\right] \qquad (78)$$

Where η and V are viscosity and molar volume of the mixture; η_i and V_i are viscosity and molar volume of i^{th} pure component, correspondingly. [231]

♣ *Viscous Synergy & Antagonism*

Rheology is the branch of science that deals with material deformation and flow, and is increasingly useful to analyze the viscous behavior of scores of pharmaceutical products, and to establish their stability and even bioavailability, because it has been firmly established that viscosity influences drug absorption rate in the body. The study of the viscous behavior of pharmaceutical, foodstuffs, cosmetics or industrial products, etc., is crucial for conforming their viscosity is suitable for contemplated use of products. [232-244]

Viscous synergy is the term used to indicate interaction between the components of a system that causes total viscosity of the system to be larger than the summation of viscosities of each component considered separately. In contraposition to viscous synergy, viscous antagonism is defined as the interaction between components of a system causing the net viscosity of the later to be reduced than the sum of the viscosities of each component considered separately. [246] If total viscosity of the system is equal to sum of the viscosities of every component considered separately, the system is said to lack interaction. [245]

Water is the most used solvent in chemical and pharmaceutical industries, since it is the most physiological and best tolerated excipient. However, in several cases water cannot be used as a solvent when the active substance or solute is insoluble or slightly soluble in water. Non-water solvents with the common characteristic of being soluble in water may be preferred in such circumstances. Such solvents can be used to increase water solubility or modifying the viscosity or absorption of dissolved solute molecules. In this respect, the nature of

intermolecular forces between solvents brings a marked effect on thermodynamic properties such as density, viscosity, refractive index and surface tension etc.

Regarding rheological behavior of solvent systems viscous synergy and antagonism is of prime importance.

The way most widely used to analyze synergic and antagonic behavior of the ternary liquid mixtures used here is that developed by *Kaletunc- Gencer and Peleg* allowing quantification of synergic and antagonic interactions taking place in the mixtures involving variable proportions of constituent components. These method compares viscosity of the system, determined experimentally, $\eta_{\exp}$, with the viscosity expected in absence of interaction, η_{cal}, as defined by simple mixing rule as follows: [247, 248]

$$\eta_{cal} = \sum_{i=1}^{j} w_i \eta_i \qquad (79)$$

Where w_i and η_i are the fraction by weight and viscosity of the i^{th} component, measured experimentally, i is an integer.

Accordingly, when $\eta_{exp} > \eta_{cal}$, viscous synergy dominates,

When $\eta_{\exp} < \eta_{cal}$, system is said to exhibit viscous antagonism.

The procedure is used when *Newtonian fluids* are involved, since non-synergy indices are defined in consequence.

In order to secure more comparable viscous synergic results, the synergic interaction index (I_S) introduced by *Howell* is taken into account: [248, 249]

$$I_S = \frac{\eta_{\exp} - \eta_{mix}}{\eta_{mix}} = \frac{\Delta\eta}{\eta_{mix}} \qquad (80)$$

When values of (I_S) are negative, it is concerned as ant agonic interaction index (I_A).

The technique used to analyze volume contraction and expansion is similar to that applied to viscosity, i.e., density of the mixture is determined experimentally, $\rho_{\exp}$, and a result is made for ρ_{cal} based on the expression:

$$\rho_{cal} = \sum_{i=1}^{j} w_i \rho_i \quad (81)$$

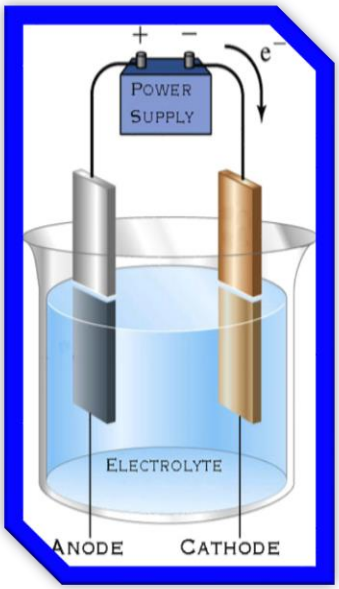
Here ρ_i is experimentally measured density of ith component. Other symbols have their standard significance. *R. Belda et al* revealed ethanol-water system is characterized by viscous synergy which in turn was correlated to volume contraction.

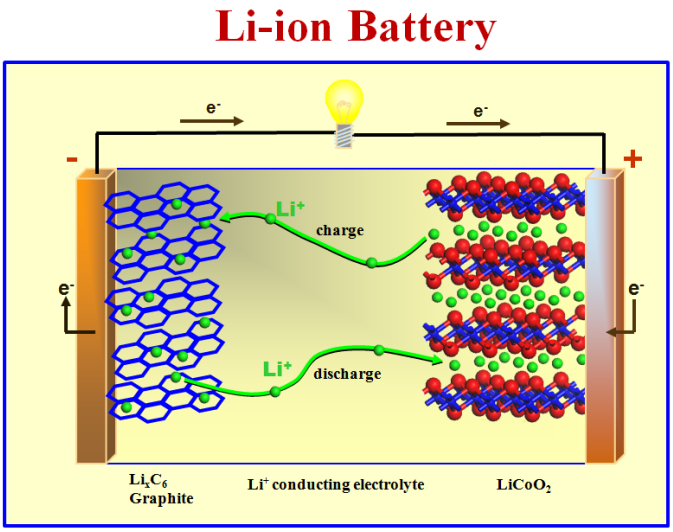
Accordingly, when $\rho_{\exp} > \rho_{cal}$, volume contraction occurs, however when $\rho_{\exp} < \rho_{cal}$, there is volume expansion in the system arises.

J. V. Herraez et al also calculated viscous synergy of pure monoalcohol mixtures in water in relation to their concentrations.

♣ *Conductometric Measurements*

One of the most specific and direct technique available to establish the extent of the dissociation constants of electrolytes in aqueous, mixed and non-aqueous solvents is the "conductometric process." Conductance data in conjunction with viscosity measurements, gives much information concerning ion-ion and ion-solvent interaction.





Dissolved Ions Conduct Electricity

The measurements can be made in a variety of solvents over wide ranges of temperature and pressure in dilute solutions where interionic theories are not applicable. Conductance measurements together with transference number determinations give an unequivocal method of obtaining single-ion values. The chief limitations, however, is colligative-like nature of information obtained. The studies of conductance measurements were pursued vigorously during the last five decades, together theoretically and experimentally and a number of important theoretical equations have been derived. We shall dwell briefly on a few of these aspects in relation to the studies in aqueous, non-aqueous, pure and mixed solvents. The successful application of *Debye-Hückel theory* of interionic attraction was made by *Onsager* to derive *Kohlrausch's equation* representing the molar conductance of an electrolyte. For solutions of a single symmetrical electrolyte equation is known by: [250]

$$\Lambda = \Lambda_o - S\sqrt{c} \qquad (82)$$

where,

$$S = \alpha\Lambda_o + \beta \qquad (83)$$

$$\alpha = \frac{(z^2)k}{3(2+\sqrt{2})\varepsilon_r kT\sqrt{c}} = \frac{82.406\times10^4 z^3}{(\varepsilon_r T)^{\frac{3}{2}}} \qquad (84)$$

$$\beta = \frac{z^2 eFk}{3\pi\eta\sqrt{c}} = \frac{82.487 z^3}{\eta\sqrt{\varepsilon_r T}} \qquad (85)$$

The equation took no account for short-range interactions and also of shape or size of the ions in solution. Ions were regarded as rigid charged spheres in an electrostatic and hydrodynamic continuum, i.e., the solvent. In subsequent years, *Pitts (1953)* and *Fuoss and Onsager (1957)* independently worked out the solution of the problem of electrolytic conductance accounting for mutually long-range and short-range interactions.

However, Λ_o values obtained for the conductance at infinite dilution using *Fuoss-Onsager theory* differed considerably from that obtained by means of *Pitt's theory* and the derivation of the *Fuoss-Onsager equation* was questioned. The original *Fuoss-Onsager equation* was further modified by *Fuoss and Hsia* who recalculated the relaxation field, retaining the terms which had formerly been neglected.

The results of conductance theories can be expressed in a general form:

$$\Lambda = \frac{\Lambda_o - \alpha\Lambda_o\sqrt{c}}{(1+\kappa\alpha)}\left(\frac{1+\kappa\alpha}{\sqrt{2}}\right) - \frac{\beta\sqrt{c}}{(1+\kappa\alpha)} + G(\kappa\alpha) \qquad (86)$$

Where $G(\kappa\alpha)$ is a complicated function of variable. The simplified form:

$$\Lambda = \Lambda_o - S\sqrt{c} + Ec\ lnc + J_1 c - J_2 \sqrt[3]{c} \qquad (87)$$

However, it has been found that these equations have certain limitations, in some cases it fails to fit experimental data. Several of these results have been discussed elaborately by *Fernandez-Prini*. Further correction of equation (87) was made by *Fuoss and Accascin*. They took into consideration change in viscosity of the solutions and assumed the validity of *Walden's rule*. The new equation thus becomes:

$$\Lambda = \Lambda_o - S\sqrt{c} + Ec\ln c + J_1 c + J_2 \sqrt[3]{c} - F\Lambda c \qquad (88)$$

where,

$$Fc = \frac{4\pi R^3 N_A}{3} \qquad (89)$$

In most cases, however, J_2 is made zero but this leads to a systematic deviation of experimental data from theoretical equations. It has been observed that Pitt's equation gives better fit to experimental data in aqueous solutions. [305-312]

♣ *Limiting Equivalent Conductance*

The limiting equivalent conductance of an electrolyte can be simply determined from the theoretical equations and experimental observations. At infinite dilutions, the movement of an ion is limited solely by the interactions with the surroundings solvent molecules as the ions are infinitely apart. Under these conditions, the validity of *Kohlrausch's law* of independent migration of ions is almost self-evident. Thus:

$$\Lambda_0 = \lambda_o^+ + \lambda_o^- \qquad (90a)$$

At the present time, limiting equivalent conductance is the only function which can be divided into ionic components by means of experimentally determined transport number of ions, i.e.,

$$\lambda_o^+ = t_+ \Lambda_0 \quad \text{and} \quad \lambda_o^- = t_- \Lambda_0 \qquad (90b)$$

Thus, from accurate value of λ_0 of ions it is possible to divide the contributions due to cations and anions in solute-solvent interactions. However, accurate transference number determinations are restricted hardly to any solvents.

In the absence of experimentally measured transference numbers it would be valuable to develop indirect methods to obtain the ionic limiting equivalent conductances in solvents for which experimental transference numbers are not yet available. Various attempts were made to develop indirect methods to acquire the limiting ionic equivalent conductance, in ionic solvents for which experimental transference numbers are not yet accessible. The scheme has been summarized by *Krumgalz* and some important points are mentioned as follows: [313-321]

(i) Walden equation

$$(\lambda_{\mathrm{o}}^{\pm})^{25}_{\mathrm{water}} \cdot \eta_{\mathrm{o,water}} = (\lambda_{\mathrm{o}}^{\pm})^{25}_{\mathrm{acetone}} \cdot \eta_{\mathrm{o,acetone}} \qquad (91)$$

(ii) $$(\lambda_{\mathrm{o,pic}} \cdot \eta_{\mathrm{o}}) = 0.267, \quad \lambda_{\mathrm{o,Et_4N^+}} \cdot \eta_{\mathrm{o}} = 0.269 \qquad (92)$$

based on $\Lambda_{o,Et_4N_{pic}} = 0.563$

Walden measured products to be independent of temperature and solvent. However, the $\Lambda_{o,Et_4N_{pic}}$ values used by *Walden* were found to differ considerably from the data of subsequent more specific studies and the values of (ii) are considerably different for different solvents.

(iii) $$\lambda_o^{25}(Bu_4N^+) = \lambda_o^{25}(Ph_4B^-) \quad (93)$$

The equality holds well in nitrobenzene and in mixture of CCl_4 but not realized in methanol, acetonitrile and nitromethane.

(iv) $$\lambda_o^{25}(Bu_4N^+) = \lambda_o^{25}(Bu_4B^-) \quad (94)$$

The technique appears to be sound as negative charge on boron in Bu_4B^- ion is completely shielded by four inert butyl groups as in the Bu_4N^+ ion while this phenomenon wasn't observed in case of Ph_4B^-.

(v) The equation suggested by *Gill* is:

$$\lambda_o^{25}(R_4N^+) = \frac{zF^2}{6\pi N_A \eta_o [r_i - (0.0103\varepsilon_o + r_y)]} \quad (95)$$

Where *Z* and r_i are charge and crystallographic radius of proper ion, respectively: η_o and ε_o are solvent viscosity, dielectric constant of the medium, respectively; r_y = adjustable parameter taken equal to 0.85 Å and 1.13 Å for dipolar non-associated solvents and for hydrogen bonded and other associated solvents correspondingly.

However, large discrepancies were observed between experimental and calculated values. In a paper, *Krumgalz* examined the *Gill's* approach more critically by means of conductance data in many solvents and found the method to be reliable in three solvents e.g. butan-1-ol, acetonitrile and nitromethane.

(vi) $$\lambda_o^{25}\left[(i-Am)_3 BuN^+\right] = \lambda_o^{25}\left(Ph_4B^-\right) \quad (96)$$

It has been found from transference number measurements that $\lambda_o^{25}\left[(i-Am)_3 BuN^+\right]$ and $\lambda_o^{25}\left(Ph_4B^-\right)$ values differ from one another by 1%.

(vii) $$\lambda_o^{25}\left(Ph_4B^-\right)=1.01\lambda_o^{25}\left[\left(i-Am\right)_4 B^-\right] \qquad (97)$$

The value is found to be true for a variety of organic solvents.

Krumgalz suggested a scheme for determining the limiting ion conductance in organic solvents. The method is based on the fact that large tetra alkyl (aryl) onium ions are not solvated in organic solvents because of the extremely weak electrostatic interactions between solvent molecules and large ions with low surface charge density and this phenomenon can be utilized as an appropriate model for apportioning Λ_o values into ionic components for non-aqueous electrolytic solutions.

Considering the activity of solvated ion in an electrostatic field as a whole, it is possible to calculate radius of the moving particle by the *Stokes equation*:

$$r_S=\frac{|z|F^2}{A\pi\eta_o\lambda_o^{\pm}} \qquad (98)$$

Where *A* is a coefficient varying from 6 (in case of perfect sticking) to 4 (in case of perfect slipping). Since in r_S values, the real dimension of non-solvated tetraalkyl (aryl) onium ions must be constant, we have:

$$\lambda_o^{\pm}\eta_0=\text{constant} \qquad (99)$$

This relation has been verified by means of $\lambda_o^{\pm}$ values determined with precise transference numbers. The product becomes constant and independent of chemical nature of the organic solvents for the i-Am_4B^-, Ph_4As^+, Ph_4B^- ions and for tetra alkyl ammonium cation starting with Et_4N^+. The relationship can be well utilized to verify $\lambda_o^{\pm}$ of ions in other organic solvents from the determined Λ_o values.

♣ Solvation

Assorted types of interactions exist between the ions in solutions. These interactions result in the orientation of solvent molecules towards the ion. The number of solvent molecules that are involved in solvation of the ion is called solvation number. If the solvent is water, this is known as hydration number. Solvation region can be classified as both primary and secondary solvation regions. Here we are concerned with primary solvation region. The primary solvation number is defined as the number of solvent molecules which surrender their own translational freedom and remain with

the ion, in a tightly bound manner, as it moves around, or number of solvent molecules which are aligned in the force field of the ion.

If the limiting conductance of the ion *i* of charge Z_i is known, effective radius of the solvated ion can be determined from *Stokes' law*. The volume of the solvation shell is thus given by the equation.

$$V_S = \left(\frac{4\pi}{3}\right)\left(r_S^3 - r_C^3\right) \quad (100)$$

Where r_c is crystallographic radius of ion. The solvation number n_s would then be obtained from

$$n_S = \frac{V_S}{V_0} \quad (110)$$

Assuming *Stokes'* relation to hold well, ionic solvated volume can be obtained, because of the packing effects, from

$$V_S^o = 4.35 r_S^3 \quad (111)$$

Where V_S^o is articulated in mol/lit. and r_S in angstroms. However, this technique is not applicable to ions of medium size though a number of empirical and theoretical corrections have been suggested in order to relate it to most of the ions.

♣ *Stokes' Law & Walden's Rule*

The starting point for most evaluations of ionic conductances is *Stokes' law* that states that limiting Walden product (the limiting ionic conductance-solvent viscosity product) for any singly charged, spherical ion is as function only of ionic radius and thus, under normal conditions, is constant. The limiting conductances λ_i^o of spherical ion of radius R_i moving in a solvent of dielectric continuum can be written, according to *Stokes' hydrodynamics*, as

$$\lambda_o^i = \frac{|z_i e| eF}{6\pi\eta_o R_i} = \frac{0.819|z_i|}{\eta_o R_i} \quad (112)$$

Where η_o = macroscopic viscosity by solvent in poise, R_i in angstroms. If radius R_i is assumed to be same in every organic solvent, as would be the case, in case of bulky organic ions, we get:

$$\lambda_o^i \eta_o = \frac{0.819 z_i}{R_i} = constant \qquad (113)$$

This is known as the *Walden rule*. The effective radii obtained using this equation can be used to estimate the solvation numbers. However, *Stokes' radii* failed to give the effective size of the solvated ions for small ions.

Robinson and Stokes, *Nightingale* and others have suggested a technique of correcting the radii. The tetra alkyl ammonium ions were unspecified to be not solvated and by plotting the *Stokes' radii* against the crystal radii of those large ions, a calibration curve was obtained for each solvent. However, the experimental results indicate that the process is incorrect as the method is based on wrong assumption of the invariance of Walden's product with temperature. The idea of microscopic viscosity was invoked without much success but it has been originated as:

$$\lambda_o^i \eta_0 = \text{constant} \qquad (114)$$

Where *p* is generally 0.7 for alkali metal or halide ions and *p* = 1 for large ions. *Gill* has pointed out the inapplicability of the *Zwanzig theory* of dielectric friction for some ions in non-aqueous and mixed solvents and has proposed an empirical modification of *Stokes' Law* accounting for dielectric friction effect quantitatively and predicts authentic solvated radii of ions in solution. This equation can be written as:

$$r_i = \frac{|z| F^2}{6\pi N_A \eta_o \lambda_o^i} + 0.0103D + r_y \qquad (115)$$

Where r_i is actual solvated radius of the ion in solution and r_y is an empirical constant dependent on nature of solvent.

The dependence of *Walden product* on dielectric constant led *Fuoss* to consider the effect of the electrostatic forces on the hydrodynamics of the system. Considering the excess frictional resistance caused by dielectric relaxation in the solvent caused by ionic motion, *Fuoss* proposed the relation:

$$\lambda_o^i = \frac{Fe|z_i|}{6\pi R_\infty}\left(\frac{1+A}{\varepsilon R_\infty^2}\right) \qquad (116)$$

or, $$R_i = R_\infty + \frac{R}{\infty} \qquad (117)$$

where R_∞ is hydrodynamic radius of the ion in a hypothetical medium of dielectric constant where all electrostatic forces disappear and *A* is an empirical constant.

Boyd gave an expression:

$$\lambda_o^i = \frac{Fe|z_i|}{6\pi\eta_o r_i\left[\left(1+\frac{2}{27}\pi\eta_o\right)\cdot\left(\frac{z_i^2e^2\tau}{r_i^4\varepsilon_o}\right)\right]} \qquad (118)$$

by considering the effect of dielectric relaxation in ionic motion; τ is *Debye* relaxation time for solvent dipoles. *Zwanzig* treated ion as a rigid sphere of radius r_i moving with a steady state viscosity, V_i through a viscous incompressible dielectric continuum. The conductance equation suggested by *Zwanzig* is:

$$\lambda_o^i = \frac{z_i^2eF}{\left[A_V\pi\eta_o r_i + A_D\left\{\frac{z_i^2e^2(\varepsilon_r^o-\varepsilon_r^\infty)\tau}{\varepsilon_r^o(2\varepsilon_r^o+1)r_i^3}\right\}\right]} \qquad (119)$$

Where ε_r^o and ε_r^∞ are static and limiting high frequency (optical) dielectric constants. $A_V = 6$ and $A_D = 3/8$ for perfect sticking, $A_V = 4$ and $A_V = 3/4$ foe perfect slipping. It has been found that *Born's and Zwanzig's* equations are very analogous and both may be written in the form:

$$\lambda_o^i = \frac{Ar_i^3}{r_i^4 + B} \qquad (120)$$

The theory predicts λ_o^i passes in the course of a maximum of $27^{\frac{1}{4}}A/4B^{\frac{1}{4}}$ at $r_i = (3B)^{1/4}$. The phenomenon of maximum conductance is illustrious. The relationship holds good to a reasonable scope for cations in aprotic solvents but fails in case of anions. The conductance, however, falls off rather more swiftly than predicted with

increasing radius. For comparison with results in different solvents, the equation (119) can be rearranged as:

$$\frac{z_i^2 eF}{\lambda_o^i \eta_o} = \frac{A_V \pi r_i + A_D z_i^2}{r_i^3} \cdot \frac{e^2(\varepsilon_r^o - \varepsilon_r^\infty)}{\varepsilon_r^o(2\varepsilon_r^o + 1)} \left(\frac{\tau}{\eta_o} \right) \qquad (121)$$

$$L^* = A_V \pi r_i + \frac{A_D z_i^2}{r_i^3 P^*} \qquad (122)$$

In order to test Zwanzig's theory, the equation (122) was useful for $Me_4N^+$and Et_4N^+ in pure aprotic solvents like methanol, ethanol, acetonitrile, butanol and pentanol . Plots of L^* against solvent function P^* were set up to be straight line. But, the radii calculated from intercepts and slopes are far apart from equal except in some cases where moderate success is noted. It is noted that relaxation effect is not predominant factor affecting ionic mobility and these mobility differences could be explained quantitatively if microscopic properties of the solvent, dipole moment and free electron pairs were considered predominant factors in the deviation from the *Stokes' law*.

It is found that *Zwanzig's theory* is successful for large organic cations in aprotic media where solvation is likely to be minimum and where viscous friction predominates over that caused by dielectric relaxation. The theory breaks down whenever dielectric relaxation term becomes large, i.e., for solvents of high *P** and for ions of small r_i. Like any continuum theory *Zwanzig* has inherent weakness of its inability to account for structural features, e.g.,

(i) It does not allow for any correlation in the orientation of solvent molecules as the ion passes by and this may be the reason why the equation is not valid to the hydrogen-bonded solvents.

(ii) The theory does not distinguish between positively and negatively charged ions and therefore, cannot give details why certain anions in dipolar aprotic media possess considerably higher molar concentrations than fastest cations.

The Walden product in case of mixed solvents does not confirm any constancy but it shows a maximum in case of DMF + water and DMA +water mixtures and other aqueous binary mixtures. To derive expressions for the variation of Walden product

with composition of mixed polar solvents, various attempts have been made with different models for ion-solvent interactions but no satisfactory expression has been derived taking into account every types of ion-solvent interactions because

(i) It is difficult to include all kinds of interactions between ions as well as solvents in a single mathematical expression, and

(ii) It is not possible to account for a few specific properties of different kinds of ions and solvent molecules.

Ions moving in a dielectric medium experience a frictional force because of dielectric loss arising from ion-solvent interactions with the hydrodynamic force. Though *Zwanzig's* expression accounts for a change in Walden product with solvent composition but doesn't account for maxima. According to *Hemmes* major deviations in the Walden products are due to variation in electrochemical equilibrium between ions and solvent molecules of mixed polar solvent composition. In cases where in excess of one types of solvated complexes are formed, there should be a maximum and/or a minimum in the Walden product. This is supported from the experimental observations. *Hubbard and Onsager* have developed kinetic theory of ion-solvent interaction within framework of continuum mechanics where concept of kinetic polarization deficiency has been introduced. However, quantitative expression is still awaited. Further, improvements naturally have to be in terms of (i) sophisticated handling of dielectric saturation, (ii) specific structural effects concerning ion-solvent interactions. From the discussion, it is apparent that the problem of molecular interactions is intriguing plus interesting. It is desirable to explore this problem using diverse experimental techniques. We have, therefore, utilized four important methods, viz., volumetric, viscometric, and conductometric etc. for the physico-chemical studies in different solvent media. [251-254]

♣ *Conductance – Some Recent Trends*

Recently *Blum, Turq and coworkers* have developed a mean spherical approximation (MSA) account of conductivity equations. Their theory starts from same continuity and hydrodynamic equations used in the more classical treatment; however, an important difference exists in the utilize of MSA terms for the equilibrium and structural properties of the electrolytic solutions. Although differences in derivation of

classical and MSA conductivity theories seem to be relatively small, it has been claimed that the performance of MSA equation is improved with a much wider concentration range than that covered by the classical equations. However, no through learning of the performance of the new equation at the experimental uncertainty level of conductivity measurement is yet available in the literature, except the study by *Bianchi et al.* They compared the results obtained using old and new equations in order to assess their capacity to describe the conductivity of different electrolytic solutions. In 2000, *Chandra and Bagchi* developed an innovative microscopic approach to ionic conductance and viscosity based on the mode coupling theory. Their revise provides microscopic expressions of conductance, viscosity in terms of static and dynamic structural factors of charge and number density of the electrolytic solutions. They claim that their new equation is applicable at low plus at high concentrations and it describes the cross over from low to high concentration smoothly. *Debye-Huckel, Onsager* and *Falkenhagen* expressions can be derived from this self-consistent theory at extremely low concentrations. In case of conductance, the agreement seems to be satisfactory up to 1 (M). [322-344]

♣ *Thermodynamics of Ion-Pair Formation*

The standard Gibbs energy changes (ΔG^o) for ion-association technique can be considered from the equation

$$\Delta G^o = -RT \ln K_A \qquad (123)$$

The values of standard enthalpy change, ΔH^o and standard entropy change, ΔS^o, can be accessed from temperature dependence values as follows,

$$\Delta H^o = -T^2 \left[\frac{d(\Delta G^o / T)}{dT} \right]_P \quad (124)$$

$$\Delta S^o = -T^2 \left[\frac{d(\Delta G^o)}{dT} \right]_P \quad (125)$$

The values can be fitted with assistance of a polynomial of type:

$$\Delta G^o = c_0 + c_1(298.15 - T) + c_2(298.15 - T)^2 \qquad (126)$$

And coefficients of fits can be compiled together with σ% values of the fits. Standard values at 298.15 K are followed by:

$$\Delta G^{o}_{298.15} = c_0 \quad (127)$$

$$\Delta S^{o}_{298.15} = c_1 \quad (128)$$

$$\Delta H^{o}_{298.15} = c_o + 298.15 c_1 \quad (129)$$

The mainly important factors which govern standard entropy of ion-association of electrolytes are: (i) size and shape of the ions, (ii) charge density on the ions, (iii) electrostriction of solvent molecules around ions, and (iv) penetration of solvent molecules inside space of ions, and influence of these factors are discussed afterwards.

The non-columbic part of Gibbs energy ΔG^{o} can furthermore be calculated by means of the following equation:

$$\Delta G^{o} = N_A W_{\pm} \quad (130)$$

$$K_A = \left(\frac{4\pi N_A}{1000}\right)\int_a^R r^2 \exp\left(\frac{2q}{r} - \frac{W_{\pm}}{kT}\right) dr \quad (131)$$

where symbols have their usual significance.

The quantity 2q/r is Columbic part of interionic mean force potential, $W_{\pm}$ is its non-columbic part. [314-324]

♣ *Solvation Models–Some Recent Trends*

The interactions amid particles in chemistry based upon empirical laws-principally on *Coulomb's law*. This is also basis of attractive part of the potential energy used in the *SchÖdinger equation*. Quantum mechanical approach for ion-water interactions was begun by *Clementi* in 1970. A quantum mechanical approach to solvation can give information on the energy of the individual ion-water interactions provided it is relevant to solution chemistry, because it concerns potential energy rather than entropic aspect of salvation. Another problem in quantum approach is the mobility of ions in solution affecting solvation number along with coordination number. Conversely, *Clementi* calculations concerned stationary models and cannot have much to do with dynamic solvation numbers. Covalent bond formation enters little into aqueous calculations; however, with organic solvents the quantum mechanical

approaches to bonding possibly essential. The trend pointing to future is thus the molecular dynamics technique. In molecular dynamic approach, a limited number of ions and molecules and *Newtonian mechanics* of association of all particles in solution is concerned. The foundation of such an approach is knowledge of the intermolecular energy of interactions between a pair of particles. Computer simulation approaches may be constructive in this regard and the last decade (1990-2000) witnessed some interesting trends in the development of solvation models and computer software. Based on a collection of experimental free energy of solvation data, *C.J. Cramer, D.G. Truhlar and co-workers* from the University of Minnesota, U.S.A. constructed a series of solvation models (SM1-SM5 series) to predict and calculate free energy of solvation of a chemical compound. These models are appropriate to virtually any substance composed of H, C, N, O, F, P, S, Cl, Br and/or I. The only input data required are, molecular formula, geometry, refractive index, surface tension, *Abraham's* a (acidity parameter) and b (basicity parameter) values, and, in latest models, the dielectric constants. The advantage of models like SM5 series is that they can be used to predict the free energy of self-solvation to be enhanced than 1 KCl/mole. These are especially useful when other techniques are not available. One can also analyze factors like electrostatics, dispersion, hydrogen bonding, etc. via these tools. They are also relatively inexpensive, available, effortless to use computer codes.

Galindo et al. have developed *Statistical Associating Fluid Theory for Variable Range (SAFT-VR)* to model thermodynamics in addition to phase equilibrium of electrolytic aqueous solutions. The water molecules are modeled as hard spheres with four short-range attractive sites to report for the hydrogen-bond interactions. The electrolyte is modeled as two hard spheres of dissimilar diameter to describe the anion and cation. The *Debye-Hückel* and mean spherical approximations are provided to describe interactions. Good agreement with experimental data is thus established for a number of the aqueous electrolyte solutions. The relative permittivity becomes very close to unity, especially when mean spherical approximation is used, indicating a good description of the solvent system. *E. Bosch et al.* of the University of Barcelona, Spain, have compared several "*Preferential*

Solvation Models" particularly for describing the polarity of dipolar hydrogen bond acceptor-co solvent mixture. [255-265]

♣ *Refractometry*

Optical data (refractive index, n_D) supply interesting information related to molecular interactions and structure of the solutions, in addition to complementary data on practical procedures, such as concentration measurement or estimation of extent of solvation of electrolytes/non-electrolytes in liquid systems.

The light bending property is a result of variation of velocity with which light is transmitted. Refractive index (n_D) of liquid, changes not only with wavelength of light used but also with temperature. Molar refractions are influenced by arrangement of atoms in the molecule or by factors like unsaturation, ring closure etc. linear optical properties of liquids and liquid mixtures have been extensively studied to obtain information on their physical, chemical, and molecular properties. *Fialkov et. al.* stated refractive index is an additive property of pure components when composition is expressed in terms of volume fraction. Several researchers have estimated the refractivity of liquid systems by means of the well known mixing rules viz. *Arago-Biot, Newton, Heller, Gladstone-Dale, Eyring-John, Eykman, Lorentz-Lorenz, Weiner and Oster relations*. These empirical approaches for scheming the excess properties attempt to give details about the non-ideality in terms of specific and non-specific intermolecular interactions. Refractive index or refractivity is a property of intrinsic interest in fields of pharmaceutical research such as formulation of eye preparations, in optoelectronic and photonic applications. [357, 358]

The ratio of the speed of light in a vacuum to the speed of light in another substance is defined as index of refraction (n_D) for the substance.

$$Refractive\ Index\ (n_D) = \frac{Speed\ of\ light\ in\ vacuum}{Speed\ of\ light\ in\ solution\ systems}$$

Whenever light changes speed as it crosses a boundary from one medium into another, its direction of travel also changes, i.e., as it is refracted. Correlation among light's speed

in two diverse mediums [V_A, V_B], angle of incidence [$\text{Sin}\theta_A$] & refraction [$\text{Sin}\theta_B$], refractive indexes of the two mediums [n_A, n_B] is revealed underneath:

$$\frac{V_A}{V_B} = \frac{\sin\theta_A}{\sin\theta_B} = \frac{n_B}{n_A} \qquad (132)$$

Thus, it is not necessary to measure the speed of light in a sample in order to establish its index of refraction. Instead, by measuring angle of refraction, and knowing index of refraction of the layer that is in contact with the sample, it is possible to determine refractive index of the sample quite accurately.

The refractive index of mixing can be correlated by application of a composition-dependent polynomial equation. Molar refractivity, was obtained from *Lorentz-Lorenz relation* by means of, n_D experimental data according to the following expression

$$R_M = \frac{(n_D^2 - 1)}{(n_D^2 + 2)}\left(\frac{M}{\rho}\right) \qquad (133)$$

Where M is mean molecular weight of the mixture and ρ is mixture density. n_D can be expressed as the following:

$$n_D = \sqrt{\frac{(2A+1)}{(1-A)}} \qquad (134)$$

where *A* is thus given by:

$$A = [\{\frac{(n_1^2 - 1)}{(n_1^2 + 2)}(1/\rho_1)\} - \{\frac{(n_1^2 - 1)}{(n_1^2 + 2)}(w_2/\rho_1)\} + \{\frac{(n_2^2 - 1)}{(n_2^2 + 2)}(w_2/\rho_2)\}\rho] \qquad (135)$$

where n_1 and n_2 are pure component refractive indices, w_j weight fraction, ρ the mixture density, and ρ_1 and ρ_2 the pure component densities.

The molar refractivity deviation is designed by the following expression:

$$\Delta R = R - \phi_1 R_1 - \phi_2 R_2 \qquad (136)$$

where ϕ_1 and ϕ_2 are volume fractions and *R*, R_1, and R_2 are the molar refractivity of the mixture and of the pure components, respectively.

The deviations of refractive index were used for the correlation of binary solvent mixtures:

$$\Delta n_D = n_D - x_1 n_{D1} - x_2 n_{D2} \qquad (137)$$

Where Δn_D is deviation of the refractive index for this binary system , n_D, n_{D1}, and n_{D2} are the refractive index of the binary mixture, refractive index of component-1, and refractive index of component-2, respectively, '*x*' is the mole fractions.

The computed deviations of refractive indices of binary mixtures are fitted using the following *Redlich-Kister expression.* [359]

$$\Delta n_{Dew} = w_e w_w \sum_{P=0}^{S} B_p (w_e w_w)^p \qquad (138)$$

where B_p are adjustable parameters obtained by a least squares fitting method, w is mass fraction, and S is the number of terms in the polynomial used.

In case of salt-solvent solution the binary systems were fitted to polynomials in the form:

$$n_{Ds,sol} = n_{Dsol} + \sum_{i=1}^{N} A_i m^i \qquad (139)$$

where $n_{Ds,sol}$ is refractive index of the salt + solvent system and n_{Dsol} is refractive index of the solvent respectively, m is the molality of salt in the solution, A_i the fitting parameters, and N is number of terms in the polynomial.[345-356]

For ternary systems of salt + solvent-1 + solvent-2 solutions a polynomial expansion has been in use, similar to that obtained for salt + solvent solutions was used to represent ternary refractive indices:

$$n_D = n_{Dw} + \sum_{i=1}^{P} C_i m^i \qquad (140)$$

where n_D is the refractive index of the ternary solution, C_i are the parameters, and P is the number of terms in the polynomial. [360]

There is no general rule that states how to compute a refractivity deviation function. However, molar refractivity is isomorphic to a volume for which ideal behavior possibly expressed in terms of mole fraction: in this case smaller deviations occur but data are more scattered for the reason that of higher sensitivity of the expression to rounding errors in the mole fraction. For the sake of comprehensiveness, both

calculations of refractivity deviation function, molar refractivity deviation was fitted to a *Redlich and Kister-type expression* and adjustable parameters and relevant standard deviation *ó* are designed for the expression in terms of volume fractions and in terms of mole fractions, respectively. [350, 266-343]

♣ *FTIR Spectroscopy*

The spectroscopic study has been established by the investigation of FTIR spectroscopy. The study has been taking into account to qualitative interpreting the molecular as well as ionic association of the electrolytes in the solutions. FTIR spectroscopy is one of the most appropriate optical properties which qualitatively interpreted the nature, mode, manner of the electrolytes and non-electrolytes in the solution system, eventually it also is able to give information about the configurational structure of the solute or solvents present in the solutions.

Infrared (IR) spectroscopy is one of the most widespread spectroscopic techniques used by organic and inorganic chemists. Simply, it is absorption measurement of different IR frequencies by a sample positioned in the path of an IR beam. The major goal of IR spectroscopic analysis is to determine the chemical functional groups in the sample. Different functional groups absorb characteristic frequencies of the IR radiation. Using diverse sampling accessories, IR spectrometers can accept a wide range of sample types such as gases, liquids, and solids. Thus, IR spectroscopy is an imperative and popular tool for structural elucidation and compound identification.

Infrared radiation spans a section of electromagnetic spectrum having wave numbers from roughly 13,000 to 10 cm^{-1}, or wavelengths from 0.78 to 1000 µm. It is bound by red end of the visible region at high frequencies and microwave region at low frequencies.

IR absorption positions are in general presented as either wave numbers (ν) or wavelengths (l). Wave number is defined as the number of waves per unit length. Thus, wave numbers are directly proportional to frequency, plus the energy of the IR absorption. The wave number unit (cm^{-1}, reciprocal centimetre) is added commonly used in modern IR instruments that are linear in cm^{-1} scale. In contrast, wavelengths are inversely proportional to frequencies and their associated energy. At the present time,

the recommended unit of wavelength is μm (micrometers), but μ (micron) is used in some older literature. Wave numbers and wavelengths can be interconnected using the following equation:

$$\nu\,(cm^{-1}) = \frac{1}{\lambda\,(\mu m)} \times 10^4 \qquad (141)$$

IR absorption information in wide-ranging presented in the form of a spectrum with wavelength or wave number as x-axis and absorption intensity or percent transmittance as the y-axis.

Transmittance, T, is ratio of radiant power transmitted by the sample (I) to the radiant power incident on the sample (I_0). Absorbance (A) is logarithm to the base 10 of the reciprocal of the transmittance (T).

$$A = log_{10}\left(1/T\right) = -log_{10}\left(T\right) = -log_{10}\left(\frac{I}{I_0}\right) \qquad (142)$$

The transmittance spectra provide improved contrast between intensities of strong and weak bands because transmittance ranges from 0 to 100% T whereas absorbance ranges from infinity to zero. Analyst should be conscious that the same sample will give quite different profiles for the IR spectrum, which is linear in wave number, and IR plot, which is linear in wavelength. It will appear as if a number of IR bands have been contracted or expanded.

The IR region is usually divided into three smaller areas: near IR, mid IR, and far IR.

	Near IR	Mid IR	Far IR
Wavenumber	13,000–4,000 cm–1	4,000–200 cm–1	200–10 cm–1
Wavelength	0.78–2.5 μm	2.5–50 μm	50–1,000 μm

This chapter focuses on the most commonly used mid IR region, between 4000 and 400 cm^{-1} (2.5 to 25 μm). [361-384]

♣ *NMR Spectroscopy*

THE Evolution of NMR Spectrometry in 1946, *Felix Bloch* and *Edward Mills Purcell* noticed that magnetic nuclei, like ^{1}H and ^{31}P, could absorb energy in the radio-frequency band when exposed to a magnetic field of a known strength. They described such absorbing

nuclei as being on resonance hybrid. *Oddly* enough at the time, however, they noted that different atoms of, say, H, within same molecule "resonated" at different frequencies even at same magnetic field strength. Their first tentative postulation that Hs were somehow in diverse local microenvironments focused on the very feature of NMR allows structural information to be gleaned from a spectrum. *Bloch* and Purcell were jointly awarded Nobel Prize in physics in 1952 for their discovery. From early 1950s until late 1970s, NMR spectrometers proliferated in laboratories globally as scientists (chemists, especially) began to appreciate and to accept potential value of the novel spectroscopic technique. This initial generation of spectrometers employed a methodology known as continuous-wave (CW) spectroscopy, where oscillating field was held at a fixed frequency and magnetic field was swept; a less regularly employed (somewhat more difficult to engineer) arrangement involved a constant magnetic field and a swept oscillating field. CW technique had several boundaries, not the least of which was that each frequency was scanned (and monitored) individually, in succession, resulting in (a) long run times, and consequently only a small number of runs in a given time interval; (b) consequently, poor signal-to-noise ratios (S/N)
observed. The landscape of practical NMR was transformed with the advent of Fourier transform (FT)-NMR. With FT-NMR, (pioneered by *Richard R. Ernst*, 1991 Chemistry laureate) acquisition time for a scan is condensed by orders of magnitude because a full range of frequencies (usually the spectral width for given analysis) is probed simultaneously. This technique has been made further practical and universal with development of computers capable of performing multiple complex mathematical data transformations. Essentially, FT-NMR engrosses exposing a sample in static, external magnetic field to short square bursts (pulses) of polychromatic radiofrequency energy. The pivotal principle here is that the Fourier decomposition of a square wave contains contributions from the entire frequencies. The polarized magnets of irradiated nuclei spin together, generating an observable RF signal. Conversely, they ultimately relax to their parallel ground state by emission of ΔE by radiative or non-radiative processes (vide supra). This decay is known as free induction decay (FID). Fourier transformation (a mathematical operation) is then subsequently used to change this time dependent pattern to a frequency-dependent pattern of nuclear resonances producing a spectrum in standard NMR format as well as the knowledge of how to generate an array of frequencies at the same time. Today, NMR spectroscopist can propose pulses with specific

shapes, widths (pulse widths), frequencies (i.e., varying pulse delays), in combinations called pulse sequences. Even subtle differences in pulse sequences can allow spectroscopist to extract a truly amazing library of information on the molecule or reacting system under revise. Another chief advancement in nuclear magnetic resonance spectroscopy is multi-dimensional NMR spectroscopy. Here, at least two pulses are employed, and as experiment is repeated, the pulse sequence is varied.

In multidimensional Nuclear magnetic resonance, there will be a succession of pulses, at slightest one variable time period.

NMR spectroscopy has emerged as arguably the most imperative spectroscopic or spectroscopic-type tool in the (organic) chemists' considerable arsenal. The pace of invention of new NMR techniques particularly pulse sequences has grown tremendously in the last decade especially and it is hard for an expert in the field to keep abreast of the changing face of NMR. As an illustration, in 1996 *Braun, Kalinowski, and Berger* published a text known as '100 and More Basic NMR Experiments'. Publishing structure of a new compound requires at the minimum a 1H-NMR and 13C-NMR spectrum on at least a 300-MHz spectrometer. Research will probably possess multiple NMR spectrometers, including at least one "walk-on" 300- or 400-MHz instrument as well as several higher field instruments. If the research involves bioorganic or biophysical chemistry, then it requires 800- or 900-MHz instrument is almost mandatory. Versatility, accuracy, and dependability of NMR spectroscopy have made it a mainstay of chemical research. Practical issues of field shielding, facile, inexpensive solid-state NMR, minimization of cryogen boil-off rates, magnet quenching safeguards, etc., still linger, but despite these and other drawbacks technique has given chemists far more than it has denied them. It is with satisfaction and confidence that we commission innovative experiments based on NMR spectroscopy and with heightened anticipation that we await the next major steps forward in this field.

NMR spectroscopy is one of the prime techniques used to obtain physical, chemical, electronic, and structural information about a molecule and/or a system undergoing chemical reactions. It is the only technique that can offer detailed information ranging from the exact 3D structure of biological molecules in solution to the kinetics of chemical reactions and yet is versatile enough to be employed in building elementary quantum computers. Arguably, most sensational use of nuclear magnetic resonance is in magnetic resonance imaging (MRI) for

medical diagnosis. Elucidation of the structure of buckminsterfullerene (the infamous C60 allotrope of carbon) by *Curl and Smalley* of Rice University in 1985 using 13C NMR (a lone singlet was obtained, indicating that all 60 carbons were equivalent) is a particularly intriguing, if not exotic, use of technology. NMR was also integral in the elucidation of the structure *Gomberg's dimer* from the coupling of triphenylmethyl radicals (in his misdirected and unsuccessful attempt to prepare hexaphenylethane). The assumption of structure as Ph3C-CPh3 had persisted for almost 70 years before a 1H-NMR spectrum showed presence, not only of non-equivalent protons, but also of a single shielded H (attached to an sp3-hybridized C); the actual dimer (prepared from Ph3CCl and silver in CCl4) being in fact 1-(diphenylmethylene)-4-trityl-2,5-cyclohexadiene. Over the course of some 15 years, *Liu et al.* made brilliant use of 19F-NMR spectroscopy to illuminate the role of vitamin A in photochemistry of vision. The technique allowed his group to describe a model of a confined, tethered chromophore of rhodopsin as compulsory for primary process of vision as well as to postulate a mechanism for thermal and photochemical processes of all intermediates in visual cycle. This investigation was also origin of hula-twist-n process: a volume-conserving process for ground-state conformational changes of retinal in confined medium of the multiple helical tertiary structure of rhodopsin. A nuclear magnetic resonance spectrum is enormously useful for analyzing samples non-destructively. Radio waves and static magnetic fields easily penetrate numerous types of matter and anything that is not inherently ferromagnetic. Particularly, biological samples, which are often difficult to obtain in high yields and with high purity (e.g., RNA, DNA, proteins, etc.), can be readily studied using NMR.

NMR spectroscopy concerns itself with certain nuclei that marked magnetic dipoles because of the juxtaposition of electric charge and mechanical spin. NMR-active nuclei are those whose spin quantum number (I). This latter condition is met either when mass number (Z) is odd (I = n/2; n is an integer) or when Z is even and atomic number (A) is odd (I = n). I = 0 whilst both A and Z are even. NMR-active nuclei are exposed to an external magnetic field (B) their magnetic dipoles align in (a quantum mechanically limited) S orientations (S = 2I + 1) or spin states, relative to the field. Such nuclei precess at a frequency,ν specified by the expression

$$\nu = \mu\beta_N\beta_0/hI \qquad (143)$$

Where μ = magnetic moment of nucleus, h = Planck's constant, and β_N = nuclear magneton constant. The magnetogyric ratio (g) is specified by

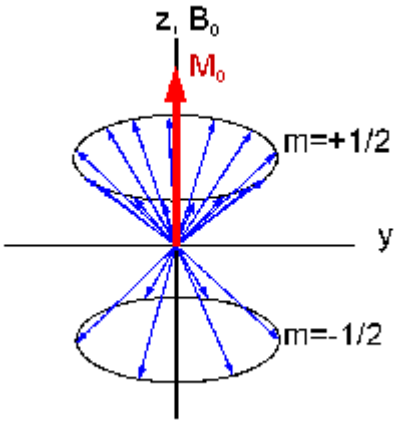
$$\gamma = 2\Pi\mu\beta n/hI \qquad (144)$$

Equation. (1) may simplify to

$$\nu = \gamma\beta_0/2\Pi \qquad (145)$$

Three points are remarkable here: (a) sensitivity of the NMR experiment depends heavily upon μ such that as value of μ increases so does the experiment's sensitivity; (b) B_0 ($\neq$B) refers to local field experienced by a given nucleus, which in turn depends predominantly upon prevailing electronic factors (largely induction and anisotropy) that affect local electron density around active nucleus; (c) while inherent spinning frequency of a particular nucleus is constant, its precessional frequency, ν, is variable and depends upon B_0 .

The various spin states possess different energy levels and ΔEs between those levels are bridgeable by photons in radio-frequency (RF) region of the electromagnetic spectrum. [385-399]

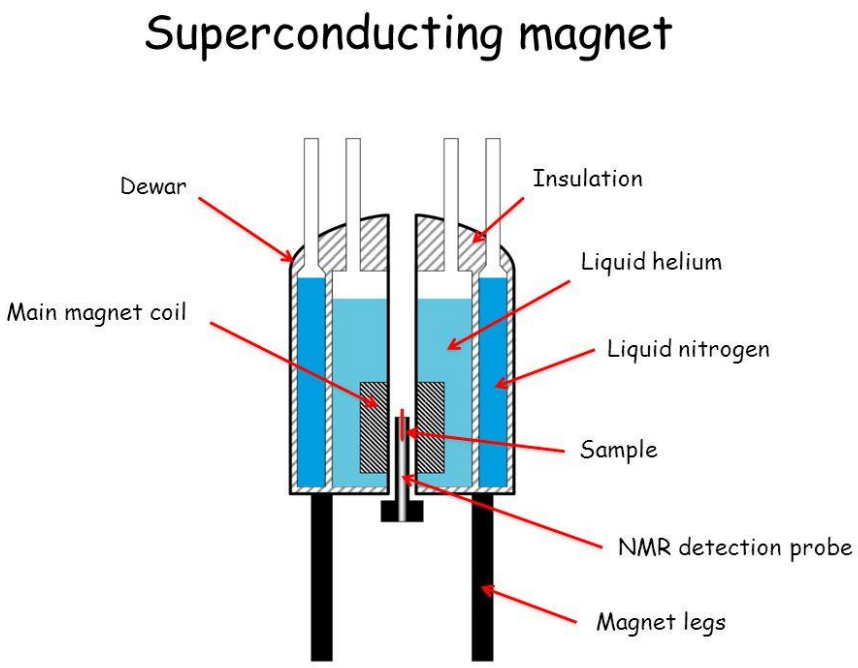


Promotions among spin states (Scheme) are allowed as long as irradiating frequency exactly matches ν (so-called resonance condition); excited nuclei are, of course, able to relax to lower spin states (spin flipping). There are numerous mechanisms by which excited nuclei may relax; two most widespread radiations less processes are spin-lattice relaxation and spin-spin relaxation. In previous, excited nucleus transfers its energy to some appropriate electromagnetic vector (e.g., a polar solvent molecule or intramolecular group undergoing vibrational-rotational phenomenon); in the latter case, exciton transfers ΔE to a different kindred relaxed nucleus. On the other hand, excited nuclei could simply re-emit ΔE. Rates of

relaxation govern rate at which net excitations occurs. If transfer of ΔE is inefficient (as in non viscous media where molecular orientations are unsystematic), then mean half-life of

Relaxation is long (~1 s) and sharp spectral lines arise. Modern NMR spectrometers utilize a magnetic field generated by a superconducting magnet whose coils are positioned in an inner Dewar bathed in liquid helium (Figure).

Requirement for NMR spectra: Spin quantum number (I) ≠ 0 meaning…. must be an odd number and/ or neutrons. Ex. 1H, 2H, 13C, 19F, etc.



An outer Dewar filled with liquid nitrogen serves to avoid boil-off of much more expensive, cooler liquid helium. Shim coils homogenize field and a spinner assembly is responsible for both spinning sample tube as well as moving it into and out of probe buoyed on a cushion of gas (usually air that has been treated and dried prior to use or zero-grade nitrogen). A probe head is connected to RF cables provides (^{2}H) lock 1H frequency and one X-nucleus frequency. New instruments possess changeable temperature and sample changer accessories and a coordinating workstation by a plethora of energy- and time-saving programs. Interpretation of a simple 1D, first-order NMR spectrum generally involves evaluation of five principal features: (1) number of signals; (2) chemical shift, δ-value; (3) signal multiplicity; (4)coupling constant, J; and (5) signal integrals. The number of signals reveals number of dissimilar types of the nuclei under study.

In a first-order spectrum (where the $\Delta\delta >> J$), interpretation of the splitting patterns is quite straight forward. In general, multiplicities in such spectra are governed by "n+1 rule" where n = number of neighboring protons (within 2 or 3 bond distances), equivalent nuclei do not interact with each other, and peak ratios are a statistical issue properly illustrated in Pascal's triangle.[399]

MULTIPLETS AND PASCAL'S TRIANGLE

No. of neighboring atoms	Relative intensities of split peaks	Name of multiplet	Splitting pattern
0	1	singlet	
1	1 1	doublet	
2	1 2 1	triplet	
3	1 3 3 1	quartet	
4	1 4 6 4 1	quintet	

Although the earlier four spectral parameters are useful, if not crucial in structure elucidation for most nuclei, signal integral is not universally valuable. For nuclei that relax very leisurely either inherently (13C, e.g.) or due to constraints in the methodology (low concentrations of small molecules in weakly polar solvents, e.g.), differences in relaxation rates arise for same nuclei but in diverse environments. Consequently, some nuclei undergo excitation-relaxation cycles more often than others, giving rise to more intense signals that are independent of relative numbers of nuclei. Except for those cases, however, the integrals point out the relative numbers of a given nucleus under consideration.

Although there are 118 different nuclei for whom I > 0 and are therefore, theoretically at least, observable in an NMR experiment, it is the nucleus of 1H that dominates the NMR landscape even today. While most of the examples discussed later in this work involve 1H NMR (and justifiably so), it is worth a moment of pause to discuss briefly a few other nuclei whose NMR spectra prove to be of value to a significant number of experimentalists. The 12C nucleus is not magnetically active (i.e., I ¼ 0), but the 13C nucleus (I ¼ 1 2) is. C-13 NMR spectroscopy is severely limited, however, by the fact that the natural abundance of this isotope is only 1.1% that of C-12 and its sensitivity relative to H-1 is only 1.6%. Thus the overall sensitivity of C-13 relative to H-1 is _1.75 _ 1024. Application of FT methodology (vide supra) to C-13 as well as broad band decoupling of protons have accelerated the development of, and enhanced the interest in, C-13 NMR spectroscopy. Techniques like

distortionless enhancement by polarization transfer (DEPT) and 1H-13C COSY (HETCOR) have further endeared 13C NMR spectroscopy to organic chemists. In general, 13C NMR spectroscopy allows chemists to directly observe the carbon framework of organic moieties and to make (collaborative) inferences about active nuclei attached to the carbon backbone. The technique is particularly valuable in natural products, pharmaceutical, and biochemistry research where complex cyclic species are common and often difficult to identify with only 1H NMR.14N and 15N are NMR-active nuclei and both have been used in structure elucidation in organic chemistry and its associated fields such as biochemistry, natural products, and pharmacology. Quadrupolar relaxation of excitons in N-14 (most abundant isotope), however, results in tremendous and crippling broad lines in NMR spectrum, thus diminishing make utilize of of this nucleus. On the other hand, low sensitivity in the 15N experiment is overcome (as it is for 13C) in modern instruments and 15N NMR spectroscopy provides decisive information on character (hybridization state) and connectivities (constitution) of nitrogen atoms in molecules. Although 19F (only isotope of F) is found only rarely in naturally occurring compounds, this nucleus is of interest for the reason that it coincidentally developed with 1H in the dawn of the "NMR age." The parallel improvement of 19F NMR spectroscopy is, not surprisingly, linked to the parallel properties of 19F and 1H. Thus, sensitivity of 19F is about 0.83 that of 1H and its natural abundance is 100%. Because it is monovalent, F is often used in place of H in synthetic analogue molecules to resolve the impact of stereochemistry and steric effects that may be operational in molecules (vide infra). [399]

♣ *Proton Nuclear Magnetic Resonance Spectroscopy (H-NMR)*

NMR or nuclear magnetic resonance spectroscopy is a technique used to determine a compound's distinctive structure. It identifies carbon-hydrogen frameworks of an organic compound. Using this method and other instrumental methods including infrared and mass Spectrometry, scientists are able to determine the entire configuration of a molecule. In this discussion, focus on H NMR or proton magnetic resonance is taken. Even though there are many other spectrometers including C-NMR and N-NMR, hydrogen (H-NMR) was the first and is the most widespread atom used in nuclear magnetic resonance spectroscopy.

The atomic nucleus is a spinning charged constituent part, and it generates a magnetic field. Not including an external applied magnetic field, nuclear spins are random and spin in random directions. But, when an external magnetic field is present, the nuclei align themselves either with or against the field of external magnet.

Structural Information That the NMR Spectrum tells us

1. Number of Signals

Each group of chemically equivalent protons gives mount to a signal. Chemically Equivalent Protons are those protons that are in identical environment, and they ought to be identical in every way. They experience the similar magnetic force, and therefore, will create overlapping signals on spectrum. Therefore, we can resolve how numerous sets of equivalent protons there are in a molecule by looking at number of signals in its H-NMR spectrum.

Assorted approaches are present to determine how many sets of equivalent protons in a molecule. For illustration, we can perceive if there is a line of symmetry. Protons that are aligned on a line of symmetry as a result appear to be equivalent. One more means is to substitute proton with deuterium to form two molecules, and if two molecules are same, then two protons are equivalent. Third technique to verify how many equivalent protons present, one have to gaze at the atom attached to proton (generally a carbon) and examine what that atom is bonded to, and then atom bonded to that, all the technique until a difference is observed. If there is no difference, the protons are equivalent. If there is dissimilarity, protons are not equivalent.

Usually, protons on identical carbon are equivalent. But, occasionally, they are not equivalent for the reason that they are not in matching environment. One proton could be Trans and other proton could be cis. This would generate two different signals.

2. Position of Signals

The positions of signals in an NMR spectrum are based on how far they are from signal of the reference compound. This information tells us kind of proton or protons that are responsible for the signal.

Reference compound: Tetramethylsilane (TMS) is generally used as the reference compound because it can easily be removed from the sample by evaporation due to its volatile properties. TMS is at a lower frequency than mostly other signals for the reason that its

methyl protons are in a more electron dense environment than most protons are because silicon is less electronegative than carbon (which is a significant component of organic molecules.)

Position of signals depends on chemical shift.

Chemical Shift: It is a measure of how far the signal produced from the proton is from the reference compound signal, and it usually measured by means of the δ(delta) scale. The TMS or reference compound is at zero position on the very left of spectrum, and as it moves toward the left, the ppm values become larger. Ppm stands for parts per million, and it is the unit used to calculate chemical shift. Proton chemical shifts range from 0 ppm to 15 ppm. Chemical shift is identical for a specific proton regardless of the spectrometer used. The formula for the chemical shift is

δ (delta)= distance downfield from TMS (Hz) / operation frequency of the spectrometer (MHz) = parts per million (ppm)

The nucleus of molecule is found within a cloud of electrons that partly shields it from applied magnetic field. This shielding is different for different protons in a molecule, and that is why there are lots of signals in the H NMR spectrum, instead of just one. In a magnetic field, electrons go around nuclei and induce a local magnetic field that opposes the applied magnetic field.

Effective Magnetic Field: is the nuclei sense through its electron filled environment.

$$B_{effective} = B_{applied} - B_{local}$$

B applied is magnetic field supplied by the applied external magnetic force (NMR) and the magnetic fields supplied by the earth. This number is same of the entire the nuclei in the molecule. *B* local is the magnetic field supplied by the surrounding electrons around nuclei. This number varies amid nuclei in the molecule. According to this formula, greater the electron density around the nuclei, the larger the *B* local will be, and more proton is shielded from applied magnetic field. This is known as diamagnetic shielding.

Protons in electron dense (rich) atmosphere sense a fewer significant effective magnetic field for the reason that they are more shielded by enormous amount of electrons, and consequently, will require a lower frequency to come into resonance as E (which is created due to the difference in the spin states) is smaller. The (ppm) will be minor, and lower frequencies are located on the right side of the spectrum.

Upfield: farther to right hand side of the spectrum.

Protons in electron poor environments sense a larger effective magnetic field for the reason that they are less shielded due to fewer electrons, and therefore, they require a higher frequency to get nearer into resonance for the reason that E is larger. The (ppm) determination is larger, and higher frequencies are located on left side of the spectrum.

Downfield: further than to left side of the spectrum.

The electron cloud shields nucleus from applied magnetic field, and electronegativity is defined as tendency of an atom to drag electrons toward it. Therefore, electronegative atoms eliminate electron density from the proton. This causes proton to have less electron density, and this leads to less shielding. If the proton has less shielding, it will feel the applied magnetic field more, and this leads to a higher E and an elevated chemical shift. Protons that are nearer to electronegative atom are in a less electron dense environment, which means they're chemical shifts will be superior.

An imperative concept to understand is that similar functional groups have similar chemical shifts. Characteristic chemical shifts are averages for normal or typical proton.

Therefore, this number varies between diverse molecules. We can't use these shift numbers to assign proton types to NMR signals. On characteristic proton NMR chemical shifts table, two molecules with same functional group may have different chemical shifts. This could be due to numerous factors such as being positioned near an electronegative atom. 300- MHz 1H N.M.R. spectra of deuterated species of samples were used in the various works of this thesis. In case of 1H-NMR though we cannot compare the extent of H-bonding but we can conform the positioning of H-bonding, if we tally both system's NMR according to the upfield shift, downfield shift or peaks which came all together in same position. [399-401]

♣ *Carbon-13 nuclear magnetic resonance*

Raymond Andrew pioneered development of high-resolution through his introduction of the so-called magic angle spinning (MAS) technique. This technique resulted in spectra in which resolution increases by several orders of magnitude. This area was further refined by *John Waugh* and *Alex Pines*, who introduced cross-polarization technique to enhance signals from nuclei with inherently low sensitivities and/or low natural abundance (e.g., 13C).

Carbon-13 nuclear magnetic resonance (most usually known as carbon-13 NMR or ^{13}C NMR or simply referred to as carbon NMR) is the application of nuclear magnetic resonance

(NMR) spectroscopy to carbon. It is analogous to proton NMR (1HNMR) allows the identification of carbon atoms in an organic molecule just as proton NMR identifies hydrogen atoms. As such ^{13}C NMR is an important contrivance in chemical structure elucidation in organic chemistry. ^{13}C NMR detects only the 13 C isotope of carbon, whose natural abundance is merely 1.1%, because the main carbon isotope is not detectable by NMR since it has zero net spin.

^{13}C chemical shifts follow the similar principles as those of ^{1}H, although the typical range of chemical shifts is much larger than for ^{1}H (by a factor of about 20). Chemical shift standard reference for ^{13}C is carbons in tetramethylsilane (TMS), is deliberated to be 0.0 ppm.

^{13}C NMR has a quantity of complications that are not encountered in the proton NMR. The ^{13}C NMR is much a lesser sensitive to carbon rather than ^{1}H NMR is to hydrogen as chief isotope of carbon, ^{12}C isotope, has a spin quantum number of zero and so. It is not magnetically active and therefore not visible by NMR. Much less common ^{13}C isotope, present naturally at 1.1% natural abundance, is magnetically active with spin quantum number of 1/2 (like ^{1}H) as a consequence detectable via NMR. Hence, merely few ^{13}C nuclei present resonate in magnetic field, even though this can be overcome by isotopic enrichment of e.g. protein samples. In addition, the gyro magnetic ratio (6.728284 10^{7} rad T^{-1} s^{-1}) is only 1/4 that of ^{1}H, further reducing sensitivity. Overall receptivity of ^{13}C is about 4 orders of magnitude lower than ^{1}H. Applications range from the quantification of drug purity to determination of composition of high molecular weight synthetic polymers. In a typical run on an organic compound, a ^{13}C NMR may require several hours to trace the spectrum of a one-milligram sample, compared to 15–30 minutes for ^{1}HNMR, and that spectrum would be of lower quality. The nuclear dipole is weaker, the differentiation in energy linking alpha and beta states is one-quarter that of proton NMR, and Boltzmann population difference is correspondingly less. 13C NMR is generated in similar fundamental was as proton NMR spectrum. Only 1.1 % of naturally occurring carbon is 13C and actually an improvement is noticed because of less coupling.

The ^{13}C NMR is directly related about the carbon skeleton not just the proton attached to it.

a.] The number of signals informs us about how many different carbons or set of equivalent carbons.

b.] Splitting of a signal notify us how numerous hydrogen's attached to each carbon. (N+1 rule)

c.] The chemical shift tells us regarding hybridization (sp3, sp2, and sp) of all carbon.

d.] Integration: Not cooperative for 13C NMR. The Proton–coupled spectra visualize splitting of carbon signal simply by protons attached to that carbon itself.

13C_H coupling occurs not 13C_ 13C_H or not 13C_13C_ 13C_H or not 12C_13C coupling occurs but very low.

Thus, for each carbon multiplicity of the signal depends upon the fact how many protons are attached to it. Due to low natural abundance, 13C NMR spectra do not ordinarily show carbon-carbon splitting two 13C being next to other is 1.1 % x 1.1%=0.012 % (because 12C doesn't have a magnetic moment, it can't split the signal of an adjacent 13C), and are thus enormously simplified. **Proton-Decoupled Spectrum** shows no splitting in any way; it consists of a set of single peaks, one for each carbon or each set of equivalent carbons in a molecule. Even for extremely complicated molecules, such a spectrum is remarkably simple (since overlapping multiplets very complicated to interpret) most usually run spectrum for structural analysis; and will list multiplicity of peaks in the upper left-hand corner. Chemical Shift in ^{13}C NMR spectrum arises in analogous way as in proton NMR spectrum. Each carbon nucleus has its own electronic environment, different from the environment of other, non-equivalent nuclei; it feels a different magnetic field, absorbs at different applied fields strength. Electronegative atoms and pi bonds cause downfield shifts. ^{13}C chemical shift range 0-250 ppm. [402-410]

Splitting Pattern (N+1 rule): for each carbon multiplicity of signal depends upon how many protons are attached to it.

Ex.

H			
_	_	_	_
_C_	H _C_	H _C_ H	H_C_H
_	_	_	_
No proton	one proton	two protons	three protons
Singlet	doublet	triplet	quartet

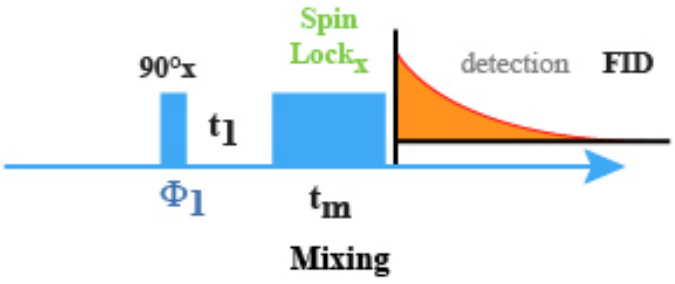
♣ 2D ROESY (Rotating-frame Overhauser SpectroscoPY)

The nuclear Overhauser effect, (NOE) experiments are invaluable in determining distances between atoms that are not covalently bonded to each other. Although it was the combined

efforts of several scientists that led to the development of 2D and multidimensional FT-NMR into a powerful technique particularly well suited for studying macromolecules (e.g., nucleic acids, proteins, etc.), much of credit is given to *Richard Ernst* and *Kurt Wu¨thrich*. They were jointly awarded Nobel Prize in chemistry in 2002 for their work in the aforesaid field. Correlation spectroscopy is one of several types of 2D-NMR spectroscopy. Other types include J-spectroscopy, exchange spectroscopy (EXSY), nuclear overhauser effect spectroscopy (NOESY). Two-dimensional NMR spectra provide additional information about a molecule than one-dimensional NMR spectra and are especially useful in determining the structure of a molecule, particularly for molecules that are too complicated to work with by means of only one-dimensional NMR. First two-dimensional experiment, COSY, was described in 1976 by *Walter P. Aue, Enrico, Bartholdi, and Richard R. Ernst*, though it was first proposed by *Professor Jean Jeener of Universite´ Libre de Bruxelles*, in 1971. For well over 40 years after the first NMR spectrometer was constructed, spectroscopy was limited to samples in the liquid phase. In solid-phase media, such as crystals, microcrystalline powders, gels, anisotropic solutions, etc., it is dipolar coupling and chemical shift anisotropy that become dominant to behavior of the nuclear spin systems. Conventional in solution-state NMR spectra, these additional interactions would direct to noteworthy spectral line broadening. Arrays of techniques are established high-resolution conditions in solid-state NMR that are equivalent to solution-state NMR spectra. Yet still today, although NMR is used to study solids, extensive atomic-level bimolecular structural detail is especially challenging to discover by this method. The intensity of NMR signals (thus the sensitivity of the technique) depends, in part, upon strength of the magnetic field. Not surprisingly, therefore, over decades since 1950s, NMR franchise has sought out ever more powerful magnets. Thus the 60-MHz instruments that proliferated in 1970s have been replaced by 900-MHz giants marketed by Varian, Bruker, and JEOL. Almost invariably, though, these devices are engaged in studies of biopolymers where access to enhanced sensitivity and resolution is critical. Advances made in audio-visual technology have also enhanced the signal generation and processing capabilities of the modern instrument. [411-416]

2D ROESY (Rotating-frame Overhauser Spectroscopy) experiment (also called CAMELSPIN (Cross-relaxation appropriate for minimolecules emulated by locked spins) experiment) offers a simple way to attain NOE information in a molecule by a single experiment and without prior

knowledgment of spectral assignment or molecular structure. In ROESY experiment, cross-relaxations are carried out in rotating-frame with spin-locked magnetization and this means that NOE in transverse plane (ROE) is always positive (no nulling condition as in NOESY-type experiments) and, in addition, chemical exchange can for all time be distinguished. It measures homonuclear NOE effects under "spin-lock" conditions. ROESY is especially valuable since ROESY cross peaks are always positive and there is no risk of getting cross peaks of zero intensity. ROESY peaks are simply positive. The ROESY spectrum must be phased. Phasing of 2D spectra is complicated and it is carefully done and somewhat intelligent to succeed. When correlation time is close to $\tau_c = 1 / \omega_0$, then no NOE effects will be noticeable. Conversely, there is a modification of NOESY experiment with a different dependence of NOE on $\omega_0\tau_c$: In ROESY (=Rotating frame NOESY) experiment, NOE (or better, ROE) is always positive, i.e., ROE cross-peaks have opposite sign as diagonal peaks. The pulse sequence for ROESY testing is relatively simple: it is identical to TOCSY sequence. After first 90° pulse and t_1 time, a spin-lock sequence follows for the period of which ROE builds up, exactly as NOE during the mixing time τ_m of NOESY. [417-423]



In ROESY experiment, relaxation does not occur in static B_0 field along z axis, but in transverse field generated by r.f. irradiation: non-equilibrium transverse component (e.g., I_{1x}) relaxes with T_{1p} while "frozen" in spin-lock field, by this means generating a transverse component I_{2x} in neighbouring spins by cross-relaxation. With the exception of different dependence on correlation time, everything else works like for NOE: again, the initial ROE build-up rate shows r -6 dependence, but with longer mixing (=spinlock) times, build-up becomes non-linear, and indirect ROEs start to occur. And, like in NOESY, dispersive antiphase peaks can take place that are not caused by ROE, but by scalar coupling. However, while NOESY experiment is

rather straight forward to evaluate, there are several additional problems to be measured with the ROESY: [433-439]

- offset dependence of the ROE and interference stuck between NOE and ROE,
- TOCSY contributions in ROESY spectrum.

Important features of ROESY spectra
only weak dependence on the correlation time, ROE always present
ROEs for all time positive, i.e., opposite sign compared to diagonal
peaks from chemical exchange show similar sign as diagonal: easily distinguishable from always positive ROEs
offset effects have to be corrected properly
interference with NOESY contributions except for $\omega_0\tau_c \gg 1$ (is vanishing NOE)
TOCSY contributions from scalar coupling can change ROESY peak integrals, ensuing in distance errors

♣ *NMR titrations*

Systematic studies of changes in NMR parameters (most frequently chemical shifts) caused by gradual addition of some agent (acid, base, complexing agent, ligand, metal ion, etc.).

Experimental techniques of (pK_a) determination for small molecules

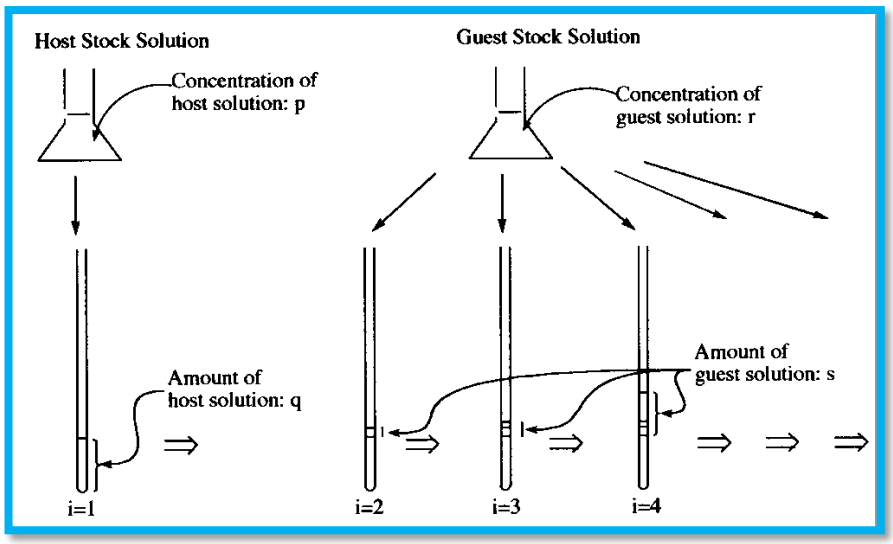
$$HA = A + H^+$$

$$K_a = [A]\,[H+]/\,[HA]$$

$$pH = pK_a + \log_{10}([A]/[HA])$$

$$pKa = -\log 10\ Ka \qquad (146)$$

pK_a determination via NMR : **NMR spectra are recorded as a function of pH.** Great amounts of material, solubility issues can arise, its laborious, separate titration curves for every anisochronous nucleus in the molecule obtained. Microscopic (pKa) values/knowledge regarding protonation/deprotonation sites can be obtained correspondingly. 13C NMR is greatly favored to 1H NMR (larger chemical shift range).



1. The advantage of pKa determination by 13C NMR is simultaneous production of multiple titration curves (= number of atoms).

2. Non-linear curve fitting to multiple curves simultaneously gives superior data.

3. NMR is the merely method that provides knowledge about protonation/deprotonation sites in the molecule.

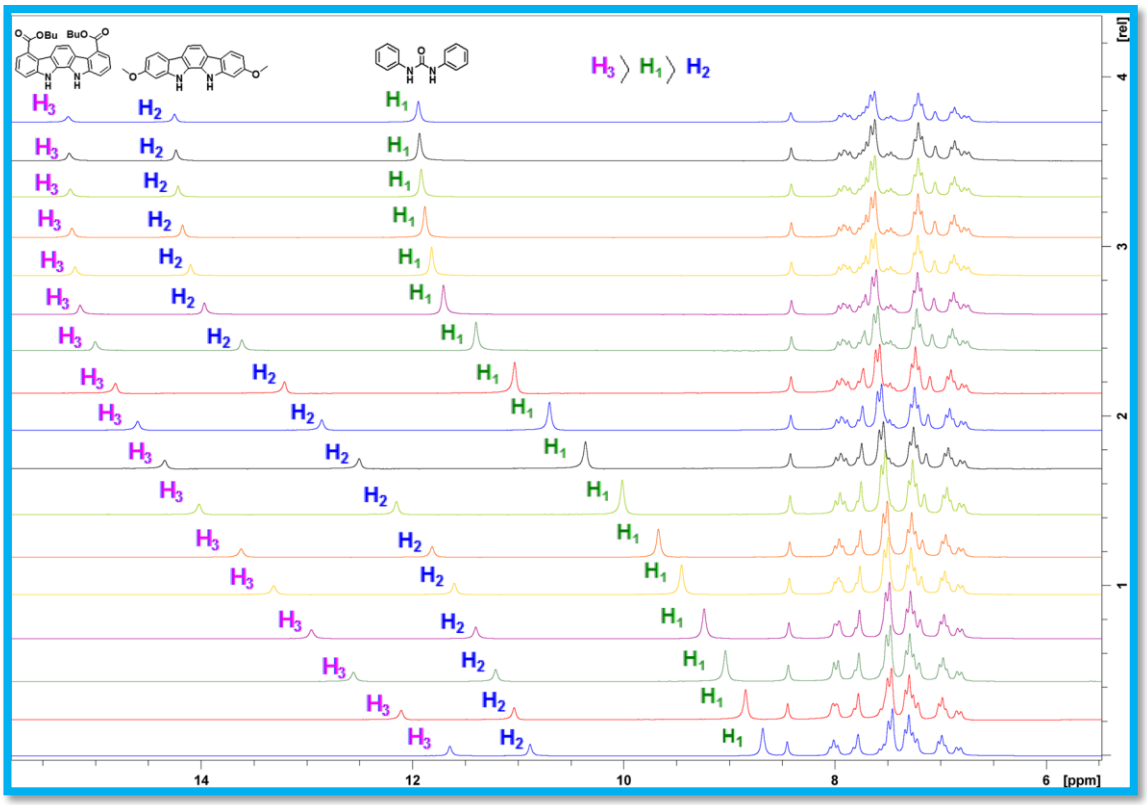
4. Excellent precision of NMR information can be obtained.

5. Technique is laborious, but at least two compounds can be NMR-titrated in a mixture.

* *Determination of Binding Constants, Enthalpy, Entropy, Free energy changes in complexation*

The intermolecular binding between each host and guest shows enantioselectivity is required to be shown by means of general parameters for example binding constant (*K*), enthalpy change (*ΔH*), entropy change (*ΔS*), free energy (*ΔG*) of complex formation instead of a brilliant color change or an appreciable difference in peak intensities. In general speaking, formation of a complex between host and guest is a basic and significant process in supramolecular chemistry. The binding constant has to be determined for quantitative analysis of complex formation. In spite of the significance of determining binding constant, it is still difficult to find documentation, where the practical issues are mentioned. The introduction of many diverse types of approximation and regression methods was important at that time from the practical point of view, in order to find an appropriate method for a wide range of certain experiments, because each approximation has severe limitation in application. Such techniques do not meet needs of a chemist nowadays. The circumstances are considerably enhanced by data-

treatment through computer development. Describing basic principle to determine the binding constants and stoichiometry is important and for the evaluation of complex concentration, precautions to be taken on setting up concentration conditions of titration experiment, practical data-treatment methods and estimation of the statistical errors host-guest chemistry is necessary but are not yet very familiar with this kind of work, mostly synthesis-oriented organic chemists. The programs for determination of binding constants of host-guest complexation were developed recently. Some of the review works are depicted here [440-442, 449]



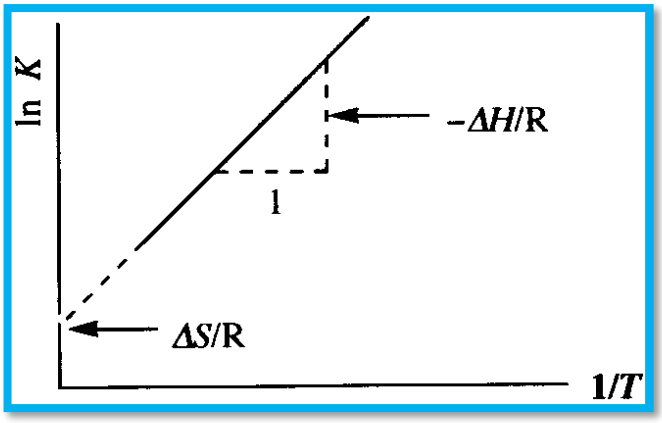
^{1}H NMR spectra for measuring relative binding affinities between receptors 3, 23, and 36 toward acetate in DMSO-d_6/H_2O (99.5%:0.5% m/m). The titration proceed from bottom to top.

General view to determine binding constants

Interpretation of basic equations for host-guest complexation

The binding constant is used as a criterion for the evaluation of host-guest complexation procedure. Thermodynamic parameters (enthalpy, entropy) and Gibbs free energy are more suitable criterion. In case where Equations (147), (148) hold good, thermodynamic parameters are related to each other as described in Figure, Equation (149), *van't Hoff*

equation. Theoretically, determination of binding constants at diverse temperatures offers these thermodynamic parameters from slope and intercept of the line in Figure. [443-448]



The vital point in the quantitative analysis of host-guest complexation is how to determine the binding constant with high reliability.

$$\Delta G = -RT \ln K \qquad (147)$$

$$\Delta G = \Delta H - T\Delta S \qquad (148)$$

$$\therefore \ln K = -\Delta H / R \,.\, 1/T + \Delta S / R \qquad (149)$$

Our investigation to determine binding constant is based on a simple binding equilibrium model: Equation (150). The binding constant, equilibrium constant, stability constant are synonymous with each other. The activity coefficients are in general unknown and the stability constant *K*, based on the concentrations, is usually employed. Judging from this condition, the question of activity coefficients of the solutes is disregarded here in order to simplify the discussion. Nevertheless, it should be remembered that this point is not for all time insignificant. The basic equations for host–guest complexation are the following four Equations (150)–(153).

$$a.\,H + b.\,G \Leftrightarrow C \qquad (150)$$

$$K = [C] / [H]^a .\, [G]^b \qquad (151)$$

$$[H]_t = [H] + a.[C] \qquad (152)$$

$$[G]_t = [G] + b.[C] \qquad (153)$$

Where H is host; G, guest; C, complex: H_a . G_b; a, b, stoichiometry: shown in Equation (150); $[H]_t$, total concentration of host molecule at initial state; $[G]_t$, total concentration of guest molecular at initial stage; [H], [G], [C], concentrations of host, guest, and complex respectively at final stage, namely, at equilibrium. Equation (154) is derived from Equations (151)–(153).

$$K = [C] / ([H]t - a.\,[C])^{a} .\, ([G]t - b.\,[C])^{b} \qquad (154)$$

Parameters are thus classified into three as follows. Constants: K, a, b {a and b are integers larger than or equal to 1}. Variables which can be set up in experimental form: $[H]_t$, $[G]_t$. Variables dependent on every equilibrium: [H], [G], [C].

Experimental guideline from the aforesaid theory

From Equation (154) and classification of its parameters is elucidated as the guideline of the experiment. When [*C*] is obtained under equilibrium in which *a* and *b* are known, *K* is derived directly according to Equation (154) from experimental condition [*H*]*t*, and [*G*]*t*. Consequently, in order to determine binding constants, following four tasks have to be carried out.

_ Determination of the stoichiometry, namely, *a* and *b*

_ Evaluation of the value [*C*]

_ Setting up concentration conditions $[H]_t$ and $[G]_t$

_ Data-treatment done

The following sections deal with the principle and also the practical issues necessary for an understanding and completion of the above four tasks in this order.

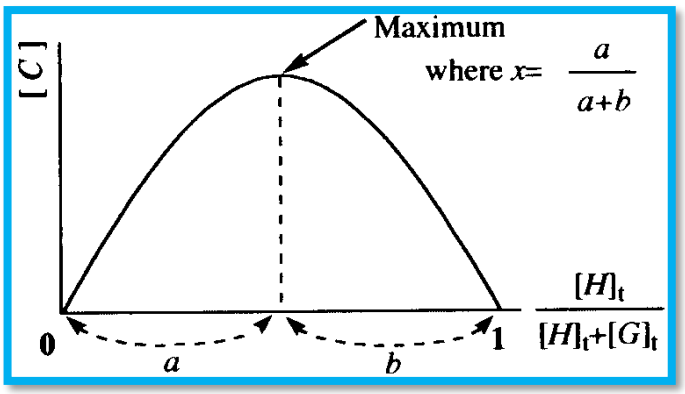
There are different methods of determining the stoichiometry, e.g., *Continuous Variation Methods, Slope Ratio Method, Mole Ratio Method,* etc. Because the Continuous Variation Method is the most well-liked among these, this method is adopted here to determine the stoichiometry. In order to determine the stoichiometry by *Continuous Variation Method,* the following four points have to be considered and carried out.

_ keeping sum of $[H]_t$ and $[G]_t$ as constant (α)

_ Changing $[H]_t$ from the value of 0 to α

_ measuring the value of [C]

_ Data treatment (*Job's plot*)



The stoichiometry (a / (a +b)) is obtained from the x coordinate at the maximum in *Job's curve* (Figure above), where the y-axis is [C] and the x-axis is

$$[H]_t / ([H]_t + [G]_t)$$

For comprehension of theoretical background of the *Continuous Variation Method*, the required Equations are

(150) – (153) and (155) – (157).

$$\alpha = [H]_t + [G]_t \qquad (155)$$

$$x = [H]_t / ([H]_t + [G]_t) \qquad (156)$$

$$y = [C] \qquad (157)$$

$[H]_t$ and $[G]_t$ will be substituted by function of x and α from Equations (155) and (156).

$$[H]_t = \alpha . \ x \qquad (158)$$

$$[G]_t = \alpha - \alpha . x \qquad (159)$$

from Equations (150)–(153) and (157)–(159).

$$K = y / \{(\alpha - b. y - \alpha . x)^{b}. (\alpha . x - a .y)^{a}\}$$

$$K. \{(\alpha - b. y - \alpha . x)^{b}. (\alpha . x - a .y)^{a}\} = y. \qquad (160)$$

Equation (160) is then differentiated, and the d*y*=d*x* is substituted by zero. Then the *x*-coordinate at the maximum in the curve is obtained.

$$K . [(\alpha - b . y - \alpha . x)^{b} . \{\alpha . x - a .y)^{a}\}' + \{(\alpha - b . y - \alpha . x)^{b}\}' . (\alpha . x - a.y)^{a}] = dy / dx$$

$$K . [(\alpha - b. y - \alpha . x)^{b}. a. (\alpha . x - a . y)^{a-1} . (\alpha - a. dy/dx) + b. (\alpha - b. y - \alpha .x)^{b-1}. (- b. dy/dx - \alpha) . (\alpha . x - a.y)^{a}] = dy / dx$$

The substitution of (d*y*=d*x)* by zero is derived as follows.

$$K . [(\alpha - b . y - \alpha . x)^{b} . a . (\alpha . x - a . y)^{a-1} . \alpha + b. (\alpha - b . y - \alpha . x)^{b-1} . (-\alpha) . (\alpha . x - a.y)^{a}] = 0$$

Subtraction by $K \cdot (\alpha - b \cdot y - \alpha \cdot x)^{b-1} \cdot (\alpha \cdot x - a \cdot y)^{a-1} \cdot \alpha$ produces

$$a \cdot (\alpha - b \cdot y - \alpha \cdot x) - b \cdot (\alpha \cdot x - a \cdot y) = 0$$

$$a \cdot \alpha - a \cdot b \cdot y - a \cdot \alpha \cdot x - b \cdot \alpha \cdot x + b \cdot a \cdot y = 0$$

$$a \cdot \alpha - a \cdot \alpha \cdot x - b \cdot \alpha \cdot x = 0$$

Subtraction by α

$$a - a x - b x = 0$$

$$\therefore x = (a / a + b) \qquad (161)$$

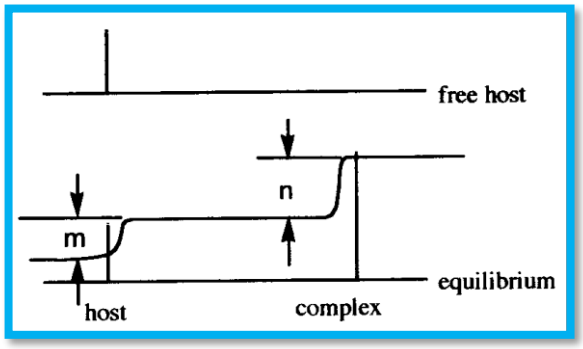
Equation (161) means $a / a + b$ is the x-coordinate at the maximum ($dy / dx = 0$) in the curve of Equation (160). Equation (161) shows the correlation between the stoichiometry and the x-coordinate at the maximum in Job's plot. For example, when **1: 1 complexation is predominant at equilibrium, the maximum appears $x = 0.5$ ($a = b = 1$). In the case of 1: 2 complexation $x = 0.333$ gives the maximum.**

The practically significant point here is the following. Even if the concentration of the complex ([C]) could not be calculated directly, the [C] (y-axis) would be replaced with a property proportional to [C]. Then the same x-coordinate can be obtained at maximum as that in Job's plot. This means stoichiometry can be determined still if [C] could not be obtained. The important point is how to adjust the y-coordinate. Depending on every experiment, there is a property which is suitable for the replacement of [C]. When observed property is the complex concentration ([C]) at equilibrium itself, there is no difficulty. But actual complex concentration is not observed directly in the majority cases. How to evaluate [C] is thus an important point. The practical way depends on property that can be observed in every experiment. In this sector, representative examples for evaluation of complex concentration at equilibrium are given: concerning to the UV-visible and NMR, examples are mentioned below.

NMR Spectroscopy

In our study concerning NMR spectrometric method, it should be classified into two cases by the difference in the exchange rate. In the case where ***host-guest complexation*** equilibrium has a similar exchange rate compared to NMR time scale, NMR peaks broaden and/or disappear, so it is impossible to measure. There are following two cases suitable for measurement by NMR spectroscopy.

Case 1: The Host-guest complexation equilibrium, which has an extremely slow exchange rate compared to NMR time scale. In this case peaks which are assigned to host parts in the complex and those to free host are observed individually in the same NMR spectrum. Those peaks emerge at individual chemical shifts.



Representation of NMR spectra for slow exchange of complexation equilibrium.

In Figure above, there is a representative NMR spectrum where the peaks, which are assigned to a free or complexed host, are observed individually with integration ratio *m* to *n*. The composition of the complex is H_aG_b. Then, the integration of host parts in the complex over the total integration of the host parts is as follows.

$$a.\,[C] / [H]_t = n / m + n$$

$$\therefore\ n / m + n\ \ [H]t = a\,.\,[C] \qquad (162)$$

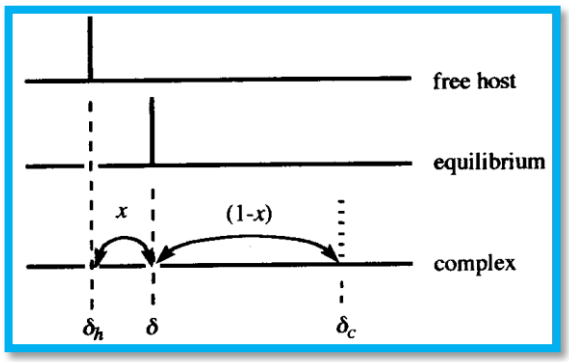
The stoichiometry is determined from the x-coordinate at the maximum in the curve which might be called a modified Job's plot where (n / (m + n)). $[H]_t$ is plotted as the y-coordinate instead of [C], for the following reasons. Equation (162) means that (n / m + n)). $[H]_t$ is proportional to [C] since a is constant.

* $[H]_t$ can be set up in the experimental condition.
* The ratio of n / (m + n) is obtained from NMR spectral data.

When the stoichiometry (a) is obtained, [C] is determined using the experimental condition ($[H]_t$) according to Equation (163), since (n / m + n) is obtained from the NMR measurement.

$$[C] = 1 / a.\ (n / (m + n)).\ [H]_t \qquad (163)$$

Case 2: The host-guest complexation equilibrium, which has a very fast exchange rate compared to the NMR time scale.



Representative of NMR spectra for fast exchange of complexation indicating correlation of complexation ratio *x* and each spectrum.

In this case the peaks which are assigned to host parts in the complex and those to the free host are fused. In Figure above, there is a representative NMR spectrum where peaks, which are assigned to the free and complexed host parts, are fused and appear at the weight average chemical shift of the free host and complexed host. In this case:δ, observed chemical shift; δ_h, δ_c, chemical shifts of the host part in free and complexed host, respectively; x, ratio of complexed host at equilibrium over total host

$$\delta = \delta_h . (1 - x) + \delta_c . x \qquad \text{where } x = a . [C] / [H]_t$$

$$\therefore [H]_t . (\delta - \delta_h) = a . [C] . (\delta_c - \delta h). \qquad (164)$$

The stoichiometry is determined from the x-coordinate at the maximum in the curve which might be called a modified Job's plot where $[H]_t . (\delta - \delta_h)$ is plotted as y-coordinate instead of [C] for the following reasons.

- Equation (164) means that $[H]_t . (\delta - \delta_h)$ is proportional to [C], since $a . (\delta_c - \delta_h)$ is constant.
- $[H]_t$ can be set up in the experimental condition.
- The $(\delta - \delta_h)$ are obtained from NMR spectral records.

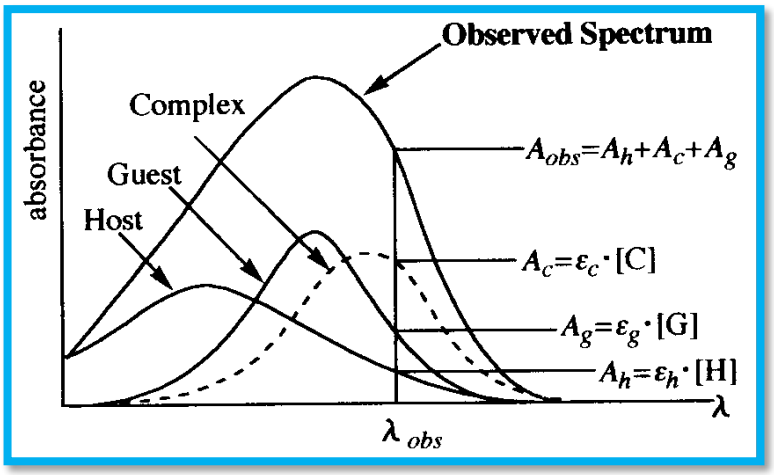
This case is often observed for complexation with crown ether and an amine. Equation (149) is derived from Equation (148) just by simple transformation.

$$[C] = 1 / a . (\delta - \delta_h) / (\delta_c - \delta_h) . [H]_t \qquad (165)$$

If all constants (a, δ_h, δ_g and δ_c) were obtained, [C] would be determined using the experimental condition ($[H]_t$). Since δ_c is not obtained directly, a titration experiment and regression are necessary for the evaluation of the complex concentration.

UV-visible Spectroscopy

In the case of investigation via UV-visible spectroscopy, the concentrations and absorbances of each species are related by the following equations (166)–(168). And the observed absorbance is expressed as Equation (169) and Figure below.



The length of cell fixed here to 1 cm as a premise. Definitions of abbreviations are given below. The definitions of other abbreviations (a, b, $[H]_t$, $[G]_t$, [H], [G], [C]) are similar as described before (A_{obs}, observed absorbance; A_h, A_g, A_c, absorbances of host, guest, and complex respectively; $\in_h$, $\in_g$, $\in_c$: molar absorptivities of host, guest, and complex, respectively).

$$A_h = \in_h . [H] = \in_h . ([H]_t - a . [C]) \quad (166)$$

$$A_g = \in_g . [G] = \in_g .([G]_t - b . [C]) \quad (167)$$

$$A_c = \in_c . [C] \quad (168)$$

$$A_{obs} = A_h + A_g + A_c \quad (169)$$

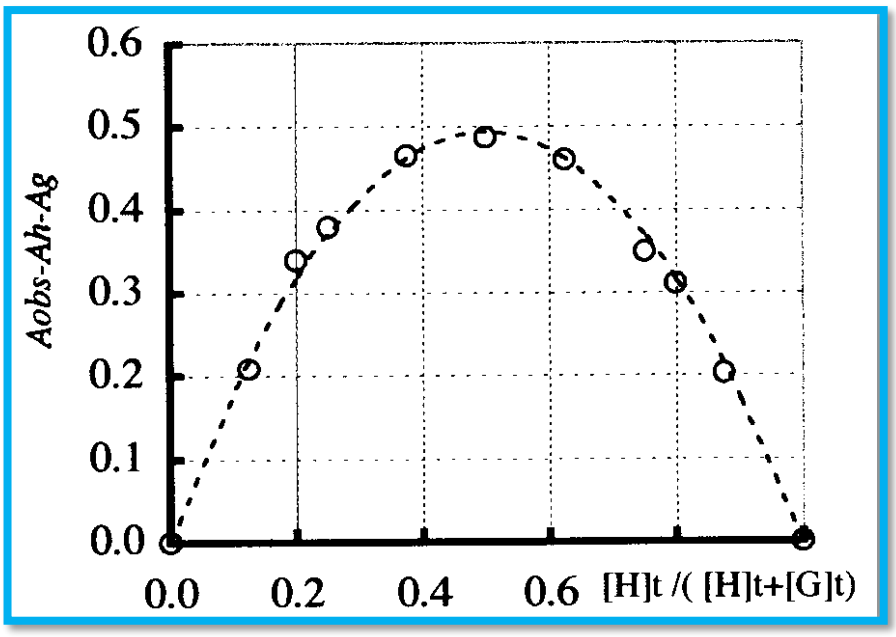
Equation (169) is transformed to Equation (170) by using Equations (166)–(168).

$$Aobs = \in_h . ([H]_t - a . [C]) + \in_g .([G]_t - b[C]) + \in_c .[C]$$

$$\therefore A_{obs} - \in_h . [H]_t - \in_g . [G]_t$$

$$= (\in_c - a . \in_h - b . \in_g). [C] . \quad (170)$$

Equation (170) shows $A_{obs} - \in_h .[H]_t - \in g .[G]_t$ is proportional to [C] because ($\in_c - a . \in_h - b . \in_g$) is constant. The molar absorptivities $\in_h$, $\in_g$ is determined from other measurements using pure host and pure guest, respectively. The concentrations $[H]_t$ and $[G]_t$, are known as they are experimental conditions. Consequently, ($A_{obs} - \in_h . [H]_t - \in_g . [G]_t$) is determined from experiments.



Case 1: the absorption bands of host, guest and complex are overlapped From Equation (170), the following equation (171) is derived.

$$[C] = A_{obs} - \epsilon_h \,.\, [H]_t - \epsilon_g \,.\, [G]_t \,/\, \epsilon_c - a \,.\, \epsilon_h - b \,.\, \epsilon_g \qquad (171)$$

If all the constants (a; b; ϵ_h; ϵ_g and ϵ_c) were known, [C] would be determined using experimental condition ($[H]_t$, $[G]_t$) and the observed property (A_{obs}). Since molar absorptivity of the complex (ϵ_c) is not measurable directly, a titration experiment and regression are necessary for evaluation of the complex concentration. This is most complicated case of host-guest complexation detecting by means of UV-visible spectroscopy because the absorption bands of all components, host, guest and complex, are overlapped. When one component (e.g., guest) whose ϵ is zero, is used, following simplification is applied. Even if ϵ is not zero, the simplification would be carried out normally in such a way that the detection-wavelength is accustomed so that absorption band of one component (e.g., guest) is not overlapped with those of other species (e.g., the host and complex).

Case 2: the absorption bands of two components are overlapped. The equation for this case is expressed by Equation (172), which is derived just by substitution of ϵg by zero from Equation (171).

$$[C] = A_{obs} - \epsilon_h . [H]_t \,/\, \epsilon_c - a\ \epsilon_c - a . \epsilon_h \qquad (172)$$

Compared to Equation (171), Equation (172) is simplified. Because three parameters (b, ϵg, and $[G]_t$) disappear from Equation (171), data-treatment is much simplified. If all constants (a, ϵ_h and ϵ_c) were obtained, [C] would be determined using experimental condition ($[H]_t$). Since

molar absorptivity of complex ($\in_c$) is not measurable directly, a titration experiment and regression are necessary for the evaluation of the complex concentration in this case.

General observation

The titration experiment in order to collect data for a reliable *K* value is known. Some are approximation methods which must be employed under some premises, and some are just a regression method. Typical examples of the approximation method are *Benesi* and *Hildebrand, Ketelaar, Nagakura and Baba, Scott, Scatchard* and *Hammond*, where $[G]_t$ is used approximately instead of $[G]$.

From Equations (151) and (153) and $a = b = 1$,

$$[G]t = [G] + K.[H].[G]$$

$$\therefore [G]t = [G](1 + K.[H]) \qquad (173)$$

If K . [H] << 1, then it would be safely assumed that [G]t = [G]. This condition is frequently encountered in weak complexation, where K is small. The condition [G]t >> [H]t is employed for the practical titration. Actually, an important point for this approximation is the condition K . [H] << 1; nevertheless, the condition [G]t >> [H]t is thought to be essential. All systems cannot be investigated under this condition [G]t >> [H]t (K . [H] << 1).

When assumption $[G]_t = [G]$ cannot be applied, other approximation or regression methods have to be employed. Here regression method is shown. Typical examples of regression techniques are *Rose and Drago, Nakano and Creswell and Allred*. Because of the wide applicability, I decided to explain a practical guide based on *Rose-Drago* method, by means of examples, one for UV-visible spectroscopy and for NMR spectroscopy. Originally the *Rose-Drago method* was used for UV-visible spectroscopy for evaluating an acid-base equilibrium, molecular addition compound of iodine. The only assumption for this original method is there are at most two observing species which obey *Beer's law* in the concentration range employed. There is no extra assumption. So it is broadly applicable. The results are presented graphically in this technique and by inspection one can quantitatively determine the precision. Firstly, a case is described where all components are observed and overlapped, which obey *Beer's law* in the concentration range employed. Secondly, the way to apply this original *Rose-Drago method* to NMR spectroscopy, especially for host-guest system with a fast exchange rate is described.

Rose-Drago method for UV-visible spectroscopy

Here equilibrium of 1: 1 host-guest complexation detected by UV-visible spectroscopy is discussed. The observed property was thus absorbance. The absorbance data of titration experiment were collected. For data-treatment of this general technique, a spreadsheet program was formatted.

$a = b = 1$ is substituted into Equation (154). Then the reciprocal is

$$1/ K = [C] – ([H]_t + [G]_t) + [H]_t . [G]_t / [C] \quad (174)$$

Combining Equation (171) with Equation (174) gives

$$1/ K = A_{obs} – \in_h . [H]_t – \in_g . [G]_t \quad / \in_c – \in_h – \in_g – ([H]_t + [G]_t) + \in_c – \in_h – \in_g / A_{obs} – \in_h . [H]_t – \in_h . [G]_t . [H]_t . [G]_t. \quad (175)$$

This is most complicated host-guest complexation, detecting by means of UV-visible spectroscopy because absorption bands of all components, host, guest and complex are overlapped. First of all, the constants $\in_h$, and $\in_g$ in Equation (175) have to be obtained without a titration experiment, because they are molar absorptivities of pure host and guest, correspondingly. Then it should be carried out to measure A_{obs} at different combinations of $[H]_t$ and $[G]_t$ followed by regression of obtained data with Equation (175). Theoretically, A_{obs} values at more than two different combinations of $[H]_t$, $[G]_t$ give two unknowns, K and $\in_c$. Measurement of absorbance at diverse combinations of [H]t and [G]t supplies matrix $\{A_{obsn}; [H]_{tn}; [G]_{tn}\}$ consisting of 3 elements: A_{obsn}, observed absorbance at nth condition; $[H]_{tn}$, total concentration of host at first stage at nth condition; $[G]_{tn}$, total concentration of guest molecule at initial stage at nth condition. Combining Equation (175) and definitions (176)–(180) leads to Equation (181).

$$Y = 1 / K \quad (176)$$

$$X = \in_c – \in_h – \in_g \quad (177)$$

$$a_n = A_{obsn} – \in_h .[H]_{tn} – \in_g . [G]_{tn} \quad (178)$$

$$b_n = [H]_{tn} + [G]_{tn} \quad (179)$$

$$c_n = [H]_{tn} . [G]_{tn} / A_{obsn} – \in_h . [H]_{tn} – \in_g . [G]_{tn} \quad (180)$$

Then

$$Y = a_n / X – b_n + c_n . X. \quad (181)$$

According to Equation (181), one combination of data (e.g., $\{A_{obs1}; [H]_{t1}; [G]_{t1}\}$, $\{A_{obs2}, [H]_{t2}, [G]_{t2}\}$ supplies a matrix of answer {X; Y}. Representative solution is as follows. As an example,

one combination of data where n = 1, n = 2 (e.g., $\{A_{obs1}, [H]_{t1}, [G]_{t1}\}$ and $\{A_{obs2}, [H]_{t2}, [G]_{t2}\}$) is used here

$$Y = a_1 / X - b_1 + c_1 . X \quad (182)$$

$$Y = a_2 / X - b_2 + c_2 . X. \quad (183)$$

Subtracting both sides, followed multiplying both sides by X results in

$$(c1-c2).X^2 + (b1 - b2) . X + (a1 - a2) = 0 \quad (184)$$

$$\therefore X = -(b1-b2) \pm \sqrt{(b1-b2)^2 - 4.(c1 - c2).(a1 - a2)} / 2 .(c1 - c2) \quad (185)$$

Substituting Equation (182) with Equation (185) derives Y. The obtained {X; Y} is merely an answer which satisfies both Equations (182) and (183), but it is not the chemically correct answer. For example, chemically Y should have a positive sign. Based on such chemical limitation, correct sets of answer should be collected. The maximum number of obtained answer pairs {X; Y} is the ${}_nC_2$ pairs for n combinations of concentration conditions. For example, 5 pairs of $\{[H]_{tn}; [G]_{tn}\}$ bestow 10(= ${}_5C_2$) pairs of {X; Y}. These {X; Y} are obtained under the principle of 1: 1 complexation. No approximation is thus introduced into this solution. The reciprocal of Y is binding constant K. The number of obtained K in this stage may be ${}_nC_2$.

Rose-Drago method for NMR spectroscopy

Using equilibrium of the 1: 1 host-guest complexation as an example, the way to apply the original *Rose-Drago method* to NMR spectroscopy is known here. As mentioned previously, host–guest complexations are classified into two for determination of binding constants by means of NMR spectroscopy. When host-guest complexation equilibrium is a very slow exchange rate compared to NMR time scale, the concentration of complex is expressed as follows (a = 1 in Equation (163)).

$$[C] = n / m + n. [H]_t \quad . \quad (186)$$

When the host-guest complexation equilibrium has a very fast exchange rate compared to the NMR time scale, the concentration of the complex is expressed as follows (a = 1 in Equation (149)).

$$[C] = \delta - \delta_h / \delta_c - \delta_h . [H]_t . \quad (187)$$

From Equations (174) and (187), the following equation is derived.

$$1/ K = (\delta - \delta_h) .[H]_t / (\delta_c - \delta_h) - ([H]_t + [G]_t) + (\delta_c - \delta_h) / (\delta - \delta_h) . [G]_t . \quad (188)$$

Here we carried out substitution using the following definitions (189)–(62).

$$Y = 1 / K \quad (189)$$

$$X = \delta_c - \delta_h \quad (190)$$

$$a_n = (\delta_n - \delta_h) \,.\, [H]_{tn} \quad (191)$$

$$b_n = [H]_{tn} + [G]_{tn} \quad (192)$$

$$c_n = [G]_{tn} / (\delta_n - \delta_h) \quad (193)$$

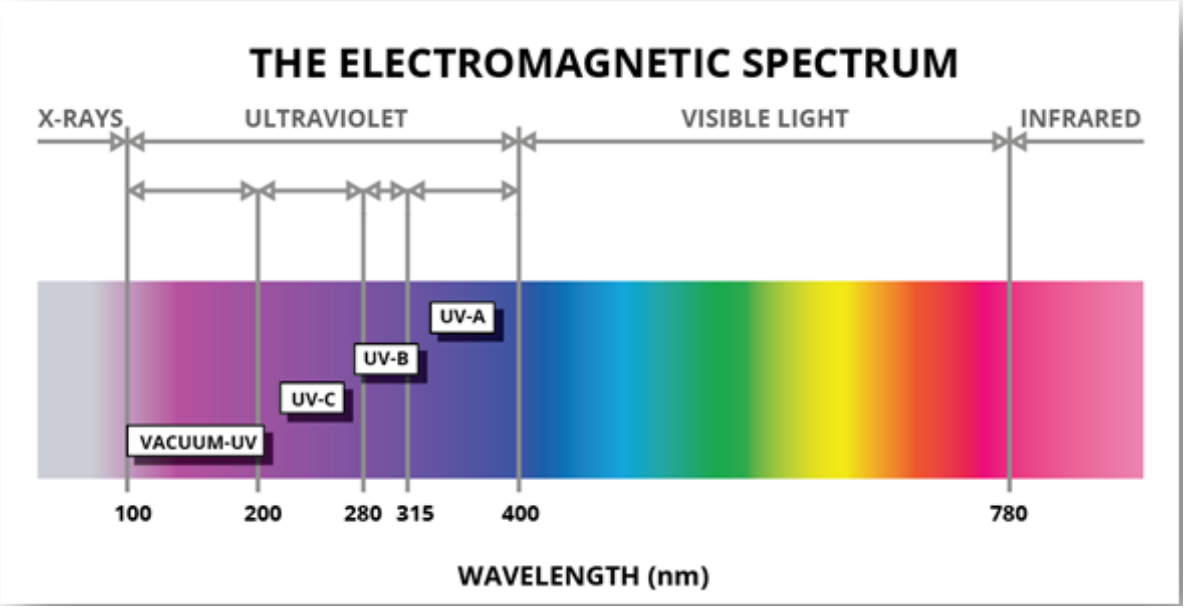
Then Equation (188) is expressed as follows.

$$Y = a_n / X - b_n + c_n \,.\, X. \quad (194)$$

Equation (194) is the same as Equation (181). So from this stage, the same procedures for UV-visible spectroscopy can be functional for NMR spectroscopy. The determination of a binding constant at assorted temperatures would be a useful way to reveal the effective criteria for molecular design under consideration of an entropy effect together with an enthalpy effect. For an understanding of basic theoretical principle, a practical measurement and also a practical data-treatment of an experiment to determine a binding constant, using a basic level of mathematics, statistics, and programs of spreadsheet software is used. It is believed the programs attached as appendices would function with commonly available spreadsheet software on computers. It is hoped the style of this article is one of the better ways at this time to provide to chemists, information on how to determine binding constants.

♣ *UV-Vis Spectrophotometric Determination*

The electromagnetic spectrum consists of Ultraviolet (UV) and visible radiation comprise only a small part, which includes such other forms of radiation as radio, infrared (IR), cosmic, and X rays. [450-455]



The visible and ultraviolet spectra of ions and molecules are associated only with transitions between electronic energy levels of certain types or functional groups of molecules and do not characterize the molecule as a whole. The energies involved in these transitions are in range of 30 –to several hundred k cal/mole.

Region	Wavelength (nm)	Region	Wavelength (nm)
Far ultraviolet	10-200	Middle infrared	3000-30,000
Near ultraviolet	200-380	Far infrared	30,000-300,000
Visible	380-780	Microwave	300,000-1,000,000,000
Near infrared	780-3000		

The human eye is only sensitive to a tiny proportion of total electromagnetic spectrum between approximately 380 and 780 nm and within this area we perceive colors of the rainbow from violet through to red.

To achieve an understanding of origins of practical absorption spectrometry, a short diversion into quantum theory is compulsory. For this reason, its best to think of radiation as a stream of particles identified as photons instead of waves considered formerly. Atoms and molecules exist in a number of defined energy states or levels along with a change of level requires absorption or emission of an integral number of a unit of energy known as quantum, or in our context, a photon. The energy of a photon absorbed or emitted during a transition from one molecular energy level to another is given by equation $E= h\nu$

where h is known as the Planck's constant and v is the frequency of the photon. We have already seen that $c= \nu\lambda$, therefore, $E= hc/\lambda$.

Thus, shorter the wavelength, greater the energy of the photon and vice versa. A molecule of any substance has an internal energy which can be considered as summation of the energy of its electrons, the energy of vibration between its constituent atoms and energy associated with rotation of the molecule. The electronic energy levels of simple molecules are extensively separated and usually the absorption of a high energy photon, that is one of very short wavelength, can excite a molecule from one level to another.

In complex molecules energy levels are more closely spaced and photons of near ultraviolet and visible light can affect transition. These substances, therefore, will absorb light in some areas of near ultraviolet and visible regions. The vibrational energy states of various parts of a molecule are much closer together than electronic energy levels and thus protons of lower energy (longer wavelength) are sufficient to bring about vibrational changes. Light absorption owing to vibrational changes occurs in infrared region. The rotational energy states of molecules are so closely spaced that light in far infrared and microwave regions of electromagnetic spectrum has enough energy to cause these small changes.

For ultraviolet and visible wavelengths, one ought to expect from this debate is that absorption spectrum of a molecule (i.e., a plot of its degree of absorption alongside wavelength of the incident radiation) must display a few sharp lines. Each line should occur at a wavelength where energy of an incident photon exactly matches energy required to excite an electronic transition. In practice it is found that ultraviolet and visible spectrum of majority molecules consists of a few humps slightly than sharp lines. These humps show that molecule is absorbing radiation over a band of wavelengths. One more cause for this band, rather than line absorption is that an electronic level transition is in general accompanied by a

simultaneous transform amongst numerous vibrational levels. Thus, a photon with a little too much or too little energy to be accepted by molecule for a 'pure' electronic transition can be utilized for a transition between one of vibrational levels associated with lower electronic state to one of the vibrational levels of a higher electronic state. If difference in electronic energy is 'E' and difference in vibrational energy is 'e', then photons with energies of E, E+e, E+2e, E-e, E-2e, etc. will be absorbed. Furthermore, each of the several vibrational levels associated with the electronic states also has large number of rotational levels associated with it. Thus a transition can consist of a large electronic component, a smaller vibrational element and even smaller rotational change. The rotational contribution to transition has effect of filling in the gaps in vibrational fine configuration. In addition, when molecules are closely packed together as they normally are in solution, they exert influences on each other which slightly agitate the already numerous, and almost infinite energy levels and blur the sharp spectral lines into bands. These effects can be seen in spectra of benzene as a vapor and in solution. In vapor, the transitions between the vibration levels are visible as bands superimposed on the main electronic transition bands. In solution they merge together and at high temperature or pressure even the electronic bands can blur to produce single wide band such as that enclosed by the dotted line.

Relationship between light absorption and color

Color absorbed	Color observed	Absorbed radiation(nm)
Violet	Yellow-green	400-435
Blue	Yellow	435-480
Green-blue	Orange	480-490
Blue-green	Red	490-500
Green	Purple	500-560
Yellow-green	Violet	560-580
Yellow	Blue	580-595
Orange	Green-blue	595-605
Red	Blue-green	605-750

A close relationship exists between color of a substance and its electronic structure. A molecule or ion will exhibit absorption in visible or ultraviolet region when radiation causes an electronic transition within its structure. Thus, absorption of light via a sample in ultraviolet or visible region is accompanied by a change in electronic state of molecules in the sample. The energy supplied by light will promote electrons from their ground state orbitals

to higher energy, excited state orbitals or antibonding orbitals. Potentially, three types of ground state orbitals may be involved: σ (bonding), π (bonding), n (non-bonding). In addition, two types of antibonding orbitals may be concerned in the transition:

i) σ* (sigma star) orbital

ii) π* (pi star) orbital

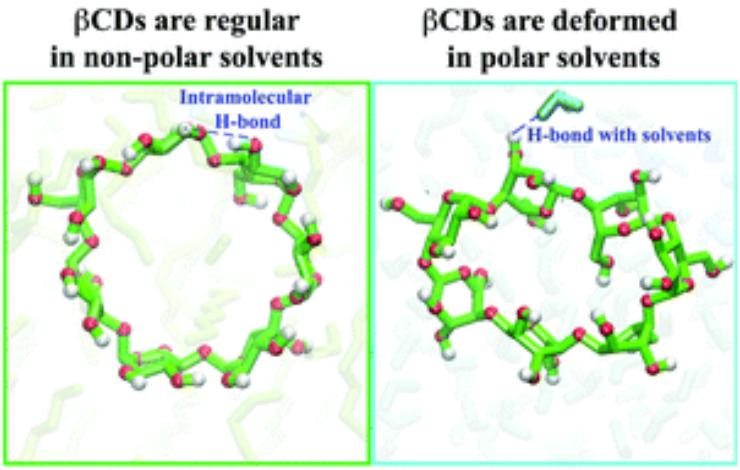
(There is no such thing as an n* antibonding orbital as n electrons do not form bonds).

A transition in which a bonding s electron is energized to an antibonding σ orbital is referred to as σ to σ* transition.In same way π to π* represents the transition of one electron of a lone pair (non-bonding electron pair) to an antibonding π orbital. Thus following electronic transitions can occur by the absorption of ultraviolet and visible light.

Both s to σ* and n to σ* transitions need an immense deal of energy and therefore occur in far ultraviolet region or weakly in region (180-240) nm. Accordingly, saturated groups don't exhibit strong absorption in ordinary ultraviolet region. Transitions of n to π* and π to π* kind occur in molecules by means of unsaturated centers; they require a smaller amount energy and arise at longer wavelengths than transitions to σ* antibonding orbitals.

It will be seen currently that wavelength of maximum absorption and intensity of absorption are determined via molecular arrangement. The transitions to π* antibonding orbitals, takes place into ultraviolet region for a particular molecule may even take place in the visible region if molecular structure is customized. A lot of inorganic compounds in solution also illustrate absorption in the visible region. These include salts of elements with incomplete inner electron shells (mainly transition metals) whose ions are complexed by hydration e.g. $[Cu(H_20)_4]^{2+}$. Such absorptions arise from a charge transfer process, where electrons are moved from one part of system to another by the energy provided by visible light.

In our investigation, UV-Visible absorption spectroscopy is a commonly used technique for the determination of equilibrium constants, particularly in biochemical applications. For example, binding constant of an inhibitor to an enzyme is a routine determination. In my lab I studied the binding of a cyclic-polysaccharide to a small molecular guest and various imperative compounds. Some of the review works are depicted as follows: Purpose was to determine the equilibrium constant for binding of ß-cyclodextrin and ß-naphthol. This reaction is a good example of a guest-host complexation.



In the aqueous solution CH bonds on rings point inward producing a hydrophobic cavity inside a cylinder of diameter 15.4 Å. The OH groups extend from top and bottom of the cylinder, providing sites for strong hydrogen bond formation. On average about 11 water molecules fit inside cylinder. The cavity volume is therefore 0.14 mL/g. Cyclodextrins bind with a broad variety of substances. Such complexes are examples of guest-host complexes, where cyclodextrin is the host which we have also used in our various investigations in lab.

ß-Naphthol is representative of a wide variety of guests; many compounds have the same bifunctional nature. ß-Naphthol is expected to bind to CD for the reason that it has a hydrophobic Guest-Host: cyclodextrin -2- group that fits into cyclodextrin cavity, while OH group participates in hydrogen bonds with the sugar OH groups. The reaction stoichiometry is 1:1

$$\text{CD} + \text{ß-naphthol} \rightarrow [\text{CD}...\text{ß-naphthol}] \qquad (195)$$

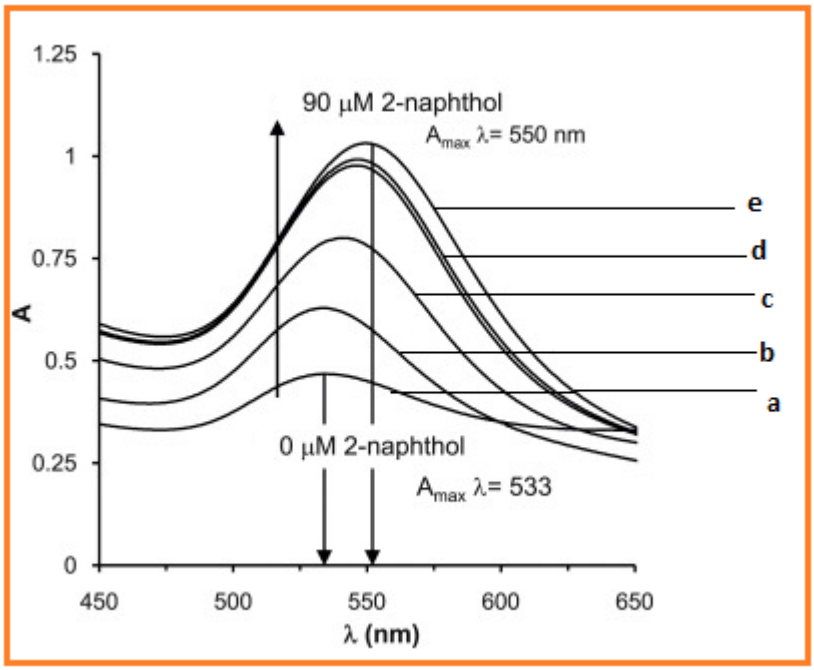
Some water molecules originally in the cavity will be excluded in the complexation. This change in number of water molecules in the cavity has an imperative effect on the binding enthalpy and entropy.

Theory: *Beer-Lambert Law* describes the absorption of light in solution. The absorbance is defined as A = -log I/Io, where Io is intensity of light falling on the cuvette, and I is light intensity leaving the cuvette. Given the path length of the cuvette, b, and the molar concentration of the absorbing species, c:

$$A = [a\ b\ c] \qquad (196)$$

where a is molar absorption coefficient. The molar absorption coefficient is unique to each substance and depends on wavelength of the light used. The complexation of ß-naphthol to

CD causes a little red shift in the absorbance maxiumum and a large increase in molar absorption coefficient, Figure below depicts it.



The increase in the molar absorption is presumably caused by naphthalene ring being complexed in hydrophobic interior of the cyclodextrin cavity. The change in absorbance with concentration of CD will be used to determine the equilibrium constant for binding. The equilibrium constant for the reaction in (Eq. 195) is:

$$K = [CDN] / [CD][N] \qquad (197)$$

where N is uncomplexed [ß-naphthol] and [CDN] is [ß-naphthol-CD] complex. The solutions in this experimentation will be made up with a constant concentration of ß-naphthol and varying amounts of CD. Let initial concentration of ß-naphthol be Co and using (Eq. 196) gives the absorbance of the solution with no CD, A^o, as:

$$A^o = a_N b C_0 \qquad (198)$$

where a_N is molar absorption coefficient of uncomplexed [ß-naphthol] . If a large excess of CD

is added, the entire of the ß-naphthol will be complexed. The absorbance with a large excess of CD, A^∞,

is: $$A^\infty = a_{CDN} b C_o \qquad (199)$$

where a_{CDN} is molar absorption coefficent of complexed ß-naphthol . For intermediate concentrations of CD, ß-naphthol will thus be in uncomplexed and complexed forms. The absorbance of the solution will be sum of the absorbances of the uncomplexed and complexed forms.

$$A = a_N\, b\, [N] + a_{CDN}\, b\, [CDN] \qquad (200)$$

Since complex is formed with 1:1 stoichiometry:

$$[N] = C_o - [CDN] \qquad (201)$$

or alternatively solving for [CDN] from Eq. 201 gives

$$[CDN] = Co - [N] \qquad (202)$$

We now need to solve for [CDN] and [N] in terms of measured absorbances. To find [CDN], first substitute Eq. 201 into Eq. 200:

$$A = a_N\, b\, C_o - a_N\, b\, [CDN] + a_{CDN}\, b\, [CDN] \qquad (203)$$

Next find the difference [A-A^o] by subtracting Eq. 198 from Eq. 203:

$$A - A^o = - a_N\, b\, [CDN] + a_{CDN}\, b\, [CDN] = (a_{CDN}\, b - aN\, b)\, [CDN] \qquad (204)$$

Finally, solving [CDN]:

$$[CDN] = A - A^o / (a_{CDN}\, b - a_N\, b) \qquad (205)$$

To find [N], first substitute Eq. 202 into Eq. 200:

$$A = a_N\, b\, [N] + a_{CDN}\, b\, C_o - a_{CDN}\, b\, [N] \qquad (206)$$

and then subtract Eq. 206 from Eq. 199:

$$A^\infty - A = - a_N\, b\, [N] + a_{CDN}\, b\, [N] = (a_{CDN}\, b - a_N\, b)\, [N] \qquad (207)$$

Finally, solving for [N]:

$$[N] = A^\infty - A / (a_{CDN}\, b - a_N\, b) \qquad (208)$$

Let nominal concentration for CD is C_b. The CD in solutions will be in excess so approximate:

$$[CD] = C_b - [CDN] \cong C_b \qquad (209)$$

We now substitute Eqs. 205, 208, and 209 into the equilibrium constant formula, Eq. 197, to give:

$$K = (A - Ao) / (A^{\infty} - A)\, C_b \qquad (210)$$

In our experiments also similarly we vary concentration of CD and measure the absorbance of resulting solutions, A. To suitably calculate K, we need to rearrange Eq. 210 into straight line form, (y=mx+b). First, cross multiply in Eq. 210 to give:

$$(A^{\infty} - A) = (A - Ao) / K\, Cb \qquad (211)$$

Now rearrange to give:

$$A = A^{\infty} - 1 / K\, ((A - A^{o}) / C_b\,) \qquad (212)$$

Therefore, a plot of A verses $(A - A^{o}) / C_b$ should give a straight line with slope -1/K. [456]

♣ *Fluorescence Spectroscopy*

Basic Principles: Absorption and Emission of Light

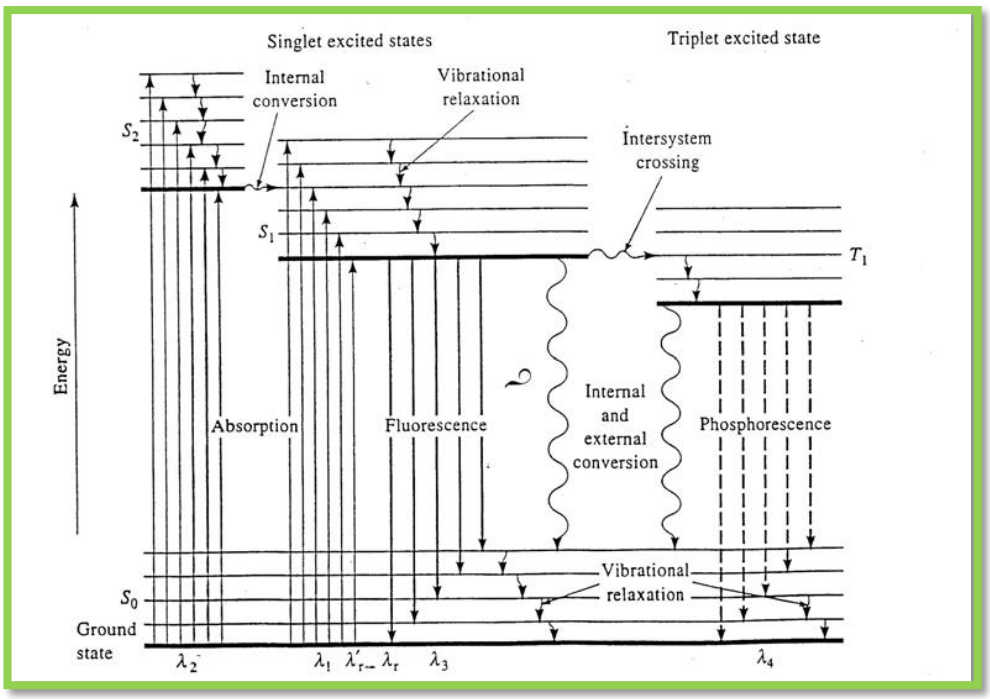
As fluorophores plays essential role in fluorescence spectroscopy and imaging we started an investigation of their manifold interactions with light. A fluorophore is a constituent that causes a molecule to absorb energy of specific wavelength and re-remit energy at a different but equally specific wavelength. The amount and wavelength of emitted energy depend on equally fluorophore and the chemical environment of the fluorophore. Fluorophores are also denoted as chromophores, historically talking the part or moiety of a molecule responsible for its color. [457]

- *Stokes Law* stated a maximum of fluorescence spectrum is red-shifted compared to a maximum of corresponding absorption spectrum. (Reasons: Franck-Condon rule).
- *Mirror Image Rule* stated a fluorescence spectrum (plotted in energy scale) strongly resembles the mirror image of the absorption spectrum. (Reason: the vibrational energy level spacing is similar for the ground and excited states).
- Universal Relationship *(*betwen *Abs-Flu):* $W_{fl}(v) = C(T) \cdot K(v)Abs \cdot \exp(- h v / kT)$.
- *Kasha-Vavilov Rule*: fluorescence spectrum shows very little dependence on the wavelength of excitation. (Reasons: the emission occurs exclusively from the lowest singlet excited electronic state).

In addition, the denotation chromophore implies that molecule absorbs light while fluorophore means that molecule, likewise, emits light. The umbrella idiom used in light

emission is luminescence, whereas fluorescence denotes allowed transitions with lifetime in nanosecond range from the higher to lower excited singlet states of molecules.

Below a wavelength of 200nm energy of the single photon is sufficient to ionize molecules. For that reason, photochemical decomposition is most probable to occur when unsaturated compounds, where all bonds are produced by σ-electrons, are irradiated with photon energies >6.2 eV. Double and triple bonds as well utilize Π-electrons in adding up to a σ-bond for bonding. In contrast to σ-electrons, which are characterized by rotational symmetry of their wave function with respect to bond direction, Π-electrons are characterized by a wave function having a node at nucleus and rotational symmetry all along a line through the nucleus. Π-bonds are generally weaker than σ-bonds because their (negatively charged) electron density is further from the positive charge of the nucleus, which requires more energy. From perspective of quantum mechanics, this bond weakness is explained by significantly less overlap between components Π-orbitals because of their parallel orientation. These less strongly bound electrons can be so excited by photons with lower energy. If two double bonds are separated via a single bond, double bonds are termed conjugated. Conjugation of double bonds additional induces red-shift in absorption (a so-called bathochromic shift). All fluorophores that have a high absorption in visible part of the spectrum possess numerous conjugated double bonds. Above 200nm only two lowest energy transitions, i.e., n $\rightarrow\Pi^*$ and$\Pi\rightarrow\Pi^*$, are achieved as a consequence of energy obtainable from photons. [458-463]



Jablonski Diagram

Explanation of the process

PART I: The molecule might lose rest of energy also in the form of heat so that the complete path is non-radiative.

PART II: Molecule releases energy in the form of light or UV radiation. This is known as Fluorescence.

PART III: Some energy may be lost in tranfer from S_1 to T_1 in the form of heat. It is known as intersystem crossing (ISC). This path is non- radiative.

Path IV: After ISC, molecule may lose energy in the form of light in going from excited triplet state to the ground state. This is known as phosphorescence.

When sample molecules are exposed to light having an energy that matches a possible electronic transition within molecule, some of light energy will be absorbed as electron will be promoted to a higher energy orbital. As a simple regulation, energetically preferential electron promotion will be from highest occupied molecular orbital (HOMO), generally singlet ground state, (S_0), to lowest unoccupied molecular orbital (LUMO), resulting species is known singlet excited state (S_1). Absorption bands in visible region of spectrum correspond to transitions from ground state of a molecule to an excited state i.e., 40–80 kcal mol^{-1} over aforesaid ground state. As mentioned beforehand, in saturated hydrocarbons in particular,

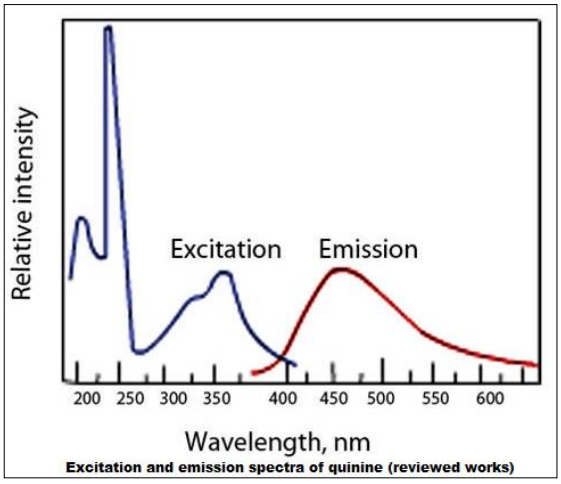
lowest electronic states are more than 80 kcal mol^{-1} greater than ground state, and therefore they do not absorb light in visible region of spectrum. Such substances are thus not colored. Compounds that absorb in visible region of spectrum (these compounds have color) usually and have some weakly bound or delocalized electrons. In these systems, energy difference between lowest LUMO and the HOMO corresponds to energies of quanta in the visible region. One of the most broadly used applications of absorption spectroscopy is the determination of the concentration of substances in solution. Through knowledge of extinction coefficient, e, absolute concentrations can be easily designed using the *Lambert-Beer relationship* ($c = A/\in d$). However, it has to be pointed out here that extinction coefficients of common fluorophores, which are generally in range of 104–105 l mol^{-1} cm^{-1}, do not represent inherently constant parameters. Conjugation of fluorophores to or interactions with supplementary molecules can change the extinction coefficient by influencing, for example, the planarity of the conjugated Π-electron system, thereby affecting transitions strength. Likewise, the extinction coefficient can show a discrepancy with the solvent. Furthermore, dimerization of fluorophores and formation of higher order aggregates in solution and solid state can induce dramatic color changes, i.e, changes of extinction coefficients.

Following absorption, a number of vibrational levels of excited state are populated. Molecules in these higher vibrational levels then relax to lowest vibrational level of the excited state (vibrational relaxation). From lowest vibrational level, several processes can cause molecule to relax to its ground state. The most imperative pathway is: Fluorescence: which corresponds to relaxation of the molecule from the singlet excited state to singlet ground state with emission of light. Fluorescence has short lifetime ($\sim 10^{-8}$ sec) so in numerous molecules it can compete favorably with collisional deactivation, intersystem crossing, and phosphorescence. The wavelength (and thus energy) of light emitted is dependent on energy gap among the ground state and singlet excited state. On the whole energy balance for fluorescence process could be written as:

$$E_{fluor} = E_{abs} - E_{vib} - E_{solv.\ relax} \qquad (213)$$

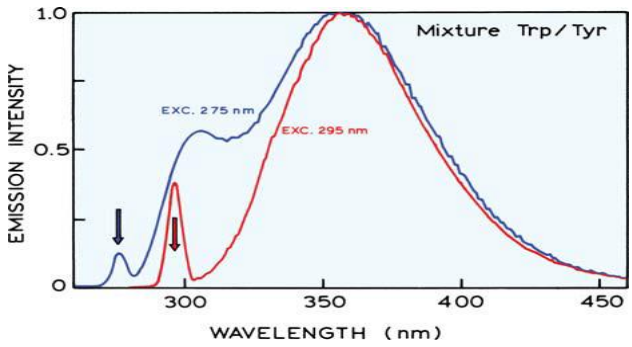
Fluorescence spectra can yield low detection limits, high sensitivity and high specificity. The high specificity is largely because of the fact that fluorophores exhibit specific excitation

(absorption) and *emission (fluorescence)* (used in my research) wavelengths. These wavelengths can be determined by means of the collection of two spectra, an excitation spectrum and an emission spectrum. Although approximate excitation and emission wavelengths for numerous molecules are known, these wavelengths should generally be optimized for the specific conditions employed.



Excitation and emission spectra of quinine (reviewed works)

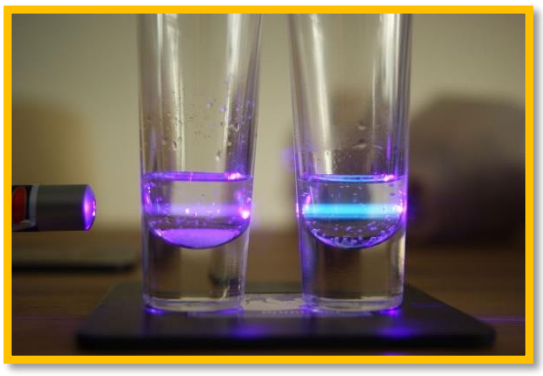
In review works it was shown that when measuring tryptophan or protein emission it is significant to recognize that the emission spectrum of a tryptophan solution that contains a minor amount of tyrosine. Upon excitation at 275 nm tyrosine results in a peak near 300 nm. The fact that this peak is due to tyrosine is shown by spectrum obtained for 295-nm excitation, which shows only tryptophan emission. If emission spectrum of tryptophan alone was recorded at lower resolution, it can readily imagine how broadened Raman line would turn out to be visually similar to tyrosine emission.



Steady-State Fluorescence Spectroscopy investigates the long-term average Fluorescence of a sample when irradiated with UV, Visible or near-IR Light. "Steady-state fluorescence" means fluorescence emitting during steady state. Steady state is statistical concept, which means contribution of fluorophor among different energy levels keeps constant. That is to say, the number of fluorophors lying in excited state and the ground state nearly keeps invariable.

Considering decay of diverse fluorophores is with same possibility, the steady-state fluorescence intensity keeps constant.

'Quenching of Fluorescence' – **Quenching** refers to assorted processes which decrease **fluorescence** intensity of a given substance. A variety of processes can outcome in **quenching**, such as excited state reactions, energy transfer, complex-formation, collisional **quenching.** If the excited molecules are deactivated, fluorescence stops, the phenomenon is known as '*Quenching*'.



- When activated molecules undergo a change from a singlet excited state to triplet excited state. This phenomenon is called *'internal quenching'*.
- When activated molecules collide with the other molecules/quenchers which are the externally added species and transfer their energy to those molecules. This phenomenon is called *'external quenching'*.

STERN-VOLMER EQUATION

The **Stern–Volmer relationship**, named after the renowedScientists *Otto Stern* & *Max Volmer*, allows us to explore kinetics of a photophysical intermolecular deactivation process. The trend for instance *fluorescence*, *phosphorescence* are examples of *intramolecular deactivation(quenching)processes*.

The *Intermolecular deactivation* region leads to subsistence of one more chemical species can accelerate decay rate of a chemical in its excited state. In general, this formula can be represented by the simple equation depicted below:

Considering $[A+h\nu \rightarrow A^* \text{ (Activation)}]$ (214)

Where [A] is chemical species, [Q] is one more (known as a quencher) and [*] designates an excited state.

$$A^* \rightarrow A+h\nu \text{ (Flourescence)} \quad k_1 \quad (215)$$

$$A^* \rightarrow A \text{ (Internal quenching)} \quad k_2 \quad (216)$$

$$A^*+Q \rightarrow A+Q' \text{ (External quenching)} \quad k_3 \quad (217)$$

Intensity of the light absorbed:

$$I_a=k_1[A^*]+k_2[A^*]+k_3[A^*][Q] \quad (218)$$

If I_f represents the intensity of fluorescence,

$$\Phi_f \text{ or } \phi_q=I_f/I_a=k_1[A^*]/k_1[A^*]+k_2[A^*]+k_3[A^*][Q]=K_1/K_1+K_2+K_3[Q] \quad (219)$$

In absence of the quencher, the quantum yield

$$\phi_o=k_1/k_1+k_2 \quad (220)$$

$$\phi_o/\phi_q=k_1+k_2+k_3[Q]/k_1+k_2=1+k_3[Q]/k_1+k_2 \quad (221)$$

Substituting $[1/k_2+k_2=$ ŕ, ϕ_o = *is intensity, or rate of fluorescence]*, without a quencher, ϕ_Q is intensity, or rate of fluorescence, by means of a quencher, k_3 is quencher rate coefficient, ŕ be lifetime of emissive excited state of A, without a quencher present, putting k_3 Ŕ = k_{sv} , i.e., Stern–Volmer constant also denoted as the binding constant in our workings, accordingly (by following previous review works), [Q] is the concentration of the quencher.

$$\phi_0/\phi_Q=1+k_3 Ŕ[Q]$$

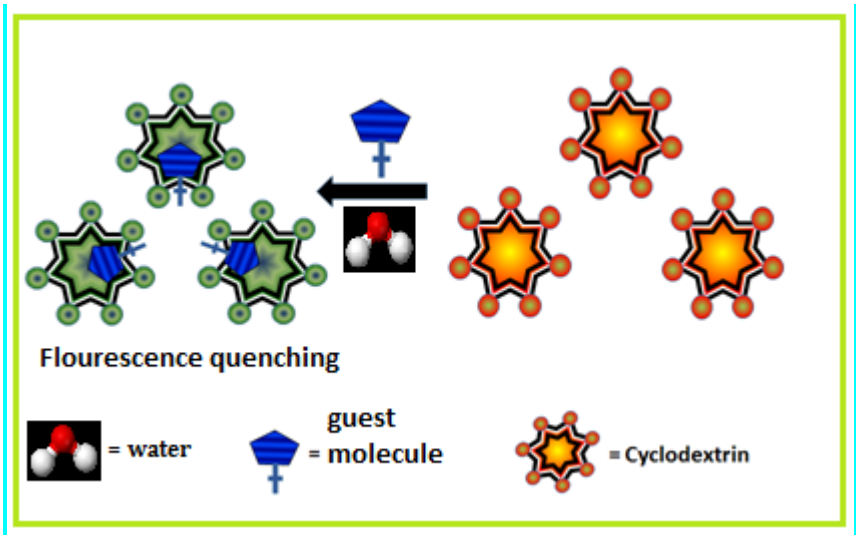
Or

$$\phi_0/\phi_Q=1+k_{sv}[Q] \quad (222)$$

This is known as ***Stern-Volmer*** equation. [471-474]

In the earlier works it was investigated that, fluorescent β-cyclodextrin vesicles (β-CD) that display host cavities available for host–guest interactions at the vesicle surface were prepared by incorporation of the hydrophobic spirobifluorene-based dye **1** into the membrane of unilamellar vesicles. Fluorescence quenching of dye **1** was observed in presence of different quenchers. Methyl viologen **2** does not quench dye **1** for the reason that it does not bind to β-CDV. 4-Nitrophenol **3** and 4-nitrophenol covalently connected to adamantane **4** quench fluorescence of

dye **1** in neutral solution, by diverse mechanisms according to lifetime measurements. The quenching efficiency of **3** is pH dependent due to presence of the phenolate form. Competition experiments with excess host and guest showed that **3** is likely to diffuse in and out of membrane, while **4** forms an inclusion complex with β-CD leading to close contact and efficient quenching. It was confirmed that this dynamic supramolecular system is a versatile model to investigate quenching and recognition processes in bilayer membranes. So, in the present thesis work I have related with the aforesaid procedures (it is represented in the form of flowchart). [463-470]



Scanning Electron Microscopy(SEM)

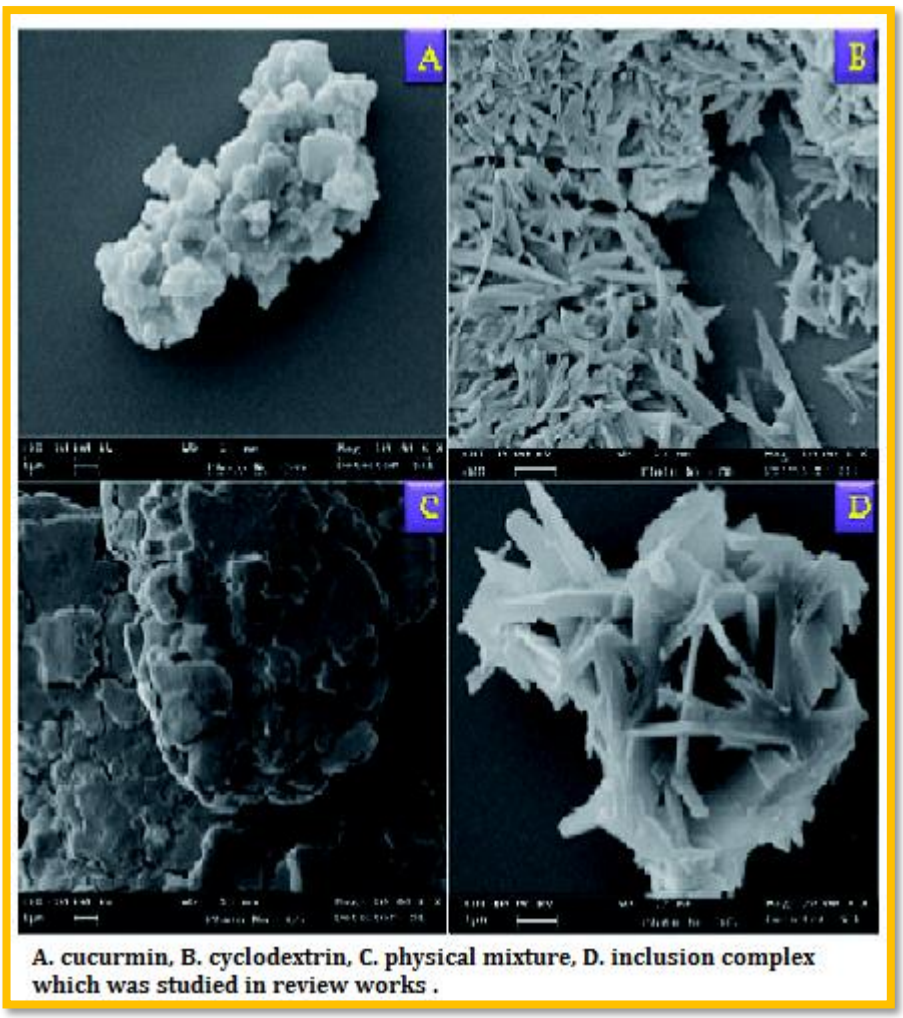
Tiny electron beam scanned across the surface of specimen, backscattered or secondary electrons detected, signal output to synchronized display.

The Scanning electron microscopy is used for inspecting topographies of specimens at steep magnifications using a piece of equipment known as the scanning electron microscope. SEM magnifications can set out to above 300,000 X but most semiconductor manufacturing applications require magnifications of less than 3,000 X accordingly. SEM assessment is habitually used in analysis of package cracks and fracture surfaces, bond failures, and physical defects on package surface. At some stage in SEM inspection, a beam of electrons is focused on a spot volume of specimen, resulting in transfer of energy to the spot. These bombarding electrons, also referred to as primary electrons, dislodge electrons from specimen itself. Dislodged electrons, also identified as secondary electrons, are attracted and collected by a positively biased grid or detector, then translated into a signal. To generate SEM image, electron beam is swept across the area being inspected, producing many such

signals. These signals are amplified, analyzed, translated into images of topography being inspected. Finally, the image is shown on a monitor of the computer that is connected with the instrument. [475-479]

The First scanning electron microscope (SEM) debuted in 1938 (*Von Ardenne*) with first commercial instruments around 1965. Its late development was due to electronics involved in "*scanning*" the beam of electrons across the studied sample.

- Electron Microscopes are scientific instruments that apply a beam of energetic electrons to examine objects on an exceedingly fine scale.
- The Electron Microscopes were developed owing to limitations of 'Light Microscopes' which are limited by physics of light.
- Early on 1930's this speculative limit had been reached and there was a scientific desire to notice fine details of the interior structures of organic cells (nucleus, mitochondria…etc.)
- This required 10,000x plus magnification which was not possible by means of current optical microscopes.
- Distinctive information deals by *Topography:* the surface features of an object or "how it looks", its texture; direct relation among these features and material properties. *Morphology*: The shape & size of particles production up object; direct relation amid composition and material properties. *Composition*: The elements & compounds that object are composed of and relative amounts of them; direct relationship connecting composition and material properties. *Crystallographic Information:* How atoms are arranged in object; direct relation connecting these measures and material properties. SEM has extra advantages above optical microscopy as has a large depth of field, which allows a great quantity of sample to be in focus at one time and produces an image that is a superior representation of three-dimensional sample. The grouping of exceedingly developed magnification, greater resolution, compositional and crystallographic information makes SEM one of the majorities heavily used instruments in academic/ national lab research areas and industry. [480]



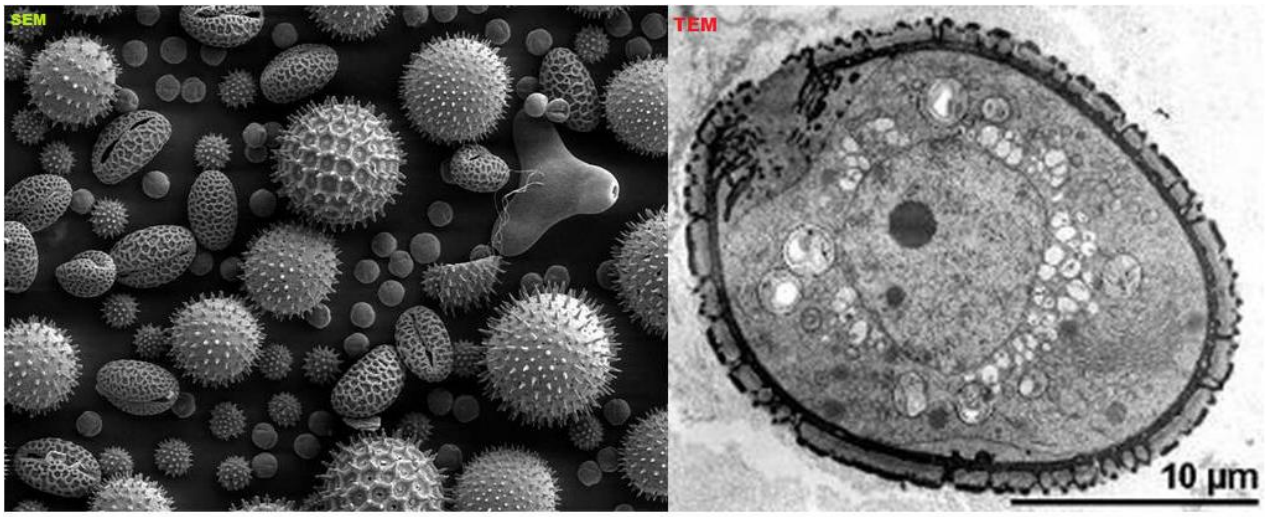
A. cucurmin, B. cyclodextrin, C. physical mixture, D. inclusion complex which was studied in review works .

Our present investigations are also investigated in the similar ways in the thesis.

♣ *Transmission Electron Microscopy*

Transmission electron microscopy (TEM) is powerful tool for imaging supramolecules (cyclodextrins as used in our works) on a nanometer scale. TEM equipment shows, specimen is illuminated using electron beams in high-vacuum conditions, and transmitted beam makes the image magnified from about fifty to over one million times. Principle, contrast of TEM image arises for basis of differences in electron density of elements constituting specimen. Three types of specimen preparation techniques follows as — negative staining, freeze-fracture, and cryogenic TEM — are commonly engaged for imaging supramolecules. TEM tomography screening shows three-dimensional structure and electron diffraction providing information on periodic ordered configuration of the specimen are described. In addition, two spectroscopic dimensions performed by means of TEM apparatus, electron energy-loss spectroscopy (EELS) and energy dispersive X-ray spectroscopy (EDS), are effective for

structural analysis of specimen. Principles and protocols for these techniques are portrayed; potential of TEM for micro-/nano-imaging in supramolecular chemistry is discussed with reference to TEM imaging examples that have been reported currently. [481-486]



Study of pollen grains in review works showing their morphological differences in SEM and TEM techniques

Advantages Real (Image) and reciprocal space (diffraction pattern) information can be obtained from similar region of sample. Chemical information by means of EDX and EELS possible (with additional attachments). Energy filtered images possible by the use of EELS filter. High resolution imaging possible (via HRLFI & HAADF in STEM). Possible to acquire amplitude and phase contrast images. Many diverse kinds of phase contrast images can be obtained.

Lower resolution/large area techniques ought to be first performed to get a 'broad picture' about the sample. This includes XRD and SEM methods. We can even initiate with optical microscopy. Phase related information should be obtained via XRD. Chemical information via EDX in SEM should be obtained (any chemical in homogeneity should be noted). On 'usual' samples conventional TEM should be performed before trying out HRTEM. In our sample investigations HRTEM was performed. The wavelength of the electrons

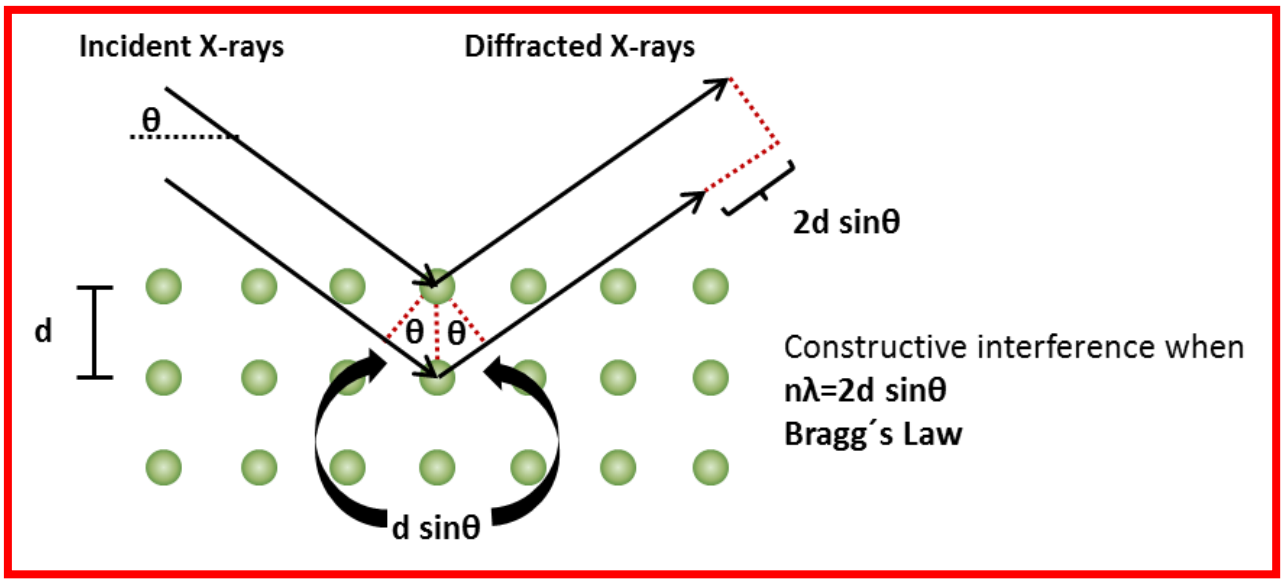
- In 10 kV SEM is 12.3 x 10−12 m (***12.3 pm***).
- In a 200 kV TEM wavelength is ***2.5 pm.***
- Wavelength of X-rays usually used in XRD is in order of ***100 pm*** (Cu kα: λ=154 pm).

♣ *X-ray Diffraction (XRD)*

Technique used for decisive atomic and molecular configuration of a crystal, in which crystalline atoms cause a beam of incident X-rays to diffract into numerous specific directions. [480]

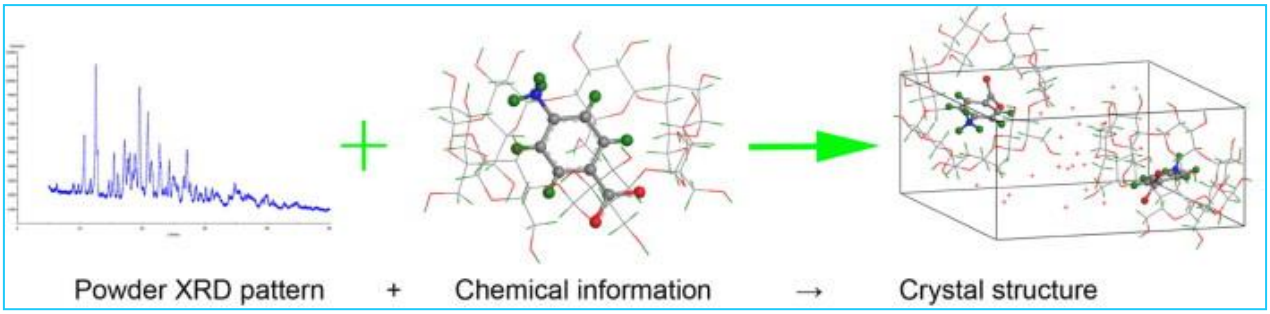
- The spacing of atoms in crystal lattices is of same order as wavelength of X-radiation (0.1 to 100 Angström). *Von Laue* discovered (1912) that a crystal could be used as diffraction grating for X-rays.
- *William Lawrence Bragg* discovered (1912) relating the spacing between atoms in a crystal to the angle at which X-rays are scattered when they strike the crystal.

$$n\lambda = 2d \sin\theta \qquad (223)$$



Generation of X-rays → When an atom is bombarded with sufficiently high energy electrons, electrons of an atom are knocked out from their shell (excited state, unstable). This leads to transition of electrons to fill up vacancy (ground state, stable). Each electron transition generates X-rays of a specific energy (with wave length in range from 0.1Å to 100Å) equivalent to that shell.

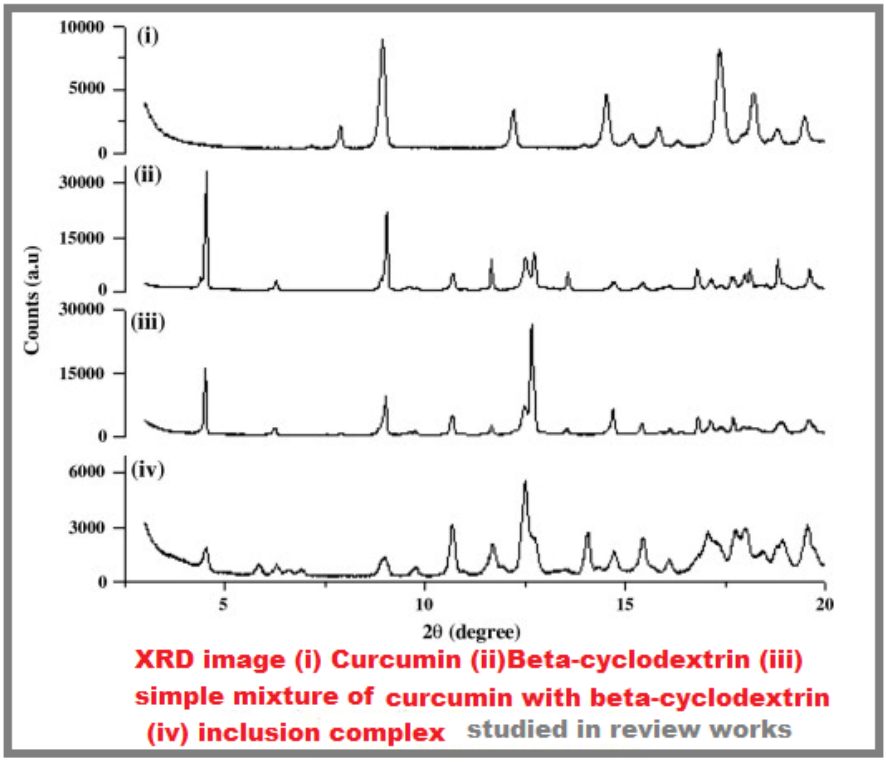
Various inorganic, organic, and biological molecules—X-ray crystallography has been fundamental in development of scores of scientific fields. The technique also discovered the structure and function of many biological molecules, including vitamins, drugs, proteins and nucleic acids such as DNA.



Applications of X-ray diffraction: X-ray diffraction has a wide and assorted applications on the chemical, biochemical, physical, material and mineralogical sciences. *Laue `s* said that has extended power of on serving minute structure ten thousand times beyond that of the optical microscope. X-ray diffraction produced a microscope with atomic resolution which shows atoms and their electron distribution. X-ray diffraction, electron diffraction, and neutron diffraction give information about structure of matter, crystalline and non-crystalline, at atomic and molecular level. In addition, they are attached to properties of all materials, inorganic, organic or biological. Due to the diffraction significance and variety of application of diffraction by crystals, a large number of Nobel Prizes were presented to studies involving X-ray. [487, 488]

In the past three decades, *powdered X-ray diffraction (PXRD) analysis* was broadly used in the characterization of cyclodextrins (CDs) and their inclusion complexes. It was studied in the previous works that the curcumin–β-CD complex from co-precipitation was evaluated by means of X-ray diffraction. The diffractograms of curcumin and β-CD exhibited a series of thin and intense lines, which are indicative of crystallinity in the inclusion complex. Thus, the X-ray diffraction corroborated results that were obtained from FT-IR, FT-Raman and photoacoustic spectroscopy techniques for the curcumin–beta-CD complex that was prepared by co-precipitation.

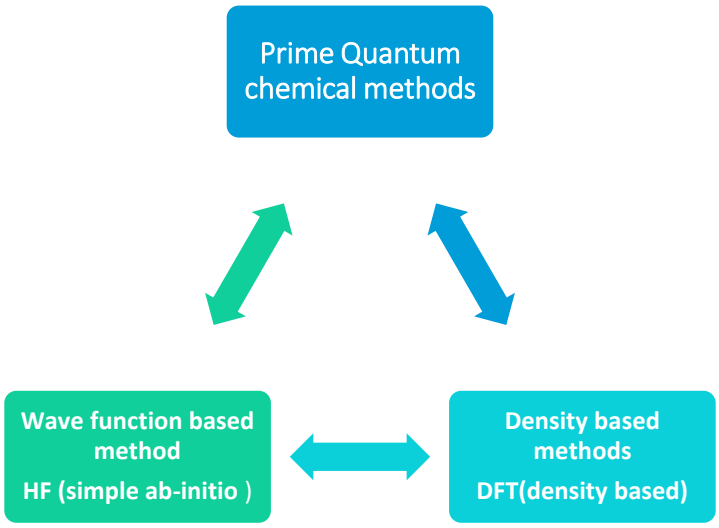
Similar to the aforesaid work I have also worked on the PXRD (powdered X-ray diffraction) analysis to determine the crystalline nature of the assorted imperative complexes during the course of my investigation. [480]



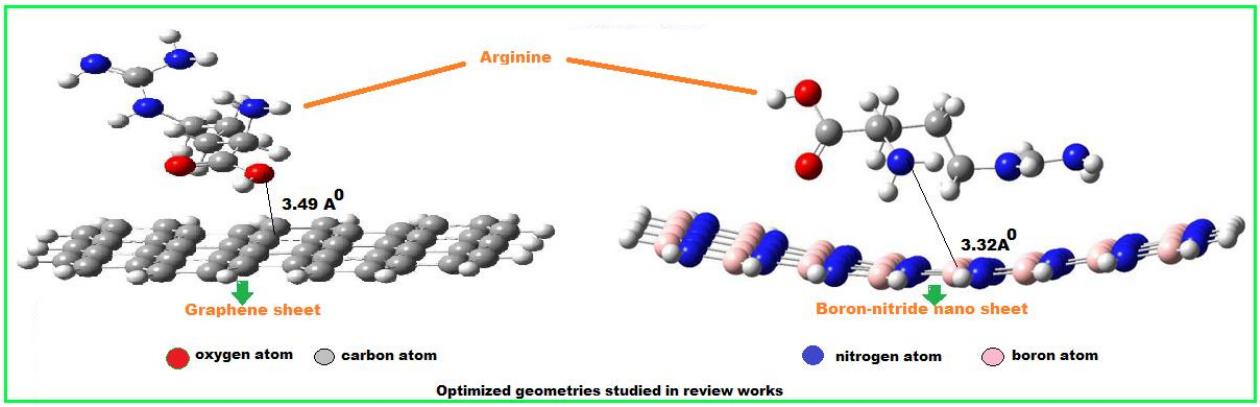
XRD image (i) Curcumin (ii)Beta-cyclodextrin (iii) simple mixture of curcumin with beta-cyclodextrin (iv) inclusion complex studied in review works

♣ *Quantum chemical methodology*

Over the past three decades, '*ab initio*' and 'DFT' in quantum chemistry has become an essential tool in the study of atoms and molecules and, increasingly, in modeling complex systems such as those arising in biology and materials science. *'ab initio'* and 'DFT' quantum chemistry has emerged as a viable and powerful approach to address the issues and problems related to the chemical systems. Quantum chemical calculations offer the real promise of being able to complement experiment as a means to uncover and explore new chemistry. It is used for predicting the properties of new materials even those which are not synthesized in the laboratory, using computer simulation technique**.** Various types of interactions related with solute-solute, solvent-solvent, solute-solvent (ion- solvent) interactions especially those related with hydrogen bonding explaining the bond lengths, bond angles was obtained by these techniques.



The work reported in the thesis deals with investigation of structural, and vibrational data analysis of some small biologically and pharmaceutically imperative molecular systems, in solution, using Quantum Chemical methods. Density Functional Theory (DFT) has been used to optimize most stable conformer and to explore ground state properties of the molecules under investigation. In order to achieve comprehensive portrayal of molecular dynamics, vibrational wave-number calculations have also been carried out at DFT level. The vibrational analysis also gives detailed information about intramolecular vibrations in characteristic region. The molecular properties such as equilibrium ground state energy, dipole moment, polarizability have been used to understand activity of molecules. [489-491]



'ab initio' methods use first principles of quantum mechanics to investigate electronic structure directly without using quantities derived from experiment. Quantum chemical models stem from Schrödinger equation first brought to light in the late *1920's*. Molecules are considered as collections of nuclei and electrons, without reference of any sort to chemical bonds. Solution to the Schrödinger equation is in terms of the motions of electrons,

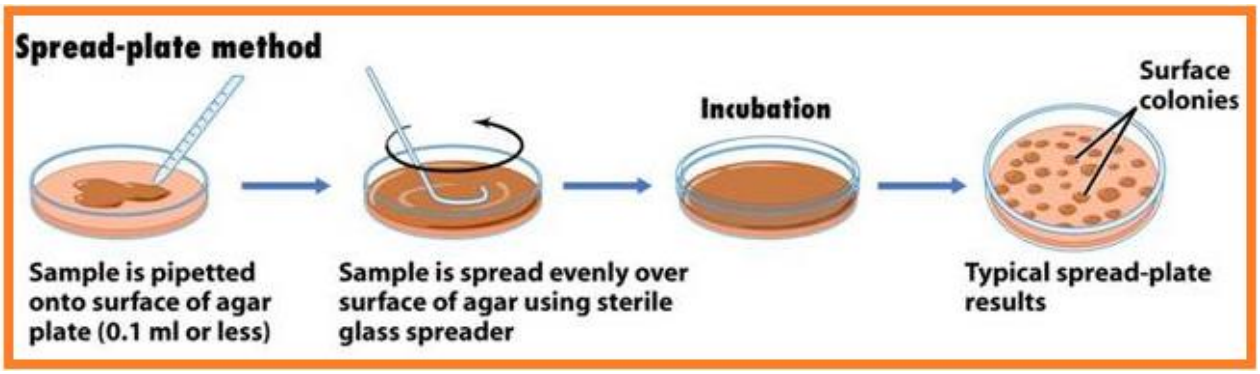
is directly related to molecular structure and energy among other observables, as well as contains information about bonding. As a matter of fact, Schrödinger equation cannot be solved in actuality, for any but a one-electron system (i.e. for hydrogen atom), and approximations are necessary to deal with many electron systems. Quantum chemical models differ from each other in form and nature of these approximations, and span a wide range, both in terms of their ability, uniformity and computational cost. There are two different approaches to obtain the solution of the electronic Schrodinger equation – Wave function based approach and Density based theory. Density functional theory is conceptually and computationally very comparable to *Hartree-Fock theory* but provides much better results and has consequently became a very popular method. Use of *Born-Oppenheimer (BO) approximation* makes *Schrodinger equation* much simpler to solve as the motions of electrons and nuclei can be separated due to their different masses. Thus, quantum mechanical methods (*ab initio*, DFT and semi-empirical) are based on solving the time-independent Schrodinger equation for electrons of a molecular system as a function of the positions of the nuclei. In classical atomistic models, atoms are regarded as basic units, and the classical potential energy functions (force fields (FFs)) represent interactions between atoms. High-level '*ab initio*' and 'DFT' calculations are computationally demanding. In *1998, Nobel Prize in Chemistry awarded to W. Kohn and J. Pople*, lead to the dramatic development of computational quantum chemistry. Density functional theory (DFT), formulated in *1964 by W. Kohn and P.* Hohenberg**,** has long been basis of electronic structure calculations of atoms from density of electron cloud surrounding them . Density functional theory (DFT) is primarily theory of electronic ground state structure. At present, there are two principal classes of functionals that have been expansively deployed and tested in large-scale applications as well as small molecule benchmarks: gradient-corrected (BLYP), and hybrid (B3LYP) functional. The work presented in the thesis for calculations of molecular properties of small imperative molecules is based on the density functional theory. In any quantum chemical calculation, the first step requires optimization of molecular geometry so is done in the various works.

Using the optimized structure (minimum energy) molecular properties like polarizability, electron affinity, dipole moment and so forth vibrational modes can also be designed by computing the second derivative of the energy with respect to the pairs of atomic Cartesian

coordinates. Simulation of infrared, which also require computation of dipole and polarizability derivatives, determination of force constants provides a useful confirmation on the geometry optimization. Since an optimized geometry corresponds to zero forces within the molecule, all leading force constants must be positive and therefore should not outcome in any imaginary vibrational wavenumber. Vibrational spectroscopy is the communal term used to describe analytical techniques- infrared spectroscopy that provide information about intra and inter molecular forces, molecular structure determination, atomic and molecular energy levels, molecular composition, molecular geometries, interaction of molecules, identification and characterization of new molecules etc. Experimental techniques for instance IR, have already their efficacy in this framework. Infrared spectroscopy is a dependable and conventional method for characterization and identification of materials for over long time. It deals with analysis of interaction of infrared light with a molecule. It is also regarded as an imperative technique for studying conformation plus bonding characteristics related with the aforesaid quantum methodologies. Molecular structure, vibrational have been calculated using density functional theory and to compare the novelty before and after the interactions in my thesis. Theoretically calculated values of mean polarizability of both forms are compared for dipole moment, FTIR to calculate the stabilization energies. [492, 493]

♣ *Cell viability and Cytotoxic activity*

Cell viability and cytotoxicity assays are used for imperative compounds (biologically active) screening and cytotoxicity tests of chemicals. Accurate determination of bacterial susceptibility to antibiotics is necessary to the successful management of bacterial infections and to the comparative analysis of antimicrobial agents. This can be done by a number of techniques, which include disc diffusion method, broth dilution assay. The effectiveness of antibiotics can be assessed by their ability to suppress bacterial growth, described by minimum inhibitory concentration (MIC), or by their ability to kill bacteria, characterized by the minimal lethal concentration (MLC). MIC is usually derived by means of tests in solid media, whereas both MIC and MLC can be determined in the broth dilution assays. A number of reports have been dedicated to comparing effectiveness of these methods. Agar diffusion assay is an important technique for assessing microbial susceptibility to antibiotics, which has net application worldwide over past 50 years. It has a number of variations, which include cup method, paper disc method, standardized single disc method etc.



Determination of MIC by these approaches, as well as using micro dilution technique, has been revealed to produce comparable results. A number of factors affect accuracy and reproducibility of the agar diffusion method, including thickness and uniformity of gel, the choice of cut-off size for the inhibition zones and breakpoints, temperature etc. When these factors are controlled or taken into consideration, analysis of data from agar diffusion assays relies on theoretical models, which incorporate a number of imperative additional assumptions. It is important to understand these assumptions, which justify use of these theoretical models and, at the same time, introduce some limitations in the validity of each model. Theoretical analysis of antibiotic diffusion data by disc method is built on assumption that antibiotics diffuse freely and diffusion-limiting factor is hydrodynamic viscous drag. The most commonly used model is based on linear diffusion in a semi-infinite space and is exemplified by the propagation of antibiotics in an agar-filled capillary. Linear diffusion is described and MIC is determined. The use of this approach allows the accurate determination of susceptibility to penicillin's and other antibiotics studied in the review works. In our investigation we have used spread plate method. [494-496]

II. (4) Imperative Compounds

♣ *Vitamins*

Vitamins are imperative organic compounds that are needed in small quantities to sustain life. The majority Vitamins required are obtained from food because the human body either

does not produce enough of them, or it does not produce any at all. Different vitamins have different roles, and they are considered necessary in different quantities. There are 13 acknowledged vitamins. They are listed as Vitamin A, B Vitamins {Thiamine, Riboflavin, Niacin, Pantothenicacid, Biotin, Vitamin B-6, Vitamin B-12 and Folate}, Vitamin C, Vitamin D, Vitamin E and Vitamin K.

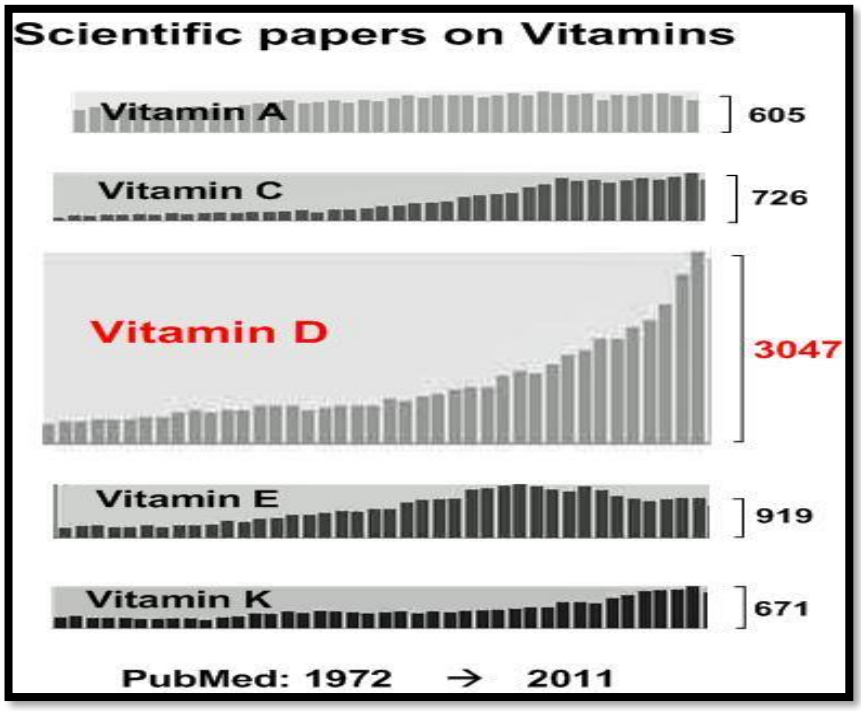
- Vitamins are either water-soluble or else fat-soluble.

[Fat-soluble vitamins are easier for body to be accumulated than water-soluble. Fat-soluble vitamins are stored in the fatty tissues of body and liver. Vitamins A, D, E, and K are fat-soluble. These are easier to store up than water-soluble vitamins, and they can stay in the body as reserves for days, and occasionally months. Fat-soluble vitamins are absorbed through intestinal tract with the help of fats, or lipids.] [Water-soluble Vitamins do not stay in the body for extended period. The body cannot store them, and they are almost immediately excreted in urine. Because of this, water-soluble vitamins need to be replaced more regularly than fat-soluble ones.]

Vitamin C and all the B vitamins are water soluble. (Most of the thesis related works are obtained by these supplements in the form of controlled delivery in our body).

- Vitamins always contain carbon, so they are described as "organic" components.

- Food is the best source of vitamins, but several people may be advised by a physician to use supplements.



People need to get mainly of their Vitamin D (needed for proper absorption of calcium; stored in bones) from exposure to sunlight, because it is not obtainable in large adequate quantities in food. However, human body can synthesize it whilst exposed to sunlight. The non-skeletal disorders, weight increase, including heart disease, mood disorders, multiple sclerosis, and metabolic disorders, the whole of which have been linked to lower Vitamin D. None of the supplemental Vitamin D showed satisfactory results against these conditions.

Vitamin B-3 (Niacinamide & Niacin)

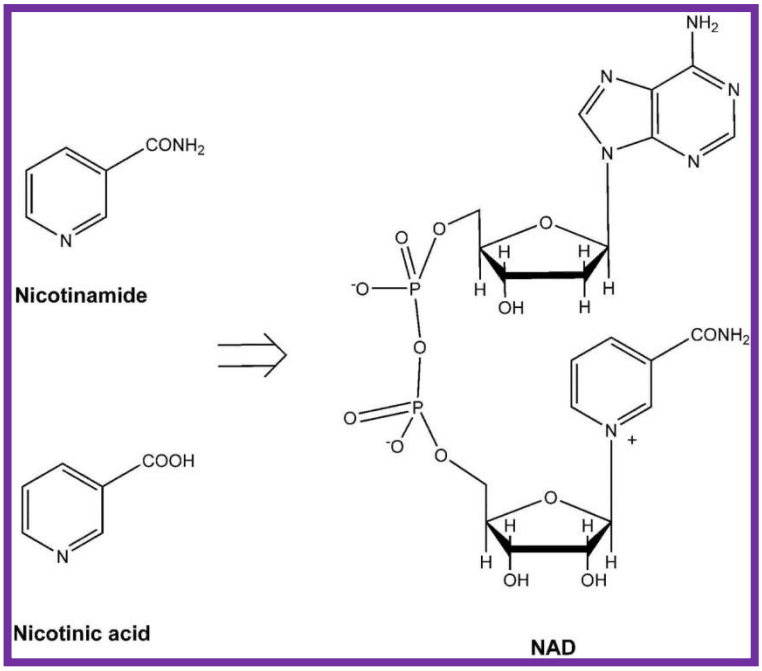
There exist two types of Vitamin B-3

- Niacinamide (*Nicotinamide*), which doesn't control cholesterol. Nicotinamide is more or less always safe to take, although a few cases of liver damage have been reported in doses of over 1000 mg/day. [Research work is based on it].
- Niacin (Nicotinic Acid) which is highly toxic in large doses. (Doses of only 50-100 mg nicotinic acid can cause dilation of blood vessels and potentially painful tingling ("niacin flush"), diarrhea, nausea, vomiting, long term liver damage).

B-3 Deficiency causes Pellegra disease (rare in Western societies), gastrointestinal disturbance, loss of appetite, headache, insomnia, mental depression, fatigue, aches, and pains, nervousness, irritability .

Most people get plenty of B-3 from their diet because it is added to white flour.

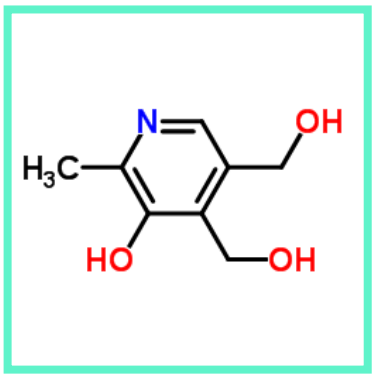
Nicotinamide is subsequently generated by conversion of nicotinic acid in liver or through the hydrolysis of NAD+. Once nicotinamide is obtained in the body, it functions as precursor for coenzyme ß-nicotinamide adenine dinucleotide (NAD+) also is crucial for the synthesis of nicotinamide adenine dinucleotide phosphate (NADP+).



B-6 Pyridoxine

Important in: Production of Red blood cells (RBC), conversion of Tryptophan to Niacin (B-3) immunity, nervous functions, reducing muscle spasms, cramps, numbness maintaining proper balance of sodium and phosphorous in the body.

High doses of Vitamin B-6 may be recommended to treat PMS (Premenstrual Syndrome), carpal tunnel syndrome, and sleep disorders, but continued use of high doses may result in permanent nerve damage.



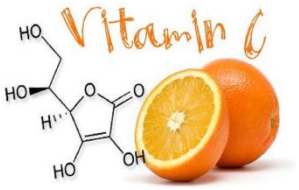
Deficiency causes diseases like nervousness, insomnia, loss of muscle control, muscle weakness, arm and leg cramps, water retention, skin lesions.

Discovery of Vitamin B6: The formula of vitamin B6 (referred to as vitB6) was former published by Ohdake in 1932. He worked on isolation from rice-polishings of what he called

“Oryzanin” (Vitamin B1) and found vitB6 as a by-product. Paul György, a Hungarian scientist, first described vitB6 as active “rat pellagra prevention factor” in yeast eluate. Pyridoxine (PN) carries a hydroxyl, pyridoxal (PL) an aldehyde, pyridoxamine (PM) an amino group.

In current years vitamin B6 has become a focus of research describing compound’s critical function in cellular metabolism and stress response. For many years sole function of vitamin B6 was considered to be an enzymatic cofactor. However, recently it became clear that it is also a potent antioxidant that effectively quenches reactive oxygen species and is of high significance for cellular well-being.

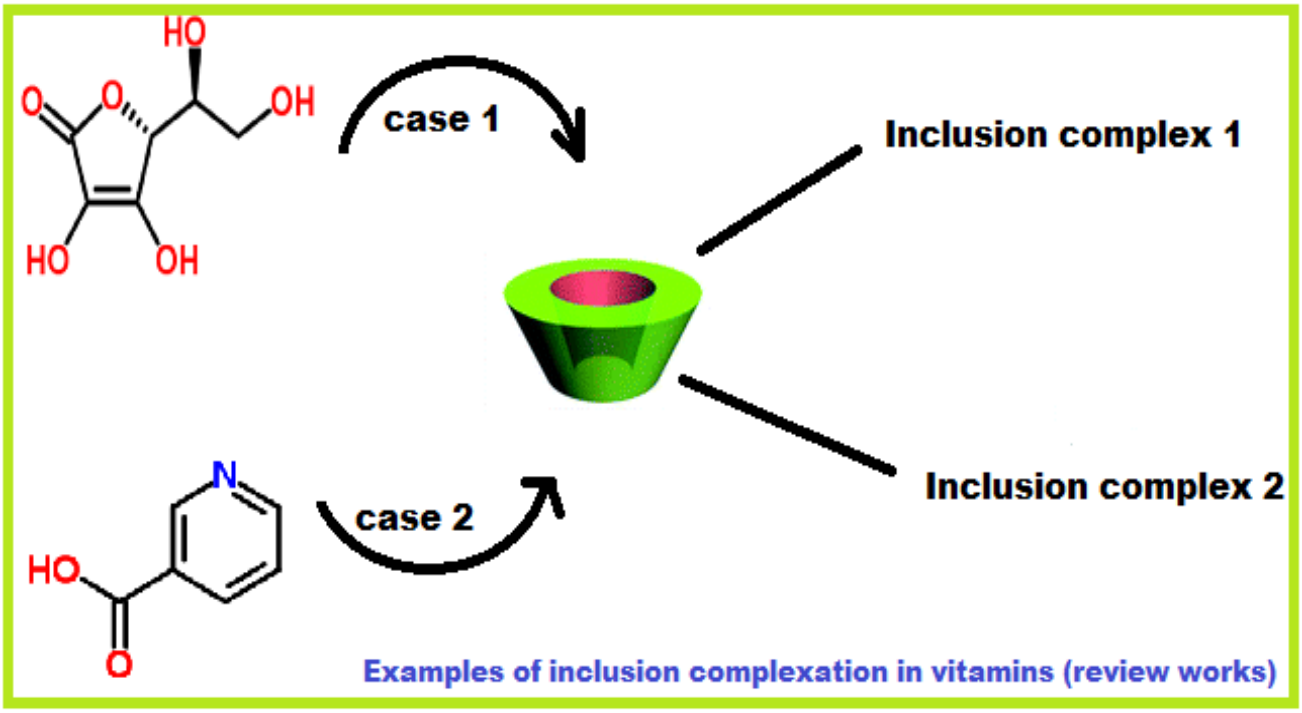
Vitamin C



“Vitamin-C” as well termed as Ascorbic acid *[extremely toxic to viruses, bacteria and several malignant tumor cells]*. It acts as antioxidant, water-soluble in nature. It functions in body by providing protection in body against free radicals, helps to form connective tissue which support bones, muscles, tissues together [collagen], aid in healing of wounds, assist body in absorbing iron from plant sources, help to keep gums healthy, helps body to scrap infections, aids in prevention of heart illness, helps to prevent various forms of cancer.

Since ‘Vitamin-C’ is soluble in water excess amounts that human body doesn’t require, will be excreted, but larger doses grounds various problems. Sources arises from Guava, Broccoli, Cantaloupe, Red Bell Pepper, Orange Juice, Strawberries, Tomato Juice, Raw Tomato, Tangerine, sweet Potato, spinach, Leafy Greens, Berries, Citrus fruits etc.,

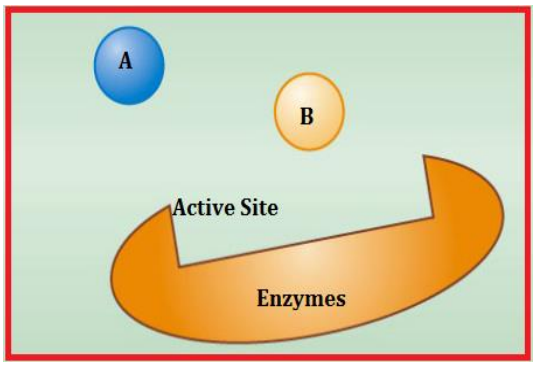
Deficiency of C causes: weight failure, tiredness, scurvy, joint Pains, (staining effortlessly, bleeding gums, and bones tendency for to fracture), condensed resistance to cold and infections, sluggish healing of wounds along by fractured bones. [496-506]



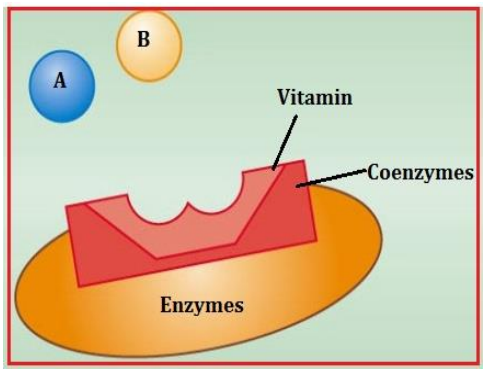
In earlier works 'Host–guest complexes'of 'β-Cyclodextrin' with Vitamins: '(vitamin-B)' verses '(vitamin-C)' in aqueous media, investigated via consistent Physico-chemical, Spectrophotometric, calorimetric procedures as preservative, transporter over and above regulatory releaser of the considered guest moieties [514].

Vitamins – water misible approach of action coupled with the *'Lock –Key mechanism'*–it performs similar like coenzymes otherwise parts of coenzymes which are enforced in favor of the proper bustle of enzymes. Accordingly they work as *'Bio-Catalysts'*.

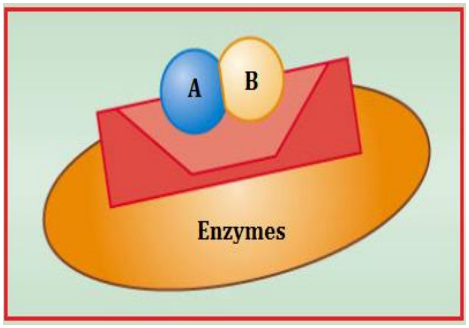
Step 1: Without coenzyme, compounds [A] and [B] don't respond to the enzyme.



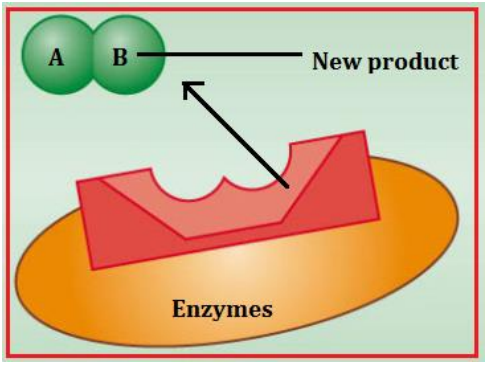
Step 2: With the coenzyme in position, compounds [A] and [B] are attracted to the active site on the enzyme, and they react.



Step 3: The reaction is completed with the formation of a new product. In this case, the product is [AB].

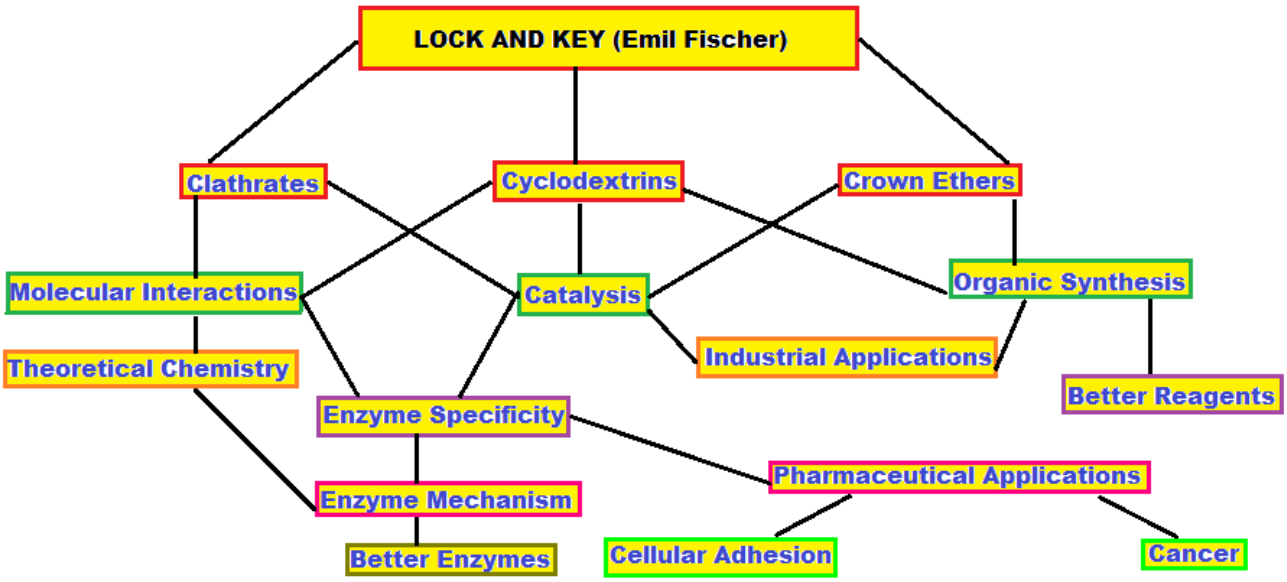


Step 4: The product [AB] is released in the controlled fashion in the body.



Lock and Key mechanism proposed in 1890 by the eminent scientist *Emil Fischer* to explain binding between the active site of an enzyme and a substrate molecule. The active site was thought to have a permanent structure (the lock), which exactly matched structure of a specific substrate (the key). Further he overviewed the whole area in the terms of molecular recognition and illustrated it as follows in the form of flowchart below.

Emil Fischer's coined for lock-and-key picture for the reaction between enzymes and substrates became a leading concept for the understanding of intermolecular interactions with proteins, and later for the rational design of drugs. With the beginning of supramolecular chemistry the idea gained an enormous momentum, as chemists began to synthetize a large variety of host compounds for basically all possible target guest molecules occurring in nature or in the environment. Although few concepts have played a comparatively imperative role in chemistry, the lock-and-key principle has limitations and extensions, which often are overlooked.

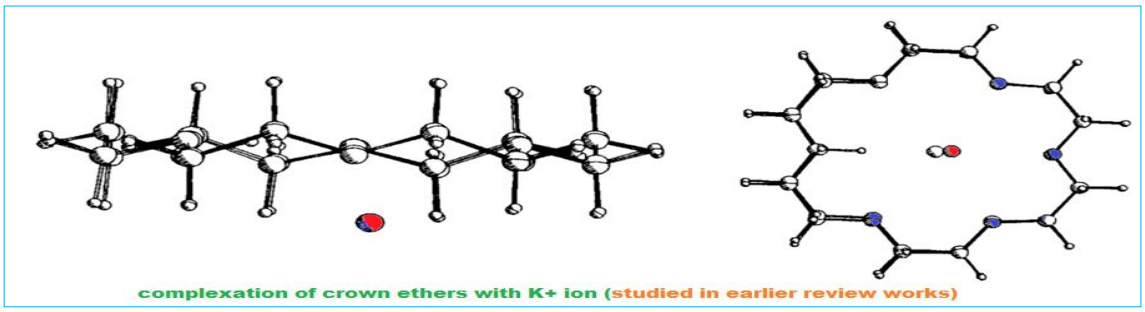


By leading us through the diverse processes which result in the molecular recognition, the scientist painted a portrait of how essential this whole area is in physical, chemical and biological sciences. Beginning with the simple example of pyrophosphate hydrolysis by Cyclodextrins and building up to how cell walls in mammalian tissue recognize sugar residues, *Friedrich Cramer* succeeded in completing an overviewed picture which was initiated by *Emil Fischer*. [507, 508]

- Dependence on Binding Mechanism / Medium, pH and Stereoelectronic Effects

In solutions, occurrence of a geometrically close-fitting cavity in a receptor is not adequate for the binding of a substrate: the price for desolvation of host and guest prior to complex formation have to be paid by compensating non-covalent forces among host and guest,

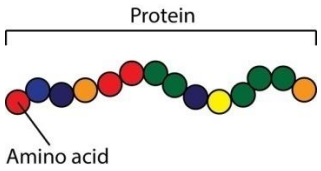
although complete desolvation might not be necessary, and desolvation alone can also contribute to a gain in free energy of the system. Solvent effects can be more decisive for complexation strength than the dimension matching. Studied in the former review works, complexation with crown ethers 18C6 and 18C5 shows that not only the absolute binding energies depend on the medium, essentially as linear function of the cation desolvation free energies of the guest metal ions as shown with a assortment of solvents, the differences between 18C6 and 18C5, which binds weaker owing to one hydrogen atom protruding into the cavity, are much smaller in water than in other solvents.



complexation of crown ethers with K+ ion (studied in earlier review works)

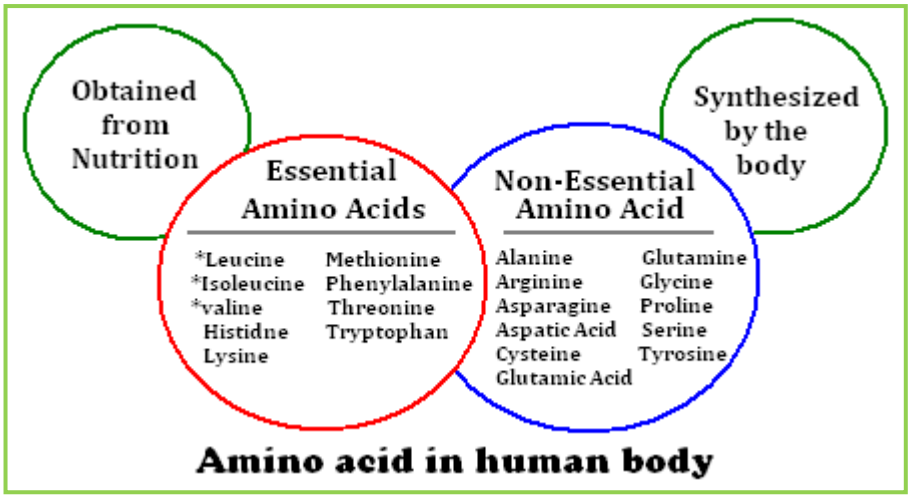
The Cyclodextrin complexes are prone to vary in both the solid and solution state, as the hydrophobic effect as significant driving force is misplaced in crystals and the interior of cyclodextrins offers just C–H bonds for non-covalent interaction, in disparity to the outside and rim. The hydrophilic compounds believed to generally bind with cyclodextrins preferentially outside the cavity; prior publications suggested similar possibilities. The lock-and-key principle is still a valuable starting point for understanding and designing of natural and non-natural supramolecular complexes. Structures and configuration of supramolecular complexes within solutions can be evaluated by spectrographic techniques, preferably by NMR spectroscopy. However there are up till now not enough conclusive spectroscopic studies for interrelated cyclodextrin complexes in the solid and solution state. [509-513]

Accordingly the thesis related studies are based on Physicochemical and the spectrometric determination of solid inclusion complexes with α, β cyclodextrins and various imperative molecules (Vitamins, aminoacids, ionic liquids) in the aqueous solutions maintaining the pH (at diverse temperatures) in conjunction with their controlled release.



♣ Amino Acids

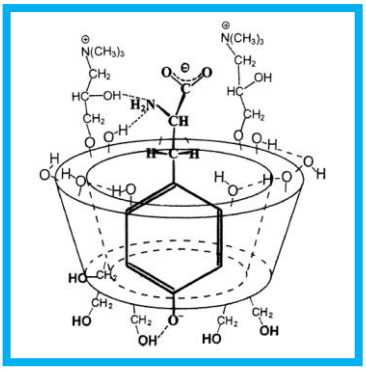
Peptide plays a crucial role in almost the intact biological processes plus Amino Acids are the construction blocks of it. A large percentage of our cells, muscles and tissue are made up of Amino Acids, indicate that they carry out a lot of imperative bodily functions, for example giving cells their structure. Amino Acids link together to create long chains. Those long chains of Amino Acids are moreover called proteins (peptides). Human body diet consists of 22 standard Amino acids either is used to synthesize proteins and further biomolecules or is oxidized to urea and carbon dioxide as a source of energy. Essential Amino Acids are listed as: *Histidine, Isoleucine, Leucine, Lysine, Methionine, Phenylalanine, Threonine, Tryptophan, and Valine*. Nonessential Amino Acids are: *Alanine, Asparagine, Aspartic Acid, Glutamic Acid, Glycine, Arginine*, Cysteine*, Glutamine*, Ornithine*, Proline*, Selenocysteine*, Serine*, Taurine*, Tyrosine** (* indicates essential only in certain cases). Essential Amino Acids ought to be obtained from food. Protein in food is broken down into Amino Acids, which are used via body for various purposes, as well as building the category of protein needed to build and maintain muscle tissue.



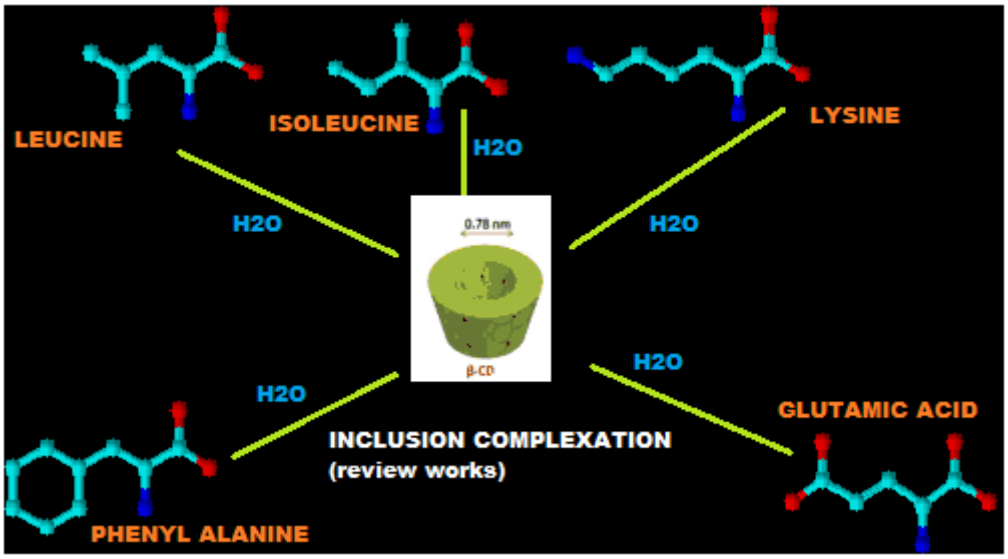
In previous works, the assignment of charges in inclusion complex formation of cyclodextrin has been investigated in terms of electrostatic interactions, hydrogen bonding and steric effects connecting the host and guest molecules. Preferred guest molecules for investigation

L- and D enantiomers of amino acids. The latter is particularly fascinating from point of view of the applications in biological systems. In case of amino acids the stability of associates can be the result of a mixture of effects: the hydrophobic part can enter the cavity, whilst the hydrated amino acid moiety remains outside of the ring and can take part in electrostatic and hydrogen bonding interactions, depending on diverse ionization states according to the pH of solution. Conversely, enantiomers of these compounds permit of the investigation of chiral recognition. Aim was to investigate the construction of some amino acid & β–cyclodextrin complex, which has higher stability constant.

Investigation of complexes of alpha-amino acids by assorted techniques like Potentiometric scheme and 1H and 13C NMR spectroscopy completed that amino acids can be classified into three types. *The utmost stability constants have been obtained for phenylalanine, tyrosine and tryptophan, in accordance with expectations: the presence of aromatic side group is especially favourable for complex formation. Complexes of leucine have also a significant stability in the middle range. The lowest stabilities are set up for the nominal or most hydrophilic compounds as threonine, and aspartic acid, glutamic acid and histidine.* The complexes are characterized through stability constants. A significant raise of the stability constants as compared to the native cyclodextrin has been found only in the case of the anionic forms of tyrosine, L-aspartic acid and L-glutamic acid with quaternary ammonium cyclodextrin. This can be understood considering that in these cases hydrogen bonding is possible with both rims of the cyclodextrin, in totaling to the improved electrostatic attraction. This effect can over compensate steric hindrance of the substituents, resulting in deeper penetration of guest moiety. The results verify deeper insertion of phenolate ring of tyrosine in the cyclodextrin cavity and the stronger interaction between the functional groups of the amino acid anion and the primary alcoholic group(s) of the cyclodextrin [515]. A probable structure of the complex of L-tyrosine with quatenary ammonium β-cyclodextrin is drawn in the review investigation as

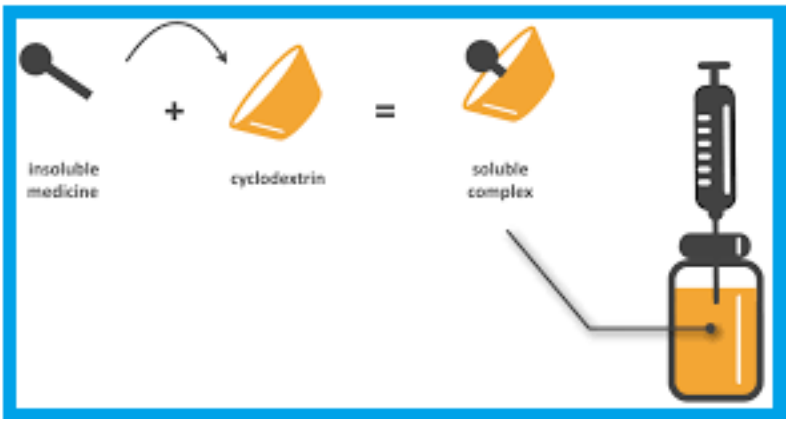


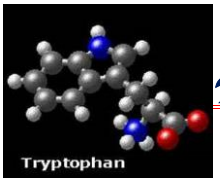
α and β-Cyclodextrin outline inclusion complex with L-Leucine and L-Isoleucine in aqueous media have been investigated which comprise diverse applications in modern science such as controlled delivery in the field of pharmaceuticals, food processing etc. L-Leucine interacts further with the hydrophobic cavity of cyclodextrin than its isomer. With the assist of stability constant by NMR titration, hydrophobic effect, H-bonds and structural effects the formations of inclusion complexes have been explained and studied previously. Various review works are depicted in the outline of graphical representation. [516, 517]



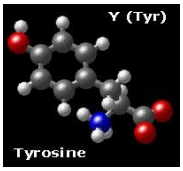
Cyclodextrin formed complexes of higher stability than the other hosts explained by Horský et.al. The stability of complexes of oligopeptides containing L-phenylalanine was invariably superior to that of L-phenylalanine itself. A model for interaction of proteins with cyclodextrins is proposed, in which the most stable complexes are formed when the native functional form of proteins is unfolded and nonpolar residues that are buried inside the structure are exposed to water. [518]

Taking in consideration of the review workings, the present dissertation consists of studies related to essential and non- essential AminoAcids in aqueous solutions screening various types of assorted interactions in both supramolecular chemistry and solution thermodynamics, to spread its novelty mainly in the field of pharmaceutical applications.

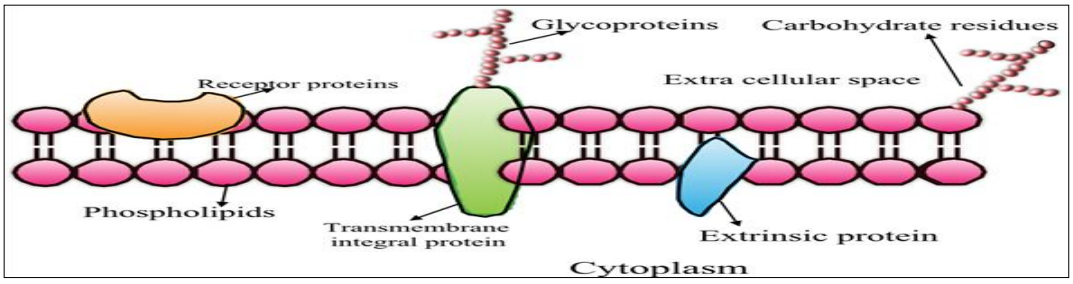




Tryptophan & Tyrosine



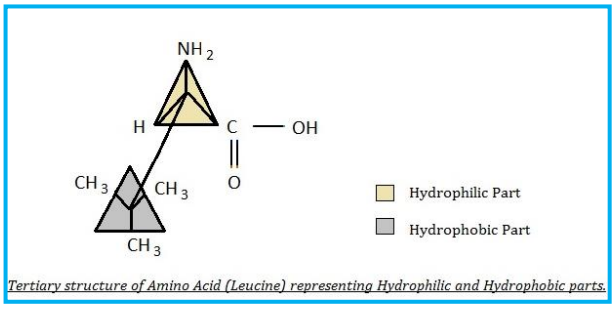
Components of superlative significance of cell membranes are a variety of proteins. The transmembrane proteins localize aromatic amino acids (especially tyrosine, tryptophan) at the membrane/water interface where they outline functionally noteworthy H-bonds with interfacial water. The present hypothesis works deals with them. [519-526]



Tryptophan is a precursor to the neurotransmitter serotonin, hormone like melatonin, and is essential in body which have to be taken from outside. Thus its molecular interactions with vitamin C and delivery

in the human body are shown in one of the thesis related works. The aforementioned interactions of tryptophan have been compared with tyrosine, which is a non-essential aminoacid and is not mandatory to be taken externally with regard to solute-solvent interactions. Details of the work are specified in chapter IV of the thesis.

Tertiary-Leucine

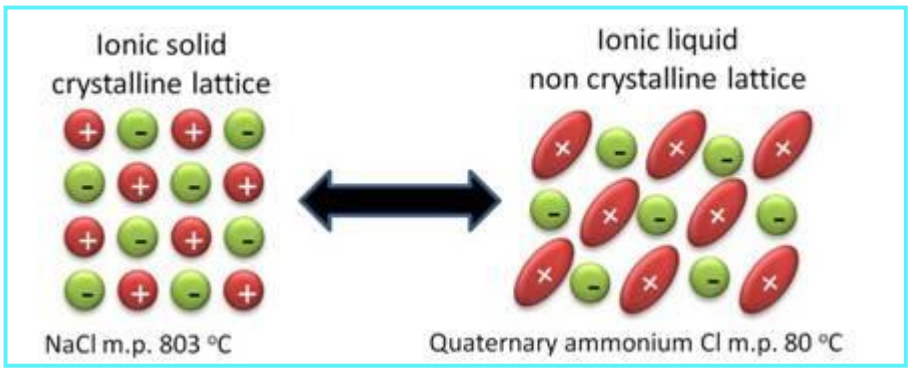


Tertiary structure of Amino Acid (Leucine) representing Hydrophilic and Hydrophobic parts.

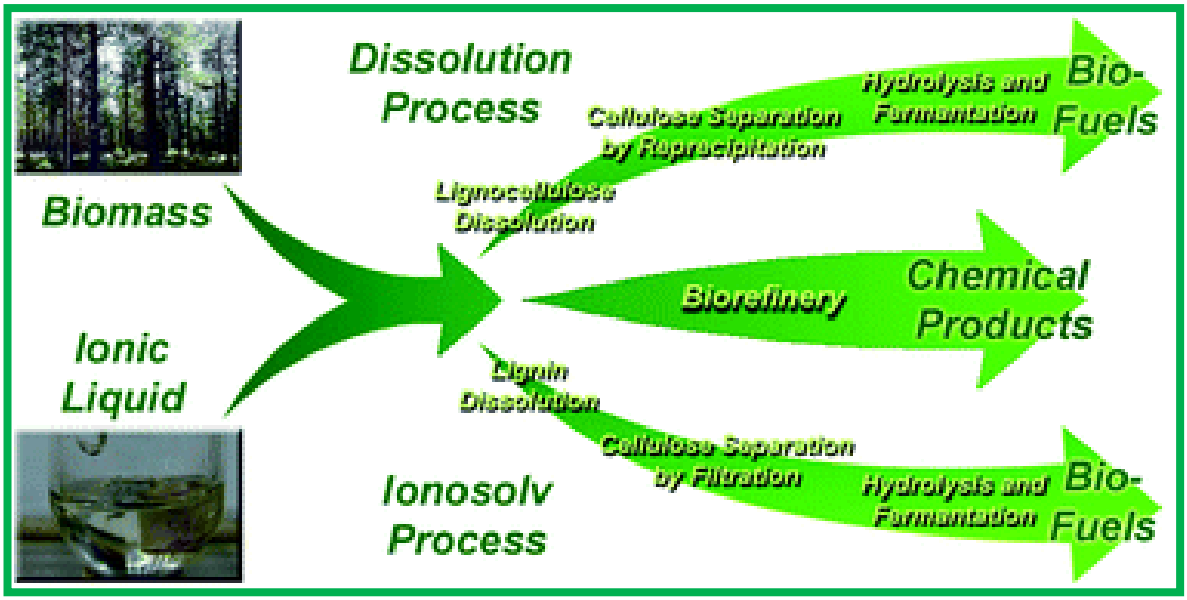
As a nonproteinogenic amino acid, Tertiary-leucine (Tle) is an imperative and attractive building block. Owing to its bulky, inflexible and hydrophobic tert-butyl side chain, enantiopure (Tle) has been comprehensively used in the synthesis of an array of pharmaceutically active compounds and chiral auxiliaries. Thus, development of schemes to synthesize enantiopure (Tle) is of immense interest. Enantiopure Tle was initially synthesized by resolution of racemic N-formyl Tle with brucine in 1934. Subsequently, a large number of chemical resolutions of racemic Tle or its derivatives with a array of resolving agents were investigated. However, biocatalytic methods usually offer bigger benefits than chemical procedures. However, penicillin G acylase (PGA) mediated kinetic resolution of N-phenacetyl-DL-Tle (N-Phac-DL-Tle) showed significant advantages over other resolution measures owing to its excellent enantioselectivity and cheap biocatalyst. [527-536] *So, for its vital role as studied from various previous datas it is being used as a guest molecule in one of the investigation by forming inclusion complex with it, by penetrating the hydrophobic part of it in the cavity of the host i.e., the cyclodextrin that is being used.* Details of the investigation are shown in chapter VI of the thesis.

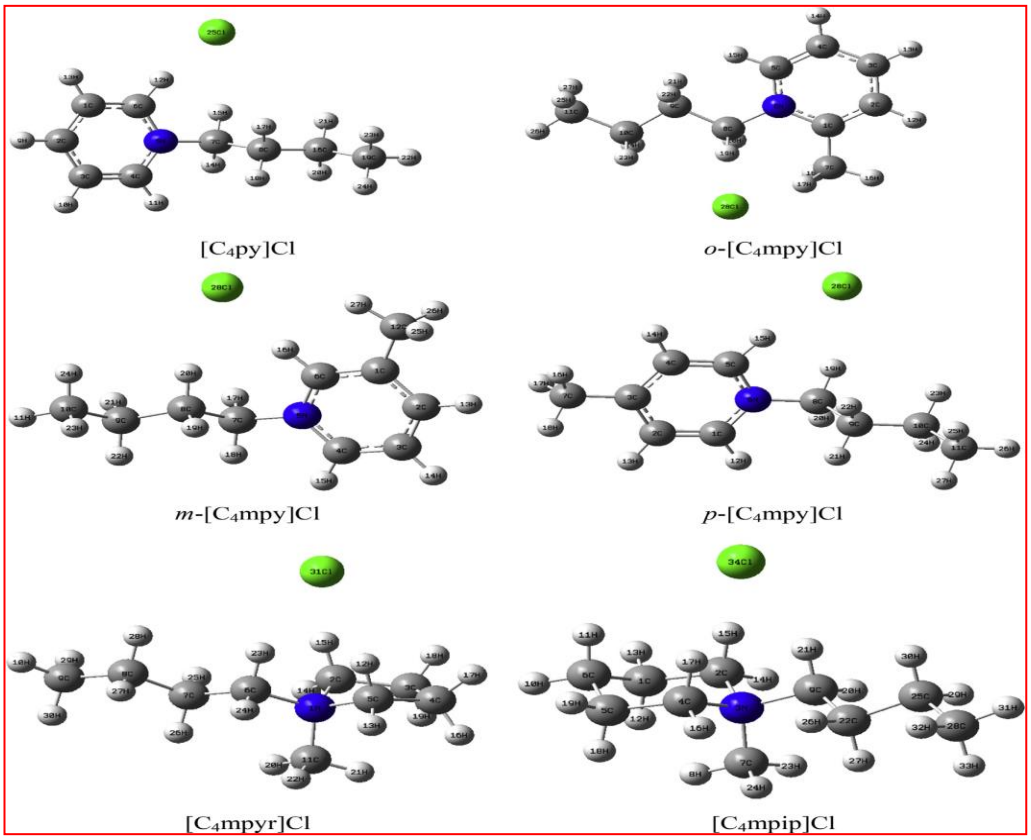
♣ *Ionic Liquids*

Ionic liquids (ILs) are a class of chemicals composed exclusively of ions having melting points below T = 373 K. Due to their unique physicochemical properties, ILs are swiftly gaining interest as greener replacements for traditional volatile organic solvents (VOCs).

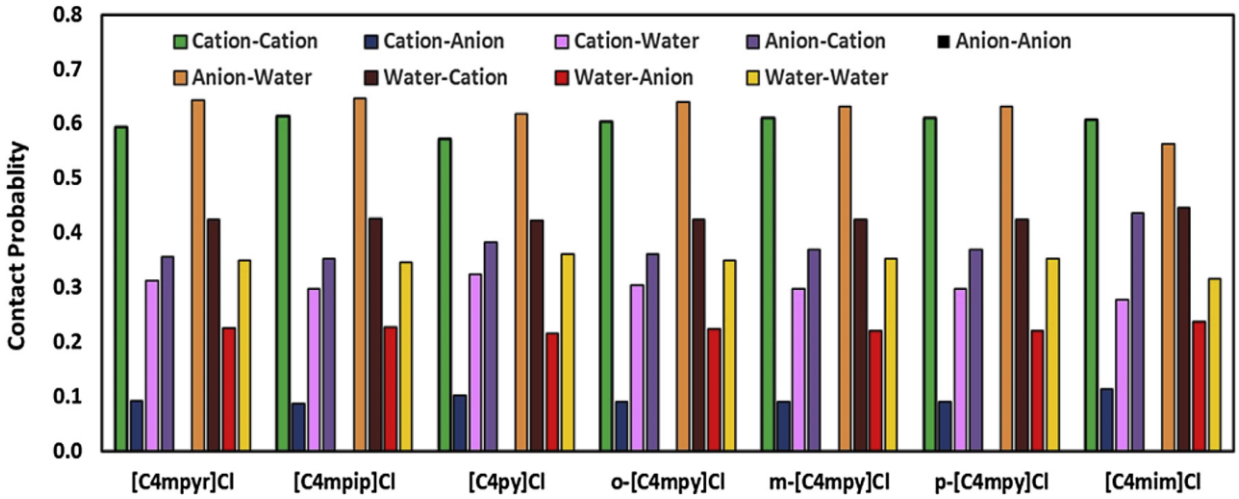


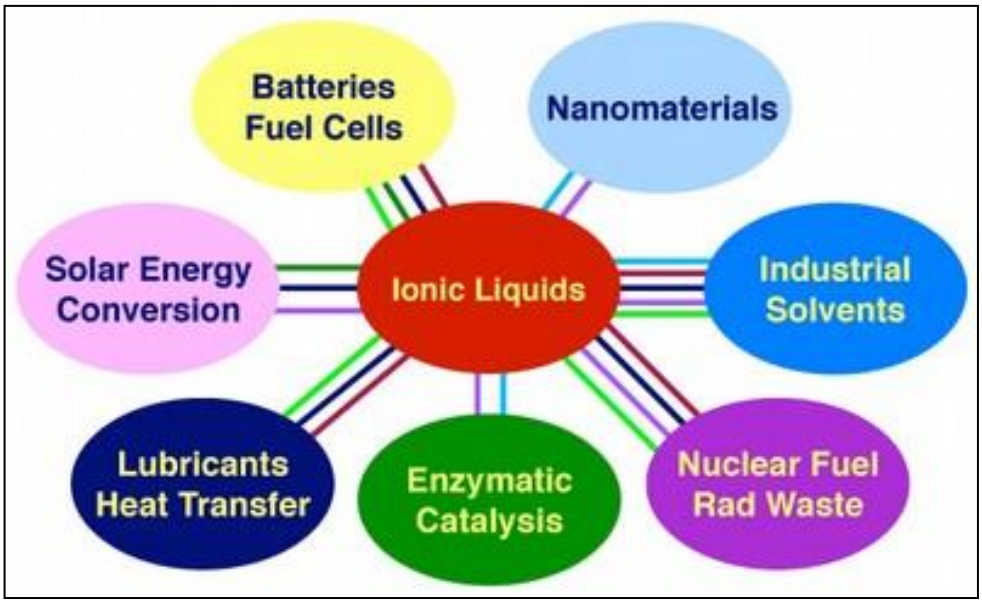
Other benefits are their large liquid temperature ranges driven by low melting temperatures and high decomposition temperatures, favourable solvation behaviour, high stability in air, high ionic conductivity, modification of selectivity in chemical reactions, which unwrap new possibilities in assorted industrial fields as catalysis, separation techniques, and electrochemical devices applications. However, some industrial development requires reliable reference data on thermodynamic properties of pure ILs and their mixtures with extra solvents. In spite of extensive applications minute information on their thermodynamic properties are published. [537-598]nearly all ILs are based on heterocyclic compounds, particularly the alkylimidazolium, alkyl pyrrolidinium, or alkylpyridinium cations. They can be broadly classified into two groups, protic and aprotic ILs. Protic Ionic Liquids (PILs) are synthesized by proton transfer from a Brønsted acid to a Brønsted base, which creates proton donor and acceptor sites and can escort to the formation of hydrogen bonds. Some examples of the ILs are shown as follows:





The research concerning PILs has in general focused on surfactant self-assembly, and their physical properties. Attributable to their excellent catalytic effects and other advantages such as easy preparation, cheap cost, and low toxicity, theirs physicochemical properties have also attracted researcher's attention. Graph below depicts the interactions studied in earlier works. [537]





For example, newly, *Nakamoto et al.* have reported that PILs are processing candidates as electrolyte for electrochemical storage and conversion devices. Recently revealed that the labile proton on PILs structure participates to the pseudo capacitance on the fast redox reactions at the electrode/electrolyte interface in the case of activated carbon-based super capacitors. However, despite the extraordinary properties of these promising electrolytes, very little study concerning the physical properties of pure PILs as well as their mixtures with classical solvents for batteries or super capacitors has been reported in the literature. Previously, a series of thermodynamic properties (such as specific heat capacities, volumetric and, rheological properties) for different PILs in mixtures with molecular solvents, such as acetonitrile, water, and alcohols was studied. Nevertheless, classical batteries electrolytes are in general composed of salt (e.g. lithium salt or an IL) dissolved in an alkylcarbonate solvents mixture. (N-alkyl-N-methylpyrrolidinium bromides + water) binary mixtures were investigated

previously and studied in terms of density, viscosity, (vapour–liquid) and (solid–liquid) phase equilibrium measurements. The gathered data allowed for estimation of pyrrolidinium bromide salts with water as a working pair for absorption refrigeration processes. Moreover this information provided scientific insight about the mutual affinity between IL and water. [538]

Interaction among ionic liquids and cyclodextrins

The innovative properties of ILs on the addition of CDs originate from the interaction between ILs and CDs, mostly the inclusion complexation between them. Thus, the revise on this topic is imperative. Diverse methods have been applied to investigate the interaction between ILs and CDs, such as the solubility (*Gao et al.*, 2005), infrared spectroscopy (*Li et al.*, 2007), Ultra-violet spectroscopy, XRD (*Gao et al.*, 2006; *Gao et al.*, 2005; *Li et al.*, 2007), conductivity (*Amajjahe & Ritter*, 2008; *He et al.*, 2009), TGA (*Gao et al.*, 2006; *Gao et al.*, 2005; *Li et al.*, 2007c), affinity CE (ACE) (*Francois et al.*, 2007), NMR (*Amajjahe & Ritter*, 2008; *Gao et al.*, 2006; *He et al.*, 2009; *Li et al.*, 2007), fluorescence competition (*He & Shen*, 2008; *He et al.*, 2009), microcalorimetry (*Amajjahe et al.*, 2008; *Amajjahe & Ritter*, 2008b; *Li et al.*), surface tension measurements (*Gao et al.*, 2006c) so on. By these techniques, formation constants of ICs, the stoichiometry for ILs and CDs can be obtained. *Gao et al.* (Gao et al., 2005a) investigated the system of [C4mim][PF6] and β-CD by means of NMR and suggested that whole imidazolium cation (C4mim+) was probably included into the cavity of β-CD, while the PF6− ion dissociated near the β-CD. They also calculated ICs formation of β-CD with three kinds of IL surfactants, [C12mim][PF6], [C14mim][PF6], and [C16mim][PF6] (*Gao et al., 2006c*). There were two kinds of inclusion complexations, *i.e.*, 1:1 and 1:2 (β-CD/IL) stoichiometries for β-CD-[C12mim][PF6], β-CD-[C14mim][PF6] ICs, and only 1:1 stoichiometry for β-CD-[C16mim][PF6] ICs due to the strong steric inhibition of [C16mim][PF6]. Unlike the possible structure suggested for [C4mim][PF6]/β-CD inclusion complex, only the alkyl side chain on imidazolium ring of these three ILs entered into the cavity of β-CD. The similar result was obtained by *Li et al.*, 2007, which indicated only alkyl side chain of [C12mim][PF6] was included into the cavity of β-CD. Also, size of the CD cavity noticeably impacts the stability of 1:1 complexes, with stronger complexes being given by β-CD. Typically, the interaction of CDs

and ILs are studied in aqueous solution. Recently, it was investigated that dissolution of β-CD could be enhanced in some hydrophilic ILs and 1:1 inclusion complexes were formed between β-CD and imidazolium cations of the ILs, *Zheng et al.* Differently, numerous inclusion complexes of β-CD with anion of ILs were also reported. [545-598]

Supramolecular assemblies based on ionic liquids

Generally, amphiphilic molecules self-assemble to outline micelle, microemulsion, lyotropic liquid crystal and vesicle. Moreover, long-chain ILs can operate as ionic surfactants and form analogous self-assembly in water or oil. *Qiu et al.* summarized studies of IL based microemulsions from the perspective of the role of ILs (*Qiu & Texter*, 2008). ILs participated in the formation of microemulsions, in which ILs replaced oil, water or surfactants. *Hao et al.* reviewed self-assembled structures (such as micelles, microemulsions, liquid crystals and vesicle) in ILs, which acted as solvent (*Hao & Zemb*, 2007). Summarizing the IL based organized assemblies, in which IL participated in the formation of micelles, microemulsions, vesicles and liquid crystals rather than acted as solvents.

Supramolecular configurations based on the host networks in ionic liquids

Generally, ILs is considered as homogeneous solvents, similar to normal molecular solvents. However, it has been found that supramolecular networks exist in pure ILs, especially in imidazolium ILs, which have already been extensively reviewed in the literature previously (*Dupont*, 2004; *Leclercq & Schmitzer*, 2009). Illustration of the organisation of ILs and several of organisations observed in pure ILs in order to raise interest in exploring how the supramolecular structures of ILs affect formation of supramolecules and supramolecular assemblies.

Effects of ionic liquids on formation of the supramolecular structures in the extraction systems based on crown ethers

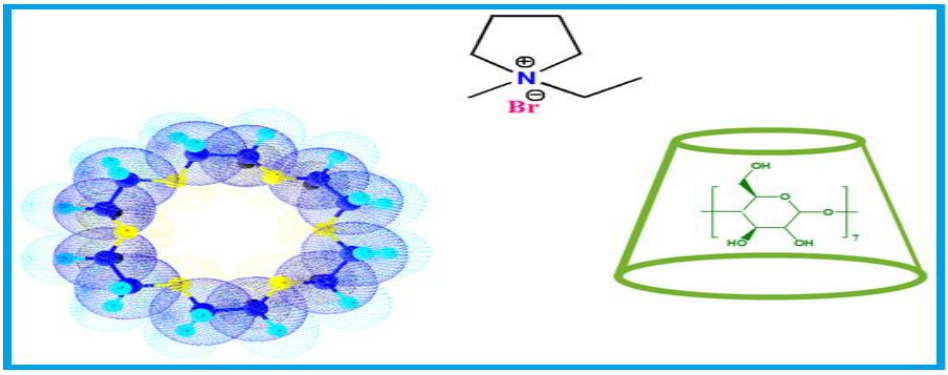
No significant close contacts are observed among ILs and crown ethers based on the study of co-crystallisation of imidazolium based salts with 18-crown-6 (18C6), though coulomb interactions between ionic (liquid) components and hydrogen bonding are important (*Gjikaj et al.*, 2008). However, because of the influence of ILs to scheme of crown ethers, they are being used in the extraction of metal ions, amino acids and so on. The extraction process can be easily tailored by varying substituting groups in imidazolium cation and the counter anions.

In succession, to a greater extent systems are involved ILs and crown ethers were investigated (*Chun et al.*, 2001; *Langmaier et al.*, 2009; *Nockemann et al.*, 2007; *Okamura et al.*, 2010; *Stepinski et al.*, 2010; *Visser et al.*, 2000; *Xu et. al.*, 2009). These consequences discovered as the alkyl group in the ILs was elongated, the extraction efficiency decreased, but extraction selectivity increased. The distribution is not only connected to the concentration and hydrophobicity of crown ethers, but also to the composition of aqueous phase.

Concluding that ILs can perform as guests to form supramolecules with several kinds of host molecules (i.e., cyclodextrins, cucurbit[n]urils and calixarenes), and can participate in constructing of supramolecular assemblies (i.e., micelles, microemulsions, lyotropic LCs, vesicles and gels However, the host-guest interaction typically takes place in aqueous solution. In case of ILs, how do the host molecules interact with guest molecules, and how do ILs affect the interaction? These are two interesting and challenging subjects. In addition, when ILs is used as solvents, how will the supramolecular structures of ILs themselves affect formation of supramolecular assemblies. In the previous works it was studied that as because trivial water is difficult to be removed and could be included in the supramolecular framework of imidazolium ILs, ILs are not pure, which makes the system more complicated. This supramolecular structure may also have an effect on the formation of supramolecular assemblies. Recently, we noticed that water plays key role in the formation of IL based microemulsions. Therefore, the effect of supramolecular structures of ILs on the formation of supramolecular assemblies is another valuable subject. Now, these fields of ILs are just commencement to be noticed. With the development of the exploration in these fields, more and more interesting phenomena and imperative results will be obtained. Thus, this assorted investigation of ILs will encounter a new chance and challenge.

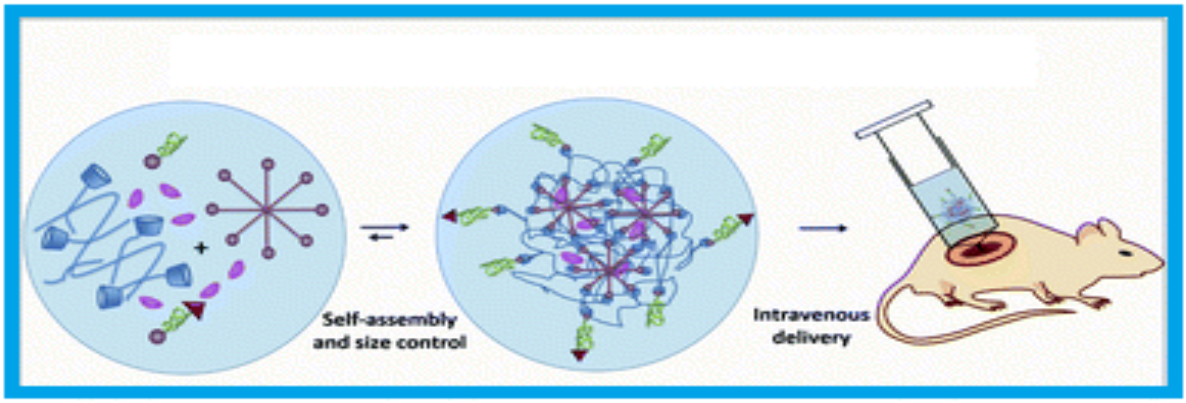
Herein, we report a thermodynamic and inclusion study of pyrrolidinium bromide- based PIL, [Pyrr] [Br], in mixture with the Cyclodextrin, Crown ether, H2O. Their volumetric, thermal and transport properties are presented as the function of temperature and composition, and then discussed in order to understand the molecular interactions between (individual ion-solvent), (cation-anion), and

(PILs ions pair-ion pair) in solution. Inclusion complexes have been also formed between cyclodextrin and pyridinium based IL.



II. (5) In Vitro Background: Controlled delivery of the Inclusion Complexes in our body

Animal based experiments lie at the very base of understanding the toxic and biological role of several compound or preparation. All such products with medicinal, toxicological or regulatory role in living systems are classified accordingly to avoid biohazard or attain beneficiary position. In the other hand, inflammation is an incredibly basic mediator of all the immunological invasions. Whenever an external pathogen is introduced in a host body, inflammation becomes the first barrier to prevent the infection of the invader. However, when present for a lengthened time, inflammation can cause a severe tissue damage and immune cell infiltration. Some of the previous works are mentioned from which we got the idea to explore inclusion in terms of in-Vitro, Firstly, bioavailability studies in rats showed the extent of absorption to be same for the free and complexed ibuprofen. Results of this report signify that β-cyclodextrin could be a useful additive to solid ibuprofen formulations as it may result in a more rapid and uniform release of the drug. Secondly, In vitro permeation and retention studies showed a higher penetration rate of vitamin E in free and encapsulated forms, from the W/O emulsion. The carriers studied appear to be promising systems for topical administration. A variety of yields are assessed for the amelioration of prolonged inflammation in the modern pharmao-medicinal systems. [599, 600] *Considering the role of Vitamins and their derivatives, we have assessed the potential role of these compounds against inflammation.*



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