

Polarization response of water and methanol investigated by a polarizable force field and density functional theory calculations: Implications for charge transfer

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Electronic polarization response in hydrogen-bond clusters and liquid configurations of water and methanol has been studied by density functional theory (DFT) and by a polarizable force field based on the chemical potential equalization (CPE) principle. It has been shown that an accurate CPE parametrization based on isolated molecular properties is not completely transferable to strongly interacting hydrogen-bond clusters with discrepancies between CPE and DFT overall dipole moments as large as 15%. This is due to the lack of intermolecular charge transfer in the standard CPE implementation. A CPE scheme for evaluating the amount of transferred charge has been developed. The charge transfer parameters are determined with the aid of accurate DFT calculations using only hydrogen-bond dimer configurations. The amount of transferred charge is found to be of the order of few hundredths of electrons, as already found in recent studies on hydrogen-bond systems. The parameters of the model are then used, without further adjustment, to different hydrogen-bond clustered forms of water and methanol (oligomer and liquid configurations). In agreement with different approaches proposed in literature for studying charge transfer effects, the transferred charge in hydrogen-bond dimers is found to decrease exponentially with the hydrogen-bond distance. When allowance is made for charge transfer according to the proposed scheme, the CPE dipole moments are found to reproduce satisfactorily the DFT data. © 2005 American Institute of Physics. [DOI: 10.1063/1.1851504]

I. INTRODUCTION

Classical molecular dynamics simulations^{1,2} have proved to be an invaluable tool to rationalize available experimental data on condensed phases of molecular systems and often to suggest further experiments. The main problem in this approach lies in the *a priori* derivation of a realistic and accurate empirical representation of the interatomic forces, whose quality and reliability, in turn, strongly influences the predictive power of the simulation itself. Usually empirical force fields³⁻⁵ are constructed by fitting on both single and many-molecules properties in a process of continuous parametric readjustment and refinement. For example, molecular dipole moments expressed by fixed atomic point charges for liquid systems are adjusted to take into account the polarizability in condensed phase, typically by a sensible enhancement of their value with respect to the gas phase.⁶

While this mean field approach works reasonably well⁷ at reproducing the structural properties of liquids (e.g., pair radial distribution functions) it does indeed suppress all fluctuations due to charge reorganization thus preventing a reliable estimate of all properties that may depend on those fluctuations (e.g., optoelectronic properties). In this respect, polarizable models have received considerable attention in recent years⁸⁻¹³ as an intermediate approach between the expensive *first principle* Car–Parrinello¹⁴ methodology and the empirical (mean field) methods.² Electrostatic polarizable models can be constructed specifically for condensed phase

by adjusting the molecular parameters in order to reproduce some condensed phase target properties,¹⁵ or can be constructed on the basis of the electronic properties of isolated molecule^{8-11,13} alone and then transferred to condensed phases without further readjustment.^{12,16,17} The latter, if viable, is clearly a much more desirable alternative, since it provides a general and effective predictive tool for molecular systems with no prior knowledge of condensed phase properties.

The chemical potential equalization (CPE) approach^{13,18,19} is one of these latter methods. CPE has been recently shown¹³ to be very suited for building up general electrostatic polarizable force fields because of the intrinsic transferability of the atomic electronegativity and hardness parameters in isolated molecules. The present study is aimed at accurately assessing the transferability of the isolated molecule CPE parametrization in the case of hydrogen-bond (H-bond) aggregates of water and methanol. This claimed transferability^{8,10,13,19} has been recently questioned^{12,20} for the case of polarizable force fields based on simple Coulomb screening. It is then important to unambiguously verify the transferability of the standard implementation of CPE (Ref. 13) in condensed phases as this would prove that a general, accurate, and inexpensive polarizable force field can be devised starting from parametrization of isolated molecules. In particular, we are interested in verifying if the *linear* CPE model is able to satisfactorily describe the strong polariza-

tion effects that occur in H-bond forming systems, possibly including implicitly²¹ charge transfer (CT) effects.

The CT effect in clusters and in bulk phases of polar molecules is not usually believed important.^{21–23} As a consequence, in the standard CPE implementations explicit intermolecular CT is usually ruled out. On the other hand, the real extent of CT in polar liquids and its impact on condensed phase properties is still a rather elusive issue.²⁴ different conclusions may be drawn⁷ depending on the way the total electron density is partitioned and assigned to individual molecules. In this respect, the comparison between CPE and density functional theory (DFT) calculations done in the present study for H-bond systems provides an alternative way for assessing the importance of CT in shaping the total electron density in condensed phases. CPE derived CT may be in turn compared to other methodologies based on standard electron density partition schemes such as *natural population analysis*²⁵ (NPA) or *atoms in molecules*²⁶ (AIM). Anticipating the results, we have found that standard CPE consistently underestimates the dipole moments of clusters by as much as 10%–15%, indicating that CT plays indeed a significant role and that must be included in the CPE based force fields. To this end, we propose and test a methodology for including intermolecular CT in the CPE model based on dimer parametrization: given a dimer configuration, an amount of charge is arbitrarily transferred from one monomer to the other, letting the excess charge to be redistributed according to the CPE protocol. Then, the true CPE transferred charge for that configuration is assumed to be the one that best reproduces the induced dipole moment calculated by DFT. Finally, the CPE CT parameters are determined by fitting the CPE transferred charge in order to reproduce its H-bond distance dependence for several dimer configurations. We find that the CPE derived CT well agrees with that estimated using different methodologies (NPA and AIM). In particular, the exponential behavior of the CPE CT as a function of the H-bond distance in the water dimer is found to be in perfect agreement with respect to that recently calculated by Gálvez *et al.*²³ using AIM analysis combined to DFT.

The paper is organized as follows. In Sec. II, the theory underlying the CPE model is described. In Sec. III we report the details of the DFT calculations and of the CPE parametrization. In Sec. IV the results are presented and discussed. In Sec. V conclusive remarks are given.

II. THEORETICAL BACKGROUND: THE CPE MODEL

In this work we use the CPE model developed in Ref. 13. The charge density on a molecule is assumed to be the superposition of single atomic charge densities, $\delta\rho_i(\mathbf{r})$, each expressed as linear combination of spherical and dipolelike functions,

$$\delta\rho_i(\mathbf{r}) = q_i s_i(\mathbf{r}) + d_{xi} p_{xi}(\mathbf{r}) + d_{yi} p_{yi}(\mathbf{r}) + d_{zi} p_{zi}(\mathbf{r}). \quad (1)$$

The $s_i(\mathbf{r})$ and $p_{ai}(\mathbf{r})$ functions are orthonormalized Gaussian form factors defined as

$$s_i(\mathbf{r}) = \left(\frac{\epsilon_i}{\pi}\right)^{3/2} \exp(-\epsilon_i |\mathbf{r} - \mathbf{r}_i|^2), \quad (2)$$

$$p_{ai}(\mathbf{r}) = 2\pi \left(\frac{\zeta_i}{\pi}\right)^{5/2} (r_\alpha - r_{ai}) \exp(-\zeta_i |\mathbf{r} - \mathbf{r}_i|^2), \quad (3)$$

where \mathbf{r}_i , r_{ai} , and r_α are the vector position of the atom i , the α th Cartesian component of \mathbf{r}_i and the α th Cartesian component of \mathbf{r} , respectively. The parameters ϵ_i and ζ_i are related to the width of the charge density distributions. With these definitions, q_i and d_{ai} in Eq. (1) take on the meaning of atomic net charge and atomic dipole moment, respectively. The CPE energy for one isolated molecule of N atoms can be written in matrix form as follows:

$$E = E_0 + \mathbf{K}^t \mathbf{c}_0 + \frac{1}{2} \mathbf{c}_0^t \mathbf{H} \mathbf{c}_0, \quad (4)$$

where E_0 is an unknown nuclear dependent term, including exchange-correlation and valence contributions, $\mathbf{c}_0^t \equiv (q_1, d_{x1}, d_{y1}, d_{z1}, \dots, q_N, d_{xN}, d_{yN}, d_{zN})$ is the charge density vector (the subscript of \mathbf{c}_0^t means that the vector is related to the isolated molecule), and $\mathbf{K}^t \equiv (\chi_1, 0, 0, 0, \dots, \chi_N, 0, 0, 0)$ is the electronegativity vector, χ_i being the electronegativity of the atom i . \mathbf{H} is the hardness matrix whose elements are equal to $\eta_s(\epsilon_i)$ for q_i^2 energy terms, $\eta_p(\zeta_i)$ for d_{ai}^2 energy terms, $\int \int s_i(\mathbf{r}) s_j(\mathbf{r}') |\mathbf{r} - \mathbf{r}'|^{-1} d\mathbf{r} d\mathbf{r}'$ for $q_i q_j$ energy terms, $2 \int \int s_i(\mathbf{r}) p_{aj}(\mathbf{r}') |\mathbf{r} - \mathbf{r}'|^{-1} d\mathbf{r} d\mathbf{r}'$ for $q_i d_{aj}$ energy terms, $\int \int p_{ai}(\mathbf{r}) p_{bj}(\mathbf{r}') |\mathbf{r} - \mathbf{r}'|^{-1} d\mathbf{r} d\mathbf{r}'$ for $d_{ai} d_{bj}$ energy terms, and zero for $q_i d_{ai}$ and $d_{ai} d_{bi}$ energy terms. The quantities $\eta_s(\epsilon_i)$ and $\eta_p(\zeta_i)$ in the definition of \mathbf{H} are independent on the nuclear configurations and may be viewed as the resistance of the atom i to lose (or to gain) charge and to polarize under an external electric field, respectively. They are related to the Gaussian atomic form factors ϵ_i and ζ_i of Eqs. (2) and (3) as follows:

$$\eta_s(\epsilon_i) = \left(\frac{2\epsilon_i}{\pi}\right)^{1/2}, \quad \eta_p(\zeta_i) = \left(\frac{2\zeta_i^3}{9\pi}\right)^{1/2}. \quad (5)$$

The charge density vector \mathbf{c}_0 is obtained by minimizing Eq. (4) under the condition that the total molecular charge Q is conserved, i.e., $\mathbf{e}^t \mathbf{c}_0 = Q$ where $\mathbf{e}^t \equiv (1, 0, 0, 0, 1, 0, 0, 0, \dots, 1, 0, 0, 0)$. This constrained minimization leads us to introduce the undetermined Lagrange multiplier χ which has the physical meaning of molecular electronegativity.¹³ The solution for \mathbf{c}_0 and χ is

$$\chi = \frac{Q + \mathbf{e}^t \mathbf{H}^{-1} \mathbf{K}}{\mathbf{e}^t \mathbf{H}^{-1} \mathbf{e}}, \quad (6)$$

$$\mathbf{c}_0 = \chi \mathbf{H}^{-1} \mathbf{e} - \mathbf{H}^{-1} \mathbf{K}. \quad (7)$$

For M interacting molecules, the energy is given by

$$E = E_0 + \mathbf{K}^t \mathbf{C} + \frac{1}{2} \mathbf{C}^t \mathbf{H} \mathbf{C} + \frac{1}{2} (\mathbf{C}^t - \mathbf{C}_0^t) \mathbf{M} (\mathbf{C} - \mathbf{C}_0), \quad (8)$$

where $\mathbf{K}^t \equiv (\mathbf{K}_1^t, \mathbf{K}_2^t, \dots, \mathbf{K}_M^t)$, \mathbf{K}_m being the electronegativity vector of the molecule m (see definition above) and

$$\mathbf{H} = \begin{bmatrix} \mathbf{H}_{11} & \mathbf{H}_{12} & \dots & \mathbf{H}_{1M} \\ \mathbf{H}_{21} & \mathbf{H}_{22} & \dots & \mathbf{H}_{2M} \\ \dots & \dots & \dots & \dots \\ \mathbf{H}_{M1} & \mathbf{H}_{M2} & \dots & \mathbf{H}_{MM} \end{bmatrix}, \quad (9)$$

$$\mathbf{M} = \begin{bmatrix} \mathbf{M}_1 & \mathbf{0} & \dots & \mathbf{0} \\ \mathbf{0} & \mathbf{M}_2 & \dots & \mathbf{0} \\ \dots & \dots & \dots & \dots \\ \mathbf{0} & \mathbf{0} & \dots & \mathbf{M}_M \end{bmatrix}.$$

The out of diagonal elements of the \mathbf{H} matrix, i.e., \mathbf{H}_{ij} , are matrices themselves whose elements represent Coulomb interactions between charge distributions of the molecules i and j . The diagonal elements \mathbf{H}_{ii} have the same form of the hardness matrix for an isolated molecule (see definition above). The elements of the \mathbf{M} matrix, i.e., \mathbf{M}_m , are matrices having the following expression:

$$\mathbf{M}_m = \frac{1}{\alpha_0} (\mathbf{X}_m \mathbf{X}_m^t + \mathbf{Y}_m \mathbf{Y}_m^t + \mathbf{Z}_m \mathbf{Z}_m^t), \quad (10)$$

where $\mathbf{X}_m^t \equiv (x_{1m}, 0, 0, 0, x_{2m}, 0, 0, 0, \dots, x_{Nm}, 0, 0, 0)$, x_{nm} being the x Cartesian coordinate of the n th atom belonging to the m th molecule (analogous expressions can be written for \mathbf{Y}_m^t and \mathbf{Z}_m^t). In Eq. (10), α_0 corresponds to the molecular polarizability, but in the present model it is treated as a variational parameter to be determined by fit. The last term in Eq. (8) is the sum of terms equal to $(2\alpha_0)^{-1} \mu_{ind}^2$ for each single molecule (μ_{ind} is the induced dipole moment on the molecule by excluding the contribution from the dipolelike charge density distributions) and accounts for the increase of the molecular energy when atomic charges are displaced by an external electric field (polarization work). This energy term has been inserted to prevent the overestimate of the polarizability as the molecular size grows.^{13,27,28} In Eq. (8), $\mathbf{C}_0^t \equiv (\mathbf{c}_{01}^t, \mathbf{c}_{02}^t, \dots, \mathbf{c}_{0M}^t)$ is the charge density vector for the system of non interacting molecules whose energy is

$$E = E_0 + \mathbf{K}' \mathbf{C}_0 + \frac{1}{2} \mathbf{C}_0^t \mathbf{H}_0 \mathbf{C}_0, \quad (11)$$

with

$$\mathbf{H}_0 = \begin{bmatrix} \mathbf{H}_{11} & \mathbf{0} & \dots & \mathbf{0} \\ \mathbf{0} & \mathbf{H}_{22} & \dots & \mathbf{0} \\ \dots & \dots & \dots & \dots \\ \mathbf{0} & \mathbf{0} & \dots & \mathbf{H}_{MM} \end{bmatrix}. \quad (12)$$

$\mathbf{C}' \equiv (\mathbf{c}_1^t, \mathbf{c}_2^t, \dots, \mathbf{c}_M^t)$ is the charge density vector for the system of interacting molecules to be found by minimizing the energy of Eq. (8) with M charge conserving conditions

$$\mathbf{e}_1^t \mathbf{c}_1 = Q_1, \quad \mathbf{e}_2^t \mathbf{c}_2 = Q_2, \quad \dots, \quad \mathbf{e}_M^t \mathbf{c}_M = Q_M, \quad (13)$$

Q_m being the net charge on the molecule m . The constrained minimization of Eq. (8) leads to a system of linear equations in the charge density vector elements,

$$(\mathbf{H} + \mathbf{M}) \mathbf{C} - \delta \mathcal{K} \mathbf{E} = (\mathbf{H}_0 + \mathbf{M}) \mathbf{C}_0, \quad (14)$$

where $\mathbf{E} \equiv (\mathbf{e}_1^t, \mathbf{e}_2^t, \dots, \mathbf{e}_M^t)$ and $\delta \mathcal{K}$ is the diagonal matrix of the difference between the molecular chemical potential of the interacting and noninteracting system.

In the present CPE model, the variational parameters to be determined by the fitting procedure (see the following section) are the atomic electronegativities used for defining the \mathbf{K} vector [see Eq. (8)], the atomic hardnesses [or the

correlated coefficients for the Gaussian form factors; see Eq. (5)], and the α_0 parameters associated to each molecule [see Eq. (10)].

III. DFT CALCULATIONS AND CPE PARAMETRIZATION

In the CPE method the parametric and environment dependent atomic electronegativities and hardnesses are trained^{10,13,29} to reproduce electronic properties calculated using *ab initio* methods (the so-called reference data). Therefore, the accuracy of the method is intimately related to the accuracy of the reference data of the training set. In previous papers some of us already proposed various CPE schemes and the corresponding parametrizations for water^{13,30} and for methanol.^{13,29} In its most recent version,¹³ the CPE scheme was parametrized for a limited set of small organic molecules, using reference data obtained using the B3LYP functional⁵³ along with the 6-311G(*d,p*) basis set. In this way, the molecular dipole moments of water and methanol are satisfactorily reproduced, while their polarizabilities are underestimated by $\sim 40\%$ and $\sim 25\%$, respectively. As the present study deals specifically with the polarization response of H bond forming compounds, from small clusters to condensed phase, we need a more accurate electronic description of the systems, especially as far as molecular polarizability is concerned. High accuracy on electrical molecular properties is also necessary in order to prevent possible sources of systematic errors when analyzing polarization response in the various states of aggregation.

The reference data used in the fitting procedure are the dipole moment, the polarizability tensor, the ionization potential I_p , and the electron affinity E_a of the isolated molecules of water and methanol. The dipole moment and the polarizability tensor have been obtained using DFT with plane wave expansion and the BLYP functional.^{31,32} The atomic core is described by Martins-Troullier pseudopotentials³³ in the Kleinman-Bylander decomposition³⁴ scheme along with a cutoff of 70 Ry in the plane wave expansion. It has been shown³⁵ that the use of diffuse functions in localized basis sets for valence electrons is essential for the correct description of polarizability and H-bond interaction. In this respect, DFT calculations using plane wave expansion with pseudopotential for *core* electrons provide at the same time (i) an effective way for introducing highly diffuse basis functions and (ii) a computationally efficient tool when dealing with large clusters or bulk systems. The BLYP functional⁵³ has been chosen since it is one of the most reliable and widely used, especially for systems characterized by the presence of H-bond interactions.³⁶⁻³⁸ The dipole moment has been computed in the Berry phase scheme,³⁹ while the polarizability by linear response theory^{40,41} (the calculations have been carried out using the CPMD program⁴²).

Going back to CPE parametrization, as prescribed elsewhere (see discussion at page 9180 of Ref. 13), I_p and E_a have been also included in the fitting procedure in order to prevent unrealistic values for the atomic parameters. Hence, their role can be considered secondary with respect to that of

TABLE I. CPE parametrization of water and methanol. C, carbon atom; Hm, methyl hydrogen atoms; O, oxygen atom; H, hydroxy hydrogen atom. χ is the atomic electronegativity (in eV e⁻¹), η_s (in eV e⁻²) and η_p (in eV D⁻²) are the hardnesses of the spherical and dipolelike charge density distributions, respectively. α_0 (in Å³) is the parameter to be used in the expression of the polarization work [see Eq. (10)].

Atom type	χ	η_s	η_p
Methanol $\alpha_0=2.94$			
C	5.01	48.64	8.43
Hm	9.71	33.67	0.00
O	14.87	19.53	21.71
H	5.03	37.19	0.00
Water $\alpha_0=0.45$			
O	19.79	33.55	12.00
H	0.89	39.99	0.00

dipole moment and polarizability. For this reason the weight factors used in the fitting target function¹³ for I_p and E_a are about 1000 times smaller than those used for the polarizability tensor and the dipole moment (the ratio between the weight factor of the dipole moment and that of the polarizability tensor is 2). This choice is sufficient to exclude several unreasonable sets of atomic charges and atomic parameters from the result. Given the marginal importance of I_p and E_a with respect to the dipole moment and polarizability in the fitting procedure, their DFT values have been taken from a previous work¹³ where the calculation was performed using the B3LYP/6-311G(*d,p*) level of theory.

The fit of the CPE parameters was performed on eight distorted configurations of the isolated molecules of water and methanol. The variational parameters obtained from the fit are reported in Table I. In principle, in addition to the atomic electronegativities and hardnesses, also the local (atomic) polarizabilities must be determined from the fitting procedure.¹³ On the other hand the atomic polarizabilities enter in the CPE model only as their sum α_0 [see Eq. (10)]. Hence, to improve the efficiency of the fit, we have reduced the number of variational parameters by assuming the sum of the atomic polarizabilities (α_0 in Table I), instead of the single atomic polarizabilities themselves, as variational parameter. Following the guideline of Ref. 13, only spherical charge density distributions have been used for the hydrogen atoms, while both spherical and dipolelike charge density distributions have been used for the oxygen and the carbon atoms.

In order to show the performance of the CPE parametrization, in Table II we report the dipole moment and the polarizability tensor of the isolated water and methanol molecules in the minimum DFT energy configuration calculated by CPE and DFT. For comparison, the experimental data⁴³ are also reported in the table. The agreement between calculation and experiment is very good. A detailed comparison of the single components of the dipole moment and of the polarizability tensor calculated using CPE and DFT shows the reliability of the former in reproducing the electronic properties in the case of isolated molecules. In particular, we stress that the polarizability tensor component of water related to the out of plane polarization, α_{yy} , is well reproduced

TABLE II. Dipole moment (in D) and polarizability tensor (in Å³) of the methanol and water molecules in their minimum DFT energy configuration calculated using CPE and DFT. $\bar{\mu}$ is the modulus of the dipole moment. $\bar{\alpha}$ is the isotropic polarizability. The methanol molecule has the C, O, hydroxy H, and one methyl H on the *xy* plane, the C–O bond coincides approximately with the *x* axis, the O atom pointing toward the positive direction of the axis. The water molecule lies on the *xz* plane, its dipole moment being directed along the *z* axis. Experimental data have been taken from Ref. 43.

	Methanol			Water		
	CPE	DFT	Expt.	CPE	DFT	Expt.
μ_x	-1.03	-1.01		0.00	0.00	
μ_y	1.44	1.43		0.00	0.00	
μ_z	0.00	0.00		1.89	1.89	
$\bar{\mu}$	1.77	1.75	1.70	1.89	1.89	1.85
α_{xx}	3.69	3.68		1.45	1.45	
α_{xy}	0.07	0.06		0.00	0.00	
α_{xz}	0.00	0.00		0.00	0.00	
α_{yy}	3.25	3.19		1.20	1.20	
α_{yz}	0.00	0.00		0.00	0.00	
α_{zz}	3.06	3.09		1.33	1.38	
$\bar{\alpha}$	3.33	3.32	3.29	1.33	1.34	1.45

by the model. This is due to the fact that the present CPE parametrization represents the charge density of a molecule as a superposition of not only atomic spherical, but also dipolar, charge distributions [see Eq. (1)].

IV. RESULTS AND DISCUSSION

As stated in Sec. I, the main aim of the present work is to determine whether the proposed CPE scheme, parametrized for the isolated molecule, is able to reproduce the relevant charge reorganization of a system subject to external perturbing electric fields. In the framework of linear response and assuming no intermolecular CT as implied in Eq. (13) with $Q_m=0$ for each molecule *m*, the CPE model can, in principle, reproduce two main sources of charge density reorganization of a molecule: one arising from the change of the nuclear potential of the molecule itself due to its distortion with respect to the equilibrium structure, the other due to the electric field produced by the neighboring molecules. The former contribution can in turn arise from both the intrinsic vibrational motion of the molecule and its structural distortion induced by the interaction with the neighboring molecules. In the CPE model such contribution can be evaluated separately from that of the external field. This is achieved by neglecting altogether the intermolecular interactions when calculating the atomic charges and atomic dipoles, i.e., using Eq. (11) instead of Eq. (8) for the energy expression.

The total CPE dipole moments calculated for various H-bond clusters and liquid phase configurations of water and methanol are reported versus the corresponding DFT counterpart in Figs. 1 and 2 (see Sec. III for details on the used DFT method). The dipole moments obtained without including intermolecular interactions (isolated molecule approximation) are also reported in the figures. In the isolated molecule approximation, the dipole moments have been calculated by summing up the contributions of each isolated

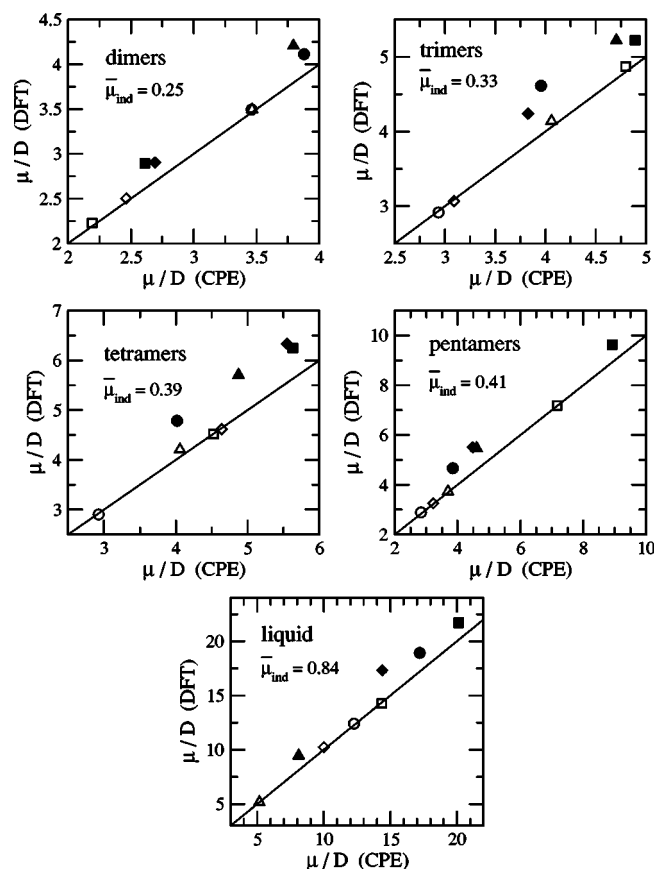


FIG. 1. Correlation diagram between CPE and DFT dipole moments for various H-bond clusters (dimer, trimer, tetramer, and pentamer) and liquid configurations of water. Open symbols: dipole moments in the isolated molecule approximation. Filled symbols: effective dipole moments. The symbol shapes refer to different configurations. The lines indicate the perfect correlation between CPE and DFT. The molecular induced dipole moment $\bar{\mu}_{\text{ind}}$ has been calculated using CPE by averaging over all sets of configurations (units of D).

molecule of the cluster/liquid. The configurations of water and methanol clusters as well as those of the liquid phase have been taken randomly from CPMD simulations. The technical details of the simulation on methanol are given in Ref. 36. The simulation of liquid water has been performed for the present aim. Thirty two water molecules in a cubic box of 9.8652 Å side length with periodic boundary conditions have been simulated. Vanderbilt⁴⁴ pseudopotentials have been used, and the plane wave expansions have been truncated at 25 Ry. Density functional calculations in the generalized gradient approximation have been performed using the PBE functional.⁴⁵ The deuterium has been utilized instead of hydrogen to allow for a larger time step. A fictitious electronic mass of 600 a.u. has been adopted to keep the system on the Born–Oppenheimer surface.

In our analysis, a collection of molecules is considered to form a H-bond cluster if every pair of molecules is connected to each other by a chain of H bonds. H bonding is defined on the basis of a geometrical criterion,^{46–48} i.e., when the O··H distance is less than 2.5 Å and the O··H–O H-bond angle is greater than 130°.

From Figs. 1 and 2 we can observe that in the isolated molecule approximation, the CPE model reproduces very

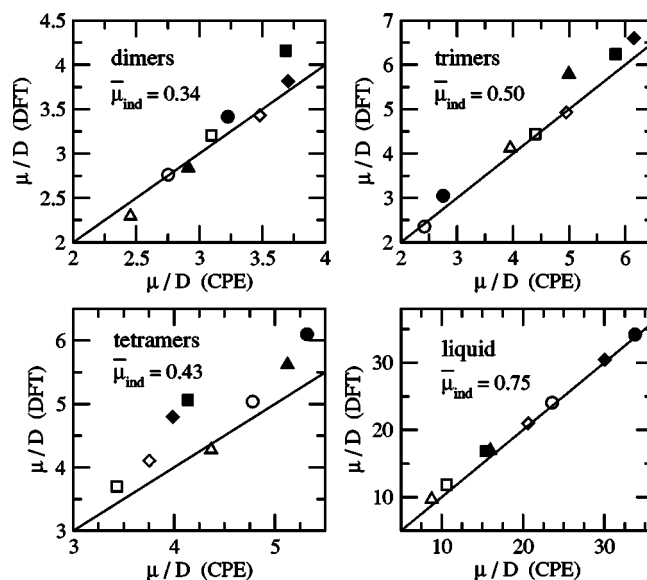


FIG. 2. Correlation diagram between CPE and DFT dipole moments for various H-bond clusters (dimer, trimer, and tetramer) and liquid configurations of methanol. Open symbols: dipole moments in the isolated molecule approximation. Filled symbols: effective dipole moments. The symbol shapes refer to different configurations. The lines indicate the perfect correlation between CPE and DFT. The molecular induced dipole moment $\bar{\mu}_{\text{ind}}$ has been calculated using CPE by averaging over all sets of configurations (units of D).

well the DFT dipole moments. This indicates that the effect of nuclear distortion on the charge density reorganization is well accounted for by the CPE approach. Two facts above all can explain this observation. In the first place we must consider that the fitting procedure has been devised precisely for reproducing electronic properties of distorted geometries of the isolated molecules (see Sec. III). Furthermore we note that the change of the dipole moment due to molecular distortions at room temperature, although significant, is not very large. For instance, the DFT dipole moments of methanol and water in the isolated molecule approximation vary in the ranges 1.6–2.0 D and 1.7–2.0 D for the systems of Figs. 1 and 2, respectively. When intermolecular interactions are taken into account, i.e., when the full CPE scheme of Eq. (8) is employed, the CPE dipole moment is found to be systematically lower than the DFT one for both water and methanol clusters, with a single exception for one methanol dimer. For the configurations taken from the liquid phase, the agreement between DFT and CPE is seemingly better, especially considering that the “corresponding states” ratio μ/N , with μ being the dipole moment of the system and N the number of molecules, is much smaller for a liquid than for a cluster configuration. In the case of the liquid, where each molecule is embedded in a rather more symmetric environment with respect to clusters, the discrepancy is very likely obfuscated, as we shall see, by compensation errors. This systematic underestimate of the CPE dipole moment of clusters suggests that either the polarization response is not linear in the local external field, as implied in the present CPE model,¹³ or that the condition of the absence of intermolecular CT is not met. A source of nonlinearity of the polarization could arise from the neglect of the higher order contributions, i.e., hyperpolarizability terms. The molecular first hyperpolarizability of

water⁴⁹ and methanol²⁹ is of the order of 10^{-1} a.u. From the knowledge of the isotropic component of the molecular polarizability in gas phase (see $\bar{\alpha}$ in Table II) and of the mean molecular induced dipole moment calculated using CPE (see $\bar{\mu}_{\text{ind}}$ in Figs. 1 and 2), the order of magnitude of the average perturbing electric field on a molecule due to the surrounding particles can be estimated. For liquid water and methanol this electric field is about 0.04 and 0.01 a.u., respectively. Even smaller electric fields are expected in clusters as can be inferred from the lower value of their molecular induced dipole moment with respect to the liquid (see Figs. 1 and 2). Finally, on the basis of the estimated first hyperpolarizability and external electric field, we can deduce that the induced dipole moment contribution from hyperpolarizability should not exceed 0.01–0.02 D in liquid phase. This contribution is even smaller for clusters, given the lower perturbing electric fields. Thus, the entity of the induced dipole moment coming from hyperpolarizability is estimated at most 1% of the gas phase dipole moment. From Figs. 1 and 2, we see that CPE model underestimates the DFT dipole moments of about 15% for some oligomers, while the discrepancy is in general less important in liquid phase, especially for methanol. Therefore, the neglect of hyperpolarizability in CPE cannot possibly be responsible of such behavior as the discrepancy with respect to the DFT data for oligomers is too large. Furthermore, a large contribution from the hyperpolarizability would lead to errors larger in liquid configurations than in small oligomers being the average perturbing electric field larger in liquid phase than in clustered systems. This was indeed not observed for water and methanol. We therefore infer that the assumption of neglecting intermolecular CT must be, to some extent, incorrect in these systems.

In principle, CPE can be straightforwardly implemented for including intermolecular CT by equalizing the chemical potential on the whole system, rather than on each molecule separately. This implies in turn to impose one single electroneutrality constraint on the whole system rather than as many constraints as the number of molecules [see Eq. (13)]. This naive approach, however, while giving the correct order of magnitude ($10^{-2}e$) for CT in H-bond dimers, fails in predicting the *sign* of the transferred charge. In fact, contrary to real systems, negative charge is predicted to be transferred from the hydrogen-donor (H-donor) molecule to the hydrogen-acceptor (H-acceptor) one. This behavior of the CPE model can be understood if we think to the CT, whether intramolecular or intermolecular, in terms of atomic electronegativities and atomic hardnesses alone: in H bonding, the more electronegative atom (oxygen) withdraws electronic charge from the less electronegative one (hydrogen). Hence, it is evident that the simple description of a system as a macromolecule is not correct and a more sophisticated modeling should be implemented for including CT in a theoretical consistent way. In DFT calculations, CT is implicitly accounted for in the unrestricted redistribution of the electron density throughout the interacting molecules. There is still debate^{22,23,50} whether the change in the electron density from gas phase to many-molecule systems reflects primarily in redistribution rather than transfer of charge effects. In this regard, it has been recently reported that the changes in elec-

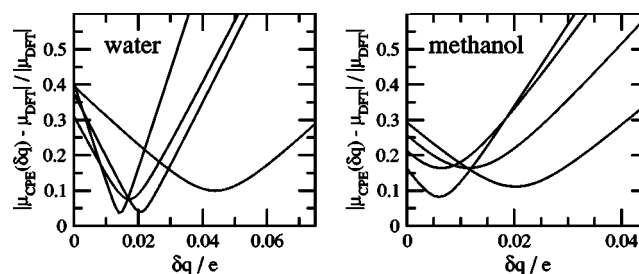


FIG. 3. Induced dipole moment error function, $|\mu_{\text{CPE}}(\delta q) - \mu_{\text{DFT}}|/|\mu_{\text{DFT}}|$, as a function of δq (charge transferred to the H-acceptor molecule) for four water and methanol H-bond dimers. The charge corresponding to the minimum value of the induced dipole moment error function is assumed to be the effective charge transferred between the molecules (δq_{ct}).

trostatic potential upon formation of water clusters can be accurately represented by changes in dipole or quadrupole moments with monopoles kept unchanged.²¹ On the other hand, using standard electron density partition schemes such as NPA (Ref. 25) or AIM (Ref. 26) yields consistently CT of the order of $0.01e$ – $0.05e$ in H-bond systems.^{22,23,50,51} In this respect, it is therefore of interest to evaluate the amount of CT needed in CPE to possibly recover DFT dipole moments in clusters and to verify whether this amount of CT is of the same order of magnitude and sign of that reported in previous studies.^{22,23,51} To this end, we proceed by forcing an *a priori* transfer of charge between H-bonded molecules, still using the provision of chemical potential equalization on each molecule. In practice, using the charge conserving constraints of Eq. (13), we have imposed a net charge δq on the H-acceptor molecule and an opposite net charge $-\delta q$ on the H-donor one (we remark that δq can be whether positive or negative). The charge density and the corresponding dipole moment have been then calculated applying the usual CPE equations [see Eq. (14)]. Using this protocol we have evaluated, for H-bond dimers, the relative deviation of the CPE induced dipole moment from the DFT counterpart, $|\mu_{\text{CPE}}(\delta q) - \mu_{\text{DFT}}|/|\mu_{\text{DFT}}|$, as a function of the δq charge. In the previous definition the dependence of the CPE induced dipole moment on the transferred charge δq is shown explicitly. This induced dipole moment error function as a function of δq is reported in Fig. 3 for four H-bond dimers of water and methanol taken randomly from CPMD simulations. The function exhibits a single minimum and its behavior is symmetric with respect to δq_{ct} , that is, the δq value corresponding to the minimum. We assume that δq_{ct} corresponds to the quantity of transferred charge in H-bond dimers. Using this criterion, very reasonable values for δq_{ct} are obtained,^{22,23} being slightly larger for water than for methanol. It should be also noted that the proposed computational scheme for CT predicts the correct sign of the transferred electronic charge, i.e., from the H-acceptor to the H-donor molecule. By definition, the induced dipole moment error function for $\delta q=0$ corresponds to the deviation of the standard CPE model (absence of CT) from DFT. In this case we note that errors in the induced dipole moment as large as 40% for water and 30% for methanol are obtained. When CT is imposed, the error decreases below 20% and in several cases below 10%.

Of course one should not expect in general very low errors, given the extreme simplicity of the model.

In the CPE based approach described above, we assume that the *a priori* transferred charge δq is rearranged on the two H-bonded molecules according to the standard CPE protocol with the charge conserving conditions $e_1^t \delta c_1 = \delta q$ and $e_2^t \delta c_2 = -\delta q$. In the following we shall refer to this charge density redistribution scheme as CT1. An alternative modeling of charge density redistribution could be that of constraining the transferred charge to be localized on the oxygen atom of the H-acceptor molecule, while the balancing charge to be localized on the H-bond hydrogen atom. The basic underlying hypothesis of this model is that CT is confined in the space occupied by the atoms directly involved in H bonding. The practical implementation of this scheme consists in adding to the system of the two H-bonded molecules two Gaussian charge density distributions [see Eq. (2)], one on the oxygen and the other on the hydrogen atom involved in H bond. These additional charge density distributions are assumed to have the same width (η_s parameter in Table I) of the host atoms. The global system is made now of two molecules and two dummy particles bearing the transferred charge. The CPE equations are then applied with charge conserving conditions that impose the electroneutrality on the molecules and a charge of δq and of $-\delta q$ on the dummy particles placed on the oxygen and hydrogen atoms, respectively. In this approach, the expression of the CPE energy reported in Eq. (8) is used with additional self-energy terms for including the interaction of the dummy particle charges with the spherical type charge density of the host atoms. Such terms are $\eta_o q_o \delta q$ and $-\eta_h q_h \delta q$, where η_o and η_h are the oxygen and hydroxy hydrogen hardnesses, respectively (O and H atom types in Table I), while q_o and q_h are the corresponding charges on the electroneutral molecules. The resulting net charges on the oxygen and hydrogen are then given by $q_o + \delta q$ and $q_h - \delta q$, respectively. In the following we shall refer to this charge density redistribution scheme as CT2.

Using the CT1 and CT2 schemes and the algorithm of the induced dipole moment error function for the evaluation of the CT, we have calculated the transferred charge δq_{ct} for two sets of H-bond dimers of water and methanol taken from CPMD simulations. The results are compared to those obtained by NPA at the B3LYP/6-311++G(*d,p*) level of theory in Fig. 4. (The calculations have been carried out using the GAUSSIAN98 program⁵²). The good correlation existing between CPE-CT1 and DFT-NPA for both water and methanol gives a crucial support to the underlying hypothesis of the CT1 model, namely, that the transferred charge is unrestrictedly redistributed on the molecule and not localized on the H-bonded atoms alone. In particular, the CPE underestimate of the induced dipole moment is confirmed to be originated by the absence of CT. CT is estimated to be larger in water than in methanol, and in both cases less than $0.1e$. From Fig. 4 we also note that CT2 systematically overestimates CT.

In order to evaluate the redistribution of the excess charge within the molecule coming from CT, we have calculated the fraction of charge transferred on the single atoms

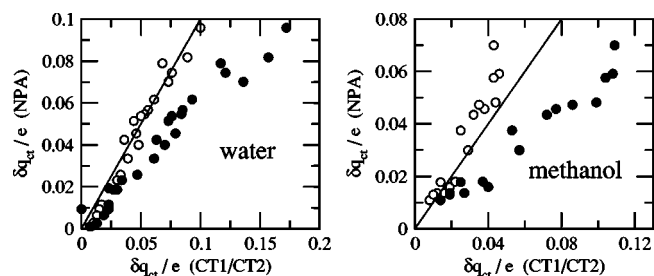


FIG. 4. Correlation diagram between the intermolecular transferred charge predicted by CPE and by natural population analysis (NPA) as obtained from the B3LYP/6-311++G(*d,p*) level of theory. Twenty four H-bond dimer configurations of water and methanol have been considered. Open circles: data obtained from the CT1 charge density redistribution scheme. Filled circles: data obtained from the CT2 charge density redistribution scheme. The lines refer to the perfect correlation between CT1/CT2 and NPA.

with respect to the total amount of charge (δq_{ct}) transferred in the molecule. This fraction has been obtained by subtracting the atomic charge obtained by CPE in absence of CT from the charge on the same atom as obtained in presence of CT and then dividing by the absolute value of δq_{ct} . In Table III the charge fractions obtained for water and methanol using the CT1 and CT2 charge redistribution schemes are reported. The data have been averaged on 359 and 654 H-bond dimers of methanol and water, respectively (taken from CPMD simulations). In the case of CT1 charge density redistribution on the whole molecules occurs. In methanol the transferred charge is equally distributed on the hydroxy and methyl groups independent on the role (H donor or H acceptor) played by the molecule in the dimer. In general a small excess of charge is observed for atoms directly involved in H bonding with respect to the non-H-bonded ones. This effect is obviously more evident using the CT2 scheme. In fact, whether for methanol or for water, the H-bonded atoms have a fraction of charge much larger than those not involved in H bonding (i.e., non-H-bonded hydrogen atom of water and methyl group). As expected, large fraction of positive charge is found to be localized on the oxygen, while negative charge is mainly redistributed on the donated hydrogen.

TABLE III. Charge fraction on the atoms of H-bond dimers of water and methanol with respect to the total amount of transferred charge δq_{ct} . The results obtained using the CT1 and CT2 charge density redistribution schemes are given. The data, averaged on 359 and 654 dimers of methanol and water, respectively, are reported considering the possible H-donor or H-acceptor function of the molecules in the H bonding.

	CT1		CT2	
	H donor	H acceptor	H donor	H acceptor
Methanol				
C	-0.02	0.02	-0.02	-0.14
O	-0.32	0.40	0.70	1.76
Hydroxy H	-0.16	0.09	-1.54	-0.48
Methyl H	-0.17	0.16	-0.04	-0.05
Water				
O	-0.32	0.37	0.28	1.39
H	-0.32	0.32	-0.04	-0.19
H (donated)	-0.36		-1.23	

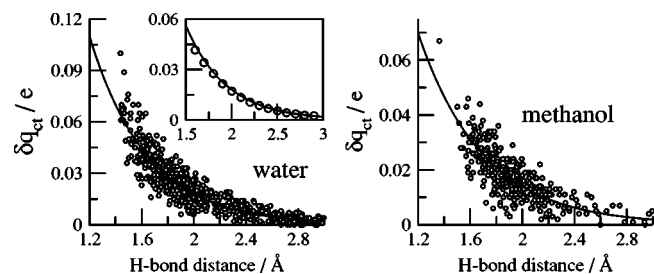


FIG. 5. Transferred charge for H-bond dimers of water and methanol (654 and 359 configurations, respectively) as a function of the $O \cdots H$ H-bond distance (open circles). Solid line: curves resulting from the fit with exponential functions. In the inset the curve resulting from the fit on water dimers is compared to early data (Ref. 22) (open circles) by Gálvez *et al.* Calculations have been performed using the CPE-CT1 model.

The results of Fig. 4 and Table III suggest that in H-bond systems, such as water and methanol, CT cannot be viewed as a process involving only (or mainly) the directly H-bonded atoms. A more extended electron density redistribution, involving at least the first neighboring atoms of the H-bond group, must occur.

In water and methanol H-bond dimers, CT can span the entire set of values below around $0.1e$ (see Fig. 4) in dependence of configurational factors mainly related to the H-bond geometry. In Fig. 5 we report the transferred charge as a function of the $O \cdots H$ H-bond distance calculated using CPE combined to the CT1 charge density redistribution scheme. The calculation has been performed on a set of H-bond dimers of methanol and water taken from CPMD simulations. In this case, in order to explore a large range of H-bond distances, a cutoff radius of 3 \AA on the $O \cdots H$ distance and no constraint on the $O \cdots H-O$ H-bond angle have been employed for the definition of H bond. A relevant spread of the data is observable for both systems. This spread can be explained considering the many configurations existing for a given H-bond distance. However two important features can be noted. The first one is the enhancing of the CT for dimers with shorter H-bond distance. The second characteristic is that CT is more important for water than for methanol. This can be quantitatively assessed by fitting the data with an exponential function of type $y = a \exp(-bx)$. We have obtained $a_m = 0.78e$ and $b_m = 2.01 \text{ \AA}^{-1}$ for methanol and $a_w = 1.67e$ and $b_w = 2.26 \text{ \AA}^{-1}$ for water. The resulting functions give a CT of $0.014e$ and $0.018e$ at H-bond distance of 2 \AA for methanol and water dimers, respectively. For water and methanol, CT seems to persist, even if at a very small extent, up to $O \cdots H$ distances of 3 \AA . All these features of CT versus H-bond distance, and in particular the almost exponential behavior, have been also observed in a recent theoretical study by Gálvez *et al.*²² on H-bond water dimers and others H-bond forming systems. Using a method based on DFT, Gálvez *et al.* found a CT versus H-bond distance dependence for water dimers in very good agreement with our fitted curve (see inset of Fig. 5).

Using the exponential functions obtained from the fit described above for evaluating the transferred charge at a given H bond distance, and assuming that CT coming from H-bonds is additive (in the sense that the total transferred charge on a molecule is the sum of the charges transferred

through single H bonds), we can, in principle, calculate the effect of CT on clusters made by more than two molecules, or even on condensed phase configurations. To this aim we have first determined the total transferred charge on the water and methanol molecules. On the basis of the aforementioned hypotheses, the net charge on a water molecule i is

$$\delta q_{ct}^{(i)} = a_w \left[\sum_{j \neq i} e^{-b_w |\mathbf{r}_{O(i)} - \mathbf{r}_{H(j)}|} - \sum_{j \neq i} e^{-b_w |\mathbf{r}_{H1(i)} - \mathbf{r}_{O(j)}|} - \sum_{j \neq i} e^{-b_w |\mathbf{r}_{H2(i)} - \mathbf{r}_{O(j)}|} \right], \quad (15)$$

where $\mathbf{r}_{O(i)}$, $\mathbf{r}_{H1(i)}$, and $\mathbf{r}_{H2(i)}$ are the vector positions of the oxygen and of the two hydrogen atoms of the molecule i . The sums over j are extended to all molecules that form a H bond of distance less than 3 \AA with the i molecule. For methanol the net charge on a molecule i is

$$\delta q_{ct}^{(i)} = a_m \left[\sum_{j \neq i} e^{-b_m |\mathbf{r}_{O(i)} - \mathbf{r}_{H(j)}|} - \sum_{j \neq i} e^{-b_m |\mathbf{r}_{H(i)} - \mathbf{r}_{O(j)}|} \right]. \quad (16)$$

In Eqs. (15) and (16), the a and b parameters have been obtained by the fit (see above). Once all molecular charges have been assigned, the new charge density on the system (corrected for CT) has been computed using the CPE-CT1 model. The CT corrected dipole moments for the same cluster and liquid configurations of Figs. 1 and 2 are reported in Figs. 6 and 7 for water and methanol, respectively, and compared in the form of correlation diagram to the DFT counterpart. For comparison, the dipole moments obtained using CPE without CT are also reported (data reported as filled symbols in Figs. 1 and 2). For both systems, the dipole moments predicted by CPE with CT [even in the crude approximation of Eqs. (15) and (16)] are generally closer to the DFT data with respect to the standard (no CT) CPE approach. For clusters, CPE with CT is systematically more accurate than CPE without CT with the exception of one single dimer configuration of methanol. The change in the dipole moment due to CT for water and methanol clusters is, on the average, of the order of 0.5 D or less, but in some cases, as for water pentamers, it can also reach 1 D corresponding to the 10%–20% of the total dipole moment. Furthermore we can observe that CT yields always an increase of the total dipole moment. This last feature should not be considered typical of CT, but it is to be ascribed to the specific topology of the systems into consideration. In particular, it means that the CT induced dipole moment has the same direction with respect to the permanent dipole moment of the systems. For the liquid configurations no significant improvement is observed when CT is taken into account. This can be due to the fact that in the liquid each molecule is embedded in a rather symmetric environment and therefore the inflow of transferred charge through H bonds is on the average compensated by an equivalent outflow, thus canceling out the effect of CT. This finding can be considered as a further support to the assumption that, in first approximation, CT into a molecule is originated by a superposition of several contributions coming from the neighboring H-bonded molecules.

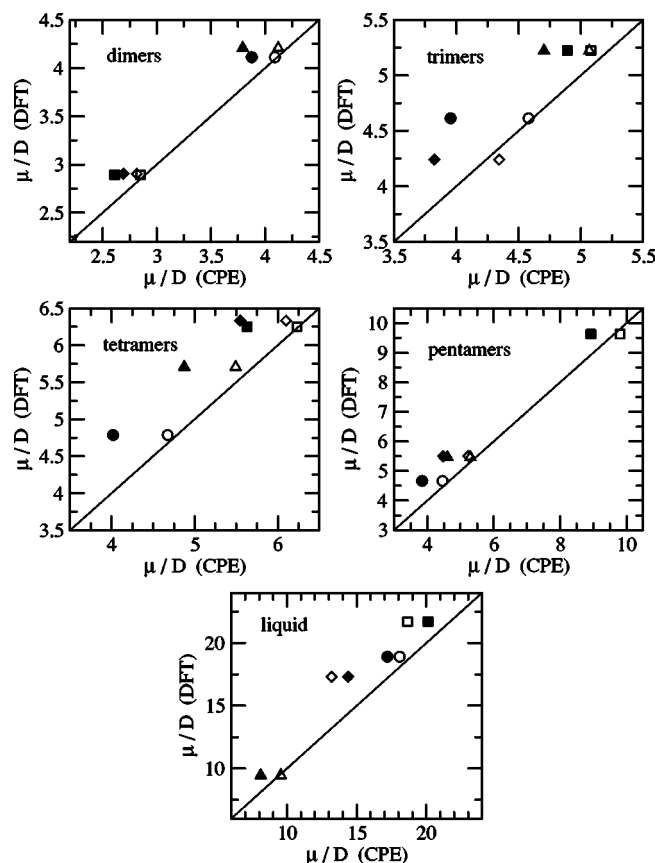


FIG. 6. Correlation diagram between CPE and DFT dipole moments for various H-bond clusters (dimer, trimer, tetramer, and pentamer) and liquid configurations of water. Open symbols: CT corrected dipole moments (the CT1 charge density redistribution scheme has been used). Filled symbols: dipole moments calculated without CT (data also reported in Fig. 1 as filled symbols). The symbol shapes refer to different configurations. The lines refer to the perfect correlation between CPE and DFT.

V. CONCLUSIONS

CPE based force fields are very promising in the modeling of complex systems as they may provide a straightforward and unambiguous protocol to evaluate their properties. In fact, CPE force fields can be, in principle, parametrized on small isolated fragments and then transferred to any aggregation state of a system without *ad hoc* parametrization. In this study we show that a very accurate isolated molecule CPE parametrization is not entirely transferable to strongly interacting H-bond clusters of water and methanol with discrepancies between CPE and DFT dipole moment as large as 15%. The discrepancy is shown to be due to the lack of CT between molecules in the standard CPE implementation. We have proposed two CPE based schemes (called CT1 and CT2) for evaluating the amount of transferred charge between H-bonded molecules. In these schemes the transferred charge is found by displacing *a priori* a charge δq from one molecule to the other and then minimizing the induced dipole moment error function (devised for estimating the deviation of the model from the reference DFT data) with respect to δq . The two schemes differ in the way of redistributing the transferred charge inside the molecules: CT1 allows the charge to be distributed over the whole molecule in accord to the CPE protocol, whereas CT2 is based

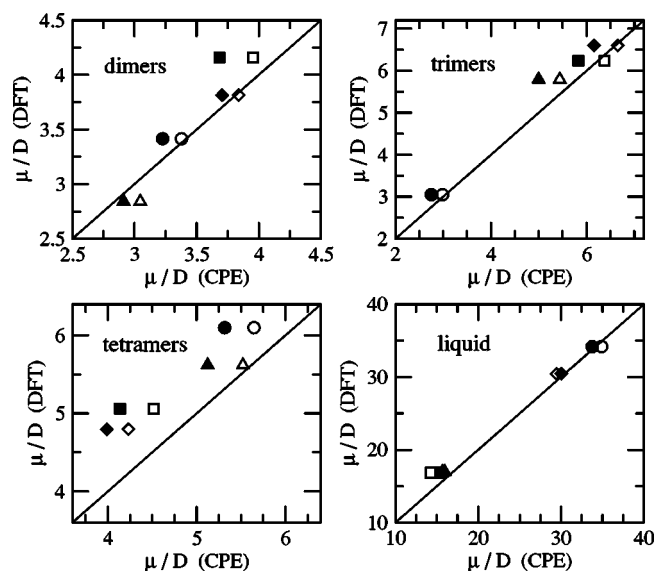


FIG. 7. Correlation diagram between CPE and DFT dipole moments for various H-bond clusters (dimer, trimer, and tetramer) and liquid configurations of methanol. Open symbols: CT corrected dipole moments (the CT1 charge density redistribution scheme has been used). Filled symbols: dipole moments calculated without CT (data also reported in Fig. 2 as filled symbols). The symbol shapes refer to different configurations. The lines refer to the perfect correlation between CPE and DFT.

on the localization of the transferred charge on the atoms directly involved in H bonding. The comparison of our approach with more standard ones for the CT estimate, as the natural population analysis combined to DFT methods, suggests that charge density redistribution must involve the whole molecular system. The average amount of CT is found to be of the order of few hundredths of electrons for both water and methanol H-bond dimers, being slightly larger that of water. The transferred charge calculated using CT1 for a large set of water and methanol dimers is then plotted against the H-bond distance in the dimers and fitted using an exponential function. The fitted curve agrees very well with results of early CT studies on water dimers. On the basis of the H-bond distance dependence of the transferred charge and assuming that CT is linearly additive (the total transferred charge on a molecule is given by the sum of pair contributions) we have estimated the CT for any aggregation state, whether in clusters or in the liquid state. When allowance is made for CT according to the proposed scheme, the CPE dipole moments are found to reproduce satisfactorily the DFT data.

According to recent studies,^{12,20} it has been speculated that, in condensed phase, the molecular polarizability is effectively reduced because of the overlap of molecular orbitals and the Pauli exclusion principle. In this regard, Giese and York²⁰ have shown that CPE schemes based on simple Coulomb screening functions and on isolated molecule parametrization systematically overestimate the polarization when molecular aggregation states are taken into account. The present CPE implementation has been found to produce overall dipole moments of H-bond clusters consistently lower than their DFT counterpart, thus indicating that the CPE model is actually underpolarized. This underpolarization has been attributed to the lack of CT. To reconcile our

results with those by Giese and York,²⁰ we could infer that the CT in H-bond systems is more than offsetting the reduction of polarizability that occurs in condensed phase. As a matter of fact, in the study of Giese and York, the polarization was evaluated for a bifurcated chain of water molecules with no H bonds (and hence CT effects) eventually leading to overpolarization. On the other hand, their basis set correction [Eq. (1) of Ref. 20], due to the use of localized basis set, might have resulted in an underestimate of the *ab initio* polarizability of the chain. In the light of this and with regard to the possibility of setting up transferable polarizable force fields, it would be therefore important to assess the relative importance of CT and underpolarization phenomena due to nonclassical effects in condensed phases. We are currently investigating in this direction and results will be presented in a forthcoming paper.

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- ¹D. Frenkel and B. Smith, *Understanding Molecular Dynamics* (Academic, New York, 1996).
- ²M. P. Allen and D. J. Tildesley, *Computer Simulation of Liquids* (Clarendon, Oxford, 1987).
- ³W. D. Cornell, P. Cieplak, C. I. Bayly *et al.*, J. Am. Chem. Soc. **117**, 5179 (1995).
- ⁴A. D. MacKerell, Jr., D. Bashford, M. Bellot *et al.*, J. Phys. Chem. B **102**, 3586 (1998).
- ⁵W. van Gunsteren and H. J. C. Berendsen, *Groningen Molecular Simulation (GROMOS) Library Manual* (Biomos, Groningen, 1987).
- ⁶H. J. C. Berendsen, J. P. M. Postma, W. F. von Gunsteren, and J. Hermans, *Intermolecular Forces* (Reidel, Dordrecht, 1981).
- ⁷L. Delle Site, A. Alavi, and R. M. Lynden-Bell, Mol. Phys. **96**, 1683 (1999).
- ⁸A. K. Rappe, C. J. Casewit, K. S. Colwell, W. A. Goddard III, and W. M. Skiff, J. Am. Chem. Soc. **114**, 10024 (1992).
- ⁹P. T. van Duijnen and M. Swart, J. Phys. Chem. A **102**, 2399 (1998).
- ¹⁰J. L. Banks, G. A. Kaminski, R. Zhou, D. T. Mainz, B. J. Berne, and R. A. Friesner, J. Chem. Phys. **110**, 741 (1999).
- ¹¹G. A. Kaminski, H. A. Stern, B. J. Berne, R. A. Friesner, Y. X. Cao, R. B. Murphy, R. Zhou, and T. A. Halgren, J. Comput. Chem. **23**, 1515 (2002).
- ¹²G. A. Kaminski, H. A. Stern, B. J. Berne, and R. A. Friesner, J. Phys. Chem. A **108**, 621 (2004).
- ¹³R. Chelli and P. Procacci, J. Chem. Phys. **117**, 9175 (2002).
- ¹⁴R. Car and M. Parrinello, Phys. Rev. Lett. **55**, 2471 (1985).
- ¹⁵G. Tabacchi, C. J. Mundy, J. Hutter, and M. Parrinello, J. Chem. Phys. **117**, 1416 (2002).
- ¹⁶S. Patel, A. D. Mackerell, and C. L. Brooks, J. Comput. Chem. **25**, 1504 (2004).
- ¹⁷S. Patel and C. L. Brooks, J. Comput. Chem. **25**, 1 (2004).
- ¹⁸A. K. Rappe and W. A. Goddard III, J. Phys. Chem. **95**, 3358 (1991).
- ¹⁹D. M. York and W. Yang, J. Chem. Phys. **104**, 159 (1996).
- ²⁰T. J. Giese and D. M. York, J. Chem. Phys. **120**, 9903 (2004).
- ²¹A. A. Rashin, I. A. Topol, G. J. Tawa, and S. K. Burt, Chem. Phys. Lett. **335**, 327 (2001).
- ²²O. Gálvez, P. C. Gómez, and L. F. Pacios, J. Chem. Phys. **115**, 11166 (2001).
- ²³O. Gálvez, P. C. Gómez, and L. F. Pacios, J. Chem. Phys. **118**, 4878 (2003).
- ²⁴D. Barker and M. Sprik, Mol. Phys. **101**, 1183 (2003).
- ²⁵A. E. Reed, R. B. Weinstock, and F. Weinhold, J. Chem. Phys. **83**, 735 (1995).
- ²⁶R. F. W. Bader, *Atoms in Molecules: A Quantum Theory* (Clarendon, Oxford, 1990).
- ²⁷R. Chelli, P. Procacci, R. Righini, and S. Califano, J. Chem. Phys. **111**, 8569 (1999).
- ²⁸K. Shimizu, H. Chaimovich, J. P. S. Farah, L. G. Dias, and D. L. Bostick, J. Phys. Chem. B **108**, 4171 (2004).
- ²⁹R. Chelli, S. Ciabatti, G. Cardini, R. Righini, and P. Procacci, J. Chem. Phys. **111**, 4218 (1999).
- ³⁰R. Chelli, R. Righini, S. Califano, and P. Procacci, J. Mol. Liq. **96-97**, 87 (2002).
- ³¹C. Lee, W. Yang, and R. G. Parr, Phys. Rev. B **37**, 785 (1988).
- ³²A. D. Becke, Phys. Rev. A **38**, 3098 (1988).
- ³³N. Troullier and J. L. Martins, Phys. Rev. B **43**, 1993 (1991).
- ³⁴L. Kleinman and D. M. Bylander, Phys. Rev. Lett. **48**, 1425 (1982).
- ³⁵A. D. Rabuck and G. E. Scuseria, Theor. Chem. Acc. **104**, 439 (2000).
- ³⁶M. Pagliai, G. Cardini, R. Righini, and V. Schettino, J. Chem. Phys. **119**, 6655 (2003).
- ³⁷D. Barker and M. Sprik, Mol. Phys. **101**, 1183 (2003).
- ³⁸I. F. W. Kuo, C. J. Mundy, M. J. McGrath *et al.*, J. Phys. Chem. B **108**, 12990 (2004).
- ³⁹J. S. Tse, Annu. Rev. Phys. Chem. **53**, 249 (2002).
- ⁴⁰A. Putrino, D. Sebastiani, and M. Parrinello, J. Chem. Phys. **113**, 7102 (2000).
- ⁴¹A. Putrino and M. Parrinello, Phys. Rev. Lett. **88**, 176401 (2002).
- ⁴²J. Hutter, A. Alavi, T. Deutch, M. Bernasconi, S. Goedecker, D. Marx, M. Tuckerman, and M. Parrinello, *CPMD* (MPI für Festkörperforschung, and IBM Zurich Research Laboratory, Stuttgart, 1995-1999).
- ⁴³D. R. Lide, *Handbook of Chemistry and Physics* (CRC, Boca Raton, 1993), Vol. 74.
- ⁴⁴D. Vanderbilt, Phys. Rev. B **41**, 7892 (1990).
- ⁴⁵J. P. Perdew, K. Burke, and M. Ernzerhof, Phys. Rev. Lett. **77**, 3865 (1996).
- ⁴⁶P. Sindzingre and M. L. Klein, J. Chem. Phys. **96**, 4681 (1992).
- ⁴⁷L. J. Root and B. J. Berne, J. Chem. Phys. **107**, 4350 (1997).
- ⁴⁸M. Ferrario, M. Haughney, I. R. McDonald, and M. L. Klein, J. Chem. Phys. **93**, 5156 (1990).
- ⁴⁹G. Maroulis, J. Chem. Phys. **113**, 1813 (2000).
- ⁵⁰L. Delle Site, A. Alavi, and R. M. Lynden-Bell, J. Mol. Liq. **98-99**, 79 (2002).
- ⁵¹A. van der Vaart and J. K. M. Merz, J. Chem. Phys. **116**, 7380 (2001).
- ⁵²M. J. Frisch, G. W. Trucks, H. B. Schlegel *et al.*, GAUSSIAN 98, revision A.7, Gaussian, Inc., Pittsburgh, PA, 1998.
- ⁵³J. B. Foresman and E. Frisch, *Exploring Chemistry with Electronic Structure Methods* (Gaussian, Inc., Pittsburgh, PA, 1996), and references therein.