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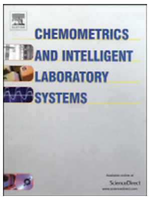

A quantum chemical approach using classical concepts to characterization and descriptive analysis of various reactions of metal ions and organic compounds

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ABSTRACT

Combined with the calculation of quantum chemical reactivity indices and the concept of the four-element theory, four major types of chemical interactions involved in various reactions can be integrated. This theoretical approach was applied to predict many kinds of reactions of metal ions and organic compounds in aqueous solutions — such as, hydration, diffusion, deprotonation, precipitation, redox reaction, and complexation; onto solid surfaces — such as, adsorption, ion exchange reaction, and sorption by organoclay; and for biological activity — such as, median effective concentrations measured from *Photobacterium phosphoreum* and *Chlorella vulgaris*. Results of analysis revealed that the quantum four-element model – which is constructed on the basis of 1) electronic chemical potential $-\mu^+$ and μ^- (electron flow), 2) condensed local softness s^+_{max} and s^-_{max} (polarization), 3) atomic partial charge $\rho^+_{max(H)}$ and $-\rho^-_{max}$ (electrostatic interaction), and 4) the inverse of apolar surface area 1/APSA (hydrophilic interaction) – provides a general meaning for chemical reactivity and has great potential to probe mechanism of action.

1. Introduction

Traditionally, considering the Born hydration model, the standard Gibbs free energy of hydration is often explained as the difference between potential energy in a vacuum and a continuous dielectric medium [1]. The diffusion of metal ions in electrolyte solutions can be described in terms of activity gradient and limiting equivalent ionic conductance of metal ions [2]. The ratio of the ionic charge and size of the metal ion can be used to indicate the deprotonation and precipitation trends of metal aquo-ions [3,4]. With respect to the stability of metal–ligand complexes, charge and size of metal ions, stabilization resulting from crystal-field and ligand-field effects are recognized as important factors [5]. The cation hydration and anion field strength models were proposed to predict the cation-exchange selectivity coefficients [6]. There are, however, several drawbacks in the above-mentioned conventional theorems, when used to characterize aqueous and surface reactions of metal ions. Since the shortcoming in continuum dielectric assumption, hydration free energies obtained from the conventional model were different from the experimental measurements. Because of the electron-sharing effect, the simple electrostatic model for chemical reactivity is unable to rationalize the behavior of metal ions with different electronic configurations. In describing the reaction trends of metal ions, the metal ions must be classified into different groups according to their electronic configurations [1–6].

For predicting and explaining the chemical reactivity of organic compounds, Kamlet, Taft, and their colleagues proposed a type of linear free energy relationship (LFER), called the linear solvation energy relationship (LSER) [7–9]. The approach relates a bulk property to molecular parameters thought to account for cavity formation, dipole moment/polarizability, and hydrogen-bonding effects. The cavity term is a measure of the energy needed to overcome cohesive solvent–solvent molecule interactions to form a cavity for the solute molecule. The dipolarity/polarizability terms are measures of the energy of solute–solvent dipole and induced dipole interactions which contribute to solution formation. Hydrogen bonding terms measure the energy of interaction when a solute–solvent complex is formed. The original LSER descriptors were derived from UV–vis spectral shifts of indicator dyes. Because of their empirical origin, their ability to make a priori predictions has been somewhat limited.

In regard to toxicity testing, both the U.S. Environmental Protection Agency (USEPA) and European Union (EU) have widely promoted the development of alternative techniques to eliminate the use of animals [10–12]. In this respect, quantitative structure–activity relationship (QSAR) was adapted as a more reliable estimation method for use in

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regulatory assessment of chemicals [10]. Octanol–water partition coefficients (log P) are often used in QSAR for toxicity assessment of organic chemicals when there is a lack of observed data [11,12]. However, conventional QSAR models, which focus on log P, are not sufficient for generating comprehensive structure–activity relationships. In order to improve the accuracy of QSAR predictions, it is necessary to select more appropriate parameters in the model.

Quantum chemical calculations are an attractive source of useful molecular descriptors, which express all of the electronic and geometric properties of chemical molecules. Moreover, electronic descriptors can be partitioned on the basis of atoms or groups, enabling the description of separate molecular regions. Therefore, it has a great advantage in developing predictive/explanatory models where quantum chemical descriptors are used [13].

Famini and Wilson have developed a set of quantum mechanical derived parameters to model conventional LSER terms [14–16]. A molecular volume is used to model the cavity term that measures the energy required to create a solute-molecule sized cavity in the solvent. The dipolarity/polarizability term, which attempts to account for dispersion, is modeled by the polarizability index. This index is defined as the average molecular polarizability divided by the molecular volume. Hydrogen bonds are modeled using covalent and electrostatic terms by the frontier molecular orbital energies and maximum partial charges, respectively.

A category of quantum chemical descriptors, such as conceptual DFT-based reactivity descriptors, have been extensively used in interpreting properties and reactions, and predicting site selectivities of various catalyst surface systems and chemical–biological interactions [17–25]. Chattaraj et al. [17] proposed a generalized concept of philicity containing electrophilic, nucleophilic, and radical reactions. By using a local version of HSAB principle, Chandrakumar and Pal presented several important studies on the interaction energy for single-site based and multiple-site based intermolecular interactions [18–20]. Padmanabhan et al. presented a series of studies for the applications of global and local reactivity descriptors [21–25]. They especially emphasized the importance of electrophilicity index in QSAR studies and charge transfer analyses. The applicability of local philicity, group philicity and multiphilic descriptor was also discussed. The combination of classical QSAR and density functional calculations used in the process of rational drug design has been developed by Yang et al. [26–30].

Our previous work represented the application of the nonlocal DFT method in constructing linear models for predicting essential reactions of metal ions in aqueous and surface systems [31]. Linear free energy relationships based on the lowest unoccupied molecular orbital energy of metal ions, the metal-oxide bond lengths, and water-binding energies of monohydrated metal ions, calculated with the Becke–Perdew–Wang density functional method have been derived and were shown to be quite useful in elucidating the interrelationship among various reactions of metal aquo-ions.

Subsequently, we applied the conceptual DFT to investigate the solvent-induced shifts of the carbonyl ($C{=}O$) stretching frequency of acetone in various organic solvents [32]. Four types of reactivity descriptors, namely, the solvation free energy of solute in continuous dielectric medium, the global interaction energy of solute–solvent system, the maximum electrostatic potential on the hydrogen atom of solvent molecule, and the maximum nucleophilic condensed local softness of solvent molecule, those which considered both the non-specific and specific effects of solute–solvent interactions were incorporated in a multiparameter equation for constructing the conceptual DFT-based predictive/explanatory model.

According to the views proposed by Cramer and Famini et al. [33], '*multiple linear regression on a given set of descriptors may legitimately be regarded as a remarkably old concept: the ancients ascribed all physicochemical properties to the proportions of earth, air, water, and fire which were present in a given substance.*' In this study, we have shown that the conceptual density functional theory and the calculation of quantum chemical reactivity indices do provide a reasonable basis for understanding the correspondence between the four "elements" and chemical interactions. Four types of descriptors, which governed electron flow, electrostatic, polarization and hydrophilic interactions, were each unique and by appropriate linear combination spanned the space of all observable properties, thus can be used to elucidate mechanisms of wide varieties of chemical reactions.

2. Computational details

2.1. Model construction

In the history of chemistry, one of the most influential information models is the concept of the four-element theory. The basis of its success highlighted pioneering concepts in various domains [34–37]. The theory stated that all substances are made up of four basic "elements" in different proportions. The allocation of these "elements" would enable the proper formation of material balance and stability. If the content of any of them were changed or unreconciled, it would lead to material changes.

After Aristotle's generalization for this concept, there were four qualities that have been proposed to constitute these "elements": hot, cold, wet, and dry (see Fig. 1a). Given the characteristics of particles as follows: 1) The mean free path (MFP) of hot particles is long — meaning, hot particles are intrinsically in a non-contact state; 2) on the contrary, cold particles are in a contact state with each other; and 3) particles gathering in a wet regime are easily deformed, and conversely, a system is non-deformable in a dry regime, two pairs of opposite attributes (contact/non-contact and deformable/non-deformable) correspond to the four qualities can be identified.

In electronic processes, a precondition is a condition that two systems must always be in a contact state prior to the transfer of electrons. Thus, in most cases, transferable and contact attributes of electrons can be regarded as synonymous. The electron flow is driven by a difference in electronic chemical potential, which leads to a charge transfer and a deformation of the electron cloud between the two systems. Hydrophilic groups attract water molecules without the deformable electron density. Water forces hydrophilic groups to hold together in a contact state, thereby minimizing their disruptive effects on the hydrogen-bonded water network. Hydrophilic groups are sometimes said to be held together by hydrophilic bonds; however, the attraction is actually caused by a repulsion of hydrophobic groups from the water. The electrostatic interaction is formed when there is complete transference of electrons from one atom to another, forming an inert gas configuration (i.e., non-deformable), and two oppositely charged ions are interacted in a non-contact state. In a polarization interaction, two atoms are attracted to each other because of the fluctuation of the deformable electron cloud. Two atoms are attracted to each other by the polarization interaction until the distance between them equals the sum of their van der Waals radii, displaying a weak bond interaction between the two atoms.

As illustrated in Fig. 1b, a model constructed by two pairs of opposites, having contact/non-contact and deformable/non-deformable electron attributes, forms four major types of chemical interactions as follows:

i) Deformable and contact attributes form an *electron flow* interaction.
ii) Contact and non-deformable attributes form a *hydrophilic* interaction.
iii) Non-deformable and non-contact attributes form an *electrostatic* interaction.
iv) Non-contact and deformable attributes form a *polarization* interaction.

Within the framework of conceptual DFT, the electronic chemical potential (μ) measures the escaping tendency of the electron density in a molecule and the chemical hardness (η) determines the resistance of the molecular species to lose electrons [38,39]. The negative of the