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An Experimentalist's Reply to "What Is an Atom in a Molecule?"

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Parr, Ayers and Nalewajski have opined in this Journal that the concept of an atom in a molecule "is an object knowable by the mind or intellect, not by the senses." This view is countered by the two hundred years of *experimental* chemistry underlying the realization that the properties of some total system are the sum of its atomic contributions. This paper concludes that an experimentalist has no doubt but that he or she is measuring the properties of atoms when performing an experiment.

Introduction

An article recently appeared in this Journal by Parr, Ayers and Nalewajski (PAN) entitled "What is an atom in a molecule?"[1] The paper argues that though the atom in a molecule (AIM) concept is highly useful—"a central vital concept, compulsively needed in chemistry—AIM remains ambiguous, subject to arbitrary (but disciplined) personal choice when specificity is required". It concludes with the espousing of Kantian philosophy that AIM is a noumenon, "an object knowable by the mind or intellect, not by the senses".

PAN are theoreticians and the conclusion stated in their paper is at odds with an experimentalist's view of chemistry. The concept of a functional group, consisting of a single atom or a linked set of atoms, with characteristic additive properties forms the cornerstone of chemical thinking of both molecules and crystals and Dalton's atomic hypothesis has emerged from the cauldron of experiment, as the operational theory of chemistry. We have no desire to enter into a philosophical discussion. Instead, our intent is to review the *experimental* justification of the AIM concept in chemistry beginning with Dalton and ending with the development of the quantum theory of atoms in molecules, QTAIM, wherein an atom is defined as a region of space bounded by a surface satisfying the quantum boundary condition of zero-flux in the gradient vector field of the electron density $\rho(\mathbf{r})$[2]

$$\nabla\rho(\mathbf{r})\cdot\mathbf{n}(\mathbf{r}) = 0 \qquad \text{for all } \mathbf{r} \text{ on the atomic surface} \quad (1)$$

As demonstrated for many properties and applicable to all, QTAIM recovers the values that are measured in the laboratory and ascribed to atoms and functional groupings of atoms. Every statement in this paper, as required in the practice of science, is based upon observation and/or quantum mechanics and subject to the single test one has of a scientific theory: prediction. It is this approach that underlies Hans Bethe's view of science:[3] "its great advantage is you can prove something is true or something is false", a statement he further paraphrased as "In science, you know you know." A recent paper details how QTAIM evolved from studies on the topology of the measurable density $\rho(\mathbf{r})$ leading to the observation of the paralleling behavior of $\rho(\mathbf{r})$ and the kinetic energy density, an observation indicating the applicability of the virial theorem and hence of quantum mechanics to such regions obtained through the action principle.[4]

The reader is reminded that QTAIM recovers all of the concepts of experimental chemistry: of atoms with characteristic, definable properties,[5] of molecular structure and structural change determined by the dynamics of the gradient vector field of $\rho(\mathbf{r})$,[6] and of electron localization/delocalization determined by the atomic expectation value of the exchange density[7] and brought to the fore in the topology of the Laplacian of the electron density.[8]

Dalton and the First Additive Atomic Property

We begin at the beginning with Dalton. In 1803 Dalton rationalized the then known combining weight relationships between the elements by postulating the atomic concept of matter with the important proviso that each atom of a given element had the same weight and this weight was an intrinsic property of the atom, free or in chemical combination. The atomic hypothesis enabled Dalton to *predict* the soon to be confirmed law of multiple proportions. Thus Dalton postulated the first additive, characteristic atomic property, boldly asserting the immutability of its mass 100 years in advance of Rutherford's demonstration of the nuclear atom in 1911. The atomic nature of matter is a consequence of the form imposed by the presence of a chemically inert nucleus and the dominance of the electron−nuclear force, a consequence of the attraction of the pointlike nuclei for the diffuse distribution of electron density. It is well to bear in mind that the nuclear-electron force is the only attractive force operative in chemistry and is the sole force responsible for chemical bonding. It is this force that determines the principal topological feature of the density − that it exhibits a maximum at a nuclear position thereby leading to the partitioning of space into atomic regions satisfying eq 1.[2] The nuclear charge thus stamps each atom with its chemical identity, thereby justifying Dalton's further postulate that the atoms of a given element maintained their individuality in any physical or chemical change.

The atomic hypothesis led to the assignment of relative atomic combining or equivalent weights and these, together with the ideas Avogadro put forth in 1811 and promulgated by Canniz-

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zaro in 1860, led to the assignment of relative atomic weights and eventually to the unified atomic mass scale. Weight relations were the quantitative experimental tool that led to the atomic concept and they continue to provide the most concrete and direct connection with the atomic composition of matter. When a chemist weighs out a given amount of some substance of known chemical composition, he or she is in effect counting the number of each of the constituent atoms. He or she is not dealing with "objects knowable by mind or intellect, not by the senses."

Thermochemistry and Origins of the Functional Group Concept

Chemistry was soon organized into disciplines that recognized that atoms, and in particular groupings of atoms, exhibited characteristic properties that enabled one to detect their presence in any molecule and to predict the properties resulting from their presence. Indeed, it was early on discovered that not only were atomic properties classifiable as characteristic but also they could in some cases be transferable, as found for molar volume, molar refraction, diamagnetic susceptibility and thermodynamic functions H, S and C_p, etc. These properties obeyed "additivity rules"; that is, the molecular value of some property equalled the sum of the additive contributions from its constituent atoms or functional groups. Thus atomic mass was but the first example of an additive atomic property.

It is important to understand how one arrives at an atom's additive contribution to a thermodynamic or field induced property. One does not measure this directly, as some would appear to deem necessary. Instead, it is obtained by taking the difference in the property between two molecules that differ in composition by the atom or group in question, the methyl and methylene groups in the series of saturated *n*-alkanes, for example. There is nothing new here. The addition and/or subtraction of measured thermodynamic quantities for chemical reactions is the standard method of determining the value of the property for some desired reaction. Thus the heat of formation of a hydrocarbon is obtained by subtracting its measured heat of combustion from the requisite number of heats of formation of CO_2 and H_2O, as detailed in the pioneering studies of Rossini.[9] The most recent compilations of additive group contributions given by Benson and co-workers[10−12] demonstrate the truly remarkable degree to which heat of formation, entropy and heat capacity, for example, may be equated to a sum of group contributions, with the classic case of the hydrocarbons providing an early striking example. The additive contributions of a methyl and a methylene group to $\Delta H_f°(C_nH_{2n+2})$ are -10.08 and -4.95 kcal/mol, respectively, with an average deviation of less that 0.1 kcal/mol in the estimation of $\Delta H_f°(C_nH_{2n+2})$ for data up to and including $n = 12$. Such thermochemical methods are used to obtain the extensive tabulations of thermodynamic properties, which, as reviewed by Cohen and Benson,[12,13] are obtained primarily from heat capacity measurements over a range of temperatures along with the values of $\Delta H_f°$ and S at some temperature.

Energy additivity appears to fail in certain applications, but what at first appears as failures of the additivity concept, result in important new concepts, that of strain energy and aromatic stabilization. Baeyer[14] introduced the concept of strain energy in 1885, predicting that compounds with three- and four-membered rings would be less stable than larger cyclic molecules because of their deviation from tetrahedral carbon geometry. This prediction has, of course, been borne out by thermochemical measurements showing, for example, that the heat of formation of cyclopropane predicts it to be less stable than predicted by 3 times the contribution from the transferable methylene group.[11] Similarly, the heats of formation of aromatic molecules indicate that they are stabilized relative to structures in which there is an absence in the alternation of single and double bonds found in a cyclic aromatic system. Various estimates of the "aromatic stabilization of energy" of benzene based on heats of formation and hydrogenation and bond energy schemes place the value of this stabilization in the range of 36−41 kcal/mol. These properties, because they are defined in terms of measured heats of formation, should be recoverable from theory.

Additivity of Field Induced Properties

The same differencing techniques are used to determine the group contributions to other molecular properties, in particular field induced properties such as magnetic susceptibility and electric polarizability. Pascal, for example, tabulated the additive group contributions to the diamagnetic molecular susceptibility,[15] the determination of similar contributions to the electric molar polarization[16] being made possible by the introduction of the Abbe refractometer in 1874. As in the case of strain and resonance energies, the apparent failure of group additivity in accounting for the enhanced magnetic susceptibility of benzene, Pascal's so-called "aromatic exaltation", led to the eventual understanding of the special role of the induced ring currents in such molecules.[17,18] Aromatic exaltation, because it is based on measured values, must, like strain and resonance energies, be recoverable from a theory of an atom in a molecule.

Spectroscopic Properties of Atoms in Molecules

In more recent times, advances in spectroscopic techniques, in nuclear magnetic resonance and photoelectron spectroscopy in particular, have enabled the measurement of properties that are directly linked to the individual atoms in a molecule. The finding that the magnetic field exerted at a nucleus is affected by the screening resulting from the magnetic field created by the current induced in the electron density distribution enables one to identify individual atoms in a molecule, distinguishing not only between atoms differing by nuclear charge but also between the same atom in chemically inequivalent sites. A similar "chemical shift" achieving similar analytical goals is observed in the energies of the electrons photoemitted from the inner shells of an atom in a molecule. Clearly, the chemical shift is in both cases determined by the atom's molecular environment, as is always the case in measuring the properties of an atom in a molecule.

These techniques were preceded by infrared (IR) and Raman vibrational spectroscopy along with visible and UV electronic spectroscopy. IR spectroscopy in particular proved invaluable as an analytical technique in enabling the determination of the presence of a particular functional group in a molecule. One need only view the extensive compilations of group frequencies given as early as 1958 by Bellamy[19] to appreciate the ability of IR measurements to identify, through the observation of a characteristic frequency, a given chemical group and identify its immediate environment: the chemical shift of IR spectroscopy. Spectroscopic techniques enjoy the advantage that a single measurement, that of a frequency, determines the energy *difference* that identifies the atom or group in the molecule.

IR intensity measurements may be linked directly to the atoms in molecule concept through the experimental determination of the atomic polar tensor. The intensities of IR fundamentals are proportional to the square of the molecular dipole moment derivatives with respect to their normal coordinates. These data are usefully summarized in the molecular polar tensor, a quantity that has been determined for numerous molecules from gas-phase fundamental intensity measurement.[20] The molecular polar tensors may be re-expressed in terms of corresponding atomic contributions, the atomic polar tensors, which have been the source of numerous attempts to assign atomic charges to atoms in molecules.[21] The atomic polar tensor is clearly a measured molecular property that should be recovered by a physically correct model of an atom in a molecule.

The experimental finding of transferable additive group properties left open the question of what carried the chemical information: was it a property intrinsic to the group and if so how was the group defined or, was it to be attributed to contributions from each of the bonds within the group? The answer to this question had to await the development of the physics of an open system, because an atom or group within a molecule, however defined, is an open system.[22]

This listing is not meant to exhaust the measured properties that link one's *measurements* in the laboratory with their reliance on, belief in or dependence upon the existence of atoms in molecules with measurable, characteristic and additive properties. We have not for example, made reference to an experimentalist's use of the known chemical properties, reactive and static, of functional groups in the design and interpretation of experiments. It is difficult to reconcile one's use of the AIM concept in the laboratory with PAN's expressed belief that "atoms in a molecule are knowable by the mind or intellect, not by the senses." Before demonstrating anew that the atoms of QTAIM recover not only the measurable properties described above but also *all* measurable properties of atoms in molecules, we first critically consider some of the statements of PAN in the light of the experimental evidence of the AIM concept presented above.

What do PAN Imply by Measurement?

The following statement of PAN appears to be self-contradictory: "... the atom in a molecule cannot be directly observed by experiment, nor can one measure enough properties of an atom in a molecule to define it unambiguously." PAN thus admit to the measurement of the properties of an atom in a molecule, while at the same time stating that the atom itself cannot be observed. It is impossible to measure the properties of an object without observing it. The act of measurement requires that one interact with the system being measured. As a simple but pertinent example, one measures the elastic scattering of X-rays by the atoms of a crystal by exposing the crystal to an X-ray beam. The measured scattering factors are related to structure factors expressed in terms of atomic contributions which, by a Fourier transform, then enable one to measure an atom's contribution to the electron density of the crystal. The fact that the atoms in the crystal reflect the impinging X-rays implies that they have been observed. All spectroscopic measurements are a result of the interaction of a molecule or crystal with the electromagnetic field and all of the atoms in the molecule are thus "observed".

If by their statement PAN imply that one cannot observe an individual atom in the course of making a measurement, their statement is irrelevant for chemistry, as such a requirement is unnecessary for the implementation of the atomic concept, as made clear by the discussion on the measurement of atomic properties. In any event, atoms are "observable", in the electron densities obtained in accurate X-ray diffraction experiments[23] and in the images obtained from an atomic force microscope, images that are determined by the measured Ehrenfest force acting on the *interatomic surface of zero-flux* separating the microscope's probe from the sample.[24]

Finally, one comes to what is the most puzzling of the PAN statements: "... we cannot conceive of any experimental measurement which would confirm one definition as uniquely correct, while refuting all other possibilities." But of course, agreement with experiment is the only test of theory. As Hans Bethe stated, because of experiment, "In science you know you know."[3] One simply looks for that definition of an atom in a molecule that recovers the experimental measurements. There is no other test of a scientific theory. As to the statement "nor can one measure enough properties of an atom in a molecule to define it unambiguously", agreement with the properties that are measured suffices to establish quantum mechanics of both the total system and its proper open systems.

Recovery of Measurable Properties by the Physics of an Open System

Thanks to Schwinger,[25] the physics of an open system is now *the* general statement of quantum mechanics (QM), the physics of a closed isolated system being a special limiting case of the variationally derived equation of motion for any observable $\hat{G}$ given in[26]

$$N\int_{\Omega} d\mathbf{r} \int d\mathbf{r}' \, \partial\{\Psi^{*}\hat{G}(\mathbf{r})\Psi + \mathrm{cc}\}/\partial t = \{(i/\hbar)\langle\Psi|[\hat{H},\hat{G}(\mathbf{r})]|\Psi\rangle_{\Omega} + \mathrm{cc}\} - \oint d\mathbf{S}\,(\mathbf{r}_s;\Omega)\{\mathbf{J}_G(\mathbf{r}_s) + \mathrm{cc}\} \tag{2}$$

Equation 2 applies to any spatial region satisfying the QM boundary condition of exhibiting a zero-flux in $\nabla\rho(\mathbf{r})$, eq 1, to *proper open systems*. The theorems of quantum mechanics for a closed isolated system result from the vanishing of the surface term on the infinite boundaries. It hardly seems necessary to point to a scientific audience that a definition of an atom in a molecule must be based on a measurable property of a system using only information contained in the wave function, thereby enabling their description by quantum mechanics, if the resulting predictions of atomic properties are to be compared with and recover what is experimentally measurable. Hirshfeld atoms,[27] as espoused by PAN for example, predict no measurable properties.

One should appreciate the utility of eq 2: it enables one to predict any measurable property of a total system or equally, of each of its component atoms or groups. There is only one quantum mechanics and because QTAIM is the generalized statement of quantum mechanics, the atoms of QTAIM will necessarily recover what is experimentally measurable. Furthermore, because the predictions of quantum mechanics are unique, only the physics of an open system as embodied in QTAIM will recover the measured atomic properties. Thus, although one is free to subscribe to the PAN statement "Consequently, what AIM are remains ambiguous, subject to arbitrary (but disciplined) personal choice when specificity is required", it is with the understanding that any choice other than QTAIM will remove one from the domain of physics and measurement.

As reviewed on a number of occasions,[2,28,29] the measured properties of atoms are recovered by QTAIM. Interestingly, this recovery of experiment by QTAIM, a point of overriding physical importance, is never acknowledged, discussed nor commented upon, neither by PAN nor by those who question QTAIM. It should be stressed that eq 2 is essential for the prediction of the properties of an atom in a molecule, the physics of an open system requiring a contribution from the flux in the measured property density through the surface of the atom.[2,30] For example, it has been shown by Martin[31] from quite general physical considerations that the polarization of a dielectric (or the dipole moment of a molecule) requires in addition to the dipolar polarizarition of the unit cell, a contribution from the position weighted transport of charge across each of the surface elements bounding the cell, a result in complete agreement with the expression obtained from the physics of an open system.[32] QTAIM has been employed in the determination of the dipole moments of the individual molecular constituents in crystals of water, urea and *p*-nitroaniline to demonstrate the enhancement of the moments caused by the intermolecular interactions within the crystal.[33−35]

The transferability of group properties defined for proper open systems has been extensively studied and documented.[36−42] One distinguishes two types of transferable behavior in the extensive tabulations of experimentally derived group properties by Benson et al.: "perfect transferability" and compensatory transferability. A reader is referred to these papers for a full accounting of this most interesting field. Perfect transferability is that observed when the properties of a given group are transferable between molecules within both experimental and theoretical error, as found experimentally for the *n*-alkanes to within 0.2 kcal/mol[11] and as found theoretically (to cite a nontrivial example) for the four interior pairs of methylene groups in $C_{12}H_{26}$, all of which have the necessary average population of 8.000 ± 0.001 e and energies deviating from the energy of the standard methylene group by 0.6, 0.3, 0.2 and 0.2 kcal/mol.[38] In comparing theoretical energies with ΔH_f values, Wiberg[43] has shown that the correlation energy, the zero-point energies and the changes in ΔH_f on going from 298 to 0 K are well represented by group equivalents. The same additivity is in any event recovered in the energies of atomization at 0 K, corrected for zero-point energies.[44] No experimental heat measurements are left unpredicted, nor unexplained. Thus, for example, the measured strain energy of 27.5 kcal/mol for cyclopropane[11] is calculated to equal 27.6 kcal/mol by QTAIM,[39] bringing Baeyer's 1885 definition of "strain" into the realm of quantum mechanics. An estimate of the "resonance energy" of benzene of 41 kcal/mol is obtained by comparing the QTAIM energies of a C|H group in benzene and of the corresponding group in cyclohexene. Clearly, QTAIM atomic energies agree with chemical expectations when these are derived from measured heats.

The measured additive group contributions to electric polarizability[40] and magnetic susceptibility[18] are, of course, also recovered by QTAIM. The prediction of magnetic properties, including Pascal's aromatic exaltation[45] required that one first use QTAIM to devise new methods to overcome the gauge origin problem for the determination of the divergence-free induced current: the method of individual gauges for atoms in molecules (IGAIM)[46] and the continuous set of gauge transformations (CGST).[47] The magnetic shielding σ_N of nucleus N is fundamentally an atomic property, as brought to the fore by the atomic contributions determined by QTAIM.[48] In addition to the anticipated result that a given functional group contributes identical amounts to the shielding of a similarly located nucleus external to it through a series of molecules, is the remarkable result that the whole of the variation in σ_N can have its origin in the basin of atom N, the contributions from the external groups remaining constant, independent of chain length and position of N within the chain, the methyl group in ethane contributing the same to shielding a methyl carbon as does the butyl group in pentane.

An atomic charge is the measurable expectation value of a Dirac observable,[49] and it, together with its change, contribute to numerous measurable properties: to all molecular moments,[50] to molecular polarizability,[40] to intensities of electronic,[51] infrared[52,53] and Raman[54−56] absorption intensities, and to the polarization of a dielectric.[32,57] The properties resulting from an applied magnetic field parallel those induced by an electric field, with the induced atomic charge being replaced by the atomic current. The phenomena of polarization and magnetization, permanent or induced, have a common physical basis when described in terms of the physics of an open system, all expressions exhibiting a single underlying structure in terms of their atomic charges, currents and electric or magnetic polarizations.[32,50] This physics and the appeal to experiment it affords are lost when one employs other definitions of an atomic charge.

Physics demonstrates that atomic polar tensors obtained from IR intensities cannot be described solely in terms of atomic charges and their vibrationally induced changes as previously assumed but require in addition the atomic dipolar polarizations and their changes to properly describe charge relaxation effects;[52] the charge-flux and atomic dipole-flux of Bruns et al.[53] Their accurate prediction by QTAIM is another recent example of the physics of an open system providing both the necessary physics and an understanding of the atomic origins of measured properties.[53,58] Table 1 lists examples of the applications of QTAIM atomic properties to the prediction of and correlation with experimentally measured properties.

With regard to the important property of transferability PAN state "..., and Hirshfeld atoms are highly transferable." They cite no examples, because there are none, as opposed to examples illustrating the contrary. As previously discussed,[50] any definition of an atom that distributes its density over the entire molecule of which it is a part, that is, an atom without the physical boundary required by the physics of an open system, can clearly never recover the observation essential to all of chemistry, that atoms and functional groups can exhibit characteristic properties *despite changes in their immediate environments*. The atoms of QTAIM on the other hand maximize any possible transferability in form and properties. Two pieces of matter (two atoms) are identical and possess identical properties only if they have identical charge distributions. Because an atom of QTAIM is defined by its charge distribution as a bounded region of real space, its form necessarily reflects its properties and they thus maximize the transferability of both form and properties from one molecule to another, a point driven home by the finding that QTAIM groups can exhibit the limiting form of "perfect transferability". Many examples from both experiment[59−64] and theory[37,65−67] have demonstrated the remarkable transferability of the charge distributions and properties of chemical groups defined as open systems, particularly of main chain and functional groups common to the amino acids and polypeptides. The transferability of groups bounded by zero-flux surfaces is utilized in the theoretical construction of large molecules by the linking together of groups defined in smaller systems, to define the properties of polypeptide[67] and complex opioids, [66] for example.

Surely the most important property exhibited by the atoms of theory is the paralleling behavior in their form and properties. Though demanded by the simple truism that two identical objects possess identical properties, it is the bounded regions defined by the physics of an open system that identifies the objects exhibiting this most fundamental of properties. This observation appears to be at odds with the theorem of Hohenberg and Kohn,[68] which states that the electron density is a unique

TABLE 1: Examples of the Application of QTAIM Atomic Properties to the Prediction of and Correlation with Experimentally Measured Properties

application	ref
Examples of the Recovery and/or Prediction of the Experimentally-Determined Additive Atomic and Group Contributions from QTAIM	
experimental additivity of heats of formation	36
experimental additivity of magnetic susceptibility	17, 18, 46, 47, 72
experimental additivity of atomic and group volumes	42
experimental additivity of moments and polarizability	73−75
interpretation and prediction of Raman intensities	54−56, 73, 75
prediction of IR intensities	53, 58, 76, 77
experimental group additivity in silanes	37
recovering the experimental transition probabilities	51
dielectric polarization in crystals and the definition of group contributions to the molecular dipole and quadrupole moments	32, 57, 78
recovering Wigner−Seitz cells in a crystal	79
recovering Pascal’s aromatic exaltations	2
providing an atomic basis for electron localization and delocalization	7, 80−82
Examples of Experimental Properties *Empirically* Related to and/or Predicted from QTAIM Atomic Properties	
prediction of pK_a from the atomic energy of the acidic hydrogen	83
prediction of a wide array of biological and physicochemical properties of the amino acids including the genetic code itself and the effects of mutation on protein stability	65
prediction of protein retention times	84
prediction of HPLC column capacity factors of high-energy materials	85
prediction of NMR spin−spin coupling constants from the electron delocalization indices	86, 87
simultaneous consistent prediction of five bulk properties of liquid HF using QTAIM charges and higher multipoles in MD simulation	88
classification of atom types in proteins with future potential applications in force fields design	89−91
reconstructing large molecules from transferable fragments/atoms in molecules	41, 65−67, 92−103
atomic partitioning of the molecular electrostatic potential	104−106
providing an atomic basis for curvature-induced polarization in carbon nanotubes and nanoshells	107

functional of the external potential, thereby excluding the transfer of the density distribution of an atom from one system to another with a different external potential. Thus DFT does not account for the fundamental observation underlying the theory of atoms in molecules: that what are apparently identical distributions of charge can be observed for systems with different external potentials and that these atoms contribute identical amounts to the energies and all other properties of the systems in which they occur.

PAN cite a paper by Bader and Becker[69] that appears to suggest that perfect transferability is an unattainable limit, a suggestion based on the extension of the theorem of Hohenberg and Kohn by Riess and Münch[70] to an arbitrary piece of some total system. However, PAN fail to mention the important conclusion given in the paper by Bader and Becker: no limit is placed on how closely elements of density from two systems may approach one another before requiring that the systems be identical. Because one finds examples of transferability of density and properties between different molecules that lie within the error limits of both experiment and theory, the limit is of no practical importance. As Dr. P. Ayers has pointed out in private discussion, the Hohenberg−Kohn theorem is stated for a closed isolated system with a fixed number of electrons and thus makes no comment on the transferability of an open system between molecules with differing numbers of electrons. Indeed, the separate changes to the external potential energy and to the repulsive contributions for a transferable group change by tens of thousands of kcal/mol between members of a homologous series. It is the virial field—the *total* potential energy density—that remains unchanged on transfer. The virial field, together with the electron and kinetic energy densities are all determined by the one-electron density matrix and it is the short-range nature of this matrix that underlies the working hypothesis of chemistry, of a functional group exhibiting a characteristic set of properties.[2,71]

A chemist can be confident in the knowledge that the measurements he or she makes in the laboratory are a result of their interacting with atoms whose form and properties are predicted by quantum mechanics.

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Note Added in Proof. After the submission of this paper, a paper appeared by T. T. Tsong in *Physics Today*, March 2006, p 31, entitled “Fifty Years of Seeing Atoms”. The paper was written to commemorate “the 50th anniversary of the first direct observation of atoms”, observations made with the field-ion microscope. The paper traces the “long journey” from the initial observations to the present day use of the transmission electron microscope, the field-emission microscope and the scanning tunneling microscope. An interested reader is invited to sample the numerous pictures of surface atoms presented in this article.

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