Chem. Rev. 1993, 93, 2339–2353

Electrostatic Interaction Potentials in Molecular Force Fields

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Received January 29, 1993 (Revised Manuscript Received May 20, 1993)

Contents

Clifford Dykstra received B.S. degrees in both chemistry and physics from the University of Illinois at Urbana-Champaign in 1973. In 1976, he received his Ph.D. from the University of California at Berkeley where he carried out thesis research on the electronic structure of certain organic molecules and on ab initio electron correlation methodology. He was Professor of Chemistry at the University of Illinois at urbana-Champaign until 1990, at which time he joined Indiana University—Purdue University at Indianapolis. He is Professor of Chemistry at Indianapolis and Associate Dean of Graduate Studies in the School of Science. His research work and continuing interests are in electron correlation, ab initio methods for calculation of molecular properties, vibrational dynamics, and weak intermolecular interaction, along with applications ranging from small molecule cluster phenomena to proteins.

I. Introduction

Electrostatics refers to the interaction of charges and charge distributions in the absence of time-dependent variations. For instance, polarization of a charge distribution by a uniform field is a problem of electrostatics so long as the field is static or not varying in time. Electrostatic analysis and electrostatic modeling have become major elements in efforts to achieve accurate molecular and intermolecular force fields and potentials. Their use represents an attempt to invoke classical physics over quantum mechanics in order to have computationally workable potentials.

Electrostatic models of interaction are mostly reserved for nonbonding interactions between molecules and for nonbonding intramolecular interactions. In the absence of strong chemical bonding forces, separation distances tend to be large. Electrostatic interaction is likely to dominate in such regions because it often persists to longer range than do interactions associated with chemical bonding. Thus, it is for such weak interactions that we have the best hope of using a classical picture as the foundation, or simply an element, of a model potential.

Electrostatics can also be a basis for refining or adapting conventional valence force fields. For instance, a four-center torsional potential for the atoms ABCD in some molecule may take the form of an electrostatic interaction between the AB and CD fragments. Or, the force field associated with some functional group may be augmented by an electrostatic term to reflect small relative effects of a varying partial charge on the group in different environments. Even though the parameters may be empirical, these are refinements or augmentations that are guided by the laws of electrostatics.

Potentials and force fields that use electrostatics through the incorporation of polarization have a qualitative difference from those that only involve the permanent charge fields. To include polarization is to model not only the forces or energetics but also the electronic structure. To say a molecule or a molecular fragment is polarized by some interaction with a neighboring species is to say that the electronic structure has changed in a specific, determinable way. That implies that information may be obtained about properties of the interacting species, and an obvious example is the dipole moment. However, there are many more properties that directly reveal small changes in electronic structure, such as NMR chemical shielding, polarizabilities and hyperpolarizabilities, magnetic susceptibilities, vibrational frequencies, and quadrupole coupling constants. The effort in my group to exploit electrostatics in weak interaction has been motivated by the prospect of understanding energetics and properties on the same footing. Out of this comes the goal of modeling properties along with forces, and eventually being able to simulate correlations between structures (from force fields) and certain spectroscopic parameters (from properties).

0009-2665/93/0793-2339$12.00/0

There are several key points to examine in considering electrostatic potentials. One is the distinction between the interaction of permanent moments and the incorporation of polarization. Another is the form of the representation of the charge fields of a molecule or molecular fragment. And then there is the choice of electrical response properties. This is a review of these points within the context of computational application. We seek to highlight the complexities, problems, and best solutions, so far, in using electrostatics for molecular mechanics force fields and potential surfaces and for property determination. There are several significant reviews and reports that provide a basis for many of the points presented here. Any discussion of electrostatic analysis for molecular systems leads back to two key papers by Buckingham.[1,2] More recent is his in-depth presentation focusing on intermolecular forces.[3] The back-to-back reviews of molecular electrostatic potentials by Williams[4] and by Politzer and Murray[5] are quite relevant and valuable. A short report I prepared 3 years ago[6] also gives some background information. To keep the scope of this review manageable, I have excluded all but passing consideration of continuum electrostatic methods. These are approaches which represent a surrounding medium as a continuum rather than a collection of atoms and molecules. Continuum methods ignore the discreteness of the solvent, as this is often a reasonable approximation. There are excellent reviews[7-10] of the substantial body of work on developing and using these methods.

II. Electrostatic Interactions

A. General Analysis

The machinery for electrostatic interaction potentials and force fields begins with the classical laws of electrostatics and proceeds through various power series expansions. Most every necessary expression can be derived or deduced from a definition of the electrical potential function, $V(x,y,z)$, in the following form. For a fixed distribution of N point charges, q_i, in space, each at respective position (x_i, y_i, z_i), the interaction energy, E, from placing the charge distribution in the potential (or turning the potential "on") is

$$E = \sum_{i}^{N} q_i \, V(x_i,y_i,z_i) \tag{1}$$

In addition, we need to know that the potential that arises from a point charge, q, at position (x_0,y_0,z_0) is

$$V^{\text{due to } q}(x,y,z) = \frac{q}{\sqrt{(x-x_0)^2 + (y-y_0)^2 + (z-z_0)^2}} = \frac{q}{r} \tag{2}$$

From eqs 1 and 2, we obtain that the interaction of two isolated point charges, q_1 and q_2, is q_1q_2/r_{12}. Other important equations of electrostatic analysis are obtained almost as readily.

Electrical potentials in the vicinity of molecules are anything but constant. So, it is reasonable to consider the variation in $V(x,y,z)$ in terms of spatial derivatives. That is, we may consider $V(x,y,z)$, whatever its form, as a power series. For conciseness, we shall replace the position coordinates (x,y,z) by (s_1,s_2,s_3), and we shall use a "0" to identify a specific choice of these coordinates.

$$V(s_1,s_2,s_3) = V(s_1^0,s_2^0,s_3^0) + \sum_{i=1}^{3}(s_i - s_i^0)\frac{\partial V}{\partial s_i}\Big|_0 + \frac{1}{2}\sum_{i=1}^{3}\sum_{j=1}^{3}(s_i - s_i^0)(s_j - s_j^0)\frac{\partial^2 V}{\partial s_i\,\partial s_j}\Big|_0 + \frac{1}{3!}\sum_{i=1}^{3}\sum_{j=1}^{3}\sum_{k=1}^{3}(s_i - s_i^0)(s_j - s_j^0)(s_k - s_k^0)\frac{\partial^3 V}{\partial s_i \partial s_j \partial s_k}\Big|_0 + \ldots \tag{3}$$

If the coordinate system origin is chosen as the expansion center, then $s_1^0 = s_2^0 = s_3^0 = 0$. The three first derivatives of V are the components of the electric field vector at the expansion center (i.e., at "0"). The second derivatives are the components of the field gradient, and so on. So, if values of the derivatives of V to some order n are known, then V can be readily evaluated at any point in space using eq 3 truncated to order n. It is important to recognize that use of fields, field gradients, and so on, in electrostatic analysis implies some truncation, and the adequacy of the point of truncation is always a concern.

The development of the standard expressions for the multipoles of charge distributions comes about from using the power series expansion for V of eq 3 in the energy expression of eq 1. For convenience, take the expansion center to be the coordinate system origin, and designate the derivatives of the potential at the origin in the following concise manner:

$$V_{ij} = \frac{\partial^2 V}{\partial s_i \partial s_j}\Big|_0 \tag{4}$$

Letting $s_i^{(n)}$ be the value of s_i for the nth charge, the interaction energy can be expressed with certain sums that are the moments of the charge distribution. The

$$E = V(0,0,0)\sum_{n}^{N} q_n + \sum_{i=1}^{3} V_i \sum_{n}^{N} q_n s_i^{(n)} + \frac{1}{2}\sum_{i=1}^{3}\sum_{j=1}^{3} V_{ij}\sum_{n}^{N} q_n s_i^{(n)} s_j^{(n)} + \ldots \tag{5}$$

individual sums over the N charges, which may be restated as spatial integrals for continuous charge distributions, are elements of the multipole moments. The order of a given moment is the order of the dependence on the position coordinates, s. In eq 5, the first of these sums is the zeroth moment (net charge), the next set of summations over the N charges corresponds to the first or dipole moment, and the second set of sums corresponds to the second moment.

There happen to be quite a number of choices of conventions for the moments, and for other electrical properties. For example, the factors of 1/2 for the second moment, 1/3! for the third moment, and so on, could be incorporated into the definition of the moment elements as in this definition of the xx-element of the second moment:

$$M_{xx} = \frac{1}{2}\sum_{n}^{N} q_n s_1^{(n)2} = \frac{1}{2}\sum_{n}^{N} q_n x_n^2 \tag{6}$$

Of course, one could just as well define the moment without the factor, and this choice is not uncommon. The difference between the conventions shows up in the energy expression. By using the definition of eq 6, generalized to all moments, the interaction energy, E, of eq 5 is simply

$$E = V_0 M_0 + V_x M_x + V_y M_y + V_z M_z + V_{xx} M_{xx} + V_{xy} M_{xy} + \ldots \quad (7)$$

As Applequist realized and cleverly exploited,[11] this expression is a dot product of two vectors. The first vector is the set of potential derivatives, and the second is an ordered list of the elements of all the moments. By the terminology of Applequist, these are rank one polytensors. The computational niceness of dot product expressions makes this convention appealing.

Another convention choice involves Laplace's condition, which is simply that outside any charge distribution,

$$V_{xx} + V_{yy} + V_{zz} = 0 \quad (8)$$

As a result, the mean value of the second moments, $\bar{M} = (M_{xx} + M_{yy} + M_{zz})/3$, does not affect the interaction energy with an external potential. Since $\bar{M}$ is the trace of the second moment tensor, a traceless form of the second moment tensor contains all the information necessary for electrostatic analysis. Similar relations hold for higher moments. These two conventions or ways of stating moment element values are distinguished by referring to the moments as Cartesian moments or traceless moments. For dipoles, there is no difference.

There are also conventions on sign choices. The interaction energy of eq 1 could be written as the negative of the value given, for instance, and various sign differences would follow. While it may be that a single convention (signs, factors, etc.) should be enforced, the reality is that several choices are in use, even by the same investigators, and so, it is best always to take note of the context in which property values are given.

B. Interaction of Two Charge Fields

The interaction of two charge fields, A and B, that arise from distributions of point charges is obtained by substituting the potential in eq 2 into eq 1:

$$E = \sum_{i=1}^{N_A} \sum_{j=1}^{N_B} \frac{q_i q_j}{r_{ij}} \quad (8)$$

This interaction expression is completely equivalent to another expression, one that is in terms of the multipole moments of the two charge distributions. This requires the generalization of eq 2 to moments beyond the zero moment (i.e., beyond the potential due to a point charge q). The usual expression for potential due to the first (dipole) moment is

$$V(x,y,z) = \frac{x}{r^3} M_x + \frac{y}{r^3} M_y + \frac{z}{r^3} M_z \quad (10)$$

where the multipole center is taken to be the coordinate system origin. The three factors that multiply the moment components in eq 10 may be collected into a rank one polytensor, $\mathbf{T}$, along with similar factors for all other moments. For each moment element, there is a corresponding factor, and so the potential may be compactly written[11-13] as the dot product of the $\mathbf{T}$ polytensor and the moment polytensor, $\mathbf{M}$.

$$V(x,y,z) = \mathbf{T} \cdot \mathbf{M} \quad (11)$$

$$\mathbf{T} = \left(\frac{1}{r}, \frac{x}{r^3}, \frac{y}{r^3}, \frac{z}{r^3}, \frac{3x^2 - r^2}{r^5}, \frac{3xy}{r^5}, \frac{3xz}{r^5}, \frac{3yx}{r^5}, \frac{3y^2 - r^2}{r^5}, \frac{3yz}{r^5}, \frac{3zx}{r^5}, \frac{3zy}{r^5}, \frac{3z^2 - r^2}{r^5}, \ldots \right) \quad (12)$$

Efficient computational algorithms have been devised and implemented[14] for finding $\mathbf{T}$-tensor elements for multipole expansions of arbitrarily high order. From knowing the potential, V, from one moment expansion, we may use eq 5 to obtain the interaction energy the multipoles of two charge fields. A rearrangement of the elements of $\mathbf{T}$ into a two-dimensional array, a polytensor of rank two designated $\mathbf{T}^{(2)}$,[11-14] yields a concise interaction expression:

$$E = \mathbf{M}^{(A)\dagger} \mathbf{T}^{(2)} \mathbf{M}^{(B)} \quad (13)$$

This expression is particularly suited to computational implementation because it is a row vector times a square matrix times a column vector, an operation that is easy to program efficiently. Also, the moment expansion can be truncated to any order with no special logic. However, the evaluation of the elements in $\mathbf{T}^{(2)}$ is a computational step that may become expensive, particularly as the point of truncation in the moment expansion is increased. The number of elements in this matrix with respect to the order of moments included, starting from zero order (point charges) is 1, 16, 169, 1600, 14641, and so on. So, the number of operations required for an evaluation of the energy in eq 13 is roughly 2×9^L where L is the highest moment order.

The interaction energy of a system of species with permanent charge fields is pairwise additive. That is, every A–B pair in a collection of species contributes to the interaction energy the amount given by eq 13. So, a specific $\mathbf{T}$-tensor is required for each pair:

$$E = \sum_{A} M^{(A)\dagger} \sum_{B>A} T^{(2)}_{AB} M^{(B)} \quad (14)$$

If the species have polarizable charge distributions, the energy associated with polarization is not pairwise additive.

The computational implication of the analysis so far is that electrostatic interaction between distributions of point charges should be inexpensive to carry out in relation to evaluation of the $\mathbf{T}$-tensors needed for a multipole interaction truncated other than at a very low order. Clearly, if the charge distributions are truly point charges, there is no reason to consider multipoles. At separation distances that are large compared to an atom's size, for instance, the interaction between two molecular ions is well treated as the interaction of point charges; in effect, at large separations, the ions *are* point charges. However, at closer separations, this may prove insufficient, and so, the question of computational efficiency is strongly linked to the problem of representing the continuous charge distribution of an atom or molecule.

C. Representations of Permanent Charge Fields

There are an infinite number of approximate ways to represent a molecular charge field (or potential). The

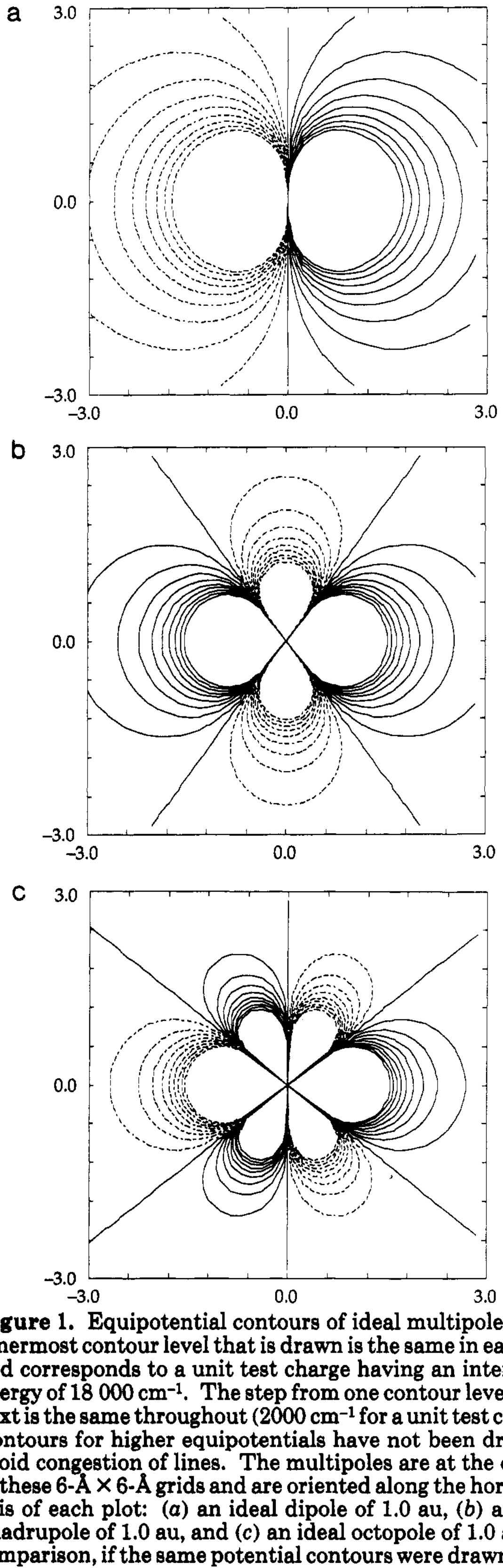


Figure 1. Equipotential contours of ideal multipoles. The innermost contour level that is drawn is the same in each plot and corresponds to a unit test charge having an interaction energy of 18 000 cm^{-1}. The step from one contour level to the next is the same throughout (2000 cm^{-1} for a unit test charge). Contours for higher equipotentials have not been drawn to avoid congestion of lines. The multipoles are at the centers of these 6-Å × 6-Å grids and are oriented along the horizontal axis of each plot: (*a*) an ideal dipole of 1.0 au, (*b*) an ideal quadrupole of 1.0 au, and (*c*) an ideal octopole of 1.0 au. For comparison, if the same potential contours were drawn about a unit charge or zeroth order multipole, the first (i.e., at 18 000 cm^{-1}) would be a circle *outside* the 6-Å × 6-Å grid.

differences amount to different truncations in an expansion of the potential, *V*. Perhaps the most common is the central multipole expansion. It is truncation in the order of included multipoles that affects accuracy in this representation. Figure 1 provides contour plots of electrostatic potentials about several low order, ideal multipoles. Representation of a molecular charge field by a central multipole expansion implies a superposition of these ideal multipole potentials. An expansion truncated at the third moment, for instance, can faithfully represent charge fields only as complicated as those in Figure 1.

The alternative to a central multipole expansion is a distributed representation, and the simplest form of this is a distribution of point charges (zero-order multipoles). The accuracy of a point-charge representation of a molecular charge field depends on the number of charges: Many small, closely spaced point charges will tend to depict a continuous charge cloud more accurately than a few sparse point charges. Point charges at atomic centers are attractive from a computational standpoint because then the electrostatic forces act directly on the atoms. However, placing point charges only at atomic centers is a concise representation that cannot be entirely accurate.

What may be regarded as a hybrid of the point charge and central multipole representations of a charge field is the distribution of low-order multipoles rather than point charges. This idea is the basis of a model called distributed multipole analysis (DMA)[15] that has been well used in the study of weakly bound complexes. This approach represents the permanent charge field in terms of distributed dipoles and quadrupoles, as well as point charges. The distribution may be dictated by or selected on the basis of a specific analysis of an ab initio wave function. Use of a Gaussian basis in the ab initio calculation means that there is some order, determined by the highest *l*-functions in the basis, at which higher order distributed moments vanish for properly chosen sites.[15] So, even for small molecules, a distributed moment representation appears to be more rapidly convergent than a central multipole representation.[15,16] A finite, and rather concise, set of distributed moments can *exactly* represent the Gaussian-basis-calculated permanent charge field of a diatomic, whereas a central multipole expansion would not be exact until infinite order. In practice, being exact in the representation is not necessary, expecially since there will be lingering errors in the ab initio calculation that yielded the electron density function. So, a smaller set of sites, the atomic centers and a site selected along each bond, are used in interaction potential applications of DMA.

Convergence advantages of almost any type of distributed multipole expansion are apparent if we consider the representation by central multipoles of a system of two well-separated ideal dipoles. This trivial system could have nonvanishing central multipoles to all order, whereas the distributed representation consisting of just the two ideal dipoles would be exact. The same could be said for separated point charges. In fact, the molecular electrostatic potential of only the skeleton of atomic nuclei would be concisely represented by distributed point charges, but an infinite set of central multipoles would be needed.

High order central moments are mostly determined by the nuclear skeleton,[17] not by fine details of the charge distribution along the bonds. In many ways, it is the low-order moments (e.g., dipole and quadrupole) that characterize bonding. This means that in small molecules (diatomics, triatomics, and tetraatomics), low-order central multipoles can succeed in representing the charge field at long range. The higher order moments become unimportant simply because of the small size of the molecule.

The important concern for molecular force fields that employ electrostatic analysis is not convergence behavior at all points in space, but accuracy of the representation in the regions of interest. Rather than an exact representation, we seek only one that is correct in the regions of interest. Probably the separation distances where charge field representations need to be most accurate are those from just under the separations associated with van der Waals radii to about twice that distance. The hydrogen fluoride dimer has an equilibrium separation distance (mass center to mass center) of about 3 Å. Accurate representation of the electrostatic fields of the two monomers when they are separated by 2.7–6.0 Å (or 90–200% of the equilibrium) is called for. At closer separations the charge distributions will tend to overlap and make invalid the physical justification for classical electrostatic potentials, and at separations beyond this range the interaction energy and forces are all weak; accuracy in the far-off regions is not important for most force field applications.

Let us examine several representations for a very simple molecule, water. Figure 2a gives the electrostatic potential, in the plane of the water molecule and in a perpendicular plane, on the basis of a large basis set, well-correlated ab initio calculation of the electronic wave function of water.[18] We shall take this as very close to a true depiction of water's permanent electrical potential. Were we to represent water's charge field by a simple dipole, we could do no better than the qualitative form of Figure 1a. However, if we truncate the central moment expansion one step further, that is, include the second moment, a reasonable representation (Figure 2b) results. Again, all we should be concerned with is the form of the potential at long range. Close in, a classical electrostatic analysis is physically inappropriate, and so there is no reason to strive for an accurate representation there or within any region of significant electron density.

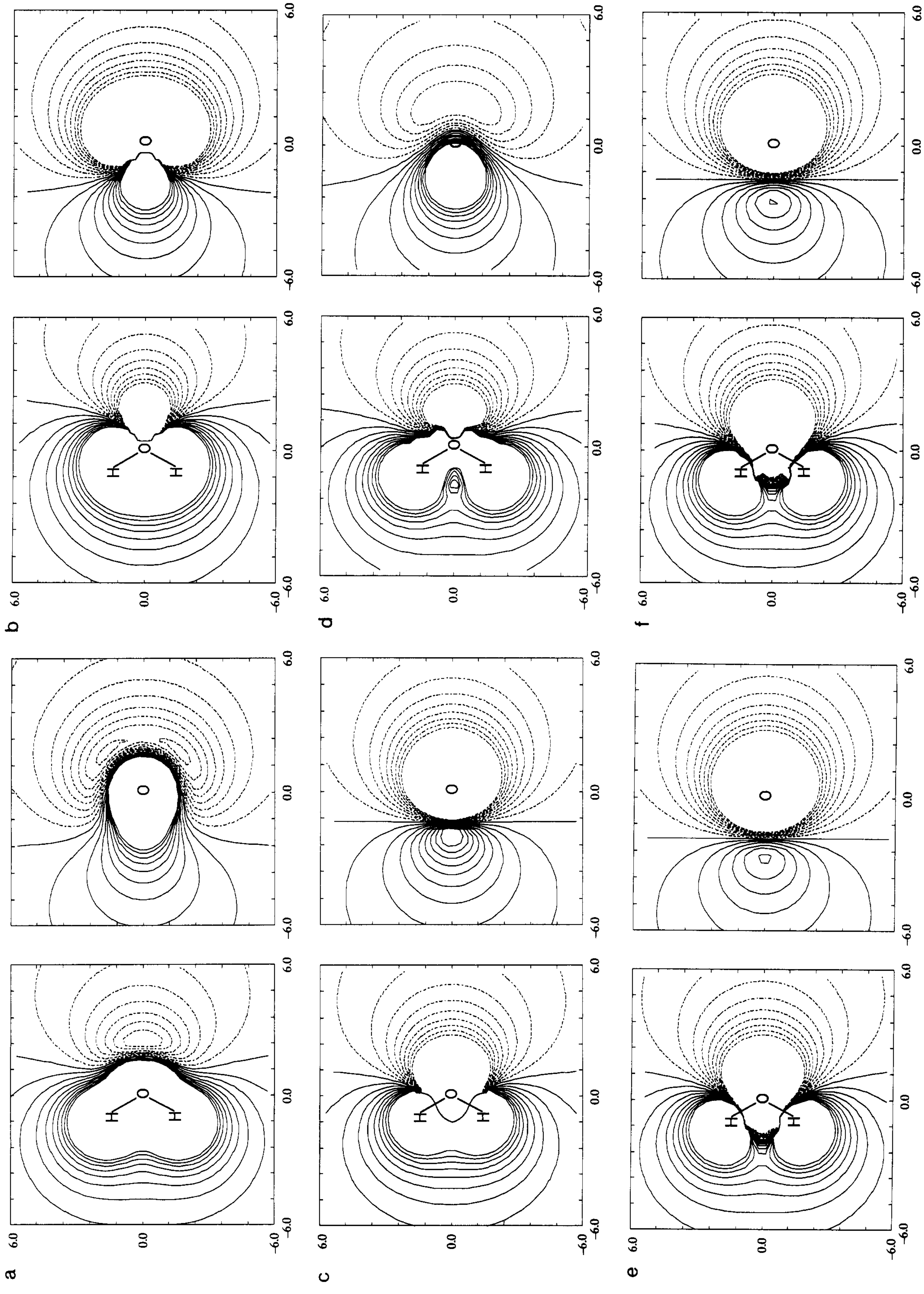
Figure 2c is a plot of the electrostatic potential of two dipoles placed essentially at the midpoints of the O–H bonds and chosen to have a magnitude and orientation such that their vector sum yields the overall permanent dipole of water. This potential is reasonably faithful to the potential of Figure 2a, although the nodal line in the contours for the perpendicular plane is off. Figure 2d is a plot of the electrostatic potential of the DMA representation of water[19] (moments through quadrupoles/atomic and bond sites), and it is rather similar to the contours in Figure 2, parts b and c. As discussed, we may expect a central multipole expansion to succeed for small molecules such as water, and so the small differences between the central multipole representation (Figure 2b) and the DMA representation (Figure 2d) are expected.

There are numerous reported point-charge representations of the charge field of water, and contours of several of these are given in Figure 2. Figure 2e shows the potential for the point charge representation of water in the OPLS (optimized potentials for liquid simulation) TIP4P model.[20,21] Figure 2f is the electrostatic potential of the SPC model,[22] and Figure 2g is of the MCY potential.[23] Relative to Figure 2a, these potentials are very good at long range, but they display a lumpiness between the hydrogens. In contrast, the four-charge ST2 model[24] does not show this lumpiness. The additional point charge makes it possible to use smaller charges, and so the otherwise sharp changes in the potential do not develop. Lumpiness is a possibility from using few charges to represent a continuous distribution, but the important concern, once again, is whether or not the undesirable artifact is found in a region of interest.

The noticeable differences in the contours in the plane perpendicular to the molecule (Figure 2) are in the location of the node line. The three-point charge representations and the bond dipole representations are the most different from the ab initio picture (Figure 2a). The central dipole and quadrupole (Figure 2b), DMA (Figure 2d), and the four-charge representation (Figure 2h) are better. This is true not only in the unimportant region close to the oxygen nucleus but also further away.

Water seems representative of small covalent molecules with one or two non-hydrogen atoms. A low-order central multipole expansion is reasonable as are other representations. This is the guidance for the representation of larger molecules; it tells us that we may be able to use a single expansion about, or in the vicinity of, a non-hydrogen center. A larger molecule in which to apply this notion is benzene. We have carried out an ab initio calculation to obtain the electron density, charge field, and multipole moments of benzene,[25] and from those results, we have compared the electrostatic potential from the calculated electron density with the electrostatic potential of a simple bond dipole representation analogous to the water representation in Figure 2c. Figure 3 shows the contours of the electrostatic potentials, including those of the DMA representation.[26] A representation we have devised (Figure 3b) that consists of six C–H bond dipoles chosen to reproduce the molecular quadrupole is effective at long range. Interestingly, the six-bond dipole representation works as well at slices above the plane of the molecule as it does in the plane of the molecule, at least for distances beyond the van der Waals radii from the atoms. This is seen by comparing Figure 3g (SCF) with Figure 3h (bond dipoles) since these give contours 1 Å above the molecular plane. That dipoles in the plane should be fairly effective at representing the electrostatic potential in benzene's π-charge cloud has to do with the dominant role of the nuclear framework in dictating the electrostatic potential of a molecule. Benzene is mostly a flat distribution of charge. Point charge representations of benzene's electrostatic field in the molecular plane are given in Figure 3, parts d and e. Distributed low-order moments, even limited to dipoles, are likely to be effective for representing molecular electrostatic potentials generally. Their advantage over point-charge distributions, if any, will be in the relative smoothness of the potentials.

The calculational differences of various representations of charge fields are much more striking than the differences in the potentials. For the calculation of an interaction energy, representing water with three point charges is very efficient. Representing it with two bond


a
b
c
d
e
f
6.0
0.0
−6.0
O
H

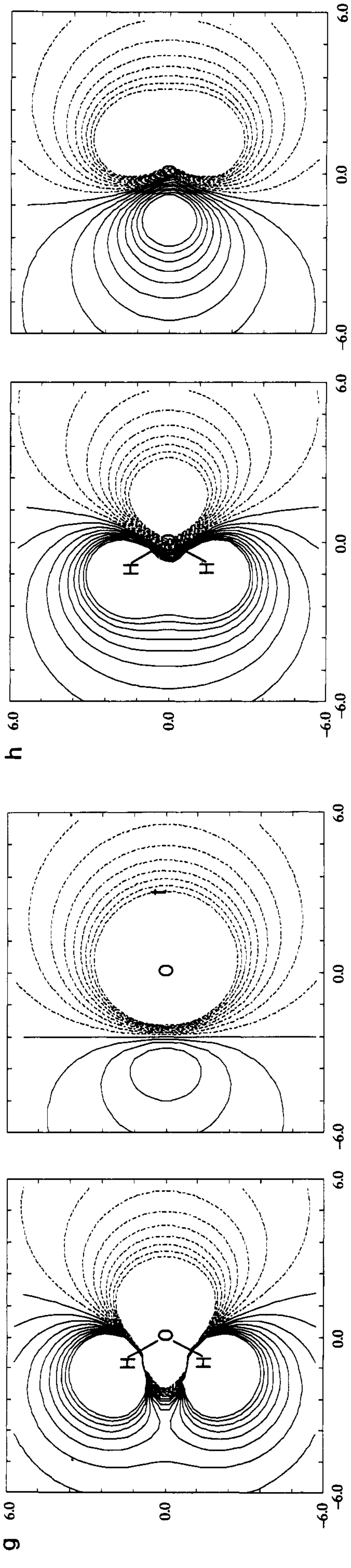


Figure 2. Electrostatic equipotential contours for the water molecule. On the left are contours in the plane of the water molecule, and on the right are contours in the plane perpendicular to the molecular plane that includes the symmetry axis. The contour spacing is the same as in Figure 1, and the distance units for the horizontal and vertical axes are atomic units (au): (*a*) The electrostatic potential obtained from the charge density of water from an ab initio calculation.[17] (*b*) The potential arising from an ideal dipole and an ideal quadrupole at the water molecule's mass center. The values of the dipole moment and the components of the quadrupole moment were obtained from the same ab initio calculation used in part a. (*c*) The potential from two dipoles placed symmetrically on the O–H bond axes at the bond mid point and with a magnitude of 0.606 au (1.541 D). The magnitude was chosen so that the vector sum of these dipoles yields the ab initio value for the molecular dipole. The position along the O–H bonds were adjusted to provide the best correspondence with the charge field from the ab initio calculation in part a. (*d*) The electrostatic potential based upon DMA analysis of an ab initio calculation on water at the SCF level.[19] Electrostatic potentials drawn for the DMA analysis[19] from MP2 and CASSCF correlated calculations show only slight differences. (*e*) The potential from three point charges of the TIP4P model.[20,21] At the hydrogens are charges of 0.52, and 0.15 Å along the symmetry axis from the oxygen is the balancing charge. (*f*) The potential from three point charges of the SPC model.[22] At the hydrogens are charges of 0.41, and the balancing charge is on the oxygen. (*g*) The MCY point charge electrostatic potential.[23] On the hydrogens are charges of 0.7175. The balancing charge is on the symmetry axis. (*h*) The potential of the ST2 model[24] which has four charges in a nearly tetrahedral arrangement. Two of the charges are on the hydrogens (0.2357), and two other point charges of opposite sign are symmetrically placed.

dipoles requires more operations, about the same as representing it with a central dipole and quadrupole. However, it is forces that are required for molecular mechanics, and in particular, forces acting on atomic centers. Central moment expansions are workable for forces if the molecule is rigid, but even then the requisite use of orientational coordinates makes the evaluations a bit cumbersome. So, there is a dilemma: The most efficient representation for calculation, point charges at atomic centers, is not the most accurate and reliable. For efficient calculation, it must be possible to quickly extract Cartesian forces on atomic centers, and this is a computational obstacle specific to each type of electrical representation.

D. Polarization

Polarization is the readjustment of a charge distribution when it experiences a static external electrical potential. Instead of the word "polarization," the term "induction" is often used for this effect on charge distributions. When both terms are used, induction is usually reserved for molecular level effects and polarization for macroscopic effects. If working entirely at the molecular level, two terms may be unnecessary; the one I will use here is "polarization" partly because this avoids possible confusion between induction and inductance, a very different quantity. And so, even though one may say that "a dipole is *induced* by an external field", we may correctly add, "because the charge distribution has been *polarized*".

The expressions for polarization energetics come about from another power series expansion. If a charge distribution experiences a uniform electric field, and if the charges are free to adjust in response to the field, the energy of interaction for the charge distribution experiencing the field can be taken to be some function of the field strength. If the charges are not free to adjust, this function is linear in the field strength, as should be evident from eq 1. Thus, a general analysis of polarization is one that allows for the interaction energy to be a nonlinear function of the field strength. The

$$E = \mathbf{F}\frac{\partial E}{\partial \mathbf{F}}\Big|_{\mathbf{F}=0} + \frac{1}{2}\mathbf{F}^2\frac{\partial^2 E}{\partial \mathbf{F}^2}\Big|_{\mathbf{F}=0} + \frac{1}{3!}\mathbf{F}^3\frac{\partial^3 E}{\partial \mathbf{F}^3}\Big|_{\mathbf{F}=0} + \ldots \quad (15)$$

$$= \mu\mathbf{F} + \frac{1}{2}\alpha\mathbf{F}^2 + \frac{1}{3!}\beta\mathbf{F}^3 + \ldots \quad (16)$$

quantities μ, α, and β, which are the dipole moment, the dipole polarizability, and the dipole hyperpolarizability, respectively, are simply derivatives of the energy with respect to the field strength. (It is a common convention choice to write E as the negative of the expression given above. That affects the signs of any stated property values.) Of course, the field, $\mathbf{F}$ is properly a vector, $\mathbf{F} = (\partial V/\partial x, \partial V/\partial y, \partial V/\partial z)$, and so the energy derivatives take the form of tensors, rank one tensor for the first derivatives, rank two for the second derivatives, and so on. Third derivatives are hyperpolarizabilities, but fourth derivatives are termed second hyperpolarizabilities. From there on, further differentiation means a higher order of hyperpolarizability.

An external electrical potential may be nonuniform, which means that in addition to derivatives with respect

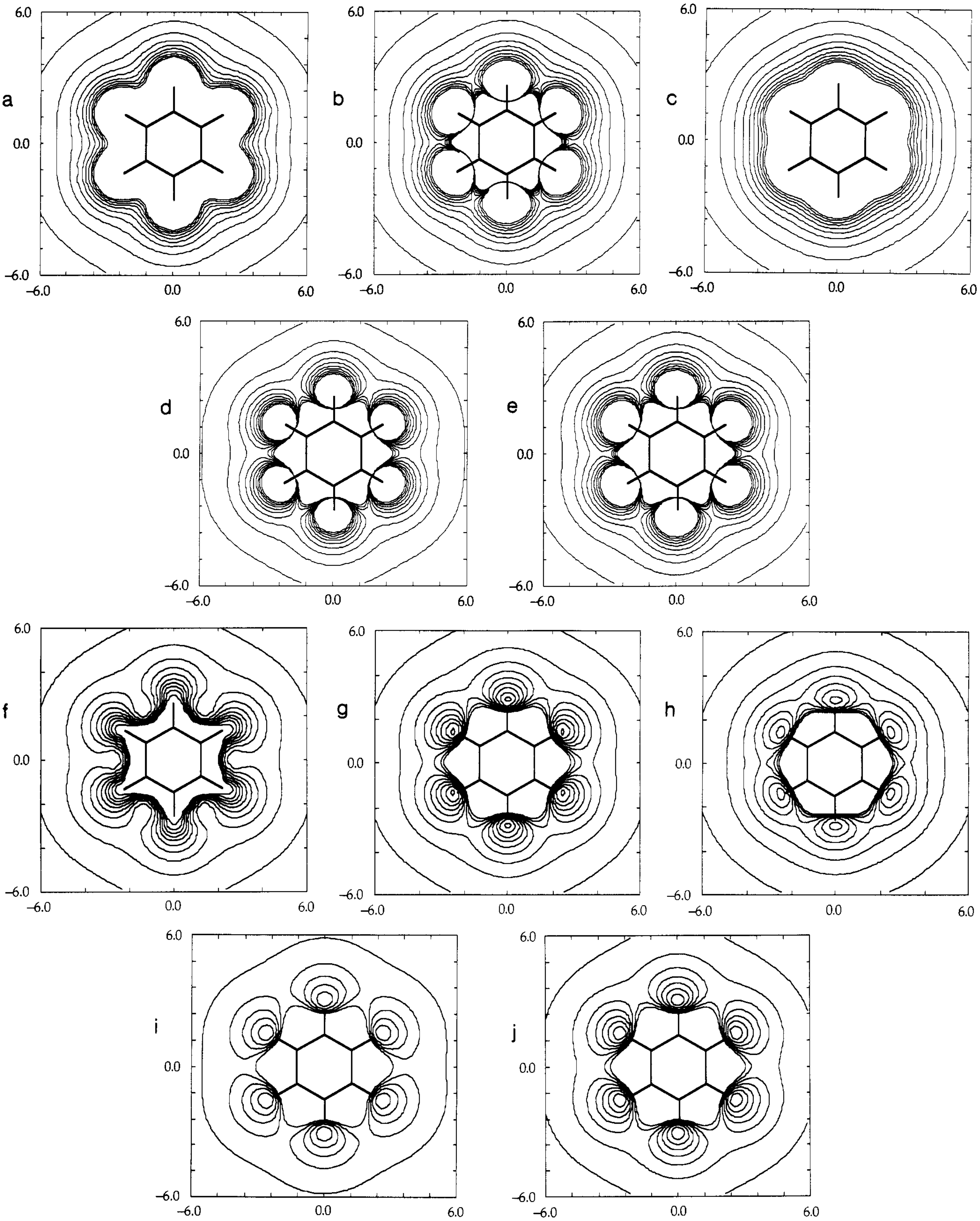


Figure 3. Contour plots of the electrostatic potential of benzene in the plane of the molecule and above the plane of the molecule.[25] The first five plots are in the molecular plane, and the last five are for a parallel plane 1 Å above the molecular plane. Contours shown represent equipotentials starting outward from 0.002 au (1.0 au test charge) and going inward to higher equipotentials in even steps of 0.002 au. The coordinate axes are labeled in atomic units (au). These plots show the in-plane potentials (*a*) from the electron density obtained from an ab initio SCF calculation with a large basis set, (*b*) an arrangement of six dipoles of magnitude 0.89 D aligned along each C–H bond at 0.503 Å out from the carbon, (*c*) the DMA representation of Price,[26] (*d*) The OPLS point charge representation,[20] and (*e*) the point-charge representation of Williams.[4] Likewise, they show the potentials in a plane above the molecule from (*f*) the SCF calculation, (*g*) the arrangement of six-bond dipoles, (*h*) DMA, (*i*) OPLS, and (*j*) Williams' point-charge representation.

to field components, the derivatives with respect to field gradient components characterize the electrical response of the charge distribution. The derivatives with respect to field gradient components (e.g., V_{xx}) carry the label "quadrupole". The first derivatives are the elements of the quadrupole moment, and the second derivatives are the elements of the quadrupole polarizability, and so on. There are also mixed derivatives such as the dipole–quadrupole polarizability, which is the set of energy second derivatives with respect to field components and field gradient components.

The polarizabilities and hyperpolarizabilities of all multipoles and to all orders may be arranged into polytensors. All moments comprise a rank one polytensor, the **M** tensor of eq 11. All polarizabilities are included in a rank two polarizability, which may be designated $\mathbf{P}^{(2)}$, and so on for all n-order derivatives in nth rank tensors $\mathbf{P}^{(n)}$. Particularly for polarization energetics, the polytensor organization allows for computation that is virtually transparent to the moment order,[12–14] and this is an important computational feature. The polarization energy of a charge distribution experiencing an external electrical potential, **V**, is simply

$$E = {}^{1}/_{2}\mathbf{V}\mathbf{P}^{(2)}\,\mathbf{V}^{\mathrm{T}} \qquad (17)$$

This expression applies regardless of the order of truncation of the multipole expansion because $\mathbf{P}^{(2)}$ may include, depending on the truncation, the dipole polarizability, the dipole–quadrupole polarizability, the quadrupole polarizability, the octopole polarizability, etc. (Most often, polarizabilities are reported opposite in sign to that implicit in eq 17. With that convention, a positive dipole polarizability value would correspond to an energy stabilization, $E < 0$, from application of a uniform field.)

Equation 17 immediately shows an important feature of polarization, that it incorporates cooperative or nonpairwise additive elements into a potential. In a system of three molecules, A, B, and C, the polarization energy will be a sum of contributions from each molecule. Different external potentials are additive in effect, and so the potential at A (neglecting back polarization) is the sum of potentials arising from the moments of B and of C following eq 11. That is, **V** in eq 17 is a sum of contributions. Since E has a quadratic dependence on **V**, cross-terms appear, and the result will be three-body terms, which in this case would be moment elements of B multiplying moment elements of C multiplying polarizability elements of A. Neglecting mutual effects means that the polarization energetics give rise to no higher than three-body terms. Hyperpolarization brings in four-body terms, and the inclusion of second hyperpolarizabilites implies five-body terms.

The detailed expressions for treating electrical polarization do not need to be restated in this review. They have been presented elsewhere in several forms (see, for example, refs 2–4, 12–14, and 27–29), and in any case, it is clear that high-order multipole representations and high-order hyperpolarization analysis will be cumbersome for the purposes of molecular force fields. Rather, the extensive treatments of polarization provide a benchmark for devising and evaluating simpler schemes. There are, however, two complications that must be considered. The first is that polarization between atoms and molecules is a mutual effect. The charge field of molecule A may polarize molecule B, but then it is the now polarized charge field of B that acts on A. Hence, the analysis of mutual charge polarization requires a solution of coupled equations. The incorporation of mutual polarization implicitly gives N-body elements for the interaction potential of an N-body system. These coupled equations become nonlinear if hyperpolarization (third derivatives of the energy) are included. Again, the details are not especially important in the context of this review, because the "back" polarization (the difference between the permanent charge field of B acting on A and the polarized field of B acting on A) tends to be small. The sizes of back polarization effects are discussed later. The second complication is that inclusion of polarization energetics adds to the computational effort for evaluating forces. This is considered in the next section.

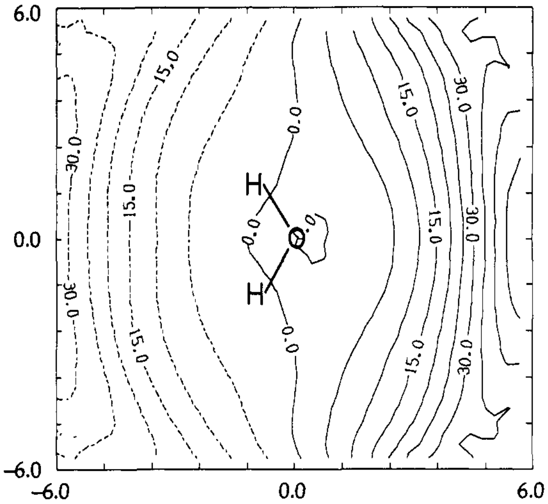


Figure 4. Contours of the relative difference in the electron density of water between isolated conditions and perturbation by an electric field along the symmetry axis of 0.01 au (5.14 × 10^7 V/cm). Difference contours are in percent of the density of isolated water and are drawn for the plane of the molecule.

An idea of the effect of polarization on molecular charge clouds can be obtained from comparing charge densities and electrostatic potentials with and without an external field. Calculations have been done on the water molecule experiencing a uniform external field along the symmetry axis of 5.14 × 10^7 V/cm (0.01 au), and results may be compared to those with zero field. This choice of a perturbing field is representative of the largest size of field that molecules experience from the charge fields of polar molecules at van der Waals separation distances. The charge densities of perturbed and unperturbed water turn out to be so similar that contour plots are almost indistinguishable. We have not presented them for that reason, but their similarity is important in showing that the overall shape and size of the molecule are not appreciably altered by the external field.

A plot of the difference in density between perturbed and unperturbed water can be presented on a meaningful scale, and on a relative basis, this is given in Figure 4. It shows the expected result that density is shifted in the direction of the field. Furthermore, the greatest relative changes are in the fringe regions of the electron density. The polarization response of a small

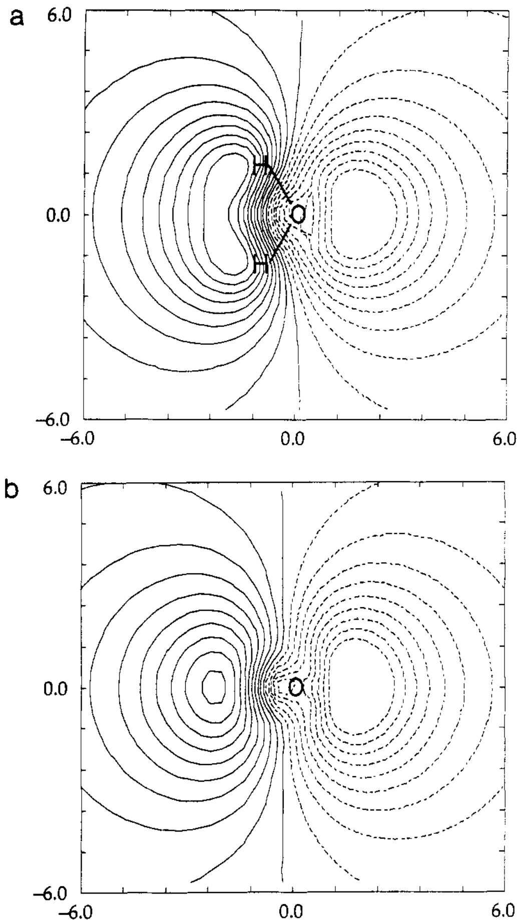


Figure 5. Difference electrostatic equipotential contours for the charge distribution of the water molecule as it experiences a uniform external electric field of 0.01 au or 5.14 × 10^7 V/cm along the symmetry axis: (*a*) contours in the plane of the molecule and (*b*) contours in the plane perpendicular to the molecular plane. These contours are obtained from the electrostatic potential of perturbed water less the electrostatic potential of isolated (unperturbed) water (as in Figure 2a). The innermost or highest contour is at 1800 cm^{-1} for a test charge of 1.0 au, and the step size between contours is 200 cm^{-1}.

molecule (one non-hydrogen atom) is mostly a response in the regions of space away from the atomic nuclei.

The electrical potential arising from the charge distribution of a molecule changes somewhat as the molecule is polarized by an external field. The difference between the electrical potential about unperturbed water and water polarized by a small field along the symmetry axis is presented in Figure 5. At van der Waals separation distances, the difference in the potential is roughly about 10% of the permanent electrical potential, or less. An interesting feature of the contours in Figure 5 is that the in-plane and out-of-plane contours are quite similar, but not exactly the same. The uniform electric field induces or affects the dipole and higher order multipoles. The asymmetry of the in-plane and out-of-plane difference contours are a manifestation of the molecular structure as well as an indication that the field affects higher order multipoles.

E. Distribution of Polarization Response

The polarization of a molecule can be characterized by the multipole polarizabilities and hyperpolarizabilities. However, the difficulties of using a central multipole expansion for a large molecule apply to the polarization as well. The alternative, again, is to distribute the polarization response. However, this is more complicated than the distribution of permanent moments because of mutual polarization. For example, one may attempt to represent the polarization response of some diatomic AB with a dipole polarizability on A and on B. If an external field is applied to the molecule, local polarization will occur at both A and B. However, the dipole induced at A gives rise to a field that B experiences. If the effect of that field is included in evaluating the polarization of B, then we are treating mutual polarization as if the charge distributions on A and B were not connected or not overlapping.

Classical electrostatics breaks down in describing mutual polarization within a molecule because the true polarization response follows from the quantum mechanically determined response properties of the molecule. However, if external electrical potentials are very weak, then the neglect of mutual polarization (classical or quantum mechanical) may be justified. That is, the direct polarization interaction energy of eq 7 should be the dominant term in a general power series expansion, such as eq 14, in the limit of weak external fields. On this basis, one may freely distribute polarizabilities provided that intramolecular mutual polarization is neglected.

The issue that arises at this point is the choice of the distributed properties. One approach is to "match" distributed properties with overall molecular response properties. For instance, the tensor sum of the distributed dipole polarizabilities may be fixed to be the same as the overall molecular dipole polarizability tensor. We have used this procedure to represent benzene.[25] Another procedure is to directly extract them from an ab initio wave function, and Stone has devised and implemented such a procedure.[30]

II. Construction of Electrostatic Potentials and Force Fields

A. Intrinsic Electrical Response Properties

Developing electrostatic potentials and force fields calls for values of electrical response properties. These values can be taken to be empirical parameters along with other force field parameters, and this is often the way atomic point charges are chosen. The role of electrostatic analysis in that case is simply to select an appropriate functional form for the given interaction term. A more rigorous, although not necessarily more effective, application of electrostatic analysis involves using intrinsic molecular electrical response properties. This removes the empiricism, but in exchange it demands that values be reliable.

Electrostatic potentials of small molecules can be well represented by a low-order central multipole expansion, and the polarization response usually requires only a few multipole polarizabilities. These are properties which are directly, and rather easily, obtained from ab initio electronic structure calculations. Distributed moments and polarizabilities can be extracted directly from ab initio calculations,[15,19,26,30] or they can be chosen to match the central moments and polarizabilities. Either way, the quality of the ab initio calculation of

Table I. Calculated and Experimental Values of Electrical Response Properties[a]

	ab initio calculation		
property	SCF	correlated	experimental
N_2 quadrupole (au)	0.886 (31)	1.085 (31)	1.09 (32a)
N_2 polarizability, α (au)	11.512 (33)	11.675 (33)	11.74 (32b)
N_2 second hyperpolarizability, γ (au)	665 (33)	830 (33)	850–865 (32c, 33)
HF dipole (au)	−0.767 (31)	−0.715 (31)	−0.707 (34)
HF polarizability, α_{axial} (au)	5.764 (35)	6.428 (35)	6.40 (35, 36)
HF hyperpolarizability, β_{axial} (au)	−8.548 (35)	−9.838 (35)	

[a] All ab initio calculations used large, multiply polarized basis sets. References are in parentheses.

the properties is central to the question of reliability of the electrical representation.

We have reviewed the ab initio calculation of molecular electrical properties,[31] and there are several ideas that have emerged to guide the choice of a calculational level. There are, of course, two factors that affect the quality of an ab initio calculation, electron correlation and basis set completeness. The effects of electron correlation on electrical properties seem rather well understood. Typically, correlation effects have an importance on polarizabilities and hyperpolarizabilities that increases with the order of differentiation associated with the property. Thus, the correlation effect on polarizabilities of small, covalent molecules is usually up to 10%, whereas a typical correlation effect on hyperpolarizabilities (third derivatives) may be up to 25%. These trends are illustrated by the examples in Table I. The relative correlation effect on permanent moments of small molecules can be small or large depending on whether the value of the moment is large or near zero. Typically, the correlation effect on a dipole moment is up to about 0.2 D (0.1 au), and the effect of the quadrupole moment is up to about 0.3 au. It should also be pointed out that basis set deficiencies can amplify the correlation effect; that is, the correlation effect may be overvalued with a poor basis.

Basis set quality is very important in electrical property calculations. Permanent moment evaluations may be suspect if the basis lacked at least one set of polarization functions. Polarizabilities require a second set of polarization functions more diffuse than the first, and hyperpolarizability requirements follow the same direction. The reason for this is that the regions of electron density that show the greatest relative effect upon polarization are the extreme or fringe regions; with conventional Gaussian bases, diffuse functions are needed to describe that response. Particularly poor values of hyperpolarizabilities can result from the use of minimal or even double-ζ valence sets for small molecules.

As molecule size increases, basis set requirements change, and in one sense that change is toward less stringent requirements. As has already been mentioned, permanent multipoles, especially higher order multipoles, of extended molecules are largely determined by the nuclear skeleton. A valence basis that is capable of roughly describing the electronic structure at each atom in a molecule will be suited to obtaining the dominant part of the contributions to the multipoles. Calculations of polarizabilities also tend to have less stringent basis set requirements as molecule size increases because the polarization response increasingly becomes a shift of charge along the molecular skeleton. Again, valence bases may be sufficient, or at least better than in a small molecules (no more than one non-hydrogen center).

B. Intermolecular Electrical Potentials

Perhaps the most valuable use of electrostatics, or at least the most suited application, is in weak intermolecular interaction. This is a long-range interaction, and so one charge cloud is weakly perturbed by another usually without strong overlap. A number of electrostatic models have been devised specifically for the treatment of weak intermolecular interaction in small molecule clusters. Even though these tend to invoke electrostatics rigorously, there is an element of modeling and empiricism because at some point, electrostatics is incomplete. Electrostatic potentials follow the laws of classical interaction, and at some point of approach, quantum mechanical effects are not ignorable. In particular, ideal multipoles will tend to coalesce, and so at the very least, some type of wall potential must be included with the electrostatic potentials to provide a realistic description over the intermolecular degrees of freedom.

The model of Buckingham–Fowler (BF)[37,38] assigns ideal permanent multipoles (zero, first, and second) to atoms according to a DMA analysis. These are embedded in perfectly (infinitely) hard spheres whose radii are atomic van der Waals radii. The hard spheres preclude approach at any distance less than a van der Waals radii contact distance, and so, they serve to represent the nonelectrical parts of the interaction energy that would prevent the coalescence of ideal multipoles. Shapes, or relative monomer orientation information, for small molecule dimers seem well predicted with this model.[37–40]

A more complete treatment of the nonelectrical part of weak intermolecular interaction is a key element of a model developed by Spackman.[41,42] This model exploits the DMA representations to obtain permanent charge field interaction energies. It also incorporates charge penetration effects. The other effects, such as the repulsive wall, are incorporated into atom–atom "exp-6" terms (i.e., for atoms separated by a distance r, "exp-6" are potential energy terms of the form exp ($-cr$) and r^{-6}). This yields a smooth, continuous potential over intermolecular coordinates. Whereas a "billiard ball" (infinitely hard) potential can be predictive of nothing more than the well depth and orientation, Spackman's model can be used to obtain the minimum-energy separation distance and other features of the full potential surface.

The molecular mechanics for clusters (MMC) model[6,14,43,44] uses empirical atom–atom "6–12" potentials (i.e., r^{-6} and r^{-12}) for the nonelectrical part of the potential, and so, as in Spackman's model, MMC has been designed to model the full intermolecular potential surface. So, both Spackman's model and MMC can be used to calculate intermolecular (weak mode) vibrational frequencies.[44,45] The permanent charge fields used in MMC are represented by central multipoles for small molecules and distributed multipoles in the limited cases where larger molecules have been treated.

Table II. Model Predictions[a] for Small Cluster Structures

cluster	model	calculated/experimental values[b]	
$(HCl)_2$	MMC	R_{com} (Å):	3.832 (79)/3.81 (80)
		θ_1:	22 (79)/0–10 (80)
		θ_2:	89 (79)/70–80 (80)
		stability (cm^{-1}):	667 (79)/817 (81)
		electrical share of stability:	567
$(HCCH)_3$	MMC	R_{com} (Å):	4.328 (82)/4.354 (83)
		orientation:	cyclic (82)/cyclic (83)
		stability (cm^{-1}):	1898 (82)
		electrical share of stability:	1772
HCCH–HF	MMC	R_{com} (Å):	3.007 (82)/3.075 (84)
		orientation:	T-shape (82)/ T-shape (84)
		stability (cm^{-1}):	2000 (82)
		electrical share of stability:	3135
H_2CO–HF	BF	θ_1:	113 (38)/115 (85)
		θ_2(COF):	110 (38)/109.5 (85)
N_2–HF	BF	orientation:	linear (38)/linear (86)
H_4C_2–HCN	BF	orientation:	HCN perpendicular to plane (38)/same (87)

[a] BF = Buckingham-Fowler (refs 37 and 38); MMC = molecular mechanics for clusters (refs 43 and 44). [b] References are in parentheses.

The multipoles are obtained from high-level ab initio calculations. The MMC model was the first to incorporate comprehensive treatment of electrical polarization. The computational techniques developed for MMC[14] provide for open-ended treatment to all orders of hyperpolarization and all orders of multipole; however, in practice low-order multipoles and hyperpolarizabilities only through the dipole hyperpolarizability are included. In MMC, the complete mutual polarization equations are solved for any number of interacting species, and so the cooperative elements of electrical interaction are not ignored.

The BF model, Spackman's model, and MMC have had generally good success in predicting structural features and a well depths of small complexes. A few examples of MMC and BF results are given in Table II. This success, in spite of the differences between the models, underscores the suitability of the electrostatic foundation for the models. Also revealed in Table II is the fact that electrostatic contributions to the total energy, at least within the MMC model, do not consistently overwhelm the other terms. Nor is the electrical share consistently less or consistently more than the total energy at equilibrium. Simply, it is not necessary that the electrical energy be a bound or even that it be dominant to use electrostatics as a primary model element.

The MMC model can be viewed as overlaying a traditional Lennard-Jones (6–12) potential with intermolecular electrostatics. The 6–12 potentials are, for problems of weak intermolecular interaction, the elements that represent all the core/valence interactions that arise quantum mechanically. Were the model not designed for rigid molecules, a more complicated form for this element would be needed, but that could easily be extracted from conventional molecular mechanics force fields. Going the other way, the potentials and force fields that develop from intermolecular electrostatic models may, with some reworking, overlay valence force fields in conventional MM programs.

C. Electrical Elements of Full Molecular Force Fields

Electrostatic elements are part of most all conventional molecular force fields,[46] and most often these elements take the form of atomic point charges. Incorporation of electrostatic elements offers a way of extending valence force fields to include intermolecular forces. Also, electrostatics terms may be the exclusive element for intramolecular interactions that are analogous to weak, intermolecular interaction. The relative orientations of two functional groups attached to adjacent carbon atoms might be properly represented by the interaction of local dipoles on the functional groups (or corresponding point-charge distributions). In intramolecular interactions, however, there may be both through-space interactions and valence interactions through the molecular framework. Empirical selection of force field parameters will not separate these, whereas realistic modeling of the electrostatic interaction may account for the through-space element.

A number of molecular mechanics force fields have gone beyond atomic point charges, and we shall consider several of these. For instance, Allinger has used both bonds dipoles and point charges for molecules with net charges in MM3,[47–49] and this has yielded good success for the structures of organic crystals.[49] The electrostatic representation of MM3 also includes atomic point charges for ionic species, and dipoles on atomic centers for certain lone pair structures. The logical choice of the orientation of the bond dipoles is along the bonds, and this seems to be the most practical choice as well.[50] Atomic dipoles (plus monopoles) could be used, but transferability may not be as good.[4,50]

Polarization energetics have been introduced in molecular mechanics force fields by several groups. Warshel and co-workers have demonstrated useful improvements upon including polarization.[9,51–53] In application to water, the polarization response in their approach is characterized by an isotropic dipole polarizability at the oxygen center.[52] A distance-dependent shielding factor is introduced to screen the polarizable centers from the full permanent moment charge field. An important aim is to achieve a representation that is transferable from small gas-phase clusters to the condensed phase.

Kollman and co-workers have also used atomic dipole polarizabilities to incorporate three-body effects.[54–56] In their approach, the atoms are perturbed by the atomic charges that constitute the permanent charge field representation. The coupled polarization equations are solved to yield the polarization energy and the dipoles induced at each atomic site. The analytical evaluation of forces due to polarization follows a procedure of Ahlström et al.[57] Kollman's results highlight the importance of nonadditivity, which arises with polarization energetics and with three-body repulsions, in the condensed phase or in extended aggregations.

There have been a number of models developed specifically for water and including polarization.[57–65] These are intended for liquid simulation. An approach used originally for water, but extended to other molecules, is the polarization model of Stillinger and David.[66] The permanent charge field representation is through point charges, and augmenting that are dipole polarizabilities that provide for charge readjustment upon interaction with neighbor species. It models the changing response of molecules to stretching and distortion through dissociation. It was used first for water simulations, but the characterization or parameter determination has been carried out for a good number of other molecules.[67]

The conclusion that seems to hold from water simulations is that polarization effects are important for constructing potentials that are suited both to isolated small clusters and to the condensed phase. Although nonpolarization effective potentials can be designed for liquid and solid simulations (e.g., OPLS[20,21]), these do not tend to give correct dimer information. The cooperative, or nonpairwise additive, feature of polarization means that it can play a crucial role in reducing molecule separations with increasing aggregation, exactly what is needed to go from a dimer to the condensed phase. So, polarization very much seems to be the essential element to achieve generally applicable potentials.

D. Forces from Electrostatic Potentials

There are a number of complications in the calculation of forces from potentials based on electrostatics. Most of these complications are associated with the representation that is employed. Atom-centered point charges and no incorporation of polarization are clearly the easiest. Multipoles beyond zero order on atoms add a directional dependence, and multipoles offset from atoms require analysis of torques. Direct polarization requires higher level electrostatic analysis to obtain forces, and mutual polarization requires solution of derivatives of the coupled polarization equations.

Forces are the derivatives of the potential energy with respect to the chosen set of geometrical parameters. For most uses of conventional molecular mechanics force fields, the chosen geometrical parameters are Cartesian displacement coordinates of the atoms. Electrostatic potentials involving only point charges on atoms yield forces directly. For example, a charge q at the point (0,0,0) will experience a force along the x axis from a charge q at the point $(x',0,0)$, as is obtained from the derivative of the potential energy from eqs 1 and 2:

$$\frac{\partial E}{\partial x}\Big|_{x=0} = \frac{\partial}{\partial x}\left(\frac{q^2}{x-x'}\right)\Big|_{x=0} = -\frac{q^2}{x'^2} \tag{18}$$

For higher permanent multipole interactions, forces may be obtained by differentiation of the energy in eq 14 with respect to the chosen internal coordinates. For those coordinates that are the same as the position coordinates of the multipole center (i.e., for the translational forces acting on the multipole), the differentiation implicitly calls for the next higher order **T** tensor, $\mathbf{T}^{(3)}$, since the order represents the differentiation with respect to the position coordinates.[13] Computational procedures have been devised and implemented to generate **T**-tensors to arbitrarily high order;[14] however, even with the most efficient algorithm, the computational cost is considerably greater to obtain $\mathbf{T}^{(3)}$ than $\mathbf{T}^{(2)}$ if there are moments beyond the dipole.

The directionality of first and higher order moments means that electrical interaction can give rise to torques as well as translation forces. One can insert a suitable direction cosine matrix into eq 14, and torques can be obtained by differentiation with respect to the angles. This is particularly useful for rigid intermolecular potentials with molecule-centered moment expansions. The calculated torques are the forces acting to twist the molecules. In the MMC model,[43] Euler angles have become the preferred choice of orientational coordinates; however, a coordinate transformation is then required so as to obtain torques about three orthogonal axes.

Multipoles not placed on atomic mass centers give rise to torques which then yield forces at the atomic centers. Explicit formulae have been presented by Price et al.[68] However, force evaluation for general multipolar distributions does not appear to be in use.

Forces that arise from polarization are computationally difficult because they include at least up to three-body effects and because they are at least quadratic in the electrostatic potential at any point. One may limit the force evaluation to direct polarization and exclude back-polarization effects in order to simplify the problem. The mutual polarization effects beyond direct polarization may offer small improvement in forces; however, the coupled equations that must be solved to find the polarization energy means there will be a further set of equations for each force. Such a treatment may be of interest for benchmarking purposes, but practical use in molecular mechanics seems unlikely now.

An ideal dipole polarizability placed along a bond but not on an atom will give rise to torques on the atoms. Analysis of these contributions follows the treatment of multipoles, except that there is a quadratic dependence on the **T**-tensor via the quadratic dependence on the potential (eq 17). From a computational standpoint, explicit treatment limited to the dipole polarizability should be much less costly than including second moment polarizabilities because of the quadratic dependence on the **T**-tensor for translational forces, and a quadratic dependence on direction cosines for torques. Explicit, analytical treatment of forces from dipole polarizable atomic centers has been reported by Kuwajima and Warshel[52] and by Ahlström et al.[57]

IV. The Intimate Connection between Electrostatic Force Fields and Properties

A strong motivation for invoking electrostatic analysis in force field construction is that it may help reveal or deduce property information. While it is true that properties could be analyzed apart from the energies and forces, simultaneous success on both fronts of attack is surely a good indication of a physically sound model or approach. The centermost issue is whether the model accounts for the electronic structure of the species, or at least the changes in electronic structure. In an electrostatic picture, this means going beyond permanent charge fields (no electronic structure change) and including polarization effects; polarization *is* a change in electronic structure. Wherever property changes are well predicted by electrical polarization effects, it is likely that polarization constitutes the primary electronic structure change.

A standard property example is the dipole moment, and Table III gives electrostatic results for two small-molecule clusters, the water dimer and a linear HCN

Table III. Polarization Contributions to Dipole Moments (D) of Small-Molecule Clusters

	$(H_2O)_2$	HCN–HCN–HCN–HCN
permanent dipoles	2.003	12.153
mutual polarization[a]		
with α	2.404	14.395
with α, A, C	2.473	14.361
with α, A, C, β	2.471	14.357

[a] Dipole moments were obtained from MMC calculations at the equilibrium structure of the cluster calculated with MMC. Solution of the mutual polarization equations was performed with the inclusion of the listed properties: α = dipole polarizability, A = dipole–quadrupole polarizability, C = quadrupole polarizability, and β = dipole hyperpolarizability.

tetramer. The series of calculations shows the permanent moment values, the values from including the dipole polarizability, and from including other polarizabilities and hyperpolarizability. For both clusters, the polarization effects beyond those associated with the dipole polarizability are small. The dipole hyperpolarizability also has a small effect. The question of whether the electrostatic analysis that yielded the values in Table III is correct, or nearly correct, may be answered by high-level ab initio calculations. The electrostatic analysis is incomplete because it neglects intermolecular quantum features, and so, the obvious comparison is with a calculation that incorporates quantum effects. We have studied properties both ways in a number of small complexes, and we consistently find good correspondence. The first study was of $(HF)_2$, and in the course of that work,[69] we calculated the dipole moment, dipole polarizability, and hyperpolarizability as a function of separation distance. Electrical analysis accounted for all the properties nicely.

Electrostatic analysis should yield simultaneous success in property evaluation and in force field determination in those cases where the relative effect on electronic structure is polarization, but only if polarization is the primary change. We have argued[6,59,70] that this is the situation for weak interaction between closed shell atoms and molecules, where by our experience, we take weak to be anything from 0 to ±10 kcal or so. It is important to indicate that within an electrostatic view, there is no distinction between hydrogen bonding and other weak interaction. The basis for, and analysis of, the interaction between water and benzene, between acetylene and nitrogen, and between nitrogen and carbon monoxide are the same. The presence of hydrogen atoms to make hydrogen bonds is only a modification of the electrical response properties, not the basic nature of intermolecular interaction. Furthermore, certain long-range intramolecular interactions likely fit the same form, although we do not yet have full knowledge of which these are.

The notion that there are situations where the electronic structures of several interacting species are changed by the interaction in a way that corresponds to simple electrical polarization is a powerful notion, when it holds. And that is when forces and energies can be predicted along with properties through one analysis, polarization electrostatics. From a number of studies, we believe this notion does hold for weak interaction, and therein is the intimate connection between electrostatic force fields and properties. The MMC model[43,44] that has been discussed earlier solves the mutual polarization/hyperpolarization equations for an assembly of species and in so doing it obtains the classical electrostatic prediction of the change in electronic structure. For instance, we find the induced moments to any order desired and the total external field and field gradient at each species. From this analysis, we may obtain changes in properties provided we know the values that characterize the response of the properties to external fields, field gradients, and so on. We have used the electrostatic machinery of MMC or its precursors to calculate changes in electrical moments,[69] in vibrational frequencies,[71-73] in vibrational transition probabilities,[74,75] in chemical shielding,[76,77] and in nuclear quadrupole coupling.[78]

V. Outlook

Molecules are distributions of charge. A question to be answered in order to construct force fields and interaction potentials is whether molecular charge distributions interact quantum mechanically or classically, that is, whether quantum mechanical analysis must always be invoked. In the limit of large separations, classical electrostatics can yield a nearly correct picture, whereas at bonding distances, classical analysis has no place. Between these limiting situations, it seems appropriate to use electrostatics supplemented with terms that correspond to nonelectrical interaction. Indeed, invoking electrostatics is commonplace.

The certain problem that is faced in constructing force fields incorporating electrostatic terms is the choice of representation. Coupled with this is the fact that except at very long range, electrical interaction is not entirely separable from other elements. Thus, accuracy in the electrical representation alone rarely seems productive. As well, errors in one part of a force field or potential may be off set in the other parts. However, the growing realization that certain properties may be calculable from electrostatic analysis implies a greater emphasis on completeness in the electrical representations.

Atomic point charges are the simplest type of electrostatic force field, from the standpoints of both implementation and computation. But enhancing these simple representations through distribution of higher order multipoles (dipoles, or dipoles and quadrupoles) and through incorporation of polarization energetics seems essential for reliable treatment of weak intra- and intermolecular interaction. What we may expect to emerge are general models that are applicable in the condensed phase and for small gas-phase species as well. The results that have been achieved so far make this appear likely.

Acknowledgments. I very much wish to thank Kenneth A. Franken for preparing Figures 1–3 and 5. Discussions with collaborators Dr. Joseph D. Augspurger, Professor H. S. Gutowsky, Professor E. Oldfield, and Professor T. S. Zwier have been extremely valuable in the pursuit of certain of the problems that I have discussed here. The support of the National Science Foundation through grants from the Physical Chemical Program is gratefully acknowledge. In addition, support from the donors of the Petroleum Research Fund and support from a grant of the National Institutes of Health has been extremely important in our developments in this area.

VI. References

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