Computation of Forces arising from the Polarizable Continuum Model within the Domain-Decomposition Paradigm

Paolo Gatto,[1] Filippo Lipparini,[1] and Benjamin Stamm[1]

I. INTRODUCTION

This paper is organized as follows. Section II reviews the ddPCM and ddCOSMO methods that we have previously developed. In Section III we describe the derivation of the ddPCM forces and discuss their efficient implementation. Section IV is devoted to numerical experiments. Finally, in Section V we draw conclusions from the presented work and point to possible future directions of research.

II. A BRIEF REVIEW OF THE DDPCM STRATEGY

A. The Polarizable Continuum Model

The foundation of Polarizable Continuum Solvation Models (PCSM's) is the assumption that the solvent in a solute-solvent system can be treated as either a dielectric, or a conducting continuum medium on the outside of the molecular cavity Ω of the solute. We follow the customary approach of taking the cavity to be the so-called Van der Waals cavity[?] , i.e., the union of spheres centered at each atom with radii coinciding with the van der Waals radii. Within this approach, the topologically similar Solvent Accessible Surface (SAS) cavity can be treated as well. Models based on the Solvent Excluded Surface (SES) have recently been proposed but are not considered here.

The electrostatic part of the solute-solvent interaction is given by $E_s = \frac{1}{2}\, f(\varepsilon)\, \int_\Omega \rho(x) W(x)\, dx$, where $f(\varepsilon)$ is an empirical scaling that depends on the dielectric constant of the solvent (and which is only applied in the case of the COSMO), ρ is the charge density of the solute, and W is the polarization potential of the solvent. The quantities W and E_s are usually referred to, respectively, as the reaction potential and the electrostatic contribution to the solvation energy.

The reaction potential is defined as $W = \varphi - \Phi$, where φ is the total electrostatic potential of the solute-solvent system and Φ is the potential of the solute *in vacuo*. In the case of the PCM, the total potential φ satisfies a (generalized) Poisson equation with suitable interface conditions[? ?] . Indeed, if ε_s is the macroscopic, zero-frequency relative dielectric permittivity of the solvent, and define $\varepsilon(x) = 1$ when $x \in \Omega$ and $\varepsilon(x) = \varepsilon_s$ otherwise, the

reaction potential fulfills

$$\begin{cases} \Delta W = 0 & \text{in } \mathbb{R}^3 \setminus \Gamma \\ [W] = 0 & \text{on } \Gamma \\ [\varepsilon\, \partial_\nu W] = (\varepsilon_s - 1)\partial_\nu \Phi & \text{on } \Gamma \end{cases} \tag{1}$$

Here $\Gamma = \partial\Omega$ is the boundary of the cavity, ∂_ν is the normal derivative on Γ, and $[\,\cdot\,]$ is the jump operator (inside minus outside) on Γ.

Recalling potential theory, W can be represented as $W(x) = (\tilde{\mathcal{S}}\sigma)(x)$ when $x \in \mathbb{R}^3 \setminus \Gamma$, or $W(s) = (\mathcal{S}\sigma)(s)$ when $s \in \Gamma$. The surface density σ defined on Γ is the so-called apparent surface charge, $\tilde{\mathcal{S}}$ is the single layer potential and $\mathcal{S}$ is the single layer operator, which is invertible[?] . Note that both $\tilde{\mathcal{S}}$ and $\mathcal{S}$ are based on the surface Γ. It can be shown that σ satisfies the equation $\sigma = 1/4\pi\,[\partial_\nu W]$, so that it is possible to recast the PCM problem (1) as a single integral equation for σ. In fact, if we define the operators

$$\mathcal{R}_\varepsilon = 2\pi \frac{\varepsilon + 1}{\varepsilon - 1}\,\mathcal{I} - \mathcal{D} \qquad , \qquad \mathcal{R}_\infty = 2\pi\,\mathcal{I} - \mathcal{D} \tag{2}$$

where $\mathcal{I}$ is the identity and $\mathcal{D}$ is the double layer boundary operator (also based on Γ). It can be shown[?] that the apparent surface charge satisfies

$$\mathcal{R}_\varepsilon\, \mathcal{S}\, \sigma = -\mathcal{R}_\infty\, \Phi \qquad \text{on } \Gamma \tag{3}$$

which is known as the IEF-PCM equation. It involves operators $\mathcal{R}_\infty$ and $\mathcal{R}_\varepsilon$, which are both invertible. Furthermore, when the dielectric constant ε_s approaches infinity, the IEF-PCM equation simplifies to $\mathcal{S}\,\sigma = -\Phi$ on Γ, which is the Integral Equation Formulation of the Conductor-like Screening Model (COSMO)[?] .

B. The ddPCM-method

Let us recall how to solve equation (3) within the domain-decomposition paradigm. The first step is to write the IEF-PCM integral equation (3) as a succession of two integral equations, one of which is equivalent to the COSMO equation[?] . Indeed, if we define $\Phi_\varepsilon = \mathcal{S}\,\sigma$, equation (3) becomes

$$\mathcal{R}_\varepsilon\, \Phi_\varepsilon = \mathcal{R}_\infty\, \Phi \qquad \text{on } \Gamma \tag{4}$$

$$\mathcal{S}\,\sigma = -\Phi_\varepsilon \qquad \text{on } \Gamma \tag{5}$$

The ddPCM strategy is an extension of ddCOSMO in the following sense: first, equation (4) is solved in order to compute the right-hand side $-\Phi_\varepsilon$ of equation (5); secondly, ddCOSMO is employed to solve equation (5) with the modified potential $-\Phi_\varepsilon$, and compute the solvation energy E_s. Both steps are carried out through a domain-decomposition approach.

Step 1. As anticipated above, let the cavity Ω be the union of M spheres $\Omega_j = B(x_j, r_j)$ with boundaries Γ_j. Let $U_j : \Gamma_j \to \mathbb{R}$ be the characteristic function of $\Gamma_j^{\text{ext}} := \Gamma_j \cap \Gamma$, and define extensions $\Phi_j, \Phi_{\varepsilon,j} : \Gamma_j \to \mathbb{R}$ as $\Phi_j(s) = U_j(s)\,\widetilde{\Phi}(s)$ and $\Phi_{\varepsilon,j}(s) = U_j(s)\,\widetilde{\Phi}_\varepsilon(s)$ for $s \in \Gamma_j$, where $\tilde{(\cdot)}$ indicates the trivial extension to $\overline{\Omega}$.

First, we enforce (4) on each Γ_j^{ext} and $\Phi_{\varepsilon,j} = 0$ on Γ_j^{int} by one joint equation

$$\alpha(1 - U_j)\Phi_{\varepsilon,j} + U_j\left(\mathcal{R}_\varepsilon\,\Phi_\varepsilon\right) = U_j\left(\mathcal{R}_\infty\,\Phi\right) \qquad \text{on } \Gamma_j \tag{6}$$

for any $\alpha > 0$.

Second, since we extended the both $\Phi_j, \Phi_{\varepsilon,j}$ trivially on Γ_j^{int}, the double layer operator $\mathcal{D}$ can be decomposed as

$$(\mathcal{D}\,\Phi)(s) = (\mathcal{D}_j\,\Phi_j)(s) + \sum_{k\neq j}(\tilde{\mathcal{D}}_k\,\Phi_k)(s)$$

where $\mathcal{D}_j$ and $\tilde{\mathcal{D}}_j$ are, respectively, the local double layer operator and the local double layer potential on Γ_j. We refer to[?] for concise details for these operators. Thus, we can also decompose $\mathcal{R}_\varepsilon$ in (6) as

$$\mathcal{R}_\varepsilon\,\Phi_\varepsilon = \mathcal{R}_{\varepsilon,j}\,\Phi_{\varepsilon,j} + \sum_{k\neq j}\tilde{\mathcal{R}}_{\varepsilon,k}\,\Phi_{\varepsilon,k} \qquad \text{on } \Gamma_j^{\text{ext}} \tag{7}$$

where the operators $\mathcal{R}_{\varepsilon,j}$ and $\tilde{\mathcal{R}}_{\varepsilon,j}$ are defined as

$$\mathcal{R}_{\varepsilon,j} = 2\pi\frac{\varepsilon+1}{\varepsilon-1}\,\mathcal{I} - \mathcal{D}_j \qquad , \qquad \tilde{\mathcal{R}}_{\varepsilon,j} = -\tilde{\mathcal{D}}_j$$

with the obvious extension to the case $\varepsilon = \infty$.

Inserting (7) into (6), in combination with the particular choice $\alpha = 2\pi(\varepsilon+1)/(\varepsilon-1)$, yields a convenient form in terms of the local double layer potentials and double layer operators:

$$2\pi\,\frac{\varepsilon+1}{\varepsilon-1}\,\Phi_{\varepsilon,j} - U_j\left(\mathcal{D}_j\Phi_{\varepsilon,j} + \sum_{k\neq j}\tilde{\mathcal{D}}_k\,\Phi_{\varepsilon,k}\right) = 2\pi\,U_j\Phi_j - U_j\left(\mathcal{D}_j\Phi_j + \sum_{k\neq j}\tilde{\mathcal{D}}_k\,\Phi_k\right) \qquad \text{on } \Gamma_j \tag{8}$$

This constitutes our domain-decomposition strategy for equation (4). It is important to remark that, because of the summation, every subdomain Ω_j interacts with all other subdomains. We anticipate that this contrasts with the ddCOSMO strategy for equation (5).

Step 2. Local problems for equation (5) arise from the fact that each restriction $W_j := W|_{\overline{\Omega}_j}$ is harmonic over each subdomain Ω_j. Thus, it can be represented as

$$W_j(x) = (\tilde{\mathcal{S}}_j\,\sigma_j)(x) \quad , \quad x \in \Omega_j \qquad ; \qquad W_j(s) = (\mathcal{S}_j\,\sigma_j)(s) \quad , \quad s \in \Gamma_j \tag{9}$$

where σ_j is an unknown surface charge, and $\mathcal{S}_j$ and $\tilde{\mathcal{S}}_j$ are, respectively, the single layer potential and the single layer operator on Γ_j. The local problems (9), are coupled together by decomposing W_j as

$$W_j(s) = -U_j(s)\,\Phi_{\varepsilon,j}(s) + \big(1 - U_j(s)\big)\,n_j(s) \sum_{k \in N_j} W_k(s) \qquad s \in \Gamma_j \tag{10}$$

where N_j is the set of all neighboring subdomains of Ω_j, W_k is understood as its trivial extension to Ω, and n_j is a normalization factor. If s does not belong to any neighbor of Ω_j, then $n_j(s)$ vanishes. Otherwise, $n_j(s)$ is the reciprocal of the number of neighbors. When we substitute the local problems (9) into the decomposition (10), and define $(\tilde{\mathcal{S}}_{jk}\,\sigma_k)(s) = n_j(s)\,(\tilde{\mathcal{S}}_k\,\sigma_k)(s)$, we obtain

$$\mathcal{S}_j\,\sigma_j = -U_j\,\Phi_{\varepsilon,j} + \big(1 - U_j(s)\big) \sum_{k \in N_j} \tilde{\mathcal{S}}_{jk}\,\sigma_k \qquad \text{on } \Gamma_j \tag{11}$$

As opposed to the local problem (8) which features a global interaction of all subdomains, the ddCOSMO step (11) is characterized by the interaction of subdomain Ω_j with only its neighbors. This results in a sparse, rather than dense, discrete operator.

We discretize equation (8) and (11) by expanding Φ_j, $\Phi_{\varepsilon,j}$ and σ_j as truncated series of spherical harmonics. If Y_ℓ^m indicates the spherical harmonic of degree ℓ and order m on the unit sphere $\mathbb{S}$, we approximate the surface charge σ_j as

$$\sigma_j(s) = \sigma_j(x_j + r_j y) = \sum_{\ell=0}^{L_{\max}} \sum_{m=-\ell}^{\ell} [X_j]_\ell^m\, Y_\ell^m(y)$$

If I understand correctly, the σ_j is not scaled as in the ddCOSMO-papers. for some unknown coefficients $X = [X_j]_\ell^m$ and a prescribed integer parameter $L_{\max}$. Here y is the variable on $\mathbb{S}$. We approximate $\Phi_{\varepsilon,j}$ and Φ_j in the same fashion, namely

$$\Phi_{\varepsilon,j} = -\sum_{\ell=0}^{L_{\max}} \sum_{m=-\ell}^{\ell} [G_j]_\ell^m\, Y_\ell^m \qquad , \qquad \Phi_j = -\sum_{\ell=0}^{L_{\max}} \sum_{m=-\ell}^{\ell} [F_j]_\ell^m\, Y_\ell^m$$

where $G = [G_j]_\ell^m$ and $F = [F_j]_\ell^m$ are the coefficients of the expansions, and the minus signs have been introduced for convenience. In the following, we shall use the condensed notation $\sum_{\ell,m}$ to indicate the double sum. We interpret each local problem (8) and (11) in a variational setting that uses spherical harmonics as test functions, see Appendix A. We employ orthogonality conditions of the spherical harmonics, along with Lebedev grids to perform numerical quadrature to derive discretizations of the global problems (4) and (5). Respectively, we obtain

$$A_\varepsilon\, G = A_\infty\, F \qquad , \qquad L\, X = G \tag{12}$$

and the expressions for the entries of the discrete operator A_ε are given in (A2) and (A3).

III. COMPUTATION OF FORCES

The solvation energy can be written as a sum of subdomain contributions, which perfectly fits the ddCOSMO paradigm.

First, for a classical solute's charge distribution of the form of $\rho = \sum_j q_j \delta_{x_j}$, we can develop

$$E_s = \frac{1}{2} \int_\Omega \rho(x) W(x)\, dx = \frac{1}{2} \sum_j q_j W(x_j)$$

This easily generalizes to point multipolar charge distributions.

Indeed, the spherical harmonics addition theorem implies that

$$W_j(x) = (\tilde{\mathcal{S}}_j\, \sigma_j)(x) = \sum_{\ell,m} [X_j]_\ell^m (\tilde{\mathcal{S}}_j\, Y_\ell^m)(x) = \sum_{\ell,m} [X_j]_\ell^m \frac{4\pi}{2\ell+1} \frac{r^\ell}{r_j^{\ell+1}}\, Y_\ell^m(y)$$

where $x = x_j + r\, y$, so that the solvation energy can be determined as

$$E_s = \tfrac{1}{2} \sum_{j=1}^M \int_{\Omega_j} \rho(x) W_j(x)\, dx = \tfrac{1}{2} \sum_{j=1}^M \sum_{\ell,m} [X_j]_\ell^m \frac{4\pi}{2\ell+1} \frac{1}{r_j^{\ell+1}} \int_{\Omega_j} \rho(x)\, r^\ell\, Y_\ell^m(y)\, dx$$

If we define

$$[\Psi_j]_\ell^m = \frac{4\pi}{2\ell+1} \frac{1}{r_j^{\ell+1}} \int_{\Omega_j} \rho(x)\, r^\ell\, Y_\ell^m(y)\, dx$$

we can compactly write the energy as

$$E_s = \tfrac{1}{2} \sum_j \sum_{\ell,m} [\Psi_j]_\ell^m [X_j]_\ell^m =: \tfrac{1}{2} \langle \Psi, X \rangle$$

where the angular brackets indicate the double scalar product over j and ℓ, m.

The force acting on the i-th particle can be computed as

$$\mathcal{F}_i = -\nabla E_s = -\tfrac{1}{2}\, f(\varepsilon)\, \langle \Psi, \nabla X \rangle$$

where the gradient is understood with respect to x_i. Here we used the fact that Ψ is independent of the atomic positions. On the other hand, since both the COSMO operator and right-hand side depend on $x_1, \ldots, x_M$, so does the unknown X. The idea is consider the adjoint problem $(A_\varepsilon\, L)^* s = \Psi$ and compute the quantity $\langle \Psi, \nabla X \rangle = \langle s, A_\varepsilon\, L\, \nabla X \rangle$ through an integration-by-parts-like approach.

If combine equations (12), the fully discretized problem becomes $A_\varepsilon\, L\, X = A_\infty\, F$, and Leibnitz differentiation rule allows to move derivatives from X onto the other terms, namely

$$A_\varepsilon\, L\, \nabla X = \nabla A_\infty\, F + A_\infty\, \nabla F - \nabla A_\varepsilon\, L\, X - A_\varepsilon\, \nabla L\, X =: h$$

Thus, once the solution s of the adjoint problem and vector h have been determined, the forces can be computed as

$$\mathcal{F}_i = -\tfrac{1}{2}\, f(\varepsilon)\, \langle s, h \rangle$$

The derivatives ∇L of the ddCOSMO discretization were discussed in. The quantity ∇F is *a priori* nonzero since F_j is the discretization of $\Phi_j = U_j\, \tilde{\Phi}$. In remainder of this section we discuss the derivatives of the ddPCM matrix.

Let $\{s_n\}$ be the N_{grid} Lebedev integration points and define the following quantities

$$t_n^{jk} = \frac{|x_j + r_j s_n - x_k|}{r_k} \quad , \quad s_n^{jk} = \frac{x_j + r_j s_n - x_k}{|x_j + r_j s_n - x_k|} \quad , \quad U_j^n = U_j(x_j + r_j s_n)$$

The blocks A_{jk}^ε of the ddPCM matrix A_ε, see (A2) and (A3), have the form

$$[A_{jj}^\varepsilon]_{\ell\ell'}^{mm'} = 2\pi\, \frac{\varepsilon + 1}{\varepsilon - 1}\, \delta_{\ell\ell'}\delta_{mm'} + \frac{2\pi}{2\ell' + 1} \sum_{n=1}^{N_{\text{grid}}} w_n\, U_j^n\, Y_\ell^m(s_n)\, Y_{\ell'}^{m'}(s_n)$$

$$[A_{jk}^\varepsilon]_{\ell\ell'}^{mm'} = \qquad\qquad - \frac{4\pi\ell'}{2\ell' + 1} \sum_{n=1}^{N_{\text{grid}}} w_n\, U_j^n\, Y_\ell^m(s_n)\, \left(t_n^{jk}\right)^{-(\ell'+1)}\, Y_{\ell'}^{m'}(s_n^{jk})$$

where $\{w_n\}$ are the weights associated to the integration points. Since the derivatives are independent of ε, we drop the ε-dependency for ease of notation.

The case of the diagonal blocks yields

$$[\nabla A_{jj}]_{\ell\ell'}^{mm'} = \frac{2\pi}{2\ell' + 1} \sum_n w_n\, \nabla U_j^n\, Y_\ell^m(s_n)\, Y_{\ell'}^{m'}(s_n)$$

so that it only requires the derivatives of the characteristic function. The function U_j is, in practice, a smoothed version of the (discontinuous!) characteristic function, and is defined as

$$U_j(x_j + r_j y) = \begin{cases} 1 - f_j(y) & f_j(y) \leq 1 \\ 0 & \text{otherwise} \end{cases} \quad , \qquad f_j(y) = \sum_{k \in N_j} \chi\left(\frac{|x_j + r_j y - x_k|}{r_k} \right)$$

where y varies on $\mathbb{S}^2$ and χ is a regularized characteristic function of $[0, 1]$. We conclude that ∇U_j and, consequently, ∇A_{jj} are *a priori* nonzero only when $i \in N_j$ or $i = j$.

The case of the off-diagonal blocks, i.e., $j \neq k$, is more involved since it includes the gradient of the product of three functions, namely

$$[\nabla A_{jk}]_{\ell\ell'}^{mm'} = -\frac{4\pi\ell'}{2\ell'+1} \sum_n w_n \, Y_\ell^m(s_n) \, \nabla \Big[U_j^n \left(t_n^{jk}\right)^{-(\ell'+1)} Y_{\ell'}^{m'}(s_n^{jk}) \Big] \tag{13}$$

However, since t_n^{jk} and s_n^{jk} depend only upon x_j and x_k, if we assume $i \neq j$ and $i \neq k$, we obtain

$$[\nabla A_{jk}]_{\ell\ell'}^{mm'} = -\frac{4\pi\ell'}{2\ell'+1} \sum_n w_n \, Y_\ell^m(s_n) \, \nabla U_j^n \left(t_n^{jk}\right)^{-(\ell'+1)} Y_{\ell'}^{m'}(s_n^{jk}) \tag{14}$$

Thus, since U_j depends only upon x_i such that $i \in N_j$, we conclude that ∇A_{jk} vanishes whenever $i \neq j$ and $i \neq k$ and $i \notin N_j$. In order to discuss the opposite case, i.e., $i = j$ or $i = k$ or $i \in N_j$, notice that the events $(i = j)$ and $(i = k)$ are mutually exclusive, as are $(i = j)$ and $(i \in N_j)$. We obtain the subcases $i = j$, and $i = k$, and $i \in N_j$, $i \neq k$, which we address individually.

Standard differentiation implies that

$$\begin{aligned} \nabla \Big[U_j^n \left(t_n^{jk}\right)^{-(\ell'+1)} Y_{\ell'}^{m'}(s_n^{jk}) \Big] &= \nabla U_j^n \left(t_n^{jk}\right)^{-(\ell'+1)} Y_{\ell'}^{m'}(s_n^{jk}) - \\ &+ U_j^n \, (\ell'+1) \left(t_n^{jk}\right)^{-(\ell'+2)} \nabla t_n^{jk} \, Y_{\ell'}^{m'}(s_n^{jk}) + U_j^n \left(t_n^{jk}\right)^{-(\ell'+1)} \left(D \, s_n^{ji}\right)^T \nabla Y_{\ell'}^{m'}(s_n^{jk}) \end{aligned} \tag{15}$$

where D emphasizes that the gradient of the vector quantity s_j^{jk} is indeed its Jacobian matrix. We proceed to evaluate ∇t_n^{jk} and $D \, s_n^{jk}$. When $i = j$, differentiation implies

$$\nabla t_n^{jk} = \frac{s_n^{jk}}{r_k} \qquad , \qquad D \, s_n^{jk} = \frac{I - s_n^{jk} \otimes s_n^{jk}}{|x_j + r_j s_n - x_k|^3}$$

where I is the identity matrix and $\otimes$ indicates the outer product. We remark that the Jacobian matrix $D \, s_n^{jk}$ is symmetric, so that the transpose in (15) is redundant. Analogously,

the case $i = k$ yields $\nabla_j\, t_n^{jk} = -\nabla_k\, t_n^{jk}$ and $D_j\, s_n^{jk} = -D_k\, s_n^{jk}$, where the extra subscripts refer to the variables with respect to which differentiation is taken. Those relationships imply

$$\nabla_j\Big[U_j^n\,\big(t_n^{jk}\big)^{-(\ell'+1)}\,Y_{\ell'}^{m'}(s_n^{jk})\Big] + \nabla_k\Big[U_j^n\,\big(t_n^{jk}\big)^{-(\ell'+1)}\,Y_{\ell'}^{m'}(s_n^{jk})\Big] = \Big[\nabla_j\, U_j^n + \nabla_k\, U_j^n\Big]\big(t_n^{jk}\big)^{-(\ell'+1)}\,Y_{\ell'}^{m'}(s_n^{jk})$$

which provide a convenient way of evaluating $[\nabla_k\, A_{jk}]_{\ell\ell'}^{mm'}$ from $[\nabla_j\, A_{jk}]_{\ell\ell'}^{mm'}$. In fact, we obtain the quasi-skew-symmetric relation

$$[\nabla_j\, A_{jk}]_{\ell\ell'}^{mm'} + [\nabla_k\, A_{jk}]_{\ell\ell'}^{mm'} = -\frac{4\pi\ell'}{2\ell'+1}\,\sum_n w_n\, Y_\ell^m(s_n)\Big[\nabla_j\, U_j^n + \nabla_k\, U_j^n\Big]\big(t_n^{jk}\big)^{-(\ell'+1)}\,Y_{\ell'}^{m'}(s_n^{jk})$$

for ∇A_{jk}. Finally, the case $i \in N_j$, $i \neq k$ reduces to (14).

IV. NUMERICAL EXPERIMENTS

V. CONCLUSIONS

ACKNOWLEDGMENTS

Appendix A: ddPCM discretization

The derivation ddPCM discrete operator A_{jk}^ε rests upon the fact that the spherical harmonics Y_ℓ^m are eigenfunctions of the double layer potential on $\mathbb{S}$, i.e., $\mathcal{D}\, Y_\ell^m = -2\pi/(2\ell+1)\, Y_\ell^m$, along with the following jump relation for the double layer operator

$$\lim_{\delta\to\pm 0}\big(\tilde{\mathcal{D}}\, Y_\ell^m\big)(y \pm \delta\nu) = \pm 2\pi\, Y_\ell^m(y) + (\mathcal{D}\, Y_\ell^m)(y) \tag{A1}$$

where ν denotes the outward normal at $y \in \mathbb{S}$. We shall employ the translation-invariance property $(\mathcal{D}_j\, \Phi_{\varepsilon,j})(s) = (\mathcal{D}\, \hat{\Phi}_{\varepsilon,j})(y)$, where $y = (s - x_j)/r_j$ and $\hat{\Phi}_{\varepsilon,j}$ is defined on $\mathbb{S}$ through the push-forward-like transformation $\hat{\Phi}_{\varepsilon,j}(y) = \Phi_{\varepsilon,j}(s)$. We begin by discussing the diagonal term $2\pi f_\varepsilon\, \Phi_{\varepsilon,j} - U_j\, \mathcal{D}_j\, \Phi_{\varepsilon,j}$ where, for brevity, we set $f_\varepsilon = (\varepsilon+1)/(\varepsilon-1)$. As customary, in order to obtain a numerical discretization, we multiply by a test function φ and integrate over Γ_j. The change of variable $y = (s - x_j)/r_j$, yields an integral over $\mathbb{S}$ which involves the hatted quantities, namely

$$\int_{\Gamma_j}\big(2\pi f_\varepsilon\, \Phi_{\varepsilon,j} - U_j\, \mathcal{D}_j\, \Phi_{\varepsilon,j}\big)\,\varphi = 2\pi\, f_\varepsilon\, r_j^2\,\int_{\mathbb{S}} \hat{\Phi}_{\varepsilon,j}\,\hat{\varphi} - r_j^2\,\int_{\mathbb{S}} \hat{U}_j\,\mathcal{D}\,\hat{\Phi}_{\varepsilon,j}\,\hat{\varphi}$$

We proceed to expand $\hat{\Phi}_{\varepsilon,j}$ as a series of spherical harmonics with coefficients $-[G_j]_{\ell'}^{m'}$, and select as a test function $\hat{\varphi}$ the rescaled spherical harmonic $r_j^{-2}\, Y_\ell^m$. The orthogonality of the spherical harmonics, together with the fact that they are eigenfunctions of the double layer potential, yield

$$\int_{\Gamma_j} \left(2\pi f_\varepsilon\, \Phi_{\varepsilon,j} - U_j\, \mathcal{D}_j\, \Phi_{\varepsilon,j}\right) \varphi = \\ = -2\pi\, f_\varepsilon \sum_{\ell',m'} [G_j]_{\ell'}^{m'}\, \delta_{\ell\ell'}\delta_{mm'} - \sum_{\ell',m'} [G_j]_{\ell'}^{m'}\, \frac{2\pi}{2\ell'+1} \int_{\mathbb{S}} \hat{U}_j\, Y_{\ell'}^{m'}\, Y_\ell^m$$

The last step to obtain the diagonal block A_{jj}^ε is to approximate the integral through a suitable quadrature formula with weights $\{w_n\}$ and nodes $\{s_n\}$. Once the numerical quadrature is carried out and the spherical harmonics expansion is truncated, we derive the final expression

$$[A_{jj}^\varepsilon]_{\ell\ell'}^{mm'} = 2\pi\, \frac{\varepsilon+1}{\varepsilon-1}\, \delta_{\ell\ell'}\delta_{mm'} + \frac{2\pi}{2\ell'+1} \sum_{n=1}^{N_{\mathrm{grid}}} w_n\, \hat{U}_j(s_n)\, Y_{\ell'}^{m'}(s_n)\, Y_\ell^m(s_n) \tag{A2}$$

The computation of the off-diagonal term $-U_j\, \tilde{\mathcal{D}}_k\, \Phi_{\varepsilon,k}$ employes the fact that the double layer operator satisfies the translation-invariance property $(\tilde{\mathcal{D}}_k\, \Phi_{\varepsilon,k})(x) = (\tilde{\mathcal{D}}\, \hat{\Phi}_{\varepsilon,k})(u)$ where $x \in \mathbb{R}^3 \setminus \overline{\Omega}_k$ and $u = (x - x_k)/r_k$. In particular, when $x \in \Gamma_j$, i.e., $x = s = x_j + r_j y$ for some $y \in \mathbb{S}$, then $u = u(y) = (x_j + r_j y - x_k)/r_k$. As the quantity $U_j\, \tilde{\mathcal{D}}_k\, \Phi_{\varepsilon,k}$ in indeed well-defined on the whole Γ_j, we can proceed as before and obtain

$$\int_{\Gamma_j} U_j(s)\, (\tilde{\mathcal{D}}_k\, \Phi_{\varepsilon,k})(s)\, \varphi(s)\, ds = \int_{\mathbb{S}} \hat{U}_j(y)\, (\tilde{\mathcal{D}}\, \hat{\Phi}_{\varepsilon,k})(u(y))\, Y_\ell^m(y)\, dy = \\ = -\sum_{\ell',m'} [G_k]_{\ell'}^{m'} \int_{\mathbb{S}} \hat{U}_j(y)\, (\tilde{\mathcal{D}}\, Y_{\ell'}^{m'})(u(y))\, Y_\ell^m(y)\, dy$$

where $-[G_k]_{\ell'}^{m'}$ are the coefficients of the expansion of $\hat{\Phi}_{\varepsilon,k}$ as a series of spherical harmonics. The function $\tilde{\mathcal{D}}\, Y_{\ell'}^{m'}$ is harmonic on $\mathbb{R}^3 \setminus \overline{B(0,1)}$, so that is has to coincide with the unique harmonic extension of its boundary value. The jump relation (A1), along with the eigenfunction property, provide the boundary value

$$\lim_{\delta \downarrow 0} \left(\tilde{\mathcal{D}}\, Y_{\ell'}^{m'}\right)(y + \delta\nu) = 2\pi\, Y_{\ell'}^{m'}(y) + \left(\mathcal{D}\, Y_{\ell'}^{m'}\right)(y) = \frac{4\pi\ell'}{2\ell +' 1}\, Y_{\ell'}^{m'}(y)$$

and, by elementary notions on harmonic functions, we conclude

$$(\tilde{\mathcal{D}}\, Y_{\ell'}^{m'})(u) = \frac{4\pi\ell'}{2\ell'+1}\, \frac{1}{|u|^{\ell'+1}}\, Y_{\ell'}^{m'}(u/|u|)$$

After truncation the series expansion and performing numerical integration we obtain the final result

$$[A_{jk}]^{mm'}_{\ell\ell'} = -\frac{4\pi\ell'}{2\ell'+1}\sum_{n=1}^{N_{\text{grid}}} w_n\,\hat{U}_j(s_n)\,\frac{1}{|u(s_n)|^{\ell'+1}}\,Y_{\ell'}^{m'}(u(s_n)/|u(s_n)|)\,Y_\ell^m(s_n) \qquad \text{(A3)}$$

This concludes the derivation of the ddPCM discretization.

Appendix B: ddCOSMO discretization

Here, just for convenience, we repeat some ddCOSMO equations and derivations. This will not be included in the article.

Single layer potential:

$$(\tilde{\mathcal{S}}_j\,\sigma^j)(x) = \int_{\Gamma_j}\frac{\sigma^j(s')}{|s'-x|}\,ds' \quad , \quad x\in\Omega_j$$

Single layer operator:

$$(\mathcal{S}_j\,\sigma^j)(s) = \int_{\Gamma_j}\frac{\sigma_j(s')}{|s'-s|}\,ds' \quad , \quad s\in\Gamma_j$$

We defined

$$W_j(x) = (\tilde{\mathcal{S}}^j\,\sigma^j)(x) \quad , \quad x\in\Omega_j \qquad ; \qquad W_j(s) = (\mathcal{S}_j\,\sigma^j)(s) \quad , \quad s\in\Gamma_j \qquad \text{(B1)}$$

and the ddCOSMO-equations become

$$W_j(s) = -U_j(s)\,\Phi_{\varepsilon,j}(s) + \big(1-U_j(s)\big)\,n_j(s)\sum_{k\in N_j} W_k(s) \qquad s\in\Gamma_j \qquad \text{(B2)}$$

This is equivalent to

$$(\mathcal{S}_j\,\sigma^j)(s) = -U_j(s)\,\Phi_{\varepsilon,j}(s) + \big(1-U_j(s)\big)\,n_j(s)\sum_{k\in N_j}(\tilde{\mathcal{S}}_k\,\sigma^k)(s) \qquad s\in\Gamma_j \qquad \text{(B3)}$$

In practise, we rescale σ^j:

$$\sigma^j(x_j + r_j\hat{s}) = \tfrac{1}{r_j}\sigma_j(\hat{s}) \qquad \Leftrightarrow \qquad \sigma^j(s) = \tfrac{1}{r_j}\sigma_j\left(\tfrac{s-x_j}{r_j}\right), \qquad \hat{s}\in\mathbb{S}^2, s\in\Gamma_j.$$

Then

$$(\mathcal{S}_j\,\sigma^j)(s) = \int_{\Gamma_j}\frac{\sigma^j(s')}{|s'-s|}\,ds' = \tfrac{1}{r_j}\int_{\Gamma_j}\frac{\sigma_j\left(\frac{s'-x_j}{r_j}\right)}{|s'-s|}\,ds' \quad , \quad s\in\Gamma_j$$

and

$$(\tilde{\mathcal{S}}_j\,\sigma_j)(x) = \int_{\Gamma_j}\frac{\sigma_j(s')}{|s'-x|}\,ds' = \int_{\Gamma_j}\frac{\sigma_j(s')}{|s'-x|}\,ds' \quad , \quad x\in\Omega_j$$