The interaction between theory and experiment in charge density analysis

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Abstract
The field of x-ray charge density analysis has gradually morphed into an area benefiting from the strong interactions between theoreticians and experimentalists, leading to new concepts on chemical bonding and of intermolecular interactions in condensed phases. Some highlights of the developments culminating in the 2013 Aminoff Award are described in this paper.

PACS numbers: 61.05.C−, 61.50.Cf

Shortly after the discovery of x-ray diffraction early in the 20th Century, it was clear that the new technique would be a breakthrough in atomic structure determination, and should allow the mapping of electron distribution in crystalline solids [1]. Nonetheless, it would take decades before significant progress was made in the latter case. Even an authority such as James [2] concluded in the 1954 edition of his book that 'any attempt to determine the state of ionization of atoms in a crystal is likely to fail, since the scattering factor curves will differ appreciably only at angles at which no spectra exist'. This conclusion was reached after an exhaustive analysis of the scattering of sodium chloride. It was certainly warranted at that time, as the capabilities of available x-ray sources and x-ray detection devices, compounded by the complete absence of computing power, interfered with the exceptional efforts that were nevertheless made. Statements like James' created considerable skepticism and some disdain for those who doggedly pursued the field, reminiscent of the way the development of direct methods was discarded by many in its early stages of direct methods for solving crystal structures. The skepticism was, in part, due to the fact that the least-squares adjustment of structural parameters based on spherical atomic scattering factors, introduced by Hughes in 1941 [3], although highly successful, accounted for bonding features by a subtle adjustment of structural and thermal parameters. This artificially flattened the electron-density *difference* maps showing the change between the experimental x-ray density and that of a thermally smeared superposition of spherical atoms. But new tools that became available in the following decades gradually produced more convincing evidence and new methods of analysis taking into account the asphericity of atoms in solids and their

net charges were developed. The absence of atomic charge neutrality had, of course, already been recognized in the concept of electronegativity. In particular, noteworthy is the introduction by Stewart [4, 5] of aspherical atomic scattering factors based on a spherical harmonic 'multipole' expansion of the atomic electron densities. It followed less general earlier work, and a parallel method of Hirshfeld [6], who succinctly summarized the situation by stating that 'An accurate set of nuclear coordinates and a detailed map of the electron distribution can be obtained via x-ray diffraction only jointly and simultaneously, never separately or independently'.

A demonstration of the power of the new experimental tools that were becoming available was provided by the combined x-ray and neutron diffraction study of the heterocyclic molecule s-triazine, which clearly showed the bias in the x-ray structural parameters through X–N Fourier *difference* maps in which the spherical-atom reference density was based on unbiased neutron structural parameters. The maps revealed the predicted electron lone-pair density at the back of the nitrogen atoms and overlap density in the covalent bonds [7]. Soon after, the field started to catch the attention of theoretical chemists. In particular, Vedene Smith [8, 9] of Queens University became a frequent contributor and participant in meetings such as the seminal 1977 Bat-Sheva seminar on Electron Density Mapping in Molecules and Crystals, organized by Fred Hirshfeld, and the Sagamore Conferences on Charge Spin and Momentum Densities. Smith was one of the founding co-chairs (with the writer of this comment) of the Gordon Research Conference series on Electron Distributions and Chemical Bonding, the first one of which took place in 1978, and the Organizing Chair of Sagamore VI in 1979.

The first comparisons between theory and experiment used *deformation*-density maps based either on Fourier summation of the observed x-ray structure factors or on theoretical calculations. But a more than qualitative comparison with static theoretical densities was hampered by the thermal smearing of the electron density inherent in the x-ray method. A solution evolved from the continuing development of least-squares refinement of more accurate x-ray data with aspherical-atom density functions. Since in such refinements the charge density and thermal smearing are accounted for separately, it became possible to plot the static density represented by the refined density functions. The procedure is valid within the approximations inherent in the thermal motion model, which became less severe as the experimental temperature was lowered. It was at this time that Richard Bader of McMaster University was developing his topological analysis of the total density, emphasizing that a host of molecular properties were implied in the details of the *total* charge density [10]. The effort culminated in an outstanding book that has lost none of its importance at this time [11]. It firmly established a strong connection between theory and the x-ray experiment. It caught the attention of many young theoretical chemists such as Gatti, who with Simonetta applied the method to derive molecular properties by topological analysis of the total density [12]. Gatti subsequently joined the Bader group for a series of most productive stays totaling 6 months during the years 1986–1989. The work included the effect of electron correlation on the charge density [13], and in later years led to a large series of independent papers exploiting the usefulness of topological analysis, such as [14–16], and defending the theory against misconceptions [17]. Many of the publications that followed were in collaboration with experimentalists, for example [18–20]. Thus, while Bader's work represented a new paradigm in the field, much of the following work was Tools-Driven [21]. The increased accuracy of experimental charge densities resulting from computer-driven automatic diffractometers, much better detectors and computer-based analysis of data sets with large redundancy, stimulated the comparison with theory. Here Gatti's contributions were crucial. He wrote the two programs TOPOND-96 [16], matched to the CRYSTAL package for calculating the electronic structure of periodic solids by Dovesi, Pisani and Roetti at Turin University [22], and TOPXD [19]. The latter interfaces with the comprehensive aspherical-atom refinement program XD [23, 24], which had become the most popular program for analyzing the charge distribution from accurate x-ray diffraction data. Gatti continued to create new concepts based on topological analysis which are directly applicable to both theoretical and experimental densities. Foremost among these is the Source Function, first described in a joint paper with Richard Bader [25]. It allows analysis of electron conjugation, aromaticity and the contribution of more than two atoms to a chemical bond [26]. Gatti's development of the implications of the Source Function is summarized in his recent 93 page article [27]. In parallel, multicenter bonding was analyzed by Macchi and co-workers [28, 29] in combined theoretical–experimental studies of metal–metal bonding and metal–carbonyl interactions in organometallic compounds, using the topology of the total electron density, as described

by its second derivative Laplacian and the delocalization function.

A second theoretical solid-state program WIEN, based on a linear augmented plane-wave density-functional method, by the group of Karl-Heinz Schwarz in Vienna [30], was oriented toward inorganic solids. It became an additional popular tool for experiment–theory interactions, including topological analysis. Applications include comparative theory–experiment studies of the high-T_c superconductor $YBa_2Cu_3O_{6.98}$ [31] and the mineral forsterite [32].

A key concept in Bader's theory is the *bond path*, i.e. the gradient path in the total electron density connecting two nuclear attractors, generally coinciding with the nuclear positions. Bader's statement that 'the presence of such an atomic interaction line satisfies both the necessary and sufficient conditions that the atoms be bonded to one another' [11] became a subject of controversy. An alternative and more general interpretation of the topological bond path between two atoms in terms of the exchange integration between the atoms was reported by Pendas, Francisco and Blanco from Oviedo, Spain and Gatti [33]. Much of this work is continuing, leading to a more general understanding of chemical bonding.

These developments led to a striking evolution of the type of attendees at electron-density-oriented conferences. Whereas the early Gordon and Sagamore conferences almost exclusively attracted experimental crystallographers and physicists, more recently theoreticians have become increasingly involved in the meetings, leading to a substantial enrichment of the field.

A second aspect that has come to the forefront is based on the realization that molecules in crystals differ in many aspects from isolated molecules not subject to external forces. In general, more complex molecules and molecular complexes have too low a vapor pressure to be experimentally accessible in the gas phase. As condensed phases, rather than isolated molecules, are relevant in materials science and biological processes, such differences cannot be ignored.

Mark Spackman contributed extensively to this aspect. In early work he placed emphasis on intermolecular interactions as derived from experimental charge distributions [34] and wrote a comprehensive survey on the enhancement of the dipole and higher electrostatic moments by the intermolecular environment, such as, but not limited to, hydrogen bonding [35]. This work was followed up by subsequent analyses [36, 37], the latter again concentrating on the effect of intermolecular interactions, which is shown to be substantial for hydrogen-bonded crystals. On the other hand, a careful combined x-ray–neutron study of benzene showed excellent agreement of the molecular quadrupole moment in the crystal with the results of gas-phase and solution measurements [38]. Gatti and co-workers contributed a theoretical analysis of the matrix effect in crystals of urea [16] and water [39]. Furthermore, in collaboration with Destro and co-workers Gatti showed an unexpectedly large enhancement of the dipole moment of the 3,4-bis(dimethylamino)-3-cyclobutene-1,2-dione (DMBCA) molecule on crystallization, due to often underestimated intermolecular CH–O interactions [20]. Again, the availability of new theoretical approaches to the calculation of the

electronic structure of solids [22] played an essential role. Spackman defined the *interaction density*, visualizing the effect of intermolecular interactions on the multipole-refined electron density [40, 41]. He introduced a new definition of a molecule in a crystal [42], based on Hirshfeld's density partitioning scheme [43], which he subsequently expanded along with McKinnon and Jayatilaka into the use of Hirshfeld surfaces, an ingenious and powerful way of analyzing intermolecular interactions [44].

Thus, thanks to the experiment–theory interaction, some major concepts of chemical bonding are redefined and attention is focused on the real differences between isolated molecules and molecules in a condensed environment. Theory can be a house of cards, building on itself, if not supported by experimental observations. While it provides information beyond what is experimentally accessible, the experiment remains an essential component as it can confirm the theoretical approach selected and distinguish between different theoretical methods. Crystallography is playing a major role in this effort, which is recognized by the awarding of the 2013 Aminoff Prize jointly to a theoretician and an experimentalist both active in the field.

Acknowledgment

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