Extending electrostatics of dielectric spheres to arbitrary charge distributions with applications to biosystems

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A previously developed classical model of electrostatic interactions, based on a formalism of dielectric spheres, which has been found to have surprising accuracy for S state atoms, is extended by allowing higher order moments of the intrinsic charge distribution. Two methods to introduce the charge distribution (point moments at the center vs surface charge) are shown to be equivalent and are compared with another common model for polarizable atoms that utilizes polarizable point dipoles. Unlike the polarizable point dipole model, the polarizable sphere models do not suffer from a divergence at small separation of atoms and are easily generalized to higher multipoles.

I. INTRODUCTION

While electrostatic interactions are generally an important aspect of physics at the molecular level, they are particularly crucial for biomolecular systems, which are comprised of many charged molecules embedded in the polar solvent water. It is not practical to apply precise quantum methods to even a moderately large biomolecular system. Consequently, there is much interest in classical approaches [1], which are sometimes categorized according to how they handle the water in which the molecules of interest are embedded. Explicit solvent methods treat each water molecule at the level of atomic detail, while implicit solvent methods replace the individual water molecules with some type of smoothed out version. The implicit solvent methods [2, 3] are in principle less computationally intensive and larger systems can be investigated. However, their application is limited to systems where fine details of solute-solvent interactions do not play a large role.

Explicit solvent methods, such as TIPnP [4], allow description of biomolecular systems at much finer detail and with a more predictable level of accuracy, but the absence of mutual polarization of molecules can be a critical deficiency in some situations.

In order to overcome the lack of mutual response between molecules, polarizable force fields, such as AMOEBA [5], were developed. They introduced variable dipole moments at various locations within the system (often at each atom) that adjust self-consistently to the local electric field [5]. The inducible dipole model is a significant step forward in the quest of designing a physically sensible and yet computationally efficient model of electrostatic interactions at atomic scale. One has to be careful, however, since the inducible dipoles can amplify each other to unphysically large magnitudes and eventually diverge if they are too close to each other [4]. Ad hoc damping terms need to be introduced [6] to suppress such divergences.

We have earlier suggested an alternative classical model of dielectric spheres [7] and used it to approximate atoms and molecules by dielectric polarizable bodies [8]. This model can incorporate the best of two worlds. If the bodies are embedded in a dielectric medium, the model becomes an implicit solvent model and the bodies represent the biomolecules while the solution is modeled by the dielectric continuum. If, however, the bodies are considered to be in the vacuum, the model becomes an explicit solvent model in which biomolecules and water molecules are modeled explicitly, with their own parameters. The surface charge method (SCM) properly calculates polarization effects while avoiding the problem of potential divergence faced by the inducible dipole model. Another advantage of the model is that higher order multipoles are naturally included in the dielectric response formalism.

This model was previously used to investigate the limits of applicability of a classical formalism to accurate description of interactions between atomic-sized objects [8]. It was found that the dielectric spheres model is surprisingly accurate down to distances where chemical bonds start to form. The formalism introduced in [7] allows one to find a solution with arbitrary accuracy for an arbitrary number of interacting dielectric spheres with point charges at their

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centers. The limitation of the formalism, however, was that it represented only objects with no permanent dipole or higher order moments, such as atoms in S states.

In this work we present an extension of this previously developed formalism which allows one to consider arbitrary configurations of arbitrary number of dielectric spheres now with an arbitrary charge distribution within each sphere. This formalism is readily applicable to, for example, studying limits of applicability of classical approach to interactions between atoms in P, D, ... non-spherically symmetric states. We also demonstrate that the dielectric spheres approach is less susceptible to unphysical amplification of the induced dipole moments.

II. POLARIZABLE SPHERES MODEL

In the previous article [7] the electrostatic problem of an arbitrary arrangement of an arbitrary number of dielectric spheres, each with a point charge at its center, was solved. The example of two charged dielectric spheres was also explicitly worked out. One of the main results of the article was the boundary condition for the scaled multipole components Q_{lm} of induced charge on the surfaces of an arbitrary arrangement of spheres:

$$\frac{\sqrt{4\pi}(\epsilon_k l + \epsilon_o(l+1))}{(2l+1)} Q_{lm}^k -$$

$$\sum_{\substack{l'>0,m',m'' \\ i\neq k}} \frac{(\epsilon_o - \epsilon_k)\sqrt{4\pi}(-)^{l-m''}l(l+l')!t_{ik}^{l'}t_{ki}^{l+1}\mathcal{D}_{m''m'}^{(l')}(R_{i\rightarrow k})\mathcal{D}_{mm''}^{(l)}(R_{i\rightarrow k}^{-1})}{((2l+1)(2l'+1)(l-m'')!(l'-m'')!(l+m'')!(l'+m'')!)^{1/2}} Q_{l'm'}^i =$$

$$\frac{(\epsilon_o - \epsilon_k)}{\epsilon_o} \sum_{i\neq k} \frac{4\pi q_i l t_{ki}^{l+1}}{(2l+1)} Y_{lm}^*(\vartheta_{ik}, \varphi_{ik}) \tag{1}$$

where ϵ_o is the solvent dielectric constant, ϵ_k is the dielectric constant of the kth sphere, $t_{ik} \equiv a_i/L_{ik}$ (a_i is the radius of the ith sphere and L_{ik} is the center to center separation of spheres i and k), $\mathcal{D}_{mm'}^{(l)}$ is the Wigner rotation function, $R_{i\rightarrow k}$ is the rotation that takes the local z axis pointing from sphere i to sphere k to the global z axis, q_i is the charge at the center of the ith sphere, and $(\vartheta_{ik}, \varphi_{ik})$ are the spherical angles of $\mathbf{n}_{ik}$, pointing from the center of sphere k to the center of sphere i, and Y_{lm} are the spherical harmonic functions. Note that here we incorporated the constant and rotationally invariant $l' = 0$ monopole term into the term on the right hand side which now is proportional to q_i/ϵ_o instead of q_i/ϵ_i. Hence the sum over l' starts now at 1 as opposed to 0 in the original work [7].

The variables Q_{lm} are just the scaled coefficients σ_{lm} in the standard expansion of the induced surface charge:

$$\sigma = \sum_{lm} \sqrt{4\pi}\sigma_{lm}Y_{lm}, \tag{2}$$

$Q_{lm} = 4\pi a^2 \sigma_{lm}$. The factor $\sqrt{4\pi}$ serves to make σ_{00} the effective net surface charge density.

The boundary condition (1) is a system of linear equations that allows one to find all the multipole components of the induced surface charges and hence the other physical properties of the system, such as energy.

In the present work we extend the formalism of Ref. [7] to include an arbitrary fixed charge distribution within each sphere. The charge distribution on each sphere can be represented either as a set of point multipoles at its center or as a properly chosen surface charge distribution. As we will show, these two routes lead to completely equivalent results.

A. Point Multipoles at Center of Dielectric Spheres

Let there be a charge distribution completely within each sphere. For simplicity, if there is a monopole we treat it separately as in the previous formalism. We ignore the details of the charge distribution and represent it by a set of multipoles q_{lm} calculated with respect to the center of the sphere.

The multipoles will contribute two additional terms to the boundary condition: one term for the multipoles within the sphere where the boundary condition is being applied, and another term for the multipoles of all the other spheres. We now derive these in turn.

Recall the customary multipole expansion

$$\Phi = \int \frac{\rho(\vec{r}')}{|\vec{r} - \vec{r}'|}d\vec{r}' = \sum_{lm} \frac{4\pi}{2l+1}q_{lm}Y_{lm}(\theta, \phi)r^{-l-1},$$

where

$$q_{lm} = \int \rho(\vec{r}')r'^l Y_{lm}^*(\theta', \phi')r'^2 \sin\theta' \, \mathrm{d}r' \, \mathrm{d}\phi' \, \mathrm{d}\theta'$$

The expansion is valid for points outside the charge distribution that generates the multipoles, in this case, points outside the sphere that represents the atom. For the boundary condition we need the normal derivative evaluated at the surface:

$$\left.\frac{\partial \Phi}{\partial r}\right|_{r=a} = \sum_{lm} \frac{4\pi q_{lm} Y_{lm}(\theta, \phi)(-l-1)}{(2l+1)a^{l+2}}$$

This term should be multiplied by $1/\epsilon$ because the charges that comprise the multipoles each attracts induced charge that screens it by this factor. The resulting expression provides an additional source term on the right hand side of the boundary condition (Eq. 1):

$$\frac{(\epsilon_k - \epsilon_o)4\pi q_{lm}^k(l+1)}{\epsilon_k(2l+1)a_k^l}$$

Now we consider the effect on the boundary condition of the multipoles within the other spheres. In fact, this has been already derived in [7] in order to handle the effect of the surface charge at the other spheres. One can simply add an additional term for each sphere that is the same as the term with the Wigner rotation functions except with the replacement $Q_{lm}^k \to \overline{Q}_{lm}^k/\epsilon_k$ where $\overline{Q}_{lm}^k = \sqrt{4\pi}q_{lm}^k/a_k^l$. Essentially, we have employed a specific charge distribution that has the required multipole distribution. And since it does indeed have the required multipoles, it must have identical effect at a distance. Note that the $\overline{Q}_{lm}^k$ are known sources whereas the Q_{lm}^k remain the unknown variables that we are seeking as a solution of the set of linear equations.

With the additional terms just described, the boundary condition becomes

$$\frac{\sqrt{4\pi}(\epsilon_k l + \epsilon_o(l+1))}{(2l+1)}Q_{lm}^k \, -$$

$$\sum_{\substack{l'>0,m',m'' \\ i\neq k}} \frac{(\epsilon_o - \epsilon_k)\sqrt{4\pi}(-)^{l-m''}l(l+l')!t_{ik}^{l'}t_{ki}^{l+1}\mathcal{D}_{m''m'}^{(l')}(R_{i\to k})\mathcal{D}_{mm''}^{(l)}(R_{i\to k}^{-1})}{((2l+1)(2l'+1)(l-m'')!(l'-m'')!(l+m'')!(l'+m'')!)^{1/2}}Q_{l'm'}^i \, =$$

$$\frac{(\epsilon_o - \epsilon_k)}{\epsilon_o}\sum_{i\neq k}\frac{4\pi q_i l t_{ki}^{l+1}}{(2l+1)}Y_{lm}^*(\vartheta_{ik}, \varphi_{ik}) + \frac{(\epsilon_k - \epsilon_o)\sqrt{4\pi}\,\overline{Q}_{lm}^k(l+1)}{(2l+1)\epsilon_k} \, +$$

$$\sum_{\substack{l'>0,m',m'' \\ i\neq k}} \frac{(\epsilon_o - \epsilon_k)\sqrt{4\pi}(-)^{l-m''}l(l+l')!t_{ik}^{l'}t_{ki}^{l+1}\mathcal{D}_{m''m'}^{(l')}(R_{i\to k})\mathcal{D}_{mm''}^{(l)}(R_{i\to k}^{-1})}{((2l+1)(2l'+1)(l-m'')!(l'-m'')!(l+m'')!(l'+m'')!)^{1/2}\epsilon_i}\overline{Q}_{l'm'}^i \tag{3}$$

B.   Multipoles Charge Distribution on the Surface of the Spheres

Now, instead of placing arbitrary point multiples at the center, we place an equivalent fixed surface charge distribution on the surface of the sphere. The fixed (as opposed to induced) surface charge quantities will be denoted by an overbar, as in the previous subsection.

In order to derive a representation of a given arbitrary multipole distribution q_{lm} on the surface of a sphere, substitute the expansion

$$\rho(\vec{r}') = \delta(r' - a)\sum_{l'm'}\sqrt{4\pi}\overline{\sigma}_{l'm'}Y_{l'm'}(\theta', \phi')$$

into the definition of q_{lm} to find:

$$q_{lm} = \sqrt{4\pi}\overline{\sigma}_{lm}a^{l+2} \tag{4}$$

Write this using $\overline{Q}_{lm}$ instead of $\overline{\sigma}_{lm}$ and solve for $\overline{Q}_{lm}$:

$$\overline{Q}_{lm} = \frac{\sqrt{4\pi}q_{lm}}{a^l}$$

As before, this expression may be used to form a boundary condition term that represents the effects of an internal charge distribution of the sphere away in the region outside the sphere.

The procedure for applying the boundary condition is now slightly different because we now have fixed charge at the surface where we are applying the boundary condition. We must therefore use the more general expression:

$$-\epsilon_{\text{ex}} \left.\frac{\partial \Phi_{\text{ex}}}{\partial r}\right|_{r=a} + \epsilon_{\text{in}} \left.\frac{\partial \Phi_{\text{in}}}{\partial r}\right|_{r=a} = 4\pi\sigma_{\text{f}}$$

where, according to standard convention, we use the outward normal. The only term in the boundary condition at the surface of sphere k that is different is due to the potential due to the fixed surface charge $\overline{Q}_{lm}^k$ that we now attribute to sphere k in lieu of the set of multipole moments q_{lm}^k. The potential due to fixed surface multipole at sphere k is

$$\Phi = \sum_{lm} \frac{\sqrt{4\pi}\, \overline{Q}_{lm}^k r_<^l Y_{lm}(\theta,\phi)}{(2l+1)r_>^{l+1}}$$

On the outside we have $r_< = a_k, r_> = r$, and on the inside we have $r_< = r, r_> = a_k$. Therefore

$$-\epsilon_o \left.\frac{\partial \Phi_{out}}{\partial r}\right|_{r=a_k} + \epsilon_k \left.\frac{\partial \Phi_{in}}{\partial r}\right|_{r=a_k} = \sum_{lm} \frac{\sqrt{4\pi}\, \overline{Q}_{lm}^k (\epsilon_o(l+1) + \epsilon_k l) Y_{lm}(\theta,\phi)}{(2l+1)a_k^2}$$

In terms of $\overline{Q}_{lm}$, $4\pi\sigma_{\text{f}}$ is

$$4\pi\sigma_{\text{f}} = \sqrt{4\pi}\, \overline{Q}_{lm} Y_{lm}/a^2.$$

The procedure for obtaining the boundary condition in [7] involved multiplying each term by a_k^2 and dropping the sum and the spherical harmonics Y_{lm} because of the independence and completeness of the spherical harmonics. The boundary condition becomes

$$\frac{\sqrt{4\pi}(\epsilon_k l + \epsilon_o(l+1))}{(2l+1)} Q_{lm}^k -$$

$$\sum_{\substack{l',m',m'' \\ i\neq k}} \frac{(\epsilon_o - \epsilon_k)\sqrt{4\pi}(-)^{l-m''} l(l+l')! t_{ik}^{l'} t_{ki}^{l+1} \mathcal{D}_{m''m'}^{(l')}(R_{i\to k}) \mathcal{D}_{mm''}^{(l)}(R_{i\to k}^{-1})}{((2l+1)(2l'+1)(l-m'')!(l'-m'')!(l+m'')!(l'+m'')!)^{1/2}} Q_{l'm'}^i =$$

$$\frac{(\epsilon_o - \epsilon_k)}{\epsilon_o} \sum_{i\neq k} \frac{4\pi q_i l t_{ki}^{l+1}}{(2l+1)} Y_{lm}^*(\vartheta_{ik}, \varphi_{ik}) - \frac{\sqrt{4\pi}(\epsilon_k l + \epsilon_o(l+1))}{(2l+1)} \overline{Q}_{lm}^k + \sqrt{4\pi}\, \overline{Q}_{lm}^k +$$

$$\sum_{\substack{l',m',m'' \\ i\neq k}} \frac{(\epsilon_o - \epsilon_k)\sqrt{4\pi}(-)^{l-m''} l(l+l')! t_{ik}^{l'} t_{ki}^{l+1} \mathcal{D}_{m''m'}^{(l')}(R_{i\to k}) \mathcal{D}_{mm''}^{(l)}(R_{i\to k}^{-1})}{((2l+1)(2l'+1)(l-m'')!(l'-m'')!(l+m'')!(l'+m'')!)^{1/2}} \overline{Q}_{l'm'}^i \tag{5}$$

C. Equivalence of the Sphere Models

In the previous two subsections, we have found modifications of the boundary condition (1) for the sphere model from [7] for two methods of incorporating a fixed multipole distribution at each sphere. For the point multipoles, the new boundary condition (3) contains a $\overline{Q}_{lm}^k$ term from the sphere under consideration and a $\overline{Q}^i$ term for each other sphere. The two terms in Eq. (3) with Wigner rotation functions are identical except for the identity of the Q variable. Combining these terms allows us to rewrite the boundary condition in terms of a new variable $\breve{Q}_{lm}^k = Q_{lm}^k + \overline{Q}_{lm}^k/\epsilon_k$. The $\overline{Q}_{lm}^k$ moments correspond to the fixed multipole moments and are scaled by a factor of $1/\epsilon_k$ to account for the direct screening of the charges within the sphere from which the fixed multipole moments are constructed. The Q_{lm}^k moments are the induced surface charge. Therefore the new variables $\breve{Q}_{lm}^k$ represent the total effective charge distribution of sphere k as seen by an observer outside of the sphere. Thus for point multipoles the boundary condition

becomes

$$\frac{\sqrt{4\pi}(\epsilon_k l + \epsilon_o(l+1))}{(2l+1)}\breve{Q}_{lm}^k -$$

$$\sum_{\substack{l'>0,m',m'' \\ i\neq k}} \frac{(\epsilon_o - \epsilon_k)\sqrt{4\pi}(-)^{l-m''}l(l+l')!t_{ik}^{l'}t_{ki}^{l+1}\mathcal{D}_{m''m'}^{(l')}(R_{i\to k})\mathcal{D}_{mm''}^{(l)}(R_{i\to k}^{-1})}{((2l+1)(2l'+1)(l-m'')!(l'-m'')!(l+m'')!(l'+m'')!)^{1/2}}\breve{Q}_{l'm'}^i =$$

$$\frac{(\epsilon_o - \epsilon_k)}{\epsilon_o}\sum_{i\neq k}\frac{4\pi q_i l t_{ki}^{l+1}}{(2l+1)}Y_{lm}^*(\vartheta_{ik},\varphi_{ik}) + \sqrt{4\pi}\overline{Q}_{lm}^k \qquad (6)$$

For surface multipoles, for sphere k there is an additional 'diagonal' term and again a $\overline{Q}_{lm}^i$ term for each other sphere. In this case, the total effective charge distribution is now $\breve{Q}_{lm}^k = Q_{lm}^k + \overline{Q}_{lm}^k$. The $\overline{Q}_{lm}^k$ moments still correspond to the fixed multipole moments imposed on the system. However, the direct screening will in this case be captured by the induced moments Q_{lm}^k. Consequently, the variables $\breve{Q}_{lm}^k$ still represent the total effective charge distribution of sphere k as seen by an observer outside of the sphere. If we now similarly rewrite the boundary condition in Eq. (5) in terms of $\breve{Q}_{lm}^k$, we arrive once again at Eq. (6), exactly the same equation as before.

Thus, the two methods of incorporating a fixed multipole distribution at each sphere are completely equivalent. Since the form of the two boundary conditions is exactly the same when rewritten in terms of $\breve{Q}_{lm}^k$, it follows that the solutions for $\breve{Q}_{lm}^k$ must be the same. Furthermore, in each case $\breve{Q}_{lm}^k$ represents the net charge distribution as seen by an external observer so the physical properites of the systems, including their energy, should be identical.

D. Interaction Energy for the Sphere Models

The energy of a multipole distribution in a field is usually written in terms of the Cartesian moments [9]:

$$U = \frac{1}{2}\int \rho_{\mathrm{f}}(\vec{r})\Phi(\vec{r})\,\mathrm{d}\vec{r}$$

$$= \frac{1}{2}\sum_k q_k\Phi|_k - \frac{1}{2}\sum_k \vec{d}_k \cdot \vec{E}|_k - \frac{1}{12}\sum_k\sum_{i,j}[\mathcal{Q}_k]_{ij}\left.\frac{\partial E_i}{\partial x_j}\right|_k + \dots \qquad (7)$$

where $\vec{d}_k$ is the dipole of the atom k in Cartesian coordinates and $[\mathcal{Q}_k]_{ij}$ are the Cartesian components of the traceless quadrupole moment of atom k (not to be confused with the components of the surface charge Q_{ij}^k). This is a generalization of the energy expression in [7], where only the the first term was present. The potential Φ refers to the total potential at the location of the multipole distribution, $\Phi = \Phi_k + \sum_i \breve{\Phi}_i$. The potential near the center of sphere k due to the induced surface charge on sphere k is

$$\Phi_k = \frac{Q_{00}^k}{a_k} + \sum_{l\geq 1,m}\frac{\sqrt{4\pi}Q_{lm}^k}{(2l+1)a_k^{l+1}}r_k^l Y_{lm}(\theta_k,\phi_k)$$

where we have explicitly shown the $l=0$ term which does not explicity appear in the boundary condition equations because it was combined with the term for the fixed monopole for simplicity. Since this is evaluated at the center of the sphere ($r_k = 0$), only a single l term survives for each term of the multipole expansion. The potential near sphere k due to both the induced and fixed surface charge on sphere i is given by [7]

$$\breve{\Phi}_i = \frac{q_i}{\epsilon_o L_{ki}} + \sum_{l,m,l',m',m''}\frac{\sqrt{4\pi}(-)^{l-m''}(l+l')!t_{ik}^{l'}\mathcal{D}_{m''m'}^{(l')}(R_{i\to k})\mathcal{D}_{mm''}^{(l)}(R_{i\to k}^{-1})\breve{Q}_{l'm'}^i}{L_{ki}^{l+1}((2l+1)(2l'+1)(l-m'')!(l'-m'')!(l+m'')!(l'+m'')!)^{1/2}}r_k^l Y_{lm}(\theta_k,\phi_k)$$

where the components of the surface charge distibution are given by solving the boundary condition and again only a single l survives for each term of the multipole expansion.

Often one is interested in the interaction energy and the full energy above includes the self energy or solvation energy. The solvation energy for a sphere containing a general charge density with multipole moments q_{lm} with respect to the center of the sphere is the usual energy expression $1/2\int\rho_{\mathrm{f}}(\vec{r})\Phi(\vec{r})\,\mathrm{d}\vec{r}$ where the potential is given by

the solution of the boundary value problem for such an isolated sphere embedded in the ϵ_o medium with the given multipoles at the center:

$$\sum_{lm} \frac{4\pi(\epsilon - \epsilon_o)(l+1)q_{lm}}{(2l+1)\epsilon[\epsilon l + \epsilon_o(l+1)]a^{2l+1}} r^l Y_{lm}(\theta, \phi) \ \ \text{for } r < a$$

Consequently, the solvation energy for sphere k is

$$U_s^k = \sum_{lm} \frac{2\pi(\epsilon_k - \epsilon_o)(l+1)q_{lm}^k q_{lm}^{k\,*}}{(2l+1)\epsilon_k[\epsilon_k l + \epsilon_o(l+1)]a_k^{2l+1}}$$

For a monopole $q_{00}^k = q^k/\sqrt{4\pi}$ the $l = 0$ term survives and gives the Born energy. For a dipole $q_{10}^k = \sqrt{3/4\pi}d$ the $l = 1$ term survives and gives

$$\frac{(\epsilon_k - \epsilon_o)d^2}{\epsilon_k[\epsilon_k + 2\epsilon_o]a_k^3}$$

Similar expressions are easily obtained for higher multipoles. The interaction energy is $U_{\text{int}} = U - \sum_k U_s^k$.

III. DISCUSSION

A. Linear Chain of Inducible Dipoles

As mentioned in the Introduction, for a more accurate representation of biomolecular systems it is sometimes necessary to go beyond implicit solvent models and beyond explicit solvent methods in which water molecules are represented by a set of fixed partial charges. One way to do so is to use polarizable force fields, such as AMOEBA [5], where a inducible dipole is added to the characterization of each molecule or atom.

The inducible dipole model is an appealing framework, allowing one to account for mutual self-adjustments of charge densities within molecules in the presence of other bodies or electric fields. This model, however, does not have an intrinsic mechanism for limiting the magnitude of the induced moments. Thus, one should be careful not to enter the unphysical regime of unrestricted positive feedback when the induced moments amplify each other to unreasonably large magnitudes or even diverge.

Let us illustrate this potential problem using an example of two atoms, separated by vector $\vec{r}$, each with a fixed and an inducible dipoles. The solution for this toy system is well-known (e.g. [6]) and is characteristic of the physics captured in polarizable force fields. (When a large number of atoms is present, the linear system that determines the induced dipoles is usually solved for computational efficiency via an equivalent, self-consistent iterative procedure rather than by a direct approach.)

Let atom A with fixed dipole $\vec{d}_f$ be at point A and let atom B with the same fixed dipole $\vec{d}_f$ be at point B. In each atom, the electric field of the other atom induces an additional dipole, proportional to the local electric field $\vec{E}_{A(B)}$:

$$\vec{d}_{A(B)} = \alpha \vec{E}_{A(B)},$$

where for simplicity we assume that the atoms have same polarizability α. Recalling that the field of a dipole is

$$\vec{E}_{\text{dipole}} = \frac{3(\vec{d} \cdot \hat{r})\hat{r} - \vec{d}}{r^3},$$

the induced dipoles are given by

$$\vec{d}_A = \alpha \frac{3((\vec{d}_f + \vec{d}_B) \cdot \hat{r})\hat{r} - (\vec{d}_f + \vec{d}_B)}{r^3}$$

$$\vec{d}_B = \alpha \frac{3((\vec{d}_f + \vec{d}_A) \cdot \hat{r})\hat{r} - (\vec{d}_f + \vec{d}_A)}{r^3},$$

where $\hat{r} \equiv \vec{r}/r$. Substituting the expression for $\vec{d}_A$ into equation for $\vec{d}_B$, we can solve for $\vec{d}_B$:

$$\vec{d}_B = \left(\frac{\alpha}{r^3} \left[3(\vec{d}_f \cdot \hat{r})\hat{r} - \vec{d}_f \right] + \frac{\alpha^2}{r^6} \left[3(\vec{d}_f \cdot \hat{r})\hat{r} + \vec{d}_f \right] \right) \left[(1 - \frac{\alpha_B \alpha_A}{r^6})I - \frac{3\alpha_B \alpha_A}{r^6}\hat{r}\hat{r} \right]^{-1}$$

where I is the three dimensional identity operator and $\hat{r}\hat{r}$ is a dyad operator. Let the z axis lie along the line joining the atoms so that $\hat{r}\hat{r}$ only has one non-zero entry. Then

$$\vec{d}_B = \left(-\frac{\alpha}{r^3 + \alpha}\, \vec{d}_f \cdot \hat{x}, \quad -\frac{\alpha}{r^3 + \alpha}\, \vec{d}_f \cdot \hat{y}, \quad \frac{2\alpha}{r^3 - 2\alpha}\, \vec{d}_f \cdot \hat{z} \right)$$

Due to the symmetry, $\vec{d_A} = \vec{d_B}$.

As the atoms approach each other, the z-components of the induced dipole moments grow and eventually diverge when $r^3 = 2\alpha$. Consequently, the interaction energy also diverges. For a hydrogen atom with $\alpha = 4.5$ a.u., the divergence distance is $\approx 1.1 \mathring{A}$.

The divergence distance may be significantly larger, depending on the number and configuration of the inducible dipoles. For example, for an infinite uniform linear chain of atoms with fixed dipoles d_f aligned along the chain's axis, the induced dipole d_A is found by summing the electric fields created by the fixed d_f and induced dipoles d_n located at all other atoms

$$d_A = 2 \sum_{n=1}^{\infty} \frac{2\alpha(d_f + d_n)}{(nr)^3}.$$

Here r is the distance between adjacent dipoles, n enumerates other atoms, the factor 2 in front of the sum is due to the symmetric contributions from the dipoles located above and below the given dipole d_A. Because of the translational symmetry, all the induced dipoles are equal, so that $d_A = d_n \equiv d$. Thus,

$$d = \frac{4\alpha\zeta(3)}{r^3 - 4\alpha\zeta(3)} d_f \tag{8}$$

where ζ is Riemann's ζ-function. The induced dipoles diverge when $r^3 = 4\alpha\zeta(3) \approx 4.81\alpha$.

Damping/screening terms can be introduced to counteract the unlimited growth of the induced moments [4, 6]. However, the presence of such terms does not follow from the assumed physical model. In fact, the application of the inducible dipole model relies on the linear response assumption. It thus becomes unjustifed when the induced dipoles become too large, which actually happens well before they diverge. One criterion that perhaps can be used for defining the range of validity of the inducible dipoles model is the condition that the magnitude of the induced dipole be less than the magnitude of the fixed dipole $d < d_f$, i.e. the induced field is weaker than the inducing field. For the above example of linear chain, the cut-off distance would then be $r^3 = 8\alpha\zeta(3)$.

B. Range of Applicability of the Dielectric Spheres Models in Biomolecular Systems

Applicability of the dielectric spheres model is limited not by the presence of divergences, as is the case for point-like inducible dipoles, but rather by the finite radii of the spheres and by the non-spherical shapes of molecules. The spherical shape of the dielectric objects within the model is, of course, a limitation. However, even for objects moderately deviating from spherical shape, the spherical approximation will be adequate at separations large compared to the length scale of the irregularities. Moreover, at closer separations the impact of the details of the shapes of the objects is to create an irregular spatial distribution of charge. Since the dielectric spheres model quite naturally accommodates multipoles of arbitrary order, the irregular spatial distribution of charge caused by non-spherical molecular shape can be faithfully taken into account by allowing higher multipole moments. On the other hand, the spherical geometry makes possible a rigorous solution with controlled accuracy. When applied to systems of approximately spherical components, the formalism of dielectric spheres allows one to establish how well the bulk dielectric model of atoms and molecules works at atomic scales. The dielectric model is surprisingly accurate when applied to atoms in S states [8] and it is important to test the dielectric model on systems with higher order intrinsic multipole moments.

The shortest distance between the atoms allowable within the dielectric spheres model is when the spheres touch, i.e. the sum of the spheres' radii. According to the model [8], each dielectric sphere is characterized by its radius a and dielectric constant ϵ. While a radius can be assigned to a chemical entity with a smaller or larger degree of arbitrariness, the concept of dielectric function is not readily defined for individual molecules and even less so for individual atoms. However, these two quantities are connected in the expression for the dipole polarizability of a dielectric sphere:

$$\alpha = \frac{\epsilon - 1}{\epsilon + 2} a^3. \tag{9}$$

Thus, one of the model parameters can be expressed via an experimentally observable quantity, the dipole polarizability. Our systematic study of interactions between atoms in S states [8] suggested that the interaction energies are not sensitive to the choice of the other parameter, as long as Eq. (9) holds. This equation also defines the minimum radius of the sphere to be $(\alpha)^{1/3}$. For instance, the minimum radius of a sphere representing a water molecule ($\alpha \approx 1.47 \mathring{A}^3$ [10]) would be approximately 1.137 Å.

The presence of a dielectric medium inside the sphere allows for the introduction of internal dynamics into the system. For example, the dielectric constant may be made dependent on the radial distance [11] and furthermore on angular variables. But even for a uniform dielectric medium, one can consider reaction of the electronic subsystem (i.e., the polarizable dielectric medim) not only to external, but also to the internal, fields. Consider, for example, the boundary condition (6) when there is a single sphere and no external fields and no other bodies. This situation would correspond to solvation of a sphere with an arbitrary charge distribution. An observer at a distance would simply measure the sphere to have multipole moments $\breve{Q}_{lm}$. The variable $\breve{Q}_{lm}$, however, includes both the fixed $\overline{Q}_{lm}$ moments and the polarization at the surface Q_{lm} due to the sphere with its charge distribution being immersed in a different medium. The boundary condition reveals that the combination of the original multipole and its induced counterpart is

$$\breve{Q}_{lm} = \frac{2l+1}{\epsilon l + \epsilon_o(l+1)}\overline{Q}_{lm} = \frac{2l+1}{\epsilon l + \epsilon_o(l+1)}\left(\frac{\sqrt{4\pi}q_{lm}}{a^l}\right)$$

Effectively, a multipole at a distance is screened not by ϵ_o (as a point multipole would have been in a medium with ϵ_o), but by the factor $(\epsilon l + \epsilon_o(l+1))/(2l+1)$. Interestingly, the amount of screening of a multipole depends on l, the order of the moment. Consequently, in order to get the 'dressed' multipole to match that of the inducible dipole model, one must make the replacement

$$\frac{\sqrt{4\pi}q_{lm}}{a^l} \rightarrow \frac{\epsilon l + \epsilon_o(l+1)}{2l+1}\left(\frac{\sqrt{4\pi}q_{lm}}{a^l}\right)$$

for the input moments of the dielectric spheres model.

Thus, a direct comparison of the dielectric spheres model to the inducible point dipole model is not as simple as it might at first appear and one should not expect to obtain comparable behavior simply by inserting the same multipoles into the inducible dipole model and the dielectric spheres model. Let us demonstrate their comparison on the example of a linear chain of dipoles from section III A.

C. Linear Chain of Dielectric Spheres

In the dielectric spheres model, the induced dipole and higher multipole moments are determined by solving the system of boundary condition equations (6). If all the spheres are arranged in a linear chain, the rotations $R_{i\to k}$ aligning the vector connecting spheres i and k along the global z-axis become either identities (for the spheres below the given sphere) or simple flips of the vectors' directions (for the spheres above). The Wigner functions for identity rotations are simply $\delta_{m\,m'}$ and for the flip-the-direction rotations $\mathcal{D}^{(l)}_{mm'}(R_{i\to k}) = (-1)^{l+m}\delta_{m\,-m'}$. Thus, the general system of equations (6) is reduced to

$$\frac{\epsilon_k l + \epsilon_o(l+1)}{(2l+1)}\breve{Q}^k_{lm} - \sum_{\substack{l'>0,m',m'' \\ i\,\text{below}\,k}} \frac{(\epsilon_o-\epsilon_k)(-)^{l-m''}l(l+l')!t^{l'}_{ik}t^{l+1}_{ki}\delta_{m''\,m'}\delta_{m\,m''}}{((2l+1)(2l'+1)(l-m'')!(l'-m'')!(l+m'')!(l'+m'')!)^{1/2}}\breve{Q}^i_{l'm'}$$
$$- \sum_{\substack{l'>0,m',m'' \\ i\,\text{above}\,k}} \frac{(\epsilon_o-\epsilon_k)(-1)^{l-m''}l(l+l')!t^{l'}_{ik}t^{l+1}_{ki}(-1)^{l'+m''}\delta_{m''\,-m'}(-1)^{l+m}\delta_{m\,-m''}}{((2l+1)(2l'+1)(l-m'')!(l'-m'')!(l+m'')!(l'+m'')!)^{1/2}}\breve{Q}^i_{l'm'} = \overline{Q}^k_{lm} \tag{10}$$

Because of the Kronecker deltas, each equation in system (10) will retain only one m. Thus, if $\overline{Q}^k_{lm} = 0$ for a particular m, all $\breve{Q}^k_{lm}$ of the same m vanish. Furthermore, because all the dipoles are aligned along the z-axis, the system has azimuthal symmetry and only $m = 0$ terms will survive. Therefore, we will omit the index m from now on. Translational symmetry for an infinite chain guarantees all spheres to be equivalent, $\breve{Q}^k_l = \breve{Q}^i_l \equiv \breve{Q}_l$, and also $t_{ik} = t_{ki} = a/(|i-k|r)$, where a is the radius of the spheres, and $|i-k|r$ is the distance between the spheres i and k in terms of the nearest neighbor distance r. For the infinite chain, the sums over the spheres above and below the sphere k are equal in magnitude. They add up to zero if l and l' are of different parity, and they add up to double

the magnitude of one sum if l and l' are of the same parity. In our example the source terms are dipoles ($l = 1$), so both l and l' must be odd. Thus, Eq. (10) further reduces to

$$\frac{\epsilon l + \epsilon_o(l+1)}{(2l+1)}\breve{Q}_l - 2 \sum_{l'=1,3,5,..} \frac{(\epsilon_o - \epsilon)(-)^l l(l+l')! a^{l+l'+1} \zeta(l+l'+1)}{(l)!(l')!\sqrt{(2l+1)(2l'+1)}} \frac{\breve{Q}_{l'}}{r^{l+l'+1}} = \overline{Q}_1. \tag{11}$$

Allowing only dipoles to be induced ($l' = 1$ only), the solution of Eq. (11) is immediately found as

$$Q_1 = \left(\frac{3}{\epsilon + 2\epsilon_o} \frac{r^3}{r^3 - 4\alpha\zeta(3)} - 1\right)\overline{Q}_1 \tag{12}$$

where we have formally introduced the dipole polarizability of a dielectric sphere in dielectric medium ϵ_o as $\alpha = a^3(\epsilon - \epsilon_o)/(\epsilon + 2\epsilon_o)$ and recalled that the observed dipole moment $\breve{Q}$ is the sum of the fixed and induced moments, $\breve{Q}_1 = Q_1 + \overline{Q}_1$. If $\epsilon = \epsilon_o = 1$ (a dipole in vacuum with no dielectric sphere), we immediately recover relation (8) between the induced and the inducing dipoles.

In contrast to the inducible point dipoles, the induced dipole on dielectric sphere does not vanish when the distance between the dielectric spheres is made infinitely large:

$$Q_1^{(s)} = \left(\frac{3}{\epsilon + 2\epsilon_o} - 1\right)\overline{Q}_1. \tag{13}$$

This limit corresponds to the case of solvation of an isolated sphere. For dielectrics, there is a finite induced dipole moment, even on an isolated sphere, which counteracts the fixed dipole moment. For a remote observer, the measurable dipole moment of the sphere

$$\breve{Q}_1 = Q_1 + \overline{Q}_1 = \frac{3}{\epsilon + 2\epsilon_o}\overline{Q}_1,$$

as discussed in the previous subsection.

In Figure 1 we plot the ratio of the induced dipole moments to the fixed dipole moments for a linear chain of inducible point dipoles with polarizability α (black dashed-dotted line) and for a linear chain of dielectric spheres for $\epsilon = 4$ and $\epsilon = 20$ (solid red and dashed blue lines, respectively) with the radii calculated from Eq. (9) to get the same polarizability. The induced dipole moment Q_1 starts negative at large separations ($Q_1 = Q_1^{(s)}$, $r \to \infty$) and remains negative (counteracting the fixed dipoles) all the way until the point where the dielectric spheres touch (shown on the figure as two touching spheres on top of the respective curves). It is important to note that the induced dipoles remain smaller in magnitude than the inducing dipoles. Thus, the assumption of linearity of the response is never violated.

Mathematically, expression (12) for Q_1 (as well as solutions of the full system Eq. (11)) can be used even when the dielectric spheres overlap. While the underlying physical model is not valid when the dielectric spheres overlap, the mathematical expressions can still be used even in that physically prohibited area. This sort of analytic continuation might be helpful because the condition for linear reponse is broken at shorter distances for the dielectric spheres model than for the inducible point dipole model. The divergence takes place at the same distance for both models.

Another advantage of the dielectric spheres model is that it can be used in the context of implicit solvent. The same linear chain of dielectric spheres can be placed in a dielectric medium with $\epsilon_o \neq 1$ and the solutions of system Eq. (11) are still valid. In Figure 2 we plot the ratio of the induced dipole moments to the fixed dipole moments as a function of normalized distance for $\epsilon_o = 80$ and for several cut-off values in the sum in Eq. (11). For such a high value of ϵ_o the sum converges very quickly, and it is enough to have only one value for l'. Again, mathematically the solution can be used even for the distances where the spheres overlap (at $r/a < 2$) and in this case the solution for the induced dipole does not diverge at all.

Finally, we note that the interaction energy would be the same in the dielectric spheres model and in the inducible point dipole model, if the fixed dipoles are properly normalized (see discussion in the previous section).

D. Conclusions

We have examined a model for molecular or atomic systems that is an extension of a previously solved system of charged dielectric spheres. In addition to point charges, the extension introduces an arbitrary charge distribution for each sphere. There are two readily apparent ways to do this: either by introducing point multipoles at the center of each sphere or by placing multipole distributions on the surface of each sphere. We have shown that these two
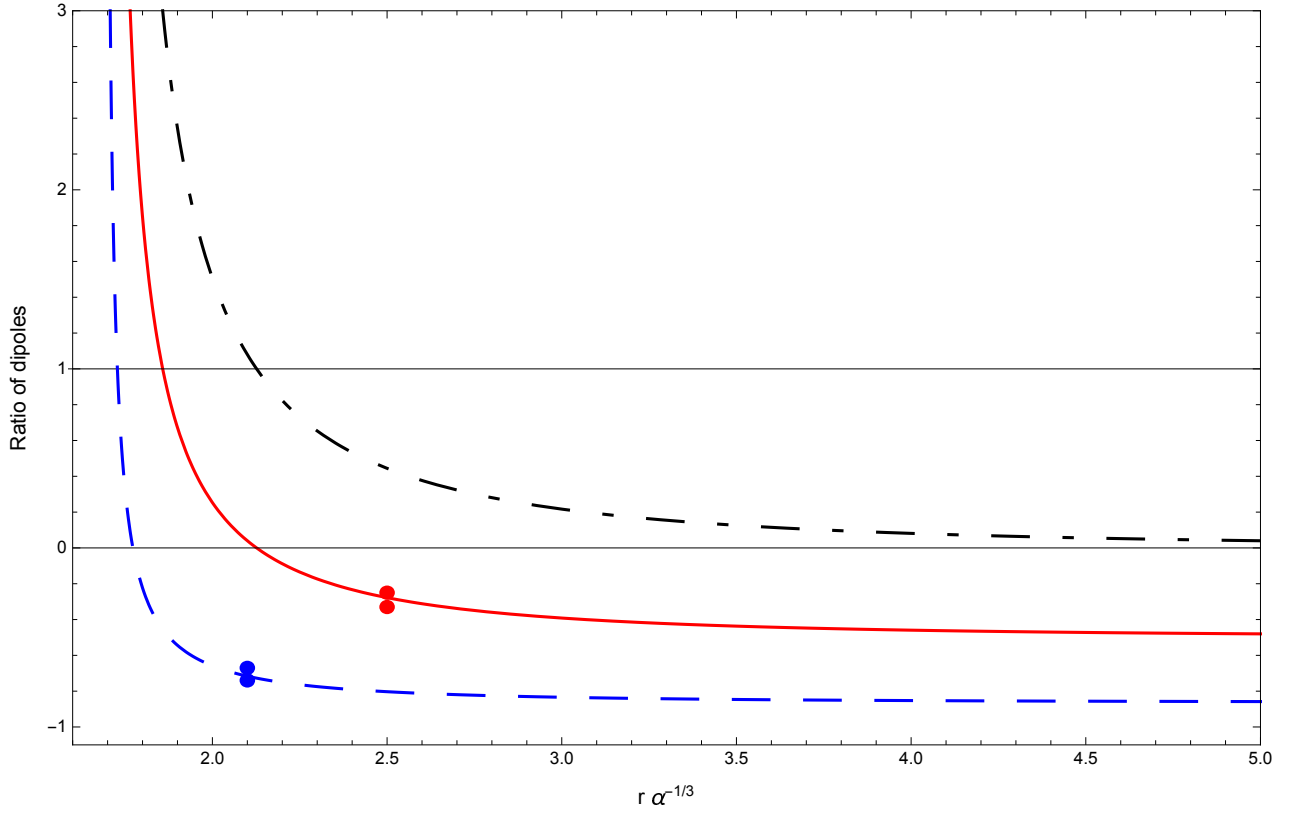
FIG. 1: (Color online) The ratio of induced dipole moments to the fixed dipole moments for a linear chain of inducible point dipoles with polarizability α (black dashed-dotted line) and for a linear chain of dielectric spheres. The solid red line shows the ratio $Q_1/\overline{Q}_1$, Eq. (12), for $\epsilon = 4$ and the dashed blue line for $\epsilon = 20$. The radii of the dielectric spheres are calculated from Eq. (9) to get the same polarizability. Two touching disks on top of the curves indicate the distance at which the dielectric spheres touch. The horizontal line where the ratio is equal to 1 serves to indicate the linear response region.

approaches are entirely equivalent , a result that is intuitively reasonable. Because the previous model of charged dielectric spheres is capable of systematically handling induced charge to any order of induced multipoles, the extension to arbitrary fixed multipoles turns out to be natural and introduces little additional computational complexity.

The computational cost of the dielectric sphere model can be estimated from the size of the system of linear equations that needs to be solved in Eq. (6). If there are N_s spheres and the expansion in spherical harmonics is cut off at $l = l_{\max}$, then the linear system will be of size $(N_s[(2l_{\max}+1)^2-1]) \times (N_s[(2l_{\max}+1)^2-1])$. On the other hand, for the polarizable dipole model, the linear system will be of size $(3N_d) \times (3N_d)$ where N_d is the number of dipoles. If $N_s \approx N_d$ and only the dipolar response is desired, then the two methods will have similar computational costs. The dielectric spheres model can produce physically consistent results in the presence of higher order multipoles, although this is naturally at the cost of more intensive computation. For a specific application, the particular circumstances will determine the trade-off between including higher multipole moments and more intensive computation.

While the spherical geometry can be a limitation, it also permits rigorous calculations to any desired degree of accuracy. An alternate model of inducible point dipoles sometimes used for polarizable force fields encounters a divergence of the induced dipoles at small separations that is typically avoided by introducing *ad hoc* damping terms. The finite size of the polarizable spheres considered here means that there is no divergence of the induced moments. When the mathematical formalism for dielectric spheres is pushed into the region of overlap, a divergence does eventually occur but the induced moments remain in the range consistent with linear response to shorter separations than in the case of inducible point dipoles. However, the completely consistent way to proceed when the dielectric spheres overlap is to merge the spheres into a single new (non-spherical) geometry, such as that devised by Connolly [12]. Although an analytical solution will not generally be available in this case, an argument based on the underlying physics of dielectrics demonstrates that this revised dielectric model will not be subject to divergences. The energy U written as a functional of the polarization density $\vec{P}$ for a linear dielectric system is [11]

$$U[\vec{P}] = \frac{1}{2} \int \left[\rho_{\mathrm{f}}(\vec{r}) - \nabla \cdot \vec{P}(\vec{r}) \right] \frac{1}{|\vec{r} - \vec{r}'|} \left[\rho_{\mathrm{f}}(\vec{r}') - \nabla \cdot \vec{P}(\vec{r}') \right] \mathrm{d}\vec{r}\,\mathrm{d}\vec{r}' + \frac{1}{2} \int \frac{\vec{P}(\vec{r}) \cdot \vec{P}(\vec{r})}{\chi(\vec{r})} \mathrm{d}\vec{r} \tag{14}$$
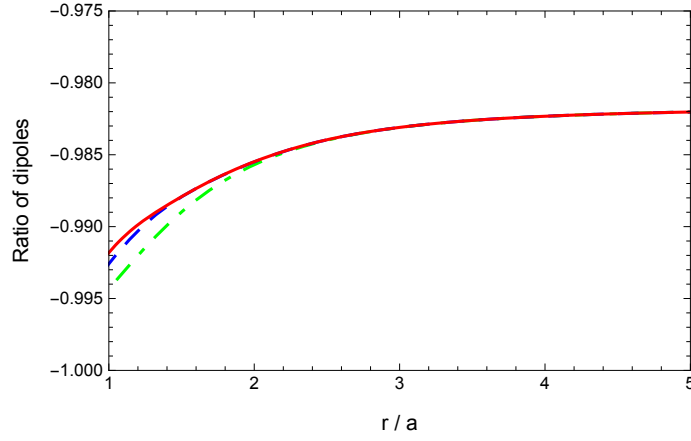
FIG. 2: (Color online) The ratio of induced dipole moments to the fixed dipole moments for a linear chain of dielectric spheres with $\epsilon = 4$ placed in a medium with $\epsilon_o = 80$. The ratios are shown for three cut-off values in the sum over l' in Eq. (11). For $l'_{\max} = 1$ the dashed-dotted green line is used, for $l'_{\max} = 3$ the dashed blue line is used, and for $l'_{\max} = 5$ the solid red line is used. The spheres touch when $r/a = 2$.

where ρ_{f} is the fixed charge density and $\chi(\vec{r})$ is the linear susceptibility. Since $-\nabla \cdot \vec{P}(\vec{r})$ is the induced charge density, the factor in square brackets is the total charge density and the first term is clearly the Coulomb energy of a set of fixed and induced charges. The second term functions as a quadratic restoring force and serves as a penalty against the creation of large polarizations even if such a polarization configuration is very favorable in terms of the Coulomb energy alone. Much as a Hookean spring prevents a mechanical system from generating an infinite response, this restoring force ensures that the polarization in reaction to the presence of the fixed charges will remain finite. We conclude that the absence of divergence is general for any finite surface provided the boundary conditions are enforced in a physically consistent manner. While numerical methods would be required for such a system, it would be a very reasonable and useful generalization of the dielectric model.

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