THEORETICAL STUDIES ON SOME ASPECTS OF CHEMICAL REACTIVITY USING DENSITY BASED DESCRIPTORS

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CERTIFICATE

This is to certify that the work presented in this thesis entitled, "**Theoretical Studies on Some Aspects of Chemical Reactivity Using Density Based Descriptors**" by **K. R. S. Chandrakumar**, for the degree of Doctor of Philosophy, was carried out by the candidate under my supervision in the Physical Chemistry Division, National Chemical Laboratory, Pune, India. Any material that has been obtained from other sources has been duly acknowledged in the thesis.

Date :26-08-02

Place : Pune

Prof. Sourav Pal

(Research Guide)

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"*If you find a solution and become attached to it, the solution may become your next problem!!!*" - As I think of my research guide, Prof. Sourav Pal, the above words of him glimpses to my mind with my own perception on the academics. Although his unconventional thoughts sometimes appeared to be pessimistic to me, those hot arguments have, in fact, elevated my confidence and given a new dimension to each problem. I was strongly motivated by his inspiring classroom lectures. It is my great pleasure to acknowledge him for the freedom that he has given to me to pursue the research independently and for his constant encouragement with critical appraisal on my work. His guidance and association have been very friendly rather than like a formal student-guide relationship and this would evolve with the time even in my future carrier also.

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Chapter 1 General Introduction

Chapter 4 A Critical Study on the Calculation of Interaction Energy Using Global and Local Reactivity Descriptors: Effects of Basis set, Electron Correlation and the Use of Different Electron Partitioning Methods

Chapter 5 Study of Local Hard-Soft Acid-Base Principle to Multiple-Site Interactions

Chapter 6 The Influence of Electric Field on the Global and Local Reactivity Descriptors: Reactivity and Stability of the Hydrogen Bonded Complexes

Abstract of the thesis

The present thesis deals with some aspects of the reactivity of molecular systems using the recently proposed density functional theory based global and local reactivity descriptors, viz., chemical potential, hardness, Fukui function and local softness. In particular, an attempt has been made in this thesis to correlate the reactivity pattern of molecular systems using these descriptors in a semi-quantitative way. Essentially, we will provide a method to evaluate the stabilization or interaction energy of the molecular complexes in terms of these reactivity descriptors of the individual interacting systems. The basis of these models emerges from the second order energy-density perturbation method using the external potential and the number of electrons as basic perturbation variables. One of the models developed by Gazquez and co-workers, known as local HSAB principle, forms the basis of the proposed model presented in the dissertation. This model can describe the interaction between the molecular systems occurring only through single-site. We have demonstrated the efficacy of the model by taking suitable examples. We have further generalized this model to account for the variety of molecular interactions taking place through multiple reactive sites as well. The present work also rationalizes the relative influence of the hardness, softness parameters in determining the nature of bonding between different types of systems and in stabilizing these molecular complexes in a semi-quantitative way. The present thesis dissertation is organized as follows.

In chapter 1, we briefly review the earlier theoretical developments made towards the broad subject of chemical reactivity using the quantum chemical methods. We will describe how the empirical conceptual ideas (electronegativity, chemical potential, hardness, softness, etc.) have been theoretically quantified within the framework of DFT. The success and failure of these descriptors in predicting the reactivity of molecular systems will be discussed in detail along with other recent developments and applications that are relevant to the present objective of the thesis. We will then outline the energy-density perturbation methods within the domain of DFT and the different semi-quantitative models, including local HSAB principle, in finding a direct correlation between the density based descriptors and the molecular stabilization or interaction energy.

Chapter 2 contains two parts. In the first part of the chapter, a qualitative study has been made on the applicability of the local reactivity descriptors in predicting the reactivity and selectivity of molecules towards the various cation-exchanged zeolite-A.

The ambiguities raised in the prediction of the reactivity order obtained only through these descriptors are discussed. In the second part, we start with the detailed description of the quantitative local HSAB model based on second order energy density perturbation method, initially formulated by Gazquez and co-workers. We discuss each term present in the model and their role in evaluating the interaction energy of the molecular complexes. We also point out the lacuna present in the definition of one of the important parameters λ present in the expression and its arbitrary definition that has been followed in the literature. We have shown that the arbitrary definition or complete neglect of that term may lead to erroneous results even at the qualitative level. However, there is no rigorous way to define this term. Subsequently, we have defined this parameter λ as the charge transfer term i.e. change in the electron densities of the systems before and after the interaction process. Using the present definition of the parameter λ, we have made an attempt to evaluate the interaction energy of the gaseous molecules with different cations present in the various reactive sites of zeolite-A. The reliability of the parameter λ in the calculation of interaction energy has been validated by comparing the experimental adsorption energy values and trends of the adsorption patterns over different cations.

Chapter 3 rationalizes the relative influence of the hardness, softness parameters in determining the nature of bonding between different types of systems and in stabilizing the molecular complexes. It also explains the principal role of electronegativity (or chemical potential) equalization and the charge distribution process in stabilizing the complexes. The effect of correlation has been studied on the reactant descriptors and subsequently, on the soft-soft as well as hard-hard kind of interactions. To solve these critical issues, we have undertaken a systematic study of the Lewis acid-base complexes, the interaction between the Lewis acid, BH_3 and the Lewis base NH_3 and its fluoro- and methyl- derivatives and some of the known hydrogen-bonded complexes.

In Chapter 4, we will make a critical study on the applicability and reliability of the semi-quantitative model proposed in the earlier chapters based on the local HSAB principle in calculating the interaction energy of the molecular systems. In particular, the effects of basis sets, the correlation and the electron partitioning methods on the calculation of interaction energy using the descriptors will be studied. The cases that we have considered for the present study are the Lewis acid-base interactions, the interaction of acids BH_3 and BF_3 with bases NH_3 and CO. Since these complexes are well studied by both experimental and other conventional theoretical methods, these serve as the benchmark systems for the study of the above mentioned effects.

The methods, described in the earlier chapters, are applicable only to the interactions on single-site. However, there are many complexes interacting through multiple-sites, like the intra and inter- molecular hydrogen bonding interaction in DNA, RNA and peptides kind of systems. The description of such interactions through local HSAB principle requires modification of the local HSAB principle to describe these multiple-site interactions and accordingly, in chapter 5, we have made an attempt to generalize the local HSAB principle using the group softness concept as one of the important concepts. Essentially, we find there are two limiting cases, so-called localized reactive model and the global reactive model. Their origin stems from the nature and location of the reactive sites present in the molecular systems. The feasibility of this development has been tested by selecting some prototype inter molecular hydrogen bonded systems where the multiple-site interactions are important. We also discuss the nature of these different approaches and the domain of their applicability. The model can describe various interactions, which are intermediate between fully local and global in nature.

In the chapter 6, a preliminary study has been undertaken to study the effect of external electric field on the global and local reactivity descriptors to explain the reactivity and stability of the simple hydrogen bonded acid-base complexes in the presence of external field. The present study is also extended to an another important class of multiple-site interacting complexes, Watson-Crick DNA base pair models, Guanine-Cytosine and Adenine-Thymine. Since the molecular interaction has been considered in terms of the density response functions, it would be interesting to study the variation of these functions due to the external field. The study of the response of molecular systems due to the external field through the density based descriptor gives the information about the behavior of the monomers in forming the complexes and eventually, it will be helpful in simulating other external effects. Using the inverse relationship between the global hardness and softness parameters a relationship is obtained for the variation of hardness in terms of the Fukui function under the external electric field. It is shown that the variation of hardness in the presence of external field does not necessarily imply that the reactivity of a specific site or an atom present in the molecule would be enhanced or deactivated.

List of Publications

1. **K. R. S. Chandrakumar**, S. Pal, A. Goursot, R. Vetrivel, "Influence of Cation Distribution on the Electric Field Strength Inside the Na-A Zeolite Cavity: A Molecular Modeling Approach", Recent Trends in Catalysis, Ed. by V. Murugasen *et al.* p.197-202, **1999,** Narosa Publishing House, New Delhi.

2. S. Pal and **K. R. S. Chandrakumar**, "Critical Study of Local Reactivity Descriptors for Weak interactions: Qualitative and Quantitative Analysis of Adsorption of Molecules in the Zeolite Lattice", *J. Am. Chem. Soc*. **2000**, 122, 4145-4153

3. **K. R. S. Chandrakumar** and S. Pal, "A Novel Theoretical Model for Molecular Recognition of Multiple-Site Interacting Systems Using Density Based Response Functions" *J. Phys. Chem. B* **2001**, 105**,** 4541-4544

4. **K. R. S. Chandrakumar** and S. Pal, " Study of Local Hard-Soft Acid-Base Principle to Multiple-Site Interactions" *J. Phys. Chem. A* **2002**, 106, 5737-5744

5. **K. R. S. Chandrakumar** and S. Pal, "DFT and Local Reactivity Descriptor Studies on the Nitrogen Sorption Selectivity from Air by Sodium and Calcium Exchanged Zeolite-A", *Colloids and Surfaces A* **2002,** 205, 127-138

6. **K. R. S. Chandrakumar** and S. Pal, "The Concept of Density Functional Theory Based Descriptors and Its Relation with the Reactivity of Molecular Systems: A Semi-Quantitative Study" *Int. J. Mol. Sci.* **2002,** 3, 324-337

7. S. G. Sudrik, S. P. Chavan, **K. R. S. Chandrakumar,** S. Pal, S. K. Date, S. P. Chavan, H. R. Sonawane, "Microwave Specific Wolff Rearrangement of α-Diazoketones and Its Relevance to the Nonthermal and Thermal Effect" *J. Org. Chem.* **2002,** 67, 1574-1579

8. **K. R. S. Chandrakumar** and S. Pal, "A Systematic Study on the Reactivity of the Acid-Base Complexes through the Local Hard-Soft Acid-Base Principle" Communicated to *J. Phys. Chem. A*

Chapter 1

General Introduction

1.1 Introduction and Motivation for the Present Thesis

One of the important questions concerning the reactivity of molecules is the prediction and interpretation of the preferred direction of a reaction and product formation under different conditions. The study of molecular interactions has been a great challenge from the experimental and theoretical point of view. Although, the quantum chemical methods provide a basic framework to study the molecular interaction in an accurate way, the applicability of these methods was limited to small molecular systems with the precision to the experimental findings. For large molecular systems, these methods become prohibitively expensive from the computational point of view. The molecular orbital wave function obtained from the Hartree-Fock method or highly correlated methods, embodies all the information about the structure, stability and reactivity of the system. However, the wave function containing this information is in such a complex form that is difficult to translate into heuristic concepts and ad-hoc models that are familiar to the chemists.[1-7] In general, what we need in chemistry, in addition to specific details about individual molecules, is an understanding of how the reactivity of molecular systems differs within the broad classes of molecules. Hence, it is necessary to develop very systematic and effective models, which should at least provide the correct qualitative order and a good prediction of the phenomenon involved. Such approximate models or indices have been used in the literature to explain the reactivity of molecular systems, e.g. valency, charge density, electrical moments, delocalization, molecular electrostatic potential and several other molecular orbital indices.[1-12]

In recent years, Density Functional Theory (DFT) has been shown to provide a framework for the simple physical interpretations of complex reactive phenomena and build a bridge to the chemist's intuitive concepts in an elegant way.[13-19] The quantification of some of the most widely utilized concepts in chemistry, such as, electronegativity, hardness, softness and the Fukui function or frontier orbitals, as realized in terms of the basic parameters in the DFT, presents a significantly important development in quantum chemistry.[13-19] Using these density-based parameters, two important chemical principles, viz., Hard-Soft Acid-base (HSAB) principle and the principle of maximum hardness, have been proved under some constraints.[20-22] The development made in this area has illustrated the usefulness of these parameters in a great detail to understand the structure, stability and the chemical reactivity of molecules. An elaborate discussion on this topic will be made in the subsequent sections.

The present thesis also deals with some aspects of the reactivity of molecular systems using the recently developed novel density-based descriptors. In particular, an attempt has been made to correlate the reactivity pattern of molecular systems using these descriptors in a semi-quantitative way. Essentially, a method is provided to evaluate the intermolecular interaction energy of the molecular complexes in terms of these descriptors. The basis of these models emerges from the second order energy-density perturbation method using the external potential and the number of electrons as the basic perturbation variables. Although there have been few such semi-quantitative models in the literature, in this thesis we would essentially follow the method given by Gazquez and Mendez or so called Local HSAB principle.[23-24] This model can describe the interaction between the molecular systems occurring only through single sites. The formulation of a novel theoretical model to describe the intermolecular interactions that are occurring through the multiple reaction sites is also presented. These models have been tested through some of the systems that are well studied experimentally as well as theoretically. The validity of the approximation that is used in the proposed model is also discussed. In addition, the present thesis also rationalizes the relative influences of the hardness, softness and other local parameters in determining the nature of bonding between the different types of systems and in stabilizing these molecular complexes. The limitation and weakness of the models are also addressed in detail.

First, we will start the details of the thesis by projecting a brief overview of the underlying concepts of the reactivity descriptors in view of the present objectives of the thesis. Following the review of the general concepts and rigorous definition off these descriptors, applications of these in predicting the reactivity of molecular systems will be discussed in detail along with the other recent developments. During the course of present review, some of the key issues that are pertinent to the structure and reactivity relationship with these descriptors will be addressed. We will then outline the energy density perturbation method within the domain of DFT and different semi-quantitative models that will establish the relation between the total energy changes with the changes in the density based descriptors and in their derivatives.

1.2 Brief Overview of Reactivity Descriptors

Many of the chemical phenomena can be understood and predicted by some theoretical quantities that have a direct relationship with the characteristic sets of important chemical properties. These quantities are, in general, called descriptors. The reactivity descriptors are very much pertinent to the reactivity of the molecular systems and are intended to provide a qualitative and semi-quantitative measure of the extent to which a particular site will be affected in a given condition. In the last two centuries, there have been several attempts to explain the nature of bonding and reactivity of molecular systems based on some intuitive ideas, models and empirical rules in terms of the reactivity descriptors.[1-7] These are essentially derived from several experimental observations and many of the chemical facts. This empirical rule, conceptual models and the studies, which have led to the present understanding, have contributed much to the definition of the problem of early chemistry. These ideas are more *connected* with respect to the small domain of experimental facts rather than to *be systematic* in a general sense and hence, it was only partially successful in explaining the chemical and physical aspects of the systems. It has also been realized that the formulation of a systematic generalization is not so simple from these qualitative ideas and models. This fact is due to the existence of the limitless number of different classes of molecule and consequently, the fascination as well as frustration started emerging out from chemist's community.

Quantum mechanics in terms of Molecular orbital theory tried to advance the degree of integration of all the conceptual models and principles, and formed mathematical foundations to it. The development of quantum chemical methods led to the rigorous definition of many of the empirical chemical concepts and has provided a method for the calculation of the properties of chemical systems and the bonding that is involved in the molecular systems.[1-7,25] Among all the important developments in the field of descriptors, some have been remarkably successful in explaining the reactivity of the molecular systems. In particular, the concept of the highest occupied molecular orbital and lowest unoccupied molecular orbital (HOMO-LUMO) developed by Fukui (frontier molecular orbital theory),[4] Woodward-Hoffmann's molecular orbital symmetry (correlation diagrams),[10] Mulliken's donor-acceptor concept (overlap and orientation principle)[26] and Pearson's hardness and softness concept (Hard-Soft Acid-Base principle).[22] These descriptors or principles have made a profound impact on our understanding of the experimental observations at the microscopic level in an elegant way. Along with these descriptors, other descriptors have also been proposed, such as charge density and its derivatives (Bader's Atoms in Molecule),[12] molecular electrostatic potential,[11] electric field,[3] etc. Thus, there have been many such descriptors and all of them have their own merits and demerits. Hence, it is very essential to know which parameters represent molecular structure and reactivity, and which are the most appropriate representatives of the tendency of a given molecule to undergo a certain class of reactions. In the present thesis, special attention is focused on the developments of the recently proposed density-based descriptors, such as chemical potential, hardness, softness, Fukui function and their derivatives. More importantly, we are interested in extending these concepts to investigate the reactivity of molecular systems in a semi-quantitative way.

1.3 The Concepts of Hardness and Softness Parameters: A Historical Perspective

Concepts such as hardness and softness have been part of the vocabulary of the chemists since the period of Berzelius, mainly to explain the occurrence of natural metal ores with several other groups or ligands, such as sulfides, oxides or carbonates.[27] The foundation for the concept of chemical hardness lies in the study of Ahrland and Chatt.[28] They showed that the metal ions are simply one group of electrophiles and which in turn can be divided into two classes (a) and (b), depending on the relative affinities for ligands with various donor atoms. The class (a) metal ions react strongly with nucleophiles, which are normally basic to the protons. The class (b) metal ions react strongly with nucleophiles that can be easily oxidized. For instance, considering the affinity of some of the metal ions towards oxides and sulfides, the reactivity order for these metal ions has been given as,

$Mg^{2+} > Fe^{2+} > Ca^{2+} > Zn^{2+} > Pb^{2+} > Cu^{2+} > Cd^{2+} > Hg^{2+}$.

This order has been later shown to be in the increasing order of softness or decreasing order of hardness. Most of these works were focused to explain the reason for the preference of metal ions with some specific ligands. Although these classifications and explanations were satisfactory for the occurrence of many natural ores and other complexes in terms of the hardness and softness concepts, it was merely a conclusion from the observed results. However, there was no explanation for the variation in the stability of these complexes and it was probably due to the lack of knowledge of electronic structure of the systems and nature of the chemical bonds.

The first detailed explanation on the basis of electronic structure theory was given by Mulliken.[26,29] He suggested that the bond between the molecular systems, A and B, is predominantly ionic in character with a single electron transfer from the Lewis base B to to the Lewis acid A. Mulliken also explained the stability or the strength of the molecular Lewis acid-base complex with the help of quantum mechanical formulation. He further argued that stability of the complex AB increases with the increasing heat of formation from system A and B, which in turn depends upon the resonance energy (i.e. resonance between the no bond and ionic bond structure of A and B). From the corresponding energy profiles of the no bond and ionic bond structures, he concluded that the lower the vertical ionization potential of B and higher the electron affinity of B, the more is the resonance, which implies greater strength of Lewis acid A and base B. Mulliken also showed that when both A and B are soft chemical species (by 'soft' he meant less exchange repulsion between the two systems) the resultant compound AB is more stable than the case when both of them are hard species (again by 'hard' he meant more exchange repulsion between two). So, according to him, softness in A or B should tend to make it a better acid or base, respectively,. On the basis of the above definition of "softness" or hardness", he also explained the "exothermicity" and "endothemicity" of the molecular compound AB.

This general idea of classifying reagents with respect to their chemical behavior stimulated further research on the physical properties of the complexes. Among all, the work contributed by Pearson is considered to be one of the most important works and it has been found to be very useful for correlating and better understanding of a very large amount of chemical information in terms of the hard and soft parameters.[20,22,30,31,32] More over, these concepts have got further momentum and it became one of the most useful concepts among the chemist's community after the proposition of HSAB principle by Pearson in 1963.[30] He has actually classified the molecular systems in terms of the hard-soft acid-base in a general way and the details are given below:

(a) Hard acid (acceptors or nucleophiles): High positive charge, low polarizability and small in size. e.g. H^+, Ca^{2+}, BF_3, etc

(b) Soft acid: Low positive charge, high polarizability and larger in size e.g. Hg^{2+}, BH_3, I^+

(c) Hard base (donors or electrophiles): High electronegativity, difficult to oxidize and low polarizability. e.g. F^-, NH_3, OH^-

(d) Soft base: Low electronegativity, easily oxidizable and higher polarizability. e.g. H^-, I^-, C_2H_4, CN^-

HSAB principle says that there is an extra stabilization if hard acids bind to coordinate with hard bases and soft acids bind to coordinate with soft bases. It is a condensed statement of very large amount of chemical information from experimental observations. This concept, which found its first applications in rationalizing inorganic stability constants, was shown to be useful even in organic chemistry. An account on the usefulness of the HSAB principle can be found in different areas through several proceedings and monographs or shorter overview articles. Some examples are given below that will explain the HSAB principle. For example, Li^+ is a hard acid, F^- a hard base, Cs^+ a soft acid, and I^- a soft base. The exothermic nature of the reaction shows that hard-hard (Li and F) and soft-soft (Cs and I) interactions are preferred over hard-soft or soft-hard interactions. In a similar way, one can also explain the other reactions through the HSAB principle.

Hard-soft + Soft-Hard = Hard-Hard + Soft-Soft ΔH in kcal/mol

$Li^+I^- + Cs^+F^- = Li^+F^- + Cs^+I^- \quad \Delta H = -12.1$

$H^+C1^- + Li^+H^- = H^+H^- + Li^+Cl^- \quad \Delta H = -56.1$

$H^+Br^- + I^+OH^- = H^+OH^- + I^+Br^- \quad \Delta H = -26.4$

$HO^+F^- + Li^+H^- = HO^+H^- + Li^+F^- \quad \Delta H = -144.1$

$$Li^+F^- \quad + \quad H^+Br^- \quad = \quad H^+F^- \quad + \quad Li^+Br^- \qquad \Delta H = -10.8$$

$$CH_3{}^+F^- \quad + \quad H^+I^- \quad = \quad H^+F^- \quad + \quad CH_3{}^+I^- \qquad \Delta H = -12.3$$

$$CH_3{}^+OH^- \quad + \quad H^+I^- \quad = \quad CH_3{}^+I^- \quad + \quad HO^-H^+ \qquad \Delta H = -12.6$$

There are many possible factors that might affect the strength of the hard-hard and soft-soft interactions. Indeed, it is probable that these factors may have different effects depending upon the particular situation. Although the foregoing discussion is sketchy, it touches on most of the factors, which seem likely to be important in controlling the nature of hard-hard and soft-soft interactions. Because of the complexity of these factors, a more detailed discussion would scarcely be justified. However, the theoretical proof for the HSAB principle will be discussed in the foregoing sections.

A more interesting idea is the one that relates the hard-hard and soft-soft character, respectively, to ionic and covalent interaction.[30-35] A simple explanation for hard-hard interactions is by considering them to be primarily electrostatic or ionic interactions. Most of the typical hard acids and bases are those that might be supposed to form ionic bonds such as Li^+, Na^+, etc and F^-, OH^-. As the electrostatic or Madelung energy of an ion pair is inversely proportional to the inter-atomic distance, the smaller the distance, the greater is the attraction between the hard acid and base. Since an electrostatic explanation cannot account for the apparent stability of the soft-soft interactions, it has been suggested that the predominant factor here is a covalent one. This would correlate well for transition metals, Ag, Hg, etc. It is usually assumed that bonds such as Ag-Cl are considerably more covalent than the corresponding ones of the alkali metals. In this regard, the polarizing power and the polarizability of d orbital electrons becomes important. Π-bonding has also been suggested for the soft-soft interactions. Π-bonding occurs more readily in those metal ions that have low oxidation states and large number of d electrons and hence, these conditions favor the soft-soft type of interactions. There are two final conclusions that can be drawn. One is that soft molecules are more reactive than hard molecules in all reactions where electron transfer or rearrangement is necessary. The second one is that the hard molecules resist change, not only in the number of electrons, but also in the distribution about the nuclei.

An empirical equation was suggested by Drago to correlate heats of formation of acid-base complexes, such as $-\Delta H = E_A E_B + C_A C_B$, where the term E represents the susceptibility of the acid or the base to undergo electrostatic interaction, and the term C represents their ability to participate in covalent bonding.[36] This equation seems to give excellent agreement with experiment and compares very favorably with that suggested by Pearson. However, its empirical nature and the number of independent parameters involved in the calculations make it very impractical to use. In addition, no physical reason or explanation for hard and soft behavior is provided by such an approach. Apart from the celebrated HSAB principle, one more principle was also proposed by Pearson, known as the principle of maximum hardness (PMH).[20] It states that there is a rule in nature that every system tries to be as hard as possible. We will make a detailed study of this principle in section 1.12.

1.4 Klopman's Quantum Mechanical Interpretation on HSAB Principle

Owing to the applicability of HSAB principle and its considerable success, Klopman attempted to give a theoretical basis using perturbation method based on the quantum mechanical theory.[34,37] He assumed that when two reactants approach each other, a mutual perturbation of the molecular orbitals of both reactants occurs and the resulting change in energy can be estimated from molecular orbital calculations. The total perturbation energy is produced by two distinct effects: (a) the neighboring effect which accounts for the interaction due to the formation of an ion pair without any charge or electron transfer, and (b) the partial charge transfer usually accompanied by covalent bonding. Following these assumptions under second order perturbation treatment, the expression for the change in the energy of the systems is given as,

$$\Delta E = -\sum_{ab} (q_a + q_b)\beta_{ab} S_{ab} + \sum_{k<l} \frac{Q_k Q_l}{\varepsilon K_{kl}} + \sum_{r}^{occ} \sum_{s}^{unocc} - \sum_{s}^{occ} \sum_{r}^{unocc} \frac{2\left(\sum_{ab} C_{ra} C_{sb} \beta_{ab} \right)^2}{E_r - E_s} \quad \text{---- (1.1)}$$

where q_a and q_b are the electronic population in the atomic orbitals of a and b. β and S are the resonance and overlap integrals; Q_k and Q_l are the total charges on atoms k and l; ε is the local dielectric constant; K_{kl} is the distance between the atoms k and l; C_{ra} is the coefficient of atomic orbital a in the molecular orbital 'r' where r refers to the molecular orbital on one molecule and similarly, C_{sb} is also defined.

In Eq. (1.1), when the difference between E_r and E_s for the frontier orbitals is large, there will be little charge transfer and hence, the contribution of the third term will be very less. In such cases, it is apparent that the perturbation energy is primarily determined by the total charges on the two reagents and thus, called as charge controlled reaction. Such an effect can be expected when E_r is very low (i.e. it is very difficult to ionize or polarize) and when E_s is very high (i.e. it has a low tendency to accept electrons). Since all the properties correspond perfectly to those associated with hard-hard interactions the charge-controlled effect can thus be directly related with the hard acid-base interaction cases.

On the other hand, when two frontier orbitals are nearly degenerate, i.e. $|E_r - E_s| \sim 0$ in Eq.(1.1), then their interaction becomes predominant and strong electron transfer occurs between them. In such cases, it is called as frontier-controlled reaction. It occurs only in reactions between nucleophiles with low electronegativity and electrophiles with high electronegativity involving a good overlap of the interacting orbitals. It can also be enhanced by high polarizability of the reagents, low solvation energies, and, in fact, by all properties reverse to the hard-hard interactions. Such interactions can be associated with the soft-soft interactions. The numerical results obtained from the above equation agree well with the qualitative description of softness and hardness given by Pearson. The above treatment also leads to a reasonable theoretical explanation of hard-hard and soft-soft interactions. This was the only model that could explain the HSAB principle during the period when the definition of hardness or softness concepts was disputed. In absence of any such formulation it would have been difficult to ascertain the justification for the hard-hard and soft-soft reactions.

1.5 Need For a More Quantitative Definition

As the general concept of hardness and softness suffers from the lack of physical basis, the predictions and explanations based on these descriptors remained only at the qualitative level. There is no scale of hardness or softness for the chemical species by which we can rank-order it. It was also not very clear how the reactivity of any base or acid is significantly influenced by both acids and bases with which it reacts as well as the medium in which the reaction occurs in terms of the hardness and softness parameters. It is clear that there is no universal ordering of this reactivity. The above weakness of this concept has been noted by several authors and subsequently, many analogies have been proposed to relate these concepts with several other molecular properties, such as electronegativity, polarizability, oxidation state, energy of the orbitals, etc. Most of these, however, do not correlate very well with the experimental facts and do not have a well-defined physical basis or account for all the properties attributed to hard and soft parameters. Although Klopman[34,37] tried to establish a theoretical basis for the hard and soft interactions, the definition of hardness or softness was not provided. The interpretation was valid only for reactions in solution and required the knowledge of other parameters, e.g. dielectric constant, ionic radius etc. Consequently, there was a high demand for an intuitive and correct theoretical approach to form a physical basis for these concepts. Advancement in this direction was possible only after the introduction of DFT, which can now be used to explain the hardness and softness parameters along with other local quantities.

1.6 Chemical Potential and Hardness from Density Functional Theory Viewpoint

The theorem due to Hohenberg and Kohn forms the basis of DFT.[13,38] The theorem states that the electron density $\rho(r)$ determines all properties of a non-degenerate ground state of an atom or molecule. The ground state electronic energy is a functional of the density, given by the formula,

$$E[\rho] = \int \rho(r)v(r)\, d\Gamma_1 + F[\rho] \qquad \text{---- (1.2)}$$

Here v is the external one particle potential and $F[\rho]$ is the sum of electronic kinetic energy and electron repulsion energy, $T[\rho]+ V_{ee}[\rho]$.

The density is spin free and may be expressed in terms of the wave function,

$$\rho(r) = N \int | \Psi(1,2, \ldots,N)|^2\, dw_1dx_2dx_3\ldots dx_n \qquad \text{---- (1.3)}$$

where $dx_i = dw_i d\Gamma_i$ is a space-spin volume element and dw_i the spin part. The number of electrons is given by the formula, $N=N[\rho]=\int\rho(r)d\Gamma_1$ ---- (1.4)

The density ρ and energy E are determined from the stationary principle,[13,39]

$\delta\{E_v[\rho'] - \mu N[\rho']\} = 0$ ---- (1.5)

where μ is a Lagrange multiplier. Of all possible solutions one picks the one or ones making E an absolute minimum. The associated value of μ is characteristic of the system of interest and is commonly called as the chemical potential of the system. From the above equation, μ can be written as,

$\mu = [(\delta E[\rho]/\delta\rho(r))_v]_{\rho=\rho(v)}$ ---- (1.6)

The quantity $\delta E/\delta\rho(r)$ is the functional derivative of the Hohenberg-Kohn functional with respect to the density. It is evaluated at the correct ground state density at an arbitrary point in space. The corresponding functional derivative with respect to the potential v, will be,

$\rho(r)=(\delta E[\rho]/\delta v(r))_\rho$ ---- (1.7)

The Lagrange multiplier μ associated with the constraint $N[\rho'] = N$ in the stationary principle, is the partial derivative of energy with respect to number of electrons.

In other words, the quantity μ is the partial derivative,

$\mu = (\partial E/\partial N)_v$. ---- (1.8)

The physical meaning of chemical potential in DFT measures the escaping tendency of an electron cloud. It is constant in three dimensional space for the ground state of an atom, molecule or solid and equals the slope of E versus N curve at constant external potential.[39]

At this point, it is very pertinent to note that the above quantity, chemical potential, is exactly identical with the definition of one of the important concepts, electronegativity (χ). In the literature, one can find a large number of definitions for the concept of electronegativity starting from Pauling's work which are essentially based on some intuitive ideas and experimental facts.[18] However, the rigorous theoretical justification has been now provided within the framework of DFT especially by Parr and his collaborators.[39] According to Iczkowski and Margrave definition, the electronegativity is expressed as,[40]

$\chi = -dE/dN$. ---- (1.9)

Using a harmonic approximation of the energy as a function of the number of electrons, the above Eq.(1.9) can be written as,

$$\chi = (IP+EA)/2 \quad \text{--- (1.10)}$$

where, IP and EA are the first ionization potential and first electron affinity, respectively.

The connection with Mulliken's definition of electronegativity is also more relevant with the present definition of chemical potential.[41] Mulliken defined electronegativity as the arithmetic average of IP and EA. The expression is just the finite difference approximation to the term, -(dE/dN). This is exactly identical to the present definition of chemical potential.

The corresponding second derivative of E(N) with respect to N, keeping the external potential or the nuclear charge fixed is defined as the absolute hardness.[42]

$$\eta = ½ (\partial^2E/\partial N^2)_v \quad \text{--- (1.11)}$$

From Eq. (1.11), hardness can be related to electronegativity or chemical potential through the identity,

$$2\eta = (\partial\mu/dN)_v = -(\partial\chi/dN)_v \quad \text{--- (1.12)}$$

The inverse of the hardness has been known as the softness.

$$S = 1/2\eta = (\partial N/\partial\mu)_v \quad \text{--- (1.13)}$$

Thus, the parameter hardness is interpreted as the resistance of the chemical potential to change in the number of electrons or resistance to deformation or change. The minimum value of hardness is zero and it corresponds to the maximum softness. Since these parameters (chemical potential, harness and softness) are obtained by averaging over atomic or molecular space, these are called as global reactivity descriptors (GRD).

As shown below, the definition of the chemical potential or electronegativity and hardness can be expressed in terms of the ionization potential and electron affinity.[39]

Consider an N-electron atom (or molecule) with electron density ρ_N and energy $E_N = E_v[\rho_N]$. The corresponding negative and positive ions have the same v; let their energies be, respectively,

$E_{N+1} = E_v[\rho_{N+1}]$ and $E_{N-1} = E_v[\rho_{N-1}]$

Let, their densities be $\rho_{N+1} = \rho_N + \Delta\rho_+$ and $\rho_{N-1} = \rho_N - \Delta\rho_-$

On expanding the energy expression in terms of the density increments,

$$E_{N+1} = E_N + \int \frac{\delta E_v}{\delta\rho(r)}\Delta\rho_+(r)d\tau + \frac{1}{2}\iint \frac{\delta^2 E_v}{\delta\rho(r)\delta\rho(r')}\Delta\rho_+(r)\Delta\rho_+(r')d\tau\ d\tau'\ + ... \quad \text{--- (1.14)}$$

$$E_{N-1} = E_N - \int \frac{\delta E_v}{\delta\rho(r)}\Delta\rho_-(r)d\tau + \frac{1}{2}\iint \frac{\delta^2 E_v}{\delta\rho(r)\delta\rho(r')}\Delta\rho_-(r)\Delta\rho_-(r')d\tau d\tau' + ... \quad \text{--- (1.15)}$$

Here all the functional derivatives are evaluated for $\rho = \rho_N$. Using Eq. (1.7), it can be shown that,

$$\frac{\delta^2 E_v}{\delta\rho(r)\delta\rho(r')} = \frac{\delta^2 F}{\delta\rho(r)\delta\rho(r')} \quad \text{--- (1.16)}$$

Similarly, the functional derivatives can be abbreviated as,

$$\delta^2 F[\Delta\rho] = \frac{1}{2}\iint \frac{\delta^2 F}{\delta\rho(r)\delta\rho(r')}\Delta\rho(r)\Delta\rho(r')d\tau\ d\tau' \quad \text{--- (1.17)}$$

Using the above two expressions, one can find that,

$$IP = E_{N-1} - E_N = -\mu + \delta^2 F[\Delta\rho-] + ... \quad \text{--- (1.18)}$$

$$EA = E_N - E_{N+1} = -\mu - \delta^2 F[\Delta\rho_+] + ... \quad \text{--- (1.19)}$$

Hence,

$$\frac{IP + EA}{2} = -\mu + \frac{\delta^2 F[\Delta\rho_-] - \delta^2 F[\Delta\rho_+]}{2} + ... \quad \text{--- (1.20)}$$

$$IP - EA = \delta^2 F[\Delta\rho_-] + \delta^2 F[\Delta\rho_+] + ... \quad \text{--- (1.21)}$$

The above Eq. (1.20), is a modified form of Mulliken's formula.[41] If we would have expanded the energy expression in terms of the particle number instead of the density expansion, the second order correction would have vanished identically.

Using the hardness kernel definition η(r,r') (it will be shown in the next section) Eq.(1.17) can be written as ,

$$\delta^2 F[\Delta\rho] = \frac{1}{2}\iint \frac{\delta^2 F}{\delta\rho(r)\delta\rho(r')}\Delta\rho(r)\Delta\rho(r')d\tau d\tau' = \frac{1}{2}\iint \eta(r,r')\Delta\rho(r)\Delta\rho(r')d\tau d\tau' \quad \text{--- (1.22a)}$$

In systems for which $\Delta\rho_+$ and $\Delta\rho_-$ are nearly equal and the application of the above relation Eq. (1.22a), provides the value of hardness up to the second order correction,

$$IP - EA = \eta \quad \text{--- (1.22b)}$$

The evaluation of chemical potential and hardness/softness values from Eq. (1.9) or Eq. (1.20) is not practically feasible, as it is not possible to derive the change of energy with respect to the fractional number of electrons. So the operational definition of μ and η are provided by the finite difference approximation from the E(N) vs N curve.[42] Under this approximation, the first energy derivative ($\partial E/\partial N$), μ, is given as the average of left and right derivatives. The left derivative is obtained as the finite difference of energy of (N-1) and N electrons. This is simply equal to negative of IP. Similarly, the right derivative is obtained as difference of energy of N and (N+1) electrons. This is equal to the negative of EA. The finite-difference approximation to second order energy derivative ($\partial^2 E/\partial N^2$), η, is then expressed as the difference between the right and left derivatives. Thus μ and η can be expressed as,

$\mu = -(IP + EA)/2$

$\eta = (IP - EA)/2$ ---(1.22c)

On comparing Eqs.(1.22b) and (1.22c), it is clear that the parabolic approximation and finite difference method give the same result for the definition of hardness. However, in literature, the definition of hardness is defined as, (IP-EA)/2 in view of the Eq.(1.11). Here, the factor 2 is added arbitrarily to make the hardness definition symmetrical with that of chemical potential

One can also relate the above two quantities to the frontier orbital energies. This can be obtained through the Koopmans' approximation within the molecular orbital theory wherein IP and EA can be related to HOMO and LUMO energy as,[43,20]

$-E_{HOMO} = IP$ --- (1.23)

$- E_{LUMO} = EA$ --- (1.24)

Hence, μ and η can be written in terms of HOMO and LUMO as

$\mu = (E_{LUMO} + E_{HOMO}) / 2$ --- (1.25)

$\eta = (E_{LUMO} - E_{HOMO}) / 2$ --- (1.26)

Here it is imperative to note that the hardness now represents half of the energy gap between HOMO and LUMO.

The present theoretical formulation of the electronegativity, hardness and softness parameters have paved a way for the enhanced understanding of the HSAB principle and the principle of maximum hardness.

1.7 The Local Reactivity Descriptors and Their Importance

In the last section, the mathematical formulation of electronegativity and the global hardness/softness parameters was elaborately discussed. These quantities proved to be useful for analyzing the thermodynamic aspects of chemical reactions and provided some information about the overall properties of the chemical systems. These are especially useful in defining the reactivity pattern of a molecule, which are obtained by averaging over all atomic or molecular space. These descriptors, however, can not identify the reactive part or site of the molecule that has the high propensity to undergo chemical reactions. In other words, the information about the concept of selectivity or local reactivity can not be obtained using GRD. Most of the chemical reactions are primarily concerned with the properties associated with atoms, or groups of atoms or one part of the molecule. Moreover, concerning the concept of chemical reactivity, the important aspects are how the charge or density fluctuations will affect in chemical systems, and how these are related to the observed reactivity trends. Since the electron density distribution ρ(r) contains all the information about the system in its ground state, it is thought that the chemical reactivity should be reflected in its sensitivity to perturbations. These facts have necessitated or demanded the proposition of descriptors that are local or non-local in nature, so-called local reactivity descriptors (LRD). These local reactivity descriptors are highly desirable in establishing a reactivity-oriented description of the molecule because electron density distribution is the basis for understanding chemical reactivity.[44]

In particular, three local properties are of great interest, namely, the Fukui function f(r), the local softness s(r) and the local hardness η(r). These are defined by the following formula, respectively, [45-50]

$$\mathrm{f(r)} = \left[\frac{\partial \rho(r)}{\partial N}\right]_v = \left[\frac{\delta \mu}{\delta v(r)}\right]_N \qquad \text{--- (1.27)}$$

$$\mathrm{s(r)} = \left[\frac{\partial \rho(r)}{\partial \mu}\right]_v \qquad \text{--- (1.28)}$$

and $$2\eta(r) = \frac{1}{N}\int \frac{\delta^2 F}{\delta\rho(r)\delta\rho(r')}\rho(r')dr' \qquad \text{--- (1.29)}$$

These local descriptors are inter-related to each other. In what follows, we will discuss briefly on the development of these descriptors in view of its close association with the concept of the chemical reactivity.

1.8 Fukui Function and Its Relation with the Reactivity of Chemical Systems

The second order change in the energy due to the changes in electron number and external potential reveals more information about the reactivity and this comes from the first order change of chemical potential,[49,54,52]

$$d\mu = \eta dN + \int \delta\mu/\delta v(r)\, dr \qquad \text{--- (1.30)}$$

The first term in Eq.(1.30) has been identified as the absolute hardness, η; the second term ($\delta\mu/\delta v(r)$) is known as the Fukui function. Using Maxwell relation, the Fukui function can be rewritten as,[51]

$$f(r) = \delta\mu/\delta v(r)|_N = \partial\rho/\partial N|_v \qquad \text{--- (1.31)}$$

The Fukui function is formally defined as the derivative of electron density with respect to the total number of electrons N in the system, at constant external potential v(r).

If a reagent approaches another, which direction will be preferred (from among several directions that produce the same type of chemical potential)?. Parr and Yang attempted to answer the above question from the Eq.(1.30) in terms of the quantity $d\mu$ that measures the extent of the reaction.[49] They argued that the preferred direction is the one for which the initial $|d\mu|$ should be maximum. The first term on the right side of the Eq.(1.30) involves only global quantities and in general, it is less direction sensitive than the second term at large distances. The integrand, however, describes a local behavior and implies that energy or chemical potential changes are governed by the function f(r). Hence, the preferred direction is the one with the largest f(r) at the reaction site and the reactivity is measured by the Fukui index of Eq.(1.30). In other words, the above argument reveals that when any two different sites with similar dispositions interact with another given reagent, the reagent prefers the one which, on the reagent's approach, is associated with the maximum response of the system's chemical potential.

The physical meaning of the f(r) is implied by its definition, i.e. it measures the response of the chemical potential to an external potential at a particular point. The second definition implies, how the electron density of the systems changes with respect to the small changes in the number of electrons. While applying the finite difference approximation to f(r), it will, in general, have one value from left, one from the right and average value.

$f^+(r) = \left[\frac{\partial \rho(r)}{\partial N}\right]_v^+$ (derivative as N increases from N_0 to $N_0+\delta$) ---(1.32a)

$f^-(r) = \left[\frac{\partial \rho(r)}{\partial N}\right]_v^-$ (derivative as N increases from $N_0-\delta$ to N_0) ---(1.32b)

$f^0(r) = 1/2[f^+(r) + f^-(r)]$ (mean of left and right derivatives) ---(1.32c)

Now applying the frontier molecular orbital (FMO) theory of reactivity invented by Fukui and collaborators, the Fukui function can also be written as, (under frozen density approximation)[4,8]

$f^+(r) \approx \rho_{LUMO}(r)$ measures reactivity toward a nucleophilic reagent --- (1.33a)

$f^-(r) \approx \rho_{HOMO}(r)$ measures reactivity toward an electrophilic reagent --- (1.33b)

$f^0(r) \approx 1/2[\rho_{LUMO}(r) + \rho_{HOMO}(r)]$ measures reactivity toward an innocuous radical reagent --- (1.33c)

Here, the term HOMO and LUMO represent the highest occupied molecular orbital and lowest unoccupied molecular orbital, respectively. FMO theory predicts that the preferable electrophilic reaction in a molecule will take place at the site where the relative density of the HOMO is high and the position, which has a relatively high LUMO density, is preferable for the nucleophilic reaction. One of the important implications of the above result is that the function f(r) has been useful in rationalizing the concept of Fukui's FMO theory in a rigorous density functional theory framework and hence the function f(r) is termed as the "Fukui Function".

1.9 The Concepts of Local Softness and Local Hardness

Berkowitz and Parr[48] have derived the expression for local softness that reveals its relation to its reciprocal property, local hardness.[46,47,52] The idea is to define the appropriate two-variable kernels for hardness and softness, and then to generate local hardness and local softness from the corresponding kernel equations.

Here, we consider a ground state, or change of one ground state to another for which ρ(r) determines all properties, it determines μ and v(r). Starting from the Hohenberg-Kohn theorem, the modified potential can be written as,

$$u(r) = v(r) - \mu = \frac{\delta F[\rho]}{\delta \rho(r)} \qquad \text{--- (1.34)}$$

In other words, u(r) is a functional of ρ(r) and the functional derivatives,

$$-2\eta(r,r) = \frac{\delta u[r]}{\delta \rho(r')} = \frac{\delta u[r']}{\delta \rho(r)} \qquad \text{--- (1.35)}$$

The quantity, η(r,r') is called as the hardness kernel.

Similarly, ρ(r) is a functional of u(r) and its functional derivative also exists. This quantity is called as the softness kernel and it is defined as,

$$-s(r,r') = \frac{\delta \rho[r]}{\delta u(r')} = \frac{\delta \rho[r']}{\delta u(r)} \qquad \text{--- (1.36)}$$

Since the above two functional derivatives exist, a proper reciprocity can be written as,

$$2 \int s(r,r')\, \eta(r,r'')\, dr' = \delta(r-r'') \qquad \text{--- (1.37)}$$

In other words, it can be seen that the hardness and softness kernels are reciprocals of each other from the Eq. (1.37).

Using the above Eq. (1.36) and Eq. (1.35), one can now identify the local softness and local hardness terms, respectively,

$$s(r) = \int s(r,r')dr' \qquad \text{--- (1.38)}$$

$$\eta(r) = 1/N \int \eta(r,r')\rho(r')dr' \qquad \text{--- (1.39)}$$

These two quantities are also local in nature, i.e.,

$$2 \int s(r)\, \eta(r)\, dr = 1 \qquad \text{--- (1.40)}$$

In the above Eq. (1.38), the local softness, s(r), is given by,

$$s(r) = \frac{f(r)}{2\eta} = f(r)S \qquad \text{--- (1.41)}$$

$$= \left[\frac{\partial \rho(r)}{\partial N}\right]_v \left(\frac{\partial N}{\partial \mu}\right)_v$$

$$= \left[\frac{\partial \rho(r)}{\partial \mu}\right]_v \qquad \text{--- (1.42)}$$

In Eq. (1.41), f(r) is the Fukui function. Since the Fukui function is normalized function, the local softness must yield the global softness on integration.

$$\int s(r)\, dr = S \int f(r)\, dr = S \qquad \text{--- (1.43)}$$

To obtain the explicit formula for $\eta(r)$, one can use the Eq. (1.16).

$$2\eta(r) = \frac{1}{N}\int \frac{\delta^2 F}{\delta\rho(r)\delta\rho(r')}\rho(r')dr' \qquad \text{--- (1.44)}$$

The global hardness can be expressed in terms of the local hardness as,

$$\eta = \int f(r)\eta(r)\, dr. \qquad \text{--- (1.45)}$$

It should be noted that the definition of local hardness is not very clear and is defined in an ambiguous manner. It has been pointed out by Harbola, Chattaraj, and Parr that the derivative is ambiguous for a ground state due to the Hohenberg-Kohn theorem.[50] The concept of local hardness can be considered as a generalized classical electrostatic potential[53] and the detail of this relation will be shown in section 1.13.

As it can be seen from the equations for the local quantities, the local softness is the measure of the response of the electron density to a perturbation in the chemical potential at constant external potential. Since the chemical reaction are, in general, considered as a perturbation in the number of electrons, the local softness can be effectively used as an appropriate descriptor to probe the chemical reaction. In particular, this has direct implications to the area of catalysis where the fluctuation in charge density is shown to be very important.[45] In other words, larger the density fluctuation at a particular reaction site, larger will be the value of the Fukui functions, hence, the reactivity at that site or point will be greater.[49] Recently, Gazquez and Mendez have proposed one more reactivity principle from the value of these Fukui function or local softness, known as the local version of the HSAB principle, that involves the descriptors of both of the reacting systems for prediction of reactive sites.[23,24] It states that the interaction between any two molecules will occur not necessarily through their softest atoms, but rather through those atoms of the two systems whose Fukui functions are identical. The details of this principle and proof will be explained in the later section. A considerable advantage of using the LRD is that such quantities are local functions, in contrast to the global quantities, which are obtained by averaging over all space, and therefore LRD should reveal finer details about the behavior of a system. The reactivity analysis based on these descriptors for the chemical systems and its relation with the molecular properties is explicitly discussed in the section 1.13. Although these indices were successful in generating the experimentally observed intra-molecular reactivity trends in several cases, the study by Roy *et al.* showed trends are not always very reliable.[54] Based on the condensed Fukui functions (or local softness), Roy *et al*. introduced two different local reactivity descriptors, relative electrophilicity and relative nucleophilicity, to locate the preferable site for nucleophilic and electrophilic attack, respectively. These two reactivity descriptors are shown to generate improved intra molecular reactivity trends than those obtained from condensed FF indices.

1.10 Methods for Computing the Local Quantities

In section 1.8 and 1.9, it is shown that the local quantities, namely, Fukui function and local softness, contain the vital information about the reactivity of the molecular systems and there are useful in predicting the site reactivity and selectivity. Herein, we will make a detailed discussion on the computation of these local quantities. As already stated, the local softness, s(r) is itself defined as the product of the Fukui function, f(r), and the global softness of the system and hence, it is realized that the calculation of Fukui function is very important to probe the reactivity of molecular systems.

The formal definition of the Fukui function, as introduced by Parr and Yang, is a function of position r in the given molecular space, varying from one position to another.[49] By plotting these functions on some surface, one can identify the part of the molecule with the largest value of the function and hence, the most reactive part. Although, the definition of the function and the calculated plot seem to be simple in identifying the reactive part of a system, it is often difficult to plot the surface as well as to interpret the information provided by such plots. Moreover, the chemist is mostly concerned with the properties associated with atoms, or groups of atoms or functional groups, rather than the properties associated with points in space. Hence, it is necessary to condense the values of f(r) and s(r) around each atomic site into a single value that characterizes the atomic contribution in a molecule to describe the site-selectivity or site reactivity of an atom in a molecule. From the viewpoint of conceptual utility, the condensed values are rather more descriptive and comprehensive than the value of the function at a particular point r. This can be achieved by electronic population analysis or in other words, by performing integration over a specific region of the molecule. This is known as regional or condensed functions. This method was first proposed by Yang[55] and Mortier in 1986 based on the Mulliken population scheme.[56] From Eqs.(1.32a-c), for an atom x in a molecule, depending upon the type of electron transfer, we have three different types of condensed Fukui function.

$f_x^+ = q_x(N+1) - q_x(N)$ nucleophilic attack --- (1.46a)

$f_x^- = q_x(N) - q_x(N-1)$ electrophilic attack --- (1.46b)

$f_x^0 = ½[q_x(N+1) - q_x(N-1)]$ radical attack --- (1.46c)

where q_x is the gross charge of the atom x in a molecule. The corresponding condensed local softnesses, s_x^+, s_x^-, and s_x^0 can be also defined.

This simplified expression for the Fukui function and the local softness has received overwhelming attention from the theoretical chemists and it has facilitated to probe the reactivity of the molecular systems for different cases, for e.g. the intra and intermolecular interactions, inorganic solids-zeolites and metal oxides, catalysis, etc.(see section 1.14).[58-61] Other population schemes, such as, Löwdin partitioning method,[62] natural population analysis (NPA),[63] Bader's atoms-in-molecules (AIM) partitioning method,[64] the charges derived from molecular electrostatic potential[65] and electronegativity equalization[66] methods are also employed. Nalewajski introduced atom-in-molecule (AIM) Fukui function indices in an original, normal representation.[57] Komorowski *et al.* calculated atomic and group FF indices and hardness by the semi-empirical method.[67] Balawender *et al.* introduced a similar scheme at the *ab initio* level.[68] Thus, the concept of atomic charge in a given molecule has become one of the important parameters in the development of the density-based descriptors. At the same time, this has brought an important issue in defining the atomic charge in an unambiguous manner. Because, there is no rigorous definition for the atomic charge and more over, the partitioning methods are not unique to each other. As a result, the charge has only been empirically defined.[69] These partitioning methods are very sensitive to the basis sets and the level of the theory used in the calculation. In addition to these problems, the computation of these functions requires three different calculations for N, N+1, N-1 cases. The main problem here lies in the fact that there will always be a change of multiplicity of the electronic state that may lead to some computational convergence trouble, especially in those cases where strongly correlated states are generated by adding electrons to the system. In light of the above arguments and other technical problems, development of some new schemes has become more important for the computation of the local reactivity descriptors, which has firm theoretical basis.[70-85] The numerical Fukui function approximations and their applicability as chemical reactivity descriptors has been recently reviewed by Chermette.[77] Without going into many details, we will herein, try to describe the other methods that have been worked out in the literature. Chattaraj *et al.* proposed a different approach based on the gradient expansion of Fukui function and the expression is given as,[78]

$$f(r)=\frac{\rho(r)}{N}+\frac{\alpha}{N\rho^{2/3}(0)}\left\{\left[\left(\frac{\rho(o)}{\rho(r)}\right)^{2/3}-1\right]\nabla^2\rho(r)-\frac{2}{3}\left(\frac{\rho(o)}{\rho(r)}\right)^{2/3}\frac{\nabla\rho(r)\nabla\rho(r)}{\rho(r)}\right\} \quad \text{--- (1.47)}$$

where $\rho(0)$ is the value of the density at the nucleus and α is an empirical parameter. It should be noted that the expansion of this type produces only one Fukui function and $f^+(r)$ and $f^-(r)$ is not found.[78,79] Variational method for determining the Fukui function was also proposed by Chattaraj *et al.*[70] On defining the hardness kernel as,[13,48]

$$\eta(r,r')=\frac{\delta^2 E_{v0}[\rho]}{\delta\rho(r)\delta\rho(r')}=\frac{\delta^2 F[\rho]}{\delta\rho(r)\delta\rho(r')}=\frac{\delta(\mu-v_0(r))[\rho]}{\delta\rho(r')} \quad \text{--- (1.48)}$$

The functional $\eta(g)$ is then minimized with respect to g(r),

$$\eta(g) = \iint g(r)\, g(r')\, \eta(r,r')\, dr\, dr' \quad \text{--- (1.49)}$$

Applying the normalization constraint,

$$\int g(r)\, dr = 1 \quad \text{--- (1.50)}$$

Then, the Fukui function, f(r), is the function which minimizes the above Eq. (1.50) and $\eta[f(r)] = \eta$, the absolute hardness. Recently, Ayer and Levy have remarked that this variational method should be the method of choice for generating the Fukui function.[76] Unfortunately, the accurate determination of the hardness kernel is complicated by the lack of an accurate explicit kinetic energy functional.

Using Kohn-Sham theory and Janak formalism, Yang *et al.* have provided another approach for the computation of Fukui function, [80]

$$f^{+}(r) = |\phi_{N+1}(r)|^2 + \sum_{i=1}^{N} \left(\frac{\partial |\phi_i(r)|^2}{\partial N} \right)_v^{+} \quad \text{--- (1.51)}$$

$$f^{-}(r) = |\phi_{N}(r)|^2 + \sum_{i=1}^{N-1} \left(\frac{\partial |\phi_i(r)|^2}{\partial N} \right)_v^{-} \quad \text{--- (1.52)}$$

Here N is the number of electrons in the system and ϕ_i are Kohn-Sham spin orbitals. Under the frozen-core approximation, the above two equations revert to the Eqs.(1.33a-c) which are the basic elements of the approximate frontier molecular orbital theory.

Recently, Contreras *et al.* provided a simple formalism to obtain the regional Fukui functions.[75] The model is based on an exact relationship between these local reactivity descriptor and the frontier molecular orbitals. Within this approach, it becomes possible to define an orbital Fukui function that directly yields the condensed-to-atom quantity. Within the Kohn-Sham theory, Senet has presented an exact definition for the frontier orbital density as,[72]

$$f_s(r)^{\alpha} = |\phi^{\alpha}{}_{KS}(r)|^2 \quad \text{--- (1.53)}$$

where F is LUMO for α=+ (electrophilic attack) or HOMO for α= - (nucleophilic attack). From the above Eq. (1.53), the condensed Fukui function at the atom k is written as,

$$f_k^{\alpha} = \sum_{v \in k}^{AO} |c_{v\alpha}|^2 + \sum_{v \neq k}^{AO} c_{\chi\alpha} c_{v\alpha} S_{\chi v} \quad \text{--- (1.54)}$$

Eq. (1.54) satisfy the normalization condition,

$$\sum_k f_k^{\alpha} = \sum_k \sum_{v \in k}^{AO} \left[|c_{v\alpha}|^2 + \sum_{v \neq k}^{AO} c_{\chi\alpha} c_{v\alpha} S_{\chi v} \right] = 1 \quad \text{--- (1.55)}$$

where $c_{v\alpha}$ are the molecular frontier orbital coefficients and $S_{\chi v}$ are the atomic orbital overlap matrix elements. By this procedure, one can avoid the additional calculations for the cation and anion cases and thereby, one can maintain the spin multiplicity of the system.

Many other different methods have been proposed to compute the Fukui function and all of them have their own merits and demerits.[81-85] However, the difficulty of the accurate calculations of Fukui function makes the qualitative or quantitative application of these important chemical entities rare in studying regional chemical reactivity of a molecular system. Many of these approaches have not yet been developed into a workable calculation scheme except for the method provided by Contreras *et al.*[75] Despite the fact that there have been many approaches to compute the Fukui function, it should be remarked that the finite difference approach suggested by Yang and Mortier is still considered to be one of the best and easy ways of computing the local quantity-Fukui function. The validity of the condensed Fukui functions evaluated by the Mulliken partitioning method will be shown in the later sections even for the semi-quantitative studies.

1.11 HSAB Principle: What Does DFT Say about It?

Having defined the physical basis and the implications of GRD and LRD within the framework of DFT, the subsequent studies focused in providing the formal proof for the HSAB principle. These studies we were essentially based on DFT based energy-density perturbation methods. One of the earlier proofs proposed by Parr and Pearson was derived on the basis of energy perturbation with respect to number of electrons alone and it was only partially successful in explaining the HSAB principle.[42] Nalewajski employed both the number of electrons and external potential as the perturbation variables.[86] Later, Parr and his collaborators have used a different method for the proof of HSAB principle and this method was based on the minimization of the interaction energy expression with respect to the softness parameter keeping other factors, like chemical potential and softness of the other reactants as constants.[87] More recently, Li and Evans employed the softness kernels and other local reactivity descriptors in their proof, which has brought out many interesting relationships between the HSAB principle and the Fukui's FMO theory.[88] Thus, there have been many different approaches for the proof of the HSAB principle and herewith, we have outlined a few of them in detail.

In 1983, Parr and Pearson gave the first theoretical proof for the HSAB principle with the use of the Taylor series energy expansion in terms of the number of electron (N) as a perturbation variable.[42] Assuming that the systems A and B are the interacting systems, the energy expression for each system is expressed as,

$$E_A = E_A^o + \mu_A(N_A - N_A^o) + \eta_A(N_A - N_A^o)^2 + \ldots \qquad ---(1.56)$$

$E_B = E_B^o + \mu_B(N_B - N_B^o) + \eta_A(N_B - N_B^o)^2 + \dots$ ---(1.57)

If one ignores all other effects except the second order, total change in the energy will have the form as,

$\Delta E = (\mu_A - \mu_B)\,\Delta N + (\eta_A - \eta_B)\,(\Delta N)^2$ ---(1.58)

where, $\Delta N = N_B^o - N_B = N_A - N_A^o$ ---(1.59)

The energy stabilization due to such a charge transfer is the second order in $\mu_B - \mu_A$. On minimizing (E_A+E_B) with respect to ΔN, the result is $\mu_A = \mu_B$. ---(1.60)

Where, $\mu_A = \mu_A^o + 2\eta_A\Delta N + \dots$ ---(1.61)

$\mu_B = \mu_B^o + 2\eta_B\Delta N + \dots$ ---(1.62)

Consequently, to first order,

$$\Delta N = \frac{\mu_B - \mu_A}{2(\eta_A + \eta_B)} \qquad \text{---(1.63)}$$

On substituting the expression for ΔN, the interaction energy can be expressed as,

$$\Delta E_{AB} = -\frac{(\mu_B - \mu_A)^2}{4(\eta_A + \eta_B)} \qquad \text{---(1.64)}$$

It can be observed from the Eq.(1.64), that the energy lowering results from electron transfer and the differences in electronegativity or chemical potential drive the electron transfer. This process is assumed to take place continuously till the equilibrium is attained and it is referred as the chemical potential or electronegativity equalization process. If both acid and base are soft, $(\eta_A+\eta_B)$ is a small number, and for a reasonable difference in electronegativity, ΔE is substantial and stabilizing. This explains the HSAB principle, in part: soft prefers soft. It does not explain, however, the hard-hard preference (large denominator). Following this work, Nalewajski pointed out that the hard-hard interaction can be described by the inclusion of the first order contribution due to the perturbing external potential (i.e. E(N,Z)).[86] The basic expression is written as,

$$\Delta E_{AB} = -\frac{(\mu_B^0 - \mu_A^0)^2}{2(\eta_A + \eta_B)} + \frac{(\mu_B^0 - \mu_A^0)(\alpha_B \Delta Z_B - \alpha_A \Delta Z_A)}{\eta_A + \eta_B} + (v_A^0 \Delta Z_A + v_B^0 \Delta Z_B) \qquad \text{--(1.65)}$$

where, v is the electron-nuclear attraction per unit charge, $(v = V_{ne}/Z < 0)$; $\alpha = 1/2(\partial\mu/\partial Z)_N = 1/2(\partial v/\partial N)_Z < 0$, and $\beta = 1/2(\partial v/\partial Z)_N < 0$.

In Eq.(1.65), the second term is always small due to the cancellation of terms in the numerator for the case of hard-hard and soft-soft cases. Even in case of the hard-soft/soft-hard cases also, the cancellation of terms in the numerator is substantial. From the first term, one can explain the soft-soft interaction, as discussed by Parr and Pearson.[42] For hard-hard combinations, the magnitude of the first term becomes small (large $\eta_A+\eta_B$), and the stability originates from the last term in Eq.(1.65). For such a pair of hard-hard reactants, both ΔZ's and |v| are large, so that the favorable effect from the external field (predominantly ionic bond), due to relatively unshielded nucleus of the partner, becomes dominant. The essential feature of the present explanation is in agreement with the Klopman's explanation of HSAB principle as outlined in section 1.4.[34,37] This completes the theoretical basis for the HSAB principle.

Later, Chattaraj, Lee, and Parr have derived the proof for the HSAB principle in an elegant way.[87] In particular, they have established that among potential partners of a given electronegativity, hard likes hard and soft likes soft. If we rewrite the above Eq. (1.64) in terms of softness parameter, the expression for ΔE becomes,

$$\Delta E_{AB} = -\frac{(\mu_B - \mu_A)^2}{4(\eta_A + \eta_B)} = -\frac{(\Delta\mu)^2}{2}\frac{S_A S_B}{S_A + S_B} \qquad \text{--- (1.66)}$$

Assume that for a given S_A, $S_B = \alpha . S_A$

$$\Delta E_{AB} = -\frac{(\Delta\mu)^2}{2}\frac{S_A \alpha}{1+\alpha}, \qquad \text{--- (1.67)}$$

where alpha is, $0 \le \frac{\alpha}{1+\alpha} < 1; 0 \le \alpha < \infty$

The supremum value of $\alpha/(1+\alpha)$ is one which corresponds to maximum energy lowering and in such cases, the hardness will be minimum. On the other hand, the value of α can be zero, which directly relates to the case of maximum hardness. Since simultaneous satisfaction of maximum energy lowering and maximum hardness is not possible, the natural compromise is to take the average value of the term, $\alpha/(1+\alpha)$ which is ½. This implies that the value of α is one and hence, $S_A=S_B$. There is also another proof by Lee and Parr based on the minimization of the molecular grand potential.[87] Other proofs are just sketched out here without many details.

Gazquez had derived an alternative proof for the HSAB principle.[89] He derived an approximate total energy expression in terms of the chemical potential μ and the hardness η, $E[\rho] = \mu N_e - 1/2\ N_e^2\ \eta + E_{core}[\rho]$. Using this expression, he has shown that the interaction between species whose softnesses are approximately equal is energetically favored, relative to the interaction between species whose softnesses are very different from each other. Here, N_e is an effective number of valence electrons and $E_{core}[\rho]$ represents the core contribution to the total energy. If one takes the derivative of the interaction energy expression with respect to S_B, keeping all the other variables constant, the optimum value of the softness of system B for a given softness of the system A can be found out. Following this idea, Gazquez has shown that the equality of the softness criterion, i.e. $S_A=S_B$, emerges out naturally for specific values of other parameters.

Besides the above proof, Li and Evans[88] have demonstrated the HSAB principle, which is similar to the Nalewajski's work. However, Li and Evans employed the local descriptors and softness kernel in their proof rather than using the global descriptors alone. One of the impressive features of their study is that the Fukui function is shown to be one of the key concepts in relating the frontier molecular orbital theory and the HSAB principle. Herewith, we give the final expression for the interaction energy, considering the interaction between two molecules i and j.

$$\begin{aligned}
\Delta E_{ij} \;=\; & (\mu_i - \mu_j)\Delta N + (\eta_i - \eta_j)\Delta N^2 + \\
& \int \left[\rho_i(r)\Delta v_i(r) + \rho_j(r)\Delta v_j(r)\right]dr + \\
& \Delta N \int \left[f_i(r)\Delta v_i(r) - f_j(r)\Delta v_j(r)\right]dr + \qquad \text{--- (1.68)} \\
& \frac{\eta_i a}{2}\left(\int (s_i(r)\Delta v_i(r)dr\right)^2 + \frac{\eta_j a}{2}\left(\int s_j(r)\Delta v_j(r)dr\right)^2 - \\
& \frac{a}{2}\int [s_i(r)(\Delta v_i(r)))^2 + s_j(r)(\Delta v_j(r))^2]dr
\end{aligned}$$

Here a and b are constants and all other terms carry the same meaning as explained before. One can explain each term present in Eq.(1.68) in the same way as we have explained in the case of the interaction energy expression (1.65) derived by Nalewajski. Based on their proof, they proposed the following rule: for hard-hard interaction cases, the site of minimum Fukui function is preferred; on the other hand, the site with the maximum Fukui function is preferred in case of the soft-soft interaction cases. They have further shown that the global hardness indicates the chemical reactivity of a molecule as a whole, where as the Fukui function determines chemical selectivity.

From the above discussions, the energy-density perturbation method with the properly chosen perturbation variables, within the framework of DFT, indeed provides a formal proof for HSAB principle. The origin and the physical basis of both the soft-soft and hard-hard interactions are illustrated with proper theoretical rigor. There have also been many numerical studies that have supported the HSAB principle.[90-95]

1.12 The Principle of Maximum Hardness and the Concept of Hardness Profiles

The principle of maximum hardness proposed by Pearson has received considerable attention over the past few years.[20,96] The PMH states that there is a rule in nature that every system tries to be as hard as possible. Parr and Chattaraj have proposed a proof based on fluctuation-dissipation theorem of statistical mechanics.[97] They have shown that the hardness of a system becomes maximum at equilibrium nuclear configuration, under conditions of constant chemical potential and temperature. The proof rests on the assumption that all nonequilibrium states near the equilibrium can be generated by small perturbations of the equilibrium state. However, relaxation of these constraints appears to be permissible, and in particular, it has been found that PMH still holds even though the electronic chemical potential varies along the reaction coordinate.[20,98-108] Datta has shown that the exchange reaction always moved into a direction that produced the hardest molecule or the product with highest average hardness where μ and $v(r)$ are not constant.[90] PMH has been numerically studied and its validity was shown by several groups.[98-104] The variation of hardness along reaction path has been studied to validate maximum hardness criterion in the chemical reactions and this has been commonly referred as "hardness profile".[100] Datta has first studied the hardness profiles for the inversion of ammonia and the intra-molecular proton transfer in malonaldehyde.[100] From these hardness profiles, he observed that the profile goes through a minimum at the transition state. The maximum hardness criterion complements the minimum energy criterion for stability. Since a chemical species is the most reactive at the transition state, its hardness value is minimum there, on the reaction profile, i.e., at the transition state a species becomes most soft. Although, the above observations have further validated PMH for a variety of cases such as the molecular inversion, internal rotation, rearrangement cases, and for various types of simple reaction etc., there are cases where the hardness does not pass through a minimum near or at the transition state.[110-113]

Pearson and Palke observed that the totally symmetric distortions do not show any sign of a maximum or minimum hardness near the equilibrium geometry and the hardness keeps increasing steadily as the nuclei approach each other.[99] However, the condition of constant chemical potential is observed for small asymmetric vibrations about a symmetric equilibrium position and this is in agreement with the formulation of Parr and Chattaraj.[97] Pal *et al.* have made a critical study on the validity of PMH by considering the symmetric and asymmetric variations around the equilibrium geometry of water molecule using the highly correlated wave function method.[102] They also found that for symmetric variations neither the chemical potential nor hardness is at an extremum and for asymmetric variations both μ and η were extrema. Further they noted that among all symmetric configurations with the equilibrium chemical potential, hardness at the equilibrium geometry is globally maximum. These results confirm the Pearson and Palke's observations.[99] Makov has further demonstrated that all the invariant (e.g., energy, chemical potential, hardness) will be extremal with respect to asymmetric variations about a symmetric nuclear configuration.[114] This has been derived by employing group theoretical symmetry arguments with in the framework of "pure-state" DFT. The above statement holds to be true whether the asymmetric distortions are carried out around symmetric equilibrium or non-equilibrium geometries. It should be noted that the symmetry principles derived by Makov do not determine by themselves whether such extrema will be minima or maxima.

Although many groups have studied PMH, the principle still lacks from the exact formal proof and it is still not well understood. None of the evidence is rigorous or general enough to make any possible conclusions. One of the difficulties associated with this principle is how the chemical potential and external potential can be kept constant during a reaction when the hardness is varied. The feasibility of maintaining these restrictions is not possible in most of the reactions.[20] Sebastian questioned the validity of the formal statistical-mechanical proof and he argued that it is valid only for specific types of ensemble distribution.[115] Recently, Liu and Parr had demonstrated the PMH with several constraints and it states that at fixed electron number, external potential and chemical potential, the global hardness should go to a maximum as the total energy approaches a minimum.[116] Despite all these criticisms, it has been generally observed that the variation of hardness along a chemical reaction is found to be useful in understanding in various chemical reactions. However, further work is still required to understand the behavior of hardness variation along the reaction path.

1.13 Applicability of the Global and Local Reactivity Descriptors: Correlation with the Physical Properties

The developments discussed in the earlier chapters on the concept of global and local reactivity descriptors have paved way for the achievement of many aspects that are closely related to chemical problems. Parallel to the development in this field, some efforts have also been made to relate these descriptors with the electronic properties of chemical systems. In particular, the correlation between GRD and the polarizability of the atomic and molecular systems have been quite successful and it has led to a better understanding of these descriptors. One of the key interests for these conceptual developments lies with the fact that the reactivity descriptors are not experimentally observable quantities and hence, the further works have necessitated in exploring a suitable relationship for these descriptors with the observable quantities. This can critically rationalize the quantitative definition of these descriptors.[117-120] As it has been discussed in the section 1.3, the softness has been directly related with the polarizability (α) and this relation is mostly valid for atomic systems.[30,37] The hardness values would then have a correlation with the inverse of polarizabilities. Sen *et al.* has shown a linear correlation between η and $1/\alpha$ for a large number of atoms.[121] Politzer showed numerically that the atomic hardness is inversely proportional to approximated Hartree-Fock atomic polarizabilities.[122] Since α is directly related to the atomic radius and molar refractivity index, these descriptors have also been found to be correlating with the above quantities.[118,123-126] Ghanty and Ghosh have made a detailed study on the hardness parameter and its relationship with the atomic radius, polarizability through a unified procedure, which requires the solution of the Kohn-Sham equation only once, for the neutral atom.[126] This relation has also been analytically derived by Simon-Manso and Fuentealba using a local functional model for the hardness kernel.[127] Using empirical arguments, Hati and Datta found analytical expressions, including a relationship with the ionization potential, consistent with the above relationship for atomic systems.[128] Komorowski has pointed out that the collection of polarizability data and the softness (S = IP-EA) for neutral atoms shows a rather poor correlation coefficient of 0.77.[118] In case of poly atomic cases also, it has been found out that there is a linear relationship between the $\alpha^{1/3}$ and global hardness parameter. Since the atomic systems are spherical in nature, the above linear relation is validated. On the other hand, the molecular systems are not spherical and if there is any distortion of a particular bond in the systems, it further leads to more asymmetry in their structure. In this regard, Pal and co-workers have studied the variation of hardness and polarizability with the bond distortion in polyatomic systems and demonstrated that the relationship of η and $\alpha^{1/3}$ is dominantly linear.[107] This trend has been further supported by many numerical studies. Pal and chandra have proposed a simple linear relationship between the hardness (or inverse of the cubic root of polarizability) of N-electron system with the dipole moment of neutral and mono-positive and mono-negative ions.[119] Their study actually shows that the relation between the second order property in terms of only the first order properties. The correspondence between the variation of hardness, polarizability, molecular valency and various energy components has also been investigated as a function of the reaction coordinate or the bond distortion in simple molecular systems.[101, 103, 105, 107-113]

On the basis of the inverse relationship of hardness and polarizability, a minimum polarizability principle (MPP) has been postulated as a complement to the PMH.[105,129] MPP states that the natural direction of evolution of any systems is toward a state of minimum polarizability. The hardness value of the transition state will be lower than that of the initial state and this can be understood from PMH. On the other hand, one can expect from MPP that the polarizability values of the transition state would be greater than that of the initial reactants. It should be noted that there is no rigorous theoretical proof for the existence of such a principle and it is supported only on the basis of numerical studies.[109,110,130] Chattaraj *et al.* recently validated the minimum polarizability principle and their results show that the excited state polarizability is always greater than the ground state polarizability for singlet-singlet excitation, which is in accordance with the minimum polarizability principle.[131] However, for the transition involving a change in the spin multiplicity the minimum polarizability principle is not always obeyed. Comparison of the profile of hardness with that of the molecular valency along the reaction coordinates has also been invoked by many workers.[100,101,105,107,109,111,126] These studies have shown that the molecular valency reaches its minimum value at the transition state for isomerization type of reactions. On the other hand, it attains maximum value at the equilibrium configuration for normal modes of vibrations and internal rotations.

There have been relatively few works in relating the local quantities, such as Fukui function with static dipole polarizability. The study of Vela and Gazquez represents the first such attempt to derive systematically from density functional theory an expression for the static-density linear response function in terms of local and nonlocal components that are proportional to the Fukui function and the global softness.[132] Ghanty and Ghosh have also shown connectivity for the above two terms for atomic systems from density functional viewpoint.[126]

Relation of chemical potential to electrostatic potential and bonding distances is another important application to this area. Considering the Euler equation of DFT,[13]

$$\mu = \frac{\delta T[\rho(r)]}{\delta\rho(r)} + \frac{\delta E_{xc}[\rho(r)]}{\delta\rho(r)} + V(r) \qquad \text{--- (1.69)}$$

Politizer, Parr and Murphy have noticed that at any point r at which,[122]

$$\frac{\delta T[\rho(r)]}{\delta\rho(r)} = \frac{\delta E_{xc}[\rho(r)]}{\delta\rho(r)}$$

then, $\mu = V(r)$ --- (1.70)

Politzer, Parr and Murphy have shown that using the Thomas-Fermi-Dirac model, the above Eq, (1.70) is satisfied at $\rho(r)=0.00872$.[53] This suggests that the distance r_μ has a special significance with respect to the bonding properties of atoms.[124] Sen and Politzer found out the electrostatic potential will be minimum at the ionic radius of the negative ion.[133]

In the similar context, Harbola *et al.* has related the hardness parameter with the electrostatic potential.[134] Accordingly, the hardness is defined as the electrostatic potential at the covalent radius (r_c) due to the Fukui function.

$$2\eta = \int f(r)/(r-r_c)\, dr \qquad \text{--- (1.71)}$$

As explained in the section 1.9, the ambiguity present in the definition of local hardness has actually prohibited the applicability of this local descriptor in analyzing the intermolecular reactivity sequences. Within the Thomas-Fermi-Dirac energy-density relationship, Berkowitz and Parr have shown that the local hardness can be related to the electrostatic potential (v(r)) as, $\eta(r) = - v(r)/2N$.[48] The present definition for the local hardness has been found to be very useful for the description of intra- and intermolecular reactivity sequences.[135]

1.14 Applicability of the Global and Local Reactivity Descriptors: Chemical Reactivity and Selectivity

The prime objectives for the formulation of these reactivity descriptors are essentially to quantify and analyze the conceptually important quantities such as chemical reactivity, selectivity and stability of the molecular systems from a general theoretical framework point of view. There have been numerous works in terms of monograph and reviews in this field bringing out the usefulness of these descriptors in generalizing the chemical reactivity problem with in the framework of DFT.[13, 17-22, 32, 60-61, 77, 136, 139] Many attempts have also been made to scrutinize the applicability of these descriptors. In this section, the purpose is not to make an exhaustive review on the reactivity descriptors. However, a brief discussion on some of them would be pertinent.

A first application is in providing a quantitative measure of aromaticity. Parr and co-workers have successfully correlated resonance energy per Π-electron, which is a conventional valence-bond measure of aromaticity, with absolute hardness or relative hardness.[140] It has been shown that for electrophilic aromatic substitution reactions, the change in hardness from reactant to transition state on a potential energy surface, is a measure of the activation energy of a reaction.

Parr and Zhou argued that the absolute hardness is generally a most useful quantitative index for marking the closing of electronic shells, and they pointed out that the closing of shells can be described as a consequence of the principle of maximum hardness.[140] It is also shown that the hardness of completely filled s-shells and half-filled p-shells is seen to be a local maxima. Harbola has shown that the hardness criterion has been very successful in predicting the stability of different types of metal clusters (magic numbers) for Li clusters.[141] Alonso and Balbas have studied the different cluster size and the corresponding hardness variation in predicting its stability and reactivity.[142]

The local softness s(r) contains the same information as the Fukui function plus additional information about the total molecular softness. Accordingly, it has been suggested that f(r) and s(r) can reveal the reactivity criterion to study the intra-molecular reactivity sequences (relative site reactivity in a molecule) and for the intermolecular reactivity sequences, respectively.[137, 143] Langenaeker *et al.*[154] have shown that a more reliable reactivity order for the intermolecular reactivity can be obtained using the local hardness parameter rather than using the local softness or the Fukui function parameters. Since the intermolecular reactivity is charge controlled (hard-hard interaction), the hardness related reactivity descriptors will be more suitable to measure this kind of reactivity. On the other hand, the intra-molecular reactivity is dominated by the covalent interaction because it is orbital controlled. So any orbital controlled reactivity descriptor (e.g., local softness, Fukui function index) will be more suitable to measure the intra-molecular reactivity sequence.[137,143]

Gazquez and Mendez have stated that the interaction between two molecules A and B will not necessarily occur through the softer atoms but through those whose Fukui functions are approximately equal.[23,24] The proof of this principle, so called, local HSAB principle, will be presented latter part of this chapter. The interpretation the orientation phenomena in the organic reactions on the basis of both global and local HSAB principle have also been studied.[60,137] The local concepts of these descriptors have been reasonably successful for the interpretation of both the regiochemistry and the mechanism of the Diels-Alder reactions.[106,135,137,144-147] In addition, it has also been applied for the chemical problems related to the regioselectivity of α,β-unsaturated aldehydes and ketones, substituted benzynes and hexarynes, and the nucleophilic and electrophilic reactions of monosubstituted benzenes.[147-160] Recently, the regioselectivity in the fullerene chemistry has been adequately rationalized by means of condensed local softness.[151] The local hardness, in one or another approximate form, has been used in studies on intermolecular reactivity sequences, reactivity of monosubstituted benzenes, acidity of substituted acetic acids, simple hydrides, model systems for zeolites, and alkyl alcohols.[152-154]

Although these descriptors have been demonstrated to be one of the promising tools in generating the experimentally observed molecular reactivity trends, some studies have also shown its failures for some specific cases.[54,109,161,162,165] A study carried out by Mineva *et al*. has claimed that the orbital Fukui indices do not provide the correct reactivity pattern for the well known case of protonation sites of aniline in the gas phase.[113] Recently Roy *et al.* have reported some mismatch for a specific more complex systems like, α,β-unsaturated aliphatic and aromatic ketones.[54] On the basis of condensed FF (or local softness) indices, they introduced two different local reactivity descriptors, relative electrophilicity (s_k^+ / s_k^-) and relative nucleophilicity (s_k^- / s_k^+) of any particular atom k, to locate the preferable site of nucleophilic and electrophilic attack on it, respectively. These two newly defined reactivity descriptors are shown to generate improved intra-molecular reactivity trends than those obtained from condensed FF indices.[54,164-165] Further, the description of the inter molecular reactivity has been recently analyzed by Krishnamurty and Pal using the concept of group softness where in the group consists of the reacting atoms and the atoms that are directly connected to the reacting atoms.[162] Recently, Parr *et al*. have defined a specific quantity of a chemical species, the square of the electronegativity divided by its chemical hardness, ($\mu^2/2\eta$) known as electrophilicity index (w).[166] This quantity is found to be useful in predicting the extent of partial electron transfer that contributes to the lowering of the total binding energy by maximum flow of electrons. The local version of this quantity has also recently been quantified by Contreras *et al.* and they have also immediately examined the usefulness of this local quantity in predicting the regioselective isomers in the Diels-Alder reactions.[167]

In addition to a significant advance in acquiring the reactivity information for simple organic molecular systems, the applicability of these descriptors has also been extended to more complex systems.[164,165,168-175] For instance, the chemical reactivity of solid surfaces as complicated as the Si(111)-surface and zeolites have been analyzed through these descriptors. In particular, the acidity and basicity of zeolites which are the two important factors for the determination of the catalytic activity of the zeolite system, has been analyzed using these LRD.[165,168-171] The influence of changes in the average framework electronegativity, (by the variations in the composition of the zeolites or by the isomorphous substitution of Si and Al atoms by other atoms), on the acidity of the bridging hydroxyl groups has been recently investigated using the reactivity descriptors by Geerlings *et al.*, Pal and co-workers, Deka *et al.* and Chatterjee *et al.*[164,165,169,171] Fuentealba *et al.* have introduced the concept of density of states in defining Fukui function.[175] They have also studied the basicity of alkaline-exchanged zeolites using this empirical parameter index and found that this empirical model assesses well the experimental basicity trend of zeolites, and it gives a better description of basicity than the FMO approximations for the Fukui function and local softness or Mulliken population analysis.

Let us now discuss the important chemical applications of these descriptors for the excited states of molecular systems.[176,177] The study of GRD and LRD for the systems at the excited states is very scarce due to the fact that Hohenberg-Kohn theorem is valid strictly for the ground state and consequently the energy of an arbitrary excited state can not be a unique functional of density. Hence, the extension of ground state DFT formalism for studying the descriptors for the excited state poses a problem. This problem disappears, however, if the excited state happens to be the lowest state of a given geometry. The recent work by Chattaraj and coworkers has focused on extending the conceptual tools of the ground state DFT to excited states.[129,176,177] These studies have the potential to significantly deepen the understanding of excited state chemistry. Their study shows that the hardness value decreases for most of the excited states of atomic and molecular systems. On the other hand, the surface plots of different local quantities like charge density, the Laplacian of the charge density, the quantum potential, the molecular electrostatic potential and the Fukui function reveal an increase in the molecular reactivity with the excitation of the systems. In the context of DFT-quantum fluid dynamics also, Chattaraj and his co-workers have studied the time evolution of various reactivity parameters such as chemical potential, hardness, polarizability and entropy associated with an ion-atom collision process and an atom-field interaction process for both the ground and the excited electronic states.[177] These studies have shown the validity of PMH and electronegativity equalization principle in the ground and excited states.

The another important conceptual developments established by Nalewaski and co-workers and Mortier and co-workers are the charge sensitivity analysis (CSA)[178-181] and the electronegativity equalization method,[182,183] respectively. The CSA is based upon the phenomenological electronegativity equalization from the view point of atoms-in-molecules (AIM) approach. The molecular CSA in the AIM resolution represents a systematic procedure for determining chemically interesting charge responses, to be used in diagnosing trends in chemical reactivity of very large systems from the model AIM hardness matrix: $\eta = d^2E/dN\ dN = du/dn \sim \{\gamma_{i,j}\}$; here E is the system electronic energy, $N=\{Ni\}$ is the row vector of the AIM electron populations, $u=\{\mu_i\}$ stands for the row vector of the AIM chemical potentials, $u=dE/dN$, and $\{\gamma_{i,j}\}$ are the valence-shell electron repulsion integrals. Such stability data in the electron population space, allows one to identify important electronic structure factors influencing the catalytic mechanism, eventually leading to an assessment of the charge instability role in influencing relative preferences for alternative courses of catalytic reactions. The charge response diagrams for all these levels (reactants mutual polarization, intra-reactant electronegativity equalization) of description can be quickly generated within the CSA in a truly two-reactant approach, which takes into account the reactant interaction.

Electronegativity equalization was first introduced by Sanderson as a method for estimating atomic charges in molecules based on the relative electronegativities of the atoms before and after the molecular formation.[184,185] Analogous to macroscopic thermodynamics, the chemical potential of an equilibrium ground state electronic system is equal everywhere. The idea behind the electronegativity equalization methods, as the name suggests, is that when atoms or molecules interact, their corresponding electronegativity must equalize. From the view point of density-functional theory, this follows directly from the variational principle for the ground-state electron density. A major advance was realized with the development of a rigorous mathematical formalism for electronegativity equalization based on density-functional theory by Nalewajski[179-181] and Mortier *et al.*[170] Methods derived from this formulation predicted atomic charges and other properties that were geometry and connectivity dependent. Recently, the concept of electronegativity equalization has been used to probe reactivities using charge sensitivity analysis, and provide a method for determining dynamic charges for molecular simulations.[186-187] In general, these methods rely on empirical parameterizations of individual atoms and, hence, have the advantage that they can be applied to any molecule.

These illustrative applications of the DFT based descriptors to the chemical problems demonstrate the potentiality of these descriptors in extracting several information on the reactivity of the molecular systems. In addition, this present thesis work will demonstrate further developments that has been established in this area, in formulating semi-quantitative models based on local HSAB principle to evaluate the stability of the complexes.

1.15 Some Critical Remarks on GRD and LRD

The success of these descriptors in analyzing the reactivity, physicochemical properties and for investigating the reaction mechanisms as well as the role of DFT in defining the theoretical foundation have been demonstrated in the preceding sections. Still, despite the successes, there are many issues, which have not yet been addressed lucidly and in a distinct manner. Herein, we will now briefly make some critical remarks on certain fundamental issues, such as the applicability of the Fukui functions in reactions; the ambiguity in relating the absolute hardness from the finite difference methods; the validity of the operational definition of the descriptors.

In most of the cases, the criticism is often leveled against the computational part of the electronegativity and hardness.[13,188-191] It is still not known how to accurately compute these quantities. The reason is that the exact and explicit form of the universal energy density functional is not known. In general, N has been treated as a continuous variable. If we draw a plot of E vs N for any system, then μ is simply the instantaneous slope of such a curve. There is no assurance that the curve will be continuous and $\mu(N)$ appears as a step function, i.e. constant between jumps at integral values of N. Hence the derivatives with respect to μ may not exist. Experimentally we only know the points on the curve for integral values of N, from the data such as ionization potential and electron affinities. Levy and coworkers have discussed in detail the differentiability of E with respect to integer and non-integer number of electrons and they have shown that the curve of lowest average energy E(N) versus N is found to be a series of straight line segments with slope discontinuities at the integral N.[191]

Although most of the applications have employed the finite difference approximations in computing chemical potential and hardness parameters, the use of the finite difference approximations is appropriate only if the value of the partial derivative, $\partial\mu/\partial N$ does not vary appreciably over the interval $\Delta N=2$. Thus the usage of the finite difference approximation requires that the absolute hardness should be essentially independent of charge over an interval of two units of charge. In other words, it should be a quadratic function of charge. This does not appear to be the case for the absolute hardness of atoms or molecules, which are in fact significantly dependent on charge.[188]

As we have noted down in section 1.8, the Fukui function is defined as the change in the electron density at the constant external potential. It reflects the component of chemical reactivity that is conveyed through the charge transfer between systems. However, it completely ignores the effects of external potential of the approaching reagent and the resultant charge distribution is assumed to be taking place only within the isolated molecule. This can happen if one assumes that that the system is well isolated from the other partner.[57,76] Thus, the reactivity, defined in terms of the Fukui function is good for a reaction, which is taking place at the early stage or at the transition state. Moreover, $\rho(r)$ and $v(r)$ are not independent variables. Therefore, any derivative of $\rho(r)$ at constant external potential is not well defined.[84] The atomic Fukui indices are usually obtained from atomic charges obtained from Mulliken population analysis. However, in light of the unreliability of population analyses based on the non-unique partitioning procedure, these values may not always yield correct trends.[69,76] Despite the potential importance of the Fukui indices in understanding the site selectivity and reactivity, the subject concerning the accurate evaluation of these has not drawn adequate attention from theoretical chemists. In practice, for semi-quantitative analysis, these points raised above have not presented any particular problem. Nevertheless, from a theoretical point of view it is important to find a better formal justification for the use of all indices.

Apart from the above remarks, Cohen *et al.* has recently raised some important fundamental issues that may further strengthen the applicability of these descriptors for general cases.[81,82,192]

1) By defining the chemical reactivities (Fukui function or local softness) as derivatives of the electron density with respect to electron number or chemical potential, one can assign them to responses to global perturbations. In a chemical reaction, however, the electron density undergoes a nonlocal response to a local perturbation. How should the concept of chemical reactivity be generalized to reflect this?

2) The focus in the theory on LUMOs and HOMOs or states at the chemical potential is inadequate for condensed matter extended in one or more dimensions. Such

materials have continuous bands of energy levels and correspondingly continuous bands of LUMOs and HOMOs. How does one weigh the contributions of the various neighboring states in a band to the chemical reactivity?

3) The present formulations entail a static response to a static perturbation, whereas interacting chemical systems have internal dynamics. How does one generalize the reactivity descriptors from a static to a dynamic theory?

4) The focus in the existing theory is on the internal response of one of the systems or subsystems in the initial stages of a chemical reaction to an external stimulus. Yet the stimulus is provided by another subsystem in interaction with the first. What is the analogous characterization of the chemical stimulus?

5) Finally, how do the stimulus and response come together to generate the change in total energy consequent to the initiation of a reaction? In other words, how does one relate the elements of chemical reactivity theory to the total energy and hence to the reaction pathway?

1.16 Non-negativity of Condensed Fukui Function

In section 1.10, it has been remarked that the condensed FF indices or the local softness are generally computed by the method suggested by Yang and Mortier.[55] It is probably because of the simplicity and readiness of the method by which the FF and local softness can be evaluated.[76,77] At the same time, it has been pointed out that there exist some difficulty in analyzing the reactivity of the atomic centers within the molecular systems when these condensed FF indices become negative.[54] In such cases, any physical explanations can hardly be given. From Eqs.(1.32) and (1.33), it can be presumed that the condensed FF indices can have negative values when $q_x(N+1) < q_x(N)$ (for nucleophilic attack) and $q_x(N) < q_x(N-1)$ (for electrophilic attack). If the FF indices are expected to have positive values, then the above equalities should not occur, in other words, $q_x(N+1) > q_x(N) > q_x(N-1)$. Although no theory has been proposed regarding the sign of the FF indices, it is expected that the change of $\rho(r)$ for an infinitesimal change of the number of electrons should be positive. This is because a negative value indicates that the electron density is depleted at any particular site or atom, although the overall electron number of the system has been increased by one. Since the atomic charge (q_x) is not well defined quantity, any small error or any arbitrariness introduced in the computation of this quantity can also cause for the occurrence of negative valued FF indices. This demands the need for a unique partitioning method, since the method would then generate different values depending on the partitioning method that is employed in the calculation. In addition to the problem with the partitioning techniques, there is one more issue concerning the value of ΔN in the differential equation ($\partial\rho/\partial N$) pertaining to the present problem. The condensed FF indices are normally derived by finite difference approximation (Eq.(1.46)) with ΔN equal to one. However, the analytic definition of the FF is valid at the limit of $\Delta N \rightarrow 0$. When ΔN is one, there will be a significant change in the electron density distribution due to large relaxation in the corresponding cation or anion. This may cause the depletion or accumulation of electron density at a particular site even though the global electron number is increased (or decreased) by 1. In view of these arguments, the following two points might be the prime reasons for the appearance of negative FF values:

(i) The improper charge partitioning techniques adopted to evaluate FF indices

(ii) Large change in the electron number ΔN when FFs are evaluated in condensed form using the finite-difference approximation.

For the first time in literature, the problem regarding the non-negativity of the condensed FF indices have been raised by Pal and co-workers.[193,194] They have made a detailed study for the occurrence of the negative valued FF indices and its most probable origins. Their study reveals that the stock-holders charge-partitioning technique, as proposed by Hirshfeld, produces non-negative FF indices. To understand the foregoing discussions, we will briefly describe the Hirshfeld population scheme (HPA).[195]

The effective atomic charge is defined in HPA scheme as,

$$q_k = - \int \rho_d(r) w_k(r)\, dr \qquad \text{--- (1.72)}$$

where, $\rho_d(r)$ is called as the deformation density which is the difference between the molecular and the unrelaxed atomic charge densities, known as "promolecular density".

$$\rho_d(r) = \rho_{mol}(r) - \rho_{pro}(r) = \rho_{mol}(r) - \sum_k \rho_k(r - R_k) \qquad \text{--- (1.73)}$$

Here, $\rho_{mol}(r)$ is the molecular charge density at a site r; $\rho_{mol}(r)$ is the promolecular charge density at the same site; $\rho_k(r\text{-}R_k)$ is the spherically averaged ground state charge density of the free atoms k, suitably positioned at the coordinate R_k; $w_k(r)$ is the sharing function which measures the relative share of the atom k in the promolecular density at position r and it will always have a positive value ranging between 0 to 1.

$$w_k(r) = \frac{\rho_k(r-R_k)}{\sum_l \rho_l(r-R_l)} \quad \text{--- (1.74)}$$

where the summation runs over all the constituent atoms "l" of the molecule.

It has been observed that employing Hirshfeld population scheme for the computation of FF indices within the finite difference approximation, furnishes positive condensed FF indices on different atoms even when the electron number is changed by 1 (i.e., ΔN=1). The reason may be attributed to the fact that in MPA,[56] LPA,[62] NBO,[63] and MESP analysis,[65] the partitioning of the electron charge density of N-electron systems to the individual atoms is different from that of (N+1) and (N-1) electron systems. New restricted orbitals redefine the charge partitioning in the later two cases. On the other hand, the partitioning of electron density to different atoms is fixed for N, (N-1) and (N+1) electron systems in HPA scheme. This is due to the fact that the partitioning of electron density at a point r to the various atoms is based on the ratio of electron densities at that point of the corresponding free atoms. The use of this constant ratio in N, (N-1), and (N+1) electron systems [ensured by the sharing function, w(r)] is the probable reason for the occurrence of non-negative FF indices in HPA. In a recent study, Fuentealba *et al.* has also discussed the occurrence of nonnegative FF indices.[196] They computed the FF indices using the Eq.(1.54), and showed that the FF values are comparable with the values obtained from Hirshfeld population scheme.

In an another important paper, Pal and co-workers have analyzed the effect of ΔN in defining FF indices.[197] To validate this particular point, they have calculated the condensed FF indices through MPA for several molecular systems using the fractional molecular charges (ΔN=1, 0.5, 0.05, 0.01 and 0.001) instead of using the integer value as one. More interestingly, the results show that the condensed FF values still have negative sign as it is observed in the usual case (ΔN=1). They also claimed analytically that nothing could be predicted about the sign of condensed FF indices, even when it is evaluated by using very small fractional molecular charge. This strongly emphasizes that the negative value of the FF indices are due to the three different weight factors for neutral, cation and anion systems that are employed in the Mulliken and other partitioning schemes. As it was discussed earlier, these weight factors are constant in HPA and this fact may explain the occurrence of non-negative FF indices in HPA.

Recently, Ayer, Morrison and Roy has derived an expression for the condensed Fukui function index in terms of the condensed hardness kernel using the variational principle.[198] Using this relation, they have hypothesized that the strong diagonal dominance of the condensed hardness kernel is sufficient for the non-negativity of the Fukui function. They have also claimed that the arbitrariness introduced in the partitioning of molecules into atoms as well as the inadequate treatment of correlation effects are the principal reasons for the negative condensed Fukui functions.

1.17 A Brief Discussion on the Higher Order Derivatives

In the preceding sections, the problem of reactivity of molecular systems was addressed in terms of the first and second order global and local functions. Accordingly, several derivatives like μ, η, $s(r)$ and $f(r)$ etc. were derived using the electron number and external potential as the perturbation variables. Using Legendre transformed representations, Nalewajski obtained different energy and chemical potential derivatives with respect to many parameters (such as N, $\rho(r)$, $v(r)$ etc.).[51] He also derived their inter relationships through Maxwell relations. These relations brought the analogy between classical thermodynamics and Legendre transformed energy derivatives closer. However, much attention has not been paid to the other higher order global reactivity descriptors from the chemical applications point of view.[199-203] The development of other higher order derivatives is not possible due to the ambiguous nature of E(N) vs N curve as a continuous function. There are other obvious technical drawbacks and limitations in evaluating these quantities.

In an interesting paper by Fuentealba and Parr, the higher order derivative, especially the hardness derivative was discussed in detail.[200] The derivative of hardness with respect to the electron number at constant potential is specified as γ. Similarly, the variation of hardness with respect to the external potential at constant electron number is termed as $\eta(r)$, $\delta\eta/\delta v(r)$. These two quantities are obtained by constructing the Legendre transform of $\eta[N,v]$ and its associated Maxwell relations.

Considering that the energy is a function of N and functional of v(r), the energy differential can be written as,

$$dE = \mu dN + \int \rho(r) dv(r)\, dr \qquad \text{--- (1.75)}$$

Similarly, the change in chemical potential, where, $\mu = \mu[N, v(r)]$,

$$d\mu = 2\eta dN + \int f(r) dv(r) dr. \qquad \text{--- (1.76)}$$

$$d\eta = 3\gamma dN + \int \eta(r) dv(r)\, dr \qquad \text{--- (1.77)}$$

where $\gamma = 1/3(d\eta/dN)_v$ and $\eta(r) = \delta\eta/\delta v(r)$ --- (1.78)

Using, the Equations (1.7,1.8,1,11 and 1.27), the Maxwell relations can be derived from Eqs. (1.75) and (1.77),

$$\begin{aligned} \left(\frac{\delta\mu}{\delta v(r)}\right)_N &= \left(\frac{\partial\rho(r)}{\partial N}\right)_{v(r)} \\ \left(\frac{\delta\eta}{\delta v(r)}\right)_N &= \frac{1}{2}\left(\frac{\partial\rho(r)}{\partial N}\right)_{v(r)} \end{aligned} \qquad \text{--- (1.79)}$$

The quantity γ measures the change in hardness associated with a variation in the electron number and it can be related with the stiffness of the system.[200] Since the parameters μ and η have already been identified as the first and second order derivatives in the Taylor series expansion of E vs N, the other higher order derivatives can only include only minor modifications of the formulae for μ and η or rather only small changes in their numerical values. This would also characterize the convergence of the energy series. On the basis of the arguments, Fuentealba and Parr[200] have shown that the value of γ is small for atoms, ions and molecules by constructing an approximate energy function.[203]

1.18 A Semi-Quantitative Approach for Chemical Reactivity Using Energy Density Perturbation Methods

From the earlier discussions in this chapter, it is evident that the GRD and LRD have been successful in describing about the nature of the reactivity and stability of the molecular systems. These developments discussed above have also substantially helped in laying the foundations of chemical reactivity theory within the framework of DFT.[25,192] Despite the partial success in describing the reactivity of the chemical systems, such studies have remained primarily qualitative. Although the HSAB model permits the organization of a very large number of reactions based on the knowledge of molecular structure and the properties of the constituent atoms, it does not provide the reaction energies. It merely predicts interactions between the molecular systems qualitatively. It should also be noted that the transformation of this qualitative principle into a quantitative form has been considered to be one of the challenging and difficult problems. This particular issue has been emphasized by many groups in the context of explaining the relative bond strengths or reaction energies of the acid-base complexes.[30-37,95,100,192,204,205] Drago and coworkers have given an expression to calculate the stabilization energy of the complexes in terms of the covalent and ionic (C and E parameters) terms which are shown to have a close relationship with the softness and hardness parameters.[36] This equation seems to give results in close agreement with the experimental results and compares very favorably with the HSAB principle. However, its empirical nature and the number of independent parameters involved in the calculation makes it very impractical for general cases. Also, no physical reason or explanation for hard/soft behavior is provided by such an approach. Similarly, the model proposed by Klopman gives a reasonable picture about the change in reaction energy in terms of the orbital energy differences or the orbital populations.[34,37] However, the model does not contain the hardness or other descriptors explicitly. Thus, the issues on the calculation of reaction energy using the reactivity descriptors (GRD and LRD) have remained unresolved problem for few decades. This clearly indicates a need for the development of a theoretical formulation in order to establish the relation between the total energy changes with the changes in the chemical potential and hardness parameters and in their respective derivatives.[204] Since the reaction enthalpy is an experimental quantity, the reproduction of this quantity would be a greater challenge than the qualitative reactivity order. Thus, the prediction of reaction enthalpy in terms of the descriptors is an interesting subject of research and such studies may further throw light on the successes and limitations of these descriptors. The present thesis work focuses on the formulation of such relations. In addition, it also discusses various critical aspects of chemical binding in terms of these descriptors. Before we address details of the present problem, we will present a pedagogical review on some of the earlier approaches pertaining to the present problem.

In general, the interaction between the chemical systems can be qualitatively perceived from the evaluation of the responses of a system to any perturbation due to other chemical systems or external fields.[206-210] In other words, the chemical effects may be described by some suitable response functions of the unperturbed isolated systems. Such descriptions have been known for many decades ago. Examples of such approximate methods are the computation of intermolecular interaction energies in terms of the experimental multipole moments of empirical atomic contributions.[206,208] Here, it is assumed that the interactions arise from the electric moments of the systems and perturbation from the other systems. In particular, the first and second order electric moments (dipole moments, quadrupole moments and polarizability, etc) are considered to be the major driving force for the long-range interactions. The long-range interaction models have been extensively studied by several groups. The description of short-range interactions can be understood from the quantum mechanical base. The practical use of this approach for quantitative interpretation of reactivity and physicochemical properties has been reasonably successful.

In a density functional description, chemical binding has been viewed as a result of the reorganization and redistribution of electron density among the atoms in a molecule.[13] In other words, when the atoms or molecules approach to form the complex molecule, the electron density over the whole space undergoes rearrangement. The basis for the quantification of such qualitative ideas for the chemical bonding can be developed through a perturbation theory approach. This chemical perturbation theory has been mainly developed by Parr and collaborators and is based on the density functional response function.[13] In particular, it comprises of the energy and density response functions (global and local function) of the reagents, i.e. the response of the electrons to a local or global change of the electron number of the system. The total interaction energy can be partitioned into several terms involving different density response quantities by truncating the perturbation series. This can facilitate the understanding of the role of the individual descriptors in stabilizing the molecular complexes.

The formalism developed by Ghanty and Ghosh was probably the first method to study the process of chemical binding with numerical demonstration using DFT as a starting point.[211,212] Their model was based on a two-step process. In the first step due to electronegativity difference of the atoms, charge transfer takes place from A to B (assuming $\mu_B > \mu_A$) leading to the formation of two species $A^{\delta+}$ and $B^{\delta-}$ with the equalization electronegativities. In the second step, the two charged species are brought to equilibrium inter-nuclear separation, where the chemical potential of two charged atoms attain an equilibrium chemical potential which is the same in the atomic as well as in the bonding region. The energy associated with the first and second steps corresponds to the ionic and covalent contribution to the bond energy, respectively. Thus, the chemical bonding is essentially viewed here as a charge-transfer and reorganization effect. Their first model, so called, "bond electronegativity" based model for chemical bonding involves atomic electronegativity and hardness parameters and the expression for the bond energy for AB_n system is given as,[211]

$$D_{AB} = D_{AB}^{cov} + (1/4n)(\mu_A - \mu_B)^2 / (\eta_A + \eta_B/n) \qquad \text{--- (1.80)}$$

where, $D_{AB}^{cov} = ½[(D_{AA}+D_{BB})/2 + (D_{AA}D_{BB})^{1/2}]$

The above expression that was derived from DFT concepts is closely related to the model proposed by Pauling.[1] Later, they have described chemical binding through more generalized electronegativity and hardness parameters within the framework of spin-polarized DFT, which includes the effects due to the electron spin also.[212] Using these models, the bond energy of a number of diatomic alkali halides, hydrogen halides and polyatomic halides of the alkaline earth atoms have been calculated and the results are in good agreement with the experimental values. These methods have been very useful in understanding the chemical binding in simple polyatomic systems (AB_n type) mainly through the atomic parameters.[212]

There have been some other approaches for the chemical binding based on perturbation theory. These models also assume that the chemical binding is assumed to take place in two processes, namely charge distribution and reorganization of charges, as described above. The interaction energy expressions obtained by using the different perturbation variables (electron number, external potential, chemical potential etc.) with various approximations have already been explained while demonstrating the proof for the HSAB principle.[42,86-89,104,146] Although the above schemes provide a reasonable quantitative model to relate the interaction behavior of the molecular systems based on these physical parameters, none of these models have been tested numerically. They also have some practical disadvantages. The important problem was the determination of these response functions and softness kernels for which there is no simple relation available. In this respect, the application of these quantitative models to general molecular interaction case remains to be developed.

Recently, Geerlings and his co-workers have made an attempt to calculate the adsorption energy of small molecules with point charges or with the cations present in the zeolite cages.[213] They obtained the interaction energy expression from the total differential of energy with respect to the electron number and external potential. Assuming the electron transfer is zero, the energy expression is given as,

$$\begin{aligned} dE &= \int \rho(r)dv(r)dr + \Delta V_{NN} + \iint w(r,r')dv(r')dv(r)dr'dr \\ &= dE_1 + dE_2 \end{aligned} \qquad \text{--- (1.81)}$$

where, w(r,r') is the linear response equation and it is defined as,

$$w(r,r') = \left(\frac{\delta\rho(r)}{\delta v(r')}\right)_N \qquad \text{--- (1.82)}$$

The first term, dE_1, in this equation describes the electrostatic interaction between two molecules in terms of the unperturbed electron density of the adsorbed molecule and the change in the external potential for this system due to the presence of the adsorbing molecule (in case of zeolite systems). The second term, dE_2, is a correction term arising from the fact that the electron density of the adsorbed molecule changes upon its introduction within the zeolite cage. Both terms are the counterparts of the well known electrostatic and polarization terms arising via a more conventional perturbation approach. The applicability of their work is more restricted to simple ion-molecule interactions and the generalization of this equation is still an issue. The difficulty with this model is due to the presence of w(r,r') which prohibits the straightforward evaluation of the interaction energy. The proper modeling of the softness kernel and the linear response function in terms of local softness parameters can further improve the applicability of these models to the general cases.

In what follows, we will now present a detailed description of one more important quantitative approach, formulated by Gazquez and coworkers, for the study of intermolecular interactions.[23,24,89,104] It forms the basis for the local HSAB principle, which states that the interaction between two molecular systems is favored, when it occurs through those atoms whose local softnesses are approximately equal. The interaction energy expression obtained by the above group provides a more detailed description of molecular interaction phenomena in terms of the reactivity descriptors of the isolated systems.[214-216] First we will give a proof of the local HSAB principle by deriving the interaction energy expression from the energy-perturbation method. The proof is based on an approximate expression for the interaction energy between two chemical systems A and B, in terms of the chemical potentials and the softnesses of the isolated species, such that, it allows one to establish the optimum value of the softness of system B for a given softness of system A.

1.19 Study of Intermolecular Interactions by Local HSAB Principle

Let us consider the general molecular interaction case,

$$A + B \rightarrow AB \qquad \text{--- (1.83)}$$

Here, the interaction is taking place between the molecular systems A with K atoms, and B with L atoms and the interaction energy between these two chemical systems is given as, according to DFT,

$$\Delta E_{int} = E[\rho_{AB}] - E[\rho_A] - E[\rho_B] \qquad \text{--- (1.84)}$$

where $\rho_{AB}(r)$ is the electron density of the system AB at equilibrium and $\rho_A(r)$ and $\rho_B(r)$ are the electronic densities of the isolated systems.[214]

It is assumed that the interaction can be divided into steps. In the first step, when A and B are located far apart from each other, their chemical potentials, μ_A and μ_B, change to reach a common value of μ_{AB} at constant external potential. The energy change in this case can be written as,

$$\Delta E_v = \Delta E_v(A) + \Delta E_v(B) \qquad \text{--- (1.85)}$$

where, $\Delta E_v^A = E[\rho_A^*] - E[\rho_A]$ --- (1.86)

and, $\Delta E_v^B = E[\rho_B^*] - E[\rho_B]$ --- (1.87)

Here $\rho_A^*(r)$ corresponds to system A with v_A and μ_{AB} and $\rho_B^*(r)$ corresponds to system B with v_B and $\mu_{AB.}$

In the second step, A and B evolve towards the equilibrium state through changes in the electronic density of the global system AB produced by changes in the external potential v_{AB}. This step occurs under conditions of constant chemical potential, and can be expressed in the form,

$\Delta E_\mu = E[\rho_{AB}] - E[\rho_{AB}^*]$ --- (1.88)

where, ρ_{AB}^* (r) = $\rho_A^*(r)+\rho_B^*(r)$ is the electronic density of the system AB with μ_{AB} when A and B are far away from each other. Adding Eqs. (1.85) - (1.88), one can find that,

$\Delta E_{int} = \Delta E_v + \Delta E_\mu$ --- (1.89)

The above Eq.(1.80) is exactly equal to the interaction energy expression, ΔE_{int}, Eq. (1.84).

Hence, $\Delta E_{int} = \Delta E_v + \Delta E_\mu$.

We will now derive the expression for each term (ΔE_v and ΔE_μ) present in the Eq.(1.89) separately. This will together form the basis for the local HSAB principle. It is derived from atoms-in-molecule viewpoint starting from the change in their grand potential.

Expression for ΔE_v:

Considering the interaction between the system A and B, the change in the energy of each system can be given by performing the Taylor series expansion,

$E_A = E_A^o + \mu_A(N_A - N_A^o) + \eta_A(N_A - N_A^o)^2 + \ldots$ --- (1.90)

$E_B = E_B^o + \mu_B(N_B - N_B^o) + \eta_A(N_B - N_B^o)^2 + \ldots$ --- (1.91)

If one ignores all other effects except the second order, the total change in energy will have the form as,

$\Delta E = (\mu_A - \mu_B)\,\Delta N + (\eta_A - \eta_B)\,(\Delta N)^2$ --- (1.92)

where, $\Delta N = N_B^o - N_B = N_A - N_A^o$ --- (1.93)

The energy stabilization due to such a charge transfer is second order in $\mu_B - \mu_A$. On minimizing (E_A+E_B) with respect to ΔN. The result is,

$\mu_A = \mu_B = \mu_{AB}$ --- (1.94)

Where, $\mu_A = \mu_A + 2\eta_A\Delta N+\ldots$ --- (1.95)

$\mu_B = \mu_B + 2\eta_B \Delta N + \ldots$ --- (1.96)

Consequently, to the first order,

$$\mu_{AB} = \frac{\mu_A S_A + \mu_B S_B}{S_A + S_B} \quad \text{--- (1.97)}$$

$$\Delta N = \frac{\mu_B - \mu_A}{2(\eta_A + \eta_B)} \quad \text{--- (1.98)}$$

On substituting the expression for ΔN, the interaction energy can be expressed as,

$$\Delta E = -\frac{(\mu_B - \mu_A)^2}{4(\eta_A + \eta_B)} \quad \text{--- (1.99)}$$

If we write the above Eq. (1.99) in terms of softness parameter, the expression for ΔE becomes,

$$\Delta E = -\frac{(\mu_B - \mu_A)^2}{4(\eta_A + \eta_B)} = -\frac{(\Delta\mu)^2}{2}\frac{S_A S_B}{S_A + S_B} \quad \text{--- (1.100)}$$

Consider the grand potential, $\Omega_A = E_A - \mu_A (N - N_A^o)$ --- (1.101)

$\Delta\Omega_A = \Delta E_A - \Delta\mu_A \Delta N_A - \mu_A \Delta N_A$ --- (1.102)

From Eqs.(1.94)-(1.97), one can see that $\Delta\mu_A = \mu_{AB} - \mu_A = \eta_A \Delta N_A$ --- (1.103)

Applying Eqs.(1.98) and (1.103), the expression can now be written as,

$\Delta\Omega_A = (\mu_A \ \Delta N_A + 1/2\ \eta_A (\Delta N_A)^2) - \eta_A(\Delta N_A)^2 - \ \mu_A \Delta N_A$

$= -1/2\ \eta_A(\Delta N_A)^2$ --- (1.104)

From the expression for ΔN, $\Delta\Omega_A = -\frac{(\mu_B - \mu_A)^2}{2(S_A + S_B)^2} S_A S_B^2$ --- (1.105)

Similarly, for the system B, the change in the grand potential, $\Delta\Omega_B$ can be expressed as,

$$\Delta\Omega_B = -\frac{(\mu_B - \mu_A)^2}{2(S_A + S_B)^2} S_A^2 S_B$$

Hence,

$$\Delta\Omega_A + \Delta\Omega_B = -\frac{(\mu_B - \mu_A)^2}{(S_A + S_B)} S_A S_B \quad \text{--- (1.106)}$$

From the above expression, it can be seen that,

$\Delta\Omega_A + \Delta\Omega_B = \Delta E_A + \Delta E_B = \Delta\Omega_{AB} = \Delta E_{AB}$ ---(1.107)

Considering, an "atoms-in-molecule" viewpoint, the atoms can be seen as open subsystems leading to a consideration of the grand potential Ω_A or Ω_B as natural quantity to describe the interactions in terms of atoms, in analogy with macroscopic thermodynamics. Supposing now that the interaction between molecule A and B occurs between atoms k and l, one can get the expressions ΔE_{Ak} and ΔE_{Bl} in the same way as we have described above. Here, the chemical potential must fulfill the condition,

$$\mu_{AB} = \mu_A + \eta_{AK}\,\Delta N_{AK} = \mu_B + \eta_{BK}\,\Delta N_{BK} \qquad \text{--- (1.108)}$$

and $\Delta N_{AK} + \Delta N_{BK} = 0$.

Accordingly, from the expression for μ_{AB}, one finds that,

$$\Delta N_{Ak} = \frac{(\mu_B - \mu_A)}{(S_A + S_B)} S_A S_B f_{Ak} \qquad \text{--- (1.109)}$$

Similarly, $\Delta N_{Bl} = \dfrac{(\mu_B - \mu_A)}{(S_A + S_B)} S_A S_B f_{Bl}$ --- (1.110)

Using the expression ΔN, the change in grand potential $\Delta\Omega_{Ak}$ and $\Delta\Omega_{Bl}$ are,

$$\Delta\Omega_{Ak} = -\frac{(\mu_B - \mu_A)^2}{2(S_A + S_B)^2} S_B^2 S_A f_{Ak} \qquad \text{--- (1.111)}$$

and $\Delta\Omega_{Bl} = -\dfrac{(\mu_B - \mu_A)^2}{2(S_A + S_B)^2} S_{Ak}^2 S_B f_{Bl}$

Rewriting $\Delta\Omega_{Ak}$,

$$\Delta\Omega_{Ak} = -C \frac{S_A}{(S_A + S_B)^2}$$

where, $C = -\dfrac{(\mu_B - \mu_A)^2}{2} S_{Bl}^2 f_{Ak}$

On minimizing the grand potential $\Delta\Omega_{Ak}$ with respect S_A at fixed $(\mu_B - \mu_A)$, S_{Bl} and f_{Ak} allows one to establish an optimum value of the softness of system B for a given softness of system A.

$$\frac{d(\Delta\Omega_{Ak})}{dS_A} = -C \frac{d}{dS_A}\left(\frac{S_A}{(S_A + S_B)^2}\right) = C\left(\frac{S_B - S_A}{(S_A + S_B)^3}\right) \qquad \text{--- (1.112)}$$

The minimization condition demands that S_A should be equal to S_B

$$S_A = S_B \qquad \text{--- (1.113)}$$

Minimization of $\Delta\Omega_{Bl}$ with respect to S_B also leads to the same result. Thus, the global HSAB principle implies that the grand potential of all the atoms in A and of all the atoms in B become minimum, when both species have an approximately equal global softness. Hence, the expression for $\Delta\Omega_{Ak}$ at the minimum may be expressed as,

$$\Delta\Omega_{Ak} \quad = \quad -\frac{1}{2}\frac{(\mu_B-\mu_A)^2}{4S_A^2}S_A^3 f_{Ak} \quad = \quad -\frac{1}{8}(\mu_B-\mu_A)^2 S_A f_{Ak} \qquad \text{--- (1.114)}$$

similarly, $\Delta\Omega_{Bl} \quad = \quad -\frac{1}{2}\frac{(\mu_B-\mu_A)^2}{4S_A^2}S_A^3 f_{Bl} \quad = \quad -\frac{1}{8}(\mu_B-\mu_A)^2 S_A f_{Bl}$

Since we have considered that the interaction between A and B occurs through the kth atom of A and the lth atom of B, one may assume that the most favorable situation corresponds to,

$$(\Delta\Omega_{Ak})_{\min} \approx (\Delta\Omega_{Bl})_{\min} \qquad \text{--- (1.115)}$$

Immediately, it implies that $f_{Ak} \approx f_{Bl}$ --- (1.116)

Since minimization of the grand potential $\Delta\Omega$ has demanded that, $S_A = S_B$, and applying the above expression (1.116), one can get $S_{Ak} = S_{Bl}$. --- (1.117)

That is, the interaction between A and B is favored when it occurs through those atoms whose softnesses are approximately equal. The important consequence of this statement is that although the softest atoms in a molecule A is, in general, the most reactive site, there may be other sites, though not as soft, which may become the most reactive sites, depending on the softness of the reacting molecule B. This proves the local HSAB principle.

When f_{Ak} is equal to f_{Bl}, the total interaction energy expression at the minimum is given as,

$$\Delta E_{Ak} + \Delta E_{Bl} \quad = \quad -\frac{(\mu_B-\mu_A)^2}{2(S_A+S_B)}S_A S_B f_{Ak} \qquad \text{--- (1.118)}$$

From Eq. (1.118), it can be seen that the greater the values of f_{Ak} and f_{Bl}, the greater the stabilization energy. If we assume that the Fukui function of the reacting atoms are equal, then the interaction between A and B will not necessarily occur through the softer atoms but rather through those the atoms whose Fukui functions are approximately equal.

Expression for ΔE_μ[104]

Let us write the Hohenberg-Kohn equation,

$$E[\rho] = F[\rho] + \int dr\rho(r)v(r) \qquad \text{--- (1.119)}$$

The corresponding Euler-Lagrange equation,

$$\mu = \frac{\delta F[\rho]}{\delta\rho(r)} + v(r) \qquad \text{--- (1.120)}$$

From Eq. (1.119) and Eq.(1.120)

$$E[\rho] = F[\rho] + \mu N - \int dr \, \frac{\delta F[\rho]}{\delta\rho(r)}\rho(r) \qquad \text{--- (1.121)}$$

The energy difference between a ground state characterized by μ_i, $\rho_i(r)$, N_i, $v_i(r)$ and another ground state characterized by μ_f, $\rho_f(r)$, N_f, $v_f(r)$, may be expressed by, from the expression (1.121),

$$Let, \Delta E = E[\rho_f] - E[\rho_i]$$

$$\Delta E = N_f\mu_f - N_i\mu_i - F[\rho_f] - F[\rho_i] + \int \rho_i(r)\frac{\delta F}{\delta\rho(r}\bigg|_{\rho_i(r)} + \int \rho_f(r)\frac{\delta F}{\delta\rho(r)}\bigg|_{\rho_f(r)} \qquad \text{--- (1.122)}$$

Now, if one performs a Taylor series functional expansion of $F[\rho_f]$ around $F[\rho_i]$, and of $\delta F/\delta\rho(r)\,|\rho_f(r)$ around $\delta E/\delta\rho(r)|\rho_i(r)$, the above expression for ΔE can be written as,

$$\Delta E = \left(N_f\mu_f - N_i\mu_i\right) - \frac{1}{2}\iint drdr'\eta_f(r,r')\rho_f(r)\rho_f(r') + \frac{1}{2}\iint drdr'\eta_i(r,r')\rho_i(r)\rho_i(r') \qquad \text{--- (1.123)}$$

Where, the expression for $\eta(r,r')$ is used, and in the first integral $\eta_i(r,r')$ has been replaced by $\eta_f(r,r')$, and the higher order terms are neglected.

If we assume that, $f(r) = \rho(r)/N$, one can relate the above integral to global hardness as defined in the Eq.(1.44) and (1.45). Hence,

$$\Delta E = (N_f\mu_f - N_i\mu_i) - \frac{1}{2}N_f^2\eta_f + \frac{1}{2}N_i^2\eta_i \qquad \text{--- (1.124)}$$

Now if we assume that the total number of electrons are not changing, i.e. $N_i = N_f = N$ and if the two ground states have the same chemical potential, $\mu_i = \mu_f$, then Eq.(1.124) becomes,

$$\Delta E_{\mu} = -\frac{1}{2} N^{2} \Delta \eta \qquad \text{--- (1.125)}$$

Since $\eta > 0$, Eq. (1.125) implies that $\Delta E > 0$ when $\Delta\eta < 0$ and $\Delta E < 0$ when $\Delta\eta > 0$. Thus one can see that when a system evolves towards a state of greater hardness ($\Delta\eta > 0$), under the conditions of constant chemical potential, its stability increases. Thus this relation leads to the principle of maximum hardness. It should be noted that ΔE_{μ} is proportional to $\Delta\eta$ and the factor N^2 can be considered as the proportionality constant. It is a constant for a fixed value of N. Hence, Eq.(1.125) is written as,

$\Delta E_{\mu} = - ½\ K\, \Delta\eta$

Thus, the expression for the total interaction energy can be written from the Eqs. (1.118) and (1.125) ,[23,24,214,216]

$$\Delta E_{\text{int}} = -\frac{(\mu_B - \mu_A)^2}{2(S_A + S_B)} S_A S_B f_{Ak} - \frac{1}{2} K \Delta \eta \qquad \text{--- (1.126)}$$

The details of the above interaction energy expression will be analyzed critically in the next chapter. The above expression of the interaction energy is a starting point of the present thesis to study the different types of intermolecular interactions. The present dissertation will critically study such interactions for different cases through the local HSAB principle and develop the principle to more general cases of interactions. We will now briefly outline the objectives and organization of the present thesis.

1.20 Organization of the Thesis

In the present thesis, a special attention is focused on the development of a theoretical formulation to establish the relation between the total energy changes with respect to the changes in the chemical potential and hardness parameters and in their derivatives. More importantly, we are interested in establishing these concepts to investigate the reactivity of molecular systems in a semi-quantitative way.

In chapter 2 of the present thesis, we will first ascertain the possibility of calculating the interaction energy of the complexes from the expression derived in section 1.19. The arbitrary definition of one of the important parameters, referred as λ, present in the interaction energy expression is explicitly pointed out. This parameter is arbitrarily defined in the literature. We have shown that the arbitrary definition or complete neglect of this term may lead to erroneous results even at the qualitative level. Subsequently, the need for an accurate definition of this parameter is explained for a quantitative study. We have defined this parameter λ as the charge transfer term, i.e., change in the electron density of the system before and after the interaction processes. Using the present definition of the parameter λ, we have made an attempt to evaluate interaction energy for some of the weakly interacting systems. In particular, we have considered small molecular interactions with the extra framework cations present in the zeolite solid systems. A focus has also been kept to validate the reliability of the interaction energy obtained from the present method by comparing the experimental and other theoretical adsorption energy values.

In chapter 3, we will address the reliability of the present model that has been discussed in the earlier chapter, in evaluating the bond energy of various types of molecular complexes with varying degrees of bond strength (weak to strong complexes). We will also discuss in detail on the principal role of electronegativity (or chemical potential) equalization and the charge distribution process in stabilizing the complexes. To solve these critical issues, we have undertaken a systematic study of the Lewis acid-base complexes, the interaction between the Lewis acid, (BH_3) and the Lewis base, (NH_3) and their respective fluoro and methyl derivatives.

In Chapter 4, we will make a critical study on the applicability and reliability of the semi-quantitative model proposed in earlier chapters based in local HSAB principle in calculating the interaction energy for some of the well-studied systems. We essentially study the effect of different basis sets, the electron correlation and different electron population partitioning methods in the calculation of interaction energy for the complexes using the present model. The cases that we have considered for the present study, are the Lewis acid-base complexes, the interaction of acids, BH_3 and BF_3 with bases NH_3 and CO. Since these complexes are well studied by both experimental and other conventional theoretical methods, these serve as the benchmark systems for the study of the above mentioned effects.

The methods, described in the earlier chapters, are applicable only to the interactions based on single-site. However, there are many complexes interacting through multiple-sites, like the intra- and intermolecular hydrogen bonding interaction in DNA, RNA and peptides. The description of such multiple-site interactions through local HSAB principle requires a modification and accordingly, in chapter 5, we have made an attempt to generalize the local HSAB principle using the group softness concept as one of the important concepts. Essentially, we find there are two limiting cases, so-called localized reactive model (fully local) and the global reactive model (fully global). Their origin stems from the nature and location of the reactive sites present in the molecular systems. The reactive atoms present in a system can either be directly bonded to each other or they can be located at different places and accordingly, one can handle the cooperative and non-cooperative types of multiple-site interactions based on the proposed models. The feasibility of development has been tested by selecting some prototype inter molecular hydrogen bonded systems where the multiple-site interactions are important. We also discuss the nature of these different approaches and the domain of their applicability. These models can describe various interactions, which are intermediate between fully local and global in nature.

In chapter 6, a preliminary study has been made to understand the effect of external field on the individual values of the reactivity descriptors and the influence of these in the calculation of interaction energy of the complexes. Since the whole molecular interaction has been considered in terms of the perturbation parameters (most of the reactivity descriptors), it would be interesting to study the variation of these parameters due to the external field. The study of the response of molecular systems due to the external field through the density based descriptor provides further understanding about the behavior of the monomers in forming the complexes and eventually it will be helpful in simulating other external effects.

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Chapter 2

Critical Study of Local Reactivity Descriptors for Weak Inter-molecular Interactions: A Qualitative And Quantitative Analysis of Adsorption of Molecules in Zeolite Lattice

Abstract

In this chapter, an attempt has been made to evaluate the interaction energy between the molecular complexes using a model based on local HSAB principle . The principle was initially proposed by Gazquez and co-workers and derived the using second order energy density perturbation method. The details for the derivation of this principle and subsequently the proposed models are discussed elaborately. The definition of one of the important parameters, referred as λ, present in the interaction energy expression is explicitly pointed out. It is also shown that any arbitrary definition or complete neglect of the term λ may lead to erroneous results even at the qualitative level. In the model proposed in the present chapter, the parameter λ has been defined as the charge transfer term i.e. change in the electron densities of the systems before and after the interaction process. Using the present definition of the parameter λ, a critical study has been made in predicting the inter-molecular interaction energy for the weakly interacting systems. The systems that we have chosen in the present study are small molecular interactions (N_2, CO_2 and CO) with different cations (Li, Na and K) exchanged zeolite-A. The applicability of the local reactivity descriptors in predicting the reactivity of various active sites, present in zeolite-A has also been studied. Attention is focused on the validation of the definition of the parameter λ by calculating of interaction energy and comparing it with the experimental adsorption energy value and trend of the adsorption patterns over different cations. This represents the first case where local HSAB principle has been used for quantitative description of weak adsorption cases.

2.1. Introduction

The interaction between the molecules or between the molecule and any metal surface is the major governing factor for the reactions occurring at the interface.[1,2] There can be several reaction sites and it is important to develop simple descriptors to probe the reactivity of the different sites of a system. In recent years, DFT has emerged as a powerful tool through which, chemical concepts like reactivity, selectivity, reaction path of a system have been studied.[3-7] In chapter 1, the global and local reactivity descriptors (GRD and LRD) have been discussed elaborately along with the two important chemical principles, HSAB and PMH, in relating stability and reactivity of the molecular systems.[4,8,9] It should be noted that the earlier attempts made by several groups on such studies, in particular, the interaction between molecules by employing the local reactivity descriptors are primarily at the qualitative level only. The cases studied are the cases of medium and strong chemical interactions. However, there are very few reports or studies of weak interactions using local reactivity descriptors. It would be interesting to assess the performance of the reactivity descriptors for the case of weak interactions. For such cases, it is important to have a quantitative description by the use of descriptors. Local HSAB principle allows the possibility of such a quantitative study. This paper will represent first such study for weak interaction in the literature. Similar quantitative study of local HSAB principle has been done only sparingly by Gazquez and Mendez[10] and Mendez *et al*[11] for the case of strong interactions. The theoretical basis for the quantitative analysis of local HSAB principle was proposed by Gazquez and Mendez.[10]

As we have discussed in section 1.19, the formulae of interaction energy derived by Gazquez and Mendez consist of two parts. The first term, ΔE_v,[12] corresponds to the energy change due to chemical potential equalization process at constant external potential and the second term ΔE_μ[13] corresponds to reshuffling of the charge distribution at constant chemical potential μ, which is actually a manifestation of the principle of maximum hardness. The second term, ΔE_μ, involves a constant λ. It has been physically related to the effective number of valence electrons involved in the interaction between the molecules.[10] The term λ bears the information on the stability of the system. In an earlier study by Gazquez and Mendez,[10] the reactivity of enolate anions and pyridine derivatives, was studied using an arbitrary value of λ as 0.5. Mendez *et al*[11] have studied the reactivity of benzonitrile oxides using the value of λ as 1.0. They could relate the reactivity of various sites of the given molecule with the energy that is involved in the interaction only at the qualitative level. However, the term λ, representing the dynamical behavior of electron cloud during a chemical reaction, may become dominant in case of weak interaction. Hence, an arbitrary definition of λ or complete neglect of that term may lead to erroneous results even at the qualitative level. Consequently, there is a high demand for an intuitive and correct theoretical approach to investigate the problem of obtaining a reliable value of λ for the study of interaction energy and more so for weak cases.

To study the above factors for weak interaction, in the present work we have taken weak adsorption of gaseous molecules at different cationic sites of zeolites as an example problem. There has been a lot of interest[14-16] in studying the reactivity of various sites and the effect of exchange of various metal cations in the zeolite framework using a cluster model from the point of view of adsorption and catalysis. However, experimentally it is difficult to access or observe the effect of interaction of the molecules at different cationic sites due to the complex framework nature of zeolites. Hence, a theoretical study to explore the effects of zeolite framework structure and the cations present inside the zeolite cavity on the interaction of molecules is a pertinent exercise. This study will constitute an important calibration and application of the local HSAB principle to the area of weak interaction and will at the same time greatly help in the understanding of zeolite-molecular interaction. Specifically we would like to focus our attention on the following issues: (i) prediction of the preferable adsorption reactive site among the various cationic adsorption sites in the zeolite lattice surface and the energy involved at the each reactive site. (ii) importance of the parameter λ in the case of various molecular interaction processes and the ability to distinguish the interaction process of N_2, CO_2 and CO towards the various cationic sites (Li, Na and K). (iii) reliability of our calculation with the experimental adsorption energy values and trends of the adsorption patterns over different cations.

The present chapter is organized as follows: In section 2.2, we give a brief theoretical background of the local HSAB principle and the reactivity descriptors. section 2.3 deals with the interaction energy expression using local HSAB principle and the definition of the factor λ and in section 2.4 the methodology and computation details are given. In section 2.5, we present the results of our study and discuss the implications of our results. While discussing about the absolute site reactivity of zeolite and the energy associated with each cationic site, a focus has been made on a systematic study of the parameter λ and its effect on the adsorption energy.

2.2. Theoretical Background

2.2.1 Global Quantities

The detailed description on the reactivity descriptors, (GRD and LRD) has already been presented in the pervious chapter. However, a brief outline of the reactivity descriptors would be helpful before we go into the details of the present chapter.

In density functional theory, the ground state energy of an atom or a molecule in terms of its electron density ρ(r) is written as,[17]

$$E[\rho] = F[\rho] + \int dr v(r)\rho(r) \qquad \text{-------}\ (2.1)$$

where v(r) is the external potential that includes the nuclear potential also, and F[ρ] is the universal Hohenberg-Kohn functional composed of the electronic kinetic energy and the electron-electron interaction energy. The first and second partial derivatives of E[ρ] with respect to the number of electron N under the constant external potential v(r) are defined as the chemical potential μ and the global hardness η of the system respectively.[8,9,18]

$$\mu = \left(\frac{\partial E}{\partial N}\right)_{v(r)} \qquad \text{---}(2.2)$$

$$\eta = \left(\frac{\partial^2 E}{\partial N^2}\right)_{v(r)} \qquad \text{---}(2.3)$$

The inverse of the hardness is expressed as,

$$S = 1/2\eta \qquad \text{---}\ (2.4)$$

The global descriptor of hardness has been an indicator of overall stability of the system. A rigorous principle of maximum hardness (PMH) relating hardness to stability at constant chemical potential has been proposed by Pearson[19] and proved by Parr and Chattaraj.[20] It has been customary to use a finite difference approximation for μ and η.[4] Using the energies of N, (N+1) and (N-1) electron systems, we get the operational definition of μ and η as,

$$\mu \approx -(IP + EA)/2 \qquad \text{---}(2.5)$$

$$\eta \approx (IP - EA)/2 \qquad \text{---}(2.6)$$

where IP and EA are the first vertical ionization energy and electron affinity of the chemical species respectively.

2.2.2 Local Quantities

The site-selectivity of a chemical system, can not, however, be studied using the global descriptors of reactivity. For this, appropriate local descriptors need be defined. An appropriate definition of local softness s(r) is given by,[4]

$$s(r) = \left(\frac{\partial \rho(r)}{\partial \mu}\right)_{v(r)} \qquad \text{---(2.7)}$$

such that,

$$\int s(r)dr = S \qquad \text{---(2.8)}$$

Combining Eqs. (2.8) and (2.4), we can write

$$s(r) = \left(\frac{\partial \rho(r)}{\partial N}\right)_{v(r)} \left(\frac{\partial N}{\partial \mu}\right)_{v(r)} = \left(\frac{\delta \mu}{\delta v(r)}\right)_{N} S$$

$$= f(r)\ S \qquad \text{---(2.9)}$$

where f(r) is defined as the Fukui function (FF).[21] It is obvious that the local softness contains the same information as FF (i.e. the sensitivity of the chemical potential of a system to a local external potential)[22] as well as the additional information about the molecular softness. Using left and right derivatives with respect to the number of electrons, electrophilic and nucleophilic FF and local softness can be defined. To describe site-selectivity or reactivity of an atom in a molecule, it is necessary to condense the values of f(r) and s(r) around each atomic site into a single value that characterizes the atomic contribution in a molecule. This can be achieved by electronic population analysis. Thus for an atom x in a molecule, depending upon the type of electron transfer, we have three different types of condensed FF of the atom k_x[23]

$f_{x+} = [q_x(N+1) – q_x(N)]$ for nucleophilic attack --- (2.10a)

$f_{x-} = [q_x(N) – q_x(N-1)]$ for electrophilic attack --- (2.10b)

$f_{x0} = [q_x(N+1) – q_x(N-1)]$ for radical attack --- (2.10c)

where q_x is the gross electronic population of atom k in the molecule. The corresponding condensed local softnesses s_{x+}, s_{x-} and s_{x0} can be defined. Parr and Yang proposed that larger value of FF indicate more reactivity.[21] Hence, greater the value of the condensed

FF, the more reactive is the particular atomic center in the molecule. This can determine the behavior of different reactive sites with respect to the hard and soft reagents.

2.3. Local HSAB Principle: The Expression for the Interaction Energy and the Definition of λ

Considering the interaction between the stable systems A and B with the number of electrons N_A and N_B, respectively, the interaction energy between these two chemical species can be written within the framework of DFT as,[4,10]

$$\Delta E_{int} = E[\rho_{AB}] - E[\rho_A] - E[\rho_B] \qquad \text{----(2.11)}$$

where ρ_{AB}, ρ_A and ρ_B are the electron density of the systems AB at equilibrium and of the isolated systems A and B respectively. It has been shown by Gazquez that the interaction between A and B is assumed to be taken place in two steps.[9,13] In the first step, the interaction will take place at constant external potential through the equalization of chemical potential. In the second step, A and B evolve towards the equilibrium state through changes in the electron density of global system produced by changes in the external potential at constant chemical potential. This step is actually a manifestation of the principle of maximum hardness.[13]

We have already derived the expression for interaction energy in the section 1.19 as shown by Gazquez and Mendez. Hence, we will now directly write the expressions and discuss further.

According to the Eq.(1.89), the total interaction energy between A and B can be given as,

$$\Delta E_{int} = \Delta E_v + \Delta E_\mu \qquad \text{---(2.12)}$$

Following Gazquez *et al*,[9,10] the expression for each term in Eq. (2.12) can be written,

$$\Delta E_v \approx \frac{-1}{2}\left(\frac{(\mu_A - \mu_B)^2}{\eta_A + \eta_B}\right) \qquad \text{---(2.13)}$$

and $$\Delta E_\mu \approx -\frac{1}{2} N^2 (\eta_{AB} - \eta^*_{AB}) \qquad \text{--- (2.14)}$$

In Eq.(2.14) η_{AB} is the hardness of the system AB at equilibrium and η^*_{AB} is the hardness of the system when the constituents of the system are far away from each other.

Eq.(2.13) can be written in terms of softnesses as,

$$\Delta E_v \approx \frac{-1}{2}\left(\frac{(\mu_A - \mu_B)^2}{S_A + S_B}\right)(S_A\ S_B) \qquad \text{--- (2.15)}$$

However, the corresponding changes in the Eq. (2.14) are not so simple, as it involves the total hardness of the system. One has to relate the total hardness of the system AB in terms of the softnesses of the individual systems. In general, the total softness of the system AB at equilibrium can be written as,[9]

$$S_{AB} = k\,(S_A + S_B) \qquad \text{---- (2.16)}$$

Where k is the proportionality constant, S_A and S_B are the softness of the isolated systems A and B. It has been shown by Yang *et al*[24] that the molecular softness of a system at equilibrium can be replaced by the average of the softness of each constituent of the molecular system. In the limit of separation or dissociation of the molecule into its constituents, the proportionality constant can be approximated as 1 and in the interacting limit, the total softness decreases (conforming to the principle of maximum hardness) and thus k attains a value less than 1. The lower the value of k, the more stable the system is expected to be. In that sense, the proportionality constant k contains information about the stability of the system AB. It can be, thus, related to the extent of overlap between the isolated atomic species in the molecule. As the total molecular softness is insensitive to the number of electrons, the difference in the softness (S_{AB} - S^*_{AB}) can be approximated by,

$$\Delta S = k'\,(S_A + S_B) \qquad \text{---- (2.17)}$$

where k' is another proportionality constant. By applying Eq.(2.17) in Eq.(2.14),

$$\Delta E_{\mu} \approx -\frac{1}{2} N_{AB}^{2} K \left(\frac{1}{(S_A + S_B)} \right) \qquad \text{---- (2.18)}$$

where N_{AB} is the total number of electrons of the system AB. The product of the terms N_{AB}^2 and K, known as λ,[10] can be related physically to the effective number of valence electrons that have participated in the interaction between A and B. We define the parameter λ as the change in the electron densities of the systems before and after the interaction process. This change will give the effective number of valence electrons participating in the interaction process. Thus an expression for the term λ can be written as the difference of electron densities of the system A before and after the interaction,

$$\lambda_A = \sum_{i=1}^{M} \rho_{Ai}^{eq} - \sum_{i=1}^{M} \rho_{Ai}^{0} \qquad \text{---- (2.19)}$$

Alternately, the term λ can be defined as the difference of electron densities for the system B,

$$\lambda_B = \sum_{j=1}^{N} \rho_{Bj}^{eq} - \sum_{j=1}^{N} \rho_{Bj}^{0} \qquad \text{---- (2.20)}$$

where the first terms of the right hand side of the Eqs.(2.19) and (2.20) refer to the sum of the electron densities of each atom in A and B in the molecule AB at equilibrium respectively and the second terms in Eqs.(2.19) and (2.20) refer to electron densities of each atom in the isolated systems A and B respectively. The number of electrons that are donated effectively to another system will be equal to the number of electrons that have been accepted by the other system. Hence, in principle, the change in electron density of the system A, λ_A in isolated system A and in the system AB should be equal to the corresponding change in electron density of the system B, λ_B, but with the opposite sign.

From a local point of view, if the interaction between two chemical systems A and B occurs through the kth atom of A, one can express the interaction at the kth atom by replacing global softness of A by the local softness of the site k in A as,

$$(\Delta E_{\text{int}})_{Ak} \approx \frac{-1}{2}\left(\frac{(\mu_A - \mu_B)^2}{S_A f_{Ak} + S_B}\right)(S_A \ f_{Ak} S_B) + \frac{-1}{2}\left(\frac{\lambda}{S_A f_{Ak} + S_B}\right) \qquad \text{--- (2.21)}$$

where f_{Ak} is the Fukui function value of the site k of the system A. According to the Eq. (2.21), in case S_B is large, there is a greater stabilization when the interaction occurs at the site with the greater value of f_{Ak} and vice versa. If the change in the electron density of system A is only at the site of interaction k of A, then the factor λ can be conveniently given as the change in electron density at the site k,

$$\lambda_{Ak} = q_{Ak}^{eq} - q_{Ak}^{o} \qquad \text{--- (2.22)}$$

where q_{Ak}^{eq} *and* q_{Ak}^{o} are the density of the kth atom of the system A in the complex AB and in the isolated system A respectively.

2.4. Methodology and Computational Details

The unit cell of Li-A, Na-A and K-A zeolite was generated from the crystal structure as reported in the literature, where the Si/Al ratio is one.[25] The three distinctive cationic sites were located. To study the nature of reactivity of sites SI and SIII towards the incoming molecules, we have considered a dimer cluster model. The dimer cluster for each site SI and SIII has been cut from the 6 membered (6-m) ring and 4-m ring respectively and the Si-O and Al-O dangling bonds of the cluster are saturated with hydrogen atoms. The O-H bond distance of the terminal OH bond is kept fixed at $0.96A^0$

and the H atoms are aligned in the direction of T-O-T (T = Si, Al) bond axis. The zeolite cluster and the complexes of molecules studied are shown in Figures 2.1-2.4. All the calculations using this model were performed at the level of *ab initio* Hartree-Fock (HF) method using 3-21G(d,p) and a more extensive basis set 6-31G(d,p) basis set. Since in case of potassium, the 6-31G(d) basis set is not available in Gamess *ab initio* program[26], the basis set is given externally.[27] To examine the effect of cluster size, we have also considered a trimer cluster model (Fig. 2.5) and studied the interaction of the molecules for the site SI using 3-21G(d,p) and 6-31G(d,p) basis sets. Since the trimer model cluster cannot be generated from a 4-m ring (site SIII), we have considered only the site SI and it has been generated from 6-m ring, as in the case of dimer cluster model of site SI. Restricted HF method has been used for the energy calculation of neutral species and for the corresponding anionic and cationic systems the ROHF method has been performed.

Condensed FF and local softness for each cationic cluster were calculated via Eq.(2.10a) using Mulliken[28] and Löwdin[29] population analysis (MPA and LPA) . MPA and LPA are based on the partition of the electrons into net atomic populations in the atomic basis functions $\psi_{n.}$ In MPA, the population on an atom is defined to be sum over the diagonal elements centered on that atom of (**PS**) matrix, where **P** is the density matrix over the atomic orbital basis and **S** is the overlap matrix of atomic orbitals. On the other hand, LPA atomic population is the sum of the corresponding diagonal elements of ($\mathbf{S}^{1/2}$ $\mathbf{P}$ $\mathbf{S}^{1/2}$). Thus in LPA, the total number of electrons is the trace of the density matrix in terms of a symmetrically orthogonal basis. The *ab initio* calculations were performed using the GAMESS[26] system of programs on the IRIX-6.2 Silicon Graphics work station. Since the extra framework cations are the usual adsorption sites in zeolites that are electrophilic in nature, the condensed local reactivity descriptors s_x^+ and f_x^+ (x = Li, Na and K) for the cations at different reactive sites of the zeolite were calculated. Along with these local descriptors, we have also used the recently proposed new descriptor, namely, relative electrophicity (s_x^+/s_x^-), defined as the ratio of s_x^+ and s_x^- to obtain the site reactivity of the various cationic sites.

The bond between cation and the molecule in the complex is only optimized. The molecules are allowed to interact perpendicularly with the cationic site and the angle between the cation-molecule is kept at 180^0. Throughout our calculations, the interaction site for the zeolite model is the cation and for the molecule, the end part of it has been considered i.e. N atom in N_2, O in CO_2 and C in CO are considered as the interacting part. As the geometry of molecules is less affected in the presence of zeolite lattice, we have fixed the experimental geometry for the above molecules and hence the only the cation - molecule distance is varied.

2.5. Results and Discussions

2.5.1 Site Reactivity Order in Various Cation Exchanged Zeolite-A: A Qualitative Analysis

The zeolites are alumino silicates materials[31] and most of the zeolites will show the varying catalytic properties that are related to several factors,[32] namely (i) the Al content in the framework, Si/Al ratio, (ii) the shape and pore size of the cavity and (iii) the presence and nature of the cations at various positions. For e.g. the cations can be found at the big cavities or small member ring like 6-membered (6-m) or 4-m ring depending upon the framework structure of zeolite, and thus it offers different types of reactive sites for the interaction of the molecule.[33] At all sites the interaction of molecules with the cations are critical in determining the catalytic transformation of the molecules,[34] or in the molecular gas separation processes.[35] In A type zeolite, three different types of cations are distributed which are located at the 6, 8 and 4–m rings in the zeolite lattice[31] and we will hereafter refer to these as SI, SII and SIII respectively as shown in the Fig. 2.1. The extra framework cations are the actual adsorption sites for the interaction of any incoming molecule and the adsorption or any kind of catalytic transformation of molecules will normally take place at the cages of zeolite. Since the cationic site SII is located at 8-m ring, i.e. at the entrance of the zeolite alpha cage (see Fig. 2.1), it hinders the incoming molecule to enter inside the cages and hence the site SII is of least importance. Hence we have not considered the site SII for the present study. We have not optimized any cluster fully, as the complete relaxation of the cluster leads to structures that do not resemble experimental geometry. Especially for our calculations we would like to address the reactivity of the available sites that depends on the structural geometry of the local sites and therefore we have not optimized any of the clusters. The difficulty of geometry optimization of a cluster model was pointed out in a study by Hill et al.[16] This fact has also been realized in a recent study by Deka *et al* [36] and Brand *et al*,[37] and it has been shown that the full relaxation of cluster does not lead to experimental acidity sequence of various metal exchanged zeolite clusters. Table 2.1 contains the chemical potential and the global softness values of the zeolite model cluster as well as the interacting molecules at both 3-21G(d,p) and 6-31G(d,p) basis sets. The global softness values of the zeolite and the adsorbed molecules differ significantly and hence the mapping of reactivity of adsorbed molecules with the cationic zeolite model clusters becomes difficult on the basis of the softness values.

We now consider the reactivity of site SI. The values of condensed FF, local softness and the relative electrophilicity, obtained through Mulliken and Löwdin population schemes are tabulated in Table 2.2. The FF values of the site SI cations calculated through the Mulliken population analysis (MPA) in 3-21G(d,p) and 6-31G(d,p) basis set, is in the increasing order of Li > K > Na and K > Li > Na, respectively. The trend of FF values obtained from the Löwdin population analysis (LPA), is in the order of K > Na > Li. On the other hand, the local softness parameter follows the reactivity order as K > Na > Li. The reactivity order obtained by the relative electrophilicity values, is in the increasing order of Li > K > Na and it is important to note that the reactivity order derived from the relative electrophilicity parameter follows the same order irrespective of the basis set and the electron population analysis.

We now turn to the reactivity of site SIII. The SIII cations are generally found in the alpha cage of the zeolite, in front of the 4-m ring. The Li ion exchanged zeolite is normally synthesized with sodium cation.[25] Li ions are located at sites SI and SII, but at site SIII sodium cations are occupied. Hence the SIII reactivity of Na and K-A zeolites are only described here. Based on the FF and local softness values, one can infer from the Table 2.3 that the reactivity order of SIII in K-A should be greater than that of Na-A zeolite model cluster. The relative electrophilicity values for both the cationic sites indicate that the reactivity order of SIII in Na-A should be greater than that in K-A, which is contradictory with the reactivity order derived from the FF and condensed local softness values. From the above arguments, a definite conclusion on the site reactivity order for the different cations from the reactivity parameters like FF, local softness values and relative ratio term is not so obvious. In spite of this apparent conflict in the conclusion on the reactivity order drawn from the reactivity parameters, we believe that the relative electrophilicity term is a good parameter to locate the reactive site, as the values give a consistent trend irrespective of the basis set and electron population analysis. From the various systematic studies like the acidity order for the various metal exchanged zeolites[36] and the electrophilic or nucleophilic attack of the molecules at the various sites of the aromatic and aliphatic carbonyl compounds,[30,38] we have confirmed that the relative ratio term gives a better description of the intra-molecular site reactivity than the other reactive parameters.

Although the ambiguity arises in the prediction of the reactivity order in the above systems, one can observe in all cases that the site SIII is more reactive than SI on the basis of FF and the relative ratio terms. In case of Na-A, the difference between the values of FF for the site SI and SIII is less compared to that of the relative electrophilicity terms. Both the FF and relative electrophilicity values in cases of K-A zeolite for the sites SI and SIII are differing marginally. The reason for the more reactivity of SIII is clearly indicated by the spatial extra stability of SI cations, as they are coordinated to more number of oxygen atoms, in contrast to the naked site SIII cations (Figures 2.2 and 2.3). Hence the reactivity of site SIII cation is expected to be more than that of partially shielded SI cationic site. The local reactivity descriptors nicely interpret the trend on the reactivity of the cationic sites. The recent study carried out by our group[39] on the determination of electric field exerted by the zeolite lattice ions shows that the electric field strength is more at the site SIII than the other cationic sites SI and SII. Moreover, the experimental studies based on infra-red[40] and molecular dynamics studies[41] reveal that the interaction of methane and nitrogen molecule takes place at the site SIII of the Na-A zeolite. It should be mentioned here that in spite of the small size of the model cluster considered in our calculations, we could retain the structural reactivity of each site consistent with the experimental studies and other theoretical studies.

2.5.2 Interaction of N_2, CO_2 and CO Molecules with the Cluster Model: A Quantitative Analysis

The quantitative energy analysis through the local HSAB principle is expected to solve the ambiguity raised in the interpretation of the site reactivity order obtained from the reactivity descriptors as discussed in section 2.5.1. Local HSAB principle can give a quantitative estimate of this using only local quantities. However, this demands the definition of the parameter λ empirically as we discussed in section 2.3. Gazquez and Mendez as well as Geerlings and co-workers have used an arbitrary value of 0.5 and 1.0 for λ to describe the reactivity of enolate ions and 1,3-cyclo addition reactions of benzonitrile oxide with an alkene respectively.[10,11] This was adequate to describe the above reaction. However, the bonding involved in that case is quite different from the ones we would like to study. Our study involves weak interaction for which no λ value exists in the literature. In course of our study as detailed in what follows, we would establish the value of this quantity for the weak interaction of gaseous molecules N_2, CO_2 and CO with the zeolite extra framework cations Li, Na and K. We would conclude that the value of λ is substantially different from the cases of stronger interactions.

Considering the case of nitrogen, the interaction of nitrogen molecule with the cationic sites of zeolite lattice is a weak interaction that is evidenced by the experiment[42] as well as theoretical[43] values of the interaction energy below 20 kJ/mol. As shown in the Table 2.5, the ΔE_v for sites SI and SIII of Li, Na and K in dimer cluster model, ranges from 14.16 to17.89 kJ/mol. These quantities cannot be regarded as large compared to the ordinary covalent or ionic bond energy. At the same time, the calculation of ΔE_μ becomes difficult, as the value of the parameter λ is not defined and it is also observed that the nature of binding changes with the value of λ. For example, for the value of λ from 0.0 to 0.5, the corresponding ΔE_{int} is calculated. The linear relationship between λ and ΔE_{int} is plotted in Fig. 2.6 for all molecules. It can be seen from the plot of λ vs ΔE_{int}, the stability of nitrogen complexes increases with increasing value of λ. The results show the need for accurate λ value. As we know from chemical intuition that the binding nature of N_2 with Na cation is a weak interaction, it is expected that the effective electron transfer should be very less. To obtain this, the zeolite model cluster with Na cation and the N_2 molecule are allowed to interact in a linear fashion and the optimization of the cluster cation- molecule is carried out. MPA gives a better description of the reactive sites in a molecule through the descriptors and hence the factor λ has been calculated through MPA. MPA usually results in larger charge separation between the atoms. This may be a probable reason, why it performs well in ionic systems like zeolites.

In the determination of λ, it can implicitly be assumed that when A and B are interacting weakly through the kth atom of molecule A and lth atom of molecule B, only those two atoms participate in the reshuffling process of charge distribution. Hence the changes in the electron population on all other atoms can be neglected. Although this may be an approximation, it can be reasonably assumed that the greatest change in the population will occur at the atomic sites that participate directly in the interaction. In Table 2.4, the electron population on each atom in the Na-A zeolite model clusters for the cationic site SIII is explicitly given. Evidently, it can be seen from Table 2.4 that the most significant change in the electron population has occurred only at the cationic site of the zeolite model cluster. Using Eq.(2.22), the λ value for the Li, Na and K zeolite cluster complexes of N_2 is calculated. It can be seen that the listed λ values in Table 2.5 are all positive and small. This λ value is used to calculate the interaction energy arising out of reshuffling. In the case of interaction of nitrogen molecule with the cations, the energy term ΔE_v calculated by 6-31G(d,p), contributes to a larger extent rather than the reshuffling of the charge distribution. However, the energy terms ΔE_v and ΔE_μ calculated from 3-21G(d,p) indicate that both are contributing equally. It may be due to the overestimation of the electron population on the reactive sites by the use of 3-21G(d,p) basis set. In order to verify the efficiency of this method, some available experimental data is also shown in Table 2.5, for comparison with our computed adsorption energy. It can be seen that the overestimation in order of few kJ/mol, is present in all the complexes listed here probably because of the limited accuracy in the calculation of structural parameters and the cluster termination. Nevertheless, such overestimation is systematic and consistent and there is an excellent linear relationship between the computed and the experimental adsorption energy. The computed ΔE_{int} of N_2 with the cationic sites at SIII is significantly greater than that of the site SI which unambiguously supports our earlier discussion on the greater site reactivity of SIII as explained by the relative electrophilicity term and the FF.

The adsorption mechanism of N_2 with cations is well established and it is essentially electrostatic in nature and the interaction arises due to the quadrupolar interaction of nitrogen molecule with the electric field generated by the cation. The quadrupole moment of N_2 molecule is –1.093 in atomic units.[44] The charges of the molecule are less affected by the presence of cations, which clearly indicates that the interaction of N_2 is influenced by the larger quadrupolar moment of the N_2 and the field generated by the cation. When we exchange the Na cation by Li and K, the interaction behavior is affected significantly and it is due to the variation in the electric field that is exerted by the cations.

The interaction of CO_2 follows the same trend as in the case of N_2 interaction. As the dipole moment of CO_2 is zero and the interaction with cations partially arises due to the electrostatic interaction as well as by the notable charge transfer process. The interaction energy for CO_2 with cations is expected to be higher than that of nitrogen case. It should be noted that the mean polarity of the C-O bond in CO_2 is greater than that of N_2 bond polarity. Hence contribution of the interaction energy due to the charge transfer will be more than that of nitrogen case. In other words, the value of the factor λ should be considerably higher compared to the value of λ in case of nitrogen interaction. The inspection of the energy values in Table 2.6 indicates that ΔE_v is less and ΔE_μ is higher than that of nitrogen case that can be easily analyzed by looking the value of quadrupole moment of N_2 and CO_2. Since the quadrupole moment of N_2 is higher than that of CO_2, the contribution of interaction energy due to the ΔE_v term will be small but the contribution of ΔE_μ is high due to the increase in the cation-dipole interaction. The energy value that is calculated using the basis set 6-31G(d,p) for the case of CO_2 is less than the experimental value. However, it essentially follows the same trend as expected in the experimental studies.[45,46] The usage of basis set 3-21G(d,p) gives better interaction energy values which is comparable to the experimental energy values.

Finally, in case of CO molecule, the most significant aspect is that the maximum part of the interaction energy comes from the ΔE_μ term and the parameter λ has a vital role in determining the interaction energy, as results presented in Table 2.7. Agreement between the interaction energy calculated using local HSAB principle and the experimental values[47] are quite satisfactory. The recent DFT[47,48] study on the CO molecular interaction with the alkali metal cation exchanged zeolite cluster also predicts the interaction energy as -19.7, -15.0 and -8.8 kJ/mol for the cations Li, Na and K respectively which is very close to our results.

To check the effect of cluster size, the interaction energies of the above molecules with the cations in a trimer model cluster of zeolite have been reported in Table 2.8. It can be seen that the interaction energy follows essentially the experimental order, Li > Na > K in all cases. On comparing these interaction energy values with those obtained using the dimer model cluster, one can see that the variation is only in marginal and the order of change in the interaction energy values is in the order of ±2-3 kJ/mol. Thus we can conclude that the interaction energies obtained through the local HSAB principle and using the reactivity descriptors are quite stable with respect to the dimension of the cluster model of zeolites.

2.6. Conclusions

We have critically analyzed the site-reactivity and the effect of zeolite framework on the adsorption of the molecules using the local reactivity descriptors. We observed that all the reactivity descriptors suggest the site SIII to be the most reactive site in zeolite-A irrespective of the cation present in the sites. We have studied adsorption of N_2, CO and CO_2 molecules in zeolite lattice. The condensed FF reproduces the reactivity order in most of the cases, only when it is evaluated using Mulliken population. Local softness fails to produce the correct reactivity order for each case. However, the relative electrophilicity furnishes the correct site reactivity order most reliably independent of the population scheme or the basis set. We have also used local HSAB principle for a quantitative estimate of the adsorption energy using only variables of the reacting molecules. The estimate of interaction energy was done by evaluating the value of the parameter λ as charge transfer at the reactive site. This scheme results in the interaction energies, which are in good agreement with experimental and other theoretical interaction energy values. This suggests the efficacy of local HSAB principle in describing the weak intermolecular interaction and the validity of our quantitative definition of the parameter λ. Our work in this chapter suggests the possible use of local HSAB principle in describing weak interactions and the simplicity of this approach will allow for the systematic investigation of structural and energetic trends.

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Table 2.1: Global property values for the zeolite-A model cluster and molecules (in atomic units) SV3 and SV6 refer to 3-21G(d,p) and 6-31G(d,p) basis sets, respectively.

System	Chemical potential		Global softness	
	SV3	SV6	SV3	SV6
Li SI	-0.134	-0.142	7.280	6.719
Na SI	-0.143	-0.151	8.411	8.070
SIII	-0.137	-0.148	8.330	7.764
K SI	-0.136	-0.144	8.303	7.855
SIII	-0.135	-0.145	8.325	7.697
N_2	-0.216	-0.227	2.758	2.788
CO_2	-0.183	-0.192	3.351	3.364
CO	-0.176	-0.175	3.147	3.137

Table 2.2: Condensed Local softness and Fukui function values for the zeolite-A model cluster from Mulliken and Löwdin population analysis for the cationic site Li, Na and K at site SI. (in atomic units)

System	Fukui Function f_x^+		Local softness s_x^+		Relative electrophilicity (s_x^+/s_x^-)	
	SV3	SV6	SV3	SV6	SV3	SV6
Li						
Mulliken	0.955	0.948	6.951	6.368	52.058	44.452
Löwdin	0.880	0.852	6.404	5.727	30.873	39.833
Na						
Mulliken	0.920	0.924	7.736	7.452	18.629	23.893
Löwdin	0.923	0.922	7.767	7.440	19.395	27.025
K						
Mulliken	0.949	0.975	7.880	7.663	25.789	45.560
Löwdin	0.953	0.905	7.911	7.106	23.800	38.197

Table 2.3: Condensed Local softness and Fukui function values for the zeolite-A model cluster from Mulliken and Löwdin population analysis for the cationic site Na and K at site SIII (in atomic units)

System	Fukui Function f_x^+		Local softness s_x^+		Relative electrophilicity (s_x^+/s_x^-)	
	SV3	SV6	SV3	SV6	SV3	SV6
Na						
Mulliken	0.921	0.937	7.672	7.273	39.940	46.590
Löwdin	0.913	0.909	7.605	7.060	27.198	41.033
K						
Mulliken	0.947	0.978	7.886	7.531	26.187	41.438
Löwdin	0.951	0.960	7.916	7.387	24.214	43.165

Table 2.4: The Mulliken Electron population on each atom[a] in the nitrogen adsorbed complex of Na-A zeolite model cluster at site SIII . The numbering of the atoms is given in Figure 2.4

Atom	Complex far away from equilibrium		Complex at equilibrium	
	SV3	SV6	SV3	SV6
Na1	10.543	10.346	10.644	10.380
O2	8.803	8.866	8.803	8.867
Al3	11.823	11.591	11.820	11.587
O4	8.657	8.850	8.657	8.850
H5	0.752	0.678	0.753	0.678
O6	8.677	8.849	8.678	8.849
H7	0.778	0.696	0.779	0.697
O8	8.720	8.873	8.720	8.873
H9	0.751	0.675	0.753	0.676
Si10	12.445	12.514	12.442	12.510
O11	8.650	8.741	8.650	8.742
H12	0.687	0.627	0.687	0.627
O13	8.683	8.730	8.683	8.731
H14	0.678	0.618	0.680	0.619
O15	8.652	8.714	8.653	8.715
H16	0.701	0.634	0.702	0.634
N17	7.000	7.000	7.006	7.008
N18	7.000	7.000	6.892	6.958

Table 2.5: Interaction energy of N_2 with Li, Na and K - zeolite-A dimer model cluster (energy values are in kJ/mol and λ value is given in atomic unit, ΔE_{TE} is the available theoretical and experimental interaction energy. [a] reference 42,43)

Cation	λ		ΔE_v		ΔE_μ		ΔE_{tot}		
	SV3	SV6	SV3	SV6	SV3	SV6	SV3	SV6	ΔE_{TE}^a
Li									
SI	0.12	0.05	-17.69	-18.15	-16.39	-6.77	-34.09	-24.93	-27.2
Na									
SI	0.09	0.03	-14.16	-15.24	-12.39	-4.31	-26.55	-19.56	-20.0
SIII	0.10	0.03	-16.69	-16.49	-12.83	-4.47	-29.52	-20.96	
K									
SI	0.08	0.02	-17.18	-18.17	-10.80	-3.43	-27.98	-20.82	----
SIII	0.09	0.03	-17.87	-17.79	-11.60	-3.67	-29.47	-21.37	

Table 2.6: Interaction energy of CO_2 with Li, Na and K - zeolite-A dimer model cluster (energy values are in kJ/mol and λ value is given in atomic unit, ΔE_{TE} is the available theoretical and experimental interaction energy. [a] reference 45,46)

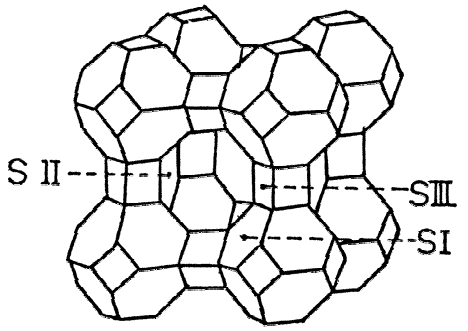
Cation	λ		ΔE_v		ΔE_μ		ΔE_{tot}		
	SV3	SV6	SV3	SV6	SV3	SV6	SV3	SV6	ΔE_{TE}
Li									
SI	0.12	0.05	-7.30	-7.16	-15.86	-6.92	-23.18	-14.08	-54.4
Na									
SI	0.11	0.04	-4.94	-5.11	-13.06	-4.47	-17.95	-9.59	-48.2
SIII	0.11	0.04	-6.54	-5.92	-12.48	-4.48	-19.03	-10.76	
K									
SI	0.10	0.02	-6.84	-6.96	-11.79	-2.92	-18.63	-9.87	-46.9
SIII	0.11	0.03	-7.31	-6.73	-13.35	-3.58	-20.66	-10.31	

Table 2.7: Interaction energy of CO with Li, Na and K - zeolite-A dimer model cluster (energy values are in kJ/mol and λ value is given in atomic unit, ΔE_{TE} is the available theoretical and experimental interaction energy. [a] reference 48)

Cation	λ		ΔE_v		ΔE_μ		ΔE_{tot}		
	SV3	SV6	SV3	SV6	SV3	SV6	SV3	SV6	ΔE_{TE}^{a}
Li									
SI	0.11	0.15	-5.23	-2.94	-14.27	-20.16	-19.65	-23.09	-19.7
Na									
SI	0.09	0.09	-3.22	-1.65	-10.39	-10.92	-13.62	-12.57	-15.07
SIII	0.09	0.09	-4.55	-2.12	-10.67	-11.50	-15.22	-13.62	
K									
SI	0.06	0.06	-4.79	-2.72	-7.48	-7.82	-12.28	-10.38	-8.79
SIII	0.08	0.07	-5.18	-2.58	-9.2	-9.00	-14.90	-11.58	

Table 2.8: Interaction energy of N_2, CO_2 and CO with Li, Na and K **at site SI** - zeolite-using trimer model cluster (energy values are in kJ/mol and λ value is in atomic unit)

Cation at site SI	λ		ΔE_v		ΔE_μ		ΔE_{tot}	
	SV3	SV6	SV3	SV6	SV3	SV6	SV3	SV6
N_2								
Li	0.115	0.034	-19.72	-20.81	-15.58	-5.01	-35.30	-25.82
Na	0.099	0.031	-18.58	-19.55	-12.63	-4.09	-31.22	-23.65
K	0.062	0.013	-20.29	-21.14	-7.55	-7.55	-27.85	-22.76
CO_2								
Li	0.109	0.039	-8.75	-9.02	-13.90	-5.42	-22.65	-14.44
Na	0.096	0.034	-7.85	-7.95	-11.61	-4.25	-19.45	-12.19
K	0.065	0.013	-8.99	-8.95	-7.54	-1.53	-16.53	-10.48
CO								
Li	0.09	0.12	-6.42	-4.42	-12.45	-16.70	-18.87	-20.87
Na	0.09	0.08	-5.64	-3.36	-10.81	-10.12	-16.45	-13.48
K	0.06	0.04	-6.57	-3.39	-6.76	-4.89	-13.33	-8.96



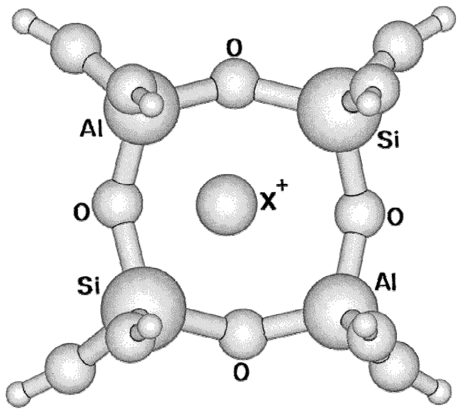
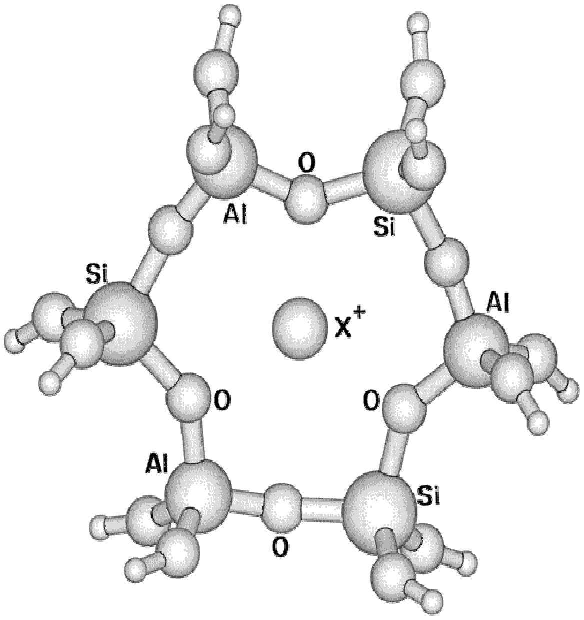


Figure 2.1 Unit cell of A-type zeolite are and the reactive site SI, SII and SII located at 6-m, 8-m, 4-m ring, respectively

Figure 2.2 The cationic (X^+) position at the 4m-ring, site SIII. All Si and Al atoms are terminated by hydroxyl group. The nearest oxygen-cation distance is 2.59 and 2.95Å for Na and K, respectively.



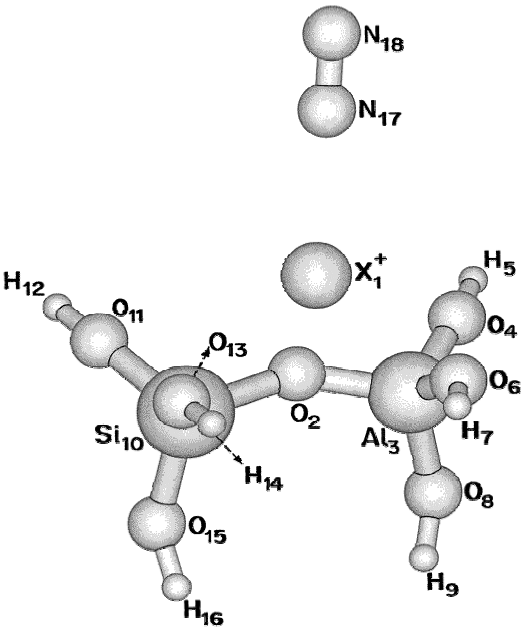


Figure 2.3 The cationic (X^+) position at the 6-m ring, site SI. The nearest oxygen--cation distance is 1.88, 2.32 and 2.60 Å Li, Na and K types of zeolites, respectively.

Figure 2.4 The dimer model cluster with N_2 for X^+ cations (Li, Na and K) used for the interaction energy calculations

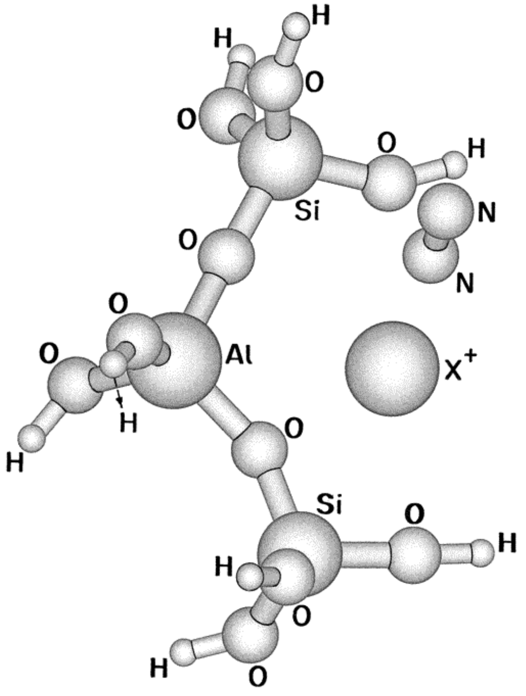


Figure 2.5 The trimer model cluster with N_2 molecule for X^+ cations (Li, Na and K) of site SI, used for the interaction energy calculation

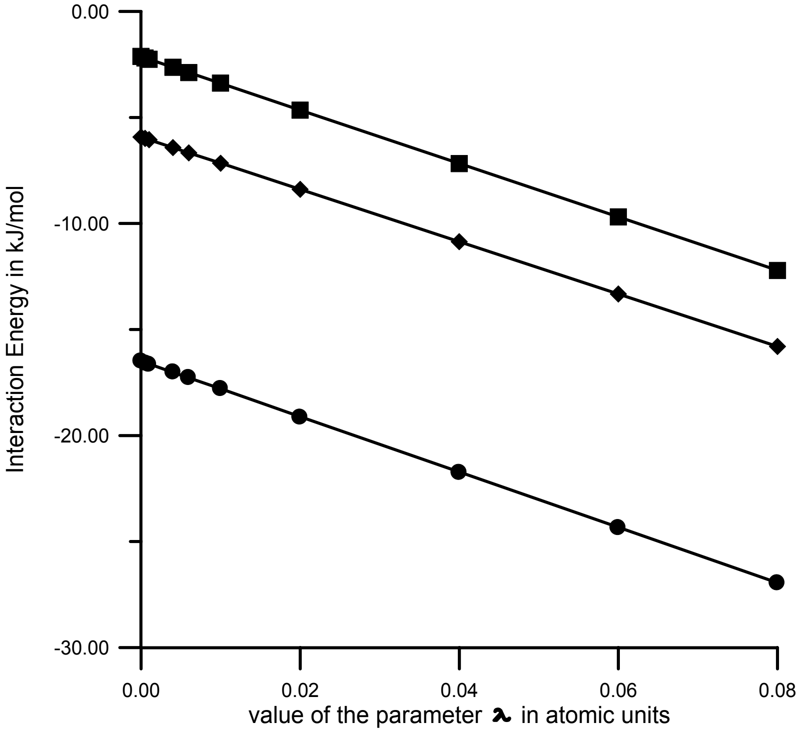


Figure 2.6 The variation of interaction energy ΔE_{int} with the parameter λ, only for the cationic site SIII of sodium at the 6-31G(d,p) basis set level is given. (● = N_2; ◆ = CO_2; ■ = CO

Chapter 3

A systematic Study on the Reactivity of Lewis Acid-Base Complexes through the Local Hard-Soft Acid-Base Principle

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Abstract

The present chapter addresses the stability of Lewis acid-base complexes using the recently developed local Hard-Soft Acid-Base (HSAB) principle. The present study will explain how the individual molecular reactivity descriptors determine or distinguish the nature of various types of interactions that are normally observed in the formation of complexes. The soft-soft and hard-hard types of interactions are distinguished primarily by the electron transfer parameter. The principal role of electronegativity equalization and the charge redistribution process in stabilizing the complexes is demonstrated. The effect of correlation on the reactivity descriptors and subsequently on the soft-soft as well as hard-hard interactions has also been studied in this chapter. The validity of the present model in calculating the interaction of these complexes with varying degrees of strength is demonstrated.

3.1. Introduction

The use of the DFT based descriptors for chemical binding, especially to evaluate the stability of the molecular complexes, is an important issue. As it has been illustrated in the previous chapters, few attempts have been made in the literature to quantify the molecular interactions in terms of the global and local reactivity based descriptors. However, these methods involve many empirical parameters.[1-5] The method, formulated by Ghanty and Ghosh, is based on the Pauling's electronegativity model and it involves covalent radii and other empirical parameters that can be related to electron density.[1] In other method, they obtained the interaction energy expression through the concept of generalized electronegativity equalization procedure. The calculated bond energies for simple hetero-nuclear diatomic molecules are in agreement with the experimental results. Pal *et al.* has discussed the energetics of the systems with the changes in the hardness and chemical potential parameters.[2] Gazquez has calculated bond energies for several diatomic molecular systems using GRD.[3a] He has also shown that activation energy of a chemical reaction depends mainly on the difference between the hardness of the initial state of a reaction and hardness of the transition state.[3b] All these models have been formulated to calculate the bond energy only for some simple diatomic molecules in terms of the chemical potential and hardness parameters. For the case of complex poly-atomic molecular systems, the models are not directly applicable and it requires many parameters which are essentially empirical in nature.

In a recent study, we have also made an attempt to calculate the intermolecular interaction energies for weakly interacting complexes.[6-8] The method is basically derived using the second order density perturbation theory and is based the local HSAB principle developed by Gazquez and Mendez.[9] The chemical bonding is viewed as resulting from the charge transfer (chemical potential equalization) and the reorganization or redistribution of electron density in the presence of various atomic nuclei in the molecules.[9,6] The model involves a parameter λ, related to the ratio of softness of the complex and the sum of the softnesses of the reacting systems.[6] Without taking recourse to the calculation of the complex, several ad hoc definitions have been proposed by different groups depending on the systems.[3,4,6,9] However, in the preceding chapter of the thesis, we have defined this parameter as charge transfer term and the same expression is used irrespective of the nature of the molecular systems.[6-8] The model merits detailed discussion and analysis. The applicability of this model has been shown in our earlier study on the interaction of various small molecules (N_2, CO_2 and CO) at the different cationic sites (Li, Na and K) of zeolite systems.[6] The obtained interaction energy was in agreement with the experimental results. Recently, this model has also been used to study the reactivity of several cationic sites in dioctahedral clays by Chatterjee and co-workers with some degree of success.[10] The systems studied are only weakly interacting systems and further, they are restricted to ionic electrostatic interactions. In order to establish and validate the present semi-quantitative approach for the purpose of study of chemical binding in a broad way, a detailed study is in order. In this chapter, the objective is to undertake such a study. Specifically, we would like to address the following issues: (i) the validity of the present model in calculating the interaction energy of the molecular complexes with varying degrees of strength, especially, weak to moderate type of interactions. (ii) the effect of electron correlation on GRD and LRD and subsequently on the interaction energy calculations and on the parameter λ. (iii) how important are chemical potential equalization process and maximum hardness principle during the molecular interactions? (iv) what parameters act as driving forces for the interaction between them so as to have a maximum stabilization?

We hope that study of such a nature will help us explain how these individual molecular descriptors determine or distinguish the nature of various types of interactions that are normally observed in the formation of complexes. To solve the above issues, we have considered the typical Lewis Acid-Base complexes (LABC) of BH_3-NH_3 and its flouro and methyl derivatives. Different kinds of acid-base complexes have been synthesized and used as reagents and catalysts to accelerate organic, organo-metallic and biochemical reactions.[11] These types of complexes are ideally suited for the present study and these complexes are well studied in the literature by experimental and by theoretical methods.[11-14] Moreover, the softness/hardness (S/η) values of these complexes can easily be tuned by substituting a group of atoms by single atom in acids and bases. LABC comprises of molecules that can be formed by electrostatic, covalent or van der Waals interactions and hence the present study will encompass bond strength from weak to medium nature. We will confirm our results with the well-documented experimental and theoretical studies.

The chapter is organized as follows: In Section (3.2), we give a brief theoretical background of the reactivity descriptors and the quantitative model. In Section (3.3) the methodology and computational details are given. In Section (3.4), we present the results of our study and discuss the implications as well as limitations of the results.

3.2. Theoretical Background

The detailed description of the reactivity descriptors and its quantitative definitions has already been discussed in earlier chapters. Hence, we will now briefly present the expression for the interaction energy.

Using energy as a functional of number of electrons (N) and the external potential (v), the interaction energy is defined as the difference between the two interacting model systems A and B, and it is given as, [9,6,4]

$$\Delta E_{int} = \Delta E_v + \Delta E_\mu \qquad \text{-------} \quad (3.1)$$

$$\Delta E_v \approx \frac{-1}{2}\left(\frac{(\mu_A - \mu_B)^2}{(\eta_A + \eta_B)}\right)_v \qquad \text{-------} \quad (3.2)$$

$$\Delta E_\mu \approx -\frac{1}{2} N^2 \, (\eta_{AB} - \eta^*_{AB})_\mu \qquad \text{------} \quad (3.3)$$

where η_{AB} and η^*_{AB} are the hardness of the complex at the equilibrium and at the non-interacting limit of AB respectively. For the details of the mathematical part of derivation for the Eqs. (3.1)-(3.2), one can refer the work of Gazquez and Mendez [4,9] and by us.[6] Here the interaction between the system A and B is assumed to take place in two steps. In the first step, the interaction takes place at constant external potential through the equalization of chemical potential (ΔE_v). In the second step, A and B evolve toward the equilibrium state through changes in the electron density of the global system at constant chemical potential (ΔE_μ). The second step is actually a manifestation of the principle of maximum hardness. One can relate the difference in the hardness terms present in the above Eq.(3.3) to the softness of system A and B with a proportionality constant (K). Thus, Eq.(3.3) can be now rewritten in terms of the softness of the systems A and B as,

$$\Delta E_{\mu} = -\frac{1}{2} N_{AB}^{2} K \left(\frac{1}{(S_A + S_B)} \right) = -\lambda \ [\ 1/\ (\ \mathrm{S_A + S_B}\ )\ ]\ /\ 4 \qquad \text{---------} (3.4)$$

Herein, we introduce an ad-hoc term λ as the product of $2N^2$ and the proportionality constant K. The term λ introduces in a way the change of total softness of AB, as the complex is formed. There is no rigorous way to obtain this term without the actual calculation of softness of AB vis-à-vis the ones of the interacting systems. In the literature, there are several different definitions of this ad-hoc parameter.[3,6,9] Geerlings and co-workers have used the value of λ as 0.5 and 1.0 for certain organic reactions.[3c,d] In the preceding chapter of this thesis, we have defined the parameter λ as the changes in the electron densities of the systems before and after the interaction process that will give the effective number of valence electrons that has participated in the interaction process.[6,7] Thus, an expression for the term λ can be written as the difference of electron densities of the system A before and after the interaction,

$$\lambda_A = \sum_{i=1}^{M} \rho_{Ai}^{eq} - \sum_{i=1}^{M} \rho_{Ai}^{0} \qquad \text{----------} (3.5)$$

Alternately, the term λ can be defined as the difference of electron densities for the system B,

$$\lambda_B = \sum_{j=1}^{N} \rho_{Bj}^{eq} - \sum_{j=1}^{N} \rho_{Bj}^{0} \qquad \text{---------} (3.6)$$

where the first terms in Eq.(3.5) and Eq.(3.6) refer to the sum of the electron densities of the each atom in A and B in the molecule AB respectively and the second terms of these equations refer to electron densities of isolated systems A and B. The densities of each atom are obtained by population analysis and there are several choices in this. We have used in our earlier calculation as well as in the present work Mulliken population analysis. This model has also been recently used by Chatterjee and co-workers with some degree of success.[10]

If the interaction between the systems occur through the kth atom of A with the lth atom of B, one can express the total interaction energy from the local point of view, as,

$$\Delta E_{\mathrm{int}}^{AB} = \left(\mu_A - \mu_B\right)^2 \left(\frac{s_{Ak} s_{Bl}}{s_{Ak} + s_{Bl}} \right)_v - \frac{\lambda}{4} \left(\frac{1}{s_{Ak} + s_{Bl}} \right)_{\mu} \qquad \text{----}(3.7)$$

Where, μ_A and μ_B are the chemical potential of the A-B, respectively. The s_{Ak} and s_{Bl} refer to the condensed local softness of the atom k in the system A and l of the systems B, respectively.

3.3. Methodology and Computational Details

Ab initio Hartree-Fock (HF) and Möeller-Plesset second order (MP2) quantum chemical calculations have been used to evaluate the global and local reactivity descriptors. All the monomers and molecular complexes were optimized without any symmetry constraints, using HF and MP2 level of theory through the standard split valence basis set 6-31G(d,p). The restricted HF method has been used for the energy calculations of neutral and for the corresponding anionic and cationic systems, the restricted open shell HF method has been performed. The condensed Fukui function and local softness for each reactive atom were calculated using Mulliken population analysis.[15] The *ab initio* molecular orbital calculations were carried out using the GAMESS[16] system of programs on an IRIX-6.2 silicon graphics workstation. The parameter λ was calculated using Eq.(3.5) through the Mulliken population scheme.

3.4. Results and Discussions

The optimized geometry and the structural parameters of the LABC are compared with the reported literature values. In Table 3.1, the chemical potential, global and local softness values of acids and bases are given. It can be seen that there is a substantial decrease in the values of the global and local softness of acids and bases by the successive fluorine substitutions. The chemical potential of the Lewis acids is less than that of Lewis bases and it indicates that the electrons will flow from the bases to acids. It should be noted that the values obtained by HF and MP2 follow the same trend. However, the HF predicts the values of global and local softness higher than MP2 and in case of chemical potential, MP2 value is greater than HF. From the values of the softness parameters, one can order the softness of the given Lewis acids and bases. Accordingly, with reference to BH_3, the soft acid will be BH_3 and the hard acid will be BF_3. Similarly, NH_3 will be the soft base and NF_3 will be the hard base, with reference to NH_3. CO can be considered as a harder base than NH_3. Based on these values, one can qualitatively predict the reactivity and stability of the Lewis acids and bases using the HSAB principle. We now explain to what extent these global and local properties will determine or control the stabilization (or the interaction energy) of the complexes.

Table 3.2 presents the computed interaction energy of all possible combination of Lewis acids and bases along with the available experimental and other theoretical interaction energy values. It is remarkable to note that the agreement between the calculated energy using our model and the experimentally observed and theoretically calculated results (MP2 and HF) is quite satisfactory. [11-14,17,18,] The interaction energy of the complexes computed through the expression (3.7) by HF method is consistently improved by adding the correlation effects. In most of the complexes, the HF value is considerably lesser than the value obtained by MP2 method. For instance, the experimentally observed interaction energy for BH_3-NH_3 complex, is -34.4 kcal/mol and this value is more comparable to the value obtained by MP2 method (-31.82 kcal/mol) than that of HF method (-26.67 kcal/mol). Thus, it shows the effectiveness and validity of the usage of our model. The correlation effect is observed to be important in describing both the soft-soft and hard-hard interactions. In particular, for the most weakly interacting complexes (BH_2F-NF_3, BHF_2-NF_3, BF_3-NF_3, CO-BF_3 and CO-BCl_3), there is a strong correlation effect in predicting the stabilization order and the interaction energy. Although the lack of appropriate experimental interaction energy values of some complexes prevents the direct verification of our theoretical prediction, it is interesting to note that our results are in complete agreement with other available theoretical calculations. The interaction energy of BH_3-NH_3 (soft acid-soft base) is higher than other complexes and it changes from -31.8 to -17.5 kcal/mol, for BH_3 with NH_3 to NF_3. Similarly, the stability order for other set of complexes, BH_2F, BHF_2 and BF_3 with NH_3 to NF_3, can also be found. The lowest interaction energy (less stable complexes) is observed for the case of maximum fluorine substitution. For instance, BF_3-NF_3 complex is less stabilized than BH_3-NF_3 complex by an amount of ~16 kcal/mol and BH_3-NH_3 is more stabilized than BH_3-NF_3 by 14kcal/mol. In these series of complexes involving the interaction of BH_3 to BF_3 with NH_3 to NF_3 (decreasing order of softness and the parameter λ), one can see the direct influence of the S/η parameters on the interaction energy or the stability of the complexes.

It is also interesting to compare the stability of carbon monoxide (CO) with BH_3 and BF_3, with that of NH_3. Owing to the strong basic nature of NH_3, the Lewis acid, BH_3 and BF_3 are more stabilized with NH_3 rather than with CO, by an amount of 12 kcal/mol for BH_3 and the interaction energy for BF_3 with CO is significantly lower than that of NH_3. The calculated interaction energy of the CO-BX_3 (X=H, F and Cl) shows that the substitution of H by F and Cl in the Lewis acids has a predominant effect on the determination of bond strength and it can even alter the nature of bonding. This result is consistent with the literature predictions. Although we have followed a different method to predict the interaction energy, it is gratifying to note that the essential bonding effects are still captured in our model. To illustrate the effect of methyl group substitution in the base, NH_3 and its binding ability with other Lewis acids (BH_3 and BF_3), we have considered TMA-BH_3 and TMA-BF_3 complexes, where TMA is tri-methyl amine. The substitution of methyl group in NH_3 increases the softness of TMA and hence, it is expected that the stability should be greater than that of the unsubstituted NH_3. Evidently, one can see from Table 3.2, that the interaction energy for TMA-BH_3 and TMA-BF_3 complexes (-40.5 and -38.9 kcal/mol, respectively) are higher than that of any other complexes that has been studied in the present study. The difference between the interaction energy of NH_3 and TMA complexes with BH_3 and BF_3, is ~8.5 and 6.2 kcal/mol, respectively.

There has been a lot of interest in studying the puzzling features of the formation of these complexes and, in particular, considerable efforts have been made to correlate the charge transfer and the stability of the complexes.[11,16,14,19,20] In a recent study, Schaefer *et al*[12] have made a detailed study on these complexes and shown that there is no correlation between the stability and the degree of charge transfer. They have also concluded that the electrostatic interaction plays a significant role in the formation of these LABC and this study is in agreement with the earlier work made by Reetz *et al.*[18a] The Morokuma analysis of the NH_3-BH_3 complex suggests that the stabilization is mainly due to the electrostatic interaction and for the CO-BH_3 is due to the significant non-electrostatic forces.[19] On the other hand, Glendening and Streitwieser predicted that the main contribution of bonding of the above complexes is due to the charge transfer interactions.[20] Using our model, we are in a position to provide insight into the driving force for the formation of the complexes and the underlying factors that govern the strength of these complexes. A closer inspection of the contribution of the energy terms to the total interaction energy, tabulated in the Table 3.2, reveals that for the soft-soft complexes, the most important component arises from the ΔE_μ term, and other term, ΔE_v contributes marginally to the total interaction energy. This trend remains same at MP2 level, though the individual values are affected by correlation effects. The term, ΔEv, signifies the chemical potential equalization principle, i.e. the process of flow of electrons from the Lewis base to acid at constant external potential will continue until the system attains an equilibrium state. The second term actually is related to the charge redistribution process within the complex at constant chemical potential. In view of this argument, we can arrive at a conclusion that these complexes are actually more stabilized by the charge redistribution process (maximum hardness) than the energy contribution due to the chemical potential equalization. The process of charge distribution among the atoms in the molecules at the equilibrium geometry actually increases the hardness of the complex and consequently, the molecules become more stable. For the weakly bound complexes, which are of hard-hard type, both the terms ΔE_v and ΔE_μ, contribute significantly in the stability of the complexes. Here one can observe that the trend of relative importance of these two terms is changed due to correlation effects. At the Hartree-Fock level, though the relative importance of ΔE_v is same in case of soft-soft interactions, the ΔE_μ term still contributes to a larger extent. On the other hand, at the MP2 level, this trend is not necessarily observed. ΔE_v term is relatively as important or even more important compared to ΔE_μ at this level for such complexes.

One common factor that can be noticed in Table 3.2, is that the parameter λ plays an important role in predicting the stability of the LABC. The contribution of the second term ΔE_v, largely depends on the parameter λ and this term is actually related to the effective number of valence electrons (or frontier orbital electrons) that has been transferred from the system A to B (see Section (3.2)). It can be seen that the value of λ for soft-soft interaction cases is significantly greater than that of hard-hard interaction cases. The quantification of the parameter λ in terms of the frontier orbitals and its relation with interaction energy confirms that the soft-soft interaction is controlled by the orbital electrons and this argument is exactly similar to the Klopman's chemical reactivity theory.[21,22] Klopman has shown that the soft-soft interaction is highly dependent on the energy difference between the frontier orbitals of the interacting systems.[21] From the definition of λ, one can infer that the BH_3, NH_3 and the corresponding TMA complexes (soft-soft interaction) are more stabilized by the term λ. By substituting more number of fluorine atoms in the acids and bases, the hardness increases considerably and hence, the reactivity is directly affected by lowering the parameter λ. It can be considered as one of the reasons that the hard-hard interaction is weaker than the soft-soft interaction. In a similar way one can also observe that there is a linear correlation between the factor λ and ΔE_v term for the complexes of BH_3 to BF_3 with NH_3 to NF_3 and for the complexes CO with BX_3 (X=H, F and Cl). It implies that the interaction energy of the complexes is varied in the proportion with the degree of charge transfer. This linear correlation is valid only within a set of complexes. For a general case, there is no correlation between the value of λ with the interaction energy of the complexes. For instance, the value of λ is same for BH_3-TMA and BH_3-NH_3, 0.307 in atomic unit, but the computed interaction energy through MP2, differs significantly by ~9 kcal/mol. It is pertinent to note that the above conclusions drawn from our calculations are significantly consistent with the experimental and other theoretical results.

Before we conclude this section, we would like also to mention the limitations of our present approach. In particular, the effectiveness and accuracy of the present method lies on the computation of the local descriptors and these are highly dependent on the basis set and level of theory that is used in the calculation. However, it should be noted that these issues are quite common in any kind of models and the accuracy will ultimately depends on the price that we pay for the computation. Despite the arbitrary nature of the population analysis and the basis set that has been applied in the computation of each term present in our approach, we could still get the reliable interaction energy values that are in agreement with the experimental or available theoretical results. These values can be further improved by making judicious choice of basis set and population methods. The problem of defining the factor λ is still an issue. Further, we would like to make a remark that emerges from our study on the applicability of the descriptors and the perturbation methods for the interaction study. It is generally known that the perturbation method (with truncated lower order perturbation series) can give the information about the behavior of the molecular interactions only at the initial stages and it restricts only to the weak interaction cases that occur at relatively large distances.[21,23,24] It becomes difficult to apply the perturbation method when the interaction is influenced by the short range and other complex multiple type of interactions. In this present study, we have considered a wide variety of complexes ranging from the covalent, van der Waals and other weak electrostatically held molecules and the interaction energy ranges from -40.5 to -1.5 kcal/mol. Although the energy expression is derived by second order perturbation theory we could demonstrate that it is even applicable for the more complex interaction cases, such as charge transfer or donor-acceptor complexes, having moderate to weak interaction cases. The present approach may be valid for the systems where the influence of each molecule on another systems is relatively small.

3.5. Conclusions

In this present chapter, we have presented the effect of softness or hardness parameters on the simple Lewis acid-base interactions in evaluating the bond energy of the acid-base complexes. These factors can be considered as among the deterministic factors to control the strong or weak kind of interactions along with other factors μ and λ. The soft-soft and hard-hard types of interactions are related to the parameter λ or the participation of effective number of valence electrons during the interaction between the molecular systems. The role of the chemical potential equalization and the maximum hardness principle in the formation of acid-base complex is explained. It is also observed that there is a consistent improvement in the interaction energy values of the acid-base complexes by the inclusion of the correlation effects. These effects are observed to be important in describing the very weak interaction cases. A further study should be made in this direction to investigate more complex type of interactions by considering the higher order terms in the perturbation series.

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Table 3.1: The Chemical potential (μ), Global (S) and local softness (s(r)) values of the acid and bases, values are given in atomic units. For the acids, the reactive atom is boron (S_k^+) and for the bases, NH_3 and for CO is N and C (S_k^-), respectively. HF and MP2 refer to HF/6-31G(d,p)//HF/6-31G(d,p) and MP2/6-31G(d,p)//MP2/6-31G(d,p)

System	μ		S		Local softness	
	HF	MP2	HF	MP2	HF	MP2
BH_3	-0.198	-0.216	1.897	1.845	1.023	0.913
BH_2F	-0.180	-0.185	1.785	1.783	1.041	0.836
BHF_2	-0.190	-0.196	1.512	1.495	0.989	0.706
BF_3	-0.187	-0.215	1.327	1.245	0.957	0.592
BCl_3	-0.194	-0.201	2.165	1.837	0.569	0.232
NH_3	-0.063	-0.095	1.789	1.700	0.943	0.813
NH_2F	-0.089	-0.116	1.704	1.641	0.805	0.797
NHF_2	-0.115	-0.132	1.619	1.549	0.672	0.755
NF_3	-0.122	-0.162	1.423	1.459	0.518	0.716
$N(CH3)_3$	-0.023	-0.061	2.067	1.886	0.700	0.414
CO	-0.174	-0.181	1.587	1.548	1.147	1.356

Table 3.2a: The calculated interaction energy (in kcal/mol) of the complexes at the level of HF and MP2. The value of the parameter λ is given in atomic units.

Acid-base complexes	λ		ΔEv		ΔEμ	
	HF	MP2	HF	MP2	HF	MP2
BH_3-NH_3	0.263	0.307	-5.67	-3.94	-20.99	-27.88
-NH_2F	0.237	0.273	-3.38	-2.63	-20.24	-25.03
-NHF_2	0.193	0.229	-1.78	-1.79	-17.84	-21.53
-NF_3	0.121	0.175	-1.26	-0.72	-12.29	-16.80
BH_2F-NH_3	0.239	0.280	-4.29	-2.10	-18.90	-26.66
-NH_2F	0.205	0.247	-2.37	-1.20	-17.46	-23.73
-NHF_2	0.142	0.201	-1.10	-0.68	-12.97	-19.81
-NF_3	0.003	0.015	-0.74	-0.13	- 0.29	- 1.47
BHF_2-NH_3	0.228	0.267	-4.91	-2.42	-18.49	-27.60
-NH_2F	0.180	0.227	-2.84	-1.48	-15.72	-23.69
-NHF_2	0.008	0.158	-1.42	-0.92	- 0.79	-16.93
-NF_3	0.004	0.007	-0.99	-0.25	- 0.39	- 0.80
BF_3-NH_3	0.228	0.264	-4.61	-3.11	-18.81	-29.49
-NH_2F	0.178	0.218	-2.63	-2.08	-15.79	-24.59
-NHF_2	0.005	0.143	-1.30	-1.42	- 0.47	-16.64
-NF_3	0.003	0.004	-0.89	-0.57	- 0.25	- 0.50
BH_3-TMA	0.257	0.307	-7.99	-4.24	-23.34	-36.31
BF3-TMA	0.199	0.226	-6.80	-3.60	-18.84	-35.28
CO-BH_3	0.222	0.264	-0.20	-0.42	-16.04	-18.25
CO-BF_3	0.018	0.033	-0.05	-0.31	-1.37	- 2.62
CO-BCl_3	0.006	0.014	-0.09	-0.05	-0.58	- 1.36

Table 3.2b: The calculated interaction energy (in kcal/mol) of the complexes at the level of HF and MP2. ΔE^{TE} is the available interaction energy of the complexes in the literature, obtained by MP2/6-31G(d,p) and the values are written in the parenthesis corresponds to the HF/6-31G(d,p).

Acid-Base Complexes	ΔE_{tot}		ΔE_{tot}
	HF	MP2	
BH_3-NH_3	-26.67	-31.82	-34.4[a] (-23.4[b])
-NH_2F	-23.62	-27.66	-30.9[a]
-NHF_2	-19.62	-23.32	-23.9[a]
-NF_3	-13.55	-17.52	-13.3[a]
BH_2F-NH_3	-23.20	-28.76	-24.8[a]
-NH_2F	-19.83	-24.93	-18.6[a]
-NHF_2	-14.07	-20.49	---
-NF_3	- 1.03	-1.60	----
BHF_2-NH_3	-23.40	-30.02	-21.5[a]
-NH_2F	-18.56	-25.17	---
-NHF_2	- 2.21	-17.85	---
-NF_3	- 1.38	- 1.05	---
BF_3-NH_3	-23.42	-32.61	-26.7[a] (-20.8[b])
-NH_2F	-18.42	-26.67	---
-NHF_2	- 1.75	-18.06	---
-NF_3	- 1.17	- 1.07	-3.6[a]
BH_3-TMA	-31.33	-40.54	-41.3[b] (-25.5[b])
BF3-TMA	-25.63	-38.88	-36.1[b] (-25.0[b])
CO-BH_3	-16.24	-18.67	-25.6[b] (-9.2[b])
CO-BF_3	-1.42	- 2.93	- 4.0[b] (-2.5[b])
CO-BCl_3	-0.66	- 1.41	- 2.0[b] (-0.7[b])

[a] Ref. 18b ; [b] Ref. 18a

Chapter 4

A Critical Study on the Calculation of Interaction Energy Using Global and Local Reactivity Descriptors: Effects of Basis set, Electron Correlation and the Use of Different Electron Partitioning Methods

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Abstract

In this present chapter, we will make a critical study on the applicability and reliability of the semi-quantitative model proposed in the earlier chapters based on local Hard-Soft Acid-Base (HSAB) principle in calculating the interaction energy. In particular, the effects of basis sets, correlation and electron partitioning methods on the calculation of interaction energy using the descriptors will be studied. The cases that we have considered for the present study, are the Lewis acid-base interactions, the interaction of acids BH_3 and BF_3 with bases NH_3 and CO. The interaction energy ranges from ~ -32 to-2 kcal/mol. Since these complexes are well studied by both experimental and other conventional theoretical methods, these serve as the benchmark systems for the study of the above mentioned effects.

4.1 Introduction

In recent years, there have been a few attempts in developing theoretical formulations to establish relation between the total energy changes with the changes in the chemical potential, hardness parameters and in their respective derivatives.[1-3] In particular, some of the recent studies have demonstrated the possibility of calculating the interaction energy (IE) between different molecular systems using density based descriptors within the framework of DFT.[4-7] In connection to this problem, the development of such quantitative models and their applicability have been critically addressed with suitable examples in the preceding chapters. These studies have demonstrated the validity of these models in terms of quantitative aspects and the estimated IEs are reasonably close to the experimental and other standard theoretical values. These studies can, in principle, provide the information about the nature of the molecular systems in three different ways: (i) identification and nature of the reactive centers, (electrophilic or nucleophilic sites) by examining the values of the global and local reactivity descriptors; (ii) estimation of the IEs between the molecular systems through the density based reactivity descriptors; (iii) to gain information about the role played by the chemical potential equalization and charge transfer processes.

Over the years, the potential applicability of these descriptors have been extensively studied in identifying the reactive centers in organic molecular systems and inorganic solid oxides, etc.[4-10] The global and local reactivity descriptors (GRD and LRD) are, however, sensitive to the level of the theory and basis set employed in the calculations. In addition, LRD also depend on the type of electron partitioning scheme. The electron partitioning schemes are inherently arbitrary and their reliability in defining the charge of an atom in a molecule is not guaranteed with respect to the use of different basis set and the level of theory.[11-13] Despite all these drawbacks, it has generally been observed that there is not much change in the reactivity order or trend when different levels of theory and basis sets are used in the calculations.[7-10] Hence, these issues have not yet posed a real problem for qualitative studies. On the other hand, these issues can cause a serious problem in quantitative estimation of the IE of the molecular complexes using these descriptors because the errors introduced in the calculations can be of a different sign and their cancellation may lead to inconsistent results. Thus, it is extremely important to study the effect of all these factors in the calculation of these descriptors and the IEs using these descriptors. At the same time, it should be noted that these problems are common even in case of the standard method for the calculation of IE. The state-of-art of selecting the correct basis set along with a good level of theory is still considered to be as a matter of experience.[14-16] In addition, there are several methods, which employ the atomic charge as a basic quantity. For instance, molecular dynamics, molecular mechanics and Monte-Carlo calculations heavily rely on these atomic charges for the interpretation of the physical properties of the solids, liquids and for the chemical binding problems. Despite the arbitrariness involved in all these calculations, these models have been found to be very useful for the qualitative and semi-quantitative studies.

Accordingly, in the present chapter of the thesis, some of the pertinent questions are addressed. This work aims towards a systematic description of the basis set effects, different electron partitioning schemes and the effect of electron correlation contributions in the calculation of the IE for the complexes using the reactivity descriptors. Accordingly, to study the above factors and to clarify the issues as detailed above, we consider the Lewis acid-base interactions, viz., BH_3 and BF_3 with NH_3 and CO, described in chapter 3. In particular, we calculate the IE for the four Lewis acid base complexes, BH_3-NH_3, BH_3-CO, BF_3-NH_3 and BF_3-CO using different split valence basis sets along with the polarization and diffuse functions. These calculations are performed using different population methods, namely, Mulliken,[17] Lowdin[18] and molecular electrostatic potential derived charges[19] (MPA, LPA and MESP). There are many other electron partitioning schemes available in the literature apart from the above three methods, like Bader's atoms-in-molecule (AIM) method,[20] natural population analysis (NPA),[21] Hirshfeld population analysis (HPA)[22] etc. Among all these methods, MPA, LPA and MESP methods are often used in this area of research extensively and hence, we have used at present only these three methods for the calculation of the LRD and the IE of the complexes. In addition, we also calculate IE of the complexes using different DFT functionals and MP2 method to explore the effects of the electron correlation. We discuss the importance of the large basis sets and electron correlation correction in evaluating the bond energies of the above complexes using the IE expression that has been described in earlier chapters.

4.2 Methodology and Computational Details

The computation of the global and local reactivity descriptors has been described in the earlier chapters and these methodologies are followed in this chapter also. The expression (2.21) has been used to calculate the IE for the molecular systems. The calculation of the electron transfer λ parameter has been done through the Eq. (2.19).

Ab initio Hartree-Fock (HF) and density functional calculations were performed to study the effect of different basis sets and population schemes on the reactivity descriptors and subsequently on the IE of the various complexes. We have employed split-valence and double-Zeta valence basis sets in this present study and in particular, 3-21G, 3-21G(d,p), 6-31G, 6-31G(d,p), 6-31++(d,p), 6-31++G(2d,2p) and DZV(d,p) have been employed to study the effect of basis set at the HF level. Moller-Plesset (MP2) and DFT methods are applied to include the effect of electron correlation using 6-31G(d,p) basis set level. Different DFT functionals have been employed at DFT level, namely, Slater-VWN,[23] PBE-LYP,[24] Becke-LYP,[25] B3-LYP[26] and BHH-LYP.[27] The Slater-VWN functional uses the Slater exchange and Vosko, Wilk and Nusair correlation functional. In all the four functionals, the correlation part is introduced through the Lee-Yang-Parr method. The abbreviations PBE and Becke refer the exchange effect is introduced by Perdew-Burke-Ernzerhof (PBE) and Becke exchange functionals, respectively. In case of BHH-LYP, it uses the larger proportion of the exchange effects computed by HF and Becke methods. The restricted HF method has been used for the energy calculation of the neutral systems and for the corresponding anionic and cationic systems, the restricted open shell HF method has been used. The *ab initio* and the DFT calculations have been performed using the PC-Linux version of GAMESS system of programs.[28] We have used the grid based DFT in GAMESS which employs a typical grid quadrature to compute the integrals. During the SCF procedure, the grid consists of 96 radial shells with 36 and 72 angular points. We have used Mulliken, Lowdin and the molecular electrostatic potential derived charges (MPA, LPA and MESP) methods for the calculation of LRD and the parameter λ. In case of MESP, the Spackman algorithm is used to fit the atomic charges constrained to reproduce the total molecular charge along with other default options. In conventional methods, the IE will be evaluated from the difference between the energy of the complex AB and sum of the energy of the monomer A and B, $\Delta E_{int} = E_{AB} - (E_A + E_B)$.

4.3 Results and Discussion

4.3.1 Effect of Basis Set and Electron Population Schemes

The first aspect of the present discussion is to investigate the effect of different basis sets in calculating the GRD and LRD, and subsequently for the IE of acid-base complexes at the HF level. Table 4.1 presents the chemical potential and the hardness parameters for the monomers, BH_3, BF_3, NH_3 and CO. In general, it can be seen that the chemical potential of all monomers steadily increases with increasing the number of basis functions. However, the effect is observed to be marginal. In case of hardness parameter, the values are slightly reduced with the number of basis functions. The local softness values for the reactive atoms, which are evaluated using the different population methods, MPA, LPA and MESP, are presented in Table 4.2. MPA and LPA values for the condensed local softness are generally seen to be less systematic than the values calculated by MESP method. The inclusion of the polarization (d,p) functions in the standard 6-31G basis set affects the local softness values marginally. On the other hand, the value of local softness increases considerably by adding the diffuse functions along with the polarization functions (6-31G++(d,p)) except for the case of carbon in CO. In case of CO, the effect of polarization functions is observed to be more than that of the diffuse functions. For all the molecular systems, the values of the local softness predicted by MESP are significantly greater than that of other methods for all the basis sets. On replacing fluorine in place of hydrogen in BH_3, there is a significant change in the values of chemical potential, hardness, and condensed local softness of boron atom. The predicted values of local softness of boron in BH_3 and BF_3 by all the three population methods using different basis sets show that the reactivity of BH_3 is greater than that of BF_3 and this is in agreement with the expected reactivity trend. The trend obtained by MPA method differs when the polarization and diffuse functions are included in the 6-31G(d,p) basis set. In case of NH_3 and CO, it is known that the reactivity of NH_3 is greater than that of CO. More interestingly, it can be seen that the prediction of the reactivity order for NH_3 and CO is strongly dependent on the types of basis set used in the calculations. MPA predicts the correct reactivity trend only at the higher basis sets, 6-31G++(d,p) and 6-31G(2d,2p). LPA predicts the correct reactivity trend at a reasonable basis set starting from 6-31G. However, the reactivity order predicted by MESP does not change with respect to the number of basis sets.

Let us now discuss the effect of the basis sets and different population schemes on the calculation of IE of the different complexes using the expression (2.21) at the HF level. The charge transfer term λ calculated by MPA, LPA and MESP methods is tabulated in Table 4.3. Although charges assigned in this fashion are inherently arbitrary, the approach remains useful for a comparison between similar complexes. It is, however, expected that the arbitrariness or errors introduced in the calculation of the charges through the different partitioning methods may cancel each other when the difference between the absolute values of charges are considered. The calculated IEs are shown in the Figure 4.1 and 4.2 in case of BH_3-NH_3, BH_3-CO and BF_3-NH_3, BF_3-CO, respectively. Inspection of Figures 4.1 and 4.2 indicates that trend in the calculated IEs is not inordinately sensitive to basis sets. The IE values are more comparable to the values calculated by standard quantum chemical methods (hereafter refereed as IE-QM) at the higher level of basis sets than at the lower level. For all the molecular complexes, LPA overestimates the IE more than the values calculated from MPA and MESP at the different level of basis sets. This could be due to the large value of the electron transfer parameter, λ, calculated by LPA. In general, it is observed that the IE for most of the molecular complexes follows in the increasing order of, LPA > MPA > MESP. However, IE-QM values calculated at the same level of basis sets is lying in between MPA and MESP and in most of the cases, it is comparable to the MPA values. However, in few cases, the above order changes as LPA > MESP > MPA. For instance, the calculated IE at the 6-31G(d,p) basis set using MPA, LPA and MESP for BH3-NH3 complex, is -26.7, -35.0 and -26.0 kcal/mol, respectively. The IE-QM calculated at the same basis set is -22.93 kcal/mol.

In case of BH_3-CO, the IE calculated by the 3-21G and 3-21G(d,p) basis set using MPA is too less compared to IE-QM and the difference is almost 10kcal/mol. Adding more number of basis functions along with diffuse and polarization functions remarkably improves the IE value by more than 10 kcal/mol. An interesting feature of our results is that the discrepancies of results of the different basis sets become reasonably narrow as one goes from 3-21G to 6-31++G(2d,2p). To investigate the role of polarization and diffuse functions on the IE values, we consider 6-31G, 6-31G(d,p), 6-31++G(d,p) and 6-31+G(2d,2p) basis sets using MPA, LPA and MESP methods for the BH_3-NH_3 complex. The calculated IE values are listed here according to the above basis set order: -23.0, -26.7, -16.0, -15.5 kcal/mol by MPA; -33.7, -35.0, -16.2, -19.4 kcal/mol by LPA; -29.0, -26.0, -12.2, -11.8 kcal/mol by MESP; -24.7, -22.9, -21.0, -20.0 kcal/mol by IE-QM. The comparison between the values calculated by the 6-31G and 6-31G(d,p) basis set using MPA and LPA shows that the IE values increase by ~3kcal/mol while MESP values show a decrease of ~3kcal/mol. On the other hand, the addition of diffuse and polarization functions, i.e., use of (6-31++G(d,p) and 6-31++G(2d,2p)) basis reduces the IE values considerably and this trend is observed for all the three population schemes. This is also in accordance with the IE-QM. The above arguments also suit well for the other three complexes.

Considering the case of BF_3-CO complex, the IE is ~2-4 kcal/mol, which is considerably less than other complexes (Figure 4.2). For weak interaction cases, in general, the use of an adequate basis set and the level of theory is the most important consideration in obtaining accurate IE values, and the basis sets usually required are much larger than those used for the strong interaction cases. The typical basis set often includes diffuse s, p, and d orbital functions in order to describe accurately the induced polarization of electrons in such weak interactions. Analysis of the results for BF_3-CO complex, obtained by different basis sets, reveals that the effect of basis set is less and the predicted values are within the error limit of ~1kcal/mol. The IE values calculated by MPA using 3-21G, 6-31G, 6-31G(d,p), 6-31++G(d,p) and 6-31++G(2d,2p) basis sets, are -2.38, -2.78, -1.42, -2.77, and -1.84 kcal/mol, respectively. It is also interesting to note that the IE values obtained by different basis sets, are comparatively less dependent on the types of electrons population scheme (See Figure 4.2). Although LPA predicts high IE, the values are completely in agreement with the other scheme, MPA and MESP at the higher basis sets of calculations. It is gratifying to note that the present method could describe the weak interaction cases satisfactorily even at the HF level itself and the method is considerably less dependent of basis sets and population methods. The earlier works based on the present methodology have also shown to be successful for the case of weak interactions, for instance, interaction of small guest molecular interactions with the zeolite non-frame work cations and weak to strong hydrogen bonding cases. The results are in remarkably agreement with the experimental and other theoretical results within the error limit of ~1-2kcal/mol.[29]

The basic working equations are derived from the second order perturbative methods and they involve the descriptors of the isolated reactants. Hence, these models are more applicable to the weakly interacting complexes. In the case of weakly interacting molecules, the influence of one reactant molecule on another molecule will be comparatively less, and hence the present method of the calculation of IE is expected to describe the weak intermolecular interaction process more accurately than the stronger cases. It also justifies the use of local reactivity descriptors, which are essentially useful for the description of molecular interactions taking place at relatively long distances, or at the transition states. For the strong interaction cases, the influence of one molecule on the other system can be high, and in addition, other higher order perturbation terms can become more important.

4.3.2 Effect of Electron Correlation

In this Section, we will now study effect of correlation using MP2 method and different exchange-correlation DFT functionals, namely, Slater-VWN, PBE-LYP, Becke-LYP, B3-LYP and BHH-LYP. Further, the effect of different population schemes, MPA, LPA and MESP has also been studied at various theoretical levels and the split-valence basis set, 6-31G(d,p) is employed in this present study. It is known that the order of electron correlation exhibited by the five DFT functionals follow as, BHH-LYP > B3-LYP > Becke-LYP > PBE-LYP > Slater-VWN. The effect of correlation obtained by MP2 methodology is known to be better than B3-LYP and BHH-LYP. In most cases, it is observed that the HF method predicts more accurate results than the DFT Slater-VWN functional. The chemical potential and hardness values are presented in Table 4.4 and the local softness values are tabulated in Table 4.5. On comparing the values of chemical potential, the values obtained by MP2 and other DFT functionals are greater than that of HF method. Comparing the hardness values, one observes that MP2 predicts the hardness values higher than that of HF method and the HF values of hardness are greater than the values obtained from the DFT functionals. When one goes from Slater-VWN to BHH-LYP, the local softness values of the reactive atom B in BH_3, BF_3 and the nitrogen atom in NH_3

cases decrease by small amounts. The values obtained by HF method are greater than MP2 and other DFT functionals. In case of carbon atom in CO, the MP2 values are slightly higher than that of HF. In most of the cases, MESP values are substantially more than that of MPA and LPA values.

The calculated IE values for the BH_3 and BF_3 complexes with NH_3 and CO are presented in Figure 4.3 and 4.4, respectively. The λ values that are tabulated in Table 4.6 are used to calculate the IE of all the systems. On analyzing the Figures 4.3 and 4.4, it indicates that there is a remarkable agreement between the values calculated by IE-QM and by our methodology using different DFT functionals. The changes in the IE values with respect to the different functionals are rather stable and discrepancies are less than the effect exhibited by different basis sets. The IE values for BH_3-NH_3 complex calculated by the present methodology is -26.7 and -31.5 kcal/mol using HF and MP2 methods respectively and the experimental IE value is -31.1kcal/mol. The DFT functionals predict the IE values using MPA as -30.2, -30.9, -29.6, -30.5, -31.5 kcal/mol calculated through Slater-VWN, Becke-LYP, BHH-LYP, B3-LYP, PBE-LYP, respectively. However, the IE calculated by LPA always overestimates in comparison with MPA and MESP values. It also indicates that the correlated level calculations are more reliable than the HF results for strong interaction cases like BH_3-NH_3, BF_3-NH_3 and BH_3-CO. Although the HF level calculation captures a large portion of the bonding energy 26.7, -23.4, -16.3 kcal/mol for BH_3-NH_3, BF_3-NH_3 and BH_3-CO, respectively, the electron correlation correction improves the calculated bonding energy into -30.5, -25.0, -17.1 kcal/mol by B3LYP DFT functional. In case of BH_3-NH_3, BF_3-NH_3 and BH_3-CO complexes, the interactions are soft-soft kinds of interactions for which the standard *ab initio* calculations have also shown that the electron correlation corrections are essential in order to predict the correct interaction pattern. From the Figures 4.3 and 4.4, it is imperative to note that the IE-QM calculated by Slater-VWN functional produces largely overestimated IE which are eventually corrected by other better DFT functionals. The inclusion of the HF exchange term (BHH-LYP and MP2) reduces the IE values dramatically, providing results in better agreement with the available theoretical data. The most noticeable change is produced for the case of weak interaction (BF_3-CO system).

It has been noted earlier that the reactivity order for BH_3 and BF_3 predicted by MPA, LPA and MESP is $BH_3 > BF_3$. This order is in agreement with the expected trend. Let us now compare the IE for the complexes, BH_3-NH_3 and BF_3-NH_3. MPA and MESP produce the correct IE order compared to the other theoretical results, at all the correlated level calculations except that MPA deviates at the MP2 level. In case of LPA, the predicted IEs are almost similar for both the molecular complexes. However, at the HF level, most of the basis sets predicted that the IE for BF_3-NH_3 is greater than that of BH_3-NH_3. In case of NH_3 and CO, the correct qualitative reactivity order is given only by MESP method. MPA and LPA gave the correct reactivity order at the higher-level basis sets. Now if we compare the IEs of NH_3 and CO complexes with BH_3 and BF_3, it can be seen that the strength of BH_3-NH_3 and BF_3-NH_3 complexes is more than the BF_3-NH_3 and BF_3-CO complexes. This trend does not change with the use of different basis sets, population scheme and with the different DFT functionals.

For the BF_3-CO complex, the agreement between the IE-QM and values obtained by the present methodology is remarkably better than the other stronger interaction cases (see Figure 4.4). It is also worth noting that IEs do not drastically change with the inclusion of electron correlation except in the case of Slater-VWN functional, which is generally known to overestimate the IE for most of the complexes. This observation is also completely in agreement with our earlier claim, made in the section 4.3.1, that the present methodology can give better reliable description for the weak interaction cases than the stronger cases. Finally, we would like to also point out that the problem of defining the factor λ is still an important issue. Although, the present definition of λ works well in most cases, it may not work where the charge transfer is negligible or zero.

4.4 Conclusions

A systematic description of the basis set effects, different population methods and the effect of electron correlation on the calculation of IE of the complexes using global and local reactivity descriptors has been reported. The effect of electron correlation on the calculation of IE is observed to be more systematic and important than the effect of basis set. The discrepancy between the IE-QM and the IE calculated by the present methodology is found to be more in case of the strong interactions than the weak interaction cases. Despite the arbitrariness involved in all electron partitioning schemes and the inclusion of the ad-hoc definition of the parameter λ in the present methodology, the IE calculated by this method, is, in general, found to be reliable and in agreement with the experimental and other theoretical results. In general, among the different population schemes studied in this present chapter, we observe that LPA overestimates the IE. Based on our present and earlier observations, we have argued that the present method can describe the weak interaction cases better than the stronger one. These conclusions are very important in justifying the applicability and reliability of the present method in predicting the intermolecular interaction energies using the global and local reactivity descriptors. Further work should focus on the general classification of the types of interactions that is involved in a large number of complexes based on the mean values of these descriptors.

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Table 4.1: The value of global reactivity descriptors, chemical potential and hardness values of all the monomers calculated at the HF level. (values in atomic units)

Basis Set		BH_3		BF_3	
		μ	η	μ	η
3-21G	**1**	-0.207	0.262	-0.199	0.364
3-21G(d,p)	**2**	-0.204	0.262	-0.199	0.364
6-31G	**3**	-0.201	0.263	-0.222	0.354
6-31G(d,p)	**4**	-0.198	0.264	-0.187	0.377
6-31++G (d,p)	**5**	-0.216	0.246	-0.260	0.311
6-31++G (2d,2p)	**6**	-0.216	0.246	-0.259	0.310
DZV(dp)	**7**	-0.210	0.252	-0.211	0.359

Basis Set		NH_3		CO	
		μ	η	μ	η
3-21G	**1**	-0.025	0.290	-0.177	0.318
3-21G(d,p)	**2**	-0.026	0.296	-0.177	0.318
6-31G	**3**	-0.048	0.270	-0.190	0.306
6-31G(d,p)	**4**	-0.063	0.280	-0.174	0.315
6-31++G (d,p)	**5**	-0.150	0.193	-0.204	0.289
6-31++G (2d,2p)	**6**	-0.152	0.195	-0.204	0.287
DZV(dp)	**7**	-0.063	0.280	-0.186	0.305

Table 4.2: The calculated local softness values s(r) using different population schemes at the HF level. The number in the basis set column refers to the corresponding basis set given in the Table 4.1. The bolded atoms are the reactive atoms. (values in atomic units)

Basis Set	Local softness s(r)					
	BH3			**B**F3		
	MPA	LPA	MESP	MPA	LPA	MESP
1	1.234	1.523	2.668	0.944	0.920	1.615
2	1.274	1.544	2.638	0.944	0.920	1.615
3	1.024	1.427	2.464	0.923	0.908	1.477
4	1.024	1.452	2.442	0.957	0.853	1.452
5	1.656	1.800	4.628	2.664	1.481	2.602
6	1.616	1.799	4.619	2.788	1.487	2.621
7	1.644	1.755	3.456	1.236	1.069	2.896

Basis Set	Local softness s(r)					
	NH3			**C**O		
	MPA	LPA	MESP	MPA	LPA	MESP
1	0.744	1.058	2.054	1.117	1.112	1.571
2	0.736	1.071	1.869	1.117	1.112	1.571
3	0.997	1.290	2.453	1.129	1.084	1.584
4	0.943	1.250	1.946	1.147	1.116	1.585
5	1.652	1.973	2.949	1.089	1.027	1.723
6	1.693	1.883	2.745	0.871	1.099	1.745
7	1.003	1.293	2.003	1.160	1.139	1.139

Table 4.3: The value of the parameter λ calculated using electron population methods and at the different basis sets for the BH_3NH_3, BH_3CO and BF_3NH_3, BF_3CO complexes. The number in the basis set column refers to the corresponding basis set given in the Table 4.1. (values in atomic units)

Basis Set	Value of the parameter λ					
	BH_3-NH_3			BH_3-CO		
	MPA	LPA	MESP	MPA	LPA	MESP
1	0.257	0.445	0.395	0.047	0.415	0.441
2	0.253	0.438	0.381	0.033	0.414	0.433
3	0.200	0.409	0.365	0.145	0.381	0.422
4	0.263	0.469	0.377	0.222	0.423	0.385
5	0.290	0.328	0.357	0.191	0.292	0.383
6	0.283	0.399	0.350	0.213	0.307	0.366
7	0.355	0.415	0.404	0.293	0.330	0.409

Basis Set	Value of the parameter λ					
	BF_3-NH_3			BF_3-CO		
	MPA	LPA	MESP	MPA	LPA	MESP
1	0.204	0.439	0.320	0.029	0.114	0.121
2	0.209	0.436	0.308	0.029	0.114	0.121
3	0.217	0.467	0.321	0.320	0.071	0.100
4	0.228	0.470	0.301	0.018	0.044	0.069
5	0.201	0.495	0.281	0.029	0.059	0.064
6	0.310	0.591	0.278	0.013	0.056	0.059
7	0.379	0.459	0.302	0.023	0.071	0.065

Table 4.4: The value of global reactivity descriptors, chemical potential and hardness values of all the monomers calculated by different DFT functionals and MP2 method at the 6-31G(d,p) basis set. (values in atomic units)

Theoretical Method **(TM)**		BH_3		BF_3	
		μ	η	μ	η
HF	**1**	-0.198	0.264	-0.187	0.377
MP2	**2**	-0.216	0.267	-0.216	0.290
SVWN	**3**	-0.220	0.251	-0.171	0.355
BLYP	**4**	-0.212	0.257	-0.160	0.350
BHHLYP	**5**	-0.220	0.265	-0.211	0.371
B3LYP	**6**	-0.218	0.260	-0.194	0.348
PBELYP	**7**	-0.212	0.257	-0.160	0.349

Theoretical Method **(TM)**		NH_3		CO	
		μ	η	μ	η
HF	**1**	-0.063	0.280	-0.174	0.315
MP2	**2**	-0.095	0.291	-0.182	0.317
SVWN	**3**	-0.118	0.284	-0.200	0.314
BLYP	**4**	-0.112	0.282	-0.193	0.313
BHHLYP	**5**	-0.100	0.286	-0.201	0.319
B3LYP	**6**	-0.109	0.284	-0.199	0.316
PBELYP	**7**	-0.112	0.283	-0.191	0.314

Table 4.5: The calculated local softness values s(r) using different DFT functionals and MP2 method for BH_3, BF_3 and NH_3, CO molecules. **TM** refers the Theoretical Methods. The number in the theoretical method column refers to the corresponding theoretical methods given in the Table 4.4. The bolded atoms are the reactive atoms. (values in atomic units)

TM	Local softness s(r)					
	BH3			**B**F3		
	MPA	LPA	MESP	MPA	LPA	MESP
1	1.023	1.452	2.442	0.957	0.853	1.452
2	0.927	1.401	2.370	0.610	0.630	1.122
3	1.289	1.492	2.433	1.594	1.021	1.564
4	0.949	1.458	2.382	1.577	1.015	1.513
5	0.987	1.434	2.397	0.933	0.838	1.407
6	0.969	1.451	2.388	0.965	0.870	1.437
7	0.945	0.945	3.747	1.574	1.015	1.515

TM	Local softness s(r)					
	NH3			**CO**		
	MPA	LPA	MESP	MPA	LPA	MESP
1	0.943	1.250	1.947	1.147	1.116	1.585
2	0.822	1.172	1.780	0.900	1.282	1.717
3	0.858	1.193	1.769	1.147	1.087	1.458
4	0.830	1.180	1.721	1.129	1.078	1.441
5	0.885	1.205	1.835	1.123	1.084	1.507
6	0.856	1.192	1.775	1.128	1.081	1.473
7	0.819	1.174	1.701	1.128	1.075	1.434

Table 4.6: The value of the parameter λ calculated by the different DFT functionals and MP2 method using different electron population methods for the BH_3NH_3, BH_3CO and BF_3NH_3, BF_3CO complexes. **TM** refers the Theoretical Methods. The number in the basis set column refers to the corresponding DFT functionals given in the Table 4.4. (values in atomic units)

TM	Value of the parameter λ					
	BH_3-NH_3			BH_3-CO		
	MPA	LPA	MESP	MPA	LPA	MESP
1	0.263	0.469	0.377	0.222	0.423	0.386
2	0.307	0.500	0.405	0.264	0.420	0.385
3	0.367	0.054	0.444	0.240	0.341	0.331
4	0.318	0.492	0.423	0.218	0.351	0.323
5	0.304	0.495	0.406	0.235	0.402	0.369
6	0.315	0.496	0.417	0.227	0.374	0.345
7	0.324	0.496	0.427	0.230	0.352	0.324

TM	Value of the parameter λ					
	BF_3-NH_3			BF_3-CO		
	MPA	LPA	MESP	MPA	LPA	MESP
1	0.228	0.470	0.334	0.018	0.044	0.080
2	0.264	0.481	0.301	0.033	0.066	0.070
3	0.318	0.500	0.351	0.137	0.300	0.258
4	0.265	0.440	0.339	0.038	0.062	0.079
5	0.265	0.480	0.325	0.035	0.070	0.083
6	0.268	0.462	0.333	0.037	0.066	0.081
7	0.275	0.446	0.343	0.048	0.076	0.088

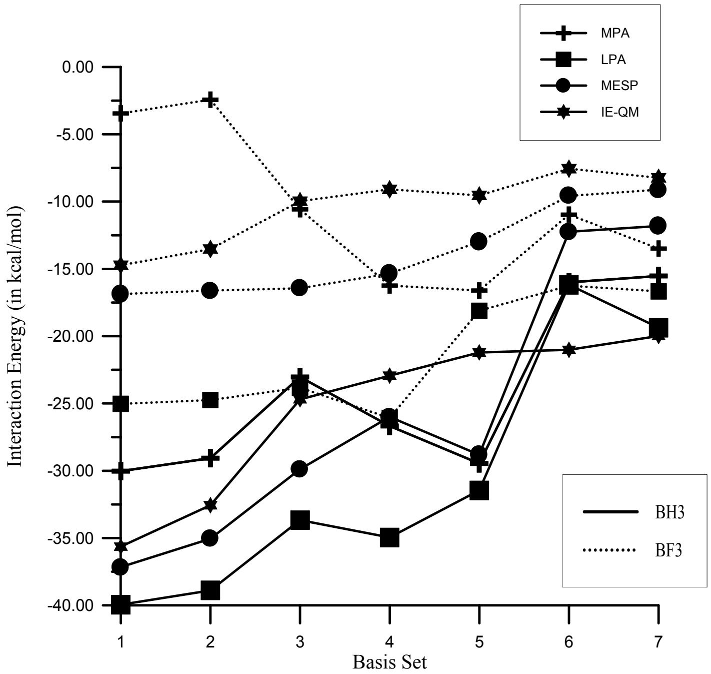

Figure 4.1 The interaction energy calculated by MPA, LPA and MESP using different basis sets at HF level for the BH_3-NH_3 and BH_3-CO complexes. The numbers in X-axis refer to the corresponding basis set given in the Table 4.1

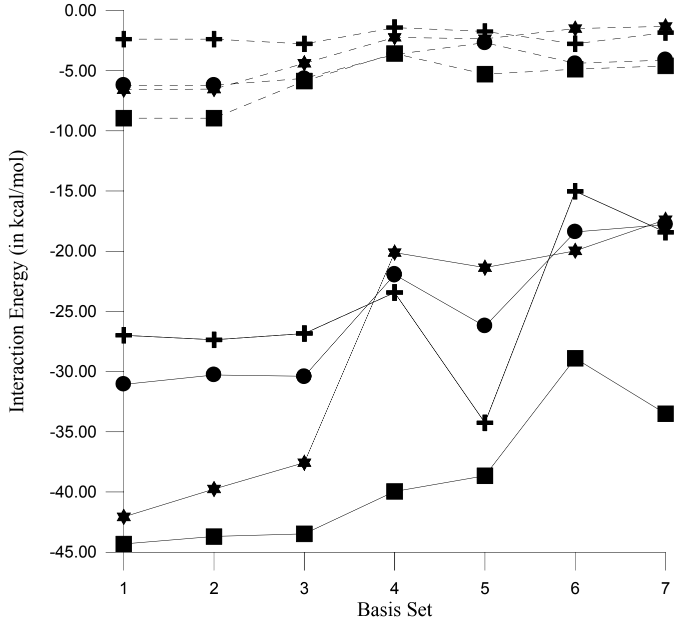

Figure 4.2 The interaction energy calculated by MPA, LPA and MESP using different basis sets at HF level for the BF_3-NH_3 and BF_3-CO complexes. The numbers in X-axis refer to the corresponding basis set given in the Table 4.1

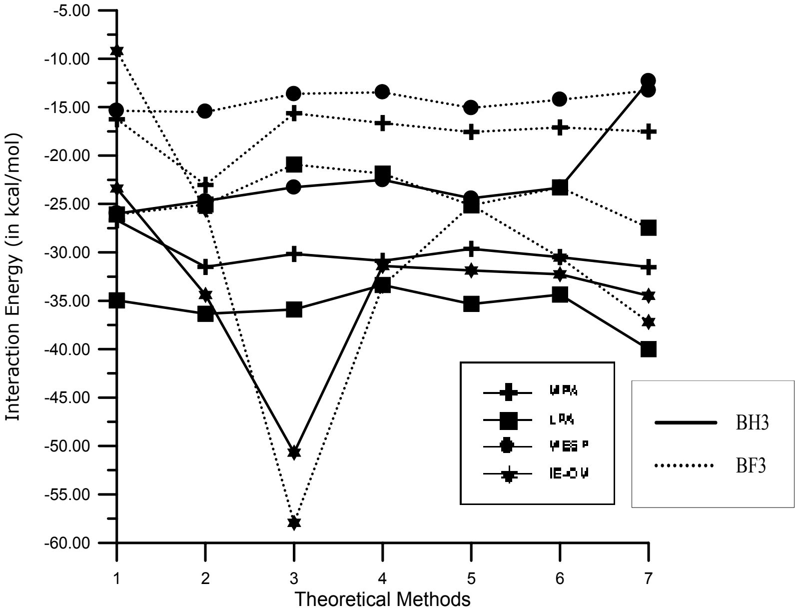

Figure 4.3 The interaction energy calculated by different DFT functionals and MP2 method using MPA, LPA and MESP population schemes at 6-31G (d,p) basis set for the BH_3-NH_3 and BH_3-CO complexes. The numbers in X-axis refer to the corresponding theoretical methods given in the Table 4.4

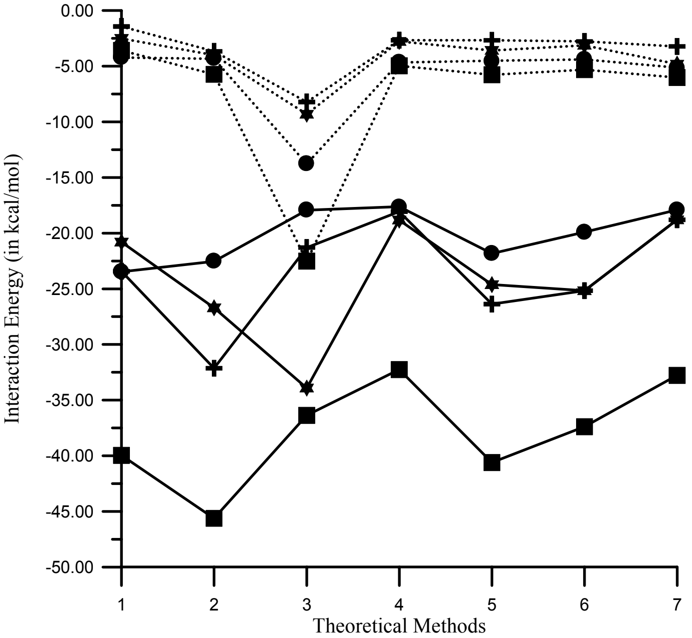

Figure 4.4 The interaction energy calculated by different DFT functionals and MP2 method using MPA, LPA and MESP population schemes at 6-31G (d,p) basis set for the BF_3-NH_3 and BF_3-CO complexes. The numbers in X-axis refer to the corresponding theoretical methods given in the Table 4.4

Chapter 5

Study of Local Hard-Soft Acid-Base Principle to Multiple-Site Interactions

Abstract

In this chapter, we have presented a detailed study of local hard-soft acid-base (HSAB) principle for describing multiple-site interactions between the molecular systems. The local HSAB principle, which has been proposed in the previous chapters to study single-site based interactions, can be generalized for the description of more general interaction types, which take place through either multiple sites or a group of atoms around one or many sites cooperating in the interaction processes. We show that local HSAB principle and consequently, our model can be generalized to handle all such interactions. Thus, we will establish the model completely local to semi-local, semi-global to fully global types of interactions. We show the local and global HSAB principle arising out of the two limits of the general expressions presented in this chapter. A detailed numerical study on model prototype interactions that are relevant to biological molecular interaction processes has been undertaken. Some of the specific molecular interactions, such as the molecular associations with and without the cooperative effects are described in detail through the models proposed in this chapter.

5.1. Introduction

In the previous chapters 2 and 3, the local HSAB principle[1-3] of Gazquez and Mendez has formed the basis of the model that we have proposed to describe the molecular interactions.[4,5] The equations of local HSAB principle, based on energy perturbation method within the framework of DFT involve an ad-hoc parameter λ, which can not be computed rigorously. By assigning this parameter to theoretical charge transfer, we have proposed a model that has been demonstrated to yield reliable interaction energies ranging from weak to moderate types of molecular complexes.[4,5] However, so far application of the local HSAB principle has been restricted to molecular interactions where the interaction proceeds through one pair of sites. Local HSAB principle has not been applied to more complicated interactions involving multiple interaction sites of the two systems. In most of the covalent bonded complexes, the interactions proceed via multiple sites, e.g., the weak intra and inter molecular Hydrogen bonding (H-bond) interaction in nucleic acids (DNA and RNA), the peptide linkages in proteins and in most of the supra-molecular complexes.[6-8] In the present chapter, we make an important generalization of the local HSAB principle to be applicable to more general class of interactions taking place through a group of cooperative atoms or individual reactive atoms based on multiple sites. Specifically, we derive the expressions for such general interactions, which can now range from strictly local to semi-global to fully global types and show how the ad-hoc parameter λ can be defined for this general model. The general model will be applied to important multiple-site interaction cases by selecting several inter-molecular H-bonded systems. The complexes studied in this present paper are of biological relevance and several groups have approached the study of molecular interactions through the available theoretical methods.[6-8] The acid amide-model nucleic acid interactions (formamidine) and other H-bonded complexes are also studied. Some other interesting interaction of Π-electron cloud with hydrogen and lithium cations is also studied.

The chapter is organized as follows: In section 5.2, we give a brief theoretical background of the global and local reactivity descriptors. In section 5.3, we will describe the local HSAB principle for the single-site interactions and then explain how to adopt this to study the interaction through multiple interaction sites. In section 5.4, the methodology and computational details are presented. In section 5.5, we will present our results for the multiple-site interaction cases and discuss the validity of the proposed models based on the numerical results.

5.2. Local HSAB Principle

5.2.1 Local HSAB Principle for the Single Interacting Site

Using energy as a functional of number of electrons (N) and the external potential (v), the interaction energy is defined as the difference between the two interacting model systems A and B and it is given as,[1,4]

$$\Delta E_{\text{int}} = \frac{-1}{2}\left(\frac{(\mu_A - \mu_B)^2}{\eta_A + \eta_B}\right)_v - \frac{1}{2} N_{AB}^2 \left(\eta_{AB} - \eta_{AB}^*\right)_\mu \qquad \text{------- (5.1)}$$

where, η_{AB} and are η_{AB}^* the hardness of the complex at the equilibrium and at the isolated state respectively. For the details of the mathematical part of the derivation for the Eq. (5.1), one can refer to chapter 2. As explained earlier, the interaction between the system A and B is assumed to take place in two steps, ΔE_v and ΔE_μ. In the first step, the interaction takes place at constant external potential through the equalization of chemical potential which is referred as ΔE_v.[1] In the second step, A and B evolve toward the equilibrium state through changes in the electron density of the global system produced at constant chemical potential which is referred ΔE_μ. The second step is a manifestation of principle of maximum hardness.[2,9] One can relate the difference in the hardness terms present in the second term of the above Eq.(5.1) to the softness of system A and B with a proportionality constant (K). [10] Thus, we have shown that, introducing λ as the product of $2N^2_{AB}$ and the proportionality constant K, ΔE_μ can be rewritten in terms of the softness of the systems A and B as,

$$\Delta E_\mu = -\frac{1}{2} N_{AB}^2 K \left(\frac{1}{(S_A + S_B)}\right)_\mu = -\lambda\ [\, 1/4(\mathrm{S_A} + \mathrm{S_B})\,]_\mu \qquad \text{--------- (5.2)}$$

This parameter λ can not be computed rigorously only through the softness of the molecular complexes. On substituting the expression (5.2) in the Eq. (5.1), one can get the global model in terms of the softness parameter of the systems A and B.

$$\Delta E_{\text{int}} \approx \frac{-(\mu_A-\mu_B)^2}{2}\left(\frac{S_A S_B}{S_A+S_B}\right)_v - \frac{1}{4}\left(\frac{\lambda}{S_A+S_B}\right)_\mu \quad \text{------ (5.3)}$$

If the interaction between the systems occur through the atom x of A with the molecular system B, one can express the total interaction energy from the local point of view, as[1,4]

$$(\Delta E_{\text{int}})_{Ax} = \frac{-(\mu_A-\mu_B)^2}{2}\left(\frac{S_A f_{Ax} S_B}{S_A f_{Ax}+S_B}\right)_v - \frac{1}{4}\left(\frac{\lambda}{S_A f_{Ax}+S_B}\right)_\mu \quad \text{---- (5.4)}$$

where S_A and f_{Ax} are the global softness and condensed Fukui function of the atom x in a system A, respectively. We have used the local softness and Fukui functions of isolated systems and this approximation is justified for weak to moderately weak interactions. We have related the parameter λ as the change in the electron densities at the interacting site before and after the interaction process.[4] This change will give the effective number of valence electrons that have participated in the interaction process. Thus, an expression for the term λ can be written as the difference of electron densities of the system A before and after the interaction,

$$\lambda_A = \sum_{i=1}^{p} \rho_{Ai}^{eq} - \sum_{i=1}^{p} \rho_{Ai}^{0} \quad \text{------- (5.5)}$$

Alternately, the term λ can be defined as the difference of electron densities for the system B,

$$\lambda_B = \sum_{j=1}^{q} \rho_{Bj}^{eq} - \sum_{j=1}^{q} \rho_{Bj}^{0} \quad \text{------- (5.6)}$$

where the first terms of the right hand side of the Eqs.(5.5) and (5.6) refer to the sum of the electron densities of each atom in A and B in the molecule AB at equilibrium respectively and the second terms in Eqs.(5.5) and (5.6) refer to electron densities of each atom in the isolated systems A and B respectively. The indices p and q are the number of atoms of the systems A and B respectively.

The expression (5.4) of interaction energy is derived on the basis of the fact that only one specific atom in the molecule is interacting with the other molecule. In the next sub-section, we extend the local HSAB principle to describe simultaneous interaction of many sites of system A with different sites of B.

5.2.2. Local HSAB Principle for Multiple Interacting Sites

Let us consider the case of multiply-bonded systems A and B. The distinctive reactive sites of A and B are designated x, y, z, etc. and k, l, m, etc. respectively. We assume that the interaction is taking place simultaneously between different pairs of reactive sites of the two systems as x-k, y-l, z-m etc. These reactive sites can be located at any part of the systems A and B. To apply local HSAB principle for such cases, we extend the formula (5.4) and we will now explain the different approaches.

In the simplest version of the model, (Localized Reactive Model, hereafter referred to as LRM-I), we assume that the interaction between the different molecular systems is taking place through the individual reactive atom of the systems A and B. Each reactive atom can be located at the different part of the system and there is no co-operative between the reacting atoms. Thus, although the reaction proceeds simultaneously through many reaction centers, interaction energy may be calculated in a de-coupled manner. Hence, the total interaction energy for the complex AB may be represented as the sum of interactions arising from each part of the interacting atoms of A and B (x-k, y-l, z-m, etc.). Thus, the net interaction is obtained as a logical extension of single-site local HSAB principle to multiple sites by assuming that the interaction occurs in de-coupled manner and the additivity of energy. According to this model, the interaction energy expression is given as,

$$\Delta E_{\text{int}} \approx \frac{-(\mu_A - \mu_B)^2}{2}\left(\frac{S_A S_B f_{Ax} f_{Bk}}{S_A f_{Ax} + S_B f_{Bk}} + \frac{S_A S_B f_{Ay} f_{Bl}}{S_A f_{Ay} + S_B f_{Bl}} + \frac{S_A S_B f_{Az} f_{bm}}{S_A f_{Az} + S_B f_{bm}} + \ldots\right)_{\vartheta}$$
$$- \frac{\lambda}{4}\left(\frac{1}{S_A f_{Ax} + S_B f_{Bk}} + \frac{1}{S_A f_{Ay} + S_B f_{Bl}} + \frac{1}{S_A f_{Az} + S_B f_{bm}} + \ldots\right)_{\mu}$$

------ (5.7)

Collecting the expression for the interaction between Ax and Bk , Ay and Bl etc. from the first and the second terms of Eq. (5.7) , one can write,

$$\Delta E_{\text{int}} = \Delta E_{\text{Ax -Bk}} + \Delta E_{\text{Ay-Bl}} + \Delta E_{\text{Az-Bm}} + \ldots \qquad \text{------ (5.8)}$$

where $\Delta E_{\text{Ax-Bk}}$ defines the interaction energy derived from the site Ax and Bk. Considering the definition of the local softness, s(r)=f(r) S, a term of the Eq. (5.8) e.g. $\Delta E_{\text{Ax- Bk}}$ can be rewritten as,

$$\Delta E_{Ax-Bk} \approx \frac{-(\mu_A-\mu_B)^2}{2}\left(\frac{s_{Ax}s_{Bk}}{s_{Ax}+s_{Bk}}\right)_v - \frac{\lambda}{4}\left(\frac{1}{s_{Ax}+s_{Bk}}\right)_\mu \quad \text{-------} \ (5.9)$$

Similarly, other terms of Eq. (5.8) can be written in terms of local softness of the reacting sites of A and B.

One can generalize the formulae Eq. (5.7) or (5.9) in the cases the reacting sites consist of a group of atoms. This can arise due to the participation of neighboring atoms in the reaction site or the proximity of the two or more reacting sites, such that they may constitute one reacting site. In such cases, co-operative effects are strong. Let us now consider, the new reacting sites x, y, z , …etc of A which are located at different parts of the system, but each of which contains a group of co-operative atoms in the reaction. Let us denote the group of atoms of the reacting site x and y, as, x_1, x_2, x_3…etc. and y_1, y_2, y_3, …etc. respectively. Similarly, for the system B, one can denote the localized sets of the reacting atoms as k, l, m, …etc. Each of this site contains the connected set of atoms which can be called as co-operative. Thus, the site k contains cooperative atoms k_1, k_2, k_3 , … etc. and the site l contains a set of atoms l_1, l_2, l_3, …etc. For such a general case, one can still write the Eq. (5.7) in terms of the reacting sites, as before. The Eq. (5.8) formally holds. In this case, however, the softness of all the atoms can be added to define the total softness of the reacting site. This can be called as group softness[11] and using the group softness of the co-operating atoms in a site, each term ΔE_{Ax-Bk}, can generally be written as,

$$\Delta E_{Ax-Bk} \approx \frac{-(\mu_A-\mu_B)^2}{2}\left(\frac{(\sum_{i=1}^{n} s_{Ax_i})(\sum_{j=1}^{m} s_{Bk_j})}{(\sum_{i=1}^{n} s_{Ax_i})+(\sum_{j=1}^{m} s_{Bk_j})}\right)_v - \frac{\lambda}{4}\left(\frac{1}{(\sum_{i=1}^{n} s_{Ax_i})+(\sum_{j=1}^{m} s_{Bk_j})}\right)_\mu$$

----- (5.10)

Where, there are n participating atoms x_1, x_2, x_3, …x_n etc in the site Ax and similarly, there are m atoms, k_1, k_2, k_3, …k_m in the site Bk. One can say that the softness of these cooperative atoms is smeared in the site. ΔE_{int} is sum of all such site interactions ΔE_{Ax-Bk}, ΔE_{Ay-Bl}, ΔE_{Az-Bm}, etc. Depending on the number of sites and group of atoms in a site, one can define different interaction pattern between two systems A and B. We will refer this mode as LRM-II. In the limit, that each site contains only one atom this model reduces to the previous model LRM-I. On the other hand, the other limit is the global HSAB, where there is only one site in each system A and B and all atoms are co-operative. In such a limit, there is only one term in the Eq. (5.7) and this term now involves the group softness of all atoms, which is the global softness of the systems. LRM-II actually defines all other intermediate interactions between the limit of fully Local (LRM-I) and the global model.

5.3. Methodology and Computational Details

Ab initio Hartree – Fock (HF) quantum chemical calculations and density functional calculations were performed to examine the validity of the different approaches. The molecular geometries were completely optimized at the HF level using the split-valence basis set, 3-21G(d,p) and 6-31G(d,p), without any symmetry constraints. The restricted HF method has been used for the energy calculations of neutral and for the corresponding anionic and cationic systems, the restricted open shell HF method has been performed. The *ab initio* calculations were performed using the GAMESS[12] system of programs on an IRIX-6.2 silicon graphics work station. The DFT calculations were performed using the deMon program[13] and the energy of the systems was calculated using the 3-parameter hybrid functional of Becke[14] and the Lee, yang and Parr correlation potential[15] (B3LYP). The optimized geometry obtained from HF/6-31G(d,p) are used in the DFT energy calculations. The basis set used for C,N,O are (5,2;5,2) auxiliary and (6311/311/1) orbital basis sets (equivalent to DZV-P basis set). For H and Li, (5,1;5,1) and (5,2;5,2) auxiliary and (41/1) and (621/1*/1+) orbital basis sets were employed, respectively. Additional auxiliary basis sets are employed to describe the charge density and exchange-correlation potential. The use of the auxiliary basis set improves the numerical efficiency and the accuracy in the calculation of the total energies of the systems. During the iterative steps, the charge density is fitted analytically and the potential exchange-correlation is fitted numerically on FINE grid composed 32 radial shells. The parameter λ was calculated using Eqs. (5.5) or (5.6), through the Mulliken population scheme.[16] In conventional methods, the interaction energy will be evaluated from the difference between the energy of the complex AB and sum of the energy of the monomer A and B, $\Delta E = E_{AB} - (E_A + E_B)$.

5.4. Results and discussions

The interactions of amides and its derivatives with nucleic acid-bases are very essential for understanding most of the biological processes.[6-8] These interactions are largely determined by the multiple inter- and intra-molecular H-bonds. Hence, the knowledge of the specific multiple interactions are very essential. We have considered prototype molecular systems such as, the complexes of formamide, acetamide, acrylamide, formic acid and acetic acid with the formamidine molecule as a simple nucleic acid-base model. The amide-formamidine complexes have been studied in the past[17-19] and represent the important model complexes having many features similar to the actual nucleic acid base pairs. These complexes have essentially two types of H-bonding (Figure 5.1), namely, a) C=O group in amide and acid with formamidine H-N group, b) amide N-H, acid O-H with formamidine N-C. The multiple interactions between butyrolactam and succinimide[20] are also considered in this present study (Figure 5.2). In addition to these polar group H-bonding interactions, the multiply bonded Π-electron system with electrophilic species are also studied (Figure 5.3). These types of complexes include the complexes of acetylene and butylene with HCl and LiCl molecules.[21] Here the cations H and Li are allowed to interact with two carbon atoms of the alkyne system that are connected by the Π-electron cloud.

The global and local properties, chemical potential, hardness and condensed local softness for all systems, are tabulated in Table 5.1 and Table 5.2. In general, the chemical potential of amide and acid systems differs marginally, in the range of ± 0.002-0.018 in atomic units. The chemical potential values for the acetylene, butylene, HCl and LiCl differ considerably. However, it should be noted that the hardness values of all complexes are quite different from each other. The values of chemical potential calculated by HF method through 3-21G(d,p) and 6-31G(d,p) basis set do not vary much. When it is compared with the DFT values, HF values are lesser than the DFT values. In the case of the hardness values, HF values are considerably higher than the DFT values except for the case of LiCl. The effect of methylation at the amide NH_2 group on chemical potential, hardness and condensed local softness values of carbonyl oxygen and the hydrogen atoms is significant. It actually reduces the value of the GRD and LRD of the reactive oxygen and hydrogen atoms. Since the methyl group is an electron-donating group, the positive charge on the reactive amide hydrogen atom is reduced. Hence, the reactivity of methylated systems will be considerably reduced and the corresponding interaction energy values are expected to be less than those of un-substituted amide complexes.

We will now turn to the problem of obtaining the value of the parameter λ. In the previous chapters, we have calculated this parameter for the case of gaseous molecular interaction on zeolite surface by considering the two reacting atom charge density alone. There, the change in electron density was observed only at the interacting site and hence the approximation introduced in defining the parameter λ indeed gave a correct description of the molecular interaction. In this present study, however, the interactions occur through multiple sites and hence, total change in electron density at all interaction sites should be included. It is simpler to use the total electron transfer from A to B or vice-versa. It will be close to the sum of the change in number of electrons at all sites and it would include the effects of surrounding atoms. This fact will specifically make a difference in determining the parameter λ for the cases of rigid ionic and covalent complexes. It also emphasizes the importance of the dynamical movement of electrons in weakly held covalent bonded complexes, in determining the stability of the complexes. On examining the value of λ from the Table 5.3, it can be seen that the λ value is considerably decreased by methylating at the -NH_2 group, for the amide complexes. In case of LiCl interaction with acetylene and butylene complexes, the value of λ is almost five times greater than that of HCl complexes. This observation is consistent with our earlier discussion on the values GRD and LRD of amide and other complexes.

Let us now examine the interaction energy values obtained by models that are described in section 5.2.2. We will first consider the case of amide-fomamidine, acid-formamidine and butyrolactam-succinimide complexes. In amides, the reactive atoms are carbonyl oxygen and the -NH_2 hydrogen atom and these reactive atoms are not directly connected to each other. Similarly, the reactive atoms present in formamidine molecule are also not connected to each other (see Figure 5.1). Although there is a *non-bonded interaction (through inductive effect)* between the reactive atoms present in the systems, the reactivity of each atom will be locally dominant in nature. This suggests that the reactive atoms in the amide complexes can be considered as localized atoms and they can interact specifically with other molecule *where each type of interaction is not much influenced* by other reactive atoms. In such a case, the interaction energy can be considered as the sum of interactions arising from each pair of reactive atoms and thus LRM-I should give reasonable energy values for the amide-formamidine complexes. The same argument holds true for the interaction between butyrolactam-succinimide and acid-formamidine complexes. In Figure 5.4, the interaction energy calculated by LRM-I Eq. (5.7) is shown for all the complexes. This is compared with the interaction energy calculated by the conventional method through the difference between the complex and monomer energies from the DFT calculations as described in the section 5.3.

We will now consider the second set of complexes arising due to the interaction of acetylene and butylene with H^+ and Li^+ cations. The reactive atoms in the alkynes are *the two adjacent carbon atoms that are directly connected to each other by triple bond,* as shown in Figure 5.3. In such cases, the reactivity of the two carbon atoms will be mixed or smeared up and the individual effect of each reactive atom will be lost. Hence, the straightforward assignment of the reactivity of the atoms in the system is not possible. The reactivity of such complexes will predominantly arise from the group of the directly connected C atoms. Hence, the generalized model with the group softness (LRM-II, Eq. 5.10) should describe the interaction pattern for these types of complexes. Evidently, one can see from Figure 5.4 that the interaction energy obtained through LRM-II is very realistic and there is a good agreement between the values obtained by other theoretical results and by the present approach. This clearly indicates the relevant influence of the nearest reactive atoms on the interaction energy of the alkyne-HCl and LiCl complexes. It is gratifying to note that the interaction energy of LiCl with these triply bonded systems is significantly greater than that of HCl complexes. It is known that the lithium affinity towards the electron rich systems is greater than that of other cations and hence the interaction energy is expected to be greater than that of other cations. In general, one can see that although the GRD and LRD of methylated systems are significantly different from the un-methylated systems, the calculated interaction energy of these complexes from the present approach differs marginally in the range of 1-2 kcal/mol. It is also in agreement with other theoretical results.

As seen in Figure 5.4, the interaction energy of these complexes is less compared to the literature values in the order of a few kilo-calories. It could be due to the limited accuracy in the calculation of the parameter λ as well as the reactivity descriptors. The value obtained by HF/6-31G(d,p) basis set is less compared to that other values. Nevertheless, such variation in the estimated interaction energy values is very systematic and consistent with the available data. The accuracy of the calculation can be improved by choosing a much larger size basis set and including the correlation effects. On comparing the interaction energy calculated by HF and DFT at the 6-31G(d,p) basis set, it can be seen that HF theory tends to underestimate the interaction energy for the most of the complexes, and when the correlation is introduced, the values are improved considerably and close to the other available theoretical results. One can see a reliable agreement between the interaction energy obtained by LRM-I and the conventional method, for the formic and acetic acid-formamidine complexes. LRM-I gives the values as -9.82 and -8.89 kcal/mol and the actual values are -12.74 and -12.20 kcal/mol.[17-19] In case of the amide-formamidine complexes, HF/3-21G(d,p) and DFT values are comparable with the actual values and there is a difference between the values obtained by LRM-I and the actual values. For the Butyrolactum-Succinimide complex, LRM-I predicts the interaction energy values evaluated by LRM-I through HF/3-21G(d,p), HF/6-31G(d,p) and DFT, as -11.51, -8.19, -5.19 kcal/mol, respectively and these values are in comparable with the actual interaction energy, -8.58 kcal/mol. In case of the ACET-HCL, BUTY-HCL, ACET-LICL and BUTY-LICL interaction cases, the actual interaction energy values are -1.5, -1.77, -7.95 and -13.45 kcal/mol, respectively. The values obtained by LRM-II are very close to these values at all levels. For e.g. ACET-HCL complex, the LRM-II predicts the interaction values as -2.28, -2.87 and -1.20 kcal/mol evaluated at 3-21G(d,p), 6-31G(d,p) and DFT methods, respectively and for the case of ACET-LICL case, the values are -7.38, -10.33 and -6.56 kcal/mol. Similarly, one can also see the agreement for BUTY-HCL and BUTY-LICL cases.

A closer inspection on the contribution of the energy terms to the total interaction energy calculated by HF/3-21G(d,p) methods (Table 5.4) reveals that the most important component of the interaction energy arises from the ΔE_{μ} term. It also emphasizes that this term alone can explain the nature and stability of the complexes and it provides a driving force for the formation of the complexes. Hence, the charge redistribution process at constant chemical potential can be considered as a decisive modulating factor in determining the strength of the H-bonded and other types of complexes that have been considered in this present study. The effect of the strong directional character and relative arrangement of atoms in the actual interaction is introduced by the factor λ as defined in the Eqs.(5.5) or (5.6).

The definition of the parameter λ is ambiguous and several approximate definitions have been used in the literature.[3, 22, 23] Gazquez *et al* and Geerlings *et al* have used different values of λ (1.0, 0.5) depending on the systems studied in the literature.[3,22,23] As described earlier, we have defined the parameter λ as the number of electrons that have been transferred from one system to another system and it can be computed through the Eq. (5.5) or Eq. (5.6). An alternative way to compute this quantity is by using only the descriptors of individual systems A and B, i.e. $\Delta N = (\mu_A - \mu_B) / (\eta_A + \eta_B)$. We have also computed λ as ΔN in this work. To illustrate this, we have computed ΔN values for all the complexes in HF/3-21G(d,p) basis, which are presented in the Table 5.3. The interaction energy calculated using ΔN as well as λ, computed through Eq. (5.5) or (5.6) are presented in the Figure 5.5 and these are compared with the available theoretical values. One can see from the Figure 5.5 that the interaction energies calculated via the Eq.(5.5) or (5.6) are much more accurate than the one obtained using ΔN. This is possibly due to the fact that the parameter λ, being total charge transfer, includes the influence of molecular environment. If one computes the interaction energy through ΔN, this influence will be missed considerably. However, one can still get qualitatively correct trend of interaction energies using the expression of ΔN. The evaluation of parameter λ, being an electron transfer variable, involves the calculation of electronic population of the complex molecule. Although the calculation of the complex can not be eliminated in the local HSAB principle, the principle provides a different route to the calculation of interaction energy based on softnesses of the reacting systems A and B, compared to the traditional way of obtaining the ΔE_{int} as the difference of energies the complex and the reacting systems. The present approach allows one to study the change of interactions in terms of the hardness/softness parameters.

5.5. Conclusion

In this work, we have attempted to study the local HSAB principle to complex multiple-site based interactions and accordingly we have followed different approaches. Each of these approaches has its domain of applicability. To study the feasibility of these approaches, we have considered model prototype molecular interactions. We have explained the general interaction pattern that is observed in most of the molecular complexes. Because of the topological nature of the complexes, one can have a variety of complexes, which can be categorized broadly in certain distinguishable ways. In certain cases, the molecular systems may contain the interacting atoms that are directly connected to each other and the reactivity of these kinds of systems are solely determined by the set of such reactive atoms. Here, the molecular association is effectively taking place with the additive co-operative effects due to the other reactive atoms. It should be noted that the major dominating interacting forces in these complexes are due to the atoms that are directly involved in the interaction process. In such cases, as detailed in the earlier part of our discussion for the directly connected reactive atoms, a general model LRM-II taking into account cooperative or connected atoms in a site should predict the stability of the complexes correctly. In cases the reaction takes place through separated atoms, the net interaction will be the sum of such individual interactions that are present in the complex. LRM-I can be used to describe these types of interactions between the complexes. However, if the interaction occurs predominantly through one pair of sites, calculation of interaction energy though single site formula would suffice. In some cases, the molecular interactions can also occur with all atoms that are present in the molecular systems. In such a case, the general LRM-II reduces to the global HSAB model, which is the correct choice for such interactions. Thus, one can treat various types of specific multiple-site interactions within the framework of local HSAB principle. We note, while deriving the expressions for the general cases that the basic limitations of working within the second order perturbation method apply to these expressions also. Thus, the models can describe the general multiple-site weak interactions.

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Table 5.1: The Global properties of the systems, Chemical Potential and Hardness (values are given in atomic units)

System	Chemical Potential			Hardness		
	HF		DFT[a]	HF		DFT
	SV3	SV6		SV3	SV6	
Formamide (FOR)	-0.072	-0.063	-0.160	0.246	0.265	0.215
N-met formamide (NFOR)	-0.070	-0.078	-0.151	0.237	0.239	0.200
Acetamide (ACT)	-0.063	-0.056	-0.154	0.237	0.254	0.202
N-met acetamide (NACT)	-0.060	-0.047	-0.145	0.231	0.254	0.190
Acrylamide (AL)	-0.102	-0.107	-0.152	0.198	0.202	0.198
N-met acrylamide (NAL)	-0.098	0.104	-0.148	0.192	0.195	0.185
Formic Acid (FORMIC)	-0.113	-0.113	-0.174	0.258	0.261	0.240
Acetic Acid (ACETIC)	-0.099	-0.099	-0.168	0.247	0.151	0.219
Formamidine (F1)	-0.055	-0.049	-0.140	0.247	0.259	0.196
Butyrolactam (LACT)	-0.063	-0.067	-0.146	0.231	0.234	0.191
Succnimide (SUC)	-0.106	-0.107	-0.140	0.226	0.232	0.203
Acetylene (ACET)	-0.087	-0.082	-0.176	0.288	0.279	0.236
Butylene (BUTY)	-0.056	-0.057	-0.10 2	0.266	0.258	0.239
HCl (HCL)	-0.133	-0.138	-0.178	0.300	0.293	0.288
LiCl (LICL)	-0.170	-0.168	-0.186	0.155	0.158	0.176

[a]RHF/6-31G(d,p)//B3LYP/DZVP; SV3 and SV6 corresponds to the basis set, 3-21G(d,p) and 6-31G(d,p), respectively.

Table 5.2: The condensed local softness of the reactive atoms (values are given in atomic units) S_x^+ and S_x^- are calculated for H, Li and for O, N, C for the different systems, respectively.

System	Reactive atoms		Local Softness					
			HF/3-21G(d,p)		HF/6-31G(d,p)		DFT	
	A	B	A	B	A	B	A	B
FOR	H	O	0.229	0.844	0.490	0.958	0.126	1.112
NFOR	H	O	0.199	0.850	0.186	1.035	0.106	0.829
ACT	H	O	0.211	0.849	0.389	0.977	0.338	1.131
NACT	H	O	0.181	0.842	0.246	0.949	0.351	0.892
AL	H	O	0.305	0.965	0.299	1.177	0.127	0.772
NAL	H	O	0.164	0.977	0.156	1.204	0.098	0.696
FORMIC	H	O	0.195	0.844	0.173	0.994	0.447	1.013
ACETIC	H	O	0.180	0.844	0.159	1.001	0.493	1.022
F1	H	N	0.199	0.508	0.448	0.606	0.485	0.825
LACT	H	O	0.192	0.831	0.133	1.005	0.692	0.652
SUC	C	O	0.159	0.244	0.139	0.221	0.165	0.663
ACET	C	C	0.577	0.577	0.615	0.615	0.773	0.833
BUTY	C	C	0.498	0.498	0.532	0.531	0.446	0.443
HCL	H	---	0.104	-----	1.190	-----	1.490	-----
LICL	Li	---	2.911	------	2.809	-----	2.503	-----

Table 5.3: The value of parameter λ for the multiply bonded complexes (values are in atomic unit, the abbreviations are given in Table 5.1)

System	Value of the parameter λ			ΔN_{CT}[a]
	HF		DFT	HF/ 3-21G(d,p)
	3-21G(d,p)	6-31G(d,p)		
FOR-F1 **1**	0.013	0.007	0.005	0.036
NFOR-F1 **2**	0.012	0.006	0.018	0.033
ACT-F1 **3**	0.009	0.005	0.012	0.017
NACT-F1 **4**	0.008	0.002	0.023	0.012
AL-F1 **5**	0.011	0.007	0.024	0.106
NAL-F1 **6**	0.009	0.003	0.022	0.099
FORMIC-F1 **7**	0.043	0.029	0.041	0.115
ACETIC-F1 **8**	0.038	0.025	0.038	0.090
LACT-SUC **9**	0.222	0.013	0.017	0.099
ACET-HCL **10**	0.022	0.026	0.237	0.079
BUTY-HCL **11**	0.025	0.025	0.037	0.137
ACET-LICL **12**	0.098	0.164	0.170	0.188
BUTY-LICL **13**	0.089	0.180	0.231	0.274

[a] ΔN_{CT} is computed through the expression, $(\mu_A-\mu_B) / (\eta_A+\eta_B)$

Table 5.4: ΔE_v, ΔE_μ and total interaction energies of all complexes as described in the text, calculated by the parameters λ and ΔN using HF/3-21G(d,p) method. (Energy values are in kcal/mol). The corresponding values of λ and ΔN are given in the Table 5.3. LRM-I and LRM-II have been used to calculate the interaction energy for the complexes, FOR-F1 to LACT-SUC and ACET-HCL to BUTY-LICL, respectively.

System	ΔE_v		ΔE_μ		ΔE_{tot}	
	λ	ΔN	λ	ΔN	λ	ΔN
FOR-F1	-0.06	-0.06	-4.55	-12.96	-4.61	-13.02
NFOR-F1	-0.05	-0.06	-4.37	-12.10	-4.43	-12.16
ACT-F1	-0.01	-0.01	-3.12	-6.30	-3.13	-6.31
NACT-F1	-0.01	-0.01	-2.84	-4.45	-2.85	-4.46
AL-F1	-0.49	-0.49	-3.71	-34.60	-4.20	-35.09
NAL-F1	-0.34	-0.34	-3.24	-36.22	-3.58	-36.56
FORMIC-F1	-0.63	-0.63	-16.11	-42.85	-16.74	-43.49
ACETIC-F1	-0.36	-0.36	14.45	-34.00	-14.81	-34.36
LACT-SUC	-0.41	-0.41	-11.09	-49.30	-11.50	-49.71
ACET-HCL	-0.74	-0.74	-1.55	-5.64	-2.29	-6.37
BUTY-HCL	-1.92	-1.91	-1.94	-10.52	-3.86	-12.43
ACET-LICL	-3.60	-3.60	-3.78	-7.26	-7.38	-10.86
BUTY-LICL	-6.09	-6.09	-3.60	-10.89	-9.69	-16.99

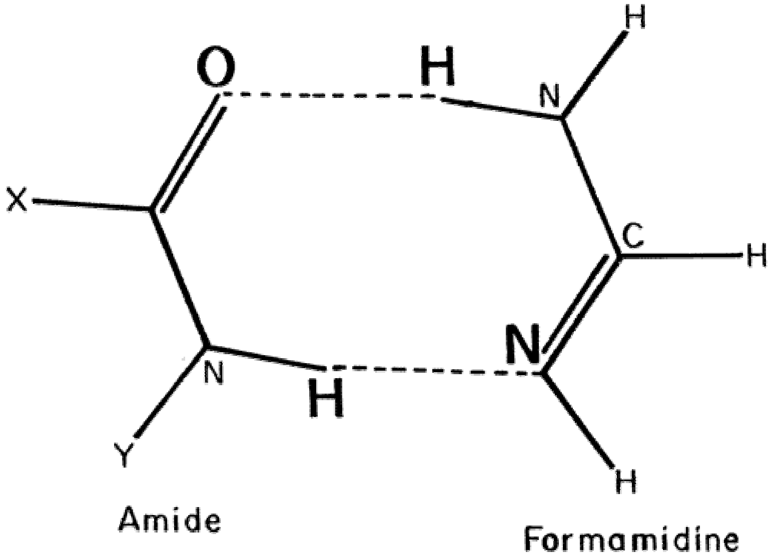

Figure 5.1 The multiple interactions between acid amide and formamidine. The bold and big letters are the reactive atoms, where, X = -H, -CH_3 and -CH_2=CH, refer to formamide, acetamide and acrylamide, respectively and in all cases Y is H. In case of N-methyl derivatives, Y is CH_3.

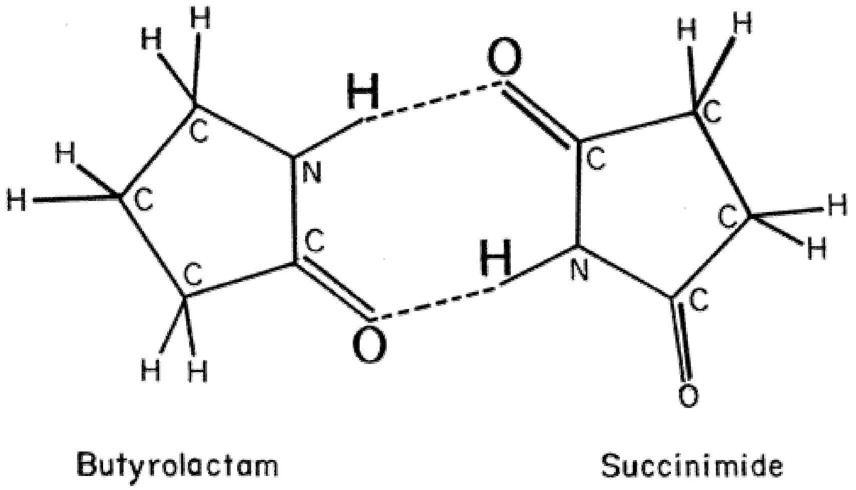

Figure 5.2 The multiple interactions between butyrolactam and succinimide

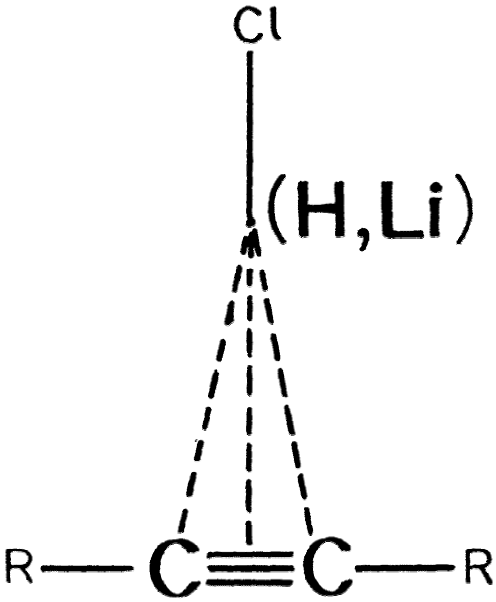

Figure 5.3 The multiple interactions between acetylene, butylene and H^+ and Li^+ cations, where, R = H and CH_3 refer to acetylene and butylene, respectively.

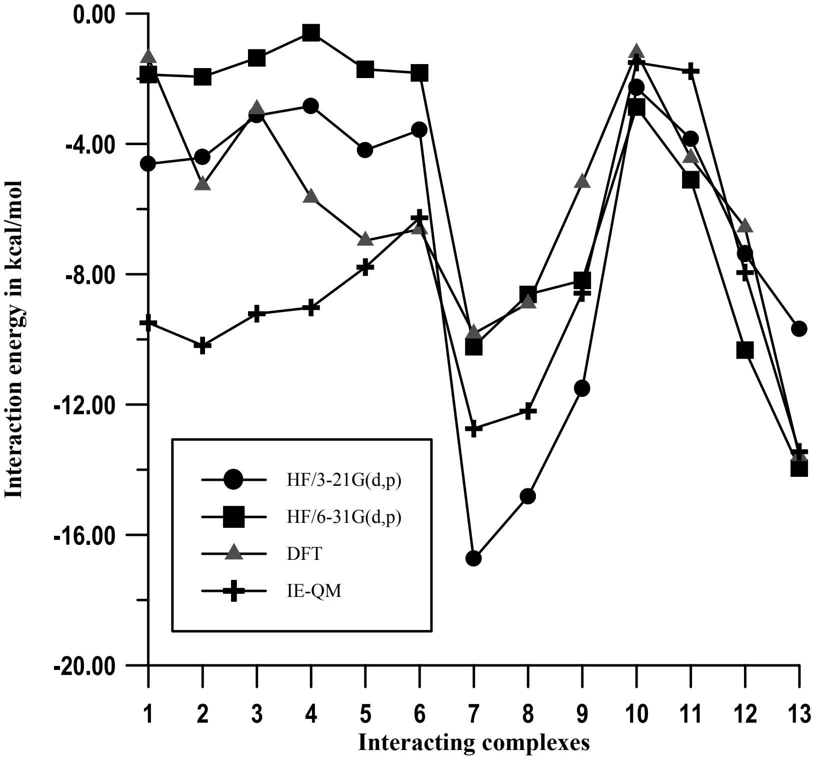

Figure 5.4 The total interaction energy of the hydrogen bonded complexes, calculated through LRM-I and LRM-II. IE-QM is the interaction energy calculated by other theoretical methods; the BSSE uncorrected ΔE, the difference between the complex and monomer energies, ($\Delta E = E_{AB} - (E_A - E_B)$), calculated through DFT method, as described in the text. The number in X-axis refers to the corresponding interacting complex given in Table 5.3.

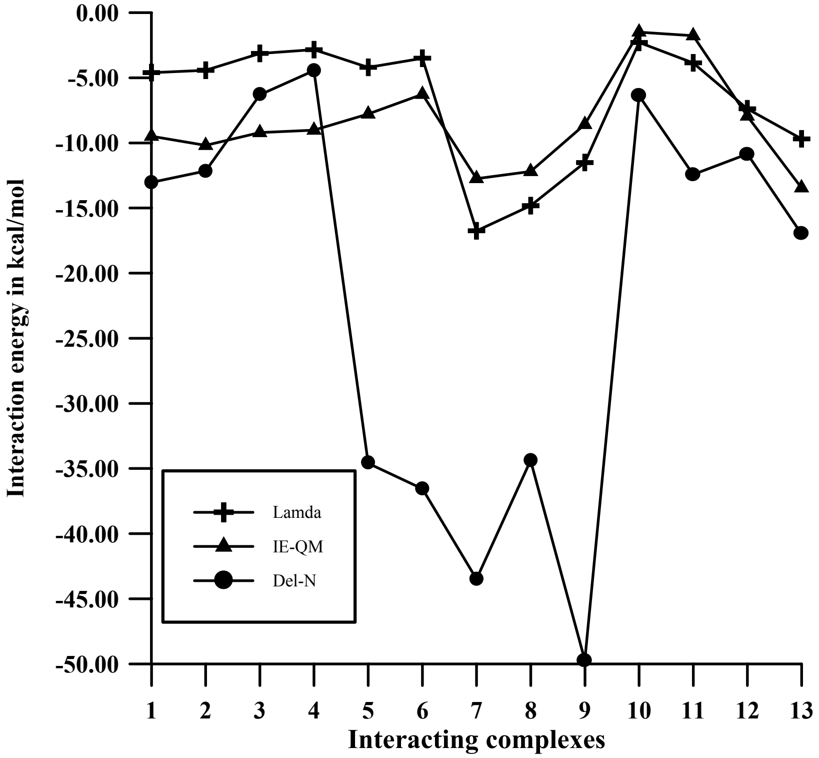

Figure 5.5 The total interaction energy of all the complexes obtained through the parameter λ and ΔN and the actual interaction energy (IE-QM). The number in X-axis refers to the corresponding interacting complex given in Table 5.3.

Chapter 6

The Influence of Electric Field on the Global and Local Reactivity Descriptors: Reactivity and Stability of the Hydrogen Bonded Complexes

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Abstract

In the present chapter, a preliminary study has been undertaken to study the effect of external electric field on the global and local reactivity descriptors to explain the reactivity and stability of the simple hydrogen bonded acid-base complexes in the presence of external field. The present study is also extended to an another important class of multiple-site interacting complexes, Watson-Crick DNA base pair models, Guanine-Cytosine and Adenine-Thymine. Using the inverse relationship between the global hardness and softness parameters a relationship is obtained for the variation of hardness in terms of the Fukui function under the external electric field. It is shown that the variation of hardness in the presence of external field does not necessarily imply that the reactivity of a specific site or an atom present in the molecule would be enhanced or deactivated. The present study shows that the complexes are more stabilized at the higher field strength than at the isolated state.

6.1. Introduction

The prediction of the changes in reactivity and selectivity of the atom centers within a molecule and the interaction between the molecular systems, in general, can be described by energy-density response functions.[1-4] A study on the behavior of electron density and its variation with respect to the small perturbations can reveal many interesting aspects concerning the reactivity pattern of the atomic and molecular systems.[5-8] The electron density of the interacting systems will be redistributed upon small perturbations which can lead to some specific strong, weak or van der Waals bond type interactions. These perturbations can be introduced in many ways. For instance, it is well known that the effect of electromagnetic radiation on the systems has largely been exploited to acquire the information about the most useful spectroscopic properties. On the other hand, the perturbation introduced by the molecular systems to an another system will define the nature of the chemical reactions. More importantly, the influence of solvent molecules or the medium in which the reaction is taking place has profound impact in determining many aspects of the reactions.[9] Owing to the importance of the solvent effects, many theoretical efforts have been devoted to study these effects. It has been experimentally well known that the acidity and basicity in organic molecules change significantly in the presence of a solvent and hence, the reactivity trend also changes. In addition, one can also have these effects by introducing homogeneous and inhomogeneous electric fields. An inhomogeneous electric field can be produced by placing fictitious point charges around the systems. These effects are generally known as environmental effects.[10, 11] These external fields can affect the physical properties and reactivity of dissolved molecules in condensed phase systems. These effects are especially important in ordered crystalline environments such as solid oxides (e.g. zeolites and other metal oxides) and biological macromolecules.[12-15] These local electrostatic fields play an important role in catalytic functions and in governing the stabilization of many bio molecular systems. When molecules are adsorbed in the zeolite cavities, they experience a strong electric field. In the cation exchanged zeolite catalysts, electric field is in the order of 1-10 V/nm and this field plays an important role in the activation of adsorbed reactant molecules.[16-18] It can also induce the abnormal adsorption capability and some of the forbidden vibration of certain bonds. Thus, the environmental effects cause a dramatic change in the reactivity and this reactivity trend can be different from the gas phase. As a result, the stability of the complexes can become more weak or strong depending on such effects. Hence, the prediction of the reactivity and stability of molecular systems in the presence of such environmental factors (solvent, electric field or point charges) would be interesting for a general study. The present work aims at a systematic description of the reactivity and stability of the molecular systems in the presence of external field in terms of the global and local reactivity descriptors.

In the previous chapters, we have developed a semi-quantitative model for the prediction of the interaction energy between the molecular systems and demonstrated its applicability in detail. The model has also been critically examined for the general types of molecular interactions and its reliability has also been systematically analyzed with respect to several theoretical factors, such as basis set, electron correlation and different electron population methodologies. The previous studies have dealt with the interactions in vacuum (or in the gas phase) where the system is completely independent of its surroundings. However, if one is interested in the features of the process in condensed media such as aqueous solution or in the presence of other external fields, it is important to include such external effects. In this paper we will study the variation of global and local reactivity descriptors (hardness and Fukui function) in the presence of an external perturbation. Since most of these descriptors are the derivatives of energy and electron density variables, they would then provide the modified reactivity information of the molecular systems in the presence of such external effects.

Using energy-density perturbation methods, Fuentealba and Cedillo have derived an expression for the variation of Kohn-Sham Fukui function under the external fields involving the Unsöld approximation.[19] In this approximation, the variation of Fukui function with respect to the external potential depends only on the knowledge of the HOMO density and the energy difference between the orbital. Senet has also recently generalized the higher order derivatives of GRD and LRD in terms of different perturbation variables and included the linear and nonlinear response functions within the framework of DFT.[20] Apart from these few works, there have been other studies explicitly considering the solvent effect on the reactivity of molecular systems in terms of LRD using the continuum dielectric model, Born-Onsager approach and effective fragment potential approach.[21-24] In the present work, we will, however, make a numerical study to examine the influence of different environmental effects on the reactivity of molecular systems in a general way. Our first attempt is to simulate these effects by applying an external electric field to the molecular systems without explicitly considering any specific environmental effects (for e.g. solvent molecules, large lattice effect in case of metal oxides, etc.) as a perturbing source. Such an approach is approximately consistent with Onsager's model for dipole fluids wherein the field of the dipole polarizes its surroundings.[25] This polarization induces a "homogeneous field" in the solute molecular spherical cavity. The homogeneous field created by these solvent dipoles and its interaction with the solute molecule affects the reactivity of the molecules and the field strength produced by these molecules depends on the nature of the solvents (dielectric constant). In the present model, these effects are simply simulated by applying the external field. Although this is an approximation, this approach can provide some useful insights about the reactivity and selectivity of the systems. Such approximations have been in practice in literature and found to be useful in explaining some specific types of molecular interactions. For instance, Jordan and Del Bene[26] have very recently studied the formation of the hydrogen-bonded complexes in the presence of electric field to simulate the environmental effects.[27] They have also predicted the proton stretching frequencies in such cases. Limbach *et al.* have made a detailed study to explore the influence of external homogeneous and inhomogeneous electric fields on the hydrogen bonded acid-base complexes and studied the proton transfer reactions in such external effects.[28] In the present study, we study the influence of the electric field on the global and local reactivity descriptors to probe the reactivity of hydrogen bonded acid-base molecular systems. Subsequently, the stability of these complexes is also studied. We have also considered these effects for other important type of complexes, the DNA base pair, multiply hydrogen bonded Guanine-Thymine and Adenine-Thymine. In this present chapter of the thesis, we have included the external field effects in the model for the interaction energy proposed in the earlier chapters for both the single and multiple site interactions.

6.2. Methodology and Computational Details

In this preliminary study, we have chosen some of the prototype acids and bases, HF, HCN and NH_3, ONH_3 and the hydrogen bonded the acid-base complexes, namely F**H**-**N**H_3, F**H**-**O**NH_3 and NC**H**-**N**H_3, NC**H**-**O**NH_3 (bolded atoms are the reactive atoms). All the systems were completely optimized at the zero field as well as in the presence of electric fields of strength 0.002 to 0.012au in the steps of 0.002. The field is applied simultaneously in x, y, z principle axis of all molecular systems. The energy of all the neutral systems were computed by MP2 method using the standard split-valence basis set, 6-31G(d,p). All the calculations were performed using the GAMESS system of programs. We have also considered the Watson-Crick DNA base pair models, Guanine-Cytosine and Adenine-Thymine for the study of multiple-site interaction cases. The geometry of the DNA bases is optimized only at the zero field using HF/6-31G(d,p) and the same geometry is employed for the higher electric field calculations. The computational details for the global and local reactivity descriptors can be referred in the earlier chapters. The expression (3.7) is used for the computation of interaction energy of the complexes interacting through single-sites (F**H**-**N**H_3, F**H**-**O**NH_3 and NC**H**-**N**H_3, NC**H**-**O**NH_3). In case of DNA base pairs, the reactive atoms are not directly bonded to each other (see Figure 6.1). The interactions that are taking place through such reactive centers of the systems A and B are assumed to be decoupled. As detailed in the chapter 5, interactions of these types can be described by Localized Reactive Model (LRM) and, accordingly, we have used the expression (5.7) for the computation of interaction energy of the complexes.

6.3 Results and Discussions

6.3.1 The Effect of Electric Field on Global and Local Reactivity Descriptors

In this section, we will first discuss the effect of electric field on global and local reactivity descriptors for the simple acids, bases (HF, HCN, NH_3, NH_3O) and for the case of guanine, cytosine, adenine and thymine. The subsequent discussion on the stability of these hydrogen-bonded complexes will be made in the next section. The effects of an increase in the electric field on GRD (chemical potential, hardness) and LRD, (Fukui functions), of acids (HF and HCN) and bases (NH_3 and NH_3O) are presented graphically in Figure 6.2 and 6.3, respectively. In general, it can be seen that the hardness values for linear molecules HF and HCN increases with the increase of electric field strength from 0.000 to 0.012 in atomic units. We also observe that there is an increment in the value of hardness for the case of NH_3 and NH_3O. The relative change in the hardness values is in the range of 0.02-0.05au. The effect is observed more for the case of HCN and NH_3O than for HF and NH_3. In case of HCN and NH_3O, the hardness value decreases at the field value of 0.006 and 0.012au, respectively and other higher field values, there is gradual increment in the hardness values for both the above cases (Figure 6.2). The values of chemical potential do not change significantly for all the cases and the effect is linear with the variation of electric field except for the case of HF. In particular, the effect of the field on the value of chemical potential of NH_3 is noticed to be very minimum and it increases gradually with the increase in the value of field by 0.001au. The similar effect is observed in case of HCN, HF and NH_3O.

It can be noticed that the influence of the field on the Fukui function (FF) of the reactive atoms is significant and the value of this function for all systems always increases with the applied electric field (Figure 6.3). Comparing the value of FF for H in HF and HCN systems, it is found that the value of FF for H in HF is more than that of HCN. However, it changes dramatically for the case of HCN at the high field strength (0.012au) and it becomes more than that of HF. Thus for the case of HCN, the influence of the field on FF is nonlinear at higher field strength. There is a significant change in the value of FF at the field value of 0.004au and the FF increases gradually at other field values. Among the bases NH_3 and NH_3O, the value of FF for O in NH_3O is always more than that of N in NH_3 and the value increases smoothly at all field values.

Let us now analyze the results of the GRD and LRD of Purines (guanine and Adenine) and pyrimidines (cytosine and thymine) under the influence of electric field (Figure 6.4 and Table 6.1). It is interesting to note that the chemical potential of guanine and cytosine remains almost constant with an increase in the field strength. The chemical potential of cytosine increases slightly only at a higher field strength. On the other hand, one observes a remarkable change in the value of chemical potential for the cases of adenine and thymine with the applied field strength. As the electric field changes from 0.000 to 0.012au (i.e. isolated state to the high field perturbed state), the chemical potential of these two systems decreases. For instance, the chemical potential for adenine and thymine changes from -0.122 to -0.110 in au and -0.106 to -0.085 in au, respectively. In case of hardness values, the effect of electric field on these systems reveals some interesting features. As discussed above, it has been found that there is an increment in the value of hardness with the increase in the value of electric field for the case of simple acids and bases. However, in the case of the bases, purines and pyrimidine, the hardness values decreases substantially with the increase in electric field strength, except for the case of cytosine (Figure 6.4). The implications of the present results have been discussed separately in the next section. Let us now examine the variation of FF under these field perturbations. It should be noted that these systems have multiple reacting sites and they are designated as RA1, RA2 and RA3 (See Figure 6.1). It can be seen that the FF indices for all the reacting atoms vary consistently and some of them are found to be constant with respect to the applied electric field. For instance, the value of FF for RA2 of guanine at the zero fields is 0.066 and it remains constant even at the field value of 0.008au. On the other hand, the FF value of RA1 increases upon applying electric field and for the other reactive atoms in RA3, reverse effect is observed. In case of cytosine, the FF for all the reactive atoms, RA1, RA2 and RA3, increases significantly. For adenine, the influence of field on all the three reacting atoms is observed to be very small. In case of thymine, FF for RA1 alone changes and for other reacting sites, RA2 and RA3, there is no substantial change in the value of FF. Comparison of the values of FF for all the reactive atoms at the isolated state and in the presence of electric field reveals that the systems, guanine and cytosine are more influenced by the electric field than the systems, adenine and thymine.

Let us now compare our results with the recent study made by Sivanesan *et al.*[22] They have studied the effect of incorporation of bulk solvent around the nucleic bases using the self-consistent reaction field (SCRF) approach on the values of FF. Their study reveals that the FF for the intrinsic reactive sites of purines and pyrimidines in water media does not have a uniform effect in the presence of water medium. It has also been noted that the FF for the electrophilic and nucleophilic sites of the bases, guanine and cytosine, increases in water medium, whereas for adenine and uracil, there is only a marginal change. This result is completely in agreement with the present study. It is also gratifying to note that the change in the value of FF for each reactive atom of these four bases due to the presence of electric field is very consistent with the results obtained from the effect produced by water solvent.

From the above results, it is clear that the possibility of finding a general relation for the variation of the global and local reactivity descriptors with the applied electric field does not appear to be simple. However, a possible explanation for these observations is presented below.

6.3.2. A General Discussion on the Variation of GRD and LRD due to the Applied Electric Field

In earlier part of the discussion, it has been noticed that there is a significant change in the hardness and Fukui function parameters upon the external perturbation on the molecular system. It is of particular interest to establish a relation for the variation of these two parameters under the external field. In a recent paper, Fuentealba and Cedillo have shown that the variation of the Kohn-Sham Fukui function with respect to the external perturbation depends on the knowledge of the HOMO density and a mean energy difference of all the occupied and unoccupied orbitals.[19] Here, the quantity, mean energy difference, has been approximately interpreted as hardness. Under this approximation, it has been stated that greater the hardness, the smaller the variation of the Fukui function under a perturbation. This statement then signifies that the system will become less reactive as the hardness of the system increases due to the external perturbation.

Contrary to the above statement, we have observed in the present study,that both the global and local reactivity descriptors of the simple acids and bases, hardness and Fukui function, increase significantly (Figure 6.2 and 6.3). At the same time, it has also been noticed that the global hardness of the guanine, adenine and thymine decreases with the increase of field values and the Fukui function of the reactive atoms does not show any significant change in their values. These results imply that the increase of hardness parameters does not necessarily mean that reactivity of the systems decreases or vice versa. In what follows, we will now provide a simple relationship for the variation of the hardness parameters and FF with respect to the electric field. An attempt has also been made to interpret the results observed in the present study.

Considering the inverse relationship of hardness with global softness, one can express the variation of hardness with respect to the field (F) as, ($\partial\eta/\partial F$), has been expressed by Pal and Chandra[29] as,

$\partial\eta/\partial F = - 1/S_0^2\ \partial S/\partial F$ --- (6.1)

Where S_0 is the global softness. Pal and Chandra have used the above expression to establish a relation between the polarizability and dipole moment as well as explain the change if hardness with respect to external field. The global hardness can be related with local softness as,

$S = \int s(r)\ dr = S \int f(r)\ dr,$ --- (6.2)

Inserting the expression (6.2), into (6.1)

$\partial\eta/\partial F = -1/S_0^2\ \partial/\partial F\ (\int S\ f(r)\ dr)$ --- (6.3)

At this stage, two comments are pertinent. First, the change in hardness with respect to the electric field is inversely proportional to the square of global softness calculated at the zero field. The second important point is that the variation of hardness with respect to the external field is directly proportional to the first order variation of sum of Fukui function at all points.

It is very essential to have the knowledge of the response of each atom present in a molecular system under external field and it would explain the atom or part of the molecule that would undergo a maximal change when an external field is applied. The influence of the field on each atom k in a molecule depends on the nature of the response of each atom present in the molecule. For simplicity, if we use the condensed Fukui functions in Eq.(6.3),

$\partial\eta/\partial f = -1/S_0^2\ \partial/\partial F\ (S\ \Sigma_k\ f_k(r))$ --- (6.4)

where the sum runs over all the atoms k in the molecule. From the above expression, it can be immediately noticed that the change in hardness parameter with respect to the electric field is actually dependent on the variation of FF of all the atoms present in the molecule. The condensed Fukui function values for some of the atoms can become more (or less) than the value of the Fukui function calculated in the isolated state or vice versa. In any case, it should be noted that the net effect would be proportional to $d\eta/dF$. It also signifies that the decrease or increase of hardness of a molecule under the external field does not necessarily imply that the reactivity of a specific site or atom present in the molecule would be enhanced or deactivated due to the variation in the hardness parameter. The variation of the hardness parameter in the presence of external perturbation is actually dependent on the net cooperative effect exhibited by the collection of all the atoms present in the molecule.

Let us consider one specific system and analyze the variation of hardness and FF in the presence of electric field. For instance, in case of HCN molecule, the f_k^+ values for all atoms along with the values of hardness at all field values are given in the Table 6.2. It can be seen that there is a gradual increment in the values of hardness as well as the f_k^+ values for the reactive atom H in HCN molecule with the increase in the field values. On the other hand, the f_k^+ value for N in HCN, decreases and for carbon, the change in the value of f_k^+ is significant. This trend is in agreement with the above discussion. Although the present argument is not very rigorous, it can, however, explain the present observation for the increase in the value of condensed Fukui function as well as the hardness parameters. A further detailed study should be made in this direction.

6.3.3 Stability of Complexes under External Field

In the earlier section 6.3.2, the influence of electric field on the determination of global and local parameters has been explained qualitatively. It is noted that the Fukui function of the reactive atoms of simple acid (HF and HCN) and bases (NH_3 and NH_3O) increases with the field strength and hence it is expected that the stability of the hydrogen bonded complexes should increase in the presence of external field. We will now examine the effect of electric field on the stability of hydrogen bonded complexes. The interaction energy (IE) for the complexes formed by single reactive sites (F**H-N**H_3, F**H-O**NH_3 and NC**H-N**H_3, NC**H-O**NH_3) are shown in the Figures 6.5 and 6.6. The value of the parameter λ is given in the Table 6.3 and 6.4. Since HF is stronger acid than HCN, it is expected that IE of HF with other bases should be greater than that of HCN. The actual quantum chemical calculation (IE-QM) for both the HF-NH_3 and HCN-NH_3 complexes shows that the complex is stabilized with the increase of electric field and the interaction energy of HF with NH_3 is found to be higher than that of HCN. It is also to be observed that the value of the parameter λ also increases linearly upon increase in the field values. The influence of electric field on the interaction of NH_3O with HF and HCN systems is not linear. It is particularly interesting to note that there is a pronounced effect on the stabilization of

HF-NH_3O complex at the field value of 0.002au and the effect is observed to be less for the case of HCN-NH_3O. On the other hand, HCN-NH_3O complex is destabilized at the higher field value of 0.012au and it is consistent with the IE-QM values.

In general, the IE calculated by the expression (5.7) also shows that these complexes are stabilized more in the presence of external field compared to the value at zero field. There is a better agreement with the actual trend for the case of HF complexes than HCN complexes. Although the value of global hardness parameter increases for all the systems, the bond strength of these complexes is further enhanced at the higher field values. This can be correlated with the increase in the value of the FF indices and the parameter λ due to the applied electric field. The IE values for HCN complexes do not vary linearly at all field values and this dissimilarity can be explained from the value of FF for H in HCN, as discussed in the Section 6.3.1. In case of NH_3O complexes, both the IE-QM and IE calculated from our method show that stabilization of these complexes does not increase gradually with the field values.

In case of multiple-site interactions, the base pair interaction energy for guanine-cytosine and adenine-thymine pairs are presented in Figure 6.7. It is particularly interesting to note that the stabilization energy for these complexes is quite sensitive to the specific value of the electric field and the stabilization trend for these two base pairs are observed to be different from each other. In particular, guanine-cytosine base pair is destabilized upon the increase in the electric field. On the other hand, the effect of electric field on adenine-thymine base pair remarkably stabilizes the base pair. At zero field, the calculated IE from the present method, for the guanine-cytosine, is -21.2 kcal/mol which is comparable to the actual value, -25.8 kcal/mol. The IE value decreases gradually with the electric field and at high field, the IE values drops down to -1.7 kcal/mol. In case of adenine-thymine, the calculated IE value is -3.7 kcal/mol, which is very less compared to the IE-QM value, -11.8kcal/mol. The value increases very rapidly and the values are overestimated at high field values. For instance, at the field value 0.008au, the value obtained by LRM and IE-QM is -25.1 and -20.0 kcal/mol. In both cases, the trend obtained from the present methodology is consistent with the actual quantum chemical calculations carried in the presence of water medium.[30] Although the global hardness values for both adenine and thymine cases decreases with the field values, the reactivity of both the systems is found to be enhanced at all the field values.

The comparison of the present results with IE-QM shows that the estimated IE values are less than that of IE-QM. It can be due to two probable reasons for this observation. The observed response of the global and local descriptors of the molecular systems is found to be insignificant due to the external field and this can be improved by employing large basis sets as well as highly correlated methods. In addition, it is generally known that there is a small variation in the density of a molecule due to solvation. The other factor can be due to the determination of the factor λ. However, a further study is required to clarify many issues on the variation of GRD and LRD due to the external perturbation and its relation with the reactivity of the molecular systems.

6.4. Conclusions

The present chapter focused on the study of influence of the environmental effects on the global and local reactivity descriptors of some of the simple acids to bases to study the reactivity and stability of the hydrogen bonded acid-base complexes. The interaction between the bases, guanine-cytosine and adenine-thymine has also been studied by the recently proposed method, localized reactive model. The environmental effect has been simulated by applying a weak electric field to the molecular systems. It is observed that the global hardness and the FF of acids and bases that are studied in this present chapter increase with the increase of electric field strength. In general, it has been shown that the increase in the value of global hardness in the presence of electric field does not necessarily imply that the reactivity of the molecular systems would be lowered and vice versa. The variation of the hardness parameter in the presence of external perturbation is actually dependent on the net cooperative effect exhibited by the collection of all the atoms present in the molecule. It is also observed that the simple acid-base complexes are more stabilized at the higher field than at the zero field (isolated state). In case of DNA base pairs, guanine-cytosine complex is destabilized upon increase in the electric field and the reverse effect is observed for the adenine-thymine case. The results are also consistent with the quantum chemical SCRF calculations carried in the water medium.

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Table 6.1 The condensed Fukui function for different reactive atoms of the purine and pyrimidine bases, at different electric field values. (values in atomic units). RA1, RA2 and RA3 refer to the reactive atomic centers of the bases, as numbered in the Figure 6.1.

System	Electric Field	Condensed Fukui function f(r)		
		RA1	RA2	RA3
Guanine	0.000	0.438	0.066	0.080
	0.002	0.434	0.066	0.083
	0.004	0.430	0.066	0.086
	0.006	0.426	0.066	0.091
	0.008	0.422	0.066	0.097
	0.010	0.418	0.043	0.501
	0.000	0.057	0.035	0.476
Cytosine	0.002	0.059	0.038	0.481
	0.004	0.060	0.041	0.487
	0.006	0.061	0.045	0.492
	0.008	0.063	0.048	0.497
	0.010	0.064	0.051	0.502
Adenine	0.000	0.063	0.060	0.105
	0.002	0.064	0.040	0.104
	0.004	0.066	0.039	0.102
	0.006	0.067	0.038	0.101
	0.008	0.068	0.038	0.101
	0.010	0.069	0.038	0.100
Thymine	0.000	0.447	0.059	0.087
	0.002	0.442	0.058	0.087
	0.004	0.437	0.058	0.087
	0.006	0.432	0.057	0.086
	0.008	0.427	0.056	0.086
	0.010	0.422	0.056	0.086

Table 6.2 The value of the hardness parameter and the f_k^+ values for all the atoms present in HCN molecule at different field values. (values in atomic units)

Electric field strength	Condensed Fukui function f_k^+			Hardness
	H	C	N	
0.000	0.160	0.465	0.375	0.334
0.002	0.164	0.466	0.370	0.336
0.004	0.998	-0.998	0.290	0.360
0.006	0.171	0.470	0.360	0.340
0.008	0.262	0.504	0.235	0.359
0.010	0.287	0.514	0.199	0.365
0.012	1.086	-0.253	0.166	0.375

Table 6.3 The value of the parameter λ for the hydrogen bonded acid-base complexes calculated at different electric field strengths. (values in atomic units)

Electric Field	Value of the λ parameter			
	F**H-N**H$_3$	F**H-O**NH$_3$	NC**H-N**H$_3$	NC**H-O**NH$_3$
0.000	0.257	0.032	0.038	0.043
0.002	0.062	0.089	0.045	0.105
0.004	0.069	0.102	0.054	0.100
0.006	0.077	0.116	0.064	0.108
0.008	0.086	0.122	0.075	0.119
0.010	0.096	0.127	0.088	0.135
0.012	0.107	0.135	0.103	0.030

Table 6.4 The value of the parameter λ for the DNA base pairs, Guanine-Cytosine and Adenine-Thymine complexes calculated at different electric field strengths. (values in atomic units)

Electric Field	Value of the λ parameter	
	Guanine-Cytosine	Adenine-Thymine
0.000	0.024	0.004
0.002	0.019	0.003
0.004	0.013	0.010
0.006	0.008	0.016
0.008	0.002	0.023
0.010	0.003	0.030

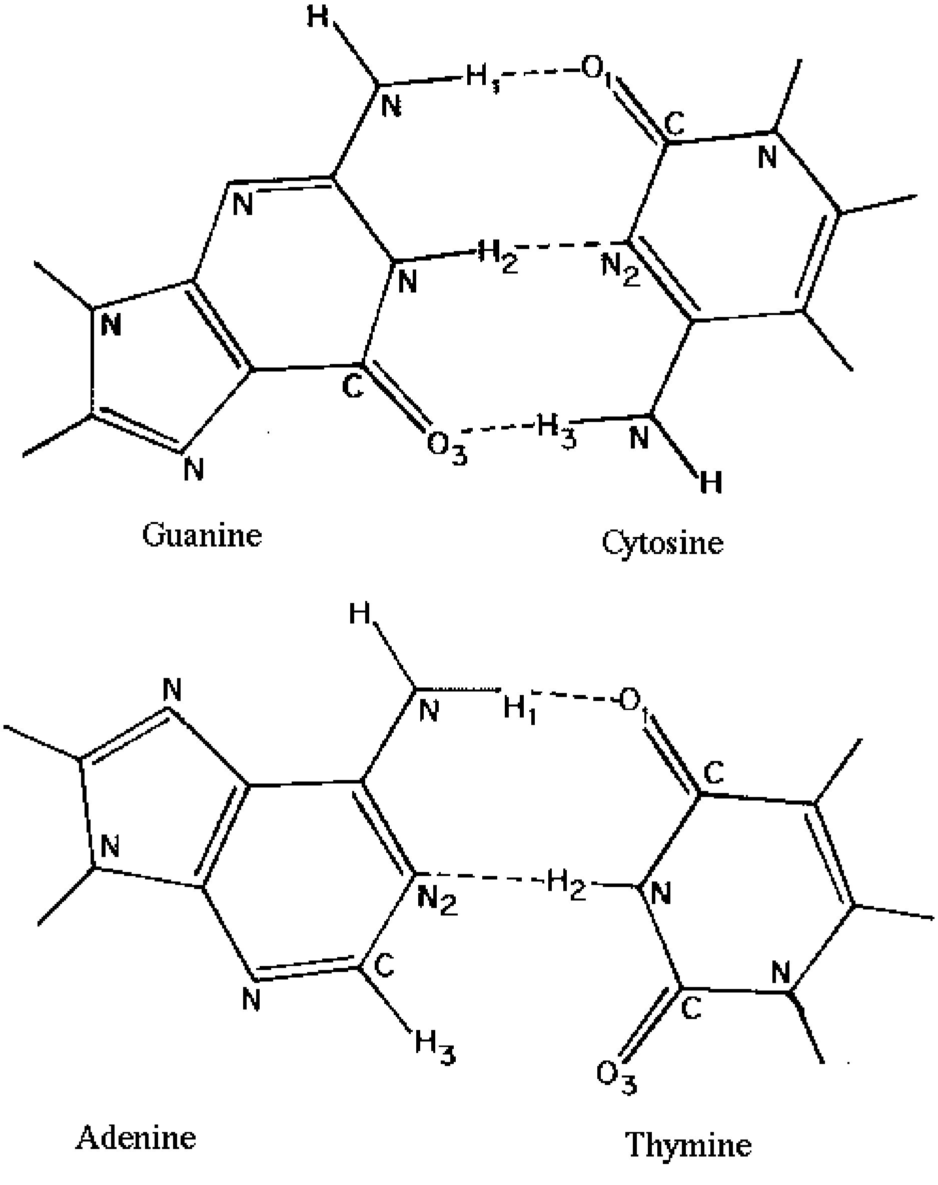

Figure 6.1 Multiple hydrogen bonding interaction between Watson-Crick DNA base pairs, guanine-cytosine and adenine-thymine complexes.

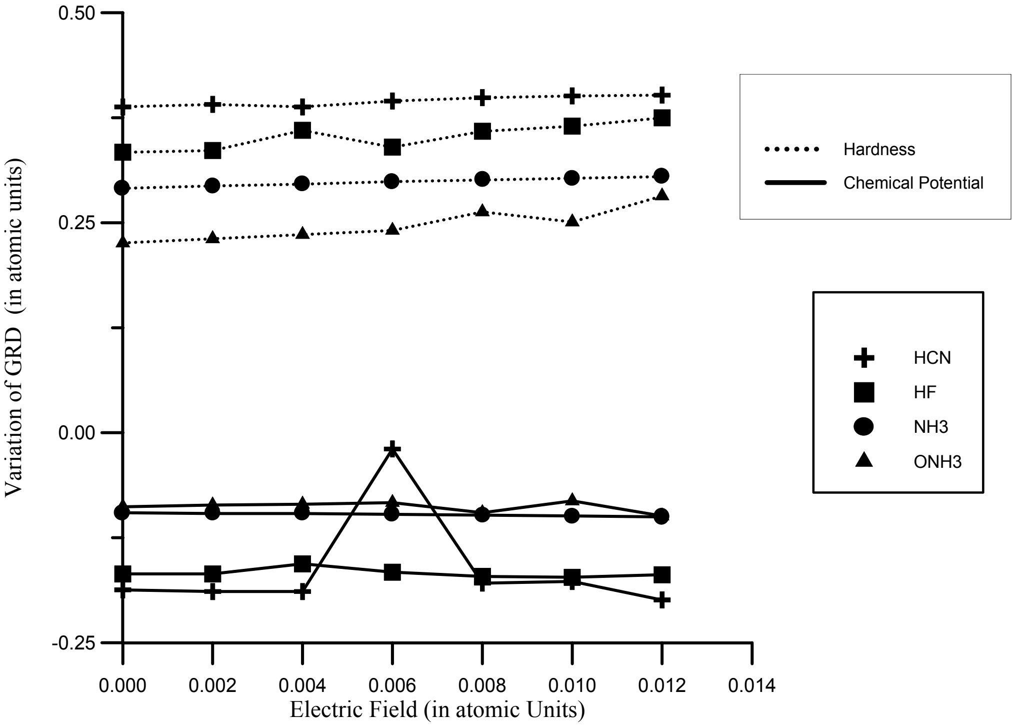

Figure 6.2 Variation of GRD, chemical potential and hardness parameter with the applied electric field for the molecular systems, HF, HCN, NH_3 and NH_3O.

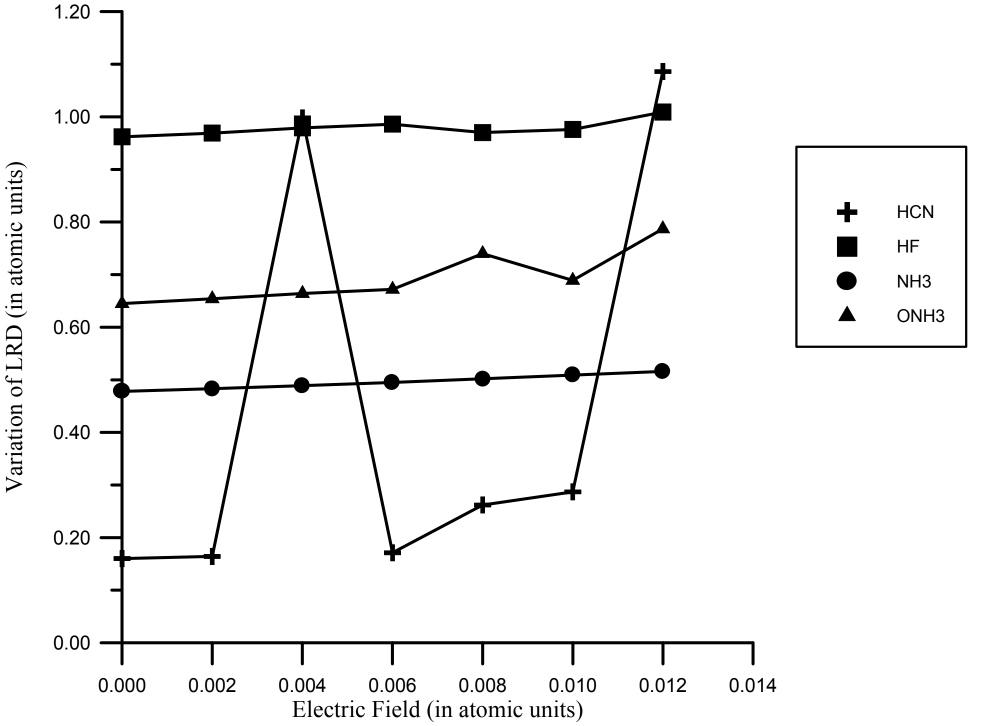

Figure 6.3 Variation of condensed Fukui function with the applied electric field for the reactive atoms of the molecular systems, **H**F, **H**CN, **N**H_3 and **N**H_3O.

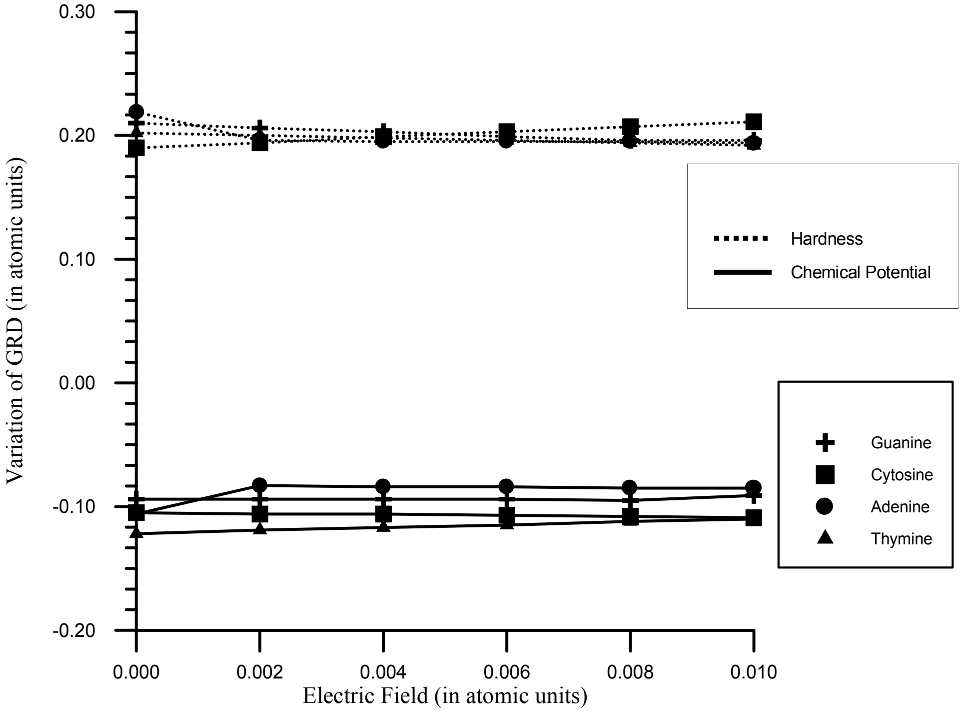

Figure 6.4 Variation of GRD, chemical potential and hardness parameter with the applied electric field for the systems, guanine, cytosine, adenine and thymine.

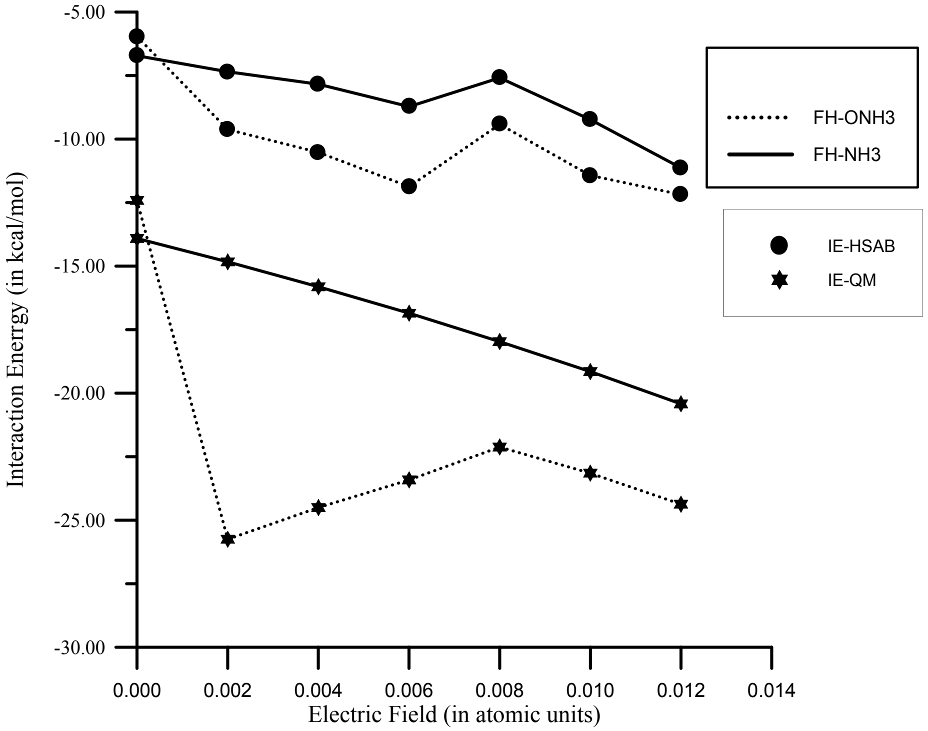

Figure 6.5 The effect of electric field on the interaction energy of HF-NH_3 and HF-NH_3O complexes

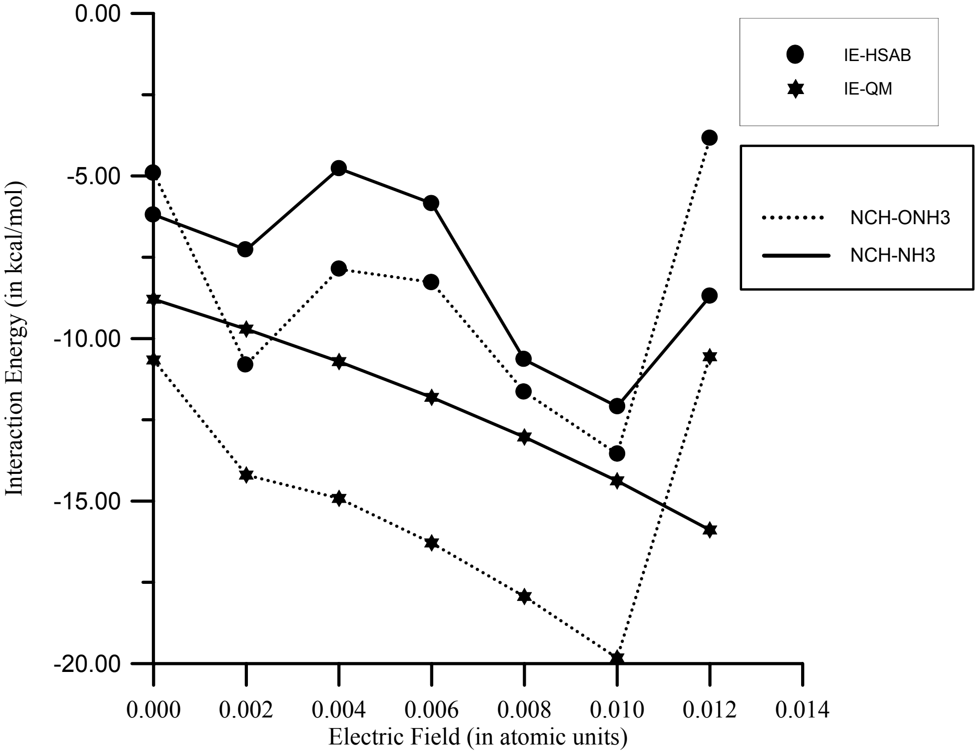

Figure 6.6 The effect of electric field on the interaction energy of HCN-NH_3 and HCN-NH_3O complexes

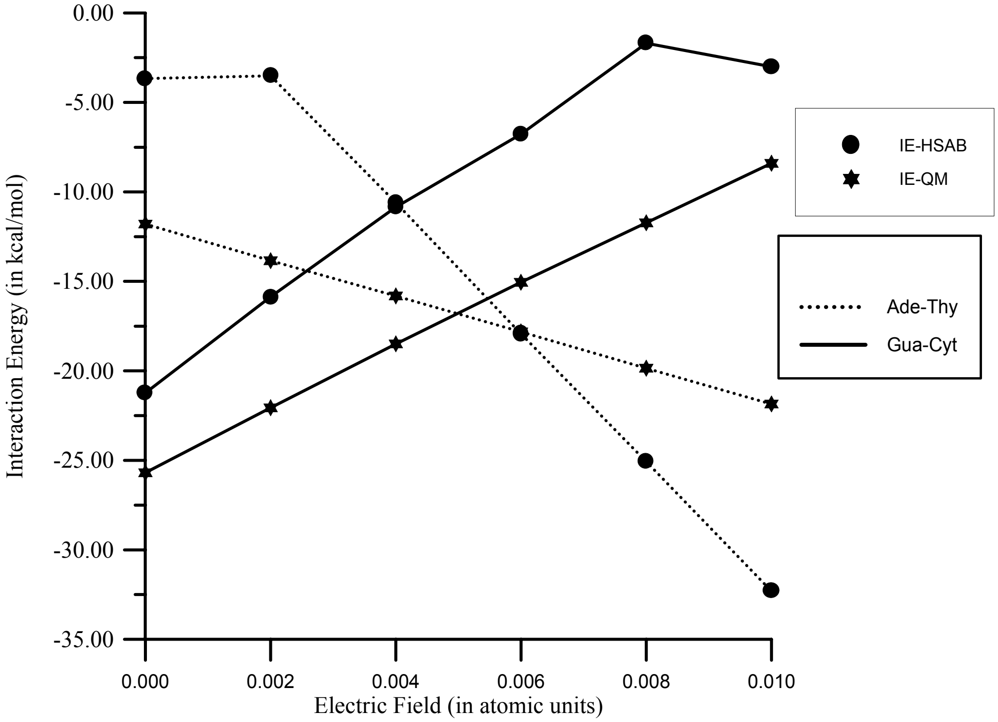

Figure 6.7 The effect of electric field on the interaction energy of DNA base pairs guanine-cytosine and adenine-thymine.