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Dielectric properties of liquid phase molecular clusters using the external field method: molecular dynamics study†

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We analyzed the dielectric properties of molecular liquids using the external field method with reaction field approximations. The applicability of this method to determine the dielectric properties of molecules with zero (1,4-dioxane) and non-zero (water and bio-molecular aqueous solutions) permanent dipole moment was studied. The relative static dielectric constant obtained using the external field method for polar and non-polar molecular liquids, including molecules with zero permanent dipole moment, agreed well with the experimental values presented in the literature. Our results indicate that the Debye relaxation time constants estimated from the non-equilibrium simulations using the external field method were accurate for molecules whose permanent dipole moments were less than 12 D.

Introduction

The dielectric properties of molecular clusters can be obtained using molecular dynamics (MD) simulations using either the fluctuation or applied external field methods. The fluctuation method uses the variation in the total dipole moment in the absence of an external field[1] whereas the external field method uses the polarization response to an externally applied electric field[2] to estimate the dielectric properties. The advantage of the external field method is that it is applicable in studying molecules with zero permanent dipole moment, where the fluctuation method cannot be applied.[2] In order to reduce computational complexity, reaction field approximation are utilised. In this approximation interactions of distant molecules (>cut-off radius) are neglected and replaced by a continuum approximated by a dielectric constant.[3] The reaction field approximation has the added benefit in that it overcomes the density fluctuations near the boundary of a small number of molecules in three dimension computer simulations.[4] Unfortunately the dielectric constant of the continuum is unknown and there is no consensus in setting the dielectric constant of the continuum. In the literature, the dielectric constant of the continuum has been set to one, infinity or the relative static dielectric constant of the

material. The quality of the results can vary dramatically depending on the value chosen. In our previous study,[5] we presented a unified method to calculate dielectric properties over frequency of a bio-molecular aqueous solution, without requiring prior knowledge of its static dielectric constant, using fluctuation method and reaction field approximations.[5] In this paper, we use the method in ref. 5 to obtain the dielectric constant of the continuum and apply it to the external field method.

To determine whether the external field method is broadly applicable, we investigate the dipole moment variation of molecular liquids with zero (1,4-dioxane) and non-zero (water and bio-molecular aqueous solutions) permanent dipole moment in a static homogeneous external electric field of strength ranging between 0.5–10 kcal (mol Å e)$^{-1}$ (0.2167 × 10^7–4.334 × 10^7 V cm^{-1}). In theory section, the external field method to compute the dielectric properties is presented. The proposed theoretical extension of the method (Method section) involves the following steps: (i) The dielectric constant of the bulk material in the reactive field outside the cut-off sphere is obtained using the fluctuation method as proposed in ref. 5. (ii) The static homogeneous external electric field is varied from 0.5–10 kcal (mol Å e)$^{-1}$ (0.2167 × 10^7–4.334 × 10^7 V cm^{-1}) and the dipole moment fluctuations are obtained for each field strength, noting that the dipole moment in the direction of electric field varies linearly and eventually saturates. (iii) The static dielectric constant is obtained from the linear region of the dipole moment response and the relaxation time constant is obtained from non-equilibrium MD simulations. This technique provides a complete method to calculate the dielectric properties of molecular liquids of both zero and non-zero permanent dipole

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moments. In the results and discussion sections we determine the static dielectric constant and Debye relaxation time constant of 1,4-dioxane, water and aqueous solutions of biological materials such as amino acids (L-alanine, L-glycine), and neurotransmitters [γ-aminobutyric acid (GABA)] from the external field method presented in this paper and compare with the results obtained from the fluctuation method and experimental values presented in the literature. We show that our extended external field method achieves good performance for polar and non-polar molecular liquids including for molecules with zero permanent dipole moment.

Theory

Static dielectric constant

The average dipole moment along the direction of applied field, $\langle M_z \rangle$, linearly increases with small field strengths, and deviates from this linear relationship for large field strengths. Static dielectric constant determination using the external field method requires the data from the linear response region of $\langle M_z \rangle$. The static dielectric constant can be obtained from the external field method[6] using the polarization response of the system, *i.e.* the average dipole moment along the direction of applied field per unit volume. This can then be related to the dielectric constant,[6]

$$\frac{4\pi}{\varepsilon_a} \frac{\langle M_z \rangle}{V E_{\text{ext}}} = \frac{(\varepsilon_0 - 1)(2\varepsilon_{\text{RF}} + 1)}{(2\varepsilon_{\text{RF}} + \varepsilon_0)} \quad (1)$$

where, $\langle M_z \rangle$ is the average dipole moment of the system along the direction of the applied field E_{ext}, ε_a is the permittivity of vacuum, ε_0 is the static dielectric constant, V is the volume of the system and ε_{RF} is the dielectric constant of the continuum. The ratio of $\langle M_z \rangle / E_{\text{ext}}$ is obtained from the slope of the linear region of variation of $\langle M_z \rangle$ with applied external field strength (see ESI†).

Debye relaxation time constant

The Debye relaxation time constant can be calculated from non-equilibrium MD simulations when an external field is applied.[2] The dipole moment along the field's direction ($\langle M_z \rangle$) can be related to the Debye relaxation time by:[2]

$$\tau_D = \tau_m \frac{[\varepsilon_0 + 2 + C_{\text{rf}}(\varepsilon_0 - 1)]}{3}. \quad (2)$$

The relaxation time τ_m can be obtained from the average dipole moment in z direction upon applying an external field at time t_0 [$\langle M_z(t) \rangle_{t_0}$] and the dipole moment at steady state [$\langle M_z(t = \infty) \rangle_t$] as

$$\langle M_z(t) \rangle_{t_0} = \langle M_z(t = \infty) \rangle_t \left[1 - \exp\left(-\frac{t - t_0}{\tau_m} \right) \right].$$

The parameter C_{rf} can be calculated from

$$C_{\text{rf}} = \frac{(2\varepsilon_0 - 2\varepsilon_{\text{RF}})(1 + \kappa R_c) - \varepsilon_{\text{RF}}(\kappa R_c)^2}{(\varepsilon_0 + 2\varepsilon_{\text{RF}})(1 + \kappa R_c) + \varepsilon_{\text{RF}}(\kappa R_c)^2},$$

where τ_D is the Debye relaxation time, κ is the Debye screening length, and R_c is the cut-off radius.[2]

Methods

Permanent dipole moments from DFT

The calculated permanent dipole moments of single molecules are shown in Table 2. These were obtained from density functional theory (DFT) using deMon2k.[10] The structure of molecules was obtained using the VEGA ZZ software.[7] In DFT calculations, VWN exchange–correlation (Local Vosko, Wilk and Nusair correlation) functional[24] and auxiliary function density (A2 Auxis set) for the calculation of the exchange–correlation energy and matrix elements of the exchange–correlation potential were used. The dipole moment calculations were performed using a double zeta valence polarization (DZVP) basis set independent of whether the energy calculations were specified using auxiliary density.

External field method

The extension of the electric field method proposed in this paper is based on the method described in ref. 5. The molecular clusters were created using VEGA ZZ software[7] and a summary of the number of molecules in the clusters and the lengths of the cubic cells are presented in Table 1. The molecular structures of amino acids and neurotransmitters shown in ref. 5 were used in the aqueous solution models. The CHARMM force fields and Gasteiger–Marsili charges were assigned using VEGA ZZ. The trajectories were generated using NAMD software.[8] Periodic boundary conditions were used and the systems were simulated in NVT (constant number of molecules, volume and temperature) ensembles. The temperature was maintained at 300 K. The dielectric constant used in the simulation was set to the dielectric constant of the continuum (ε_{RF}), obtained using the fluctuation method as described in ref. 5. Other simulation parameters such as cut-off radius and switchdist were defined as in ref. 5.

MD simulations to obtain static dielectric constant and Debye relaxation time constant

The static homogeneous external electric field of strength 0.5–10 kcal (mol Å e)$^{-1}$ (0.2167×10^7–4.334×10^7 V cm^{-1}) was applied in z direction. The external field was applied by enabling eFieldOn parameter and defining the electric field vector using eField parameter in NAMD simulations. For each external electric field strength, an equilibration simulation of 100 ps (non-equilibrium MD simulation) and subsequently, a 1 ns production run was performed, by applying harmonic constraints. The occupancy column of the PDB file was set to 1 to implement the harmonic constraint force constant. The dipole moment of the systems was obtained using VMD software[9] and the equilibrium properties were then averaged over

Table 1 Summary of the molecular structures used for the simulations

Material	N_{mat} (mol)	N_{wat} (mol)	L (Å)
1,4-Dioxane	125		25.48
Water		240	20.8
Glycine 1 M	4	212	19.98
Alanine 1 M	4	208	19.09
GABA 1 M	4	222	21.28

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45 blocks of 20 ps, for a total of 900 ps. The static dielectric constant and relaxation time were obtained from the external field method [eqn (1) and (2)]. In the results section, the computational results based on external field method are compared to the values obtained from the fluctuation method[5] and experimental values.

Results

In this paper, the applicability of the extended external field method to estimate dielectric properties of polar and non-polar molecular liquids with zero and non-zero permanent dipole moment is studied by comparing computed values to measured experimental results. As illustrated in Table 2, the permanent dipole moment values obtained in this paper compare favourably with the theoretical values and experimental values presented in the literature. The non-zero dipole moment of 1,4-dioxane obtained from DFT is due to the lower symmetry of its structure.[26] In the following, dielectric properties of 1,4-dioxane, which has a zero permanent dipole moment, water and aqueous solutions of amino acids and neurotransmitters as determined by the extended electric field method are presented.

Dielectric constant at infinite frequency, ε_∞

The MD simulations presented in this study used non-polarizable force fields ($\varepsilon_\infty = 1$). Thus the dielectric constant at infinite frequency, ε_∞, was determined from the polarizability value calculated using DFT.[5] The values for ε_∞, static dielectric constant ε_0, and the Debye relaxation time constant τ_D can be incorporated into the Debye model[27] to obtain the frequency dependent complex permittivity.[5] The dielectric constant at infinite frequency of pure 1,4-dioxane was determined as 2.025 from DFT, as per ref. 5. This is within approximately 1% of the experimental value of 2.01.[19] The value of ε_∞ for water was set to 1.37 as obtained in ref. 5 and that for bio-molecular aqueous solutions were assumed to be the same as for water.

Relative static dielectric constant, ε_0

The variation in average dipole moment of molecular liquids in the direction of the external electric field (z direction), $\langle M_z \rangle$, versus field strength is shown in Fig. 1–3. For 1,4-dioxane and water, the dipole moment $\langle M_z \rangle$ linearly increased with the field up to 10 kcal (mol Å e)$^{-1}$ and 1.5 kcal (mol Å e)$^{-1}$, respectively. The average dipole moments of glycine 1 M (Gly 1 M), alanine 1 M (Ala 1 M) and GABA 1 M along z direction linearly increased with the field up to 1.0 kcal (mol Å e)$^{-1}$, and then eventually
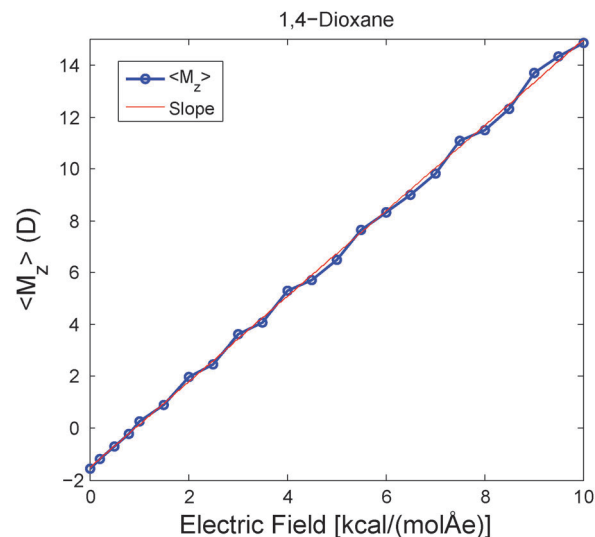

Fig. 1 Variation of the average dipole moment of 1,4-dioxane in the direction of electric field, $\langle M_z \rangle$, with the electric field strength.
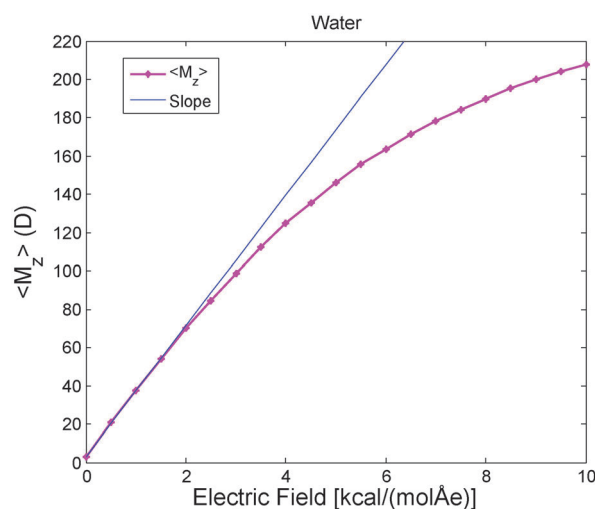

Fig. 2 Variation of the average dipole moment of water in the direction of electric field, $\langle M_z \rangle$, with the electric field strength.

saturated at larger field strengths. The relative static dielectric constants were obtained from the linear region of variation of $\langle M_z \rangle$ with the field to avoid dielectric saturation.

The relative static dielectric constants were calculated from the slope of Fig. 1–3 by substituting the ratio of $\langle M_z \rangle / E_{ext}$ (see ESI†) in eqn (1). The relative static dielectric constants of 1,4-dioxane, water and bio-molecular aqueous solutions calculated from the external field method agree well with the experimental values presented in the literature and are shown in Table 3.

Debye relaxation time constant, τ_D

The Debye relaxation time constant of 1,4-dioxane, calculated from the initial 100 ps of non-equilibrium simulation using eqn (2) varied from 0.08 ps to 2.2 ps in 0.2–3.5 kcal (mol Å e)$^{-1}$ range (Fig. 4). The maximum relaxation time of 2.2 ps was comparable with the experimental values (0.3–1 ps). As shown

Table 2 Permanent dipole moments of molecules obtained from DFT compared with the theoretical and the experimental values presented in the literature

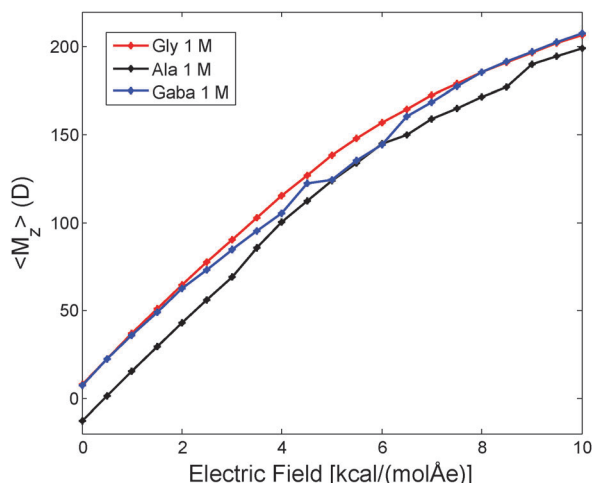| Molecule	This study (D)	Theoretical study (D)	Experimental (D)
1,4-Dioxane	0.018	0.00[11]	0.06[12], 0.45[25]
Water	2.185	2.063–2.292[13]	2.643[13]
Glycine	12.31	12.196[14]	11.6–15.7[15]
Alanine	13.696	11.561[14]	13.3[16]
GABA	22.11	20.59[17]	22[18]

Fig. 3 Variation of the average dipole moment of Gly 1 M, Ala 1 M and GABA 1 M in the direction of electric field with the electric field strength.
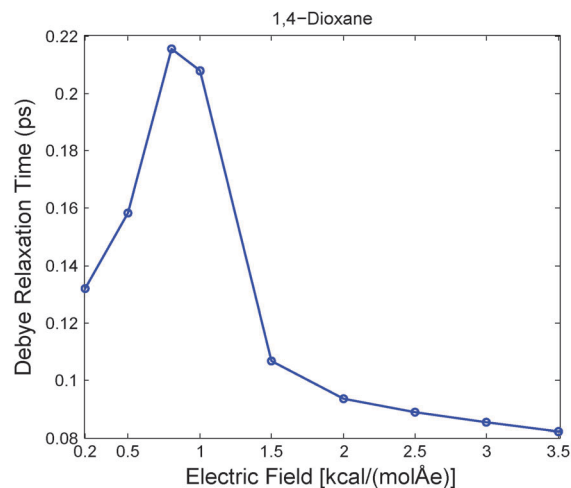

Fig. 4 Variation in Debye relaxation time of 1,4-dioxane calculated from the non-equilibrium MD simulations using eqn (2).

in Fig. 5 and 6, the Debye relaxation times of water, Gly 1 M, Ala 1 M and GABA 1 M vary in 5.2–8.15 ps, 12–20.36 ps, 12–29.16 ps and 17.83–24.56 ps ranges, respectively, for the studied electric field strengths of 0.5–10 kcal (mol Å e)$^{-1}$. The maximum relaxation times agree with the experimental values presented in the literature except for GABA 1 M (Table 3).

Discussion

In this paper, the dielectric properties of polar and non-polar molecular liquids with different permanent dipole moments were computed using the extended external field method. The average dipole moment along the direction of electric field ($\langle M_z \rangle$) linearly increased with electric field strength and saturated at larger field strengths. The molecular liquids with non-zero permanent dipole moment (water and bio-molecular aqueous solutions) deviated from the linear relationship at lower electric field strengths compared to 1,4-dioxane that has a zero permanent dipole moment. For small electric field strengths, the average dipole moment of 1,4-dioxane and Ala 1 M along the direction of electric field ($\langle M_z \rangle$) was negative indicating that $\langle M_z \rangle$ and electric field were in opposite directions.

The relative static dielectric constants of 1,4-dioxane, water and bio-molecular aqueous solutions obtained from the external field method, agree with values obtained from the fluctuation method and experimental values presented in the literature.
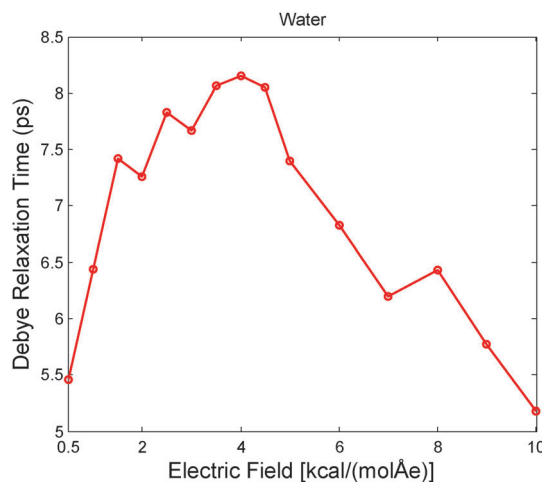

Fig. 5 Variation in Debye relaxation time of water calculated from the non-equilibrium MD simulations using eqn (2).

In our simulations we used the dielectric constant of the continuum obtained as in ref. 5, rather than the static permittivity of the materials. Our results validated the method proposed in ref. 5 for obtaining the dielectric constant of the continuum without requiring prior knowledge of the materials' permittivity.

The accuracy of the estimated relaxation time constant varied depending on the applied electric field strength.

Table 3 Static dielectric constant and Debye relaxation time constant obtained from the external field method compared with the fluctuation method and the experimental values

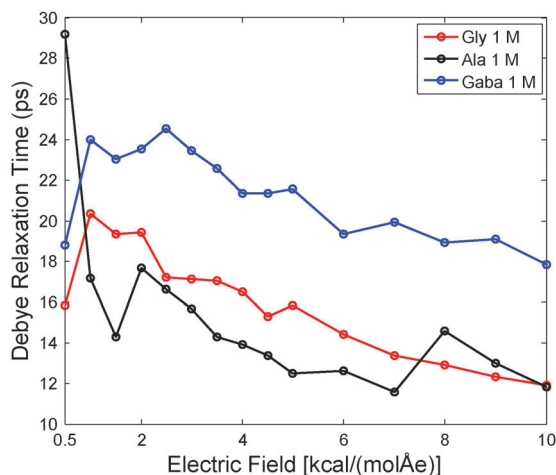| Material	External field method			Fluctuation method[5]		Experimental	
	ε_0	τ_D (ps) at 0.5 kcal (mol Å e)$^{-1}$	τ_D (ps) at 1 kcal (mol Å e)$^{-1}$	ε_0	τ_D (ps)	ε_0	τ_D (ps)
1,4-Dioxane	2.45	0.22	0.21	2.41	3	2.25[19]	0.3–1[12]
Water	81.76	5.45	6.44	81.2 ± 3	8.8 ± 0.6	78.4	8.23[20]
Glycine 1 M	98.35	15.82	20.36	97.36 ± 3.7	20.81 ± 2.6	100.44	22.7[21]
Alanine 1 M	91.31	29.16	17.18	89.52 ± 2.5	33 ± 2.4	103.54	30.87[22]
GABA 1 M	132.21	18.79	24.00	120.72 ± 1.7	126.55 ± 2.6	128	117[23]

Fig. 6 Variation in relaxation time of Gly 1 M, Ala 1 M and GABA 1 M calculated from the non-equilibrium MD simulations using eqn (2).

This may be because dissimilar field strengths perturb the molecules in various ways, causing the molecular dipoles to return to their equilibrium state differently. Fig. 4–6 show that in the given electric field range, the maximum value of the Debye relaxation time constant agrees well with the experimental values presented in the literature. The Debye relaxation time constants obtained from eqn (2) using non-equilibrium MD simulation provided reasonable estimation except for GABA 1 M. Thus for the tested compounds, the relaxation times were accurately determined using this method for molecules with permanent dipole moments in the range of 0.018–12 D. This limitation is due to external electric fields causing structural changes to polar molecules with large permanent dipole moments (see ESI†). In contrast, the Debye relaxation time constants obtained using the fluctuation method agreed well with experimental values, except for 1,4-dioxane. This may be because in the absence of an external field, the molecules with zero permanent dipole moment are randomly oriented and require a larger relaxation time to equilibrate. Thus, in computing Debye relaxation time constants the external field method is more accurate for molecular liquids with zero permanent dipole moments whereas the fluctuation method yields better performance for molecules with large permanent dipole moments.

In future work, the effect of molecular cluster size and simulation time on the estimated dielectric properties using the proposed method in ref. 5 and this paper will be studied.

Conclusions

A method based on molecular dynamics simulations is presented to determine dielectric properties of materials under external electric fields without prior knowledge of their static dielectric constant, using reaction field approximations. The external field method to obtain the relative static dielectric constant is applicable for polar and non-polar molecules with zero and non-zero permanent dipole moments. The non-equilibrium MD simulation to obtain the Debye relaxation time constant is valid for molecules with permanent dipole moments less than 12 D.

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