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ORIGINAL PAPER

Mathematical modeling and physical reality in noncovalent interactions

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Abstract The Hellmann-Feynman theorem provides a straightforward interpretation of noncovalent bonding in terms of Coulombic interactions, which encompass polarization (and accordingly include dispersion). Exchange, Pauli repulsion, orbitals, etc., are part of the mathematics of obtaining the system's wave function and subsequently its electronic density. They do not correspond to physical forces. Charge transfer, in the context of noncovalent interactions, is equivalent to polarization. The key point is that mathematical models must not be confused with physical reality.

Keywords Noncovalent interactions · Hellmann-Feynman theorem · Electrostatic potential · Polarization · Charge transfer · Dispersion · σ-hole interactions · Halogen bonding · Hydrogen bonding

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Noncovalent interactions and electrostatic potentials

In 2009, Schneider suggested that the chemistry of the twenty-first century is "…likely to be the chemistry of noncovalent bonding" [1]. The evidence so far certainly bears out this prediction. For example, during the three years 2006–2008, an average of 28.3 papers *per day* referred to the term "hydrogen bond" [2]. In the last 10 years, there has been a veritable deluge of papers dealing with halogen bonding and its analogues involving Groups IV–VI, all of which (including hydrogen bonding) come under the heading of σ-hole interactions. (There have been several recent reviews of hydrogen bonding [2–4] and of σ-hole interactions in general [5–7].)

A continuing subject of intense study has been the nature of these interactions—even though they are rather easily explained in terms of the electrostatic potentials $V(\mathbf{r})$ of the molecules involved, as will be shown. $V(\mathbf{r})$ refers to the potential that the nuclei and electrons of a molecule create at any point $\mathbf{r}$ in the surrounding space. It is given rigorously by Eq. (1), which is simply a form of Coulomb's law:

$$V(\mathbf{r}) = \sum_{A} \frac{Z_A}{|\mathbf{R}_A - \mathbf{r}|} - \int \frac{\rho(\mathbf{r}')\,d\mathbf{r}'}{|\mathbf{r}' - \mathbf{r}|} \quad (1)$$

Z_A is the charge on nucleus A, located at $\boldsymbol{R}_A$, and $\rho(\mathbf{r})$ is the molecule's electronic density. Atomic units are used throughout this discussion.

$V(\mathbf{r})$ is a real physical property, an observable, which can be obtained experimentally both by diffraction methods [8–10] and computationally. When computed on a molecular surface —e.g., the 0.001 au contour of the electronic density, as proposed by Bader et al. [11]—$V(\mathbf{r})$ has proven to be an effective guide to noncovalent interactions [12–14], since it is how the

molecule is initially "seen" or "felt" by another, approaching molecule.

Figure 1 presents the computed electrostatic potentials on the 0.001 au surfaces of (a) acetylene, H–C≡C–H, (b) bromobenzene, C_6H_5Br, (c) sulfur dichloride, SCl_2, (d) phosphorus hydrogen difluoride, PHF_2, and (e) silane, SiH_4. In each molecule, at least one atom has one or more regions of significantly positive electrostatic potential centered on the extension(s) of one or more of the covalent bonds to that atom. These regions are called positive σ-holes; they are due to the anisotropy of the atom's charge distribution that results from the formation of the covalent bond or bonds [5–7]. A positive σ-hole is often (not always) neighbored by negative regions on the same atom.

Table 1 lists the values of the most positive potentials in the σ-hole regions of the molecules in Fig. 1; the covalent bond responsible for each σ-hole is identified. Note that the sulfur in SCl_2, the phosphorus in PHF_2 and the silicon in SiH_4 have two, three and four positive σ-holes, respectively. (Note that,

Table 1 Most positive electrostatic potentials of σ-holes in the molecules shown in Figure 1, in kcal mol^{-1}. Computational level: M06-2X/6-31+G(d,p)

Molecule	Atom with σ-hole(s)	Bond producing σ-hole	Most positive σ-hole potential[a]
HC≡CH	H	C-H	32.3
C_6H_5Br	H_{meta}	C-H_{meta}	19.8
	H_{para}	C-H_{para}	19.7
	H_{ortho}	C-H_{ortho}	17.9
	Br	C-Br	10.2
SCl_2	S	Cl-S	26.9 (2)
	Cl	S-Cl	13.8
PF_2H	P	F-P	38.8 (2)
	P	H-P	22.6
	H	P-H	12.5
SiH_4	Si	H-Si	15.4 (4)
	H	Si-H	0.2

[a] If an atom has more than one σ-hole with the same maximum potential, the number of σ-holes is given in parentheses

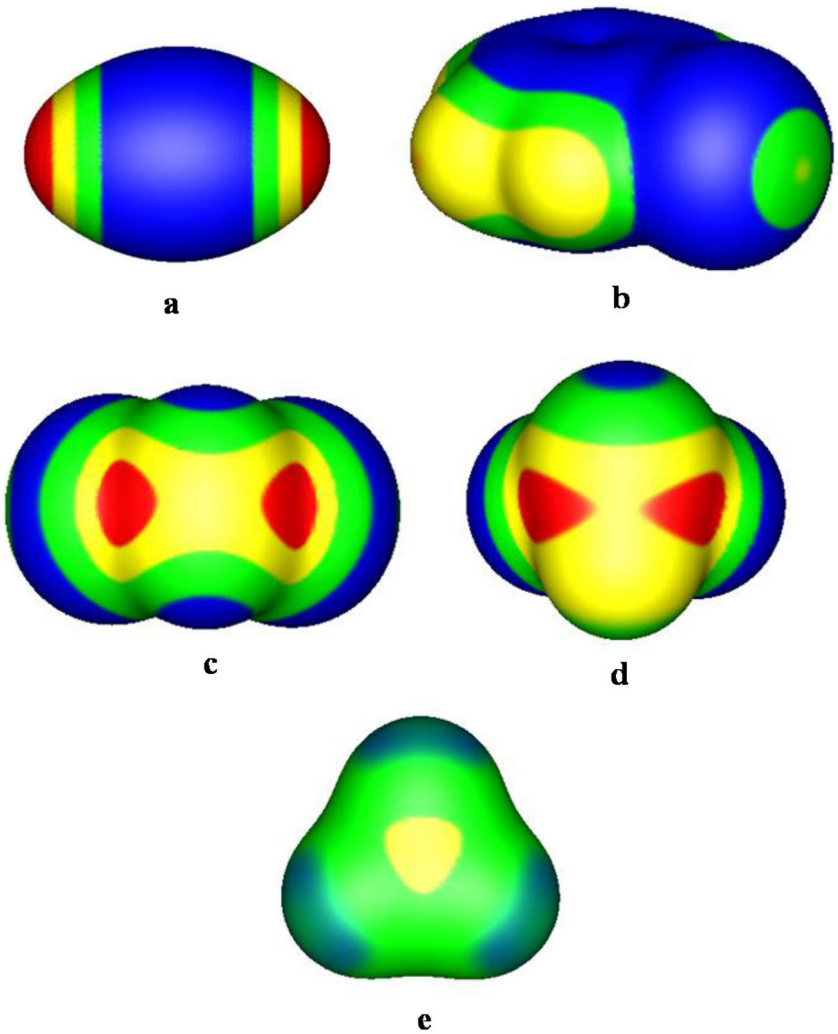
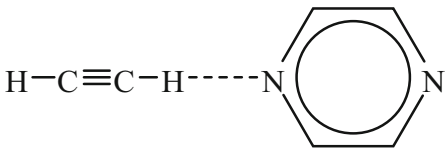


Fig. 1 **a**–**e** Computed electrostatic potentials showing σ-holes on 0.001 au molecular surfaces. **a** Acetylene, H–C≡C–H; hydrogens are at left and right ends. **b** Bromobenzene, C_6H_5Br; bromine is at right, two hydrogens at left. **c** Sulfur dichloride, SCl_2; sulfur is in center foreground. **d** Phosphorus hydrogen difluoride, PHF_2; phosphorus is in upper foreground, hydrogen in lower foreground. **e** Silane, SiH_4; silicon is in center foreground. Color ranges (kcal mol^{-1}): **a**, **b**, **c**, **e** *red* > 20, *yellow* 20–10, *green* 10–0 *blue* negative; **d** *red* > 30, *yellow* 30–15, *green* 15–0, *blue* negative. Visible σ-holes: **a**, **c**, **d** *red*; **b** *yellow* (hydrogens) and *green* (bromine); **e** *yellow*. Values of most positive σ-hole potentials are in Table 1. Computational level: M06-2X/6-31+G(d,p)

in SiH_4, the σ-holes of the hydrogens are essentially neutral and are surrounded by negative potentials; this can be attributed to the hydrogens being more electronegative than silicon.)

Through such positive σ-holes, molecules can interact attractively with negative sites to form noncovalent complexes. Three examples of negative sites are in Fig. 2: (a) the nitrogens in 1,4-diazine, NC_4H_4N; (b) the π region in ethylene, $H_2C=CH_2$; and (c) the oxygen in acetone, $O=C(CH_3)_2$. Since positive σ-holes are centered on the extensions of the bonds that produce them, the σ-hole···negative site interactions are usually highly directional, as is shown in Fig. 3 for complexes **1**–**4**:



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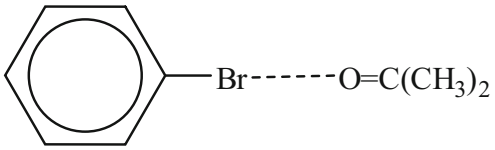

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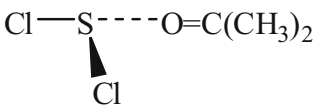

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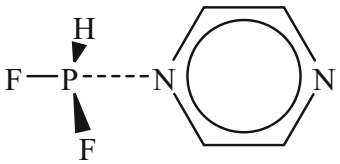

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Table 2 presents some computed properties of **1**–**4**. The C–H···N angle in **1**, the C–Br···O in **2** and the Cl–S···O in **3** are all close to 180°; the F–P···N angle in **4** deviates somewhat from near-linearity due to a secondary F···H attraction, as can be seen in Fig. 3d. The separations of the interacting atoms are all less than the sums of the respective van der Waals radii. The interaction energies are all negative, indicating that the complexes are more stable than the separated molecules.

Hydrogen bonding (as in **1**), halogen bonding (as in **2**) and other σ-hole interactions (as in **3** and **4**) can all be understood readily as Coulombic attractions between positive σ-holes and negative sites [5–7]. This will of course be accompanied by some mutual polarization; the electric field of each participant will have some polarizing effect upon the charge distribution of the other. This further stabilizes the interaction.

This Coulombic interpretation of hydrogen bonding and other σ-hole interactions is simple and straightforward—and therefore unacceptable to many theoreticians. For instance, it ignores the beloved decades-old debate over the relative degrees of electrostatics and covalence in hydrogen bonds [2]. Since covalence is purely conceptual and any attempt to quantify it is necessarily arbitrary, this is an ideal academic debate: it cannot be resolved, and can (and will) continue indefinitely.

Relentless theoretical scrutiny has led to the following description of hydrogen bonding, as stated by Arunan et al. [2]: "Today, it is well accepted that hydrogen bonding has contributions from electrostatic interactions between permanent multipoles, polarization, or induction interactions between permanent and induced multipoles, dispersion arising from instantaneous multipoles-induced multipoles, charge-transfer-induced covalency, and exchange correlation effects from short-range repulsion due to overlap of the electron distribution." The poor hydrogen bond cringes before this assault! But is it really necessary to invoke such a barrage of factors to explain an interaction that is usually just a few kcal mol^{-1}? William of Occam (1287–1347) would say: certainly not! (Occam's Razor: *Lex parsimoniae*: *Pluralitas non est ponenda sine necessitate*. Plurality is not to be posited without necessity.)

Analogous "clarification" of halogen bonding and other σ-hole interactions is being pursued mercilessly. A frequently used analytical technique is "interaction energy decomposition," whereby the interaction (stabilization) energy of a noncovalent complex is somehow separated into a set of supposedly fundamental contributions. There is no general consensus as to what these fundamental contributions are; different researchers invoke different subsets of a group that includes electrostatics, charge transfer, polarization, correlation, dispersion, exchange, Pauli repulsion, orbital interaction, distortion, etc. There is no physically meaningful way to separate these, since they are not independent of each other. This has the advantage that everyone can invent his/her own procedure, and none can be shown to be more incorrect than any other. So far, at least 16 decomposition schemes have been proposed

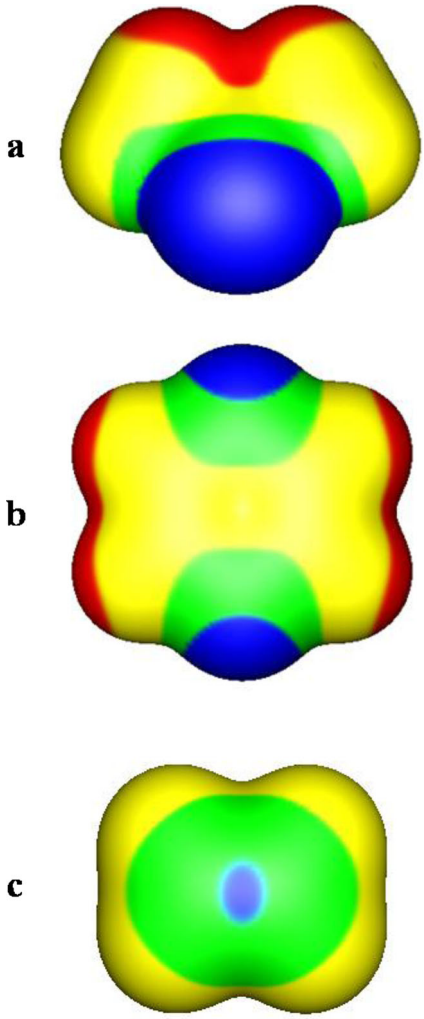


Fig. 2 **a**–**c** Computed electrostatic potentials, on 0.001 au molecular surfaces, of some molecules having possible negative sites. **a** Acetone, $O=C(CH_3)_2$; oxygen is in bottom foreground. **b** 1,4-Diazine, NC_4H_4N; nitrogens are at top and bottom. **c** Ethylene, $H_2C=CH_2$; view from above, double bond is in the center. Color ranges (kcal mol^{-1}): *red* > 15, *yellow* 15 to 0, *green* 0 to −15, *blue* more negative than −15. The most negative sites are in *blue*; their most negative values (kcal mol^{-1}) are: **a** −37.5, **b** −30.5, **c** −16.0. Computational level: M06-2X/6-31+G(d,p)

[15]. Inevitably, they sometimes disagree significantly or even directly contradict each other. A notable example are two studies of complexes formed by methyl halides and trifluoromethyl halides with formaldehyde. One study found the stabilizing effects to be primarily electrostatics and dispersion [16]; the other concluded, *for exactly the same molecules*, that charge transfer and polarization dominate, with electrostatics contributing only "slightly" [17]. Despite such annoyances, interaction energy decomposition continues to be used to "clarify" noncovalent bonding.

Fortunately for those who seek simplicity, the straightforward Coulombic interpretation of noncovalent interactions does have one powerful ally. It is the Hellmann-Feynman theorem.

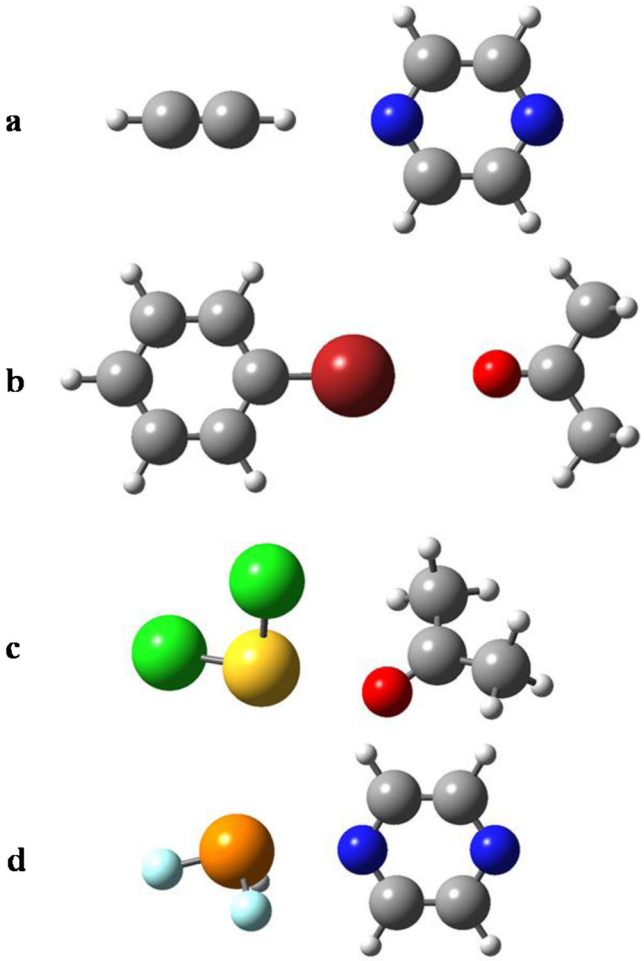


Fig. 3 Computed structures of complexes **a 1**, **b 2**, **c 3**, **d 4**. Some properties are in Table 2. Colors: *white* hydrogens, *gray* carbons, *blue* nitrogens, *red* oxygens, *light blue* fluorines, *orange* phosphorus, *yellow* sulfur, *green* chlorines, *maroon* bromine. Computational level: M06-2X/6-31+G(d,p)

The Hellmann-Feynman theorem

The first point of interest about the Hellmann-Feynman theorem is that it was initially derived neither by Hellmann nor by Feynman. It has been traced back to Schrödinger in 1926 [18],

Table 2 Computed properties of complexes **1**–**4**. Computational level: M06-2X/6-31+G(d,p)

Complex	Interaction angle (°)	Separation (Å)[a]	Interaction energy ΔE (kcal mol^{-1})[b]
1	C–H···N (180)	H···N: 2.25 (2.7)	−3.5
2	C–Br···O (180)	Br···O: 2.94 (3.4)	−3.1
3	Cl–S···O (177)	S···O: 2.76 (3.3)	−5.8
4	F–P···N (166)	P···N: 2.64 (3.4)	−7.4

[a] Sums of van der Waals radii are in parentheses [59, 60]

[b] For a complex X···Y, ΔE=E(X···Y) – [E(X)+E(Y)]

Güttinger in 1932 [19], Pauli [20] and Hellmann [21] in 1933 and finally Feynman in 1939 [22]. The theorem shows that for a system with energy E, time-independent Hamiltonian H and normalized wave function Ψ, the derivative of the energy with respect to any parameter λ that appears explicitly in the Hamiltonian is given by,

$$\frac{\partial \mathrm{E}}{\partial \lambda} = \left\langle \Psi^* \left| \frac{\partial H}{\partial \lambda} \right| \Psi \right\rangle \tag{2}$$

This seemingly simple (perhaps almost trivial [23]) result leads to a very significant conclusion when applied to a system of nuclei and electrons within the Born-Oppenheimer approximation and λ is taken to be a coordinate of nucleus A, which has a charge Z_A and is located at $\boldsymbol{R}_A$. Since the kinetic energy portion of H does not depend explicitly upon the nuclear coordinates, Eq. (2) becomes,

$$\frac{\partial \mathrm{E}}{\partial \lambda} = \left\langle \Psi^* \left| \frac{\partial V}{\partial \lambda} \right| \Psi \right\rangle \tag{3}$$

in which V is the potential energy operator. Writing Eq. (3) in turn for each coordinate of nucleus A and noting that the negative gradient of a potential energy is a force leads finally to an expression for the force exerted upon nucleus A by the electrons and the other nuclei of the system [22, 24, 25]:

$$\mathbf{F}(\mathbf{R}_\mathrm{A}) = -\mathrm{Z}_\mathrm{A} \sum_{\mathrm{B}\neq\mathrm{A}} \frac{\mathrm{Z}_\mathrm{B}(\mathbf{R}_\mathrm{B}-\mathbf{R}_\mathrm{A})}{|\mathbf{R}_\mathrm{B}-\mathbf{R}_\mathrm{A}|^3} + \mathrm{Z}_\mathrm{A} \int \frac{\rho(\mathbf{r})(\mathbf{r}-\mathbf{R}_\mathrm{A})\mathrm{d}\mathbf{r}}{|\mathbf{r}-\mathbf{R}_\mathrm{A}|^3} \tag{4}$$

In Eq. (4), $\boldsymbol{R}_\mathrm{B}$–$\boldsymbol{R}_\mathrm{A}$ and $\boldsymbol{r} - \boldsymbol{R}_\mathrm{A}$ are vectors from nucleus A to nucleus B and to point r, respectively, and $\rho(\mathbf{r})$ is the electronic density.

To demonstrate the significance of Eq. (4), we turn to the expression for the electrostatic potential $\mathrm{V}(\mathbf{r})$ at any point $\mathbf{r}$ within the system; by Coulomb's Law, this is Eq. (1), given earlier and repeated below:

$$\mathrm{V}(\mathbf{r}) = \sum_\mathrm{A} \frac{\mathrm{Z}_\mathrm{A}}{|\mathbf{R}_\mathrm{A}-\mathbf{r}|} - \int \frac{\rho(\mathbf{r}')\mathrm{d}\mathbf{r}'}{|\mathbf{r}'-\mathbf{r}|} \tag{1}$$

Now let $\mathbf{r}$ be $\boldsymbol{R}_\mathrm{A}$, the position of nucleus A. Then,

$$\mathrm{V}(\mathbf{R}_\mathrm{A}) = \sum_{\mathrm{B}\neq\mathrm{A}} \frac{\mathrm{Z}_\mathrm{B}}{|\mathbf{R}_\mathrm{B}-\mathbf{R}_\mathrm{A}|} - \int \frac{\rho(\mathbf{r}')\mathrm{d}\mathbf{r}'}{|\mathbf{r}'-\mathbf{R}_\mathrm{A}|} \tag{5}$$

Eq. (5) gives the potential at nucleus A that is created by the electrons and other nuclei. Then $\mathrm{Z_A V}(\mathbf{R}_\mathrm{A})$ is the potential energy of nucleus A and its negative gradient is the force felt by nucleus A:

$$\mathbf{F}(\mathbf{R}_\mathrm{A}) = -\nabla \mathrm{Z_A V}(\mathbf{R}_\mathrm{A}) \tag{6}$$

Carrying out the operations indicated in Eq. (6) leads to,

$$\mathbf{F}(\mathbf{R}_\mathrm{A}) = -\mathrm{Z}_\mathrm{A} \sum_{\mathrm{B}\neq\mathrm{A}} \frac{\mathrm{Z}_\mathrm{B}(\mathbf{R}_\mathrm{B}-\mathbf{R}_\mathrm{A})}{|\mathbf{R}_\mathrm{B}-\mathbf{R}_\mathrm{A}|^3} + \mathrm{Z}_\mathrm{A} \int \frac{\rho(\mathbf{r}')(\mathbf{r}'-\mathbf{R}_\mathrm{A})\mathrm{d}\mathbf{r}'}{|\mathbf{r}'-\mathbf{R}_\mathrm{A}|^3} \tag{7}$$

Equation (7) is exactly equivalent to Eq. (4)! The same equation for the force on nucleus A has therefore been reached classically, using Coulomb's Law, as quantum mechanically, starting from the Schrödinger equation. Equation (4) is often referred to as the "electrostatic theorem," to distinguish it from the more general Eq. (2). However we shall refer to both as the Hellmann-Feynman theorem.

The theorem shows that the forces that are felt by a nucleus in a molecule, complex, etc., are due to purely classical Coulombic interactions with the electrons and the other nuclei. They can be determined from just the electronic density, the nuclear positions and Coulomb's Law. These conclusions should not really be surprising, if it is considered that all of the potential terms in the Hamiltonian of a system of nuclei and electrons are Coulombic. Quoting Levine, "…there are no 'mysterious quantum-mechanical forces' acting in molecules" [24].

But what about all of the factors that delight quantum chemists: antisymmetry, exchange, Pauli repulsion, correlation, etc.? These are certainly important but, as has been pointed out [24, 26–29], their role is in obtaining the wave function from which the electronic density can be calculated. Once it and the nuclear positions are known—whether computationally or experimentally—only Coulomb's Law is needed.

Conceptually, the Hellmann-Feynman theorem is extremely significant, especially Eq. (4). Slater described it as one of the "most powerful" in the areas of molecules and solids [28]. Nevertheless, the theorem seems not to have received the recognition that it merits. Fernandez Rico et al. [25] observed that "…the possibilities that it opens up have been scarcely exploited, and today the theorem is mostly regarded as a scientific curiosity." In the past, one reason for this has been that quantitative

applications of it require electronic densities of a relatively high level of accuracy [28, 30, 31]. However the advances in computational methodology in recent years make this less of an obstacle [32]. It was suggested by Deb [33] that a second reason might be that "…the apparent simplicity of the H-F theorem had evoked some skepticism and suspicion…". It must indeed be upsetting for some theoreticians, imbued with the exotic mysteries of quantum mechanics, to be informed that the chemical bond can be explained rigorously in terms of classical physics (Coulomb's Law). What does this do, for example, to the electrostatics vs. covalence debate?

Reconciliation

Current theory views noncovalent bonding as involving an imposing array of contributions: electrostatics, charge transfer, polarization, correlation, dispersion, exchange, Pauli repulsion, orbital interaction, etc. Can this be reconciled with the Hellmann-Feynman theorem, which shows that the forces holding together a molecule or complex are the Coulombic attractions between the nuclei and the electrons? Yes, if the distinction between mathematics and physical reality is kept in mind. We will consider individually the supposed contributions listed above.

Exchange, Pauli repulsion, orbitals and correlation

As has been discussed on several occasions [24, 26–29], exchange and Pauli repulsion reflect mathematical requirements that the wave function of a molecule or complex must satisfy. Exchange is introduced as a means of accounting for the fact that electrons are indistinguishable. The Pauli exclusion principle (i.e., "Pauli repulsion") is the result of the need for the wave function to be antisymmetric. Neither exchange nor Pauli repulsion corresponds to a physical force.

Orbitals are simply mathematical constructs that are used to obtain an approximate solution of the multielectron Schrödinger equation. They have no physical reality [34], nor accordingly does orbital overlap. Finally, the wave function should be designed in such a manner as not to neglect the instantaneous correlation between the electrons' movements in response to their mutual electrostatic repulsions.

Exchange, Pauli repulsion, orbitals and correlation are all very important components of the mathematics of arriving at a satisfactory wave function and the resulting electronic density. However they do not contribute directly to the physical forces (Coulombic attractions) that hold the system together.

Electrostatics, polarization

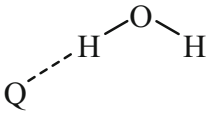
In theoretical analyses of noncovalent interactions, it is unfortunately quite common to find the term "electrostatics" used in a misleading manner, as referring to a hypothetical Coulombic interaction between the molecules in their *isolated*, *unperturbed* states but at the separation that they have in the complex. Thus for a complex X···Y, formed between the molecules X and Y, the "electrostatic" interaction energy is incorrectly written as:

$$\Delta \mathrm{E}_{\{\mathrm{electrostatic}\}} = \sum_{\mathrm{B}} Z_{\mathrm{B}}^{\mathrm{X}} \mathrm{V}^{\mathrm{Y}}\left(\mathbf{R}_{\mathrm{B}}^{\mathrm{X}}\right) - \int \rho^{\mathrm{X}}(\mathbf{r}) \mathrm{V}^{\mathrm{Y}}\left(\mathbf{r}\right) \mathrm{d}\mathbf{r} \qquad (8)$$

In Eq. (8), $Z_{\mathrm{B}}^{\mathrm{X}}$ and $\boldsymbol{R}_{\mathrm{B}}^{\mathrm{X}}$ are the charge and position of nucleus B in the unperturbed molecule X and $\rho^{\mathrm{X}}(\mathbf{r})$ is its electronic density; $\mathrm{V}^{\mathrm{Y}}(\mathbf{r})$ is the electrostatic potential of unperturbed molecule Y, as given in Eq. (1). X and Y are assumed to occupy the same relative positions as in the complex.

Equation (8) is physically unrealistic. It ignores the fact that as soon as the molecules begin to interact (and certainly by the time they have formed the complex), they are no longer isolated and unperturbed. The charge distribution of each has been polarized by the electric field of the other. Such polarization is an intrinsic part of any Coulombic interaction (unless both participants are point charges). It influences both $\rho(\mathbf{r})$ and $\mathrm{V}(\mathbf{r})$ of each molecule that is involved. Accordingly, the electrostatic potentials displayed in Figs. 1 and 2, which are for the isolated molecules, may be altered significantly when the molecules begin to interact.

The role that polarization can play was demonstrated by Hennemann et al. [35], by putting a point charge Q at a distance of 1.9 Å from one of the hydrogens of the water molecule, as in **5**. Figure 4 shows how the molecular surface electrostatic potential of the water is changed as Q is made increasingly negative. (In this study, the surface was taken to be the 0.002 au contour of the electronic density; this does not affect the key point that is being illustrated.)



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In Fig. 4a, Q is zero; the potential is accordingly that of the unperturbed H_2O molecule. The positive σ-holes of the hydrogens, on the extensions of the O–H bonds, are clearly visible. In proceeding to parts (b), (c) and (d) of Fig. 4, Q is made incrementally more negative: −0.2, −0.4 and −0.6 au. This polarizes the electronic density

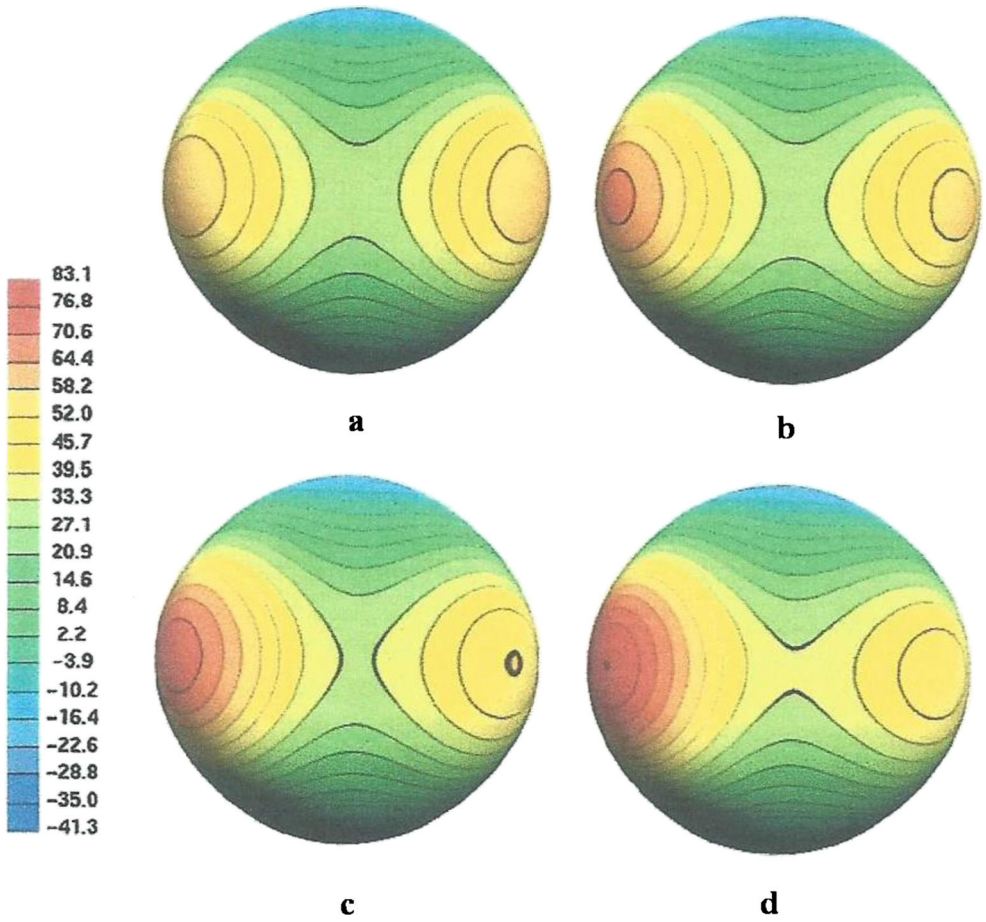


Fig. 4a–d Computed electrostatic potential on 0.002 au molecular surface of H_2O. Hydrogens are at left and right in foreground. *Color scale* Values of the potential (kcal mol^{-1}). A point charge Q is 1.9 Å from the hydrogen at left, along extension of the O–H bond as in structure **5** (see text). Values of the point charge (au): **a** 0.0, **b** −0.2, **c** −0.4, **d** −0.6. The most positive value of the σ-hole potential of the hydrogen at the left correspondingly increases from **a** 57 to **b** 66 to **c** 75 to **d** 83 kcal mol^{-1}. Computational level: MP2/aug-cc-pVTZ. Figure taken from Hennemann et al. [35] with permission from Springer

of the H_2O away from the hydrogen that is close to Q (at the left) and toward the farther hydrogen (at the right). The σ-hole of the closer hydrogen becomes increasingly positive and larger, the σ-hole of the farther hydrogen becomes less positive and smaller.

Figure 5, also taken from Hennemann et al. [35], shows how the σ-hole potential of the closer hydrogen is changed when Q is allowed to be positive as well as negative. As Q becomes increasingly positive, the electronic density of the H_2O is polarized toward the hydrogen that is closer to Q, making its σ-hole less positive. Whereas the σ-hole of the hydrogen in the unperturbed H_2O molecule (Q=0) has a maximum potential ($V_{S,max}$) of 57 kcal mol^{-1}, this diminishes to 38 kcal mol^{-1} when Q=0.4 (Fig. 5). In contrast, this σ-hole potential increases to 75 kcal mol^{-1} when Q=−0.4. Thus, positive σ-holes can be strengthened, weakened or even *induced* (see below) by polarization.

In σ-hole complexes, such as **1**–**4**, the primary polarizing electric fields are likely to be those due to the positive σ-hole and the negative site. Accordingly, it can be anticipated that the electronic densities in the molecules having the σ-holes will be shifted away somewhat from the negative sites, while the electronic densities in the molecules with the negative sites will be shifted toward the positive σ-holes, as shown schematically in **1A**–**4A**. This is exactly what is observed in

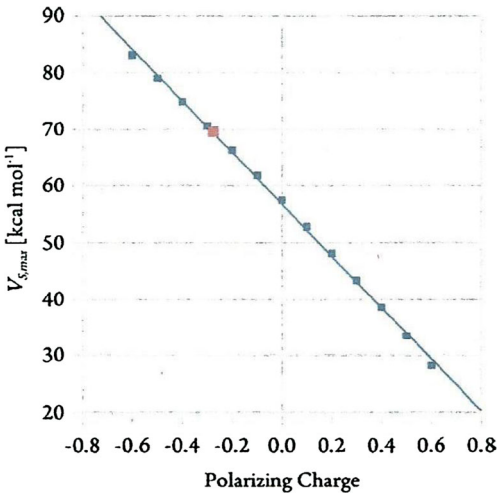
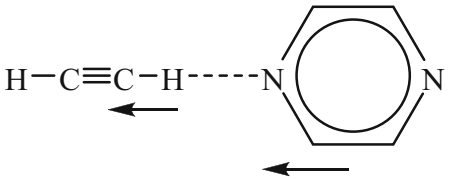
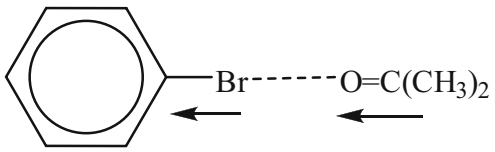


Fig. 5 Magnitude of the most positive value of the σ-hole potential of the hydrogen at the left in Fig. 4 plotted against the value in au of the polarizing charge Q, placed 1.9 Å from the hydrogen (structure **5**, see text). Computational level: MP2/aug-cc-pVTZ. Figure taken from Hennemann et al. [35] with permission from Springer

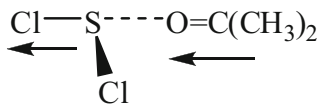
plots showing the difference between the electronic density of a complex and the sum of the electronic densities of the unperturbed component molecules, placed in the same relative positions as in the complex [36–39].



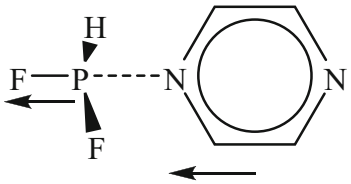
1A



2A



3A



4A

Neglecting polarization can lead to incorrect conclusions, as has been emphasized recently [40]. For instance, the σ-holes of the chlorine in H_3C–Cl [6] and the phosphorus in H_3P [41] have negative or near-neutral electrostatic potentials. It may accordingly be claimed that the computationally predicted complexes **6** [16] and **7** [42] do not represent Coulombic σ-hole interactions, and that some other stabilizing factors are involved. However this ignores the polarizing effects of the electric fields of the negative sites (the oxygen of $O{=}CH_2$ and the nitrogen of NSH) which can *induce* positive σ-holes on the chlorine and on the phosphorus [40]. It is not the Coulombic interpretation (and the Hellmann-Feynman theorem) that is inadequate to explain these interactions, but rather the restricted use of "electrostatics" as reflecting the isolated, unperturbed molecules.

H_3C-Cl----$O{=}CH_2$ **6**

H_3P----NSH **7**

Dispersion

Dispersion has traditionally been attributed to attractive interactions between instantaneous induced dipoles created by the correlated movements of the electrons as they respond to their mutual electrostatic repulsions; see, for example, London [43] and Hirschfelder et al. [26]. Feynman, on the other hand, argued that the stabilizing effects of dispersion are due to intramolecular attractions between the nuclei of each molecule and its own electronic charge that has been polarized into the intermolecular region [22]. The validity of Feynman's explanation has been confirmed on several occasions [30, 31, 44, 45], and London's $1/R^6$ dependence of the dispersion energy [46] has been derived from the Hellmann-Feynman theorem.

In terms of the present discussion, however, the key point is that dispersion—whether involving dipole/dipole or nuclear/electronic interactions—is Coulombic; it is simply part of polarization. It is not a separate interaction. This also follows from the Hohenberg-Kohn theorem [47], which tells us that the correctly polarized electronic density of a complex will yield its true total energy; it is not necessary to calculate an additional dispersion contribution. Treating dispersion as distinct from polarization is just another example of trying to separate what cannot be separated.

Charge transfer

In the context of noncovalent bonding, charge transfer and polarization are also not separate contributions to the interaction; they are equivalent. Morokuma and Kitaura observed already in 1981 that "If one uses a complete basis set, one cannot distinguish between the charge transfer and the polarization" [48]. The same point has been made by others [40, 49–53].

Polarization is a real physical phenomenon, i.e., the response of one molecule's electronic density to the electric field of another. Charge transfer is a way of modeling that response mathematically. Unfortunately, the model is often erroneously taken to correspond to physical reality.

Thus we are told that the formation of complexes such as **1**–**4** involves the transfer of some fraction of an electron from an occupied orbital on an "electron donor" (the negative site)

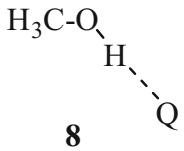
to an empty orbital, usually antibonding, of an "electron acceptor" (the molecule with a positive σ-hole). However this explanation ignores the inconvenient truths that (1) electrons are indivisible and cannot be fractionated, and (2) orbitals have no physical existence [34]!

Stone and Misquitta [52] offered a good example of how a model can affect the interpretation. Consider a noncovalent complex X···Y. The usual quantum chemical treatment would be in terms of orbitals centered on the atoms of both X and Y. The form of the resulting X···Y wave function, which in itself has no physical meaning, might suggest that some transfer of electronic charge has occurred, e.g. from Y to X. The same complex could be described equally well using only orbitals centered on Y, provided that a sufficient number and variety were included. The two treatments would produce comparable electronic densities that show the polarization within the complex. However the second X···Y wave function could not possibly imply charge transfer from Y to X since there are no orbitals on X to receive electronic charge. *The illusion of charge transfer is in the model*; *the reality of polarization is in the electronic density*, *the physical observable*.

Density-difference plots indicating the shifting of electronic charge that accompanies a σ-hole interaction, as depicted schematically in **1A**–**4A**, may show what could be interpreted as charge transfer into an antibonding orbital of the molecule containing the σ-hole. However Clark et al. [39] demonstrated, for the F_3C–Cl···OH_2 interaction, that this inference would be incorrect. They showed that essentially the same density difference plot is obtained when each participant is polarized *separately* through an iterative process in which the other is represented by point charges. Since the participants are treated separately, no charge transfer can take place.

A σ-hole interaction is typically accompanied by a change in the stretching frequency of the bond on the extension of which is the σ-hole (i.e., the C–H in **1**, the C–Br in **2**, the Cl–S in **3** and the F–P in **4**). The frequency usually decreases (a red shift), but in some cases an increase (blue shift) is observed [2, 54, 55]. The occurrence of red shifts has been claimed to support the notion of charge transfer into an antibonding orbital of the molecule with the σ-hole, which would presumably weaken the bond in question and diminish its stretching frequency. However, Hermansson [56] and Qian and Krimm [57] have developed formalisms that allow both the red and the blue shifts in σ-hole complexes to be explained and predicted in terms of just the electric field of the negative site and the permanent and induced dipole moments of the molecule having the σ-hole. Such calculations have been carried out for numerous σ-hole complexes [54, 55], confirming that electric field and polarization considerations suffice to explain the observations.

This was further demonstrated by Hennemann et al. [35]. They placed point charges Q along the extensions of the O–H bond of H_3C–OH and the C–H bond of F_3C–H, as in **8** and **9**. Q was put at the position that the oxygen of the H_2O molecule occupies in the complexes H_3C–OH···OH_2 and F_3C–H···OH_2. When the Q in **8** was made negative, the O–H stretching frequency decreased; when it was positive, the frequency increased. In **9**, the opposite was observed: a negative Q increased the C–H frequency, a positive Q decreased it. Thus, the polarizing effects of the electric fields of the Q in **8** and **9** were sufficient to produce both red and blue shifts; no charge transfers could be involved since the Q are point charges and have no electronic charge to transfer nor orbitals to receive it. The frequency changes, both increases and decreases, are the consequences of polarization.



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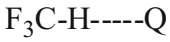

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Concluding comments

The elegant mathematics of quantum chemistry—which deals with exchange, Pauli repulsion, electronic correlation, orbital representations, etc.—plays an essential role in arriving computationally at a description of the charge distribution in a noncovalent complex. Once that has been achieved, however, the Hellmann-Feynman theorem and even the Hamiltonian itself tell us that the interactions within the system are purely Coulombic—which encompasses polarization and therefore dispersion.

It is important to resist the seductive allure of mathematical models, no matter how gratifyingly complex they may be. Mathematical models should not be confused with physical reality, even if the latter is exasperatingly straightforward. Newton recognized this perverse tendency of physical phenomena, "Nature is pleased with simplicity" [58], as did Einstein, "Nature is the realization of the simplest conceivable mathematical ideas" [58].

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