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Results from an Early Polarization Model Based on Maxwell's Invariant Multipole Form

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Abstract: This paper reviews the cooperative water model of Campbell and Mezei based on the Maxwellian form of multipole interaction. The Maxwellian form is described, and the algorithms and software for their implementation in both disordered and ordered phases are presented, followed by the specifics of the model. The model has been used in a number of calculations on various water clusters, liquid, and crystal models. The results of these calculations are briefly summarized, and their implications, relevant to polarization model in general, are discussed.

Introduction

Standard statistical mechanics offers a systematic treatment of cooperative interactions by partitioning the total energy into sums of two-body, three-body, etc. terms. This approach is quite general and does not take advantage of the specific nature of interactions. Terms beyond the two-body represent the cooperativity of the interaction.

For interacting molecules, the cooperativity is due to the deformability of the electron density upon interaction. For water clusters, Del Bene and Pople[1] demonstrated that such cooperativity is indeed significant. This led to the idea of representing the cooperativity of water−water interactions with interactions of induced moments albeit at first in a negative manner: the idea was first discarded out of hand based on the fact that dipoles represent cylindrical symmetry but that the charge distribution of water has only planar symmetry.[2] As the results reviewed here on Ice Ih calculations show, this skepticism is not unfounded in the sense that the contributions beyond dipole polarizability are not negligible. However, the use of dipole polarizability has proven to be very useful in modeling the cooperativity of water, as witnessed by subsequent work in the Stillinger Laboratory[3] as well as the model, contemporary to Stillinger's, reviewed here.

Background

The Maxwellian Form of Multipole Interaction. The energy of the electrostatic interaction of two nonoverlapping charge distributions A and B can be expressed through a double Taylor series of $1/|\mathbf{r}_B - \mathbf{r}_A|$ about the two origins $\mathbf{O}_A$ and $\mathbf{O}_B$

$$E_{AB} = \sum_{N=0}^{\infty} \sum_{0 \le N_A + N_B \le N}^{\infty} E_{N_A,N_B} \tag{1}$$

with

$$E_{N_A,N_B} = \sum_{n_{A1}+n_{A2}+n_{A3}=N_A} \sum_{n_{B1}+n_{B2}+n_{B3}=N_B}$$

$$\prod_{k=1}^{3} (\nabla_{Ak})^{n_{Ak}} \prod_{k=1}^{3} (\nabla_{Bk})^{n_{Bk}} I_A(\mathbf{n}_A) * I_B(\mathbf{n}_B)(1/(|\mathbf{r}_B - \mathbf{r}_A|))|_{r_\gamma = O_\gamma} \tag{2}$$

where $\gamma = A$ or B

$$\nabla_{\gamma k} = (\partial/\partial x_{\gamma k}) \tag{3}$$

and

$$I_\gamma(\mathbf{n}_\gamma) = \int \rho_\gamma \prod_{i=1}^{3} x_i^{n_{\gamma i}}\, d\mathbf{x} / \prod_{k=1}^{3} n_{\gamma k}! \tag{4}$$

where ρ_γ is the charge density of system γ.

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The Maxwellian formalism is based on the fact[4] that for each center and for each N, there exists a unique set of real pole vectors (called characteristic directions) $\mathbf{s}_1^N$, ..., $\mathbf{s}_N^N$ and scalar multipole moments $p^{(N)}$, such that the sum of directional derivatives in eq 2, involving only vectors along the Cartesian axes, can be replaced by a single directional derivative along a general direction:

$$E_{N_A,N_B} = \{p_A^{(N_A)} * p_B^{(N_B)}/(N_A! * N_B!)\} * \prod_{i=1}^{N_A} (\mathbf{s}_i^{N_A} \cdot \nabla_A) * \prod_{i=1}^{N_B} (\mathbf{s}_i^{N_B} \cdot \nabla_B)(1/(|\mathbf{r}_B - \mathbf{r}_A|))|_{\mathbf{r}_\gamma = O_\gamma} \quad (5)$$

Use of eq 5 not only reduces the number of directional derivatives per charge distribution from $(N + 1)(N + 2)/2$ to N but also leads naturally to an extension where the calculation of the electric field generated by the multipoles (required for the calculation of induced dipoles), field gradients, etc. involves the same computational procedure as the calculation of the interaction between the multipoles: adding unit vectors as additional characteristic directions.[5] A formalism for the calculation of torques has been also developed[6] that includes higher order induced moments as well.

Use of eq 5, however, requires first the determination of the poles $p(N)$ and characteristic directions $\{\mathbf{s}_i^N\}$. For the case of $N = 2$ an explicit formula has been developed.[7] For $N > 2$ it was shown that the characteristic directions can be obtained from the roots of a polynomial of order $2N$, and the poles can be calculated based on calculating the directional derivatives with the newly derived characteristic directions at selected points.[8]

The calculation of the characteristic directions and of the calculation of the scalar poles from the moments $I(n)$ is implemented in the program **chardir**, that is part of the package **Maxwell**.[9] The same package also includes the program **moments** that evaluates $I(\mathbf{n})$ for any **n** from single-determinant wave functions generated by the software **POLYATOM**[10] or **Gaussian**.[11] The calulated moments $I(\mathbf{n})$ can be translated and/or rotated by the program **momtrnsf** of **Maxwell**.

Since eq 5 involves only derivatives its evaluation is, in principle, simple. However, the number of terms increases exponentially with N since derivation of each term in a fraction results in two terms. Fortunately, the exponential complexity can be reduced to polynomial order since eq 5 can also be evaluated recursively, resulting in an efficient algoritm.[12] This recursion has been implemented in the program **multipol** of the Maxwell package.[9]

Periodic Systems. Calculation of the electrostatic energy of a crystal presents a nontrivial mathematical problem. Even when the unit cell is neutral but has a finite dipole moment (which is the case in most systems), the infinite sum of dipole−dipole energies not only is slow to converge but also is conditionally convergent, i.e., dependent on the order of summation which can be interpreted as dependent on the crystal's shape. The classic solution to the problem is the one presented by Ewald[13] who represented the lattice sums with two different, fast converging sums, one in real space and the other in reciprocal space. A detailed analysis of the question of which shape does the Ewald sum correspond to has been presented by Campbell.[14] Subsequently, Campbell derived the Ewald summation formulas for multipoles of arbitrarily high order, using the Maxwellian formalism of multipole expansion.[15] The general form of the electrostatic energy of a crystal consisting of a set of simple translation lattices $\{T_i\}$ containing a set of charge distributions centered at $\{\mathbf{X}_c\}$ is given as

$$U_p = \frac{1}{2} \sum_{\{\mathbf{X}_c\}} \sum_{\{T_i\}} U(\mathbf{X}_c, T_i) \quad (6)$$

Each $U(\mathbf{X}_c,T_i)$ is obtained from a multipole sum over the multipole tensors of order N_X and N_T that can be written in the form[15]

$$U(\mathbf{X}_c, T_i, \langle N_X, N_T \rangle) = \frac{(P^{N_X})(P^{N_T})}{N_X! N_T!} \sum_{\{\nu\}} K(\nu, \mathbf{X}_c - \mathbf{X}_i, \langle N_X, N_T \rangle) \sigma(\mathbf{S}(\mathbf{X}_c), \mathbf{S}(\mathbf{X}_T)) \quad (7)$$

where the summation is over the set of non-negative integer triples $\nu = \langle \nu_1, \nu_2, \nu_3 \rangle$ with $\nu_1 + \nu_2 + \nu_3 = N_X + N_T$ and $P(^{N_X})$, $\mathbf{S}(\mathbf{X}_c)$, and $P(^{N_T})$, $\mathbf{S}(\mathbf{X}_T)$ are the poles and characteristic directions at the site $\mathbf{X}_c$ and the lattice site T_i, respectively. The formulas for the so-called 'crystal constants' K and the directional derivatives σ are given in ref 15. Furthermore, for the calculation of the σ's a recursion, analogous to those used to evaluate eq 5, has been developed.[12]

The salient feature of this expression is that all geometric information about the crsytal is incorporated into the crystal constants K and that all information about the charge distributions is separated into the factor σ. The lattice sums (both direct and reciprocal space) contribute only to the crystal constants. This means that once the crystal constants are calculated for a given lattice, the calculation using different charge distributions or just different orientations of the same distribution can proceed without the need for additional lattice summation. Calculation of the crystal constants K and the recursion calculating the σ's have been implemented into the programs **cryscon** and **crysten**, respectively.[16] The calculation of the electrostatic energy of a crystal can be supplemented by the direct summation of r^{-k} ($k \geq 4$) terms with the program **cryspot**. These programs are also part of the **Maxwell** package.

Density Partitioning. There are two important facts worth remembering concerning the Taylor expansion represented by eqs 1−4 or, equivalently, eq 5. First, the series is only convergent if the charge distributions ρ_A and ρ_B do not overlap. Second, if a charge distribution ρ_γ includes only basis functions centered on the same point (usually a nucleus), then the multipole expansion of order $2n$ is exact where n is the highest order term in the wave function representing the density.[17] The nonoverlapping requirement suggests that the convergence can be improved if the molecular density is split up. This improvement comes, however, at the expense of increasing the number of interacting multipoles. The tradeoff between the two has been examined for water−water interactions using different

density partition schemes.[17] The most efficient scheme took advantage of the chance to get exact (partial) results with a finite order: it assigned all overlap densities to the oxygen atom of the water molecule and assigned to each hydrogen only the density that comes from the basis functions centered on it—a partition called 'very extreme split'.

Campbell−Mezei (CM) Water Model. The combination of the algorithms evaluating multipole interactions in the Maxwellian formalism to arbitrary high order and the (at that time) extensive data set of water dimer Hartree−Fock (HF) energies published by the Clementi Laboratory[18,19] led to the development of a fully ab initio cooperative model for water−water interactions.[20] The energy of a system of n water molecules was assumed to be of the form

$$U(n) = U_p(n) + U_i(n) + U_r(n) + U_d(n) \qquad (8)$$

where $U_p(n)$ is the electrostatic energy of the n charge distributions representing the water molecules in their respective orientation, $U_i(n)$ is the additional electrostatic energy due to the induced moments, and $U_r(n)$ and $U_d(n)$ are the repulsion and dispersion contributions, respectively.

$U_p(n)$ represents the electrostatic interaction as approximated by the multipole expansion of the static wave function of Clement et al.[18,19] The density was partitioned according to the 'very extreme split'[17] technique described above, resulting in second-order expansion of the density on the hydrogens and 10th-order expansion on the oxygen.

$U_i(n)$ represents the interaction energy due to the induced moments. The static contribution to electric field was calculated from the multipolar representation of the charge distribution by adding a unit vector to the characteristic directions, allowing the use of the algorithm calculating the interaction energy of multipoles to calulate the fields as well. $U_i(n)$ was calculated in the dipole approximation (i.e., induced moments of order higher than dipole were neglected). The polarizibility tensor α required for this calculation was obtained from the ab initio calculations of Liebmann and Moskowitz.[21] The induced dipoles were calculated using the method of Campbell.[5] This calculation involves the solution of a system of linear equations instead of the customarily employed iteration. The fact that the induced dipoles are obtained from such an unequivocal fashion suggests that the so-called 'polarization catastrophy' where the iteration diverges for centers too close is only an artifact of the iteration process and does not represent a physical phenomenon. Indeed, it is known that the iterative solution of a system of linear equations is not necessarily convergent.[22]

The terms $U_r(n) + U_d(n)$ represented the nonelectrostatic contributions to the interaction, resulting from exchange and dispersion effects. Since the HF energies do not include dispersion effects, the difference between our calculated electrostatic energy, $U_p(n) + U_i(n)$, and the HF energy calculated for the same conformation represents only the exchange repulsion term, $U_r(n)$. In the CM model the repulsion term $U_r(n)$ was represented by r_{AB}^{-k} terms whose coefficients were fitted to reproduce the difference between the $U_p(n) + U_i(n)$ terms and the corresponding HF energy. The exponent set was arrived at by testing several different values—the best fit was obtained with the exponent set {9, 12}. As expected of repulsion contributions, they were indeed positive for all dimer conformations in the Clementi dataset.

This left open the determination of $U_d(n)$. In subsequent work (vide infra) several empirical expressions were tested on ice lattice energies, and the one giving results closest to the experimenta data was selected.[23] The poles, characteristic directions, elements of the polarizability tensor, the parameters of the terms representing $U_r(n)$, and the dispersion function $U_d(n)$ found the best are also part of the **Maxwell** package.

Figure 1 shows the CM potential and its individual terms as a function of the O−O distance for a water dimer in linear hydrogen bonded orientation. It shows that the contribution of both the induced moments and the nonelectrostatic terms become negligible beyond ca. 3.5 Å. Furthermore, these two terms largely cancel in the 2.8−3.5 Å range, resulting in a remarkable good representation of the total energy with just the permanent electrostatic energy alone in the 2.8 Å−∞ range.

The computational effort required to evaluate the energy of an assembly of waters is quite high when compared to the widely used simple central-force models. While, in principle, the model could be incorporated into molecular dynamics simulations, this high cost excludes it from consideration. It is feasible, however, to evaluate the energy of a limited set of configurations (under periodic boundary conditions, if required). Such calculations were performed to show the feasibility of deriving a so-called 'effective cooperative' potential approximating a cooperative one by fitting the parameters of the pairwise additive effective cooperative potential to the cooperatively calculated *total* energy of a set of condensed-phase conformations.[24] As for incorporating the CM model into a Monte Carlo simulation, an additional, more fundamental difficulty, common to all cooperative models based on polarization, arises: the calculation of the polarization energy is an $O(N^2) - O(N^3)$ process, while the calculations at a usual Monte Carlo step without polarization requires only $O(N)$ effort. As a result, the incorporation of polarizability slows the calculation by an order of magnitude. Possible solutions to this problem are discussed by Mahoney and Jorgensen.[25]

Test of the CM Model. The HF nonadditivity given by Kistenmacher et al.[18] for the optimal closed trimer, −1.13 kcal/mol, is reproduced very well with the polarization model that gave −1.12 kcal/mol. Comparisons were also made with the trimer data set of Hankins et al.[2] The results, given in Table 1, show that the general trends are well represented by the polarization model. Since the basis set, hence the wave function, used in this trimer data set was different from the one used to build the model, the lack of quantitative agreement is understandable.

Results

Water Clusters. With a near-exact representation of the electrostatic interactions in terms of multipole interaction as well as a reasonable representation of the cooperativity through the calculation of induced dipoles several important questions can be answered: convergence of the multipole

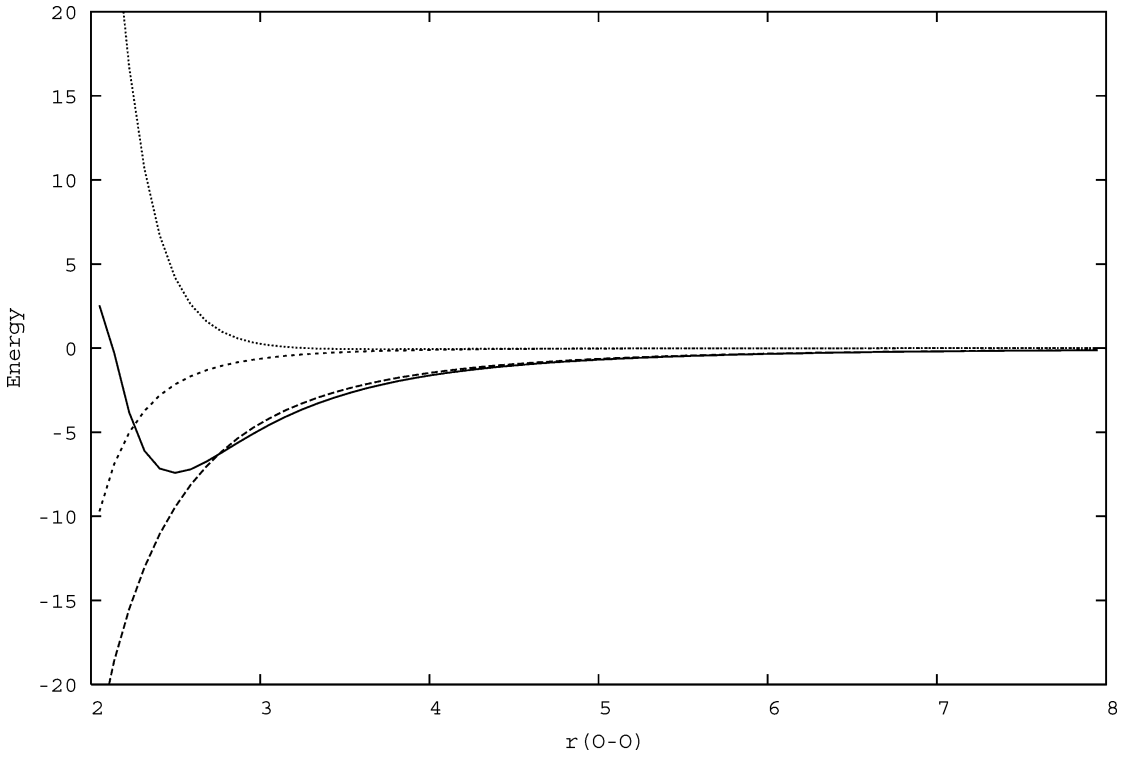

Figure 1. The contributions to the CM potential (in kcal/mol) for a linear dimer (orientation VI decribed in ref 30) as the function of the oxygen−oxygen distance r(O−O) (in Å). Full line: total energy; long-dashed line: permanent electrostatic energy ($U_p(n)$); short-dashed line: induced electrostatic energy ($U_i(n)$); dotted line: exchange and dispersion energy ($U_r(n) + U_d(n)$).

Table 1. Comparison of the HF and CM Model Nonadditivities[a−c]

R(O−O)	type	θ_{23}	E(H−F)	E(CM model)
2.76	sequential	−54.7°	−0.94	−0.77
3.15	sequential	−54.7°	−0.64	−0.44
2.76	double donor	−54.7°	1.30	1.09
3.15	double donor	−54.7°	0.38	0.42
2.76	double acceptor	−54.7°	0.77	1.26
3.00	double acceptor	−54.7°	0.37	0.68
3.39	double acceptor	−54.7°	0.10	0.28
3.00	double acceptor	−25.7°	0.49	0.29
3.00	double acceptor	−70.0°	0.36	0.85

[a] Energies are in kcal/mol. [b] Distances are in Å. [c] θ_{23} is the angle between the third water dipole and the O−O line between the second and third waters.

expansion, effect of neglecting cooperativity on the minimum energy geometries, and the estimate of the relative magnitude of three-body, four-body, etc., terms compared to the total cooperative energy and to the total energy. In a series of papers Campbell and Belford studied optimized water clusters[26,27] with $n = 4, 5, 6$ and clusters in conformations corresponding to the ones seen in Ice Ih[28] for $n \leq 33$. The highlights of these papers are summarized below.

The good performance of the CM model in reproducing the HF trimer energy was repeated in a study of the optimal tetramer,[26] where the HF and CM energies agreed within 3%. The magnitude of the induced dipole was found to be 0.25 D—this falls between the corresponding value for the dimer (0.12 D) and the average value observed in Ice Ih (0.55 D). It is also observed that the relative contribution of cooperativity (i.e., inluding the effects of the induced dipoles to the electric field) increases with cluster size: 1.7%, 2.9%, 5.2% for the optimal dimer, trimer, and tetramer, respectively. This compares with 15−20% for the different ice forms treated (vide infra).

Subsequently, clusters of 48 waters in Ice Ih configurations were studied.[28] Among the several results of this study was the partitioning of the calculated total energy into two-body, three-body, etc. contributions, allowing an estimate of the convergence of the alternative approach to multibody effects. Extrapolating the results to infinite lattice, the three- and four-body terms were found to contribute to the total lattice energy 21% and 3%, respectively. The contributions of five and higher order multibody terms were found to be 0.6% or less, with the exception of two conformations where the three- and four-body terms partially cancelled.

Still another study[27] determined a number of local minima in small water clusters containing three, four, and six waters. A major goal of that work was to find out if inclusion of cooperativity would affect the order of energies of the local minima found—the answer was affirmative for hexamers: the additive approximation favored a nearly planar ring, while the cooperative approximation favored an ice Ih-like staggered ring. Also, the optimal oxygen−oxygen distance was found to decrease with cluster size. For hexamers, it already fell into the range of vibrationally averaged oxygen−oxygen distances seen in condensed phases.

A Trifurcated Water Dimer. Ab initio calculations identified a low-energy water dimer conformation[29] that involves three hydrogen bonds: the O−H bond of one water is roughly antiparallel to the dipole vector of the other. Subsequently, several pairwise additive potentials and the CM model were used to compare the calculated dimer

Table 2. Comparison of the Ab Initio, Empirical, and Polarization Model Energies with Quantum-Mechanical Energies

		configuration					
		I	II	III	IV	V	VI
		3[a]	3[a]	2[a]	1[a]	1[a]	1[a]
ab initio models:	MCY[33]	0.41	−3.33	−3.72	−5.50	−5.25	−5.24
	YMD[34]	0.92	−3.59	−3.75	−5.34	−4.93	−5.16
empirical models:	ST2[35]	1.80	−3.05	−2.97	−6.44	−5.66	−5.99
	SPC[36]	5.16	−3.10	−3.91	−5.59	−5.36	−5.11
	TIP3P[37]	3.86	−3.45	−3.91	−5.48	−5.25	−5.10
	TIP4P[37]	5.07	−3.05	−4.29	−5.57	−5.60	−5.14
polarizable model:	CM	−3.70	−5.09	−5.89	−6.03	−6.06	−5.76
ab initio energy MP4SDQ/ 6-311G**		−3.08	−6.02	−5.84	−6.23	−6.14	−5.40

[a] Number of H bonds.

Table 3. Lattice Energy Contribution for Ice Forms[a]

form	U_p	U_i	$U_p + U_i$	U_r	U_d^a	U_d^b	U_d^c	U_t^a	U_t^b	U_t^c
Ih	−20.2	−7.0	−27.2	15.9	−3.8	−4.1	−6.6	−15.1	−15.5	−17.9
II	−17.5	−7.7	−25.2	12.6	−3.3	−3.9	−7.3	−15.9	−16.5	−19.9
IX	−18.3	−7.2	−25.5	13.8	−3.2	−3.9	−7.1	−15.0	−15.7	−18.9

[a] U_p, U_i, U_r, U_d: see eq 6; $U_t = U_p + U_i + U_r + U_d$; dispersion term parameters for U_d^a, U_d^b, and U_d^c from refs 40−42, respectively.

energies with the ab initio values at different conformations, ranging from the trifurcated to the dimer in the 'classical' linear hydrogen bond conformation.[30]

Table 2 shows the results for six conformations. Conformations I and II are both trifurcated; conformations IV−VI are linear dimers optimized with different levels of theory; and conformation III is an intermediate between linear and trifurcated. For each conformation the CM model is the closest to the ab initio values among the models tested. The difference between the CM model and the rest is particularly large for the trifurcated conformations. The poor performance of the models fitted to ab initio energies is understandable since trifurcated dimers were not in any of the data sets used for the fit. The poor performance of the empirical models, on the other hand, indicates that trifurcated dimers do not occur with significant probability in normal aqueous systems. This implies that this shortcoming is not affecting seriously calculations on aqueous systems. However, it was pointed out[30] that in situations where interactions with individual water molecules are important, these empirical potentials should be used with caution. The good performance of the CM model is particularly impressive since it was also derived without using any trifurcated structure. This supports the notion that the polarization approach can be effective in the modeling of intermolecular interactions. At a more general level, the comparison highlights the point that, in some situations, explicit calculation of the cooperativity is necessary.

It should be mentioned that a comment to this work questioned its validity since no counterpoise correction was applied to correct for the basis-set superposition error.[31] In answering this comment,[32] it was pointed out that the no correction was applied for the neglect of zero-point vibration energy either, and it was shown that the two corrections work in the opposite direction, thus reinforcing our conclusion about the potential significance of such trifurcated conformations.

Calculations on Disordered Ice Ih. The lattice energy of Ice Ih was calculated by Campbell in the dipolar approximation as a tool to assess the electrostatic nature of hydrogen bond.[38] The work was later extended to multipoles of order six.[39]

With the development of the recursion algorithm[12] to evaluate eqs 4 and 5 the permanent multipole energies were calculated up to multipole order 14, using $r_o = 2.741$ Å. The calculations were performed on Ice Ih crystals with disordered water orientations. The disorder was represented by all the possible tetrahedral orientations of waters that still satisfy the Bernal−Fowler rule (exactly one hydrogen between neighboring oxygens). All possible arrangements of a 16-site unit cell were considered, resulting in 55 classes of conformations with distinct permanent multipole energy; 10 of these had zero total dipole.[23,39]

From the convergence of the series it was estimated that the truncation error is about 0.03 kcal/mol. The spread in the permanent multipole energy for the 55 classes was 0.14 kcal/mol that was reduced to 0.1 kcal/mol for the zero-dipole subclass. While this spread was steadily decreasing as the multipole order was increased toward 14, it remained higher than the estimated trunction error. This indicates that there indeed is a residual energy difference among the different water orientations—a question that was debated at that time.

The induced dipoles and the induced energies were also calculated.[5] This increased the spread in the electrostatic energy to 1.1 kcal/mol and 0.6 kcal/mol for the whole and nonpolar class, respectively. This increase in the spread serves as an indicator of the fact that the truncation of the induced multipoles at the dipole level introduced a non-negligible error and points out the importance of considering higher order polarizibilities.

Comparison of the Energies of Different Ice Forms. The ice crystal energy calculations[23] have been extended to two additional ice forms with ordered hydrogen positions: Ice II and Ice IX. The dispersion contribution was calculated with three different approximations.[40−42] The comparison with experiment, however, is only valid if the zero-point energy, that is neglected in these calculation, is known, and the experimental value can be adjusted accordingly. This was the case only for Ice Ih, giving −14.1 kcal/mol. Comparison of the three different dispersion approximations shows that that of Zeiss and Meath[40] gave the best approximation. Subsequent work with the CM model used this dispersion contribution throughout.

Calculation of the Energies of Ice Ih Bjerrum Defects. Hassan and Campbell performed a series of calculations[43] to study the energetic penalty of a Bjerrum defect in an Ice Ih crystal: either there are two hydrogens between neigboring oxygens or there are none. They considered both 'formal defects', i.e., the waters were not allowed to relax due to the repulsion caused by the defect and allowed relaxation of the waters in involve in the defect as well as their neighbors. The system studied involved altogether 27 water

molecules placed in an arrangement corresponding to the Ice Ih lattice with all but the central water pair satisfying the Bernal−Fowler rule. Energy calculations involved both a pairwise additive potential fit to ab initio data[18] and the cooperative CM model.

Optimization of the molecular orientations and positions using the additive model was found to reduce the defect energy by ∼40% The optimization involved the defect pair and their neighbors, while the rest provided the boundary effect. It was found that relaxing the orientational degrees of freedom contributes significantly more to lowering the defect energy than relaxing the positions.

The optimization with the additive potential was followed by orientational optimization with the cooperative CM model. This yielded an additional 10% lowering of the defect energy.

These calculations also brought into focus the lower quality of the repulsive contributions in most analytical potentials. There are two major reasons for this. The simpler and easier to remedy source is the limited sampling of the repulsive conformations in the database used to fit the potentials. More difficult is the establishment of an adequate objective function to the fit since the energy surface can vary by orders of magnitude if strongly repulsive orientations are considered.

Charge Transfer. Molecular mechanics force fields that are used in most large-scale computer simulations use fixed charges on the interaction centers and thus are not equipped to handle charge transfer. Thus, it is of interest to examine the magnitude of this neglected contribution.

A set of free energy simulations was performed for monovalent cations in water and chloroform using ab initio derived parameters[44] for the ions.[45] The calculated solvation free energies were strongly underestimated when compared with experiment. This was expected, with the reasoning that polarization is neglected in the calculations.[44] To test if polarization can indeed account for the shortfall, the CM model was used to calculate the additional contribution to the solvation free energy, by evaluating the induced dipole energy of a selected set of conformations from the simulation. For this application, the program **multipol** has been extended to handle periodic boundary conditions and to use a lower order of expansion for more distant pairs of waters. The calculation showed that including polarization can indeed reduce the discrepancy between calculation and experiment, but a significant gap still remained.

It was proposed that the source of the remaining discrepancy between calculation and experiment is the neglect of charge transfer. To support this claim, ab initio calculations were performed on selected configurations containing the ion and its first solvation shell. A Mulliken population analysis showed that significant charge-transfer exists: Li^+ lost 0.32 e and Na^+ lost 0.27 e to the waters surrounding it. Note, that the Mulliken population analysis is known to be a rather simple approach to charge density partitioning. However, it was used in the present work only to demonstrate the *presence* of charge transfer and not to quantitate it.

Subsequently, van der Vaart and Merz have published analogous calculations with similar results; the conclusion held even when a more sophisticated charge partitioning scheme was used.[46] They also found that even for a hydrogen bond there is a measurable amount of charge transfer.[47]

Representation of the Exchange Repulsion. Another ingrained property of the widely used molecular mechanics force fields is the representation of the nonbonded interactions as the sum of eletrostatic and Lennard-Jones terms, i.e., terms of the form r^{-1}, r^{-6}, and r^{-12}. The r^{-6} term is usually identified with the dispersion energy and the r^{-12} term with the repulsion. While the dispersion term has its physical justification, the repulsive term's *raison d'être* is the fact that $r^{-12} = (r^{-6})^2$ and thereby it is easy to compute. Also, as discussed above, the quality of these contributions is generally lower than that of the rest.

There are two problems with this approach. First, the functions r^{-1}, r^{-6}, and r^{-12} are close to be linearly *dependent*. This was seen from least-square fit calculations aiming at obtaining the best fitting coefficients: the matrix of the resulting system of linear equation is usually very ill-conditioned.[24] This is not just a technical problem that can be simply overcome with better numerical algorithms or higher precision arithmetics—it means that a wide range of coefficient sets can give a virtually identical fit, making the identification of individual terms with physical meaning unreliable. This, in turn, is not just a question of 'esthetics' since the generally assumed transferability of atomic parameters from one molecule to another largely relies on the fact that these parameters have a physical interpretation.

The other problem is the well-known fact that the exhange repulsion is an exponential function of r (see, e.g., ref 48); the r^{-12} term results in too steep a repulsion. For simulations around room-temperature it is not a significant problem. However, one of the main justifications of the explicit inclusion of cooperativity into computer simulations is that such representation can remain valid over a wide range of thermodynamic conditions as opposed to the force fields where the effect of cooperativity is mapped to pairwise additive terms that are only valid in the thermodynamic vicinity of the state the functions were parametrized. This advantage, however, is only realized if the rest of the potential functions are parametrized well enough to represent the full range of thermodynamic conditions under consideration.

The fact that the r^{-12} repulsion is inadequate for this task was highlighted by simulations at high temperature. A comparison of (T, V, N) and (T, P, N) ensemble simulations on three polarizable and two nonpolarizable water models found that the polarizable models underestimate the density by 10−50%, leading to the suggestion that the functional form of the repulsive term has to be changed.[49] Subsequently, the comparison was extended to more models and to simulation in the Gibbs ensemble[50] to determine the critical point of each model.[51] While in this test several of the polarizable models gave critical densities close to the experimental value, the overall comparison between the pairwise additive and polarizable models failed to show the expected superiority of the polarizable models. These comparisons reinforce the suggestion that, for optimum performance, the repulsion term has to be revised concurrently with the development of polarizable models.

Summary and Conclusions

Work in the Campbell Laboratory has showed that the Maxwellian formalism[4] is an elegant and efficient way to treat electrostatic interactions in the multipole expansion approximation. The necessary formulas[15] and algorithms[8,12] for their use to describe intermolecular interactions in clusters as well as crystals have been developed and implemented in the software package **Maxwell**.[9]

The formalism was also used to derive an ab initio cooperative water potential based on Hartree−Fock energies and representing cooperativity with dipole polarizability.[20] Subsequently, the model was used in a variety of studies on water clusters[24,26−28,30,43] and ices.[23] These calculations showed that dipole polarizability can treat the cooperative contribution to water−water interactions reasonably well and also quantitated the limitations inherent in this approximation.

Calculations on Ice Ih showed that the orientational disorder results in a finite energy range even when the orientations obey the Bernal−Fowler rule and even when the unit cell dipole is zero. The calculation of induced dipole energies showed that the dipole approximation to the cooperative contributions is not fully converged.[23]

An important result from calculations with the CM cooperative model is the recognition of the significance of charge transfer. Other calculations led to the recognition of the importance of adequate treatment of the repulsion contribution.

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