

This is the peer reviewed version of the following article: Clark Timothy, Politzer Peter, Murray Jane S. Correct electrostatic treatment of noncovalent interactions: the importance of polarization. WIREs Comput Mol Sci 2015, 5: 169-177. doi: 10.1002/wcms.1210, which has been published in final form at <http://wires.wiley.com/WileyCDA/WiresArticle/wisId-WCMS1210.html> . This article may be used for non-commercial purposes in accordance With Wiley-VCH Terms and Conditions for self-archiving

Article title: Correct Electrostatic Treatment of Non-Covalent Interactions: The Importance of Polarisation

Timothy Clark,* Computer-Chemie-Centrum, Friedrich-Alexander-Universität Erlangen-Nürnberg (Tim.Clark@fau.de), Peter Politzer, Chemistry Department, University of New Orleans, Jane S. Murray, Chemistry Department, University of New Orleans

Abstract

The Hellmann-Feynman theorem assures us that the forces felt by the nuclei in a molecule or complex are purely classically electrostatic. Nevertheless, it is often claimed (incorrectly) that electrostatic considerations are not sufficient to explain non-covalent interactions. Such assertions arise largely from neglecting the polarisation that is inherently part of the electrostatic interaction, and must be taken into account. Accordingly, we now outline the requirements for a correct electrostatic treatment and discuss the difference between physical observables and quantities that arise from mathematical models. Polarisation and donor-acceptor charge transfer are shown to be equivalent for weak interactions. However, polarisation is a physical observable while charge transfer, in this context, is mathematical modelling. We also discuss some popular schemes for analysing non-covalent interactions.

Il résulte donc de ces trois essais, que l'action répulsive que les deux balles électrisées de la même nature d'électricité exercent l'une sur l'autre, suit la raison inverse du carré des distances.

Charles-Augustin de Coulomb, *Premier mémoire sur l'électricité et le magnétisme*, Histoire de l'Académie Royale des Sciences, **1785**, 569-577.

Introduction

The preceding is Coulomb's original formulation of his inverse square law for the magnitude of the force between two charged bodies, and hence of the inverse distance dependence of the interaction energy

between them. This " $\frac{1}{R_{ij}}$ " dependence forms the basis of energy calculations in modern quantum

chemistry; the potential energy terms in the Hamiltonian are all Coulombic. In fact, from the Hellmann-

Feynman theorem^{1,2,3,4} (see Sidebar 1), it follows rigorously that if the electronic density of a molecule is known, then all of the forces upon its nuclei (and hence bonding interactions) can be determined using purely classical electrostatics. As Levine put it, “...there are no ‘mysterious quantum-mechanical forces’ acting in molecules.”⁵ We need quantum mechanics to obtain the electronic density, but once we have it, we can calculate the energy using only classical electrostatics.

The Hellman-Feynman Theorem

This theorem was derived, apparently independently, by at least four persons,^{1,2,3,4} although only two of them have their names attached to it. Hans Hellmann was a German physicist who emigrated to the Soviet Union in 1934. He was executed in 1938 as part of the Great Purge. Richard Feynman derived the theorem while an undergraduate at the Massachusetts Institute of Technology.

Nevertheless, electrostatic interpretations of non-covalent (and covalent) interactions have often been viewed as inadequate. For instance, the fact that the halogen-bonded complex $\text{H}_3\text{C}-\text{Cl}\cdots\text{O}=\text{CH}_2$ is predicted to be bound⁶ despite the chlorine lacking a significant positive potential⁷ has sometimes been asserted to be a failure of the electrostatic interpretation.⁸ However, the problem is not the electrostatic interpretation but the fact that the potential on the chlorine prior to interaction does not reflect the polarisation caused by the electric field of the oxygen in $\text{O}=\text{CH}_2$. Figure 1 shows that a charge of -0.2762^9 situated 3 \AA from the chlorine nucleus along the extension of the C-Cl bond does indeed result in a positive (σ -hole) potential on the chlorine.

Figure 1

Despite such effects being extremely easy to demonstrate, it is often still argued that additional stabilizing factors must be invoked in some types of non-covalent bonding. There has even been claimed “*a new and what appears to be a fundamentally different sort of noncovalent interaction which does not have any precedent in the literature.*”¹⁰ (Actually, analogous interactions have been known experimentally and reported in the literature for decades, as is extensively documented in recent reviews.^{11,12})

We shall now show that the problem lies not with the electrostatic interpretation itself, but rather with the incomplete and unrealistic manner in which it is applied. The Hellmann-Feynman theorem tells us that this must be the case. Our present purpose is to outline a “correct electrostatic treatment” that makes it unnecessary to resort to explanations that are more complex. We will also discuss some fundamental aspects of bonding theory and examine several popular analysis schemes.

Fundamentals

The list of concepts that do not really exist (i.e. are not physically measurable) but still play important roles in our understanding of bonding is long: orbitals, correlation, net atomic charges, bond orders, atoms within molecules, chemical bonds, etc. Such concepts usually, but not always, arise from approximations made in order to make the mathematical theory tractable. None of them can be identified uniquely, but they have nonetheless played major roles in our understanding of chemistry.

It is important to understand, however, that models are simply models; one should not be tempted to think of them as reality. This sounds obvious and trivial, but examples abound in which questions that are completely meaningless outside of a given approximate model have been discussed intensely and sometimes acrimoniously.¹³ It has even been claimed, and refuted, that orbitals have been observed.¹⁴ In order to remove some of the confusion, we now present a purist view of reality vs. modelling in intermolecular interactions.

In doing this, we are immediately faced with an insurmountable problem: One of the most popular concepts of qualitative molecular-orbital theory cannot be defined rigorously. Electron donor-acceptor interactions, as made popular by Mulliken¹⁵ and Fukui,¹⁶ and which ultimately imply charge-transfer,¹⁷ cannot be defined without invoking entities that cannot be separated uniquely. Strictly speaking, molecules or collections of molecules are (within the Born-Oppenheimer approximation) groups of fixed positive nuclei within clouds of indistinguishable electrons. There are no atoms or bonds, so that electrons cannot be assigned to particular atoms or molecules uniquely; we must in some arbitrary way define borders between atoms or molecules. Charge transfer is not separable from polarisation in non-covalent complexes. It is real, however, for radical-ion pairs and for pairs of molecules at large separations.¹⁸

We are certainly not advocating abandoning concepts that have served so well in the theory of reactivity, but it must be very clear that they are models, not physical observables. As we shall point out, the complicating factor in the case of charge transfer (donor-acceptor interactions) is that a real and observable quantity, polarisation, can masquerade as charge transfer and fool the unwary.¹⁹ This can lead to confusion.

Molecular Electrostatics

A correct electrostatic interpretation of non-covalent interactions requires an accurate representation of the molecular electrostatic potential $V(\mathbf{r})$ at any point \mathbf{r} . This is the standard quantity used to define and visualize the electrostatic properties of a molecule (see Sidebar 2).

The Molecular Electrostatic Potential

The electrostatic potential $V(\mathbf{r})$ at a position \mathbf{r} in the space of a molecule is the standard quantity used to define and visualize the electrostatic properties of a molecule. It is given by:

$$V(\mathbf{r}) = \sum_A \frac{Z_A}{|\mathbf{R}_A - \mathbf{r}|} - \int \frac{\rho(\mathbf{r}') d\mathbf{r}'}{|\mathbf{r}' - \mathbf{r}|}$$

where Z_A is the charge on the nucleus of atom A situated at position \mathbf{R}_A and $\rho(\mathbf{r})$ is the molecule's electronic density. $V(\mathbf{r})$ is simply the interaction energy between the molecule (with its static electronic density) and a unit positive charge situated at \mathbf{r} . Thus, $V(\mathbf{r})$ as usually calculated does not reflect the polarisation of the molecule that is produced by an external charge or field.

Calculating $V(\mathbf{r})$ explicitly involves integrating the electronic density over space and is therefore computer-intensive. Accordingly, simplified models abound. Perhaps the most common is that in which the electrostatic effect of each atom is represented by a single point charge (monopole) at its nucleus (the net atomic charge). Numerous procedures for assigning magnitudes to such point charges have been proposed.²⁰ A seemingly reasonable one is to first calculate $V(\mathbf{r})$ at an array of points around the molecule according explicitly and then to fit the atom-centred monopoles to these $V(\mathbf{r})$ as well as possible. Even if a good fit is obtained, however, the resulting electrostatic model is often poor, failing to reproduce essential features of the actual $V(\mathbf{r})$. For instance, Figure 2 compares a rigorously computed $V(\mathbf{r})$ on the 0.001 a.u. isodensity surface of iodobenzene and the equivalent plot calculated from fitted point charges; the latter is the best possible atomic monopole model for reproducing the rigorous $V(\mathbf{r})$.

Figure 2

The colour scale in Figure 2 has been compressed to emphasize the differences. Nonetheless, it is clear that the negative equatorial belt around the iodine and its positive "σ-hole" (the positive potential on the extension of the C-I bond)^{11,21,22} are not reproduced, even by optimal atomic charges. Such inadequacy has been called the "fallacy of atomic charges."²³ The only exceptions are homodiatomic molecules, which can be represented accurately by two atomic monopoles.²⁴

A second simplified technique is to express the entire electrostatic character of the molecule in terms of its dipole moment or a series of multipole moments at a single centre within the molecule.²⁵ Such techniques can only be considered very coarse representations of molecular electrostatics. A more effective approximation to the rigorous $V(\mathbf{r})$ for fast but nonetheless accurate calculations is a distributed multipole analysis (DMA) in which multipole series are situated at several centres (e.g. atomic positions, bond midpoints) throughout the molecule.²⁶ A particular subset of such distributed multipole models is that in which a multipole series is assigned to each atomic centre.²⁷ Such atom-centred multipole models are accurate at non-bonding distances from atoms and have the advantage that they are identical to the

technique used in MNDO-like semiempirical molecular orbital theories to approximate two-electron integrals.^{28,29}

Analysing non-covalent interactions

Decomposition analyses

A common approach to analysing intermolecular interactions is to decompose them into notional “components”: electrostatics, dispersion, polarisation or induction, charge transfer, exchange, Pauli repulsion, orbital overlap, etc. (Different decomposition schemes postulate different sets of components.) There are several problems with such procedures. One is that some of these components are real (i.e. physically measurable) while others are simply constructs derived from a mathematical model. Another difficulty is that many of these components are not independent of each other, so that different decomposition schemes can increase the role of one at the cost of another.

This brings us to one of the key flaws in many current descriptions of non-covalent bonding. The electrostatic contribution is often modelled using the unperturbed electronic-density distributions of the reactants. This is incomplete and misleading because it ignores polarisation, which is an intrinsic and inseparable part of an electrostatic interaction. Failure to take it into account means that the electrostatic interaction is not being described fully.

Compounding the error, polarisation (or induction) and charge transfer are typically introduced as two separate contributions. In the context of non-covalent interactions, the latter is usually invoked as the transfer of a small quantity of electronic charge from one of the interacting molecules (the “donor”) into an antibonding molecular orbital of the other (the “acceptor”), normally the lowest unoccupied one (LUMO). However, “transferring” a portion of an indivisible electron into a non-existent orbital is simply mathematical modelling of the physical reality, which is polarisation of the “donor’s” electronic charge toward the “acceptor”.

Consider the $\text{H}_3\text{C}-\text{Cl}\cdots\text{O}=\text{CH}_2$ complex mentioned earlier.^{6,7} It is the polarisation of the chlorine by the electric field of the oxygen that induces the positive chlorine potential that results in an attractive interaction,³⁰ as is shown in Figure 3. Note that representing a halogen-bond acceptor (in this example water) in terms of one or more point charges, which cannot indulge in charge transfer, produces an electronic density redistribution in the $\text{H}_3\text{C}-\text{Cl}$, Figure 3(a), that is very similar to that found in the complete calculation with a water molecule, Figure 3(b). Furthermore, both redistributions strongly resemble the LUMO of $\text{H}_3\text{C}-\text{Cl}$, Figure 3(c). We note here that a general consensus has been established for halogen bonding in which both electrostatic interactions (including polarization) and dispersion (which according to the Feynman interpretation is also electrostatic in nature)⁴ are important.⁶ However, the Feynman

interpretation of dispersion also rests on polarization effects, so that the two notionally different types of interaction are difficult to separate.

Figure 3

A major conceptual problem with decomposition analyses is their failure to distinguish between what has a physical basis and what results from one or more of the mathematical models used in the calculations. Polarisation and donor-acceptor charge transfer are a good example of this. It is often overlooked that they are essentially equivalent. There are many ways to demonstrate this;³¹ one of the simplest is based on self-consistent-field theory:

Consider a molecule whose Fock matrix is as depicted schematically in Figure 4.

Figure 4

The only difference from a normal Fock matrix in the atomic-orbital basis is that Figure 4 shows a matrix expressed in the molecular orbital (MO) basis (i.e. the rows and columns each represent a molecular orbital rather than an atomic orbital). For the converged molecule without an external electrostatic perturbation, the diagonal (black) elements contain the eigenvalues of the MOs and all others (the coloured ones) are zero. The effect of applying an external electric field is to polarize the molecule, so that the wavefunction is no longer converged and some off-diagonal elements become non-zero. Only the occupied-virtual (yellow) elements lead to a change in the energy of the system. Mixing two occupied orbitals or two virtual ones has no effect because it does not change the overall electronic density.

In order to converge to a new polarized wavefunction, the non-zero off-diagonal elements must be eliminated. This can be achieved by mixing the virtual and the occupied orbitals to eliminate the yellow elements of the Fock matrix. The mathematical procedure used to do this is known as Givens (or Jacobi) rotation^{32,33} and is characterized by a rotation angle that defines the amount of mixing. This angle can be estimated from perturbation theory to be,

$$\omega = \frac{\mathfrak{F}_{ij}}{(\varepsilon_i - \varepsilon_j)} \quad (1)$$

where \mathfrak{F}_{ij} is the element of the Fock matrix in the MO basis that connects occupied orbital i with virtual orbital j and ε_i and ε_j are the eigenvalues of orbitals i and j , respectively.³⁴

Equation (1) shows that MOs mix most strongly in a perturbed (polarized) molecule when the occupied-virtual interaction element \mathfrak{F}_{ij} is large and/or the energy difference $(\varepsilon_i - \varepsilon_j)$ is small. The smallest energy difference between occupied and virtual orbitals is the HOMO-LUMO gap, meaning that high-lying occupied orbitals and low-lying virtual ones will mix most strongly on polarisation. This conclusion is independent of

whether the orbitals are centred on the same molecule or different ones. Thus a small HOMO-LUMO gap, which is viewed as promoting charge transfer, also corresponds to greater polarisation. In mathematical terms, therefore, polarisation and donor-acceptor charge transfer are equivalent. It has been pointed out that when polarisation and charge transfer are treated separately, the former increases and the latter decreases as the basis set becomes larger^{18,35} (and the calculations therefore more accurate); charge transfer disappears in the complete basis set limit in most types of analysis.

The arbitrary nature of charge-transfer formulations is evident in an example due to Stone and Misquitta.³⁶ Imagine calculating a dimer using *ab initio* or density-functional theory with a good, but not extremely large basis set. Most analyses will suggest that some of the dimerization energy results from a charge-transfer (donor-acceptor) interaction. Now repeat the calculation but using, instead of the original basis set, an extremely large one centred only on the atoms of one molecule. Such a one-sided calculation would give essentially the same results as one in which basis functions are situated on both molecules. However, by definition, there now cannot be any donor-acceptor interaction because one of the molecules has no basis functions. This example shows that donor-acceptor (charge-transfer) interactions are a consequence of the artificial partitioning of the basis set into functions “belonging” to one molecule or the other. Polarisation, on the other hand, appears in both of the above calculations to the same extent; the only difference is that in the first case the molecules “borrow” basis functions from one another to represent the polarisation, whereas in the second all of the basis functions “belong” to one molecule.

Invoking charge transfer is mathematically acceptable (although not physically observable), as long as it is made clear that polarisation and charge transfer are equivalent. However, we suggest that Occam’s razor^{37,38} should lead us to be content with the simple and correct electrostatic treatment (that includes polarisation), rather than implicating non-observables. Above all, it is wrong to claim that purely electrostatic treatments do not work, when the problem is that polarisation (an intrinsic part of an electrostatic interaction) is being neglected.

Symmetry-Adapted Perturbation Theory

Symmetry-adapted perturbation theory (SAPT)^{39,40} was designed for determining the interaction energy in a non-covalent complex from a single calculation for the complex (without additional ones for the separated molecules). It works well for this purpose and has been extended to DFT calculations,^{41,42} from which reliable interaction energies can also be obtained directly. SAPT is a mathematical technique that gives good results for its original purpose and contains quantities that have been related, but not uniquely, to notional components of an interaction. There is one technical problem, which was pointed out by Stone and Misquitta:³⁶ the perturbation expressions for exchange-repulsion and charge transfer (which are opposite in sign) contain terms that make their energies too large in magnitude. This is not a problem in the original theory because the errors cancel, but it renders separate estimates of these two quantities

meaningless; only their sum should be considered (which itself may or may not be significant, since it is simply part of a model). In any case, any SAPT analysis that reports large and opposing exchange-repulsion and charge-transfer energies should be treated with caution.

Quantum theory of Atoms in Molecules

The original quantum theory of atoms in molecules (QTAIM) introduced by Bader is actually very purist.⁴³ The first and second derivatives of the molecular electronic density are used to define boundaries that separate “basins.” Bader took pains to emphasize that his technique identifies what he called bond paths, not bonds, and he used the Hellmann-Feynman theorem to argue that these paths lead to stabilization. Thus his approach was purely electrostatic.

The arbitrariness in QTAIM begins when the electronic basins are labelled “atoms.” We know that this is not totally appropriate because mystical entities called non-nuclear attractors (basins of electronic density without an atomic nucleus) are sometimes observed. These can be significantly populated (experimentally, up to approximately 0.8 electrons but higher populations are possible) and have also been seen in experimentally determined electron densities.⁴⁴ This should indicate that QTAIM is not suitable as an interpretive tool because the sum of the net “atomic charges” need not add up to the charge on the molecule. It has also been pointed out that the maxima along bond paths (bond critical points) do not necessarily indicate attractive interactions between the atoms connected by the bond paths.⁴⁵

Orbital-Based Treatments

Perhaps the best-known orbital-based approach is Natural Bond Orbital (NBO) analysis.⁴⁶ Significantly, the authors noted that NBO cannot distinguish between polarisation and charge-transfer interactions, so that the two terms are synonymous (although we prefer polarisation).

Absolutely localized molecular orbital (ALMO) analysis is among the most thorough methods available;⁴⁷ it considers polarisation and charge transfer separately, treating the former self-consistently. ALMO does, by design, find some charge-transfer contributions within its localized molecular orbital picture. This represents a problem for a purist view, since it implies defining arbitrary borders between molecules, which in this case are identified via the ALMOs. However ALMO does provide a well-founded and consistent picture. Polarisation increases at the expense of charge transfer in ALMO with increasing size of the basis set, as expected, but upper and lower bounds for the polarisation energy have been estimated.¹⁸ However, the sum of polarisation and charge-transfer terms is constant, so that we prefer not to separate them.

Density-Difference Analysis

Examining the difference in electronic density between a complex and its unperturbed components allows one to visualize (qualitatively) the electronic redistribution accompanying the formation of the

complex^{17,35,48} We attribute this to polarisation.³⁰ Any attempt to use density-difference calculations to quantify charge transfer would again require introducing artificial borders between molecules.

Conclusion

The neglect of polarisation, or attributing its effects to charge transfer, often leads to incorrect assertions that purely electrostatic interpretations are inadequate. Recognition that polarisation is an intrinsic part of an electrostatic interaction, and must be taken into account, would yield the correct results. Note that this is also true for treatments based on dipole moments. It is often claimed that the dipole moment of water should lead to a symmetrical, bridged structure for the water dimer. However, the dipole moment is shifted by polarisation, so that the correct structures is predicted (see Figure 5).

Figure 5

Polarisation and charge transfer are, for weak interactions, two ways of describing the same phenomenon. Energy decomposition analyses divide this one interaction into two non-orthogonal parts; the proportion found varies with method and basis set but the sum often remains constant, depending on the analysis method. There can be no unique way of separating them. Polarisation is measurable and an integral part of Coulomb interactions that must be considered in a complete electrostatic model. We therefore define a “correct” electrostatic model as follows:

1. A satisfactory representation of the electrostatic potential of a molecule is necessary. If obtaining this explicitly is not practical, then at least an atom-centred multipole model should be used.
2. Polarisation is an inherent part of electrostatic interactions and must not be neglected. Since it can masquerade as charge transfer, it should be considered directly by point-charge modeling,^{9,30,49} ALMO^{18,47} or Stone and Misquitta’s modification of SAPT.³⁶
3. In SAPT, QTAIM and density difference analyses, care should be taken to distinguish clearly between their physically well-based aspects and more arbitrary interpretations.
4. The distinction between physical reality and mathematical modelling should always be kept in mind.

References

- ¹ Güttinger P. Das Verhalten von Atomen im magnetischen Drehfeld Z. Phys. 1932, 73:169-184.
- ² Pauli W. Principles of Wave Mechanics, Handbuch der Physik, 24. Springer, Berlin, 1933, 162.
- ³ Hellmann H. Zur Rolle der kinetischen Elektronenenergie für die zwischenatomaren Kräfte Z. Phys. 1933, 85:180-190.
- ⁴ Feynman RP. Forces in Molecules Phys. Rev. 1939, 56:340-343.
- ⁵ Levine IN. Quantum Chemistry, 5th edn. Prentice-Hall, Upper Saddle River, NJ, 2000.
- ⁶ Riley KE, Hobza P. Investigations into the nature of halogen bonding including symmetry adapted perturbation theory analyses J. Chem. Theor. Comput. 2008, 4:232-242.
- ⁷ Politzer P, Lane P, Concha MC, Ma Y, Murray JS. An overview of halogen bonding J. Mol. Model. 2007, 13:305-311.
- ⁸ To cite one such occasion: *“For example, CH₃Cl can form a halogen bond with OCH₂, which is impossible according to the σ -hole theory because of the lack of a positive potential region around the Cl.”*, Ding X, Tuikka M, Haukka M. Halogen Bonding in Crystal Engineering, Recent Advances in Crystallography. In Jason BB, ed.; 2012, ISBN: 978-953-51-0754-5, InTech, DOI: 10.5772/48592. Available from: <http://www.intechopen.com/books/recent-advances-in-crystallography/halogen-bonding-in-crystal-engineering>
- ⁹ Murray JS, Riley KE, Politzer P, Clark T. Directional Weak Interactions: σ -Hole Bonding Aus. J. Chem. 2010, 63:1598-1607.
- ¹⁰ Scheiner S. On the properties of X...N noncovalent interactions for the first-, second-, and third-row X atoms J. Chem. Phys. 2011, 134:164313-164321.
- ¹¹ Politzer P, Murray JS, Clark T. Halogen bonding and other σ -hole interactions: a perspective Phys. Chem. Chem. Phys. 2013, 15:11178-11189.
- ¹² Politzer P, Murray JS, Janjić GV, Zarić SD. σ -Hole Interactions of Covalently-Bonded Nitrogen, Phosphorus and Arsenic: A Survey of Crystal Structures Crystals 2014, 4:12-31.
- ¹³ Magnusson E. Hypercoordinate Molecules of Second-Row Elements: d Functions or d Orbitals? J. Am. Chem. Soc. 1990, 112:7940-7951.
- ¹⁴ Scerri R. Have Orbitals Really Been Observed? J. Chem. Educ. 2000, 77:1492-1494.
- ¹⁵ Mulliken RS. Molecular Compounds and their Spectra. II J. Am. Chem. Soc. 1952, 74:811-824.

- ¹⁶ Fukui K. Role of Frontier Orbitals in Chemical Reactions *Science* 1982, 218:747-754.
- ¹⁷ See, for instance, Dapprich S, Frenking G. Investigation of Donor-Acceptor Interactions: A Charge Decomposition Analysis Using Fragment Molecular Orbitals *J. Phys. Chem.* 1995, 99:9352-9362.
- ¹⁸ Azar RJ, Horn PR, Sundstrom EJ, Head-Gordon M. Useful lower limits to polarization contributions to intermolecular interactions using a minimal basis of localized orthogonal orbitals: theory and analysis of the water dimer *J. Chem. Phys.* 2013, 138:084102-084115.
- ¹⁹ Chen J, Martínez TJ. QTPIE: Charge transfer with polarization current equalization. A fluctuating charge model with correct asymptotics *Chem. Phys. Lett.* 2007, 438:315-320.
- ²⁰ Wiberg KB, Rablen PR. Comparison of atomic charges derived via different procedures *J. Comput. Chem.* 1993, 14:1504-1518.
- ²¹ Clark T, Hennemann M, Murray JS, Politzer P. Halogen Bonding: The σ -Hole *J. Mol. Model.* 2007, 13:291-296.
- ²² Clark T. σ -Holes *WIREs Comput. Mol. Sci.* 2013, 3, 13-20.
- ²³ Politzer P, Murray JS, Concha MC. σ -Hole bonding between like atoms: a fallacy of atomic charges *J. Mol. Model.* 2008, 14:659-665.
- ²⁴ Sedlak R, Deepa P, Hobza P, Why is the L-Shaped Structure of $X_2 \cdots X_2$ ($X = F, Cl, Br, I$) Complexes More Stable than Other Structures? *J. Phys. Chem. A.* 2014, 118, 3846-3855.
- ²⁵ Tomasi J, Menucci B, Cammi R. MEP: a tool for interpretation and prediction. From molecular structure to solvation effects, Molecular Electrostatic Potentials; Concepts and Applications. In Murray, JS, Sen, KD, eds. Elsevier, Amsterdam; 1996 1-103.
- ²⁶ Stone AJ, Alderton M. Distributed multipole analysis methods and applications *Molecular Physics* 1985, 56:1047-1064.
- ²⁷ See, for instance, Horn AHC, Lin J-H, Clark T. Multipole electrostatic model for MNDO-like techniques with minimal valence spd-basis sets *Theor. Chem. Acc.* 2005, 114:159-168; Erratum: *Theor. Chem. Acc.* 2007, 117:461-465.
- ²⁸ Dewar MJ S, Thiel W. Ground states of molecules. 38. The MNDO method. Approximations and parameters *J. Am. Chem. Soc.* 1977, 99:4899-4907.
- ²⁹ Clark T, Stewart JJP. MNDO-like Semiempirical Molecular Orbital Theory and its Application to Large Systems. In Reimers, JJ, ed. *Computational Methods for Large Systems*. Wiley, Chichester; 2011 Chapter 8 (ISBN: 978-0-470-48788-4).

- ³⁰ Clark T, Murray JS, Politzer P. The Role of Polarisation in a Halogen Bond *Aus. J. Chem.* 2014, 67:451-456.
- ³¹ Maroulis, G, ed. *Computational Aspects of Electric Polarizability Calculations: Atoms, Molecules and Clusters*. IOS Press, Amsterdam; 2006.
- ³² Cybenko G. Reducing Quantum Computations to Elementary Unitary Operations *Comput. Sci. Eng.* 2001, 3:27-32.
- ³³ Press WH, Teukolsky SA, Vetterling WT, Flannery BP. *Numerical Recipes: The Art of Scientific Computing*, 3rd edn. Cambridge University Press, New York; 2007.
- ³⁴ Stewart JJP, Csaszar P, Pulay P. Fast semiempirical calculations *J. Comput. Chem* 3:227-228.
- ³⁵ Sokalski WA, Roszak SM. Efficient Techniques for the Decomposition of Intermolecular Interaction Energy at SCF Level and Beyond *J. Mol. Struct. (Theochem)* 1991, 234:387-400.
- ³⁶ Stone AJ, Misquitta AJ. Charge Transfer in Symmetry-Adapted Perturbation Theory *Chem. Phys. Lett.* 2009, 473:201-205.
- ³⁷ William of Ockham (c. 1287-1347). One way of stating Occam's razor is: Given two equivalent explanations, the simpler one is usually better.
- ³⁸ Politzer P, Riley KE, Bulat FA, Murray JS. Perspectives on Halogen Bonding and Other σ -Hole Interactions: *lex parsimoniae* (Occam's razor) *Comput. Theoret. Chem.* 2012, 998:2-8.
- ³⁹ Szalewicz K. Symmetry-adapted perturbation theory of intermolecular forces *WIREs: Computational Molecular Science* 2012, 2:254-272.
- ⁴⁰ Jeziorski B, Moszynski R, Szalewicz K. Perturbation Theory Approach to Intermolecular Potential Energy Surfaces of van der Waals Complexes *Chem. Rev.* 1994, 94:1887-1930.
- ⁴¹ Podeszwa R, Szalewicz K. Accurate interaction energies for argon, krypton, and benzene dimers from perturbation theory based on the Kohn–Sham model *Chem. Phys. Lett.*, 2005, 412, 488-493.
- ⁴² Heßelmann A, Jansen G, Schütz M. DFT-SAPT with density fitting: A new efficient method to study intermolecular interaction energies *J. Chem. Phys.*, 2005, 122, 014103/1-17
- ⁴³ Bader RFW. *Atoms in Molecules: A Quantum Theory*. Oxford University Press, Oxford, 1990.
- ⁴⁴ Platts JA, Overgaard J, Jones C, Iversen BB, Stasch A. First Experimental Characterization of a Non-nuclear Attractor in a Dimeric Magnesium(I) Compound *J. Phys. Chem. A* 2011, 115:194-200.

⁴⁵ Foroutan-Jejad C, Shahbazian S, Marek R. Toward a Consistent Interpretation of the QTAIM: Tortuous Link Between Chemical Bonds, Interactions, and Bond/Line Paths *Chem. Eur. J.* 2014, 20:10140-10152.

⁴⁶ Reed AE, Curtiss LA, Weinhold F. Intermolecular Interactions from a Natural Bond Orbital, Donor-Acceptor Viewpoint *Chem. Rev.* 1988, 88:899-926.

⁴⁷ Khaliullin RZ, Cobar EA, Lochan RC, Bell AT, Head-Gordon M. Unravelling the Origin of Intermolecular Interactions Using Absolutely Localized Molecular Orbitals *J. Phys. Chem. A* 2007, 111:8753-8765.

⁴⁸ Sola M, Mestres J, Carbo R, Duran M. A comparative analysis by means of quantum molecular similarity measures of density distributions derived from conventional ab initio and density functional methods *J. Chem. Phys.* 1996, 104:636-647.

⁴⁹ Hennemann M, Murray JS, Riley KE, Politzer P, Clark T. Polarisation-induced σ -holes and hydrogen bonding *J. Mol. Model.* 2012, 18:2461-2469.

Figure captions

Figure 1: The MP2/aug-cc-pVDZ calculated MEP on the 0.001 a.u. isodensity surface of H₃C-Cl polarized by a charge of -0.2692 at a distance of 3 Å from the chlorine atom along the extension of the C-Cl bond.

Figure 2: A comparison of the MP2/aug-cc-pVDZ-calculated MEP on the 0.001 a.u. isodensity surface of iodobenzene with that calculated from MEP-fitted charges (i.e. the best possible atomic monopole fit to the MP2-data). The colour scale only extends over the 0 ± 10 kcal mol⁻¹ region to emphasise the differences between the two plots.

Figure 3: Electronic density redistribution of H₃C-Cl upon perturbation (a) by an array of point charges representing an H₂O molecule (red indicates an increase in electron density, blue a decrease) and (b) in a fully quantum-chemically described interaction with an H₂O molecule (colour scheme as in (a)). (c) The lowest unoccupied molecular orbital of H₃C-Cl (the phases have been coloured to correspond to (a) and (b)). The data for (a) and (b) are taken from reference 29.

Figure 4: Schematic depiction of the regions of a Fock-matrix in a molecular-orbital basis. The diagonal (black) elements contain the MO-eigenvalues. Only mixing within the yellow occupied-virtual block leads to a change in the electron density.

Figure 5: Schematic diagram of the effect of polarisation by a second water molecule on the dipole moment of water. The dipole moment is depicted by the red arrow with the negative pole at the arrowhead. (a) The situation as often discussed without considering polarisation. (b) A more complete model in which polarisation of the donor water molecule is taken into account.

Further Reading/Resources

The Theory of Intermolecular Forces, Anthony J. Stone, Oxford University Press, Oxford, 2013.

Molecular Electrostatic Potentials; Concepts and Applications, J. S. Murray and K. D. Sen (Eds), Elsevier, Amsterdam, 1996, 1-103.

The Chemical Bond, G. Frenking and S. Shaik (Eds), Wiley-VCH, Weinheim, 2014.

Related Articles

Article ID [or Subtopic]	Article title
CMS-016	Energy decomposition analysis
CMS-051	Electrostatic Potentials
CMS-109	Symmetry-adapted perturbation theory with density functional methods
CMS-121	Atoms in Molecules
CMS-235	Natural Bond Orbital Methods
CMS-169	Polarisation effects in molecular interactions