Key Role of the Polarization Anisotropy of Water in Modeling Classical Polarizable Force Fields

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We have evaluated the extent to which classical polarizable force fields, based either on the chemical potential equalization principle or on distributed polarizabilities in the framework of the Sum of Interactions Between Fragments Ab initio computed (SIBFA), can reproduce the ab initio polarization energy and the dipole moment of three distinct water oligomers: bifurcated chains, transverse hydrogen-bonded chains, and longitudinal hydrogen-bonded chains of helical shape. To analyze the many-body polarization effect, chains of different size, i.e., from 2 to 12 water monomers, have been considered. Although the dipole moment is a well-defined quantity in both classical polarizable models and quantum mechanical methods, polarization energy can be defined unequivocally only in the former type of approaches. In this study we have used the Kitaura−Morokuma (KM) procedure. Although the KM approach is on the one hand known to overestimate the polarization energy for strongly interacting molecules, on the other hand it can account for the many-body polarization effectively, whereas some other procedures do not. Our data show that, if off-centered lone pair polarizabilities are explicitly represented, classical polarizable force fields can afford a close agreement with the ab initio results, both in terms of polarization energy and in terms of dipole moment.

1. Introduction

In view of reliable computer simulations of large molecular assemblies, derivation of molecular mechanics potentials that explicitly encompass induction effects is the object of long-standing efforts.[1−16] Such effects are not included, or only so in a mean field spirit, in conventional force fields.[17−19] The need for explicit inclusion of polarization phenomena is becoming clearer as the algorithms[12,20−25] and computer power allow the determination of increasingly accurate free energy surfaces. For instance, the binding affinities between an active and inactive ligand for a specific biological target can differ by less than 1 kcal mol^{-1} (see ref 26), whereas the polarization energy at a binding distance may often exceed some kilocalories per mole. Several polarizable force fields have been developed. Most of them are based on the linear response and may be classified in three groups: (i) improved Applequist-like schemes (using isotropic atomic polarizabilities) that use a Thole correction,[3,14,27] (ii) approaches using distributed polarizabilities such as those published by Le Sueur and Stone,[28] or Garmer and Stevens,[29] and (iii) models based on the chemical potential equalization (CPE) principle.[30,31] The second type of procedure is used in the SIBFA (Sum of Interactions Between Fragments Ab initio computed),[4,5] EFP (effective fragment potential[16]), or the density-fitting-based GEM (Gaussian electrostatic model[13]) force fields. In the CPE-based methods, the molecular charge distribution depends on the system configuration and is described by a set of basis functions of spherical and dipolar symmetry generally centered on the atoms. This method allows for either a local molecular polarization (dipole-like basis functions) or for a global polarization originated from the intramolecular charge transfer (spherical basis functions). The above-mentioned polarizable force fields have in common the fact that (i) they are based on classical electrostatics and (ii) the electric response, in terms of induced dipole moment, is linear with respect to the external electric field.

Merits and limitations have been extensively discussed in recent papers.[32−37] Indeed, the ability of classical polarizable models to reproduce the polarization response of condensed-phase systems starting from gas-phase or small clusters has been questioned. Thus, Kaminski et al.[26] have argued that the "molecular polarizability" in condensed phases is lowered with respect to that of the gas-phase due to exchange-polarization coupling. This would limit the transferability of gas-phase derived classical polarizable models to condensed phases. In this respect, by designing a specific example consisting of a bifurcated chain of water molecules of increasing length, Giese and York[36] discussed the effect of such a coupling by comparing ab initio calculations to results obtained by the AMOEBA polarizable model[14] that uses a Thole/Applequist-like approach. They concluded that, owing to the absence of the polarization exchange-coupling, classical polarizable models could be over-polarized. By contrast, subsequent tests[38] on hydrogen-bond forming chains of water molecules have suggested that classical polarizable models with polarization centers on the atoms could be underpolarized. This was interpreted[38−40] to be due to lack of intermolecular charge transfer via hydrogen bonding. Indeed,

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in quantum chemistry, the total induction energy embodies several terms: linear response polarization, nonclassical charge-transfer, and exchange-induction energies, each with different physical origin.[41−45] Obviously, a simple polarizable force field approach using only an electric field/distributed polarizability approach can only deal with the linear response part of the induction, namely, polarization.

In the present work we compare the CPE[9] and SIBFA[4,5] polarizable models to ab initio methods, concerning two specific quantities calculated for water oligomers: the polarization energy, E_{pol}, and the dipole moment. The ab initio values of E_{pol} were obtained using the Kitaura−Morokuma (KM) energy decomposition scheme,[41] which fully accounts for the many-body polarization. Since the SIBFA and CPE force fields parameters are calibrated using different strategies, our goal is to show that polarizable models that take into account the inhomogeneity of polarization response on the isolated water molecule could correctly reproduce both E_{pol} and dipole moment. To do so, we compare the SIBFA- and CPE-based models bearing dipolar polarizabilities on the water lone pairs to a CPE parametrization where the out-of-plane polarizability is modeled by a dipolar basis function located on the oxygen nucleus.

The outline of the article follows. In Section 2 we provide some details on the ab initio energy decomposition and on the polarizable models. In the same section we also describe the studied model systems (water oligomers). The results are presented in Section 3. The conclusions are given in Section 4.

2. Computational Details

2.1. Ab initio Polarization Energy Calculations. All ab initio calculations have been performed at the HF/CEP 4-31G-(2d) level of theory[46] using the GAMESS program.[47] The most widely used decomposition methods of the ab initio energy of a many-molecules system are the restricted variational space (RVS) approach[44] and the KM intermolecular interaction energy scheme.[41] At variance with the KM approach, the RVS analysis uses antisymmetrized wave functions and embodies exchange-polarization effects. For instance, in the case of a dimer, the polarization energy of a constituent monomer is computed by relaxing its molecular orbitals through a constrained variational energy minimization. The constraint of minimization is the orthonormality condition between the molecular orbitals of the target monomer and the frozen molecular orbitals of the partner monomer. In the KM analysis, the polarization energies of both monomers are instead computed at the same time, the procedure allowing the mixing of the occupied molecular orbitals of a molecule with its virtual orbitals, the virtual orbitals of the partner molecule being excluded from the variational space. This computational strategy brings to an overestimate of the polarization energy, the exchange-polarization component being missing. On the opposite, the RVS approach underestimates the polarization response, the full wave function being incompletely relaxed as only frozen molecular orbitals are used in the variational optimization (the cross-contributions of induced multipole moments are not taken into account). For this reason, the RVS polarization can be seen as a lower bound to the polarization energy. Because of the great cooperative many-body effects expected in our rich hydrogen-bond systems, we shall consider the polarization energy obtained from the KM analysis. However, for completeness, a comparison between the polarization energies calculated using the SIBFA parametrization and the RVS method is reported in the Supporting Information.

TABLE 1[a]

	ab initio	CPE1	CPE2	SIBFA
μ (D)	1.97	1.97	1.97	1.98
α_{xx} (Å^3)	1.01	1.02 (1.02)	1.01 (1.01)	1.11
α_{yy} (Å^3)	1.28	1.28 (1.02)	1.28 (1.01)	1.34
α_{zz} (Å^3)	1.13	1.11 (1.02)	1.13 (1.01)	1.20

atomic coordinates	X (Å)	Y (Å)	Z (Å)
O	0	0	0.1172
H	0	0.757	−0.4687
H	0	−0.757	−0.4687

[a] Dipole moment and polarizability tensor of the isolated water molecule (whose geometry is reported on the bottom) obtained from the CPE1, CPE2, and SIBFA polarizable models and from an ab initio method. For the CPE1 and CPE2 models, we report in parenthesis the contribution of the dipolar charge distributions to the polarizability.

2.2. Polarizable Force Fields. We have considered three different polarizable force fields denoted as CPE1, CPE2, and SIBFA.

2.2.1. CPE Models. Both CPE1 and CPE2 models are based on the CPE principle.[30,31] In the CPE1 model the charge distribution of the water molecule is treated by means of a Gaussian basis function on each atom plus a dipole-like basis function on the oxygen. In the CPE2 model, the charge distribution is instead represented by a Gaussian basis function on each atom plus two dipole-like basis functions on the sites of the oxygen lone pairs. Details of the underlying theory regarding these models are given in ref 9. In the CPE2 model, the dipolar charge distributions are placed 0.65 Å away from the oxygen nucleus, forming a dipole−oxygen−dipole angle of 109.47°. This angle corresponds to that obtained from density functional theory calculations of an isolated water molecule[48] using Wannier function decomposition.[49,50] The oxygen−dipole distance is consistent with a recent seven-site model[51] for water where the charges corresponding to the lone pairs have been placed at a distance of 0.74 Å away from the oxygen. Moreover, this choice is consistent with findings on the spatial extension of the induction electron density of water in presence of small homogeneous electric fields[52,53] and of strong nonuniform electric fields[40] as well. The empirical parameters of the CPE1 and CPE2 models are[9] the atomic electronegativity, χ, and the atomic hardness, η, for the spherical (Gaussian) charge density distributions, the hardness, ξ, for the dipole-like charge density distributions, and the sum of the isotropic polarizabilities of the atoms, α_0. Both CPE models have been parametrized[9] to reproduce the ab initio dipole moment and the polarizability tensor of the isolated water molecule. The reference quantum mechanical calculations have been performed at the HF/CEP 4-31G(2d) level. For the CPE1 model we obtained the following fitting parameters: $\chi = 27.5$ eV e^{-1} and $\chi = 0.0$ eV e^{-1} for O and H, respectively; $\eta = 53.3$ eV e^{-2} and $\eta = 21.4$ eV e^{-2} for O and H, respectively; $\xi = 14.2$ eV D^{-2} for the dipole-like charge density distribution of the oxygen atom; finally, $\alpha_0 = 0.323$ Å^3. For the CPE2 model we obtained the following fitting parameters: $\chi = 28.3$ eV e^{-1} and $\chi = 0.0$ eV e^{-1} for O and H, respectively; $\eta = 30.1$ eV e^{-2} and $\eta = 71.3$ eV e^{-2} for the spherical charge density distributions of the O and H, respectively; $\xi = 28.5$ eV D^{-2} for each of the two dipole-like charge density distributions assigned to the lone pairs; finally, $\alpha_0 = 1000$ Å^3. The very large value of α_0 for the CPE2 parametrization means that the energy term depending on the square of the induced dipole moment (see eq 27 of ref 9) has been neglected. As can be seen in Table 1, the fitted electronic properties of the isolated molecule are well reproduced by both CPE models.

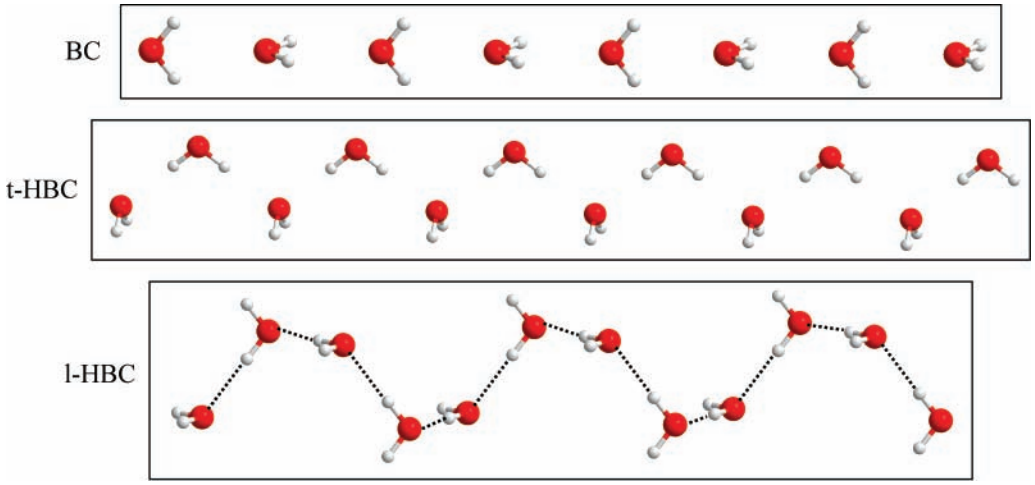

Figure 1. Graphic representation of the three types of water oligomers: bifurcated chain (BC), transverse hydrogen-bonded chain (t-HBC), and longitudinal hydrogen-bonded chain (l-HBC). In each type of chain, all interoxygen distances between neighboring (hydrogen-bonded) molecules are equal. To make clear the connection topology between the molecules in the l-HBC, we have drawn the line connecting the hydrogen and the oxygen of all hydrogen bonds.

We note that the largest contribution to the polarizability is given by the dipole-like charge distributions. This feature is necessarily obtained for correctly fitting the polarizability tensor component, α_{xx}, perpendicular to the molecular plane, which happens to be of the same order as the planar components. For the CPE1 and CPE2 models, E_{pol} is calculated by subtracting the energy of the water cluster determined without intermolecular electric induction from the energy of the water cluster evaluated in presence of electric induction.

2.2.2. SIBFA Model. In the SIBFA model[4,5] the charge distribution is represented by permanent multipole moments (up to quadrupole) distributed on the atoms and on the bond barycenters following Vigné-Maeder and Claverie's approach.[54] In addition to the permanent charge distribution there is a set of anisotropic polarizability sites that give rise to the configuration-dependent polarization. These polarizabilities are distributed on the centroids of the Boys localized orbitals (lone pairs and barycenter of the covalent bonds) using the procedure by Garmer and Stevens.[29] The electric field applied on each polarizability site of the molecule is determined by both the permanent multipole moments and the induced dipole moments of all the other molecules in an iterative fashion (see refs 55−58 for details). In addition to the electric field, such self-consistent procedure provides also the induced dipole moments on the polarizability sites. E_{pol} is the polarization energy contribution, calculated with distributed, anisotropic polarizabilities on the individual molecules. Once the electric field and the induced dipole moment on the polarizability sites (denoted as i) are determined, E_{pol} is obtained as follows:

$$E_{pol} = -\frac{1}{2}\sum_{i=1}^{N} \boldsymbol{\mu}_i \cdot \mathbf{E}_0(i) \qquad (1)$$

where

$$\boldsymbol{\mu}_i = \alpha_i[\mathbf{E}_0(i) + \mathbf{E}_\mu(i)] \qquad (2)$$

where $\mathbf{E}_0(i)$ and $\mathbf{E}_\mu(i)$ are the electric fields on the site i due to the permanent multipole moments and to the induced dipole moments, respectively, α_i is the polarizability tensor of the site i, $\boldsymbol{\mu}_i$ is the induced dipole moment at the site i, and the sum is extended to all the N polarizability sites of the system (as pointed out by Garmer and Stevens,[29] the induced dipole moments within a molecule are not interacting with each others). $\boldsymbol{\mu}_i$ is derived by successive iterations in the electric fields of all the moments (permanent and induced) applied at site i, convergence being generally obtained in five to nine iterations.[56,58] A Gaussian screening of the polarizing electric field is used[59] in order to reproduce the results of RVS and thus embodies part of the short-range effects including exchange-polarization energy. The polarization energy obtained in this way can be compared to its fully relaxed ab initio counterpart derived from the KM analysis. The SIBFA polarization energy, if calculated without iterations, can be directly compared to the RVS procedure, since the polarizing electric field exerted on a polarizability site is only from the permanent multipole moments of the system (values of the first iteration are given in the Supporting Information).

The parametrization of E_{pol} in SIBFA bears essentially on the parameters of the screening function of the polarizing electric field generated by the permanent multipole moments, namely, its multiplicative factor and the exponent of the Gaussian. This was done for water so that E_{pol} reproduces the polarization energy computed by RVS analysis at the HF/CEP 4-31G(2d) level of theory for the monoligated complex of Zn(II) with one water molecule.[59] The multipoles (up to quadrupoles) are nonparametric[54] and directly derived from the ab initio HF wave function of water computed with this basis set. The ab initio polarizability tensor and the dipole moment of the isolated water molecule obtained with the SIBFA parametrization are given in Table 1.

In the SIBFA model, E_{pol} is coupled with a short-range charge-transfer contribution E_{ct} in order to embody all the features of the "induction" term from ab initio energy decomposition. E_{ct} is the counterpart of the charge-transfer energy in the RVS procedure.

2.3. Investigated Water Oligomers. The calculations have been performed for three types of water oligomers: (i) bifurcated chains (BCs), (ii) transverse hydrogen-bonded chains (t-HBCs), where the molecular dipole moments are perpendicular to the main axis of the chain, and (iii) longitudinal hydrogen-bonded chains (l-HBCs) with helical configuration, where the molecular dipole moments are parallel to the main axis of the chain. A picture of these water chains is reported in Figure 1. The BCs and t-HBCs were previously investigated[36,38] to evaluate the polarization response. The l-HBCs have been selected in order

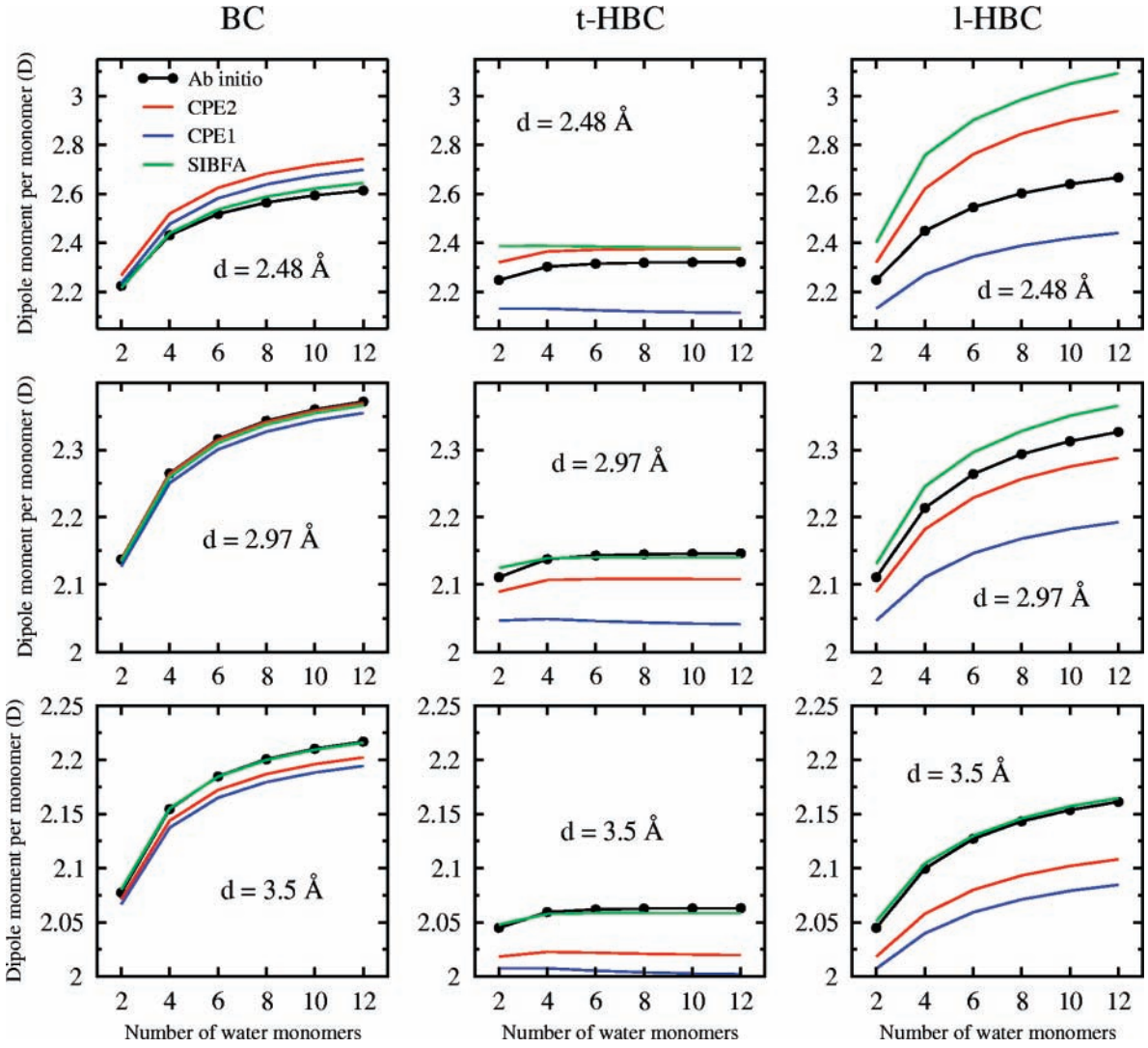

Figure 2. Dipole moments per water monomer obtained for the BCs, t-HBCs, and l-HBCs as a function of the number of water molecules in the chain. The calculations were carried out for various interoxygen distances *d* (see inside each panel) using the CPE1, CPE2, and SIBFA polarizable models and quantum mechanical methods (HF/CEP 4-31G(2d) level of theory).

to enhance cooperativity effects. For the three chain arrangements we have considered six oligomers differing by the number *n* of water molecules, $n = 2, 4, 6, 8, 10$, and 12. Three distances between the oxygen atoms of neighboring water molecules in the chains have been considered, namely, 2.48, 2.97, and 3.5 Å. Short oxygen−oxygen distances, like 2.48 Å, are rarely found in aqueous phases at normal conditions.[38] Nonetheless in simulations of condensed phases, polarizable force fields must be devised to prevent unrealistic short-range increases of E_{pol} (the so-called polarization catastrophe).

3. Results and Discussion

3.1. Dipole Moments. The dipole moments per monomer of the three water chains[60] obtained with the CPE1, CPE2, and SIBFA polarizable models are reported in Figure 2 along with those calculated ab initio at the HF/CEP 4-31G(2d) level of theory. The general performance of the models in reproducing the ab initio data follows the order CPE1 < CPE2 < SIBFA. In particular, we note that all models reproduce quite well the dipole moments of the BCs at interoxygen distances of 2.97 and 3.5 Å. In such cases the maximum error, occurring for the CPE1 model at the interoxygen distance of 3.5 Å, is about 1%. Clearly, the error increases (up to 11%) if we assume the induced dipole moment as reference. For the BC configurations at interoxygen distance of 2.48 Å, the CPE models behave less satisfactorily, consistently overestimating the ab initio dipole moment by about 5%. The SIBFA model is instead able to follow the ab initio dipole moment with good accuracy. Such an overestimate at short distances is to be expected since in the ab initio calculation the actual electron densities of two neighboring molecules strongly overlap, giving rise to exchange-polarization effects directly linked to the Pauli exclusion principle and to short-range penetration effects. Such effects, well-known in quantum chemistry, have been extensively discussed in recent papers.[26,36,38] However, in the BC configuration (see Figure 2), the overestimate of the dipole moment obtained with the SIBFA model is remarkably small. This suggests that such subtle effect can be actually accounted for by classical polarizable force fields, embodying them in the screening function used for the multipolar electric field correction.

For the t-HBCs, the dipole moments computed with the SIBFA model are closer to the ab initio data than the CPE1 and CPE2 ones, except for the water chains at interoxygen distance of 2.48 Å. In these configurations CPE1 underestimates the dipole moment. Recently, some of us interpreted such behavior as a nonclassical effect stemming from intermolecular charge-transfer,[38] an effect that would not be accounted for by

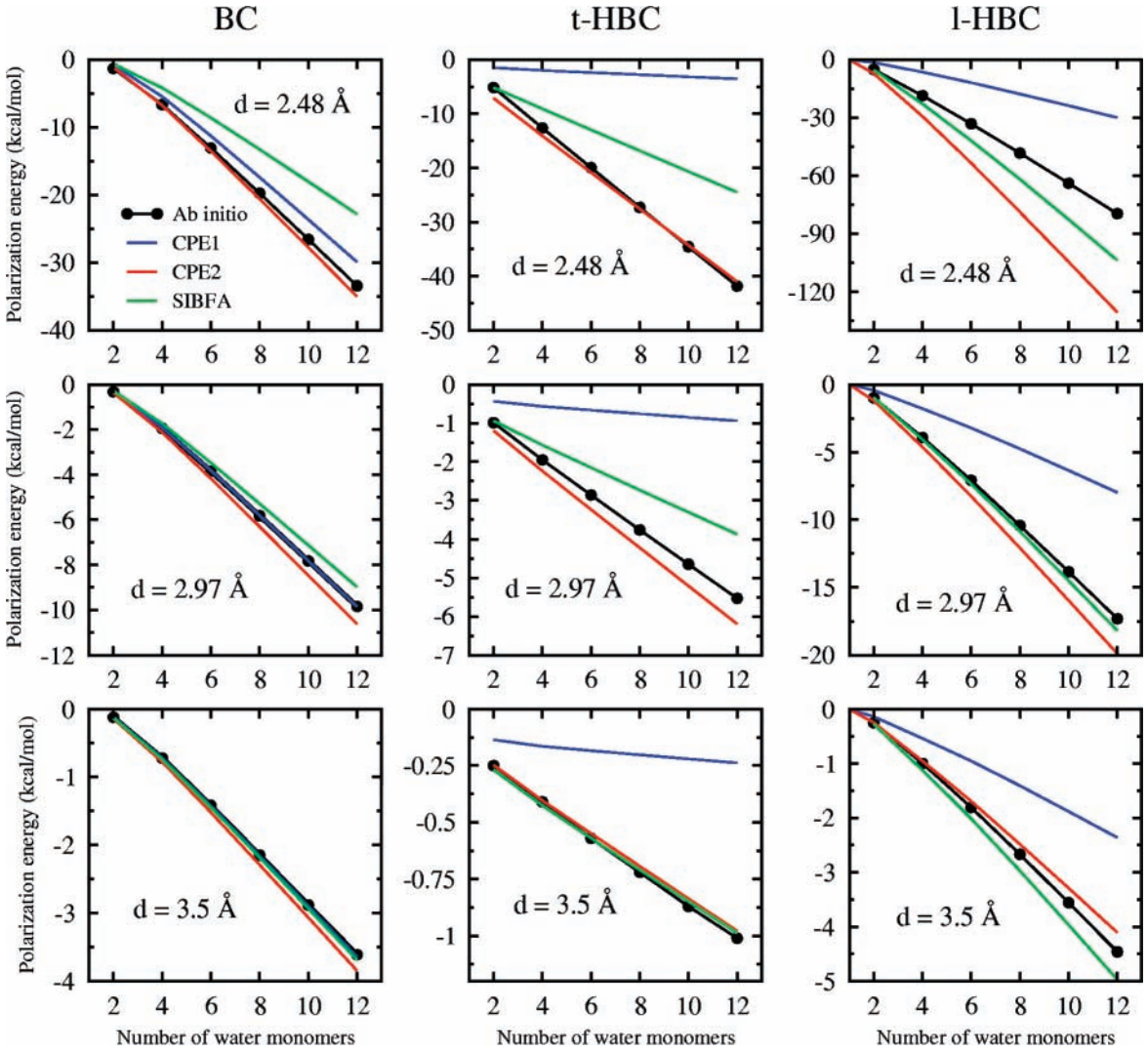

Figure 3. Polarization energies obtained for the BCs, t-HBC, and l-HBCs as a function of the number of water molecules in the chain. The calculations were carried out for various interoxygen distances *d* (see inside each panel) using the CPE1, CPE2, and SIBFA polarizable models and quantum mechanical methods (HF/CEP 4-31G(2d) level of theory). The ab initio polarization energy has been estimated by the KM decomposition.

CPE1-like models. Thus, the difference between the ab initio and the CPE dipole moment was taken[38] as an indirect "measurement" of intermolecular charge-transfer contribution to the total dipole moment. The present results indicate that such an underestimate can actually be removed by resorting to a *classical* polarizable model having a more realistic representation of the molecular polarization response that in the case of the water molecule consists of introducing off-atom polarizable centers in correspondence of the lone pair locations. On the other hand, the importance of the lone pairs in the electron density reorganization of a water molecule under the application of strong electric fields was pointed out in a recent paper.[40] In particular, it has been shown that the difference between the electron density of water after and before electric field application extends up to 1 Å far from the oxygen nucleus.

The effect of an adequate representation of the anisotropy of the water polarizability is partially observed with the CPE2 model, which bears polarizable lone pairs, and is fully exploited in the case of the SIBFA model, which also includes polarizability centers on the covalent bonds and resorts to nonisotropic polarizability tensors. We remark that in the SIBFA model, although the energy correlated to intermolecular charge transfer is directly available,[4−6] the electric charge reorganization is due to polarization. In this respect, no significant differences exist between the SIBFA and the CPE approaches. The reproduction by SIBFA may be ascribed to the more accurate representation of the molecular polarization response that also includes bond polarizabilities.

Concerning the l-HBC configurations at the interoxygen distance of 2.97 Å, which corresponds to the most energetically stable l-HBC complex, the SIBFA and CEP2 models over- and underestimate, respectively, the ab initio dipole moment by approximately 0.05 D. The CPE1 model gives an underestimate of about 0.15 D. For the shortest interoxygen distance (2.48 Å) and for $n = 12$, the models give errors of 0.2 D (CPE1) or larger (SIBFA and CPE2). For the largest interoxygen distance (3.5 Å), CPE1 and CPE2 models give deviations of about −0.05 D, whereas the corresponding SIBFA deviations are very small (less than 0.01 D).

3.2. Polarization Energies. In Figure 3, we compare the polarization energy obtained from the polarizable models to their quantum mechanical counterpart obtained with the KM procedure. The polarization energy of the BCs is satisfactorily reproduced by all models, indicating that for such a chain topology the molecule−molecule interaction can be basically described even by a polarizable dipolar charge distribution localized on the oxygen atom (e.g., the CPE1 model). A different behavior of the polarizable models is observed for the t-HBCs,

TABLE 2[a]

	E_{ct} (ab initio)	E_{ct} (SIBFA)
BC	−3.5	−3.6
t-HBC	−7.7	−7.5
l-HBC	−9.8	−9.5

[a] Charge-transfer contribution to the induction energy calculated using the SIBFA model and the ab initio RVS analysis. The data refer to the longest chains (12 water monomers) at interoxygen distance of 2.97 Å. The energies are in kcal mol^{-1}.

where water molecules act as double hydrogen donor and double hydrogen acceptor as well (except for the terminus water molecules; see Figure 1). In this case the most significant feature is the strong underestimation of E_{pol} from the three-site CPE1 model at all interoxygen distances. The better performance of the CPE2 and SIBFA models with respect to the CPE1 one is to be ascribed to the more realistic description of the polarization charge distribution in the former two models, concerning in particular the inclusion of polarizable lone pairs. In fact, if the CPE2 model is modified by setting the distance of the centroids of the lone pair dipole moments at 0.3 Å from the oxygen nucleus (instead of 0.65 Å), the polarization energy decreases by about 70% (data not shown).

The importance of the lone pairs in water, and hence the need of reproducing their polarization behavior, can be qualitatively understood by considering the polarization energy response obtained from the CPE1 and CPE2 models, when two equal point charges approach the oxygen atom of water along the line perpendicular to the molecular plane, both charges at the same distance from the oxygen. For symmetry reasons, the CPE1 model gives negligible polarization energy due to the small dipole moment induced along the direction of the permanent dipole moment of water (such induction is due to the intramolecular charge reorganization of the spherical atomic charges). Polarization energy largely different from zero would be instead obtained from the CPE2 model due to the occurrence of a quadrupole moment induced on the lone pair charge distributions. This charge redistribution mechanism is essentially the one responsible for the small polarization energy observed for the CPE1 model in the t-HBCs (Figure 3). This example shows that a proper representation of the anisotropy of the water molecule in terms of polarization sites distribution can be an essential asset for the development of polarizable force fields.

In the case of the l-HBCs, the scenario of the polarization response does not change substantially from the one observed for the t-HBCs. In fact, the CPE1 model strongly underestimates the ab initio E_{pol} at all interoxygen distances. The CPE2 and SIBFA models show again a closer agreement with ab initio data, even if a significant overestimate of E_{pol} is noted, especially at the shortest interoxygen distance. For this chain configuration the performance of the SIBFA model is very satisfactory. In general, we may state that the CPE2 and SIBFA models perform well for all chains at intermediate and long interoxygen distances, whereas they behave less satisfactorily at short interoxygen distances. However, at an interoxygen distance of 2.48 Å, even if a strong nonclassical electrostatic penetration energy contribution occurs in the polarization energy due to the overlap of charge densities, it is important to point out that the total interaction energies are highly repulsive. Therefore, these configurations are rarely explored in real systems at normal temperature. In the case of the SIBFA model, it is also worth noticing that an excellent agreement is found for the charge-transfer energy, E_{ct}, which is the remaining contribution to the polarization energy (see Table 2). As stated in section 2.2, if we only consider the permanent multipole moments as the only electric field sources, we can compare the corresponding polarization energy to that obtained from the ab initio RVS analysis. Such comparison is provided for the SIBFA model in Supporting Information. The good performance of SIBFA for this case is expected, since the model was originally parametrized to specifically reproduce the RVS polarization energy of water in its monoligated complex with a Zn(II) cation used as a probe.[59]

4. Conclusions

In this work we have studied the capability of two classical polarizable force fields (CPE and SIBFA models) in reproducing polarization properties of water oligomers. In order to amplify the nonadditive induction effects, we have used water oligomers with strong intermolecular interactions as model systems. Specifically, two properties closely related to the electronic polarization, i.e., dipole moment and polarization energy, have been calculated and compared to their ab initio counterparts. To recover the reference ab initio polarization energy, we have resorted to the KM energy decomposition. Our analysis has focused on to the understanding of the role played by the anisotropic polarizability of the water molecule stemming from the oxygen lone pairs in shaping the electric behavior of water in condensed phases. With this regard, we have shown that only polarizable models, that embody explicit polarizable lone pair sites, are able to satisfactorily reproduce the ab initio reference data. The implications of these results go well beyond the specific case of water, due to the ubiquitous presence of lone pairs in complex systems. In addition, the better reproduction of the dipole moment values by the SIBFA model suggests that the dipole moment of water in the condensed phase could be more sensitive to short-range interactions (i.e., penetration and exchange-polarization) than polarization energies and be more difficult to reproduce by a classical polarizable force field limited to simple dipolar polarizabilities. An extension of the iterative models to higher order polarizabilities could be useful.[61] Fully relaxed ab initio polarization calculation computed using antisymmetrized wavefunctions[62] will be needed to continue to explore such difficult issues, especially in the case of charged species.

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Supporting Information Available: Polarization energies calculated ab initio at the HF/CEP 4-31G(2d) level of theory using the Kitaura−Morokuma (KM) and restricted variational space (RVS) approaches; these energies are compared to those obtained from SIBFA. This material is available free of charge via the Internet at http://pubs.acs.org.

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