Physical Chemistry

A Langevin continuum model for electrostatic polarization of solvent: calculations of solvation energies of ions and molecules

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A Langevin continuum model is proposed for performing quantum-chemical calculations of the interaction energies of solute species with polar solvent. The electrostatic contribution is estimated in the framework of the dipole approximation using a Langevin-type function for description of solvent polarization. The parameters of the model for water are presented. Hydration enthalpies of organic ions and neutral polar and nonpolar molecules, whose wave functions were calculated in the 6-31G* basis set, are well reproduced using the approach proposed.

Key words: solvation, solute—solvent interaction, Langevin dipoles, quantum-chemical calculations.

The development of methods for taking account of the solvent effect in quantum-chemical calculations of the structure of solute molecules is a topical line of investigation in theoretical chemistry. Currently, the possibilities of quantum-chemical methods are limited by consideration of molecular systems consisting of several hundreds of atoms. At the same time, reliable estimates of physicochemical properties of molecules in solution can be made only by taking into account a rather large volume of the solvent around a solute molecule. This has motivated the development of combined approaches in which the classical potentials of the solvent are incorporated into schemes of quantum-chemical calculations of solute molecules.

Two main types of solvent models, discrete and continuum ones, are used in quantum-chemical calculations of the reactivity of compounds. In discrete (microscopic) models, the solvent is considered as a set of individual species, whereas macroscopic quantities that describe the properties of a medium are used in continuum models.[1—4] When simulating the solvent effect, it is the most important to correctly account for the long-range electrostatic interactions.

In this regard the known continuum models can be divided into two main groups. In the first group of models the solvent potential is calculated using the generalized Born formula.[5—8] In the second (the largest) group of models, in which the self-consistent reaction field (SCRF) approximation is used, the potential of charges induced on the surface of a cavity formed by the solute molecule in the dielectric continuum is calculated (see, *e.g.*, Refs. 4, 9—13, and references cited therein). Among microscopic approaches, the model of Langevin dipoles (LD) is most widely used. In this model, electrostatic interactions in solution are described in the dipole approximation using analytical functions of the Langevin type.[2,14—16]

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Both microscopic and continuum approaches have their advantages and drawbacks and currently there is no universal model for solvation, which in all cases would make it possible to adequately describe the interaction of solute molecules with the solvent.

In this work we present the methods and results of calculations of the energies of solute—solvent interaction in the framework of the Langevin continuum model (LC model). In this model, electrostatic polarization of the solvent is described by a Langevin type function, which makes it possible to effectively calculate the characteristics of nonspecific solvation of large molecules.

Calculation procedure

In the general case of nonspecific solvation, the free solvation energy of a molecule (ΔG_{sol}) can be represented as the sum of electrostatic (ΔG_{el}) and nonpolar (ΔG_{np}) contributions[1—4]:

$$\Delta G_{sol} = \Delta G_{el} + \Delta G_{np}. \qquad (1)$$

The electrostatic term makes the largest (in absolute value) contributions to ΔG_{sol} for ions and polar molecules and is the most sensitive to rearrangement of their electronic structure in the course of chemical reactions. The nonpolar term, as a rule, includes the energies of the van der Waals interactions and the energy of cavity formation in the solvent and is mainly determined by the size of the solute molecule.

In the discrete LD model the solvent molecules are represented as polarizable point dipoles located at the nodes of a spatial network around the solute species. In this model the polarization ($\mathbf{m}$) of such a dipole in the overall electric field (created by solute species and other solvent dipoles) of strength $\mathbf{E}$, averaged over orientations, is given by the formula:

$$\mathbf{m} = \alpha\mathbf{E} + \langle\mu\mathbf{e}\rangle\mathbf{e} = \alpha\mathbf{E} + \mu L[\mu E/(kT)]\mathbf{e}, \qquad (2)$$

where α and μ are respectively the polarizability and absolute value of the dipole moment of a point dipole (μ); $\mathbf{e}$ is the unit vector directed along the field strength vector $\mathbf{E}$; $L(x) = \mathrm{cth}\, x - 1/x$ is the Langevin function[2,14]; $x = \mu E/(kT)$; k is the Boltzmann constant; and T is absolute temperature. Further, the ΔG_{el} value is calculated using the overall potential of solvent dipoles.

The advantage of the LD model lies in the fact that formula (2) makes it possible to perform effective analytical calculations of the solvent polarization by the solute in the dipole approximation. It is the value of this polarization that determines the ΔG_{sol} value. This possibility is lost on going to more precise solvent models in which, *e.g.*, the spatial distribution of atomic charges is taken into account. At the same time, as for any other microscopic scheme, the use of the LD model requires calculations of the electric field strength E, averaged over different orientations of solvent molecules, *i.e.*, over various configurations of the network of dipoles. However, the known algorithms of averaging in this model are, on the whole, ineffective and require additional computational resources. The problem of calculating the averaged solvent field is solved on going to a macroscopic description of the system.

Continuum model for the Langevin polarization of the solvent. If a solvent is considered as a dielectric continuum, the electrostatic contribution to the ΔG_{sol} value can be represented as the integral over the solvent volume (V):

$$\Delta G_{el} = -\frac{1}{2}\int_{Solv}\mathbf{DP}\,dV, \qquad (3)$$

where $\mathbf{D}$ and $\mathbf{P}$ are respectively the vectors of the electric induction and polarization of the medium, related to the strength of the Maxwell electric field $\mathbf{E}$ by the known relationships $\mathbf{D} = \mathbf{E} + 4\pi\mathbf{P}$ and $\mathbf{P} = (\varepsilon - 1)/(4\pi)\cdot\mathbf{E}$, where ε is the dielectric constant of the medium. Polarization $\mathbf{P}_V$ of an infinitesimal volume element of the solvent dV can be represented as the sum of the orientational and induced contributions:

$$\mathbf{P}_V = \sum_{k\in dV}\left[\alpha\mathbf{E}_{ik} + \mathbf{e}_{dk}\langle\mu_k\mathbf{e}_{dk}\rangle\right] = \left[\alpha\mathbf{E}_i + \mu L\left(\frac{\mu E_d}{kT}\right)\mathbf{e}_d\right]\rho_\mu dV, \qquad (4)$$

where $\boldsymbol{\mu}_k$ is the vector of the dipole moment of the kth solvent molecule; $\mathbf{E}_i$ and $\mathbf{E}_d$ are the internal and direction components of the strength of the field exerted on the kth dipole, respectively; $\mathbf{e}_d$ is the unit vector directed along the $\mathbf{E}_d$ vector; ρ_μ is the density of solvent dipoles; and α is polarizability. In expression (4), we turned from the discrete to the continuum representation of $\mathbf{P}_V$.

The components of the electric field in the volume element of the dielectric continuum are related by the relationship $\mathbf{E}_i = \mathbf{E}_d + \mathbf{R}$, where $\mathbf{R}$ is the reaction field of the dielectric. Using the representations for contributions $\mathbf{E}_d$ and $\mathbf{R}$, known from reaction field theory,[17,18] we obtained the formula that relates the polarization $\mathbf{P}_V$ of the volume element dV to the strength of the effective electric field $\mathbf{E}'$ exerted on this element:

$$\mathbf{P}_V = \left[\alpha\mathbf{E}' + \frac{\mu}{1 - f\alpha}\mathbf{e}L\left(\frac{\mu E'}{kT}\right)\right]\rho_\mu dV, \qquad (5)$$

where

$$f = \frac{1}{a^3}\cdot\frac{2(\varepsilon - 1)}{2\varepsilon + 1},$$

and a is the size of a cavity of the solvent dipole. Formally, expression (5) corresponds to formula (4); however, it contains the dependence of both contributions (orientational and induction) on the effective strength of the electric field in solution $\mathbf{E}' = \beta\mathbf{E}$, where $\mathbf{E}$ is the strength of the Maxwell electric field, and

$$\beta = \left(\frac{1}{1 - f\alpha}\right)\cdot\left(\frac{3\varepsilon}{2\varepsilon + 1}\right).$$

It should be noted that the ratio $\mu/(1 - f\alpha)$ in Eq. (5) is the dipole moment μ_s of a solvent molecule in its own media.[18] In the case of solvation of a point ion, the relation between $\mathbf{E}(r)$ and the electric field strength of the ion in vacuum is sometimes given in the form $\mathbf{E}(r) = \mathbf{E}_m(r)/\varepsilon(r)$, where $\varepsilon(r)$ is the dielectric constant of the solvent dependent on r.

However, the use of the macroscopic concept of the dielectric constant in the vicinity of solute species[2,19] is rather poorly justified. In this connection it is more correct to interpret the

coefficient $\varepsilon(r)$ as a shielding function of the electric field of a point charge by the solvent (an analogous shielding function appears, *e.g.*, in the microscopic LD model[14,19]). This makes it possible to represent the field of a polyatomic solute molecule in a convenient form as the sum of atomic contributions:

$$\mathbf{E} = \sum \frac{q_i \mathbf{r}_i}{\varepsilon(r_i) r_i^3}, \qquad (6)$$

where the factors $\varepsilon(r_i)$ characterize the effect of shielding of the field of atomic charges in the molecule.

Parametrization of the model and calculations of solvation energies. Using Eqs. (1) and (3), it is possible to calculate the free solvation energies ΔG_{sol}. Most modern solvent models are also calibrated to calculate this value. At the same time, in many instances it is of interest to obtain separate estimates of the enthalpy and entropy contributions to the ΔG_{sol} value. In particular, this can be done using the additive scheme of estimating the entropy contribution to the hydrophobic effect.[15,20] To make the above estimates, in this work we consider the enthalpy of solvation (ΔH_{sol}). As a rule, the electrostatic contributions to the ΔG_{sol} and ΔH_{sol} values differ insignificantly (within the limits of several per cent),[21,22] whereas for the nonpolar contribution this difference is much larger. In this work, the methods used for calculating the polar (ΔH_{el}) and nonpolar (ΔH_{np}) contributions to the ΔH_{sol} value were parametrized separately.

When considering electrostatic interactions, the solvent volume is divided into two regions inside and outside a sphere of radius r_s circumscribed about a solute molecule (regions *1* and *2*, respectively, see Fig. 1). The region *1* is also bounded by the solvent-accessible surface of the molecule S_w. Electrostatic interactions in the region *1* and in the region of long-range interactions (region *2*) are respectively described by the Langevin formulas (4)—(6) and by the Born—Kirkwood formulas.[23] The ΔH_{el} value is represented as the sum of contributions from these two regions (ΔH_{Lgvn} and ΔH_{Born}, respectively):

$$\Delta H_{el} = \Delta H_{Lgvn} + \Delta H_{Born}. \qquad (7)$$

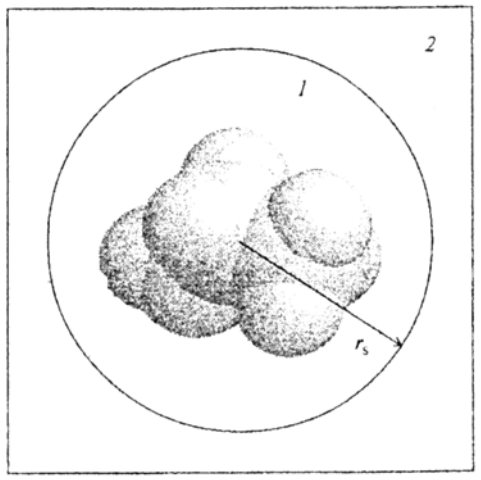

Fig. 1. Division of the space in the solute—solvent system into the regions (*1* and *2*, see text) in the LC model taking an EtOH molecule as an example; r_s is the radius of the external spherical boundary of region *1*.

Table 1. Parameters of solvation LC model for water

Solvent		Solute		
Parameter[a]	Numerical value	Type of species	r_w/Å[b] ion	atom
μ/D	2.50	H, H—N, H—O	1.8, 1.4, 1.1	1.8, 1.5, 1.4
α/Å^3	1.48	C, C_{arom}	1.7, 2.0	1.7, 2.0
a/Å	1.40	N	1.3	1.4
ε_w	78.4	O	1.2	1.4
b	0.96	Na^+	1.7[33]	—
c	1.20	K^+	2.2[33]	—

[a] Here μ is the dipole moment of the molecule; α is the molecular polarizability; a is the radius of the molecular sphere; ε_w is the dielectric constant; b and c are the coefficients of the shielding function.
[b] Atomic radii.

According to expression (4), the first term in relationship (7) can be represented as the sum of contributions of permanent ($\Delta H_{Lgvn,p}$) and induced ($\Delta H_{Lgvn,i}$) polarization. The parameters of the LC model are the dipole moment (μ), polarizability (α), the size (a) of the solvent molecule, the shielding function ($\varepsilon(r)$), and the electrostatic atomic radii (r_w) of solute species, which determine the shape and size of the solvation cavity (S_w). The shielding function $\varepsilon(r)$ is given by the Gompertz formula:

$$\varepsilon(r) = \varepsilon_w \exp(-bc^{-cr}), \qquad (8)$$

where ε_w is the dielectric constant of water, and b and c are constants. In the general case, such a dependence corresponds to the theoretically expected S-shaped curve of the dielectric constant for a system with point ions.[24—26] For water, the experimental values of ε_w and α (Table 1) were used. The dipole moment chosen (μ = 2.5 D) corresponds to the expected value for a water molecule in water.[27] The coefficients b and c were calibrated based on the solvation energy of the Na^+ cation and to meet the condition $\varepsilon(10\ Å) = 0.9\varepsilon_w$, which determines the slope of the curve (see Table 1).

The parametrization of this model takes into account an additional condition, according to which the calculated ΔH_{el} value should be stable with respect to changes in the radius of the solvent-accessible sphere (R) at medium and long distances. Since both contributions to the ΔH value depend on R as $\Delta H_{Lgvn} \sim C_1/R$ and $\Delta H_{Born} \sim C_2/R$, the condition $\delta H_{el}/\delta R = 0$ is equivalent to the equality $C_1 = -C_2$. Numerical calculations for the point ions showed that this equality is valid for the parameters of the model, which correspond to a coefficient β of 3.19.

To calculate the nonpolar contribution to the enthalpy of solvation, we used an empirical linear functional dependence of ΔH_{np} on the surface area of the solute molecule (S_{mol}). Such a representation was chosen on the basis of the known data (see, *e.g.*, the parametrization of the methods reported in Refs. 6 and 12), according to which the nonpolar contribution is mainly dependent on the size of the solute molecule rather than on the type of atoms constituting the molecule. To calibrate the linear dependence, we used the data on the enthalpies of solvation of several nonpolar compounds (inert

gases,[28] aliphatic hydrocarbons[29]) for which it can be accepted that $\Delta H_{sol} \approx \Delta H_{np}$.

The surface of the solute molecule is represented as a superposition of the surfaces of intersecting spheres circumscribed about the atoms constituting the molecule. The surface areas of the spheres were calculated using the known atomic radii.[30,31] After statistical processing we obtained two linear dependences, which make it possible to calculate the ΔH_{np} values for small (data for He, Ne, Ar, Kr, and CH_4 were taken) and large (data for Kr, Xe, C_2H_6, C_3H_8, C_4H_{10}, and *neo*-C_5H_{12} were taken) surface areas of the molecules:

$$\Delta H_{np} = 6.62 - 0.0667 S_{mol} \text{ at } S_{mol} \leq 153.05;$$
$$\Delta H_{np} = -0.44 - 0.0206 S_{mol} \text{ at } S_{mol} > 153.05. \quad (9)$$

For molecules of nonpolar compounds, estimates of ΔH_{el} were obtained by subtracting the ΔH_{np} values from ΔH_{sol} values.

The ΔH_{sol} values for polyatomic molecules were calculated using the electrostatic atomic charges obtained in *ab initio* quantum-chemical calculations in the 6-31G* basis set (see Ref. 32). In this case the molecular geometry was preliminarily optimized by the semiempirical AM1 method. Based on the calculated solvation energies of several compounds, we calibrated the values of the electrostatic atomic radii r_w (see Table 1), which provides the best agreement between the experimental and calculated data.

The calculations were carried out using an original program written in the FORTRAN77 programming language on a Convex-120 computer. Integration over the volume of region *I* (see Fig. 1) was performed numerically in polar coordinates with a radial distance increment of 0.2 Å. In all cases, region *I* included a spherical layer of thickness 20 Å around the solute species.

Results and Discussion

The enthalpies of solvation calculated for a number of ions and neutral molecules are listed in Tables 2 and 3, respectively. For the ions, good quantitative agreement was obtained between the calculated and experimental data in the range considered, *viz.*, from −60 to −110 kcal mol^{-1} (including the scatter of experimental data, which amounts to several kcal mol^{-1} when using different published data). In this case the ΔH_{el} term makes the major contribution to the ΔH_{sol} values; in turn, the permanent polarization of the solvent, $\Delta H_{Lgvn,p}$, makes the largest contribution to the ΔH_{el} value. At the size chosen of region *I*, the values of the long-range contribution, ΔH_{Born}, in all cases lie in the range from −6.13 to −6.88 kcal mol^{-1}, which is less than 10% of the ΔH_{sol} value. The calculations reproduce well the changes in the ΔH_{sol} values of protonated mono-, di-, and trimethylamines.

For the neutral molecules considered, the ΔH_{sol} values lie in the range from about −3 to −13 kcal mol^{-1}. On the whole, in this case the relative enthalpies of solvation are also reproduced correctly. For polar molecules, the electrostatic contribution dominates, whereas for nonpolar aliphatic hydrocarbons, its value is close to zero. For the nonpolar aromatic benzene molecule, the ΔH_{el} value is already ~−1.5 kcal mol^{-1}. Such a difference between the benzene molecule and those of aliphatic hydrocarbons is due to the planar configuration of low-polar C—H bonds in the benzene ring.

Table 2. Calculated and experimental enthalpies of solvation of ions and their components (ΔH/kcal mol^{-1})

Ion	ΔH_{np}	ΔH_{Born}	$\Delta H_{Lgvn,p}$	$\Delta H_{Lgvn,i}$	ΔH_{sol}^{calc}	ΔH_{sol}^{exp}
Na^+	−3.01	−6.87	−85.42	−3.51	−98.81	−98.50[a]
K^+	−3.98	−6.71	−70.67	−2.48	−83.83	−78.40[a]
OH^-	−1.00	−6.88	−110.48	−5.60	−113.91	−116.20[b]
$MeCOO^-$	−4.56	−6.41	−76.95	−3.37	−91.29	−89.70[b]
NH_4^+	−3.10	−6.65	−76.23	−2.81	−88.79	−87.00[c]
$MeNH_3^+$	−4.28	−6.40	−63.84	−2.19	−76.71	−75.40[c]
$Me_2NH_2^+$	−4.90	−6.23	−55.48	−1.81	−68.41	−69.70[c]
Me_3NH^+	−5.48	−6.22	−48.49	−1.52	−61.70	−63.30[c]
PyH^+	−5.63	−6.13	−48.70	−1.53	−61.99	−61.90[c]

[a] Data were taken from Ref. 33.
[b] Data were taken from Ref. 34.
[c] Data were taken from Ref. 35.

Table 3. Calculated and experimental enthalpies of solvation of molecules and their components (ΔH/kcal mol^{-1})

Molecule	ΔH_{np}	$\Delta H_{Lgvn,p}$	$\Delta H_{Lgvn,i}$	ΔH_{sol}^{calc}	ΔH_{sol}^{exp}
H_2O	−1.70	−7.91	−0.30	−9.91	−9.97[a]
MeCOOH	−4.70	−9.53	−0.37	−14.61	−12.7[b]
MeOH	−3.93	−5.07	−0.19	−9.18	−10.25[a]
$MeCH_2OH$	−4.67	−4.55	−0.17	−9.40	−12.05[a]
$Me(CH_2)_2OH$	−5.34	−4.92	−0.19	−10.45	−13.25[a]
NH_3	−2.50	−5.30	−0.21	−8.02	−7.87[a]
$MeNH_2$	−4.13	−3.71	−0.15	−7.99	−10.27[a]
Py	−5.49	−4.66	−0.17	−10.32	−11.98[b]
CH_4	−3.46	−0.06	0	−3.52	−2.75[a]
C_3H_7	−5.02	−0.04	0	−5.06	−4.83[a]
C_6H_6	−5.64	−1.44	−0.04	−7.12	−7.08[a]

[a] Data were taken from Ref. 29.
[b] Data were taken from Ref. 34.

Mention may be made of inadequate reproduction of the effect of methyl substituents on the ΔH_{sol} values for molecules of water, aliphatic alcohols, and aliphatic amines. Most likely, this can be explained by the fact that the model takes no account of the effects of specific solvation and, in particular, the formation of hydrogen bonds between the solute species and solvent molecules. It should be noted that more rigorous calculations using methods of molecular dynamics[36] also cannot reproduce the effects of methyl substituents in the case of aliphatic amines.

The generalized correlation of calculated and experimental values of ΔH_{sol} is shown in Fig. 2. A linear dependence with a slope close to unity, a correlation coefficient (r) of 0.999, and a standard deviation (σ) of 1.93 kcal mol^{-1} was obtained.

In the framework of the model considered the interactions in the solute—solvent system were estimated in

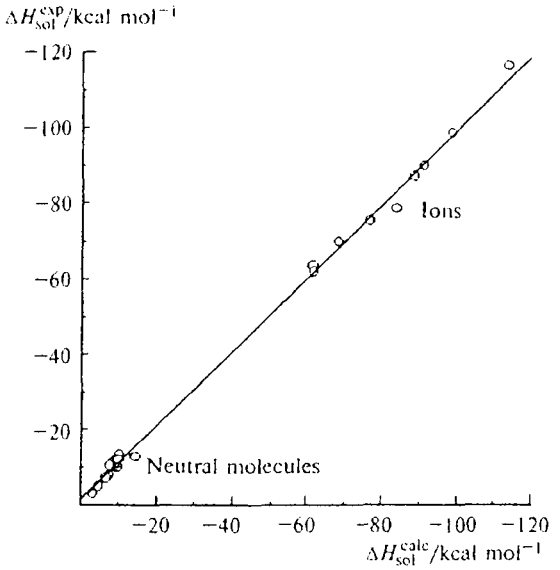

Fig. 2. Correlation of experimental (ΔH_{sol}^{exp}) and calculated (ΔH_{sol}^{calc}) enthalpies of solvation for the compounds listed in Tables 2 and 3.

the simplest manner using the atomic charges calculated from the wave function for an isolated solute molecule. As is known, there is no unambiguous definition of atomic charges for molecular systems and their values are dependent on the choice of both the quantum-chemical method and the scheme of division of the electron density overlap over the atomic centers. In this work, we used the procedure for the determination of charges that provides the most realistic description of the interactions between the molecules in solution. Nevertheless, no account is taken of polarization of the solute molecules by the solvent in such an approach. This effect can be accounted for using a quantum-mechanical Hamiltonian containing an additional term that describes the interaction of the electrons of solute molecules with the electrostatic field of the solvent (see, *e.g.*, Ref. 15), which can favor an appreciable increase in the nonuniformity of the charge distribution in the dissolved compound. However, the influence of this effect on the ΔH_{sol} values is compensated by the parametrization suggested in this work.

Integration of the solvent polarization over the solvent volume is an important distinction between the approach considered above and the existing continuum analogs, since in other computational schemes either integration over a solvent-accessible surface (modifications of SCRF models) or simplified analytical formulas (variants of the generalized Born approach) are used. The continuum approximation proposed in this work is based on the known microscopic model of Langevin dipoles and formally meets the suggested procedures for estimating the solvation energies of the ions in the framework of the Born model with a variable dielectric constant of the solvent.[24–26] However, the efficiency of calculations performed using this new approach to consideration of polyatomic molecules, in which the solvation energy is divided into atomic contributions according to Eq. (6) (see above), is highly competitive with those of the microscopic LD approximation and SCRF methods.

Thus, the computational scheme proposed makes it possible to correctly reproduce the enthalpies of solvation of polar and neutral molecules of different structure. Because of its computational efficiency, this scheme can be used in the simulation of the properties of large molecules in solution in combination with the methods of quantum chemistry and molecular dynamics.

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