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A new formulation of the PCM solvation method: PCM-QINTn

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Abstract. A new formulation of the PCM electrostatic solution problem is proposed. Through a new derivation of the PCM-CLSn expression we propose an interpolation formula that improved the convergence: PCM-QINTn. All the available formulations are applied to the evaluation of the electrostatic component of the free energy of solvation for some molecular systems. In addition, PCM-QINT derivatives of G_{el} with respect to atomic coordinates are evaluated. The computational costs are compared with those of PCM-direct formulation.

Key words: Polarizable continuum model – Free energy of solvation – Free energy derivatives

1 Introduction

We present in this paper a preliminary description of a new computational method for the study of solvation effects on molecular systems. The procedure presented here derives from that used in the polarizable continuum model (PCM) elaborated by our group, for which several variants are in use [1–3].

The PCM procedure describes the solute quantum mechanically (at the various levels of the ab initio theory but also at the semiempirical level) and there also codes using classical descriptions of the solute charge distribution. In all cases the solvent is described by continuous distributions (isotropic or with anisotropies of different type) to which the appropriate response functions are assigned (dielectric response, linear or not, dispersion response etc.).

The use of classical descriptions of the solute charge distribution has been suggested by the need to reduce computational times when the solute has a large size. Classical descriptions are not able, however, to faithfully describe the details of the influence of the solvent on the solute electronic distribution and then on its properties, especially when attention is addressed to the study of reaction mechanism.

A few years ago we suggested a simplified version of the standard PCM procedure (isotropic infinite solvent, ground electronic state, solute at the SCF level, cavity described in terms of intersecting spheres) which remarkably reduces computational costs, especially for large molecules [4]. That procedure is, however, limited to fixed solute geometry, because the implementation of automatic geometry optimization presents some problems. Later [5] we suggested using the arithmetic mean of the two first approximations of the solvation free energy [or to be more precise of its dominant part, the electrostatic contribution (G_{el})], but still without automatic geometry optimizations.

In fact the hierarchical sequence of approximations proposed in Ref. [4], called PCM-CLSn, and the practical recipe given in Ref. [5], based on PCM-CLS1 and PCM-CLS2, are not appropriate for the extension of analytical expressions of derivatives of G_{el} with respect to the molecular geometry. We present here a new derivation, a further elaboration based on an interpolation formula between PCM-CLSn and PCM-CLS(n-1) charges, named PCM-QINTn, for which analytical derivatives can be derived.

We shall report here numerical data on PCM-CLSn reaching higher n levels to show the convergence of the approximation, comparing it with the corresponding interpolation series PCM-QINTn, and some examples of the analytical derivatives obtained using both standard PCM and PCM-QINTn values.

2 Theory

The following are the equations for the calculation of the apparent surface charges (ASC) q_k (see Ref. [3] for terminology and general information about the method) at the PCM-CLS1 and PCM-CLS2 levels of theory. They were first proposed in [4]:

$$q_k^{(\infty,1)} = \frac{1}{1-A_k}\left[q_k^{(0)} - \sum_{l\neq k} B_{kl}\frac{q_l^{(0)}}{1-A_l}\right], \qquad (1)$$

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$$q_k^{(\infty,2)} = \frac{1}{1-A_k}\left\{ q_k^{(0)} - \sum_{l\neq k} B_{kl}\frac{q_l^{(0)}}{1-A_l}\right. , \qquad \left.\left[q_l^{(0)} - \sum_{n\neq l} B_{ln}\frac{q_n^{(0)}}{1-A_n}\right]\right\} \tag{2}$$

where

$$\mathbf{q}^{(0)} = \frac{\epsilon-1}{4\pi\epsilon}\mathbf{E}_n, \tag{3}$$

$$A_k = \frac{\epsilon-1}{2\epsilon}\left(1-\sqrt{\frac{\Delta S_k}{4\pi R_k^2}}\right), \tag{4}$$

$$B_{\mathrm{kl}} = \frac{\epsilon-1}{4\pi\epsilon}\Delta S_k\frac{(\vec{r}_k-\vec{r}_l)\cdot\hat{n}_k}{|\vec{r}_k-\vec{r}_l|^3}, \tag{5}$$

and

$$E_{n_k} = \Delta S_k\,\vec{\varepsilon}(\vec{r}_k)\cdot\hat{n}_k. \tag{6}$$

$\vec{r}_k$, ΔS_k, R_k and $\hat{n}_k$ are the central point, the area, the radius of curvature, and the outward unit vector of the tessera k. $\vec{\varepsilon}(\vec{r}_k)$ is the electrostatic field at $\vec{r}_k$.

The previous equations are obtained from the equation of the original iterative formulation of the PCM method:

$$q_k^{(m)} = q_k^o\left[1+A_k+\cdots+A_k^m\right] - \sum_{i=0}^{m-1}A_k^i\sum_{l\neq k}B_{kl}q_l^{(m-i-1)} \tag{7}$$

by extrapolating to $m=\infty$.With the approximation

$$q_l^{(\infty-i-1)} \simeq q_l^{(0)} \tag{8}$$

we obtain the PCM-CLS1 equation (Eq. 1). If we substitute $q_l^{(0)}$ with the expression of $q_l{}^{(\infty,1)}$ derived from the same equation, we obtain PCM-CLS2 (Eq. 2).

In the original PCM formulation [1] the set of ASC was obtained in an iterative way, with the number of iterations large enough to satisfy numerical convergence. The closure formulations Eq. (1) and Eq. (2) are not iterative and they are faster to compute and require less memory allocation.

It is convenient to consider these approximations from a different point of view. If we define the matrices **A** and **B** as following:

$$\mathbf{A} \equiv \begin{cases} 0 & k\neq l \\ A_k & k=l \end{cases} \tag{9}$$

$$\mathbf{B} \equiv \begin{cases} B_{kl} & k\neq l \\ 0 & k=l, \end{cases} \tag{10}$$

Eqs. (1) and (2) can be written in the following matrix form:

$$\mathbf{q}^{(\infty,1)} = (\mathbf{I}-\mathbf{A})^{-1}\left[\mathbf{I}-\mathbf{B}(\mathbf{I}-\mathbf{A})^{-1}\right]\mathbf{q}^{(0)} \tag{11}$$

$$\mathbf{q}^{(\infty,2)} = (\mathbf{I}-\mathbf{A})^{-1}\left[\mathbf{I}-\mathbf{B}(\mathbf{I}-\mathbf{A})^{-1}+\mathbf{B}(\mathbf{I}-\mathbf{A})^{-1}\mathbf{B}(\mathbf{I}-\mathbf{A})^{-1}\right]\mathbf{q}^{(0)} \tag{12}$$

The terms within the square brackets in two previous equations suggest that the PCM-CLS expression at order n represents the truncation of a power series. We show here that this is true through an alternative derivation of the PCM-CLSn equations. To accomplish this we next consider an alternative formulation of the PCM theory: the direct (or matrix-BEM [6]) formulation. If we define

$$\mathbf{D} = \frac{4\pi\epsilon}{\epsilon-1}(\mathbf{B}+\mathbf{I}-\mathbf{A}) \tag{13}$$

then

$$\mathbf{q} = -\mathbf{D}^{-1}\mathbf{E}_n. \tag{14}$$

Now, substituting Eq. (13) into Eq. (14), and recalling the relation between $\mathbf{q}^{(0)}$ and $\mathbf{E}_n$, we have

$$\mathbf{q} = -\frac{\epsilon-1}{4\pi\epsilon}(\mathbf{B}+\mathbf{I}-\mathbf{A})^{-1}\mathbf{E}_n = (\mathbf{B}+\mathbf{I}-\mathbf{A})^{-1}\mathbf{q}^{(0)}. \tag{15}$$

By inserting $(\mathbf{I}-\mathbf{A})^{-1}(\mathbf{I}-\mathbf{A})$ we obtain

$$\mathbf{q} = (\mathbf{I}-\mathbf{A})^{-1}\left[\mathbf{I}+\mathbf{B}(\mathbf{I}-\mathbf{A})^{-1}\right]^{-1}\mathbf{q}^{(0)}. \tag{16}$$

The expression enclosed in square brackets can be expanded in a Taylor series:

$$\left[\mathbf{B}(\mathbf{I}-\mathbf{A})^{-1}\right]^{-1} = \mathbf{I}-\mathbf{B}(\mathbf{I}-\mathbf{A})^{-1}+\mathbf{B}(\mathbf{I}-\mathbf{A})^{-1}\mathbf{B}(\mathbf{I}-\mathbf{A})^{-1}-\cdots \tag{17}$$

and by defining

$$\mathbf{K}_n = (\mathbf{I}-\mathbf{A})^{-1}\left[\sum_{m=0}^{n}\left(-\mathbf{B}(\mathbf{I}-\mathbf{A})^{-1}\right)^m\right] \tag{18}$$

as the reduced sum of the series of order n, we have the expression for the ASC with PCM-CLSn at any n:

$$\mathbf{q}^{(\infty,n)} = \mathbf{K}_n\mathbf{q}^{(0)}. \tag{19}$$

This PCM-CLSn formulation also introduces the zero-order approximation in which the ASC are strictly related to the non-polarized ASC $\mathbf{q}^{(0)}$. This new derivation of the PCM-CLSn method also establishes the following relation with the PCM-direct method:

$$\mathbf{K}_\infty = \mathbf{D}^{-1}. \tag{20}$$

From the computational results reported in next section we note that the sum of PCM-CLS ASC at the order n:

$$q_{\mathrm{tot}}^{(n)} = \sum_k q_k^{(n)} \tag{21}$$

is very far from the theoretical value given by Gauss's theorem:

$$q_{\text{theo}} = -\frac{\epsilon - 1}{\epsilon} q_{\text{int}} \tag{22}$$

where q_{int} is the charge internal to the cavity.

We note also that

$$\begin{aligned} \left| q_{\text{tot}}^{(n)} \right| &> |q_{\text{theo}}| \quad \text{if } n \text{ is even,} \\ \left| q_{\text{tot}}^{(n)} \right| &< |q_{\text{theo}}| \quad \text{if } n \text{ is odd.} \end{aligned} \tag{23}$$

For $|G_{el}|$ we have

$$\left| G_{el}^{(N_{pair})} \right| < \left| G_{el}^{(\infty)} \right| < \left| G_{el}^{(N_{\text{odd}})} \right|. \tag{24}$$

Two interpretations, one physical and one mathematical, can be proposed:

1. Physical interpretation: Each term in the sum in Eq. (18) can be interpreted as a depolarization operator if m is odd (and the sign of the term is negative), and as a polarization operator otherwise. The sum that defines $\mathbf{K}_n$ is therefore a succession of polarization and depolarization operators, each less important than the previous.
2. Mathematical interpretation: The series in Eq. (17) is a convergent alternating sign series.

The consequences of these interpretations are that the ASC given by PCM-CLSn methods converge to the PCM-direct ASC in an oscillating fashion.

On the basis of the previous considerations we have developed a method for improving the convergence of PCM-CLSn description with an interpolation scheme:

$$\begin{cases} \mathbf{Q}_n = (1 - \lambda_n)\mathbf{K}_n + \lambda \mathbf{K}_{n-1} \\ q_{\text{theo}} = (1 - \lambda_n) q_{\text{tot}}^{(n)} + \lambda q_{\text{tot}}^{(n-1)} \end{cases} \tag{25}$$

thus

$$\lambda_n = \frac{q_{\text{theo}} - q_{\text{tot}}^{(n)}}{q_{\text{tot}}^{(n)} - q_{\text{tot}}^{(n-1)}}. \tag{26}$$

We are using a PCM version where the ASC due to solute nuclei and electrons are separately treated [7]. We have:

$$q_{\text{int}} = q_{\text{int}}^{\text{nuc}} + q_{\text{int}}^{\text{ele}} \tag{27}$$

and

$$q_{\text{int}}^{\text{nuc}} = \sum^{\text{atoms}} Z_i \tag{28}$$

where Z_i are the nuclear charges. The nuclear field is independent of the SCF procedure, and so the correspondenting set of ASC is evaluated only once. The quantity $q_{\text{int}}^{\text{ele}}$ is less easy to calculate because it is the integral on the electronic charge density over the space inside the cavity. To dispense with this numerical integration, we evaluate λ_n from nuclear ASC and use this value also for electronic ASC. This approximation has been used in other PCM-direct formulations [7].

This method we have summarized here has been named PCM-QINTn (charge interpolation) and is defined by the equation

$$\mathbf{q}^{(\infty,n)} = \mathbf{Q}_n \mathbf{q}^{(0)}. \tag{29}$$

Analytical derivatives of G_{el} with respect to the nuclear coordinates are possible for the PCM-direct formulation only [8, 9]. These derivatives can be extended also to PCM-QINTn by making the approximation

$$\mathbf{D}^{-1} \simeq \mathbf{Q}_n. \tag{30}$$

This approximation cannot be used with the PCM-CLSn theory because the renormalization factor is too large and gives rise to numerical catastrophes.

3 Results

In this section will be presented some results obtained with the PCM-direct, PCM-CLSn and PCM-QINTn methods. These results illustrate the evaluation of the electrostatic component of the free energy of solvation, the analytical first derivatives with respect to nuclear coordinates and the behaviour of the PCM-QINTn method with respect to the variation of the molecular basis set.

These methods have been implemented in the HONDO8 [10] package for molecular ab initio calculation and performed on an IBM RS/6000 58H workstation. The matrix multiplications to generate $\mathbf{K}_n$ and $\mathbf{Q}_n$ were performed with the Winograd-Strassen [11] algorithm using the routine DGEMMS of the IBM ESSLV2.0 library [12]. The molecular cavity has been built with the GEPOL procedure [2] with the standard pentakisdodecahedral tessellation and Bondi van der Waals radii [13] scaled by a factor $\alpha = 1.2$. All the calculations are at the Hartree-Fock level with 6.31G** basis set. All molecular geometries are optimized in vacuo.

A systematic calculation of G_{el} up to tenth order for water, formaldehyde and glycine is reported in Table 1 and for last molecule only in Fig. 1. The results con-

Table 1. Electrostatic component of the free energy of solvation (Kcal/mol) evaluated with PCM-CLSn and PCM-QINTn methods for water, formaldehyde and glycine

N	H_2O		H_2CO		H_2NCH_2COOH	
	CLS	QINT	CLS	QINT	CLS	QINT
0	−8.434	–	−11.034	–	−16.415	–
1	−6.237	−7.166	−5.981	−7.967	−11.394	−13.470
2	−6.734	−6.518	−7.543	−6.845	−13.142	−12.379
3	−6.611	−6.665	−6.962	−7.215	−12.485	−12.775
4	−6.644	−6.630	−7.170	−7.080	−12.755	−12.641
5	−6.633	−6.638	−7.091	−7.127	−12.642	−12.694
6	−6.638	−6.636	−7.123	−7.110	−12.695	−12.674
7	−6.635	−6.636	−7.109	−7.115	−12.670	−12.682
8	−6.637	−6.637	−7.116	−7.113	−12.684	−12.678
9	−6.636	−6.637	−7.112	−7.114	−12.675	−12.679
10	−6.637	−6.637	−7.115	−7.114	−12.681	−12.679
∞	−6.635		−7.108		−12.674	

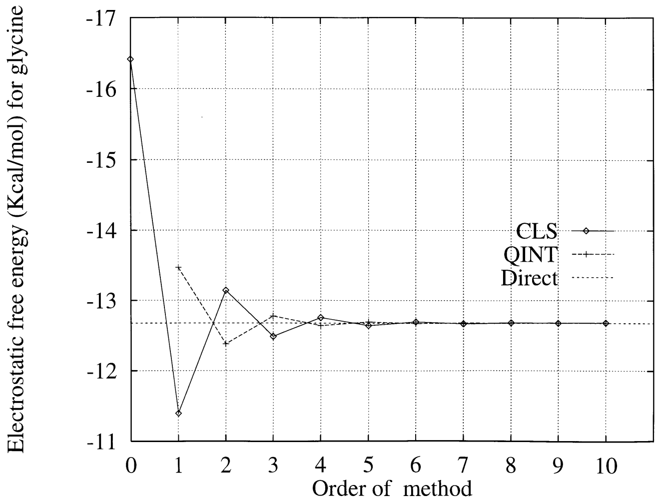

Fig. 1. Electrostatic free energy of solvation G_{el} for neutral glycine at the HF 6.31G** level versus the order of PCM-CLSn and PCM-QINTn methods

tained in Table 1 have been partially discussed in the previous section; with ∞ we indicate the PCM-direct method results. The small divergence between the PCM-CLSn and PCM-QINTn asymptotic value and the direct value (less than 0.1%) is probably due to numerical round-offs. Figure 1 gives a graphical idea of the convergence of PCM-CLSn and PCM-QINTn methods: the error of PCM-QINTn is less than half of the PCM-CLSn error and has the opposite sign.

Calculations for 17 molecules at the PCM-CLS4 and PCM-QINT2 levels, in water at standard conditions, are reported in Table 2.

Taking the PCM-direct result as reference we have the following statistical results:

PCM-CLS4 $\sigma = 1.66$, $r = 0.999942$
PCM-QINT2 $\sigma = 0.50$, $r = 0.999996$.

Table 2. Electrostatic component of the free energy of solvation (Kcal/mol) evaluated with PCM-CLS4, PCM-Direct, PCM-QINT2 methods for some molecules

Molecule	Direct	CLS4	QINT2
CH_3COCH_3	−8.536	−8.617	−8.278
CH_3COH	−5.566	−5.838	−5.566
CH_3CH_2OH	−6.708	−6.713	−6.595
CH_3OH	−5.464	−5.334	−5.320
H_2NCH_2COOH	−12.674	−12.755	−12.378
H_2CO	−7.108	−7.170	−6.845
H_2O	−6.763	−5.177	−6.519
HF	−10.845	−10.858	−10.637
NH_3	−7.065	−7.088	−6.967
OH^-	−93.898	−93.787	−93.720
$CH_3CH_2O^-$	−87.731	−87.959	−87.794
$HCOO^-$	−88.987	−89.057	−88.655
$NO_3{}^-$	−69.870	−69.813	−69.855
$CLO_4{}^-$	−59.695	−59.566	−59.687
$[Li(H_2O)_4]^+$	−52.810	−53.377	−52.784
$[Mg(H_2O)_6]^{++}$	−177.808	−177.827	−177.796
$[Al(H_2O)_6]^{+++}$	−744.804	−720.706	−737.768

These results show that PCM-direct, PCM-CLS4 and PCM-QINT2 give very close values; furthermore, about 90% of the standard deviation is due to the last system in Table 2 ($[Al(H_2O)_6]^{+++}$).

An analysis on the assumption of nuclear interpolation value also for electrons [see discussion after Eq. (26)] is reported in Table 3. For three molecules is reported the difference

$$|q^{\mathrm{ele}}_{\mathrm{tot}} - q^{\mathrm{ele}}_{\mathrm{theo}}| \tag{31}$$

obtained with six different basis sets at the last SCF cycle of PCM-direct and comparing it with PCM-QINT2 and PCM-QINT4 values. The value obtained from Eq. (31) with PCM-QINT2-4 can be larger or smaller than the PCM-direct value and increases with the flexibility of the basis set, but always is less than half an electron charge.

Only the PCM-QINTn yields goods results for G_{el} derivatives with respect to atomic coordinates [8, 9] using the approximation given in Eq. (30).

Synthetic quantities for three molecules are reported in Table 4 up to fourth order. Taking the PCM-direct gradient for reference, we report, for any gradient, the norm ($|\vec{v}|$), the norm of the difference ($|\vec{v} - \vec{v}_{\mathrm{dir}}|$) and the angle ($\widehat{\vec{v}\vec{v}_{\mathrm{dir}}}$) with the reference gradient. Some additional material is available at the URL "http://www.sns.it/~cris/qint.html".

The differences in norm and orientation of gradients computed with different PCM formulations are small.

Table 3. Error on the sum of ASC with respect to theoretical value with several basis sets and several PCM formulations

HF			
Basis set	QINT2	QINT4	Direct
6.31G	0.02021	0.02009	0.01940
6.31G**	0.02329	0.02317	0.02264
6.31++G**	0.04957	0.04951	0.04813
DZV	0.03474	0.03463	0.03345
DZP	0.03072	0.03691	0.03584
DZP++	0.05322	0.05315	0.05175
NH_3			
Basis set	QINT2	QINT4	Direct
6.31G	0.12645	0.12639	0.15854
6.31G**	0.13169	0.13163	0.16397
6.31++G**	0.38391	0.38548	0.38558
DZV	0.15352	0.15349	0.18573
DZP	0.15667	0.15674	0.18908
DZP++	0.17842	0.17843	0.21095
OH^-			
Basis set	QINT2	QINT4	Direct
6.31G	0.05782	0.05775	0.04528
6.31G**	0.05999	0.05993	0.04746
6.31++G**	0.20020	0.20031	0.18860
DZV	0.09300	0.09298	0.08053
DZP	0.09408	0.09407	0.08162
DZP++	0.20773	0.20783	0.19599

Table 4. Synthetic quantities about G_{el} gradients for several molecules and PCM formulations.

H_2O			
Method	$\|\vec{v}\|$	$\|\vec{v}-\vec{v}_{\mathrm{dir}}\|$	$\widehat{\vec{v}\vec{v}_{\mathrm{dir}}}$
QINT1	0.00598	0.0001	0.0035
QINT2	0.00581	0.0016	0.0016
QINT3	0.00594	0.0003	0.0028
QINT4	0.00598	0.0003	0.0014
direct	0.00597	0.0000	0.0000
H_2CO			
Method	$\|\vec{v}\|$	$\|\vec{v}-\vec{v}_{\mathrm{dir}}\|$	$\widehat{\vec{v}\vec{v}_{\mathrm{dir}}}$
QINT1	0.02232	0.0025	0.0663
QINT2	0.02513	0.0010	0.0231
QINT3	0.02415	0.0018	0.0180
QINT4	0.02451	0.0025	0.0587
direct	0.02430	0.0000	0.0000
CH_3OH			
Method	$\|\vec{v}\|$	$\|\vec{v}-\vec{v}_{\mathrm{dir}}\|$	$\widehat{\vec{v}\vec{v}_{\mathrm{dir}}}$
QINT1	0.00877	0.0008	0.0603
QINT2	0.00795	0.0004	0.0206
QINT3	0.00839	0.0003	0.0269
QINT4	0.00819	0.0002	0.0227
direct	0.00806	0.0000	0.0000

The complete values show three-decimal-place precision for any component of the G_{el} gradient.

Finally, PCM-CLS4 and of PCM-QINT2 are computationally convenient if the molecular surface has more than 600 tesserae. For $\left[\mathrm{Al(H_2O)_6}\right]^{+++}$, the system with the largest number of tesserae (846), PCM-QINT2 methods are around three times faster than PCM-direct. The ratio of CPU times for computing ASC is in this case 1(PCM-direct):0.33(PCM-CLS4):0.31(PCM-QINT2).

4 Conclusions

We have presented a new method to solve the PCM electrostatic problem (PCM-QINTn) and a new formulation of a pre-existent algorithm (PCM-CLSn). These methods give good values for all the molecules we have presented.

The computational costs of the PCM procedures respect to ab initio calculation are small, so the PCM-QINTn and PCM-CLSn methods can be interesting applications when coupled to more approximated methods such as semiempirical HF and molecular mechanics.

In these fields we generally have a large number of atoms and hence a large number of tesserae; the low computational complexity of PCM-CLSn and PCM-QINTn methods can thus be useful. Furthermore, in these approximated methods the electrostatic description of the system is generally limited to punctual multipoles. This characteristic eliminates the problem of the double set of nuclear and electronic charges.

Applications of the procedures described in this paper to non-ab initio methods will be described in further papers.

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