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Continuum Solvation Models

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Introduction

The following text is a summary of work I did as part of the Master-Seminar in 'Computational Engineering Science' at RWTH in winter 2018.

The first part should be considered as an introduction to Continuum Solvation Models. My studies on this part were largely based on the review by Tomasi, Mennucci and Cammi [12]. Emphasizing in particular the PCM and COSMO Model, I used the books by Mennucci and Cammi [10] and by Klamt [5], when formulating the corresponding interface problems in terms of the reaction potential. To gain some more expertise on the electrostatic background I used the book by Griffiths [3] as well as the lecture notes by Stamm [11] as further references.

In the second part I summarize the analytical solutions of both the PCM and COSMO Model for a spherical cavity. The resulting solvation energies are compared for a point charge, a dipole as well as a multipole.

Throughout the whole semester I had regular meetings with Muhammad Hassan who encouraged me to study the theoretical background necessary to carry out these calculations. I'm especially grateful for his patient and careful review of my writings as well as for the continuous support when preparing the oral presentation.

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Lucia Baltz

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1 Continuous Solvation Models (CSM)

Since the 1990s quantum chemistry methods have been able to predict properties of new molecules in the range of industrially relevant molecular sizes. By applying density functional theory (DFT) the electron correlation was (first) taken into account, and therefore accuracy improved significantly compared to previously developed Hartree-Fock methods while the computational cost remained within the same scale [5]. Quantum Mechanics based methods are primarily suitable whenever inter-molecular interactions can be neglected, as e.g. for isolated molecules in a vacuum or dilute gases. However processes relevant for chemical and biochemical industry are mainly taking place in the liquid phase where solute and solvent molecules influence one another. In order to account for the change in chemical properties of a solute molecule due to the presence of a solvent, we need to extend the general quantum mechanical description by a so-called solvation model.

Continuous solvation models (CSMs) belong to the class of implicit solvation models. Instead of including the solvent molecules individually (explicitly), CSMs neglect the atomistic nature of the solvent and describe it by a continuous dielectric medium.



Figure 1: Concept - Continuum Solvation Model

In Continuum Solvation Models the solute-solvent interaction consists of the mutual polarization of the solutes charge distribution ρ inside a molecular cavity Ω and the dielectric continuum with permittivity ϵ_s . Figure 1 shows this setup of such a molecular cavity. The resulting quantum mechanical system can be described by a so-called effective Hamiltonian H^{EF} [12]. It is given by sum of the vacuum Hamiltonian H^{solute} , modeling the solute in vacuum, and the interaction Hamiltonian $H^{solute-solvent}$, accounting for polarization effects between solvent and solute. We only account for electrostatic interactions due to polarization, neglecting any other weaker types of interactions. H^{EF} is therefore an approximation of the actual Hamiltonian H modeling the total energy of the solute in presence of a solvent. It holds

$$H \approx H^{EF} = H^{solute} + H^{solute-solvent}.$$

The change in energy E^R due to electrostatic interactions between solute and solvent molecules, modeled by the Hamiltonian $H^{solute-solvent}$, corresponds to the solution of

an interface problem in terms of the electrostatic reaction potential Φ^R . One popular approach is to model these electrostatic interactions by a charge density σ at the surface of the cavity Ω . This is called the Apparent Surface Charge approach and eases computations by rewriting the electrostatic interface problem as integral equations [9].

The methods including this type of formulation build the family of Polarizable Continuum Models (PCM). In the scope of this seminar work we consider two members, the original (D-PCM) formulation and the conductor-like screening model (COSMO or C-PCM)[10] and compare the corresponding solvation energies.

1.1 Electrostatic Problem

1.1.1 Total Potential

Let $\Omega \in \mathbb{R}^3$ be a bounded domain that represents some solute molecule, let ρ_M denote the charge distribution of this molecule. Let the solute molecule be surrounded by an isotropic and homogeneous dielectric solvent. We can therefore define a dielectric function:

$$\epsilon(r) = \begin{cases} 1 & r \in \Omega, \\ \epsilon_s & r \in \mathbb{R}^3 \setminus \overline{\Omega}. \end{cases} \quad (1)$$

We assume the charge distribution of the solute ρ_M is supported inside the cavity Ω . Then the total electrostatic potential Φ satisfies:

$$\begin{aligned} -\Delta\Phi(r) &= 4\pi\rho_M(r) & r \in \Omega, \\ -\epsilon_s\Delta\Phi(r) &= 0 & r \in \mathbb{R}^3 \setminus \overline{\Omega}. \end{aligned} \quad (2)$$

In addition Φ satisfies the following jump conditions at the cavity interface. It holds

$$\begin{aligned} (\Phi(r))_i &= (\Phi(r))_o & r \in \partial\Omega, \\ \left(\frac{\partial\Phi(r)}{\partial\mathbf{n}}\right)_i &= \epsilon_s \left(\frac{\partial\Phi(r)}{\partial\mathbf{n}}\right)_o & r \in \partial\Omega. \end{aligned} \quad (3)$$

Here $(\cdot)_i$ denotes the boundary values of the function when approaching the boundary from the interior, i.e. $(\Phi(r))_i = \lim_{\mu \rightarrow 0^+} \Phi(r - \mu\mathbf{n}(s))$. Analogously when approaching the boundary from the exterior $(\Phi(r))_o = \lim_{\mu \rightarrow 0^+} \Phi(r + \mu\mathbf{n}(s))$, with $\mathbf{n}(s)$ denoting the unit outward normal vector.

In order to obtain a unique potential Φ , we additionally impose standard decay conditions:

$$\lim_{r \rightarrow \infty} |r| |\Phi(r)| < \infty, \quad (4)$$

$$\lim_{r \rightarrow \infty} |r^2| |\nabla \Phi(r)| < \infty.$$

The problem with solving this PDE directly is that it is posed on an unbounded domain. As we shall see shortly, it is therefore advantageous to regard the total potential as sum of the vacuum potential Φ^V and the reaction potential Φ^R , thus we may write

$$\Phi = \Phi^V + \Phi^R.$$

Adopting this approach, it is possible to solve for the reaction potential Φ^R and the vacuum potential Φ^V separately and add up the results, instead of solving the electrostatic problem for the total potential Φ directly.

1.1.2 Vacuum Potential

The potential Φ^V solely generated by the solute molecule in vacuum satisfies the following problem: Find Φ^V such that

$$-\Delta \Phi^V(r) = 4\pi \rho_M(r) \quad r \in \mathbb{R}^3, \quad (5)$$

with standard decay conditions

$$\begin{aligned} \lim_{r \rightarrow \infty} |r| |\Phi(r)| &< \infty, \\ \lim_{r \rightarrow \infty} |r^2| |\nabla \Phi(r)| &< \infty. \end{aligned}$$

In this case the solution Φ^V is given by a Newton potential

$$\Phi^V(r) = \int_{\mathbb{R}^3} \frac{\rho_M(r')}{|r - r'|} dr'.$$

Since we assume the charge distribution of the solute molecule ρ_M to be supported in Ω , it holds

$$\Phi^V(r) = \int_{\Omega} \frac{\rho_M(r')}{|r - r'|} dr'.$$

For later use we additionally state the corresponding interface problem, find Φ^V such that:

$$\begin{aligned} -\Delta \Phi^V(r) &= 4\pi \rho_M(r) & r \in \Omega, \\ -\Delta \Phi^V(r) &= 0 & r \in \mathbb{R}^3 \setminus \bar{\Omega}, \end{aligned} \quad (6)$$

with zero jump conditions

$$\begin{aligned} (\Phi^V(r))_i &= (\Phi^V(r))_o & r \in \partial\Omega, \\ \left(\frac{\partial \Phi^V(r)}{\partial \mathbf{n}} \right)_i &= \left(\frac{\partial \Phi^V(r)}{\partial \mathbf{n}} \right)_o & r \in \partial\Omega, \end{aligned} \quad (7)$$

and standard decay conditions.

1.1.3 Reaction Potential

Due to linearity Φ^R can now be determined by solving the following interface problem: Find Φ^R , such that:

$$\begin{aligned} -\Delta\Phi^R(r) &= 0 & r \in \Omega, \\ -\Delta\Phi^R(r) &= 0 & r \in \mathbb{R}^3 \setminus \overline{\Omega}, \end{aligned} \quad (8)$$

with jump conditions

$$\begin{aligned} [\Phi^R](r) &= 0, \\ \left[\frac{\partial\Phi^R}{\partial\mathbf{n}} \right](r) &= g\left(\frac{\partial\Phi^V}{\partial\mathbf{n}}, \epsilon_s\right), \end{aligned} \quad (9)$$

and standard decay conditions. Here we use the notation $[\Phi^R] := (\Phi^R(r))_i - (\Phi^R(r))_o$. Using the the zero jump conditions of the vacuum potential and the jump conditions of the total potential in Equation (3), we obtain

$$\left(\frac{\partial\Phi^R(r)}{\partial\mathbf{n}}\right)_i - \epsilon_s \left(\frac{\partial\Phi^R(r)}{\partial\mathbf{n}}\right)_o = (\epsilon_s - 1) \left(\frac{\partial\Phi^V(r)}{\partial\mathbf{n}}\right)_i, \quad (10)$$

which we denoted by some function g .

We observe that the solution Φ^R to this interface problem is a harmonic function.

1.2 Polarizable Continuum Model

The main idea of the Polarizable Continuum Model is to follow the so-called Apparent Surface Charge approach. This approach suggest to represent the reaction potential Φ^R as a single layer potential in terms of the apparent surface charge distribution σ on the cavity surface $\partial\Omega$.

1.2.1 Single Layer Potential

Let's recall that the reaction potential Φ^R satisfying the the interface problem defined in Equation (8) and (9) is a harmonic function. It can therefore be represented as a single layer potential

$$\Phi^R(r) = S(\sigma)(r) = \int_{\partial\Omega} \frac{\sigma(s)}{|r-s|} ds \quad r \in \mathbb{R}^3, \quad (11)$$

where σ is a so-called apparent charge distribution on the cavity surface $\partial\Omega$. From the integral representation formula for Φ^R in [1] we find that

$$\left[\frac{\partial\Phi^R}{\partial\mathbf{n}} \right] = 4\pi\sigma. \quad (12)$$

Next we define

$$\frac{\partial \Phi^R}{\partial \mathbf{n}}(r) := \frac{1}{2} \left[\left(\frac{\partial \Phi^R}{\partial \mathbf{n}} \right)_i + \left(\frac{\partial \Phi^R}{\partial \mathbf{n}} \right)_o \right](r) \quad r \in \partial\Omega, \quad (13)$$

and introduce the double layer potential as

$$\frac{\partial \Phi^R}{\partial \mathbf{n}}(r) = D^*(\sigma)(r) = \int_{\partial C} \frac{\partial}{\partial n} \left(\frac{\sigma(s)}{|r-s|} \right) ds. \quad (14)$$

By inserting the relations (12), (13) as well as the jump conditions (7) and (3) into Equation (10) we rewrite the interface problem of the reaction potential as the following integral equation: Find $\sigma(s) \in \mathbb{C}^0(\partial\Omega)$ such that

$$(2\pi \frac{\epsilon_s + 1}{\epsilon_s - 1} - D^*)\sigma = \frac{\partial \Phi^V}{\partial \mathbf{n}}. \quad (15)$$

Notice that instead of solving the three dimensional problem in Equation (8) and (9) on an unbounded domain \mathbb{R}^3 , we only need to solve the integral equation (15) on the cavity surface $\partial\Omega \in \mathbb{R}^3$.

1.3 Conductor like Screening Model

Even though we reduced the dimensionality of the original problem in the PCM model, the resulting integral equation (15) is still not straight forward to solve.

One approach to adapt the PCM model in order to simplify the resulting integral equation, was introduced by Klamt [4] as the so-called Conductor like Screening Model (COSMO). The main idea is to treat the solvent as an ideal conductor ($\epsilon_s \rightarrow \infty$). In this case the total potential Φ on the cavity surface $\partial\Omega$ vanishes. Thus, the reaction potential $\Phi^{R^*}(r) = 0 - \Phi^{\rho M}(r)$ for all $r \in \partial\Omega$ and we can therefore obtain the following interface problem for the reaction potential: Find Φ^{R^*} , such that:

$$\begin{aligned} -\Delta \Phi^{R^*}(r) &= 0 & r \in \Omega, \\ -\Delta \Phi^{R^*}(r) &= 0 & r \in \mathbb{R}^3 \setminus \overline{\Omega}, \\ \Phi^{R^*}(r) &= -\Phi^V & r \in \partial\Omega, \end{aligned} \quad (16)$$

and decay conditions

$$\Phi^{R^*}(r) \rightarrow 0 \quad r \rightarrow \infty.$$

Here again, the solution holds the form of a single layer potential

$$\Phi^{R^*}(r) = \int_{\partial C} \frac{\sigma^*(s)}{|r-s|} ds,$$

for some unknown apparent surface charge distribution σ^* .

Therefore Equation (16) can again be written as an integral equation: Find σ^* such that:

$$S\sigma^* = -\Phi^V \quad (17)$$

with $S\sigma(r) = \int_{\partial C} \frac{\sigma(s)}{|r-s|} ds$. Since the medium is not in-fact an ideal conductor, the actual σ is obtained by multiplication with a scaling factor $f(\epsilon)$. It holds

$$\sigma = f(\epsilon)\sigma^*.$$

The scaling function $f(\epsilon)$ has been adapted by Klamt from the Onsager Reaction Field Model [4]. It describes the scaling of the screening energy of a multipole at the centre of a spherical cavity due to a dielectric medium as

$$f(\epsilon) = \frac{\epsilon - 1}{\epsilon + k}, \quad \text{where } k \in \mathbb{R}.$$

Using correct electrostatic solute-solvent energies from solvchromatic experiments, Klamt observed that only ions need a separate scaling factor, while non-ionic solutes can be well approximated using the same scaling factor $f(\epsilon)$ for dipoles and higher multipole contributions, as shown in Figure 2. Klamt proposes to choose $k=0.5$ for non-ionic solutes, but also points out a dependency on the cavity shape as well as on the distribution of charges in the solute. [5]

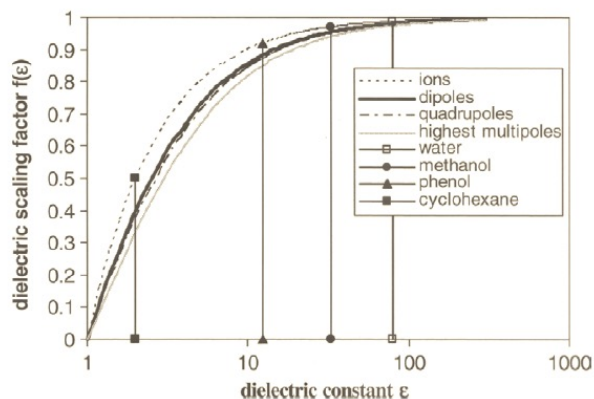


Figure 2: Dielectric scaling functions for different multipole orders [5]

1.4 Energy of Solvation

The electrostatic energy corresponding to the charge density ρ_M of a molecule in vacuum is given by

$$E_V = \frac{1}{2} \int_{\mathbb{R}^3} \rho_M(x) \Phi^V(x) dx.$$

In order to obtain the total energy, the electrostatic energy due to the presence of the solvent need to be added. It is given in terms of the reaction potential Φ^R by

$$E_R = \frac{1}{2} \int_{\mathbb{R}^3} \rho_M(x) \Phi^R(x) dx.$$

E_R is also called the electrostatic contribution to the solvation energy. We can rewrite this in terms of the apparent surface charge σ and the vacuum potential Φ^V [1] and obtain

$$E_R = \frac{1}{2} \int_{\Omega} \rho_M(x) \left(\int_{\partial\Omega} \frac{\sigma(s)}{|x-s|} ds \right) dx = \frac{1}{2} \int_{\partial\Omega} \sigma(s) \Phi^V(s) ds. \quad (18)$$

2 Analytical Solutions for a Spherical Cavity

In order to compare the COSMO and the PCM model, we solve the corresponding integral equations analytically in case of a spherical cavity $\Omega = \mathcal{S}_r^2$ with radius r and compare the resulting solvation energies.

2.1 Spherical Harmonics

Recall that $\sigma \in \mathbb{C}^0(\partial\Omega)$ and $\Phi^V \in \mathbb{C}^0(\partial\Omega)$. As we will see shortly it is beneficial to expand σ and Φ in terms of spherical harmonics. For that purpose we use spherical coordinates $\vec{x} = (r_x, \theta_x, \phi_x)$.

COSMO Equation:

The LHS of the COSMO Equation (17)

$$S\sigma^*(x) = \int_{\partial\Omega} \underbrace{\sigma^*(s)}_A \underbrace{\frac{1}{|x-s|}}_B ds \quad x \in \partial\Omega,$$

can be rewritten, using

$$\sigma^*(s) = \sum_{\ell=0}^{\infty} \sum_{m=-\ell}^{\ell} u_{\ell}^m Y_{\ell}^m(\theta_s, \phi_s) \quad s \in \partial\Omega,$$

and

$$\frac{1}{|x-s|} = \sum_{\ell=0}^{\infty} \sum_{m=-\ell}^{\ell} \frac{4\pi}{2\ell+1} \frac{r^{\ell}}{r^{\ell+1}} Y_{\ell}^m(\theta_s, \phi_s) Y_{\ell}^m(\theta_x, \phi_x),$$

such that

$$S\sigma^*(x) = \sum_{\ell=0}^{\infty} \sum_{m=-\ell}^{\ell} \frac{4\pi}{2\ell+1} r_x u_{\ell}^m Y_{\ell}^m(\theta_x, \phi_x). \quad (19)$$

with some unknown coefficients $[u]_{\ell}^m$.

Analogously, the RHS of the COSMO Equation (20) can be expressed as

$$-\Phi^V(x) = \sum_{\ell=0}^{\infty} \sum_{m=-\ell}^{\ell} g_{\ell}^m Y_{\ell}^m(\theta_x, \phi_x) \quad x \in \partial\Omega. \quad (20)$$

Here the coefficients $[g]_{\ell}^m$ depend on the known vacuum potential Φ^V . Thus, the integral $S\sigma^*(x) = -\Phi^V(x)$ can be solved by finding the set of coefficients $g_{\ell}^m, u_{\ell}^m \in \mathbb{R}$.

PCM Equation:

The solution of the PCM Equation (15) is obtained in a similar manner. By making use of the property $D^*\sigma = -\frac{1}{2r}S\sigma$, we can rewrite the PCM Equation (15) as

$$\left((2\pi \frac{\epsilon_s + 1}{\epsilon_s - 1} - D^*)\sigma \right)(x) = 2\pi \sum_{\ell=0}^{\infty} \sum_{m=-\ell}^{\ell} \left(\frac{\epsilon + 1}{\epsilon - 1} + \frac{1}{2\ell + 1} \right) u_{\ell}^m Y_{\ell}^m(\theta_x, \phi_x), \quad (21)$$

and

$$\frac{\partial \Phi^V}{\partial n}(x) = \sum_{\ell=0}^{\infty} \sum_{m=-\ell}^{\ell} h_{\ell}^m Y_{\ell}^m(\theta_x, \phi_x) \quad x \in \partial\Omega. \quad (22)$$

2.2 Point Charge

Let us first consider a single point charge q placed in the origin of a spherical cavity $\Omega = \mathcal{S}_r^2$ with radius r . Its potential generated in vacuum is given by

$$\phi_{Pointcharge}^V = \frac{1}{4\pi} \frac{q}{r} \quad (23)$$

2.2.1 Surface Charge

COSMO Model:

By inserting $\phi_{Pointcharge}^V$ into the RHS of the COSMO Equation (20) it holds

$$-\phi_{Pointcharge}^V = -\frac{1}{4\pi} \frac{q}{r} = g_0^0 Y_0^0, \quad (24)$$

where $Y_0^0 = \frac{1}{2}\sqrt{\pi^{-1}}$. Hence, we obtain

$$g_0^0 = -\frac{q}{2\sqrt{\pi}r}.$$

Combining Equation (24) with the LHS of the COSMO Equation (19) and matching coefficients yields

$$4\pi r u_0^0 Y_0^0 = g_0^0 Y_0^0 \rightarrow u_0^0 = -\frac{q}{8\pi\sqrt{\pi}r^2}$$

and $[u_l^m] = 0 \forall l > 0, m \in [-l, l]$.

The COSMO surface charge is therefore given by

$$\sigma^*(x) = u_0^0 Y_0^0 = -\frac{q}{16\pi^2 r^2} \rightarrow \sigma(x) = -\frac{\epsilon - 1}{\epsilon + k} \frac{q}{16\pi^2 r^2}, \quad x \in \partial\Omega. \quad (25)$$

PCM Model:

For the electrostatic potential of a point charge in Vacuum $\phi_{pointcharge}^V$ we obtain as the RHS of the PCM Equation (22)

$$\frac{\partial \Phi_{pointcharge}^V}{\partial n} = -\frac{1}{4\pi} \frac{q}{r^2} = h_0^0 Y_0^0,$$

where $Y_0^0 = \frac{1}{2}\sqrt{\pi^{-1}}$. Hence,

$$h_0^0 = -\frac{q}{2\sqrt{\pi}r^2}.$$

Combining Equation (26) with the ansatz for the LHS of the PCM equation (21) and matching coefficients yields

$$2\pi\left(\frac{\epsilon+1}{\epsilon-1} + r\right)u_0^0 Y_0^0 = h_0^0 Y_0^0 \rightarrow u_0^0 = -\frac{q(\epsilon-1)}{8\pi\sqrt{\pi}r^2\epsilon},$$

and $[u_l^m] = 0 \forall l > 0, m \in -l, l$.

The PCM surface charge is therefore given by

$$\sigma(x) = -\frac{q(\epsilon-1)}{16\pi^2 r^2 \epsilon}, \quad x \in \partial\Omega. \quad (26)$$

2.2.2 Energy of Solvation

We calculate the energy of solvation according to Equation (18) as

$$E_R = \frac{1}{2} \int_{\partial\Omega} \sigma(s) \Phi_{pointcharge}^V(s) ds.$$

Thus, comparing the COSMO energy without the scaling factor E_R^{COSMO*} , the COSMO energy including the scaling factor E_R^{COSMO} and the PCM energy E_R^{PCM} , yields

$$\begin{aligned} E_R^{COSMO*} &= \frac{1}{2} \int_0^\pi \int_0^{2\pi} \left(-\frac{q}{16\pi^2 r^2} \right) \left(\frac{1}{4\pi} \frac{q}{r} \right) r^2 \sin(\theta) d\varphi d\theta \\ &= -\frac{q^2}{32\pi^2 r}, \end{aligned} \quad (27)$$

$$\begin{aligned} E_R^{COSMO} &= \frac{1}{2} \int_0^\pi \int_0^{2\pi} \left(-\frac{\epsilon-1}{\epsilon+k} \frac{q}{16\pi^2 r^2} \right) \left(\frac{1}{4\pi} \frac{q}{r} \right) r^2 \sin(\theta) d\varphi d\theta \\ &= -\left(\frac{\epsilon-1}{\epsilon+k} \right) \frac{q^2}{32\pi^2 r}, \end{aligned} \quad (28)$$

and

$$E_R^{PCM} = \frac{1}{2} \int_0^\pi \int_0^{2\pi} \left(-\frac{q(\epsilon-1)}{16\pi^2 r^2 \epsilon} \right) \left(\frac{1}{4\pi} \frac{q}{r} \right) r^2 \sin(\theta) d\varphi d\theta$$

$$= -\left(\frac{\epsilon - 1}{\epsilon}\right) \frac{q^2}{32\pi^2 r}. \quad (29)$$

We observe that in case of a point charge in the center of a sphere, it holds that

$$E_R^{COSMO^*} < E_R^{PCM} < E_R^{COSMO} \quad \text{for } k > 0,$$

and

$$E_R^{PCM} = E_R^{COSMO} \quad \text{for } k = 0.$$

2.3 Dipole

Let us next consider a dipole defined by the moments $[\Phi]_1^{-1}, [\Phi]_1^0, [\Phi]_1^1$. It is again placed at the origin of the spherical cavity with radius r . Its potential generated in vacuum is given by

$$\phi_{dipole}^V(r, \theta, \phi) = \sum_{m=-1}^1 [\Phi]_1^m \frac{1}{r^2} Y_1^m(\theta, \phi) \quad (30)$$

$$= \frac{1}{r^2} [[\Phi]_1^{-1} Y_1^{-1}(\theta, \phi) + [\Phi]_1^0 Y_1^0(\theta, \phi) + [\Phi]_1^1 Y_1^1(\theta, \phi)], \quad (31)$$

2.3.1 Surface Charge

COSMO Model:

By inserting Φ_{dipole}^V into the RHS of the COSMO Equation (20), it holds

$$-\phi_{dipole}^V = -\frac{1}{r^2} [[\Phi]_1^{-1} Y_1^{-1} + [\Phi]_1^0 Y_1^0 + [\Phi]_1^1 Y_1^1] = \sum_{m=-1}^1 g_1^m Y_1^m,$$

and $g_1^m = 0 \forall \ell \neq 1$. Thus, by comparison of coefficients we obtain

$$g_1^m = -\frac{1}{r^2} [\Phi]_1^m,$$

for $m \in \{-1, 0, 1\}$.

Combining Equation (32) with Equation (19) and matching coefficients yields

$$\frac{4\pi r}{3} u_1^0 Y_1^0 = g_1^0 Y_1^0 \rightarrow u_1^0 = -\frac{3}{4\pi r^3} [\Phi]_1^0$$

for $m \in \{-1, 0, 1\}$.

The COSMO surface charge is therefore given by

$$\sigma^*(x) = -\frac{3}{4\pi r^3} [[\Phi]_1^{-1} Y_1^{-1} + [\Phi]_1^0 Y_1^0 + [\Phi]_1^1 Y_1^1], \quad (32)$$

$$\sigma(x) = -\frac{\epsilon - 1}{\epsilon + k} \frac{3}{4\pi r^3} [[\Phi]_1^{-1} Y_1^{-1} + [\Phi]_1^0 Y_1^0 + [\Phi]_1^1 Y_1^1], \quad x \in \partial\Omega. \quad (33)$$

PCM Model:

For the electrostatic potential of a dipole in Vacuum in Equation (30) we obtain as the RHS of the PCM Equation (22)

$$\frac{\partial \Phi^{V_{dipole}}}{\partial n} = -\frac{2}{r^3} [[\Phi]_1^{-1} Y_1^{-1} + [\Phi]_1^0 Y_1^0 + [\Phi]_1^1 Y_1^1] = \sum_{m=-1}^1 g_1^m Y_1^m \quad (34)$$

and $g_l^m = 0 \forall l \neq 1$. Hence, we obtain

$$g_1^m = -\frac{2}{r^3} [\Phi]_1^m,$$

for $m \in \{-1, 0, 1\}$.

Combining Equation (34) with the ansatz for the LHS of the PCM equation (21) and matching coefficients yields

$$2\pi \left(\frac{\epsilon + 1}{\epsilon - 1} + \frac{1}{3} \right) u_1^m Y_1^m = g_1^m Y_1^m \rightarrow u_1^m = -\frac{3}{4\pi r^3} [\Phi]_1^m \left(\frac{\epsilon - 1}{\epsilon + \frac{1}{2}} \right),$$

and $[u_l^m] = 0 \forall l \neq 1$.

The PCM surface charge is therefore given by

$$\sigma(x) = -\frac{3}{4\pi r^3} \left(\frac{\epsilon - 1}{\epsilon + \frac{1}{2}} \right) [[\Phi]_1^{-1} Y_1^{-1} + [\Phi]_1^0 Y_1^0 + [\Phi]_1^1 Y_1^1] \quad x \in \partial\Omega. \quad (35)$$

2.3.2 Energy of Solvation

We calculate the energy of solvation according to Equation (18). Therefore we obtain for the dipole

$$\begin{aligned} E_R^{COSMO*} &= \frac{1}{2} \int_0^\pi \int_0^{2\pi} \left(-\frac{3}{4\pi r^3} [[\Phi]_1^{-1} Y_1^{-1} + [\Phi]_1^0 Y_1^0 + [\Phi]_1^1 Y_1^1] \right) \\ &\quad \left(\frac{1}{r^2} [[\Phi]_1^{-1} Y_1^{-1} + [\Phi]_1^0 Y_1^0 + [\Phi]_1^1 Y_1^1] \right) r^2 \sin(\theta) d\varphi d\theta, \\ &= -\frac{3}{4\pi r^3} \left[([\Phi]_1^{-1})^2 + ([\Phi]_1^0)^2 + ([\Phi]_1^1)^2 \right] \end{aligned} \quad (36)$$

$$\begin{aligned} E_R^{COSMO} &= \frac{\epsilon - 1}{\epsilon + k} E_R^{COSMO*} \\ &= -\frac{\epsilon - 1}{\epsilon + k} \frac{3}{4\pi r^3} \left[([\Phi]_1^{-1})^2 + ([\Phi]_1^0)^2 + ([\Phi]_1^1)^2 \right], \end{aligned} \quad (37)$$

and

$$E_R^{PCM} = \frac{1}{2} \int_0^\pi \int_0^{2\pi} \left(-\frac{3}{4\pi r^3} \left(\frac{\epsilon - 1}{\epsilon + \frac{1}{2}} \right) [[\Phi]_1^{-1} Y_1^{-1} + [\Phi]_1^0 Y_1^0 + [\Phi]_1^1 Y_1^1] \right)$$

$$\begin{aligned}
& \left(\frac{1}{r^2} [[\Phi]_1^{-1} Y_1^{-1} + [\Phi]_1^0 Y_1^0 + [\Phi]_1^1 Y_1^1] \right) r^2 \sin(\theta) d\varphi d\theta \\
& = -\frac{\epsilon - 1}{\epsilon + \frac{1}{2}} \frac{3}{4\pi r^3} \left[([\Phi]_1^{-1})^2 + ([\Phi]_1^0)^2 + ([\Phi]_1^1)^2 \right].
\end{aligned} \tag{38}$$

We observe that in case of dipole in the center of a sphere, it holds that

$$E_R^{COSMO^*} < E_R^{PCM} < E_R^{COSMO} \quad \text{for } k > \frac{1}{2},$$

and

$$E_R^{PCM} = E_R^{COSMO} \quad \text{for } k = \frac{1}{2}.$$

2.4 Multipole

We extend our previous calculation by considering a multipole, also inside a spherical cavity. For such an multipole of order L defined by a set of moments $[\Phi]_l^m$ located inside a sphere of radius r centered at the origin, its potential generated in vacuum is given by

$$\phi_{multipole}^V(r, \theta, \phi) = \sum_{\ell=0}^L \sum_{m=-\ell}^{\ell} [\Phi]_l^m \frac{1}{r^{\ell+1}} Y_\ell^m(\theta, \phi). \tag{39}$$

2.4.1 Surface Charge

COSMO Model:

By inserting $\phi_{multipole}^V$ as well as Equation (19) into the COSMO Equation (17) it holds

$$\sum_{\ell=0}^L \sum_{m=-\ell}^{\ell} \frac{4\pi}{2\ell+1} r u_\ell^m Y_\ell^m(\theta_x, \phi_x) = - \sum_{\ell=0}^L \sum_{m=-\ell}^{\ell} [\Phi]_\ell^m \frac{1}{r^{\ell+1}} Y_\ell^m.$$

Matching coefficients yields

$$\frac{4\pi}{2\ell+1} r u_\ell^m = -[\Phi]_\ell^m \frac{1}{r^{\ell+1}} \rightarrow u_\ell^m = -\frac{2\ell+1}{4\pi} \frac{1}{r^{\ell+2}} [\Phi]_\ell^m$$

The COSMO surface charge is therefore given by

$$\sigma^*(s) = - \sum_{\ell=0}^L \sum_{m=-\ell}^{\ell} \frac{2\ell+1}{4\pi} \frac{1}{r^{\ell+2}} [\Phi]_\ell^m Y_\ell^m(\theta_x, \phi_x) \tag{40}$$

$$\sigma(x) = -\frac{\epsilon-1}{\epsilon+k} \sum_{\ell=0}^L \sum_{m=-\ell}^{\ell} \frac{2\ell+1}{4\pi} \frac{1}{r^{\ell+2}} [\Phi]_\ell^m Y_\ell^m(\theta_x, \phi_x) \quad x \in \partial\Omega. \tag{41}$$

PCM Model:

For the electrostatic potential $\phi_{multipole}^V$ in Equation (39) we obtain as the RHS of the PCM equation (22)

$$\frac{\partial \Phi^{V_{multipole}}}{\partial n} = - \sum_{\ell=0}^L \sum_{m=-\ell}^{\ell} \frac{\ell+1}{r^{\ell+2}} [\Phi]_{\ell}^m Y_{\ell}^m \quad (42)$$

Combining Equation (42) with the ansatz for the LHS of the PCM Equation (21) we obtain

$$2\pi \sum_{\ell=0}^L \sum_{m=-\ell}^{\ell} \left(\frac{\epsilon+1}{\epsilon-1} + \frac{1}{2\ell+1} \right) u_{\ell}^m Y_{\ell}^m = - \sum_{\ell=0}^L \sum_{m=-\ell}^{\ell} \frac{\ell+1}{r^{\ell+2}} [\Phi]_{\ell}^m Y_{\ell}^m,$$

Matching coefficients yields

$$2\pi \left(\frac{\epsilon+1}{\epsilon-1} + \frac{1}{2\ell+1} \right) u_{\ell}^m = - \frac{\ell+1}{r^{\ell+2}} [\Phi]_{\ell}^m \rightarrow u_{\ell}^m = - \frac{2\ell+1}{4\pi} \frac{1}{r^{\ell+2}} [\Phi]_{\ell}^m \frac{\epsilon-1}{\epsilon + \frac{2\ell}{2\ell+2}}.$$

The PCM surface charge is therefore given by

$$\sigma(x) = - \sum_{\ell=0}^L \sum_{m=-\ell}^{\ell} \frac{2\ell+1}{4\pi} \frac{1}{r^{\ell+2}} [\Phi]_{\ell}^m \frac{\epsilon-1}{\epsilon + \frac{2\ell}{2\ell+2}} Y_{\ell}^m(\theta_x, \phi_x) \quad x \in \partial\Omega. \quad (43)$$

2.4.2 Energy of Solvation

We calculate the energy of solvation according to Equation (18). Therefore we obtain for the multipole

$$\begin{aligned} E_R^{COSMO^*} &= \frac{1}{2} \int_0^{\pi} \int_0^{2\pi} \left(- \sum_{\ell=0}^L \sum_{m=-\ell}^{\ell} \frac{2\ell+1}{4\pi} \frac{1}{r^{\ell+2}} [\Phi]_{\ell}^m Y_{\ell}^m \right) \\ &\quad \left(\sum_{\ell=0}^L \sum_{m=-\ell}^{\ell} [\Phi]_{\ell}^m \frac{1}{r^{\ell+1}} Y_{\ell}^m \right) r^2 \sin(\theta) d\varphi d\theta \\ &= - \frac{1}{8\pi} \sum_{\ell=0}^L \sum_{m=-\ell}^{\ell} \frac{2\ell+1}{r^{2\ell+1}} ([\Phi]_{\ell}^m)^2, \end{aligned} \quad (44)$$

$$\begin{aligned} E_R^{COSMO} &= \frac{\epsilon-1}{\epsilon+k} E_R^{COSMO^*} \\ &= - \frac{1}{8\pi} \frac{\epsilon-1}{\epsilon+k} \sum_{\ell=0}^L \sum_{m=-\ell}^{\ell} \frac{2\ell+1}{r^{2\ell+1}} ([\Phi]_{\ell}^m)^2, \end{aligned} \quad (45)$$

and

$$E_R^{PCM} = \frac{1}{2} \int_0^{\pi} \int_0^{2\pi} \left(- \sum_{\ell=0}^L \sum_{m=-\ell}^{\ell} \frac{2\ell+1}{4\pi} \frac{1}{r^{\ell+2}} [\Phi]_{\ell}^m \frac{\epsilon-1}{\epsilon + \frac{2\ell}{2\ell+2}} Y_{\ell}^m \right)$$

$$\begin{aligned}
& \left(\sum_{\ell=0}^L \sum_{m=-\ell}^{\ell} [\Phi]_{\ell}^m \frac{1}{r^{\ell+1}} Y_{\ell}^m \right) r^2 \sin(\theta) d\varphi d\theta \\
&= -\frac{1}{8\pi} \sum_{\ell=0}^L \sum_{m=-\ell}^{\ell} \frac{\epsilon - 1}{\epsilon + \frac{2\ell}{2\ell+2}} \frac{2\ell + 1}{r^{2\ell+1}} ([\Phi]_{\ell}^m)^2.
\end{aligned} \tag{46}$$

We observe that in case of a multipole of order L inside a spherical cavity, it holds

$$E_R^{COSMO^*} < E_R^{PCM} \quad \text{for } k > 0.$$

When comparing the constant scaling factor of the COSMO Model

$$f_{COSMO}(\epsilon) = \frac{\epsilon - 1}{\epsilon + k},$$

with the corresponding factor of the PCM model

$$f_{PCM}(\epsilon) = \frac{\epsilon - 1}{\epsilon + \frac{2\ell}{2\ell+2}},$$

we observe that the contributions to the solvation energy of multipole terms of orders $\ell > 1$ are underestimated by E^{COSMO} , since for $\ell > 1$

$$f_{PCM}(\epsilon) < f_{COSMO}(\epsilon).$$

We notice that Klamt's choice to set $k = \frac{1}{2}$ for uncharged molecules corresponds exactly to the regarding a dipole ($\ell = 1$) as the most dominant mode of the multipole expansion inside a spherical cavity. In this case the solvation energy obtained by the PCM and COSMO model are equal. Since any higher order modes will decay faster in r , the underestimation of the COSMO Model for modes $l > 1$ can be neglected at sufficiently large distances $r > r_c$.

3 Conclusion

We can conclude that in case of a spherical cavity the assumption of the solvent being perfect conductor leads to $E_R^{COSMO^*}$ being an underestimation of the electrostatic contribution to the solvation energy E_R^{PCM} . The scaling factor $f(\epsilon)$, Klamt introduces in order to account for the real solvent, leads to E_R^{COSMO} becoming an upper bound instead, given a sufficiently large choice of the k . We have seen that Klamt's choice of $k = \frac{1}{2}$ for uncharged molecules, meets the physical observations of the dipole being the most dominant mode. E_R^{COSMO} is exactly equal to E_R^{PCM} in case of a dipole in a spherical cavity. Further, $k = 0$ leads to equal energies E_R^{COSMO} and E_R^{PCM} in case of a dominating point charge and therefore corresponds to charged molecules.

The most important point to take care about in the future is to investigate the dependency of these observation for a more sophisticated shape of molecular cavity.

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