Theor Chem Acc (2002) 107:80–89
DOI 10.1007/s00214-001-0302-1

Theoretical
Chemistry Accounts

Regular article

Comparison of solvent reaction field representations

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Received: 2 July 2001 / Accepted: 10 September 2001 /

Abstract. Alternative ways are examined for representing a reaction field to treat the important effects of long-range electrostatic interaction with a solvent in electronic structure calculations on the properties of a solute. Several extant boundary element methods for approximate representation of the solvent reaction field in terms of surface charge distributions are considered, and analogous new methods for approximate representation in terms of surface dipole distributions are introduced. Illustrative computational results are presented on representative small neutral and ionic solutes to evaluate the relative accuracy of various methods.

Key words: Solvent effects – Reaction field – Boundary element methods – Surface charge distributions – Surface dipole distributions

1 Introduction

The various influences of a solvent on a solute can be broadly classified as being due to attractive electrostatic and dispersion interactions along with repulsive cavitation and exchange interactions. The electrostatic interactions, which are the subject of this work, are of long range and usually dominate in polar environments. It is common and convenient to represent the electrostatic interactions approximately using reaction field theory [1–4] wherein the solvent polarization is treated by a highly simplified model.

Excellent recent reviews are available covering both theory and applications of reaction field methods in connection with electronic structure calculations [5, 6], so we will give only a cursory literature treatment here. The present work focuses on methods that provide approximate solutions of Poisson's equation through reaction fields that are generated by certain apparent surface distributions. For completeness, it should be mentioned that several other kinds of reaction field methods not considered here are also in common use. These include related methods based on the generalized Born equation [7–9], Langevin dipoles [10], and a direct reaction field approach [11].

In reaction field theory the solute is envisioned as nominally occupying a cavity that strictly excludes the solvent. If the solute charge density is entirely enclosed inside the cavity, then it is possible to represent the effect of the classical reaction field exactly by a certain apparent charge density lying on the surface of the cavity. However, any unconstrained quantum mechanical calculation on the solute inevitably leads to a tail of the wave function extending outside the cavity. There is a variety of reaction field implementations in the literature that differ mainly in how the effect of this solute charge penetration is treated.

Exact solution of Poisson's equation to include the effects of charge penetration can be achieved laboriously by using both an apparent surface charge density lying on the cavity surface and an apparent volume charge density lying outside the cavity [12–18], as in the method here denoted surface and volume polarization for electrostatics (SVPE). In this work we consider several simpler approximate solutions to this problem that involve only apparent surface charge distributions, which can be conveniently obtained in practice through solutions based on boundary element approaches. These include the method here denoted surface and simulation of volume polarization for electrostatics [SS(V)PE] [14, 15, 19, 20–22] the integral equation formalism (IEF) [23–26] and the conductor screening model (COSMO) [27–34]. In SS(V)PE there is an optimal representation of volume polarization in terms of a surface charge distribution, while in IEF and COSMO there is a more approximate representation of volume polarization in terms of a surface charge distribution.

For reference, we also consider the large group of standard methods that we denote surface polarization for electrostatics (SPE) which simply ignore volume

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polarization effects. A large group of SPE implementations utilize boundary element approaches. Many of them [35–46] represent the reaction field through apparent surface charge distributions. A few SPE boundary element approaches use a combination of apparent surface charge and apparent surface dipole distributions [47–50], or just apparent surface dipole distributions [48]. Note that use of apparent surface dipole distributions [47–50] requires that different dipole distributions, as well as volume polarization distributions, be used to represent the solution in the different regions inside, on, and outside the cavity in order to achieve a reaction potential that is continuous across the cavity surface. Still other SPE implementations avoid explicit display of the underlying apparent surface distribution by using a more direct means to represent the reaction potential either through finite-element approaches [51–55] or by use of multipole expansions [56–59].

The approximate SS(V)PE, IEF, COSMO, and SPE methods can also be classified as particular variants of the broad polarized continuum model (PCM) [60], as will be discussed in detail later. The term PCM is also usually understood to further imply certain kinds of cavity construction, called GEPOL [61] or DefPol [62], but in principle the specific cavity construction is largely independent of the reaction field equation and solution that is the main focus of the present work.

We also introduce here several new approximate methods proposed as surface dipole analogs for each of the SS(V)PE, IEF, COSMO, and SPE methods. These can also be conveniently obtained in practice through solutions based on boundary element approaches. The general advantages and disadvantages of surface dipole versus surface charge representations are compared and discussed.

In the following ‘Theory’ section, a self-contained outline is given of the formal equations defining the various reaction field methods considered. The next section on ‘Accuracy of approximate reaction field methods’ reports some illustrative calculations to assess in practice how well each of the approximate surface distribution methods provides an accurate representation of the exact reaction field. The final section gives a brief summary of the work and reviews the major findings.

2 Theory

2.1 Notation for potentials and fields

The entire three-dimensional space is denoted by $\mathbf{V}$. A closed surface $\mathbf{\Gamma}$ defines the cavity region strictly excluding solvent and nominally enclosing the solute. Thus, $\mathbf{V}$ is separated into regions $\mathbf{V}^{\mathrm{int}}$ interior to the cavity and $\mathbf{V}^{\mathrm{ext}}$ exterior to the cavity. Points that may be anywhere in $\mathbf{V}$ are denoted by $\mathbf{r}$, while points that are constrained to lie on $\mathbf{\Gamma}$ are denoted by $\mathbf{t}$. A point regarded as lying on the interior face of $\mathbf{\Gamma}$ is given by $\mathbf{t}^{\mathrm{int}}$, and similarly a point on the exterior face as $\mathbf{t}^{\mathrm{ext}}$. The unit vector parallel to the outward-directed normal to $\mathbf{\Gamma}$ at $\mathbf{t}$ is denoted as $\mathbf{n_t}$.

The symbol $\Phi(\mathbf{r})$ denotes an electrostatic potential. All potentials in this work are assumed to be well behaved at the origin and regular at infinity. As detailed later, different expressions apply for the electrostatic potential depending on whether it arises from a volume charge density, a surface charge density, or a surface dipole density. Regardless of its source, a given electrostatic potential $\Phi(\mathbf{r})$ has an associated electric field given by $\mathbf{F}(\mathbf{r}) = -\nabla\Phi(\mathbf{r})$. The outward-directed normal component of this field at any point on the surface $\mathbf{\Gamma}$ is $F_{\mathrm{n}}(\mathbf{t}) = \mathbf{n_t}\cdot\mathbf{F}(\mathbf{t})$. In cases where the normal electric field is discontinuous across the surface, we take its value on the surface to be the average of its values $F_{\mathrm{n}}(\mathbf{t}^{\mathrm{int}})$ and $F_{\mathrm{n}}(\mathbf{t}^{\mathrm{ext}})$ at the respective points on the interior and exterior faces.

A generic volume charge density $\rho(\mathbf{r})$ defined throughout all $\mathbf{V}$ has a total charge given by

$$\bar{\rho} = \int_{\mathbf{V}} \mathrm{d}^3\mathbf{r}'\,\rho(\mathbf{r}') \ ,$$

which can be resolved into contributions interior and exterior to the cavity

$$\bar{\rho}^{\mathrm{int}} = \int_{\mathbf{V}^{\mathrm{int}}} \mathrm{d}^3\mathbf{r}'\,\rho(\mathbf{r}') \quad \text{and} \quad \bar{\rho}^{\mathrm{ext}} = \int_{\mathbf{V}^{\mathrm{ext}}} \mathrm{d}^3\mathbf{r}'\rho(\mathbf{r}') \ ,$$

so $\bar{\rho} = \bar{\rho}^{\mathrm{int}} + \bar{\rho}^{\mathrm{ext}}$. A volume charge density source $\rho(\mathbf{r})$ produces the electrostatic potential

$$\Phi^{\rho}(\mathbf{r}) = \int_{\mathbf{V}} \mathrm{d}^3\mathbf{r}'\rho(\mathbf{r}')\left(\frac{1}{|\mathbf{r}-\mathbf{r}'|}\right) \ .$$

Provided that $\rho(\mathbf{r})$ is well behaved, the associated electric field is continuous everywhere. The normal component of this field at any point on the surface can be written as

$$F^{\rho}_{\mathrm{n}}(\mathbf{t}) = \int_{\mathbf{V}} \mathrm{d}^3\mathbf{r}'\rho(\mathbf{r}')\left(\frac{\partial}{\partial\mathbf{n_t}}\frac{1}{|\mathbf{t}-\mathbf{r}'|}\right) \ ,$$

where the indicated normal derivative is given by

$$\frac{\partial}{\partial\mathbf{n_t}}\frac{1}{|\mathbf{t}-\mathbf{r}'|} = -\frac{\mathbf{n_t}\cdot(\mathbf{t}-\mathbf{r}')}{|\mathbf{t}-\mathbf{r}'|^3} \ .$$

Note that in previous work [21] the notation $\partial\Phi^{\rho}(\mathbf{t})$ was used for what is here denoted as $-F^{\rho}_{\mathrm{n}}(\mathbf{t})$.

A generic surface charge density $\sigma(\mathbf{t})$ defined throughout all of $\mathbf{\Gamma}$ has a total charge given by

$$\bar{\sigma} = \int_{\mathbf{\Gamma}} \mathrm{d}^2\mathbf{t}'\,\sigma(\mathbf{t}') \ ,$$

and produces the electrostatic potential

$$\Phi^{\sigma}(\mathbf{r}) = \int_{\mathbf{\Gamma}} \mathrm{d}^2\mathbf{t}'\,\sigma(\mathbf{t}')\left(\frac{1}{|\mathbf{r}-\mathbf{t}'|}\right) \ .$$

Provided that $\sigma(\mathbf{t})$ is well behaved, the potential $\Phi^{\sigma}(\mathbf{r})$ is continuous everywhere, but the associated electric field $\mathbf{F}^{\sigma}(\mathbf{r})$ is discontinuous in passing across $\mathbf{\Gamma}$. Its value at any point on the surface is

$$F_{\mathrm{n}}^{\sigma}(\mathbf{t}) = \int_{\Gamma} \mathrm{d}^2\mathbf{t}'\sigma(\mathbf{t}')\left(\frac{\partial}{\partial \mathbf{n_t}}\frac{1}{|\mathbf{t}-\mathbf{t}'|}\right) \ .$$

A generic surface dipole density $\mu(\mathbf{t})$ defined throughout all of $\mathbf{\Gamma}$ produces the electrostatic potential

$$\Phi^{\mu}(\mathbf{r}) = \int_{\Gamma} \mathrm{d}^2\mathbf{t}'\mu(\mathbf{t}')\left(\frac{\partial}{\partial \mathbf{n_{t'}}}\frac{1}{|\mathbf{r}-\mathbf{t}'|}\right) \ .$$

Provided that $\mu(\mathbf{t})$ is well behaved the associated normal electric field component $F_{\mathrm{n}}^{\mu}(\mathbf{t})$ is continuous across $\mathbf{\Gamma}$, although the potential $\Phi^{\mu}(\mathbf{t})$ itself is discontinuous in passing across $\mathbf{\Gamma}$.

We will be especially concerned with the values of potentials and fields at and near the cavity surface, so it is convenient to adopt special notations for this case. Thus, we define $\mathscr{S}$ as the integral operator acting on a generic surface charge density $\sigma(\mathbf{t})$ that produces on $\mathbf{\Gamma}$ the corresponding electrostatic potential, i.e.,

$$\mathscr{S}\sigma(\mathbf{t}) = \int_{\Gamma} \mathrm{d}^2\mathbf{t}'\sigma(\mathbf{t}')\left(\frac{1}{|\mathbf{t}-\mathbf{t}'|}\right) = \Phi^{\sigma}(\mathbf{t}) \ .$$

We further define $\mathscr{D}^*$ as the integral operator acting on a generic surface charge density $\sigma(\mathbf{t})$ that produces on $\mathbf{\Gamma}$ the corresponding negative normal component of the electric field, i.e.,

$$\mathscr{D}^*\sigma(\mathbf{t}) = \int_{\Gamma} \mathrm{d}^2\mathbf{t}'\sigma(\mathbf{t}')\left(\frac{\partial}{\partial \mathbf{n_t}}\frac{1}{|\mathbf{t}-\mathbf{t}'|}\right) = -F_{\mathrm{n}}^{\sigma}(\mathbf{t}) \ .$$

The discontinuity of this normal field across $\mathbf{\Gamma}$ can then be expressed by

$$\mathscr{D}^*\sigma(\mathbf{t}) + 2\pi\sigma(\mathbf{t}) = -F_{\mathrm{n}}^{\sigma}(\mathbf{t}^{\mathrm{int}}) \quad \text{and}$$
$$\mathscr{D}^*\sigma(\mathbf{t}) - 2\pi\sigma(\mathbf{t}) = -F_{\mathrm{n}}^{\sigma}(\mathbf{t}^{\mathrm{ext}}) \ .$$

Similarly, we define $\mathscr{D}$ as the integral operator acting on a generic surface dipole density $\mu(\mathbf{t})$ that produces on $\mathbf{\Gamma}$ the corresponding electrostatic potential, i.e.,

$$\mathscr{D}\mu(\mathbf{t}) = \int_{\Gamma} \mathrm{d}^2\mathbf{t}'\mu(\mathbf{t}')\left(\frac{\partial}{\partial \mathbf{n_{t'}}}\frac{1}{|\mathbf{t}-\mathbf{t}'|}\right) = \Phi^{\mu}(\mathbf{t}) \ .$$

The discontinuity of this potential across $\mathbf{\Gamma}$ can then be expressed by

$$\mathscr{D}\mu(\mathbf{t}) - 2\pi\mu(\mathbf{t}) = \Phi^{\mu}(\mathbf{t}^{\mathrm{int}}) \quad \text{and}$$
$$\mathscr{D}\mu(\mathbf{t}) + 2\pi\mu(\mathbf{t}) = \Phi^{\mu}(\mathbf{t}^{\mathrm{ext}}) \ .$$

We note that $\mathscr{D}$, $\mathscr{D}^*$, and $\mathscr{S}$ are related through $\mathscr{D}\mathscr{S} = \mathscr{S}\mathscr{D}^*$, which is an example of an operator relation that takes on specific meaning when each side operates on some given surface distribution. The identity operator is denoted $\mathscr{I}$.

2.2 Exact reaction potential

It is desired to determine the equilibrium reaction potential $\Phi^{\mathrm{rxn}}(\mathbf{r})$ from some model of the solute–solvent interaction. Here we treat the solvent as a homogeneous linear isotropic dielectric continuum. The reaction potential can then be obtained from a classical approach based on Poisson's equation in which the charge density of the solute polarizes the solvent, leading to an attractive potential energy due to the mutual electrostatic attraction between solute and bulk solvent. This classical potential energy is given in atomic units by

$$\mathscr{V}^{\mathrm{rxn}} = \sum_{\nu}^{\mathrm{nuc}} Z_{\nu}\Phi^{\mathrm{rxn}}(\mathbf{R}_{\nu}) - \sum_{n}^{\mathrm{elec}} \Phi^{\mathrm{rxn}}(\mathbf{r}_n) \ .$$

The influence of the solvent in back-polarizing the solute can be treated by adding this potential energy to the gas-phase solute Hamiltonian operator, $\mathscr{H}^{\mathrm{gas}}$, that is used to determine the solute electronic wave function. In a self-consistent reaction field approach the mutual solvent and solute polarizations are iterated until full equilibration.

Quantum mechanical calculation of the solute electronic wave function, Ψ, determines the solute charge density via

$$\rho(\mathbf{r}) = \rho^{\mathrm{nuc}}(\mathbf{r}) + \rho^{\mathrm{elec}}(\mathbf{r})$$
$$= \sum_{\nu}^{\mathrm{nuc}} Z_{\nu}\delta^3(\mathbf{r}-\mathbf{R}_{\nu}) - \left\langle \Psi \middle| \sum_{n}^{\mathrm{elec}} \delta^3(\mathbf{r}-\mathbf{r}_n) \middle| \Psi \right\rangle \ .$$

In any one step of an iterative self-consistent reaction field calculation, $\rho(\mathbf{r})$ can be regarded as known and fixed. The most fundamental expression used here for the total solute–solvent interaction energy can be written in terms of these quantities as

$$\mathscr{E}^{\mathrm{rxn}} = \langle\Psi|\mathscr{V}^{\mathrm{rxn}}|\Psi\rangle = \int_{\mathbf{V}} \mathrm{d}^3\mathbf{r}'\rho(\mathbf{r}')\Phi^{\mathrm{rxn}}(\mathbf{r}') \ . \tag{1}$$

Other secondary expressions for $\mathscr{E}^{\mathrm{rxn}}$, which are formally equivalent to the fundamental expression in Eq. (1) only under certain conditions, will be given later.

The free energy of solvation is given by

$$\Delta G^{\mathrm{solv}} = [\langle\Psi|\mathscr{H}^{\mathrm{gas}}|\Psi\rangle - \mathscr{E}^{\mathrm{gas}}] + \tfrac{1}{2}\mathscr{E}^{\mathrm{rxn}} \ .$$

Here the quantity in brackets on the right hand side (RHS) represents the work of polarizing the solute. Note that only half the solute–solvent interaction energy, $\mathscr{E}^{\mathrm{rxn}}$, contributes, because the other half is expended as work in polarizing the solvent (assuming linear response).

The electrostatic potential $\Phi^{\rho}(\mathbf{r})$, which can be partitioned into $\Phi^{\rho^{\mathrm{nuc}}}(\mathbf{r}) + \Phi^{\rho^{\mathrm{elec}}}(\mathbf{r})$, represents the potential that the given charge density, $\rho(\mathbf{r})$, would produce if it were isolated in a vacuum, so it is the solution of Poisson's equation in a vacuum given by

$$\nabla^2\Phi^{\rho}(\mathbf{r}) = -4\pi\rho(\mathbf{r}) \ .$$

Together with the reaction potential it produces the total electrostatic potential of the solute–solvent system

$$\Phi^{\mathrm{total}}(\mathbf{r}) = \Phi^{\rho}(\mathbf{r}) + \Phi^{\mathrm{rxn}}(\mathbf{r}) \ .$$

In this work we consider only the solvation energy after full mutual equilibration between solute and solvent is reached, and further assume zero ionic strength. The solvent polarization is therefore characterized solely by the experimental static dielectric constant, ϵ, of the bulk pure solvent. The polarizability of the solute is automatically taken care of by the quantum mechanical calculation of its wave function, so inside the cavity the dielectric constant is taken as unity. Thus, Poisson's equation for the total electrostatic potential in the presence of a solvent is

$$\nabla^2\Phi^{\text{total}}(\mathbf{r}) = -4\pi\rho(\mathbf{r})\begin{cases} 1 & \text{for } \mathbf{r} \in \mathbf{V}^{\text{int}} \\ 1/\epsilon & \text{for } \mathbf{r} \in \mathbf{V}^{\text{ext}} \end{cases} ,$$

together with the boundary conditions that $\Phi^{\text{total}}(\mathbf{r})$ be continuous across $\mathbf{\Gamma}$ and that the associated normal electric field takes a jump across the surface given by

$$F_{\text{n}}^{\text{total}}(\mathbf{t}^{\text{int}}) = \epsilon F_{\text{n}}^{\text{total}}(\mathbf{t}^{\text{ext}}) \ .$$

By subtracting the known contribution of $\Phi^{\rho}(\mathbf{r})$ from $\Phi^{\text{total}}(\mathbf{r})$, we obtain Poisson's equation for the remaining reaction potential as

$$\nabla^2\Phi^{\text{rxn}}(\mathbf{r}) = \begin{cases} 0 & \text{for } \mathbf{r} \in \mathbf{V}^{\text{int}} \\ (\frac{\epsilon-1}{\epsilon})4\pi\rho(\mathbf{r}) & \text{for } \mathbf{r} \in \mathbf{V}^{\text{ext}} \end{cases} . \tag{2}$$

The exact reaction potential $\Phi^{\text{rxn}}(\mathbf{r})$ is continuous across $\mathbf{\Gamma}$. Since $\mathbf{F}^{\rho}(\mathbf{r})$ is continuous across $\mathbf{\Gamma}$, the reaction field must be entirely responsible for taking care of the jump boundary condition, i.e.,

$$F_{\text{n}}^{\text{rxn}}(\mathbf{t}^{\text{int}}) = \epsilon F_{\text{n}}^{\text{rxn}}(\mathbf{t}^{\text{ext}}) + (\epsilon - 1)F_n^{\rho}(\mathbf{t}) \ . \tag{3}$$

The major computational work of reaction field theory lies in obtaining an exact or approximate solution of these equations for the reaction potential. It should always be kept in mind that even an exact or highly accurate solution still represents only a highly simplified model of the actual physical effects of solvation.

The SVPE method [12, 13, 14, 15, 16, 17, 18] provides an exact solution of these reaction field equations. It is defined by the potential $\Phi^{\text{rxn}}(\mathbf{r}) = \Phi^{\text{SVPE}}(\mathbf{r})$ that combines two distinct contributions

$$\Phi^{\text{SVPE}}(\mathbf{r}) = \Phi^{\sigma^{\text{SVPE}}}(\mathbf{r}) + \Phi^{\beta^{\text{SVPE}}}(\mathbf{r}) \ . \tag{4}$$

Here $\Phi^{\beta^{\text{SVPE}}}(\mathbf{r})$ is a volume polarization potential that accounts for the Laplacian of the reaction potential not vanishing outside the cavity, as seen in Eq. (2). It is the electrostatic potential associated with the volume polarization charge density, $\beta^{\text{SVPE}}(\mathbf{r})$, defined by

$$\beta^{\text{SVPE}}(\mathbf{r}) = \begin{cases} 0 & \text{for } \mathbf{r} \in \mathbf{V}^{\text{int}} \\ -(\frac{\epsilon-1}{\epsilon})\rho(\mathbf{r}) & \text{for } \mathbf{r} \in \mathbf{V}^{\text{ext}} \end{cases} . \tag{5}$$

The other term, $\Phi^{\sigma^{\text{SVPE}}}(\mathbf{r})$, accounts for the jump boundary condition at the cavity surface, as seen in Eq. (3). It is the electrostatic potential associated with the surface charge distribution, $\sigma^{\text{SVPE}}(\mathbf{t})$, that satisfies

$$\begin{aligned} &\left[\mathscr{I} - \left(\frac{\epsilon-1}{\epsilon+1}\right)\frac{1}{2\pi}\mathscr{D}^*\right]\sigma^{\text{SVPE}}(\mathbf{t}) \\ &\quad = -\left(\frac{\epsilon-1}{\epsilon+1}\right)\frac{1}{2\pi}[F_{\text{n}}^{\rho}(\mathbf{t}) + F_{\text{n}}^{\beta^{\text{SVPE}}}(\mathbf{t})] \ . \end{aligned} \tag{6}$$

However, the exact SVPE method is laborious to implement and time-consuming to run, because it utilizes a volume polarization potential arising from a discontinuous volume charge density. With a cavity surface that is adapted to the detailed nonspherical shape of a general molecular solute, this leads to difficult integrations over just part of the full three-dimensional space. Consequently, it is of interest to investigate approximate representations that omit any explicit volume polarization charge density and that use only simple surface charge or surface dipole distributions to generate the reaction potential.

2.3 Approximate surface charge potentials

In many instances, the reaction potential is approximated by using only some surface charge distribution, $\sigma(\mathbf{t})$, yielding a reaction potential $\Phi^{\sigma}(\mathbf{r})$. Among other simplifications, such approximation leads to a convenient alternative means of determining the associated reaction field energy, $\mathscr{E}^{\sigma}$, as a surface integral via the secondary expression

$$\mathscr{E}^{\sigma} = \int_{\mathbf{\Gamma}} \mathrm{d}^2\mathbf{t}'\sigma(\mathbf{t}')\Phi^{\rho}(\mathbf{t}') \tag{7}$$

which involves the solute potential on the surface. We emphasize again that it is possible to solve the reaction field equations exactly in terms of a surface charge density alone only if no solute charge lies outside the cavity. In an unconstrained quantum mechanical treatment of the solute, representing the reaction potential through a surface charge density alone is always an approximation.

Here we briefly review several ways that have been suggested to achieve such approximate surface charge distributions. These approaches have in common that the surface charge density satisfies an equation of the generic form

$$\mathscr{K}\sigma(\mathbf{t}) = \mathscr{Y}(\mathbf{t}) \ . \tag{8}$$

Here $\mathscr{K}$ is the system operator, an integral operator depending explicitly on the cavity definition. According to the particular definition selected to determine the cavity surface, the system operator may in turn be implicitly influenced by the solute charge density, such as in the isodensity construction described later. The RHS function $\mathscr{Y}(\mathbf{t})$ depends explicitly and linearly on the charge density of the solute through the electrostatic potential and/or electric field it generates at the cavity surface. The effective system operator $\mathscr{K}$ and the function $\mathscr{Y}(\mathbf{t})$ associated with each of the approximate surface charge methods examined in this work are summarized in Table 1.

The SS(V)PE method originated with the demonstration [14] that all direct and indirect effects of the volume polarization charge density on the exact SVPE reaction potential can be exactly represented at all points inside the cavity (which is the most important region) by simulating the explicit volume charge density in terms of an additional surface charge density. Thus,

$$\Phi^{\sigma^{\text{SS(V)PE}}}(\mathbf{r}) = \Phi^{\text{SVPE}}(\mathbf{r}) \quad \text{for } \mathbf{r} \in \mathbf{V}^{\text{int}} \ .$$

Table 1. Operators and functions involved in approximate surface charge methods

Method	Operator $\mathscr{K}$	Function $\mathscr{Y}(\mathbf{t})$
SS(V)PE[a]	$\mathscr{S} - \left(\frac{\epsilon-1}{\epsilon+1}\right)\frac{1}{4\pi}(\mathscr{D}\mathscr{S}+\mathscr{S}\mathscr{D}^*)$	$-\left(\frac{\epsilon-1}{\epsilon+1}\right)\left(\mathscr{I}-\frac{1}{2\pi}\mathscr{D}\right)\Phi^{\rho}(\mathbf{t})$
IEF[a]	$\mathscr{S} - \left(\frac{\epsilon}{\epsilon+1}\right)\frac{1}{2\pi}\mathscr{D}\mathscr{S} + \left(\frac{1}{\epsilon+1}\right)\frac{1}{2\pi}\mathscr{S}\mathscr{D}^*$	$-\left(\frac{\epsilon}{\epsilon+1}\right)\left(\mathscr{I}-\frac{1}{2\pi}\mathscr{D}\right)\Phi^{\rho}(\mathbf{t}) + \left(\frac{1}{\epsilon+1}\right)\left(\frac{1}{2\pi}\mathscr{S}\right)F_{\mathrm{n}}^{\rho}(\mathbf{t})$
COSMO	$\mathscr{S}$	$-\left(\frac{\epsilon-1}{\epsilon}\right)\Phi^{\rho}(\mathbf{t})$
SPE	$\mathscr{I} - \left(\frac{\epsilon-1}{\epsilon+1}\right)\frac{1}{2\pi}\mathscr{D}^*$	$-\left(\frac{\epsilon-1}{\epsilon+1}\right)\frac{1}{2\pi}F_{\mathrm{n}}^{\rho}(\mathbf{t})$

[a] The $\mathscr{K}$ operators for the SS(V)PE and IEF surface charge methods are formally equivalent to one another. They can also be equivalently written in factorized form as $\mathscr{S}\left[\mathscr{I} - \left(\frac{\epsilon-1}{\epsilon+1}\right)\frac{1}{2\pi}\mathscr{D}^*\right]$ or as $\left[\mathscr{I} - \left(\frac{\epsilon-1}{\epsilon+1}\right)\frac{1}{2\pi}\mathscr{D}\right]\mathscr{S}$

Later the accuracy of this representation of the reaction field was verified numerically [15] and the idea was further analyzed formally [20], but at that point the method was still not very practical because it required explicit construction of the volume polarization in order to determine the additional surface charge distribution that simulates it. The culmination, and awarding of the SS(V)PE designation as a practical and desirable method, finally came with a formal synthesis [21] that allowed all the relevant surface charge density, from whatever source, to be determined from a single equation having the form of Eq. (8). The SS(V)PE operator listed in the main body of Table 1, which is one of several possible expressions as noted in the footnote to Table 1, is in the previously recommended [21] most symmetric form. While the different expressions given for this operator are formally equivalent, they may lead to slightly different results in practice when the individual operators $\mathscr{S}$, $\mathscr{D}$, and $\mathscr{D}^*$ are each separately defined over a finite grid of surface points. Note from Table 1 that the SS(V)PE method only requires determination of the solute potential on $\mathbf{\Gamma}$, rather than the more difficult to construct solute normal electric field. An independent implementation of the SS(V)PE method called implicit volume charge-PCM has also been developed recently [18], and the results compared to those from a related implementation [18] of SVPE.

The IEF method [23–26], also sometimes called IEF-PCM, is given here in a simplified form that applies to the special case of an isotropic solvent having zero ionic strength. The IEF operator listed in the main body of Table 1, which is one of several possible expressions as noted in the footnote to Table 1, is in the form specified in the original publications defining the method. Note from Table 1 that the IEF method requires determination of both the solute potential and the normal electric field on $\mathbf{\Gamma}$.

An alternative IEF method has also been suggested [19], being derived with the motivation of eliminating the solute normal electric field from the RHS of the original IEF working equation (Table 1). More recently, it was shown [22] that this alternative IEF method [19] is formally equivalent to the SS(V)PE method. However, the favorable representation of volume polarization in the resulting equation [19] was not recognized at the time of its derivation, that feature being evident only in the SS(V)PE work [14, 15, 20, 21].

The COSMO [27–34] method is based on solving the large ϵ limit of Poisson's equation exactly on the cavity surface, then scaling the result to apply to the finite dielectric case. It should be pointed out that the original COSMO formulation [27–31] uses the slightly different dielectric scaling factor of $(\epsilon-1)/(\epsilon+0.5)$ rather than the factor $(\epsilon-1)/\epsilon$ from the "generalized" GCOSMO version [32–34] that is adopted here and in C-PCM implementations.The expression used here in Eq. (7) and in most other reaction field formulations displays the reaction field energy as a linear function of the surface charge density, but in the COSMO method it is possible to take advantage of the very simple and immediate connection of the surface charge density with the solute potential (Table 1) to generate other equivalent tertiary surface integral expressions [27, 28, 32, 33] that contain terms quadratic in the surface charge density. Note from Table 1 that this method requires determination of only the solute potential on $\mathbf{\Gamma}$.

A. Klamt, the developer of COSMO, has privately informed us that he also arrived at the equivalent of the SS(V)PE [21] (and alternative IEF [19, 22]) equation some time ago by yet another approach. This previously unpublished deduction proceeds as follows. Start with the SPE equation given in Table 1 (and discussed more fully later). Let $\sigma_{\infty}^{\mathrm{SPE}}(\mathbf{t})$ be the solution of this equation in the limit of large ϵ. Use this solution to reexpress the function on the RHS of the SPE equation, leading to an expression for $\sigma^{\mathrm{SPE}}(\mathbf{t})$ in terms of its large ϵ limit as

$$\left[\mathscr{I} - \left(\frac{\epsilon-1}{\epsilon+1}\right)\frac{1}{2\pi}\mathscr{D}^*\right]\sigma^{\mathrm{SPE}}(\mathbf{t}) = -\left(\frac{\epsilon-1}{\epsilon+1}\right)\left(\mathscr{I}-\frac{1}{2\pi}\mathscr{D}^*\right)\sigma_{\infty}^{\mathrm{SPE}}(\mathbf{t}) \ .$$

Now argue that the distribution $\sigma_{\infty}^{\mathrm{COSMO}}(\mathbf{t})$ which satisfies $\mathscr{S}\sigma_{\infty}^{\mathrm{COSMO}}(\mathbf{t}) = -\Phi^{\rho}(\mathbf{t})$ provides a better description of the correct large ϵ behavior than does $\sigma_{\infty}^{\mathrm{SPE}}(\mathbf{t})$.

Thus, it is interesting to inquire what happens to the equation if $\sigma_{\infty}^{\mathrm{SPE}}(\mathbf{t})$ is replaced ad hoc by $\sigma_{\infty}^{\mathrm{COSMO}}(\mathbf{t})$. A brief manipulation shows the answer is that $\sigma^{\mathrm{SPE}}(\mathbf{t})$ becomes replaced by what is now recognized as $\sigma^{\mathrm{SS(V)PE}}(\mathbf{t})$.

Thus, we have three independent ways of arriving at the SS(V)PE equation, each arising from a somewhat different motivation. One modifies the exact SVPE method to provide an optimal simulation of volume polarization in terms of additional surface polarization [14, 15, 20, 21], one modifies the original IEF equation to eliminate the solute electric field in favor of the solute potential [19, 22], and one modifies the SPE equation to improve the behavior in the limit of large dielectric constant. These different approaches each give valuable insight into the full meaning of the SS(V)PE equation.

The most common and historically first method [35] for determining the reaction potential is here called SPE, and elsewhere PCM or sometimes standard PCM or D-PCM (without charge renormalization). The SPE method follows immediately from pretending during solution of Poisson's equation that no solute charge density penetrates outside the cavity. It can be shown using Gauss' law that the total surface charge in this method is given by

$$\bar{\sigma}^{\mathrm{SPE}} = -\left(\frac{\epsilon - 1}{\epsilon}\right)\bar{\rho}^{\mathrm{int}} \ .$$

If it were true that all the solute charge density was enclosed by the cavity, then the RHS of this equation for $\bar{\sigma}^{\mathrm{SPE}}$ would involve the known total solute charge, $\bar{\rho}$, in place of the otherwise generally unknown $\bar{\rho}^{\mathrm{int}}$. A number of different ad hoc charge renormalization schemes have been suggested that effectively alter $\sigma^{\mathrm{SPE}}(\mathbf{t})$ in a way that forces this relation to $\bar{\rho}$, but none are very firmly based in theory and we do not recommend any of them. Rather, we find the relation to be useful as a means to calculate in practice the amount of solute charge penetrating outside the cavity by turning it around to obtain

$$\bar{\rho}^{\mathrm{ext}} = \bar{\rho} + \left(\frac{\epsilon}{\epsilon - 1}\right)\bar{\sigma}^{\mathrm{SPE}} \ . \tag{9}$$

Note from Table 1 that the SPE method requires determination of the solute normal electric field on $\mathbf{\Gamma}$.

If no solute charge penetrates outside the cavity then volume polarization vanishes. In that event the SS(V)PE, IEF, and SPE methods all become formally identical to one another, and furthermore each supplies the exact SVPE solution of Poisson's equation, while the COSMO method generally still differs and becomes exact only in the limit of very large dielectric constant.

2.4 Approximate surface dipole potentials

Here we show that still other simple approximations to the reaction field are possible through invoking a surface dipole distribution in place of a surface charge distribution. In this case the reaction potential is approximated by using only some surface dipole distribution, $\mu(\mathbf{t})$, yielding a reaction potential $\Phi^{\mu}(\mathbf{r})$. Such approximation leads to a convenient alternative means of determining the associated reaction field energy, $\mathscr{E}^{\mu}$, as a surface integral via the secondary expression

$$\mathscr{E}^{\mu} = -\int\limits_{\mathbf{\Gamma}} \mathrm{d}^2\mathbf{t}' \mu(\mathbf{t}') F_{\mathrm{n}}^{\rho}(\mathbf{t}') \ , \tag{10}$$

which involves the solute normal electric field.

For $\sigma(\mathbf{t})$ being some specified surface charge distribution, the electrostatic potentials $\Phi^{\sigma}(\mathbf{r})$ and $\Phi^{\mu}(\mathbf{r})$ are equal everywhere inside the cavity provided they are equal on the inner face of the cavity. This is the case if $\mu(\mathbf{t})$ is defined to be the surface dipole distribution which satisfies

$$\left(\mathscr{I} - \frac{1}{2\pi}\mathscr{D}\right)\mu(\mathbf{t}) = -\frac{1}{2\pi}\mathscr{S}\sigma(\mathbf{t}) \ . \tag{11}$$

The reaction potentials $\Phi^{\sigma}(\mathbf{r})$ and $\Phi^{\mu}(\mathbf{r})$ still differ on and outside the cavity, but that may not matter much if most of the solute charge is enclosed by the cavity. Thus, a surface dipole formulation might be expected to give a reaction field representation similar to that of the corresponding surface charge representation. On the other hand, use of a single surface dipole distribution to generate the full reaction potential everywhere leads to a discontinuity in the potential across the cavity surface

Table 2. Operators and functions involved in approximate surface dipole methods

Method	Operator $\mathscr{L}$	Function $\mathscr{Z}(\mathbf{t})$
SS(V)PE−μ	$\mathscr{I} - \left(\frac{\epsilon - 1}{\epsilon + 1}\right)\frac{1}{2\pi}\mathscr{D}$	$\left(\frac{\epsilon - 1}{\epsilon + 1}\right)\frac{1}{2\pi}\Phi^{\rho}(\mathbf{t})$
IEF[a]−μ	$\mathscr{I} - \left(\frac{2\epsilon}{\epsilon + 1}\right)\frac{1}{2\pi}\mathscr{D} + \left(\frac{\epsilon - 1}{\epsilon + 1}\right)\left(\frac{1}{2\pi}\mathscr{D}\right)^2$	$\left(\frac{\epsilon}{\epsilon + 1}\right)\left(\mathscr{I} - \frac{1}{2\pi}\mathscr{D}\right)\frac{1}{2\pi}\Phi^{\rho}(\mathbf{t})$ $-\left(\frac{1}{\epsilon + 1}\right)\left(\frac{1}{2\pi}\mathscr{S}\right)\frac{1}{2\pi}F_{\mathrm{n}}^{\rho}(\mathbf{t})$
COSMO−μ	$\mathscr{I} - \frac{1}{2\pi}\mathscr{D}$	$\left(\frac{\epsilon - 1}{\epsilon}\right)\frac{1}{2\pi}\Phi^{\rho}(\mathbf{t})$
SPE[a]−μ	$\mathscr{I} - \left(\frac{2\epsilon}{\epsilon + 1}\right)\frac{1}{2\pi}\mathscr{D} + \left(\frac{\epsilon - 1}{\epsilon + 1}\right)\left(\frac{1}{2\pi}\mathscr{D}\right)^2$	$\left(\frac{\epsilon - 1}{\epsilon + 1}\right)\left(\frac{1}{2\pi}\mathscr{S}\right)\frac{1}{2\pi}F_{\mathrm{n}}^{\rho}(\mathbf{t})$

[a] The $\mathscr{L}$ operators for the IEF–μ and SPE–μ surface dipole methods are identical to one another. They can also be equivalently written in factorized form as $\left[\mathscr{I} - \left(\frac{\epsilon-1}{\epsilon+1}\right)\frac{1}{2\pi}\mathscr{D}\right]\left(\mathscr{I} - \frac{1}{2\pi}\mathscr{D}\right)$ or as $\left(\mathscr{I} - \frac{1}{2\pi}\mathscr{D}\right)\left[\mathscr{I} - \left(\frac{\epsilon-1}{\epsilon+1}\right)\frac{1}{2\pi}\mathscr{D}\right]$

that is not present in the exact reaction potential or in approximate surface charge representations, which may cause such approximate surface dipole methods to give poorer results in practice. In any case, it is of some interest to compare the two general approaches in practice.

Use of Eq. (11) together with the defining equation for each of the various surface charge distributions, $\sigma(\mathbf{t})$, allows us to obtain directly the SS(V)PE–μ, IEF–μ, COSMO–μ, and SPE–μ methods, which are surface dipole analogs of the SS(V)PE, IEF, COSMO, and SPE methods, respectively. These approaches have in common that the surface dipole density satisfies an equation of the general form

$$\mathscr{L}\mu(\mathbf{t}) = \mathscr{Z}(\mathbf{t}) \ . \qquad (12)$$

The effective system operator $\mathscr{L}$ and the function $\mathscr{Z}(\mathbf{t})$ associated with each of the methods examined in this work are summarized in Table 2.

It is interesting to note that if the surface distributions $\mu^{\mathrm{SS(V)PE}}(\mathbf{t})$ and $\sigma^{\mathrm{SPE}}(\mathbf{t})$ are each evaluated from the same solute charge density, $\rho(\mathbf{r})$, then it can be shown formally that

$$\mathscr{E}^{\mu^{\mathrm{SS(V)PE}}} = \mathscr{E}^{\sigma^{\mathrm{SPE}}} \ .$$

For example, this would happen in practice in the first self-consistent-field iteration starting from the gas-phase solute wave function. However, even though they accidentally produce the same reaction field energy when evaluated from the same solute density, the corresponding reaction potentials $\Phi^{\mu^{\mathrm{SS(V)PE}}}(\mathbf{r})$ and $\Phi^{\sigma^{\mathrm{SPE}}}(\mathbf{r})$ of course remain different from one another. Thus, in the course of self-consistently equilibrating the reaction field to the solute density the SS(V)PE–μ and SPE methods will eventually produce different solute charge densities and so eventually different reaction field energies.

If no solute charge penetrates outside the cavity, the SS(V)PE–μ, IEF–μ, and SPE–μ methods all become equivalent to one another, and furthermore each supplies the exact solution of Poisson's equation everywhere inside the cavity, while the COSMO–μ method generally still differs and becomes exact inside the cavity only in the limit of a very large dielectric constant.

3 Accuracy of approximate reaction field methods

Here we evaluate the relative accuracy of the SS(V)PE, IEF, COSMO, and SPE approximate surface charge methods and the SS(V)PE–μ, IEF–μ, COSMO–μ, and SPE–μ approximate surface dipole methods through calculations on several representative small solutes. By accuracy, we mean in this context how close each of these approximate representations of the reaction field comes to the exact SVPE solution of the given model of solvation. It is emphasized that this model only purports to determine long-range electrostatic contributions to solvation, and is not intended by itself to provide quantitative determination of the entire free energy of solution. That would necessitate further studies into other issues within the model such as optimum cavity size, especially for ionic solutes, and also independent evaluation of further contributions to solvation, such as those arising from cavitation, exchange repulsion, dispersion, and specific solute–solvent interactions, like hydrogen bonding, that are outside the scope of the present work.

The results reported here for the SS(V)PE, IEF, COSMO, SPE, SS(V)PE–μ, IEF–μ, COSMO–μ, and IEF–μ methods were obtained from a newly developed reaction field program [63] implemented in the HONDO [64] electronic structure package. The exact SVPE results used for comparison were obtained from the literature [15] and from additional calculations using the program described there [15].

Calculations are reported for the roughly spherical H_2O and distinctly nonspherical CH_3CONH_2 neutral solutes, and on the isoelectronic NO^+ and CN^- ions. The restricted Hartree–Fock (RHF) method is used throughout. The neutrals and the cation are each treated

Table 3. Solvation free energy for representative solutes (kcal/mol), with a high dielectric constant characteristic of water solvent

Method	H_2O	CH_3CONH_2	NO^+	CN^-
Exact treatment of volume polarization				
SVPE[a]	−8.59	−10.86	−89.49	−67.40
Approximate surface charge methods				
SS(V)PE	−8.58	−10.81	−89.47	−67.31
IEF	−8.58	−10.81	−89.41	−67.44
COSMO[b]	−8.64	−10.88	−89.49	−67.31
(COSMO)[b]	(−8.58)	(−10.80)	(−88.93)	(−66.88)
SPE	−8.67	−11.13	−94.70	−56.85
Approximate surface dipole methods				
SS(V)PE–μ	−8.53	−11.01	−94.11	−56.74
IEF–μ	−8.53	−10.99	−94.04	−56.83
COSMO–μ[b]	−8.59	−11.07	−94.13	−56.74
(COSMO–μ)[b]	(−8.53)	(−10.99)	(−93.45)	(−56.37)
SPE–μ	−8.86	−12.54	−99.62	−49.81

[a] The SVPE results, which are taken from Ref. [15], all use 1202 surface points and layers spaced at 0.1 bohr intervals out to 4.0 bohr for H_2O, CH_3CONH_2, and NO^+, and out to 12 bohr for CN^-

[b] The first line of COSMO results corresponds to the dielectric scaling factor $(\epsilon - 1)/\epsilon$, while the second line of results (in *parentheses*) corresponds to the dielectric scaling factor $(\epsilon - 1)/(\epsilon + 0.5)$

Table 4. Solvation free energy for representative solutes (kcal/mol), with a low dielectric constant characteristic of toluene solvent

Method	H_2O	CH_3CONH_2	NO^+	CN^-
Exact treatment of volume polarization				
SVPE[a]	−3.93	−5.30	−52.21	−39.42
Approximate surface charge methods				
SS(V)PE	−3.92	−5.01	−52.21	−39.35
IEF	−3.89	−4.89	−49.99	−43.85
COSMO[b]	−4.77	−5.90	−52.50	−39.36
(COSMO)[b]	(−3.89)	(−4.78)	(−43.37)	(−32.49)
SPE	−3.98	−5.17	−55.26	−35.05
Approximate surface dipole methods				
SS(V)PE–μ	−3.95	−5.14	−55.07	−32.93
IEF–μ	−3.80	−4.49	−52.73	−36.05
COSMO–μ[b]	−4.79	−6.04	−55.36	−32.94
(COSMO–μ)[b]	(−3.91)	(−4.91)	(−45.77)	(−27.16)
SPE–μ	−4.15	−6.04	−58.30	−28.43

[a] The SVPE calculations all use 1202 surface points and layers spaced at 0.1 bohr intervals out to 4.0 bohr for H_2O, CH_3CONH_2, and NO^+, and out to 12 bohr for CN^-

[b] The first line of COSMO results corresponds to the dielectric scaling factor $(\epsilon - 1)/\epsilon$, while the second line of results (in *parentheses*) corresponds to the dielectric scaling factor$(\epsilon - 1)/(\epsilon + 0.5)$

with the 6-31G** basis set [65] at the optimum gas-phase RHF/6-31G** geometry, while for the anion diffuse functions are also included through use of the 6-31+G** basis set [66], at the optimum gas-phase RHF/6-31+G** geometry. The cavity is always defined by an isodensity surface having $\rho_0 = 0.001e/a_0^3$, the value of which has previously been found [16, 17] to be nearly optimal for representing electrostatic effects of solvation on a variety of small neutral solutes. The surface integrations all used 1202 Lebedev points, which is more than adequate to reach the precision reported.

Table 3 gives the electrostatic contributions to free energies of solvation for the different solutes with a high dielectric constant of 78.304 that is characteristic of water solvent, and Table 4 gives analogous results with a low dielectric constant of 2.379 that is characteristic of toluene solvent. In both tables the first line of results is obtained from the SVPE method, which provides an essentially exact representation of volume polarization effects within the simple dielectric continuum model of solvation. The accuracy of various approximate reaction field methods can be assessed by how close they come to the exact SVPE results.

First we evaluate the results in Table 3 for a high dielectric constant solvent. Among the approximate surface charge methods, the SS(V)PE method fares extremely well, with errors less than 0.1 kcal/mol in all cases examined. The IEF method also does extremely well for all the solutes, as does the COSMO method when used with the $(\epsilon - 1)/\epsilon$ dielectric scaling factor. With the alternative $(\epsilon - 1)/(\epsilon + 0.5)$ dielectric scaling factor, the COSMO method does extremely well for the neutral solutes and still reasonably well for the ionic solutes, where the error rises to about 0.5 kcal/mol and has the same sign for both the cationic and the anionic solute. The SPE method does well for the neutral solutes, with errors of about 0.1–0.2 kcal/mol, but fares poorly for the ionic solutes, where the errors are about 5 kcal/mol for the cation and over 10 kcal/mol for the anion, with opposite signs for the latter two errors.

Among the approximate surface dipole methods, SS(V)PE–μ, IEF–μ, and COSMO–μ with either dielectric scaling all show behavior similar to one another and to the surface charge SPE method just discussed. That is, they all do reasonably well for the neutral solutes but fare poorly for the ionic solutes. The SPE–μ method is still worse, with larger errors of 0.3 and 2.7 kcal/mol for the neutral solutes, 10 kcal/mol for the cation, and nearly 18 kcal/mol for the anion.

Next we evaluate the results in Table 4 for a low dielectric constant solvent. Among the approximate surface charge methods, the SS(V)PE method fares extremely well, with errors less than 0.2 kcal/mol in all the cases examined. The IEF method does quite well for the neutral solutes, with errors of 0.2 kcal/mol or less, but not so well for the ionic solutes, where the errors range from 2 to over 4 kcal/mol. With the $(\epsilon - 1)/\epsilon$ dielectric scaling factor the COSMO method also does reasonably well, with errors of about 0.6–0.8 kcal/mol for the neutral solutes and less than that for the two ionic solutes. With the alternative $(\epsilon - 1)/(\epsilon + 0.5)$ dielectric scaling factor the COSMO method still does reasonably well for the neutral solutes, with errors of less than 0.5 kcal/mol, but fares poorly with the ionic solutes, where the errors range from 7–9 kcal/mol. The SPE method also does quite well for the neutral solutes, with errors less than 0.2 kcal/mol, but not so well for the ionic solutes, where the errors are about 3–4 kcal/mol.

Among the approximate surface dipole methods with low dielectric solvent the SS(V)PE–μ method does very well for the neutral solutes, but shows large errors of 3 to over 6 kcal/mol for the ionic solutes. The IEF–μ method does reasonably well for the neutral solutes with errors up to about 0.8 kcal/mol and has an error of just 0.5 kcal/mol for the cationic solute, but has a significant error of over 3 kcal/mol for the anionic solute. The COSMO–μ method with $(\epsilon - 1)/\epsilon$ dielectric scaling does reasonably well for the neutral solutes with errors near 1 kcal/mol, but shows large errors of 3 to over 6 kcal/mol for the ionic solutes. With the alternative $(\epsilon - 1)/$

$(\epsilon + 0.5)$ dielectric scaling the COSMO–μ method does a little better for the neutral solutes, with errors less than 0.4 kcal/mol, but fares poorly for the ionic solutes, with errors of 6–12 kcal/mol. The SPE–μ method does reasonably well for the neutral solutes with errors of 0.2–0.7 kcal/mol, but has large errors of 6 kcal/mol for the cation and 11 kcal/mol for the anion.

In most of the methods considered the reasons for the dielectric dependence of the errors are not obvious. An exception is COSMO, where the larger errors found at low dielectric constant are probably a reflection of the fact that the correct dielectric dependence is more complicated than can be described by multiplying the conductor result, which corresponds to the high dielectric limit, by any simple function of the dielectric constant.

Overall, we conclude that the SS(V)PE surface charge method fares best among the approximate methods examined. It is very good in all situations, accurately reproducing the exact SVPE results to within 0.1 kcal/mol or less in high dielectric constant solvent and within 0.2 kcal/mol or less in low dielectric constant solvent. The COSMO surface charge method with $(\epsilon - 1)/\epsilon$ dielectric scaling also performs well in high dielectric constant solvent, with errors of less than 0.1 kcal/mol, and still reasonably well in low dielectric constant solvent, with errors less than 1 kcal/mol. All other methods considered show significant errors in some of the situations examined and so cannot be recommended in general, although several of them may be satisfactory for certain special cases, especially for that of a neutral solute in a high dielectric solvent.

4 Summary and conclusion

This work considered several extant methods for approximate reaction field representation in terms of surface charge distributions, including the SS(V)PE, IEF, COSMO, and SPE methods, and discussed their formal similarities and differences. Analogous new SS(V)PE–μ, IEF–μ, COSMO–μ, and SPE–μ methods were also introduced, each based instead on the use of a surface dipole representation to give the same reaction field inside the cavity as in the respective surface charge method. All these methods can be regarded as approximations to the SVPE method, which provides an essentially exact solution of the simple solvation model considered in terms of both surface charge and volume charge distributions. If no solute charge penetrates outside the cavity, the SVPE, SS(V)PE, IEF, SPE, SS(V)PE–μ, IEF–μ, and SPE–μ methods all give the same result, while COSMO and COSMO–μ give the same result as the others only in the limit of large dielectric constant. In practice, a small but significant amount of solute charge generally does penetrate outside the cavity, and all of these methods then give different results.

The accuracy of each approximate reaction field method was assessed by comparing numerical results to those from the essentially exact SVPE method. Formally, the SS(V)PE method is expected to provide the closest approximation to the exact SVPE method, and this is borne out in practice. With several representative neutral and ionic solutes in both high and low dielectric solvents, the SS(V)PE free energies of solvation are always within 0.2 kcal/mol of the SVPE results. The COSMO method, at least when implemented with $\epsilon/(\epsilon - 1)$ dielectric scaling, also does very well compared to SVPE in a high dielectric constant solvent, but has larger errors approaching 1 kcal/mol in a low dielectric constant solvent. While several of the other approximate reaction field methods considered perform satisfactorily for the special case of a neutral solute in a high dielectric constant solvent, they each show very significant errors in some other situations and cannot be recommended in general.

Acknowledgements. The author would like to thank A. Klamt for communicating his unpublished alternative route to the SS(V)PE equation that is described here and M. Dupuis for valuable discussions. The research described herein was supported by the Office of Basic Energy Sciences of the Department of Energy. This is contribution no. NDRL-4313 from the Notre Dame Radiation Laboratory.

References

1. Born M (1920) Z Phys 1: 45
2. Kirkwood JG (1934) J Chem Phys 2: 351
3. Onsager L (1936) J Am Chem Soc 58: 1486
4. Böttcher CJF (1973) Theory of electric polarization. Elsevier, Amsterdam
5. Tomasi J, Persico M (1994) Chem Rev 94: 2027
6. Cramer CJ, Truhlar DG (1999) Chem Rev 99: 2161
7. Still WC, Tempczyk A, Hawley RC, Hendrickson T (1990) J Am Chem Soc 112: 6127
8. Cramer CJ, Truhlar DG (1991) J Am Chem Soc 113: 8305
9. Schaefer M, Karplus M (1999) J Phys Chem 100: 1578
10. Luzhkov V, Warshel A (1992) J Comput Chem 13: 199
11. de Vries AH, van Duijnen PT, Juffer AH, Rullmann JAC, Dijkman JP, Merenga H, Thole BT (1995) J Comput Chem 16: 37
12. Chipman DM (1996) J Chem Phys 104: 3276
13. Mennucci B, Tomasi J (1997) J Chem Phys 106: 5151
14. Chipman DM (1997) J Chem Phys 106: 10194
15. Zhan C-G, Bentley J, Chipman DM (1998) J Chem Phys 108: 177
16. Zhan C-G, Chipman DM (1998) J Chem Phys 109: 10543
17. Zhan C-G, Chipman DM (1999) J Chem Phys 110: 1611
18. Cossi M, Rega N, Scalmani G, Barone V (2001) J Chem Phys 114: 5691
19. Mennucci B, Cammi R, Tomasi J (1998) J Chem Phys 109: 2798
20. Chipman DM (1999) J Chem Phys 110: 8012
21. Chipman DM (2000) J Chem Phys 112: 5558
22. Cancès E, Mennucci B (2001) J Chem Phys 114: 4744
23. Cancès E, Mennucci B, Tomasi J (1997) J Chem Phys 107: 3032
24. Mennucci B, Cancès E, Tomasi J (1997) J Phys Chem B 101: 10506
25. Cancès E, Mennucci B (1998) J Math Chem 23: 309
26. Tomasi J, Mennucci B, Cancès E (1999) J Mol Struct (THEOCHEM) 464: 211
27. Klamt A, Schüürmann G (1993) J Chem Soc Perkin Trans 2: 799
28. Andzelm J, Kölmel C, Klamt A (1995) J Chem Phys 103: 9312
29. Klamt A (1996) J Phys Chem 100: 3349
30. Klamt A, Jonas V (1996) J Chem Phys 105: 9972
31. Baldridge K, Klamt A (1997) J Chem Phys 106: 6622
32. Truong TN, Stefanovich EV (1995) Chem Phys Lett 240: 253
33. Truong TN, Stefanovich EV (1995) J Chem Phys 103: 3709
34. Truong TN, Nguyen UN, Stefanovich EV (1996) Int J Quant Chem Symp 30: 403
35. Miertuš S, Scrocco E, Tomasi J (1981) Chem Phys 55: 117
36. Rashin AA, Namboodiri K (1987) J Phys Chem 91: 6003
37. Hoshi H, Sakurai M, Inoue Y, Chûjô R(1987) J Chem Phys 87: 1107

38. Zauhar RJ, Morgan RS (1988) J Comput Chem 9: 171
39. Basilevsky MV, Chudinov GE (1991) Chem Phys 157: 327
40. Wang B, Ford GP (1992) J Chem Phys 97: 4162
41. Chudinov GE, Napolov DV, Basilevsky MV (1992) Chem Phys 160: 41
42. Vorobjev YN, Grant JA, Scheraga HA (1992) J Am Chem Soc 114: 3189
43. Rauhut G, Clark T, Steinke T (1993) J Am Chem Soc 115: 9174
44. Bharadwaj R, Windemuth A, Sridharan S, Honig B, Nicholls A (1995) J. Comput Chem 16: 898
45. Tawa GA, Martin RL, Pratt LR, Russo TV (1996) J Phys Chem 100: 1515
46. Foresman JB, Keith TA, Wiberg KB, Snoonian J, Frisch MJ (1996) J Chem Phys 100: 16098
47. Yoon BJ, Lenhoff AM (1990) J. Comput Chem 11: 1080
48. Juffer AH, Botta EFF, van Keulen BAM, van der Ploeg A, Berendsen HJC(1991) J Comput Phys 97: 144
49. Xiang Z, Huang F, Shi Y (1994) J Phys Chem 98: 12782
50. Wilson WD, Schaldach CM, Bourcier WL (1997) Chem Phys Lett 267: 431
51. Gilson MK, Sharp KA, Honig BH (1987) J Comput Chem 9: 327
52. Davis ME, McCammon JA (1989) J Comput Chem 10: 386
53. Holst M, Saied F (1993) J Comput Chem 14: 105
54. Tannor DJ, Marten B, Murphy R, Friesner RA, Sitkoff D, Nicholls A, Ringnalda M, Goddard WA, Honig B (1994) J Am Chem Soc 116: 11875
55. Chen JL, Noodleman L, Case DA, Bashford D (1994) J Phys Chem 98: 11059
56. Mikkelsen KV, Ågren H, Jensen HJA, Helgaker T (1988) J Chem Phys 89: 3086
57. Karelson MM, Tamm T, Katritzky AR, Cato SJ, Zerner MC (1989) Tetrahedron Comput Methodol 2: 295
58. Wong MW, Frisch MJ, Wiberg KB (1991) J Am Chem Soc 113: 4776
59. Rivail J-L, Rinaldi D (1995) In: Leszczynski J (ed) Computational chemistry, review of current trends. World Scientific, New York, p 139
60. Amovilli C, Barone V, Cammi R, Cancès E, Cossi M, Mennucci B, Pomelli CS, Tomasi J (1999) Adv Quant Chem 32: 227
61. Pascual-Ahuir JL, Silla E, Tomasi J, Bonaccorsi RJ (1987) J Comput Chem 8: 778
62. Pomelli CS, Tomasi J (1998) J Comput Chem 19: 1758
63. Chipman DM, Dupuis M (2001) Theor Chem Acc
64. Dupuis M, Marquez A, Davidson ER (1999) HONDO 99, a computer program based on HONDO 95.3. Quantum Chemistry Program Exchange, Indiana University, Bloomington
65. Hariharan PC, Pople JA (1973) Theor Chim Acta 28: 213
66. Clark T, Chandrasekhar J, Spitznagel G, Schleyer PvR (1983) J Comput Chem 4: 294