New applications of integral equations methods for Solvation Continuum Models: ionic solutions and liquid crystals [*]

Eric Cancès [†] & Benedetta Mennucci [‡]

[†] CERMICS
Ecole Nationale des Ponts et Chaussées,
6 & 8 Avenue Blaise Pascal, Cité Descartes, Champs-sur-Marne ,
77455 Marne-la-Vallée Cedex 2, France

[‡] Dipartimento di Chimica e Chimica Industriale,
Università di Pisa, Via Risorgimento, 35
56216 Pisa, Italy

Abstract

We present a new method for solving numerically the equations associated with solvation continuum models, which also works when the solvent is an anisotropic dielectric or an ionic solution. This method is based on the integral equation formalism. Its theoretical background is set up and some numerical results for simple systems are given. This method is much more effective than three dimensional methods used so far, like finite-elements or finite-differences, in terms of both numerical accuracy and computational costs.

1 Introduction

Solvent effects play a crucial role in most of the chemical and biological processes. A convenient and fruitful way to deal with such effects in Molecular Mechanics or Quantum Chemistry calculations consists in making use of the so-called *solvation continuum models*. In particular the present paper focuses on a specific example of this kind of models, namely the *Polarizable Continuum Model* (in short PCM),

---

[*] Submitted to Journal of Mathematical Chemistry.

which has spread out since its introduction in 1981 [1] because of its adaptability and accuracy; in this method the solute molecule under study is located inside a molecular cavity surrounded by a dielectric medium which models the solvent (see Figure 1).

Fig. 1 - Scheme of solvation in the Polarizable Continuum Model.

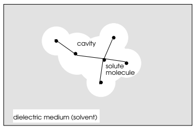

Figure 1: Scheme of solvation in the Polarizable Continuum Model

We refer the reader to [2] for a comprehensive review of the whole class of these models, with particular attention to PCM, and of the various numerical methods in use for solving the corresponding equations.

One of the basic quantities that has to be computed is the electrostatic interaction between two charge distributions ρ and ρ' carried by the solute molecule. In PCM, this interaction takes into account the polarization of the dielectric medium modelling the solvent. Its mathematical expression reads

$$E_I(\rho, \rho') = \int_{\mathbb{R}^3} \rho'(x) V(x)\, dx,$$

where $V(x)$ is the electrostatic potential generated by the charge distribution $\rho(x)$. For standard PCM, it is solution to the equation

$$-\mathrm{div}(\epsilon(x) \nabla V(x)) = \rho(x), \tag{1.1}$$

with $\epsilon(x) = 1$ inside the cavity and $\epsilon(x) = \epsilon_s$ outside (ϵ_s denotes the macroscopic dielectric constant of the solvent, $\epsilon_s = 78.6$ for water).

Equation 1.1 fully accounts for the dielectric polarization phenomenon.This equation may be rewritten as

$$-\Delta V = \rho + \rho_a, \tag{1.2}$$

where ρ_a may be regarded as an apparent charge. It is easy to see that, when ρ is located inside the cavity, the apparent charge ρ_a is supported on the interface Γ. Indeed, inside the cavity (in Ω_i), $\epsilon(x) = 1$ and then $\rho_a = -\Delta V + \mathrm{div}(\epsilon \nabla V) = -\Delta V + \Delta V = 0$, and outside the cavity (in Ω_e), $\epsilon(x) = \epsilon_s$ and therefore $\rho_a = -\Delta V + \mathrm{div}(\epsilon \nabla V) = -\frac{1-\epsilon_s}{\epsilon_s}\mathrm{div}(\epsilon \nabla V) = \frac{1-\epsilon_s}{\epsilon_s}\rho = 0$, as $\rho = 0$ in Ω_e. A classical way to get the electrostatic energy E_I consists in computing the surface density σ of the apparent charge ρ_a by an integral equation method. This technique allows one to transform the three dimensional problem (1.1) which is, moreover, posed on an unbounded domain, namely $\mathbb{R}^3$, into a two dimensional problem posed on the bounded domain Γ (see [2], and [3] for instance for the mathematical aspects). This significantly reduces the computational effort.

Over the last few years, some extensions of the standard solvation continuum models have been proposed to cover the cases when the solvent is an ionic solution or a liquid crystal.

In the former case [4], equation (1.1) is replaced by the so-called linearized Poisson-Boltzmann Equation

$$-\mathrm{div}(\epsilon(x)\nabla V(x)) + \epsilon(x)\kappa^2(x)V(x) = \rho(x), \tag{1.3}$$

with

$$\epsilon(x) = \begin{cases} 1 & \text{if } x \in \Omega_i, \\ \epsilon_s & \text{if } x \in \Omega_e, \end{cases}$$

and

$$\kappa(x) = \begin{cases} 0 & \text{if } x \in \Omega_i, \\ \kappa_s & \text{if } x \in \Omega_e. \end{cases}$$

The constant κ_s accounts for the ion screening: $1/\kappa_s$ is the Debye lenght.

In the latter case [5], equation (1.1) keeps the same formal expression,

$$-\mathrm{div}(\underline{\underline{\epsilon}}(x) \cdot \nabla V(x)) = \rho(x), \tag{1.4}$$

but the dielectric constant $\underline{\underline{\epsilon}}(x)$ is no longer a scalar: it is a 3×3 anisotropic symmetric tensor so that

$$\underline{\underline{\epsilon}}(x) = \begin{cases} \underline{\underline{I}}_3 & \text{if } x \in \Omega_i, \\ \underline{\underline{\epsilon}}_s & \text{if } x \in \Omega_e, \end{cases}$$

($\underline{\underline{I}}_3$ denotes here the 3×3 unit tensor).

In both cases, it is of course still possible to define an apparent charge ρ_a by equation (1.2), but this charge is now supported both on the interface Γ and in the external medium Ω_e. That is why integral equation methods have not been applied, so far as we know, in those cases: until now three dimensional methods have been used, like the finite difference method (FDM) for the Poisson-Boltzmann equation (1.3) [4], or a finite element type method (FEM) for equation (1.4) [5].

Our purpose here is to show that integral equation methods, which are more competitive in terms of computational effort, may actually also be used in these two cases.

In Section 2, we present the theoretical bases which underlie the method that we propose. We have chosen to collect in Section 2.1 what is necessary to know for implementing this method. We believe that the proofs of these mathematical results are useful for a deep understanding of the method. Nevertheless, we have regrouped them in Section 2.2, which is independant from the others. Thus, the reader who is less interested by the mathematical counterpart of this work, may easily skip Section 2.2, and proceed directly to Section 3 where we show how to implement these results in Hartree-Fock calculations, and where we give some satisfactory numerical results for real chemical systems. Conclusions and trends for future work concerning analytical derivatives and inhomogeneous external media are presented in Section 4.

2 Theoretical background

Let us consider two charge distributions, both located inside the cavity Ω_i. Our aim is to compute the interaction energy

$$E_I(\rho, \rho') = \int_{\mathbb{R}^3} \rho' V,$$

where the electrostatic potential V is the unique solution (in a suitable functional space) to equation (1.1) for the standard PCM, (1.3) for ionic solutions, or (1.4) for liquid crystals.

2.1 The integral equation approach

Notations: If u is a function defined on $\mathbb{R}^3$ such that $u|_{\Omega_i}$ and $u|_{\Omega_e}$ are "regular enough", we denote by u_i (resp. u_e) the trace of $u|_{\Omega_i}$ (resp. $u|_{\Omega_e}$) on the interface Γ, and by $[u] = u_i - u_e$ the jump of u passing through Γ. The usual scalar product on $L^2(\Gamma)$ is denoted $\langle \cdot, \cdot \rangle_\Gamma$ (for all v and w in $L^2(\Gamma)$, $\langle u, v \rangle_\Gamma = \int_\Gamma uv$).

We first notice that the three equations (1.1), (1.3) and (1.4) may be unified under the same formalism

$$(I)\begin{cases} L_iV = \rho & \text{in } \Omega_i, \\ L_eV = 0 & \text{in } \Omega_e, \\ [V] = 0 & \text{on } \Gamma, \\ [\partial_L V] = 0 & \text{on } \Gamma. \end{cases} \tag{2.5}$$

The operators $L_i = -\Delta$ and L_e are second-order elliptic partial differential operators with constant coefficients. We have

- $L_e u = -\epsilon_s \Delta u$ for the standard PCM (1.1),
- $L_e u = -\epsilon_s \Delta u + \epsilon_s \kappa_s^2 u$ for ionic solutions (1.3),
- $L_e u = -\mathrm{div}(\underline{\underline{\epsilon}}_s \cdot \nabla u)$ for liquid crystals (1.4).

The jump condition $[V] = 0$ means that the potential V in continuous across the interface Γ. With the notations defined above, this condition reads

$$V_i - V_e = 0 \qquad \text{on } \Gamma.$$

The equality $[\partial_L V] = 0$ is a formal expression of the jump condition of the gradient of the potential. The jump of the gradient only depends on the second-order terms of the operators L_i and L_e. The condition $[\partial_L V] = 0$ may be written as

$$\partial V_i - \partial V_e = 0 \qquad \text{on } \Gamma, \tag{2.6}$$

with, for all $x \in \Gamma$

$$\partial V_i(x) = (\nabla u)_i(x) \cdot n(x) = \left(\frac{\partial u}{\partial n}\right)_i (x)$$

and

$$\partial V_e(x) = (\epsilon_s \cdot (\nabla u)_e(x)) \cdot n(x),$$

where $n(x)$ is the outward pointing normal at point x.

For the cases of the standard PCM (1.1) and of the ionic solutions (1.3), i.e. when the dielectric constant is a scalar, equation (2.6) takes the well-known form

$$\left(\frac{\partial V}{\partial n}\right)_i - \epsilon_s \left(\frac{\partial V}{\partial n}\right)_e = 0.$$

What permits the use of integral equations to get the potential V is the knowledge of analytical expressions for the Green functions G_i and G_e of L_i and L_e considered as operators on $\mathbb{R}^3$. As explained below, this enables us to transform the first two equations in (I) into integral equations on Γ, that can be easily solved with standard numerical methods.

It is well known that the Green function of the operator $L_i = -\Delta$ on $\mathbb{R}^3$ is

$$G_i(x,y) = \frac{1}{4\pi|x-y|} \qquad \forall (x,y) \in \mathbb{R}^3 \times \mathbb{R}^3 \quad x \neq y.$$

We recall that, if ρ_0 is a charge distribution in $\mathbb{R}^3$, the potential

$$\phi_0(x) = \int_{\mathbb{R}^3} \rho_0(y) G_i(x,y)\, dy$$

is the Newton potential associated with ρ_0 and corresponds to the electrostatic potential created by ρ_0 in the vacuum. It is solution to the Poisson equation

$$-\Delta \phi_0 = \rho_0 \qquad \text{in } \mathbb{R}^3.$$

Concerning the three different operators L_e, their Green functions on $\mathbb{R}^3$ are the following ones

- for $L_e = -\epsilon_s \Delta$ (standard PCM), we have of course

$$G_e(x,y) = \frac{1}{4\pi\epsilon_s|x-y|},$$

- for $L_e = -\epsilon_s \Delta + \epsilon_s \kappa_s^2$ (ionic solutions),

$$G_e(x,y) = \frac{e^{-\kappa_s|x-y|}}{4\pi\epsilon_s|x-y|},$$

  This kernel is associated with a short-range Yukawa potential.

- for $L_e = -\mathrm{div}(\underline{\underline{\epsilon}}_s \cdot \nabla)$ (liquid crystals), we obtain

$$G_e(x,y) = \frac{1}{4\pi\sqrt{\det(\underline{\underline{\epsilon}}_s)}(\underline{\underline{\epsilon}}_s^{-1} \cdot (x-y), (x-y))^{1/2}}.$$

We denote by S_i, D_i and D_i^* the following operators: for $u \in L^2(\Gamma)$ and $x \in \Gamma$,

$$
\begin{aligned}
(S_i \cdot u)(x) &= \int_\Gamma G_i(x,y)u(y)\,dy,\\
(D_i \cdot u)(x) &= \int_\Gamma \partial_y G_i(x,y)u(y)\,dy,\\
(D_i^* \cdot u)(x) &= \int_\Gamma \partial_x G_i(x,y)u(y)\,dy,
\end{aligned}
$$

where $\partial_x G_i(x,y) = (\nabla_x G_i(x,y)) \cdot n(x)$ and $\partial_y G_i(x,y) = (\nabla_y G_i(x,y)) \cdot n(y)$.

These operators are well-known in the theory of integral equations. They are three of the four components of the Calderon projector [3]. We recall some of their properties: the operator S_i is self-adjoint and D_i^* is the adjoint of D_i for the scalar product $\langle \cdot, \cdot \rangle_\Gamma$. Besides, $S_i D_i^* = D_i S_i$. We also define similar operators for the Green function G_e, that we need below:

$$
\begin{aligned}
(S_e \cdot u)(x) &= \int_\Gamma G_e(x,y)u(y)\,dy,\\
(D_e \cdot u)(x) &= \int_\Gamma \partial_y G_e(x,y)u(y)\,dy,
\end{aligned}
$$

where $\partial_y G_e(x,y) = (\epsilon_s \cdot \nabla_y G_e(x,y)) \cdot n(y)$.

At last, if ρ_0 and ρ_0' are two charge distributions in $\mathbb{R}^3$, we denote by

$$\mathcal{D}(\rho_0, \rho_0') = \int\int_{\mathbb{R}^3 \times \mathbb{R}^3} G_i(x,y)\rho_0(x)\rho_0'(y)\,dx\,dy$$

their interaction energy in the vacuum.

We can now state our main result, which is valid for each of the three physical contexts that we consider here (standard solvent, anisotropic solvent or ionic solution).

Theorem. *Let ρ be a charge distribution located inside the cavity Ω_i.*

1. *There exists an apparent surface charge ρ_a supported on Γ so that the interaction energy between ρ and another charge distribution ρ' also located inside the cavity Ω_i reads*

$$E_I(\rho, \rho') = \mathcal{D}(\rho, \rho') + \mathcal{D}(\rho_a, \rho').$$

2. *We denote by ϕ the electrostatic potential created by ρ in the vacuum. The density σ of the apparent surface charge ρ_a is the unique solution to the equation*

$$A \cdot \sigma = g \tag{2.7}$$

with

$$A = (\frac{I}{2} - D_e)S_i + S_e(\frac{I}{2} + D_i^*)$$

and

$$g = -(\frac{I}{2} - D_e) \cdot \phi_i - S_e \cdot \partial\phi_i.$$

Remark 1: For the standard PCM, equation (2.7) may be simplified. Indeed, in this case, the Green functions G_i and G_e are proportional, and we have $S_e = \frac{1}{\epsilon_s} S_i$ and $D_e = D_i$. Denoting by $E_n = -\partial\phi_i$ the normal component of the electric field created by ρ in the vacuum and using the equality $(\frac{I}{2} - D_i) \cdot \phi_i + S_i \cdot \partial\phi_i = 0$ (see Lemma 1 below), equation (2.7) may be rewritten as

$$S_i \left[(\frac{I}{2} - D_i^*) + \frac{1}{\epsilon_s}(\frac{I}{2} + D_i^*) \right] \cdot \sigma = -\frac{(\epsilon_s - 1)}{\epsilon_s} S_i \cdot E_n.$$

After multiplication by $\frac{\epsilon_s}{\epsilon_s - 1} S_i^{-1}$, we obtain

$$\left(\frac{\epsilon_s + 1}{\epsilon_s - 1} \frac{I}{2} - D_i^* \right) \cdot \sigma = -E_n, \tag{2.8}$$

which is exactly the same as equation (A1) in [6] for instance.

2.2 Mathematical proofs

Some tools are used in this Section, which are standard in mathematics but not in theoretical chemistry. In order to simplify, we forget all considerations of functional analysis. In particular, we assume that the cavity is smooth and that the charge distributions belong to suitable functional spaces. Let us notice that the latter assumption is always satisfied for charge distributions used in practice in Molecular Mechanics or in Quantum Chemistry. On the other hand, the former one is obviously true for a spherical or an ellipsoidal cavity, and also for some molecular shape cavities (as those defined as isodensity surfaces), but not for instance for molecular cavities defined as intersections of spheres. The extension of the forthcoming theoretical results to general non-smooth cavities is a difficult mathematical issue which is out of the scope of the present article.

Proof of the Theorem.

Let us consider a charge distribution ρ' located inside Ω_i and let us denote

$$\phi'(x) = \int_{\mathbf{R}^3} G_i(x,y)\rho'(y)\,dy,$$

the electrostatic potential generated by ρ' in the vacuum. Let

$$f(x) = \begin{cases} \int_{\mathbf{R}^3} G_i(x,y)\rho(y)\,dy & \text{if } x \in \Omega_i \\ \int_{\mathbf{R}^3} G_e(x,y)\rho(y)\,dy & \text{if } x \in \Omega_e \end{cases}$$

and

$$W = V - f.$$

This latter function satisfies

$$\begin{cases} L_i W = 0 & \text{in } \Omega_i, \\ L_e W = 0 & \text{in } \Omega_e. \end{cases}$$

With these notations,

$$E_I(\rho,\rho') = \int_{\mathbf{R}^3} \rho' f + \int_{\mathbf{R}^3} \rho' W.$$

The first term is easy to compute. Indeed, since we assume that the charge distributions ρ and ρ' are supported in Ω_i,

$$\begin{aligned} E_1 &= \int_{\mathbf{R}^3} \rho'(x) f(x)\,dx \\ &= \int\int_{\mathbf{R}^3\times\mathbf{R}^3} \frac{\rho'(x)\rho(y)}{4\pi|x-y|}\,dx\,dy \\ &= \mathcal{D}(\rho,\rho'). \end{aligned}$$

Our purpose is to compute the second term. For that, we use an integral representation of the "apparent" potential W.

Lemma *(of representation). Let us consider u so that*

$$\begin{cases} L_i u = \rho_i & \textit{in } \Omega_i, \\ L_e u = \rho_e & \textit{in } \Omega_e. \end{cases}$$

Then, if u, ρ_i and ρ_e belong to "suitable" functional spaces,

1. *for all* $x \in \Omega_i$,

$$u(x) = \int_\Gamma G_i(x,y)\partial u_i(y)\,dy \;-\; \int_\Gamma u_i(y)\partial_y G_i(x,y)\,dy \;+\; \int_{\Omega_i} G_i(x,y)\rho_i(y)\,dy,$$

2. *for all* $x \in \Omega_e$,

$$u(x) = -\int_\Gamma G_e(x,y)\partial u_e(y)\,dy + \int_\Gamma u_e(y)\partial_y G_e(x,y)\,dy + \int_{\Omega_e} G_e(x,y)\rho_e(y)\,dy,$$

3. *for all* $x \in \Gamma$,

$$\frac{1}{2}u_i(x) = \int_\Gamma G_i(x,y)\partial u_i(y)\,dy \;-\; \int_\Gamma u_i(y)\partial_y G_i(x,y)\,dy \;+\; \int_{\Omega_i} G_i(x,y)\rho_i(y)\,dy,$$

4. *for all* $x \in \Gamma$,

$$\frac{1}{2}u_e(x) = -\int_\Gamma G_e(x,y)\partial u_e(y)\,dy + \int_\Gamma u_e(y)\partial_y G_e(x,y)\,dy + \int_{\Omega_e} G_e(x,y)\rho_e(y)\,dy.$$

Such results are standard in the Theory of integral equations. Nevertheless, for the reader's convenience, we will sketch a proof of this lemma at the end of the present Section.

Using statement 1 of the Lemma with $u = W$, we obtain

$$\begin{aligned}
E_2 &= \int_{\mathbf{R}^3} \rho'(x)W(x)\,dx \\
&= \int_{\mathbf{R}^3} \rho'(x)\left(\int_\Gamma G_i(x,y)\partial W_i(y)\,dy \;-\; \int_\Gamma W_i(y)\partial_y G_i(x,y)\,dy\right)\,dx \\
&= \int_\Gamma \partial W_i(y)\left(\int_{\mathbf{R}^3} \rho'(x)G_i(x,y)\,dx\right)\,dy - \int_\Gamma W_i(y)\left(\int_{\mathbf{R}^3} \rho'(x)\partial_y G_i(x,y)\,dx\right)\,dy \\
&= \langle \partial W_i, \phi_i' \rangle_\Gamma - \langle W_i, \partial\phi_i' \rangle_\Gamma .
\end{aligned}$$

We now apply twice statement 3 of the Lemma, firstly with $u = W$, which gives

$$S_i \cdot \partial W_i - D_i \cdot W_i = \frac{1}{2}W_i \tag{2.9}$$

then with $u = \phi$, and we obtain

$$S_i \cdot \partial\phi_i - D_i \cdot \phi_i = -\frac{1}{2}\phi_i. \tag{2.10}$$

Let us consider the quantity $\sigma = S_i^{-1} \cdot W_i$, which has the dimension of a surface charge density. Using equations (2.9) and (2.10), we obtain

$$\begin{aligned} E_2 &= \langle \partial W_i, \phi_i' \rangle_\Gamma - \langle W_i, \partial \phi_i' \rangle_\Gamma \\ &= \langle S_i^{-1}(\frac{I}{2} + D_i) \cdot W_i, \phi_i' \rangle_\Gamma - \langle W_i, S_i^{-1}(-\frac{I}{2} + D_i) \cdot \phi_i' \rangle_\Gamma \\ &= \langle (\frac{I}{2} + D_i^*) \cdot \sigma, \phi_i' \rangle_\Gamma - \langle (-\frac{I}{2} + D_i^*) \cdot \sigma, \phi_i' \rangle_\Gamma \\ &= \langle \sigma, \phi_i' \rangle_\Gamma . \end{aligned}$$

This equality may be written

$$E_2 = \mathcal{D}(\rho_a, \rho'),$$

where ρ_a is the surface charge of density σ. This closes the proof of the first statement of our Theorem.

Let us now turn to the proof of the second statement.

The functions W_i, W_e , ∂W_i and ∂W_e satisfy the following 4×4 system

$$(II) \quad \begin{cases} S_i \cdot \partial W_i - D_i \cdot W_i = \frac{1}{2} W_i \\ S_e \cdot \partial W_e - D_e \cdot W_e = -\frac{1}{2} W_e \\ W_i - W_e = f_e - f_i \\ \partial W_i - \partial W_e = \partial f_e - \partial f_i . \end{cases}$$

The first two equations come from a direct application of statements 3 and 4 of the Lemma with $u = W$. The two latter ones are consequences of the jump conditions, $V_i - V_e = 0$ and $\partial V_i - \partial V_e = 0$. As $f = \phi$ in Ω_i and as moreover, from statement 4 of the Lemma applied with $u = f$, $S_e \cdot \partial f_e - D_e \cdot f_e = -\frac{1}{2} f_e$, a straightforward algebraic manipulation on system (II) gives equation (2.7).

In order to prove the uniqueness result, we consider two solutions σ and σ' to equation (2.7) and we denote $\tau = \sigma - \sigma'$. We have $A \cdot \tau = 0$, and that means

$$\left((\frac{I}{2} - D_e) S_i + S_e (\frac{I}{2} + D_i^*) \right) \cdot \tau = 0. \tag{2.11}$$

Let us define $\overline{W}$ so that

$$\overline{W}|_{\Omega_i}(x) = \int_\Gamma G_i(x,y) \tau(y) \, dy$$

and $\overline{W}|_{\Omega_e}$ is the unique solution (in a suitable weighted Sobolev space) to

$$\begin{cases} L_e \mathcal{W} = 0 & \text{in} \quad \Omega_e \\ \mathcal{W} = \overline{W}_i & \text{on} \quad \Gamma. \end{cases}$$

From (2.11) we deduce $\partial\overline{W}_i - \partial\overline{W}_e = 0$. Besides, as by construction $\overline{W}$ is continuous across Γ,

$$\begin{aligned} \int_{\mathbb{R}^3} (\epsilon(x) \cdot \nabla\overline{W}(x)) \cdot \nabla\overline{W}(x) &= \int_{\Omega_i} \nabla\overline{W} \cdot \nabla\overline{W} + \int_{\Omega_e} (\epsilon_s \cdot \nabla\overline{W}) \cdot \nabla\overline{W} \\ &= \int_\Gamma \overline{W}_i \partial\overline{W}_i - \int_\Gamma \overline{W}_e \partial\overline{W}_e \\ &= \int_\Gamma \overline{W}_i (\partial\overline{W}_i - \partial\overline{W}_e) \\ &= 0. \end{aligned}$$

Thus $\nabla\overline{W} = 0$ almost everywhere, and therefore $\overline{W} = 0$, which implies $\tau = 0$.

We conclude this Section with the

Proof of the Lemma.

The proofs of the four statements of the Lemma are based upon the following Green formula, which is nothing but a multidimensional integration by part: let Ω be a bounded domain of $\mathbb{R}^3$ with a piecewise smooth boundary $\partial\Omega$, and let L be a second-order partial differential operator of the form

$$L \cdot v = -\mathrm{div}(\epsilon \cdot \nabla v) + c\, v$$

where ϵ is a 3×3 tensor field and c is a scalar field. We have, for all v and w regular enough,

$$\int_\Omega (L \cdot v) w + \int_{\partial\Omega} \frac{\partial v}{\partial n_L} w = \int_\Omega (L \cdot w) v + \int_{\partial\Omega} \frac{\partial w}{\partial n_L} v, \tag{2.12}$$

where $\frac{\partial u}{\partial n_L} = (\epsilon \cdot \nabla u) \cdot n$ (n denotes as usual the outward pointing normal).

Proof of statement 1

Let $x \in \Omega_i$ and $\eta > 0$ so that $B_x(\eta) \subset \Omega_i$ (where $B_x(\eta) = \{y / |x - y| < \eta\}$). We write the Green formula (2.12) for $\Omega = \Omega_i \setminus \overline{B}_x(\eta)$, $L = L_i$, $v(y) = G_i(x,y)$ and $w(y) = u(y)$. As $L_i \cdot v = 0$ and $L_i \cdot w = \rho_i$ in Ω, we obtain

$$\int_\Omega G_i(x,y)\rho_i(y)\, dy + \int_{\partial\Omega} G_i(x,y) \frac{\partial u}{\partial n}(y)\, dy = \int_{\partial\Omega} u(y) \frac{\partial G_i}{\partial n_y}(x,y)\, dy.$$

Thus

$$\begin{aligned}\int_\Omega G_i(x,y)\rho_i(y)\,dy &+ \int_\Gamma G_i(x,y)\partial u_i(y)\,dy - \int_\Gamma u_i(y)\frac{\partial G_i}{\partial n_y}(x,y)\,dy \\ &= \int_{S_x(\eta)} u(y)\frac{\partial G_i}{\partial n_y}(x,y)\,dy - \int_{S_x(\eta)} G_i(x,y)\frac{\partial u}{\partial n}(y)\,dy.\end{aligned}$$

We let η go to zero, which gives:

$$\int_{S_x(\eta)} u(y)\frac{\partial G_i}{\partial n_y}(x,y)\,dy \longrightarrow u(x)$$

and

$$\int_{S_x(\eta)} G_i(x,y)\frac{\partial u}{\partial n}(y)\,dy \longrightarrow 0.$$

Finally,

$$u(x) = \int_\Gamma G_i(x,y)\partial u_i(y)\,dy - \int_\Gamma u_i(y)\partial G_i(x,y)\,dy + \int_\Omega G_i(x,y)\rho_i(y)\,dy.$$

Proof of statement 2

Let $x \in \Omega_e$ and $\eta > 0$ so that $B_x(\eta) \subset \Omega_e$. Let $R > 0$ so that $(\overline{\Omega}_i \cup B_x(\eta)) \subset B_0(R)$. We use the Green formula (2.12) for $\Omega = B_0(R) \setminus (\overline{B}_x(\eta) \cup \overline{\Omega}_i)$, $v(y) = G_e(x,y)$ and $w(y) = u(y)$. As $L_e \cdot v = 0$ and $L_e w = \rho_e$ in Ω, we obtain

$$\int_\Omega G_e(x,y)\rho_e(y)\,dy + \int_{\partial\Omega} G_e(x,y)\frac{\partial u}{\partial n}(y)\,dy = \int_{\partial\Omega} u(y)\frac{\partial G_e}{\partial n_y}(x,y)\,dy$$

Thus

$$\begin{aligned}\int_\Omega G_e(x,y)\rho_e(y) &- \int_\Gamma G_e(x,y)\partial u_e(y)\,dy + \int_\Gamma u_e\partial G_e(x,y)\,dy \\ &= \int_{S_x(\eta)} u(y)\frac{\partial G_e}{\partial n_y}(x,y)\,dy - \int_{S_x(\eta)} G_e(x,y)\frac{\partial u}{\partial n}(y)\,dy \\ &+ \int_{S_0(R)} u(y)\frac{\partial G_e}{\partial n_y}(x,y)\,dy - \int_{S_0(R)} G_e(x,y)\frac{\partial u}{\partial n}(y)\,dy.\end{aligned}$$

If u and ρ_e belong to suitable functional spaces, we obtain statement 2 letting η go to zero and R go to infinity.

We skip the proofs of statements 3 and 4 which are a bit more technical (the outlines may be found in [3] for instance). We just point out that the factor $\frac{1}{2}$ comes from the fact that, when x belongs to Γ, $S_x(\eta) \cap \Omega_i$ is no longer a sphere but only half a sphere (asymptotically, when η goes to zero).

3 Numerical method and Results

We use here the notations defined in the previous Section.

3.1 Boundary element approximation

As for the apparent surface charge (ASC) method used for standard PCM [2], we use a boundary element method (BEM) to solve equation (2.7) (i.e. $A\sigma = g$), and to compute the second term $E_2 = \mathcal{D}(\rho_a, \rho')$ of the interaction energy $E_I(\rho, \rho')$. For this purpose, we firstly build a tessellation of the boundary Γ consisting of K tesserae $(T_k)_{1\leq k\leq K}$. For the calculations, we have chosen a $\mathbb{P}_0$-approximation. That means that the charge density σ is approximated by a piecewise constant function (constant on each tessera of the tessellation). Let us denote by σ_k the approximate value of the density σ on the tessera T_k. There comes at once

$$\mathcal{D}(\rho_a, \rho') = \sum_{k=1}^{K} \sigma_k \left(\int_{T_k} \phi'(y)\, dy \right). \tag{3.13}$$

With this approximation, equation (2.7) amounts to a linear system of order K denoted

$$[A] \cdot [\sigma] = [g]$$

where $[\sigma]$ is the column vector $[\sigma_k]$, $[A]$ is a $K \times K$ matrix, and $[g]$ a column vector depending on the charge distribution ρ. We obtain for all $1 \leq k, k' \leq K$,

$$A^{kk'} = \int_{T_k} dx \int_{\Gamma} dy \int_{T_{k'}} dz\ k(x,y,z) \tag{3.14}$$

with

$$k(x,y,z) = \left(\left(\frac{\delta(x-y)}{2} - \partial_y G_e(x,y) \right) G_i(y,z) + G_e(x,y) \left(\frac{\delta(y-z)}{2} + \partial_y G_i(y,z) \right) \right)$$

and

$$g^k = \int_{T_k} dx \int_{\Gamma} dy \left(- \left(\frac{\delta(x-y)}{2} - \partial_y G_e(x,y) \right) \phi_i(y) - G_e(x,y) \partial\phi_i(y) \right). \tag{3.15}$$

The two above expressions come from a variational calculation.

At this stage, the remaining problems are

- the computation of ϕ_i, $\partial\phi_i$ and ϕ'_i (we tackle this problem in the next section),

- the numerical computation of the various surface integrals in (3.13), (3.14) and (3.15). When Γ is smooth, one can prove that for fixed x, the singularities of the kernels $G_i(x,y)$, $G_e(x,y)$, $\partial G_i(x,y)$ and $\partial G_e(x,y)$ are all in $\frac{1}{|x-y|}$. Therefore, all these singularities are integrable on a (two dimension) surface. We have used Gaussian integration in suitable coordinates to perform these quadratures, which gives good results.

3.2 Application to Hartree-Fock SCF calculations

Let us deal at first with the nuclei repulsion term. In this case, $\rho = q\,\delta(\cdot - \overline{x})$ and $\rho' = q'\delta(\cdot - \overline{x}')$ are two point charges, and thus the functions ϕ_i, $\partial\phi_i$ and ϕ_i' are very easy to be computed. Indeed, for all $x \in \Gamma$

$$\begin{aligned} \phi_i(x) &= \frac{q}{4\pi|x-\overline{x}|} \\ \partial\phi_i(x) &= -q\frac{(x-\overline{x})\cdot n(x)}{4\pi|x-\overline{x}|^3} \\ \phi_i'(x) &= \frac{q'}{4\pi|x-\overline{x}'|}. \end{aligned}$$

Let us now turn to the electronic energy. From now on, $(\chi_p)_{1\le p\le N}$ denotes the set of the atomic orbitals. We use the following classical notations:

$$I_{pq}(x) = \int_{\mathbf{R}^3} \frac{\chi_p(y)\chi_q(y)}{4\pi|x-y|}\,dy$$

and

$$I_{pqrs} = \int_{\mathbf{R}^3}\int_{\mathbf{R}^3} \frac{\chi_p(x)\chi_q(x)\chi_r(y)\chi_s(y)}{4\pi|x-y|}\,dx\,dy.$$

In the PCM, the Fock matrix reads (for a spinless model to simplify the notations)

$$F_{\mu\nu} = h_{\mu\nu} + G_{\mu\nu}(P)$$

with

$$h_{\mu\nu} = \frac{1}{2}\int_{\mathbf{R}^3} \nabla\chi_\mu\cdot\nabla\chi_\nu - E_I(\rho^{nuc},\chi_\mu\chi_\nu)$$

and

$$G_{\mu\nu}(P) = \sum_{\kappa,\lambda} P_{\kappa\lambda}\left(E_I(\chi_\kappa\chi_\lambda,\chi_\mu\chi_\nu) - \frac{1}{2}I_{\kappa\nu\mu\lambda}\right),$$

where

$$\rho^{nuc} = \sum_{k=1}^{M} z_k \delta_{\overline{x}_k}$$

is the charge distribution of the M nuclei and P the one-electron density matrix. Denoting

$$\rho^{el} = \sum_{\kappa,\lambda} P_{\kappa\lambda} \chi_\kappa \chi_\lambda$$

the electronic density and using the results obtained in the previous section, we write the Fock matrix as

$$F_{\mu\nu} = F^0_{\mu\nu} + \mathcal{D}(\rho_a^{nuc} + \rho_a^{el}, \chi_\mu \chi_\nu)$$

where F^0 denotes the standard Fock matrix (for the molecule in the vacuum) and ρ_a^{nuc} and ρ_a^{el} are the apparent surface charges created by the nuclei and the electronic cloud respectively. To compute the Fock matrix, we only need to know for all $x \in \Gamma$

$$\begin{aligned}
\phi_i(x) &= \sum_{k=1}^{M} \frac{z_k}{4\pi|x - \overline{x}_k|} - \sum_{\kappa,\lambda} P_{\kappa\lambda} I_{\kappa\lambda}(x) \\
\partial\phi_i(x) &= -\sum_{k=1}^{M} z_k \frac{(x - \overline{x}_k) \cdot n(x)}{4\pi|x - \overline{x}_k|} - \sum_{\kappa,\lambda} P_{\kappa\lambda} (\nabla I_{\kappa\lambda}(x) \cdot n(x)) \\
\phi_i'(x) &= -I_{\mu\nu}(x).
\end{aligned}$$

When atomic orbitals are contracted gaussians, which is the case in most of the quantum chemistry calculations for molecules, the functions $I_{\kappa\lambda}$ and their gradients are very easy to compute and that makes this method very effective.

Remark 2. The electronic distribution is not rigorously located inside the cavity: there is always an “electronic tail” spreading outside. For standard cavities and basis functions, the approximation that we make when computing the Fock matrix as above is quite valid. In some special cases, for example when diffuse functions are used to compute excited states, this approximation may be too crude. Let us notice however that the same problem occurs when computing the standard PCM equation (1.1) with the ASC method (i.e. starting from equation (2.8)).

3.3 Numerical results

In this section we report a selection of results obtained with the implementation on GAMESS package [7] of the new formalism presented above within the PCM framework.

As the scope of the present article is the detailed presentation of the theoretical bases which underlie the method, we have limited our numerical study to some very simple systems: the solute molecules are small and the cavity is a single sphere even for polyatomic solutes. Besides, the reported values are not analyzed in their real chemical meaning, but only as a proof of the reliability of the method. Other more complex systems are studied in a parallel work [8] dedicated to a detailed analysis of the potentialities and the effective performances of this new integral equation formalism, in which we also check that the new method, when applied to standard isotropic liquids, gives the same results as standard PCM (apart from numerical approximations).

The results reported here regard two solute-solvent systems of different natures. The first one is an application to intrinsically anisotropic dielectrics, characterized by a tensorial permittivity. In the specific case that we have considered, the chosen solvent is the liquid crystal known with the acronym 7CB (4-*n*-heptyl-4′-cyanobiphenyl), which is nematic at room temperature (its transition temperature to the isotropic phase is 312 K). The main characteristic of this kind of "mesophases" is that they exhibit long-range orientational order, with the long axes of the anisometric component molecules tending to align parallel to a space-fixed axis called the *director*. From a physical point of view, a consequence of this is that their permittivity is described by a symmetric tensor which has two eigenvalues equal: for 7CB the double eigenvalue is $\epsilon_{\perp} = 5.54$ and the simple eigenvalue is $\epsilon_{\|} = 17.1$ (in other words, $\epsilon_{\|}$ is the permittivity along the direction of preferential alignment of solvent molecules, and $\epsilon_{\perp}$ the value in the plane normal to this direction). Because of the structural specificity mentioned above, solute molecules dissolved in nematic liquid crystals are subject to anisotropic forces which lead them to orient. Usually, a rodlike dipolar molecule orders such that its long axis is preferantially oriented parallel to the nematic director. One of the major sources of this orientational ordering of rigid solutes in liquid crystals is given by electrostatic interactions bewteen the polar solute and the solvent molecules. Other minor contributions come from dispersion forces and short-range repulsion. The method we have presented above allows us to get in a very efficient way the electrostatic contribution. We have limited ourselves to the calculation of this term. A more accurate evaluation of the ordering mechanism can be easily obtained within PCM framework [9], by including the cavitation term, but it is not performed here as out of the scope of the present paper. In the following figure we have reported the electrostatic contribution to the solvation free energy of HF in 7CB with respect to the angle between the solute bond and the solvent director. These results are obtained with the HF molecule embedded in a sphere of radius 1.734 Å and described with a standard DZV basis set.

Figure 2: ΔG_{sol} values of HF in 7CB with respect to the angle between the bond axis and the z axis.

As we can easily see, the differences between the various orientations are quite small, but small is also the anisotropy of the dielectric; anyway it appears that the stablest configurations (i.e. those with the most negative ΔG_{sol}) are those with the HF bond parallel to the axis along which the dielectric tensor has the greatest value (clearly the graph is symmetric with respect to the angle value of 90°). In the figure we also report as limit values, those obtained for two hypothetical isotropic media with permittivity equal to each of the two different eigenvalues of ϵ for 7CB.

The second application of the new method presented in the previous sections is the analysis of the solvation behavior of a probe solute in salt solutions of various ionic strengths. Verification of this new algorithm was accomplished by calculating the ion contribution to the solvation free energy of a spherical charged solute (here the anion H^- embedded in a sphere of radius 1.4 Å in a solution of water (dielectric constant=78.5) and a 1:1 salt at variable concentration. The ion contribution, defined as the free energy in solution minus the energy calculated at zero ionic strength, is reported in figure 3 with respect to the bulk ionic strength I expressed in mole per litre.

Figure 3: Ion contribution to the solvation free energy of H^- in water containing a 1:1 salt at variable concentrations. I is the bulk ionic strength in mole/l.

Continuum models accounting for ionic screening have found an increasing application in the modelling of hydrated molecules, particularly biological macromolecules. Our future intent is to follow this trend and try to exploit the present algorithm to understand many interesting phenomena related to biological systems. However, in the present paper we have limited our analysis to a very simple system; the reason of this choice is that for the moment our scope is to stress even if with an almost propedeutic example, the reliability of this extension of a pure integral equation methods to problems usually solved with three dimensional methods.

4 Conclusion and future trends

We have shown in this article that integral equation methods are also efficient for the above extensions of solvation continuum models when the solvent is an ionic solution or a liquid crystal. In fact, these methods are generally relevant from the moment that the medium which spreads outside the cavity is homogeneous.

In all these cases, integral equations methods are much more efficient than three dimensional methods as finite difference or finite element methods used so far, because

1. the computational effort is lower,
2. no approximation is made to account for boundary conditions.

Moreover it becomes easy to compute analytical derivatives of the energy with respect to physical parameters, as the temperature in the case of ionic solutions, or as the orientation of the molecule with respect to the principal directions of the anisotropic tensor $\underline{\underline{\epsilon_s}}$ in the case of liquid crystals. Analytical derivatives with respect to nuclear coordinates, which are useful for geometry optimization [10], are more difficult to be computed because of the change of the cavity shape, but seems nevertheless accessible. We are at the moment studying this extension [11].

On the other hand, for an inhomogeneous external medium, three dimensional methods are required. However, if there is in the model an inhomogeneous zone in the external medium, it is usually located in the neighbourhood of the molecule under study. It is therefore possible to put both the molecule and the inhomogeneous zone in a bigger cavity of simple shape (for example a cube) and to couple integral methods (for solving the external problem) with three-dimensional methods (for solving the internal problem). The advantage of such a method, compared with pure three-dimensional methods, is to take into account the boundary conditons rigourously. We intend to look soon into inhomogeneous models.

AKNOWLEDGMENTS

The authors would like to thank Pr. J. Tomasi, Dr. M. Defranceschi and Dr. C. Le Bris for helpful discussions.

References

[1] S. Miertuš, E. Scrocco and J. Tomasi, Chem. Phys. 55 (1981) 117.

[2] J. Tomasi and M. Persico, Chem. Rev. 94 (1994) 2027.

[3] W. Hackbusch, *Integral equations - Theory and numerical treatment*, (Birkhäuser Verlag, Basel, Switzerland, 1995).

[4] K. Sharp, J. Comp. Chem. 12 (1991) 454.

[5] B. Mennucci, M. Cossi and J. Tomasi, J. Chem. Phys. 102 (1995) 6837.

[6] R. Cammi and J. Tomasi, J. Chem. Phys. 100 (1994) 7495.

[7] M.W. Schmidt, K.K. Baldridge, J.A. Boatz, S.T. Elbert, M.S. Gordon, J.H. Jensen, S. Koseki, N. Matsunaga, K.A. Nguyen, S.J. Su, T.L. Windus, M. Dupuis and J.A. Montgomery, J. Comp. Chem. 14 (1993) 1347.

[8] E. Cancès, B. Mennucci and J. Tomasi, J. Chem. Phys., submitted.

[9] B. Mennucci, M. Cossi and J. Tomasi, J. Phys. Chem. 100 (1996) 1807.

[10] M. Cossi, B. Mennucci and R. Cammi, J. Comp. Chem. 17 (1996) 57.

[11] E. Cancès, B. Mennucci, manuscript in preparation.