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A modified repulsive bridge correction to accurate evaluation of solvation free energy in integral equation theory for molecular liquids

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Integral equation theory for molecular liquids is one of the powerful frameworks to evaluate solvation free energy (SFE). Different from molecular simulation methods, the theory computes SFE in an analytical manner. In particular, the correction method proposed by Kovalenko and Hirata [Chem. Phys. Lett. **290**, 237 (1998); J. Chem. Phys. **113**, 2793 (2000)] is quite efficient in the accurate evaluation of SFE. However, the application has been limited to aqueous solution systems. In the present study, an improved method is proposed that is applicable to a wide range of solution systems. The SFE of a variety of solute molecules in chloroform and benzene solvents is evaluated. A key is the adequate treatment of excluded volume in SFE calculation. By utilizing the information of chemical bonds in the solvent molecule, the accurate computation of SFE is achieved. © *2012 American Institute of Physics*. [http://dx.doi.org/10.1063/1.4733393]

I. INTRODUCTION

Solvation free energy (SFE) is one of the most fundamental thermodynamic quantities to understand chemical process in a solution. However, the accurate computation of SFE is not so straightforward because complex integration is necessary with respect to numerous degrees of freedom composing the system. One of the most popular approaches is based on molecular simulation such as molecular dynamics,[1] in which Newton's equations of motion are numerically integrated over time until a sufficient number of solvent configurations is obtained. In principle, the computed free energy is guaranteed to properly converge to the exact value[2–4] when the simulation is adequately performed, but a high computational cost is usually required. It is also important to note that a sufficient sampling is necessary to achieve statistical convergence (so-called sampling problem). Dielectric continuum model,[5] in which solvent is represented with the dielectric media, is one of the simplest and widely adopted methods to obtain SFE. The evaluation is, however, essentially based on the electromagnetic theory. An integral equation theory for molecular liquids[6–9] is an alternative to evaluate SFE, which is based on the analytical treatment of the thermodynamic integration. Thanks to this nature, the method does not require a large amount of computational resources and is free from the sampling problem, although the accuracy depends on the approximation.

A good example was shown by Kovalenko and Hirata.[10] In their work, the hydration free energy of a series of rare gases was computed using hyper-netted chain (HNC) closure coupled with Ornstein-Zernike (OZ) type equation. As expected, the computed trend was in contradiction with the experiment because of overestimation of hydrophobicity. In these systems, hydrogen atoms of solvent water are practically inside the oxygen. But the excluded volume of water is not adequately described by HNC. Hence, they proposed a promising procedure to correct this shortcoming and improve the accuracy of SFE, called repulsive bridge correction (RBC). This procedure was successfully applied to various solute molecules; from simple hydrocarbons[10] to proteins.[11] But the applications are almost limited to aqueous solution systems. As shown below, the correction loses its shine when it is applied to other solution systems since the approximated treatment gets worse as the volume of solvent is increased.

In the present study, we generalize RBC to evaluate accurate SFE for a wide range of solution systems. As the benchmarks, the method is applied to water, chloroform, and benzene solvent systems. The organization of this article is as follows: In Sec. II, after summarizing RBC, the details of the present method are described. The computational results to demonstrate the reliability are shown in Sec. III, followed by the conclusions in Sec. IV.

II. METHOD

A. Repulsive bridge correction

Since details of the integral equation theories of molecular liquids are reported elsewhere,[12–15] let us begin with closure equation in 3D space.

$$h_s(\mathbf{r}) + 1 = \exp\left[-\beta u_s(\mathbf{r}) + h_s(\mathbf{r}) - c_s(\mathbf{r}) + b_s(\mathbf{r})\right], \quad (1)$$

where $h_s(\mathbf{r})$ and $c_s(\mathbf{r})$, respectively, represent the three-dimensional total and direct correlation functions of solvent site s. $u_s(\mathbf{r})$ is solute-solvent interaction potential. β is $1/k_BT$, where k_B and T are Boltzmann constant and temperature, respectively. $b_s(\mathbf{r})$ is bridge function that is usually unknown.

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In RBC formalism, $b_s(\mathbf{r})$ is assumed to be the following equation:

$$\exp\{b_s(\mathbf{r})\} = \prod_{s'\neq s}^{n} \int d\Omega_{s'} \exp\left[-\beta u_{s'}^{\mathrm{R}}(\mathbf{r}_{s'}, \Omega_{s'})\right] \simeq \prod_{s'\neq s}^{n} w_{ss'} * \exp\left[-\beta u_{s'}^{\mathrm{R}}(\mathbf{r}_{s'})\right], \quad (2)$$

where n is the number of interaction sites in the solvent molecule. $\mathbf{r}_s$ and $\mathbf{\Omega}_s$ denote the relative position and orientation of the solvent site s. By the orientational averaging of the entire core repulsion $u_{s'}^{\mathrm{R}}$, the final equation is given using the solvent intramolecular correlation function, $w_{ss'}$. The asterisk in the above equation is a convolution integral. Using Eq. (1) and the OZ-type equation, SFE ($\Delta\mu$) is obtained with thermodynamic perturbation technique,[16,17]

$$\Delta\mu = \Delta\mu^{\mathrm{HNC}} + k_{\mathrm{B}}T \sum_{s}^{n} \rho_s \int d\mathbf{r}_s \{h_s(\mathbf{r}_s) + 1\} \times [\exp\{b_s(\mathbf{r}_s)\} - 1], \quad (3)$$

where

$$\Delta\mu^{\mathrm{HNC}} = k_{\mathrm{B}}T \sum_{s}^{n} \rho_s \int d\mathbf{r}_s \times \left\{\frac{1}{2}h_s^2(\mathbf{r}_s) - c_s(\mathbf{r}_s) - \frac{1}{2}h_s(\mathbf{r}_s)c_s(\mathbf{r}_s)\right\}. \quad (4)$$

This is the original expression of HNC + RBC introduced by Kovalenko *et al.*[10] It is noted that Eq. (3) is reduced to Eq. (4) when $b_s(\mathbf{r})$ is set to zero.

B. Generalization of RBC

RBC is a promising approach to evaluate accurate SFE for an aqueous solution system. As pointed out in the original paper, the approximation is valid for water solvent because the hydrogen-hydrogen correlation is not crucial for the correction. To put it in another way, the correction may not be suitable for complicated-shape solvent molecule. In fact, the treatment does not work satisfactorily for benzene and chloroform solvents as shown below.

Equation (2) indicates that the correction is described as a superposition of repulsive contribution from solute ($u_{s'}^{\mathrm{R}}$) through *all* the other site (s') in the same solvent molecule, namely the indirect repulsive effect is considered using $\omega_{ss'}$. This may be a good approximation for small molecule such as water. But the reliability of this simple orientational averaging through $\omega_{ss'}$ becomes worse as the solvent shape becomes complex. If the size of molecule is sufficiently large, the contributions through other sites should not be uniform and become more complicated. While contributions from neighboring sites must be taken into account, those from further sites should be eliminated.

Here, the term in Eq. (2) is rewritten as follows by introducing a filtering factor $P_{ss'}$:

$$\exp\{b_s(\mathbf{r})\} = \prod_{s'\neq s}^{n} w_{ss'} * \exp\left[-\beta P_{ss'} u_{s'}^{\mathrm{R}}(\mathbf{r}_{s'})\right] \quad \text{and} \quad P_{ss'} \equiv 1. \quad (5)$$

It is convenient and intelligible to represent the factor as square matrix $\mathbf{P}$ with a dimension of n. In the above RBC, all the elements of matrix $\mathbf{P}$ are one. If $\mathbf{P} = \mathbf{E}$ (unit matrix), the right hand side of Eq. (5) is reduced to zero because of $s' \neq s$, corresponding to HNC closure. This means that all the atoms composing the solvent molecule are virtually independent. Hence, $\mathbf{P}$ matrix may be regarded as the bridge between these two limits, i.e., RBC and HNC. Although *all* the atomic pairs in solvent molecule are explicitly taken into account in RBC, it would be reasonable to suppose that the contribution only from bonding sites participates in RBC because repulsive potential is usually a short-ranged function.

$$\mathbf{P} = \mathbf{E} + \mathbf{P}^{\mathrm{CB}}, \quad (6)$$

where $\mathbf{P}^{\mathrm{CB}}$ is defined as follows:

$$P_{ss'}^{\mathrm{CB}} = \begin{cases} 1 & \text{(if there is chemical bond between } s \text{ and } s') \\ 0 & \text{(otherwise).} \end{cases} \quad (7)$$

The matrix element is uniquely defined for any solvent molecule. For example, $\mathbf{P}^{\mathrm{CB}}$ for water and chloroform (united model) solvents are respectively presented by

$$\mathbf{P}^{\mathrm{CB}}(\text{water}) = \begin{array}{c} \\ \mathrm{O} \\ \mathrm{H} \\ \mathrm{H} \end{array} \begin{array}{c} \begin{array}{ccc} \mathrm{O} & \mathrm{H} & \mathrm{H} \end{array} \\ \begin{pmatrix} 0 & 1 & 1 \\ 1 & 0 & 0 \\ 1 & 0 & 0 \end{pmatrix} \end{array}, \quad (8)$$

$$\mathbf{P}^{\mathrm{CB}}(\text{chloroform}) = \begin{array}{c} \\ \mathrm{CH} \\ \mathrm{Cl} \\ \mathrm{Cl} \\ \mathrm{Cl} \end{array} \begin{array}{c} \begin{array}{cccc} \mathrm{CH} & \mathrm{Cl} & \mathrm{Cl} & \mathrm{Cl} \end{array} \\ \begin{pmatrix} 0 & 1 & 1 & 1 \\ 1 & 0 & 0 & 0 \\ 1 & 0 & 0 & 0 \\ 1 & 0 & 0 & 0 \end{pmatrix} \end{array}. \quad (9)$$

The present approach, called the chemical bond-RBC (CB-RBC), unifies RBC and HNC. As shown below, this treatment remarkably improves the evaluation of SFE for a variety of solvent systems including organic solvents.

Let us illustrate the role of $\mathbf{P}$ and $\mathbf{P}^{\mathrm{CB}}$ matrices by taking the Cl site of chloroform molecule as an example. Figure 1 schematically shows the exclusive areas of one Cl site (gray colored) represented by the original RBC (a), CB-RBC (b), and HNC (c) methods. In the original RBC method (a), all sites in the chloroform molecule contribute to the exclusive area because all the elements of $\mathbf{P}$ matrix are 1. As a result, effective exclusive area is much larger than the van der Waals volume (blue region). In sharp contrast, the exclusive area with HNC method (c) consists of only the repulsive core of the Cl site that is clearly insufficient. CB-RBC method (b) corrects this insufficiency by adding CH site contribution throughout $\mathbf{P}^{\mathrm{CB}}$ matrix. The exclusive area with CB-CRB method (b) is comparable with the van der Waals volume. This is the physical background of the present treatment.

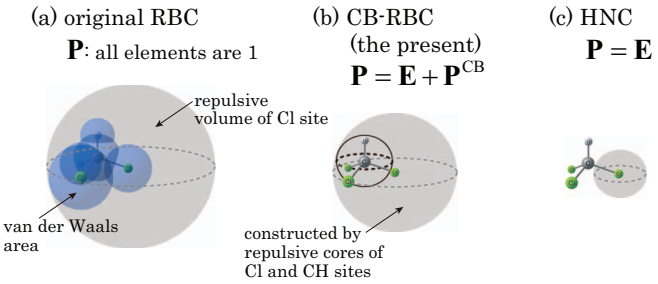

FIG. 1. A schematic picture of repulsive volumes of Cl site in chloroform molecule described by the original RBC (a), CB-RBC (the present, b), and HNC (c) methods.

C. Computational details

In this study, two types of function are employed for u_s^{R}. One is the repulsive term in Lennard-Jones (LJ) potentials (LJ12),

$$\sum_{\alpha}^{\text{solute}} 4\epsilon_{\alpha s}\left(\frac{\sigma_{\alpha s}}{r_{\alpha s}}\right)^{12}, \tag{10}$$

where $r_{\alpha s}$ denotes the distance between site α (solute) and s (solvent). The other is the repulsive part of the Weeks-Chandler-Andersen (WCA) separation of LJ potential,[18]

$$\sum_{\alpha}^{\text{solute}}\left[4\epsilon_{\alpha s}\left\{\left(\frac{\sigma_{\alpha s}}{r_{\alpha s}}\right)^{12}-\left(\frac{\sigma_{\alpha s}}{r_{\alpha s}}\right)^{6}\right\}+\epsilon_{\alpha s}\right] \times \Theta\left(2^{\frac{1}{6}}\sigma_{\alpha s}-r_{\alpha s}\right), \tag{11}$$

where Θ means Heaviside step function.

The temperature is 298.15 K and the densities of aqueous, chloroform, and benzene solutions are set to 1.000 g/cm^3 (0.033426 molecule/Å^3), 1.479 g/cm^3 (0.007460 molecule/Å^3),[19] and 0.877 g/cm^3 (0.006774 molecule/Å^3).[20] LJ parameters of solvent molecules are listed in Table I. The geometries and the LJ parameters of solute molecules are taken from Refs. 21 and 23.

Multi-center molecular OZ (MC-MOZ) method[9] was solved by coupling with HNC closure. In this study, radial 512 (logarithm) and angular 302 (Lebedev) grid points are used to solve MC-MOZ/HNC equation for all calculations. The degree of real spherical harmonics expansions, l, is set to 14. Note that MC-MOZ is more suitable for parallel computation.

TABLE I. Potential parameters of solvent water, chloroform, and benzene.

Molecule	Site	Charge (|e|)	σ (Å)	ϵ (kcal mol^{-1})
Water	O	−0.8340	3.151	0.1520
(TIP3P (Refs. 26 and 27)-like)	H	0.4170	1.000	0.0560
Chloroform[28]	CH	0.4200	3.800	0.0800
	Cl	−0.1400	3.470	0.3000
Benzene[28]	C	−0.1030	3.550	0.0700
	H	0.1030	2.420	0.0300

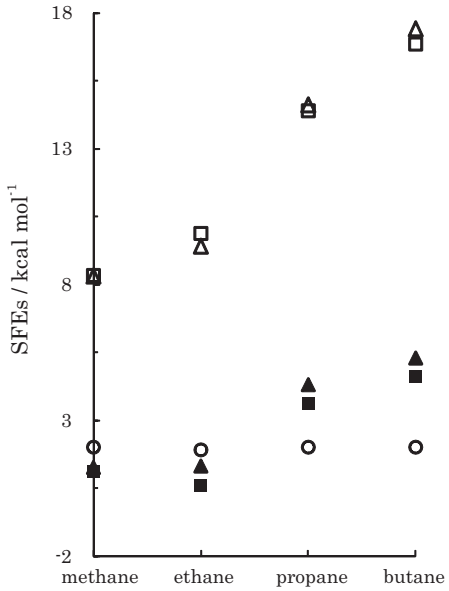

FIG. 2. Hydration free energy of methane, ethane, propane, and butane computed by MC-MOZ method (open and closed triangles), compared with 3D-RISM results (open and closed squares).[10] The open and closed symbols represent $\Delta\mu^{\mathrm{HNC}}$ and $\Delta\mu$, respectively. Open circles denote the corresponding experimental values.

III. RESULTS AND DISCUSSION

A. A series of hydrocarbon

Similar to 3-dimensional reference interaction site model (3D-RISM) theory,[8] MC-MOZ provides a 3D solvation structure. Since RBC has been applied only to 3D-RISM, SFE is evaluated using MC-MOZ to check the applicability of the correction. Figure 2 shows SFEs of a series of hydrocarbon models in SPC/E-like water computed by MC-MOZ (open and closed triangles) compared with 3D-RISM (open and closed squares) taken from Ref. 7. As displayed in the figure, both $\Delta\mu^{\mathrm{HNC}}$ (open symbols) and the corrected $\Delta\mu$ (closed symbols) are virtually identical, indicating that the original RBC is applicable to MC-MOZ.

B. Aqueous solution

Table II lists SFE of 32 solute molecules in aqueous solution and hydration free energies. SFEs computed by HNC, the original RBC, the present method (CB-RBC), and Monte Carlo (MC) simulation[21–23] are shown with their corresponding experimental values.[24] The same data are plotted in Figure 3. The two axis are taken as the calculated and experimental SFEs; if a symbol in this figure is located at the area above the line, SFE is overestimated. When the position of the symbol is lower than the line, SFE is underestimated. HNC (circle) results are obviously distributed in the upper region. Actually, the root mean square deviations (RMSDs) with respect to the experimental values are 11.76 kcal/mol (HNC), 3.97 kcal/mol (RBC, LJ12), 4.34 kcal/mol (CB-RBC, LJ12), and 1.02 kcal/mol (MC). Note that, although the highest accuracy is achieved in the MC simulation, reported data are adjusted using both solvent-accessible surface area (SASA) and some optimized parameters utilizing the experimental SFEs.

TABLE II. Computed SFEs in aqueous solution with HNC, the original RBC, the present CB-RBC, and Monte Carlo methods compared with experiments (unit: kcal/mol).

		RBC		CB-RBC			
Molecule	HNC	LJ12	WCA	LJ12	WCA	Monte Carlo	Exp.
Methanol	1.17	− 4.94	− 3.03	− 4.64	− 2.78	− 4.01	− 5.1
Methylamine	1.23	− 4.58	− 2.82	− 4.30	− 2.59	− 3.30	− 4.6
Acetonitrile	4.07	− 3.96	− 1.15	− 3.55	− 0.82	− 3.83	− 3.9
Dimethylether	7.36	− 0.10	2.14	0.30	2.48	− 1.85	− 1.9
Methanethiol	6.50	− 0.57	1.88	− 0.22	2.17	− 0.72	− 1.2
Chloromethane	6.68	− 0.69	2.00	− 0.32	2.30	− 0.32	− 0.6
Ethane	9.84	3.26	5.19	3.64	5.52	0.83	2.0
Acetamide	− 3.27	− 11.30	− 8.73	− 10.94	− 8.43	− 10.00	− 9.7
Acetic acid	0.07	− 8.30	− 5.57	− 7.91	− 5.25	− 7.40	− 6.7
Acetone	4.99	− 3.69	− 1.01	− 3.25	− 0.64	− 4.45	− 3.8
Methyl acetate	6.17	− 3.37	− 0.45	− 2.89	− 0.04	− 5.17	− 3.3
Benzene	12.31	3.13	5.89	3.65	6.33	− 1.07	− 0.8
Pyridine	8.24	− 1.03	1.85	− 0.54	2.26	− 3.91	− 4.7
Dichloromethane	8.95	− 0.62	3.22	− 0.14	3.59	− 0.49	− 1.4
Fluoromethane	6.30	0.35	2.21	0.67	2.48	− 0.87	− 0.2
Trichloromethane	11.57	0.19	4.98	0.75	5.41	0.14	− 1.1
Ethene	8.67	2.65	4.54	2.99	4.83	0.34	1.3
Cyclohexane	18.84	8.54	11.45	9.14	11.99	0.22	1.2
2-propanol	8.99	0.23	2.86	0.70	3.26	− 5.08	− 4.8
Dimethylamine	7.98	0.44	2.69	0.85	3.04	− 2.61	− 4.3
Dimethyl sulfide	11.48	2.89	5.69	3.36	6.09	− 0.48	− 1.4
Tart-butyl alcohol	11.41	1.77	4.60	2.29	5.05	− 6.00	− 4.5
Trimethylamine	12.72	4.01	6.57	4.51	7.00	− 1.43	− 3.2
Butane	16.31	7.12	9.76	7.65	10.23	0.57	2.1
Propane	13.37	5.45	7.76	5.91	8.16	0.60	2.0
Ethylamine	6.06	− 1.31	0.90	− 0.93	1.22	− 5.19	− 4.5
Ethanol	6.16	− 1.35	0.94	− 0.96	1.28	− 4.93	− 5.0
Pronene	11.55	4.10	6.36	4.53	6.72	− 0.02	1.3
Acetoaldehyde	5.00	− 2.61	− 0.12	− 2.22	0.20	− 3.79	− 3.5
Naphthalene	19.35	7.24	10.94	7.94	11.54	− 1.85	− 2.4
Phenol	11.11	1.05	4.21	1.59	4.67	− 5.01	− 6.6
Tetrahydrofuran	11.15	1.91	4.63	2.42	5.07	− 2.99	− 3.5
RMSD	11.76	3.97	6.21	4.34	6.57	1.02	

As mentioned in the previous reports,[10] HNC considerably overestimates the observations more than 10 kcal/mol, and they are adequately corrected by both RBC and CB-RBC, although these corrected values are still overestimated. It is suggested that a charge polarization of solute molecule is crucial, especially in aqueous media, to accurately evaluate SFEs.

One might notice that SFE by CB-RBC is slightly higher than RBC. This is simply attributed to the treatment in Eq. (3): Because $(h_s + 1) \geq 0$ and $\exp(b_s) - 1 \leq 0$ are satisfied for any solvent site s, the correction (second term in this equation) always negatively contributes to SFE. Because of the nature of **P** matrix, this correction is partially effective in CB-RBC. Namely, the correction in the original RBC is slightly greater in negative than that in the present CB-RBC. The difference is quite small in practice, indicating that the effect of the core repulsion is dominated by the oxygen atom in solvent water. This is consistent with the discussion on the empirical approach of Roux *et al.*[25]

The comparison of SFEs computed with LJ12 and WCA is shown in Table II. Both of them provide similar values but the difference could not be negligibly small: the LJ12 RMSD is 4.34 kcal/mol, whereas the RMSD by WCA is 6.57 kcal/mol. Since there is no clear criterion to select the core repulsive function, it is difficult to judge between them. Anyway, these numerical results show that LJ12 function provides more accurate SFEs than WCA in the case of aqueous solution.

C. Chloroform and benzene solutions

In chloroform solution, the validity of the present method is investigated for 14 solute molecules. Similarly, 12 solute molecules are examined in benzene solution. The numerical results in chloroform solution computed by HNC, the original RBC, the present CB-RBC, and MC (Ref. 23) procedures are listed in Table III. The RMSD of HNC results is 2.81 kcal/mol, which is remarkably smaller than that in aqueous solution. But all SFEs of HNC (circles) somewhat overestimate the corresponding experimental values[24] as shown in Figure 4.

In contrast to the aqueous solution, the original RBC (closed squares) considerably underestimated SFEs (the

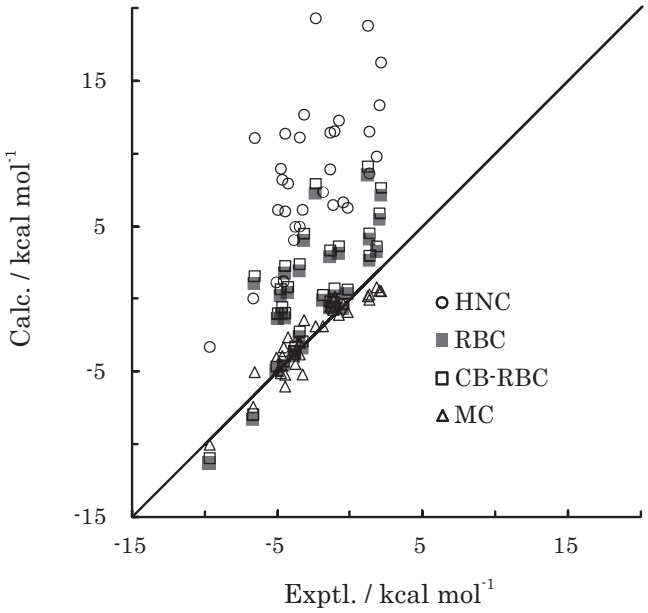

FIG. 3. Comparison between calculated and experimental SFEs. LJ12 was adopted in the original RBC and the present CB-RBC.

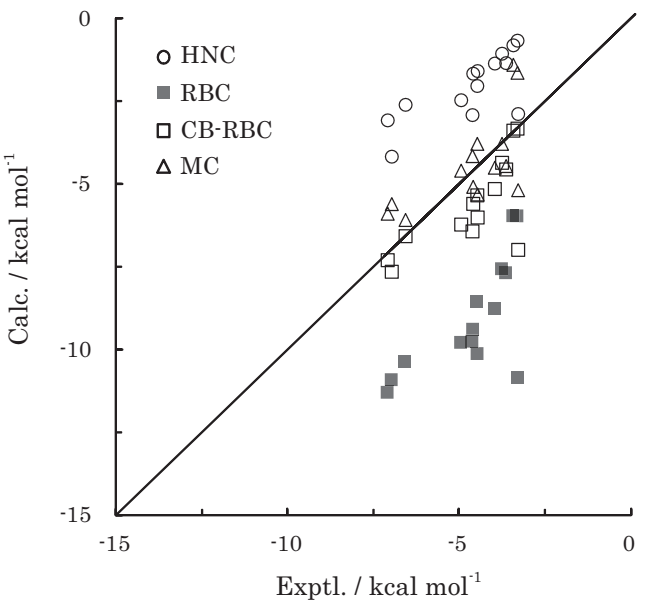

FIG. 4. Comparison between calculated and experimental SFEs. WCA was adopted in the original RBC and the present CB-RBC.

symbols are located at the lower area of the line). The values get worse compared to the HNC ones (RMSD is 4.40 kcal/mol), indicating that the correction dose not work in practice. On the other hand, as expected, the CB-RBC method (open squares) gives very reasonable results (RMSD is 1.07 kcal/mol when WCA was adopted to the repulsive function). Although the corrected value slightly underestimates the experiments, the accuracy of the present approach is comparable to that of MC simulation displayed with open triangles (RMSD is 0.66 kcal/mol). Similarly in the aqueous system, the SFE by MC simulation is modified using the result of a free-energy perturbation with SASA and 3-adjusted parameters. Here, it should be emphasized that the present CB-RBC procedure achieves high accuracy without such a treatment, i.e., simply based on the thermodynamic integration method of SFE. As listed in the table, RMSD is slightly worse (2.34 kcal/mol) when LJ12 was adopted. This is an opposite trend to the aqueous solution.

Finally, the computed SFEs in benzene solution by HNC, the original RBC, and the present CB-RBC are summarized in Table IV. Unfortunately, simulation results could not be found. As seen in Figure 5, the original RBC has a large margin of error similar to the case of chloroform solution. RMSDs of RBC and CB-RBC are 26.25 kcal/mol (WCA) and 1.77 kcal/mol (WCA), respectively. The significant underestimation by RBC may be attributed to the large size of benzene. By increasing the number of sites in solvent, the correction becomes negatively greater. In contrast, the present CB-RBC shows an excellent agreement with the experimental SFEs.[24]

TABLE III. The SFEs in chloroform solution evaluated by HNC, the present, the original, and Monte Carlo methods. The unit is kcal/mol.

		RBC		CB-RBC		Monte	
Molecule	HNC	LJ12	WCA	LJ12	WCA	Carlo	Exp.
Methanol	− 0.65	− 7.75	− 5.96	− 4.37	− 3.31	− 3.32	− 3.32
Methylamine	− 0.79	− 7.63	− 5.96	− 4.35	− 3.37	− 2.85	− 3.44
Acetonitrile	− 2.02	− 10.96	− 8.56	− 6.78	− 5.32	− 4.85	− 4.49
Acetamide	− 4.16	− 13.23	− 10.91	− 9.05	− 7.64	− 6.58	− 6.98
Acetic acid	− 2.90	− 12.18	− 9.75	− 7.90	− 6.41	− 4.90	− 4.63
Acetone	− 2.45	− 12.14	− 9.79	− 7.64	− 6.21	− 5.58	− 4.96
Methyl acetate	− 2.87	− 13.35	− 10.84	− 8.52	− 6.97	− 5.62	− 4.88
Benzene	− 1.65	− 11.73	− 9.39	− 7.00	− 5.58	− 4.76	− 4.61
Pyridine	− 2.59	− 12.83	− 10.38	− 8.06	− 6.56	− 5.39	− 6.58
Cyclohexane	− 1.57	− 12.51	− 10.13	− 7.45	− 6.00	− 5.30	− 4.48
Dimethylamine	− 1.04	− 9.52	− 7.56	− 5.52	− 4.34	− 3.77	− 3.77
Trimethylamine	− 1.34	− 10.92	− 8.76	− 6.44	− 5.13	− 4.49	− 3.98
Acetoaldehyde	− 1.33	− 9.84	− 7.68	− 5.85	− 4.54	− 4.44	− 3.65
Phenol	− 3.06	− 13.89	− 11.30	− 8.88	− 7.28	− 5.88	− 7.10
RMSD	2.81	6.65	4.40	2.34	1.07	0.66	

TABLE IV. The SFEs in benzene solution evaluated by HNC, the present, and the original methods. The unit is kcal/mol.

		RBC		CB-RBC		
Molecule	HNC	LJ12	WCA	LJ12	WCA	Exp.
Methanol	1.35	− 29.44	− 24.33	− 6.65	− 4.27	− 2.58
Methylamine	1.40	− 28.33	− 23.55	− 6.21	− 4.01	− 2.66
Benzene	2.26	− 40.03	− 33.74	− 9.12	− 5.99	− 4.55
Pyridine	1.20	− 41.64	− 35.01	− 10.56	− 7.16	− 5.28
Cyclohexane	3.36	− 41.69	− 35.33	− 9.05	− 5.87	− 4.05
2-propanol	2.13	− 37.68	− 31.58	− 8.69	− 5.67	− 3.48
Dimethylamine	2.08	− 34.03	− 28.59	− 7.44	− 4.84	− 3.01
Trimethylamine	2.62	− 37.43	− 31.59	− 8.16	− 5.29	− 2.80
Ethylamine	1.77	− 33.33	− 27.88	− 7.51	− 4.91	− 2.73
Ethanol	1.81	− 33.57	− 28.03	− 7.64	− 4.96	− 3.42
Phenol	1.08	− 44.00	− 37.01	− 11.47	− 7.85	− 7.12
Water	0.63	− 21.58	− 17.28	− 4.97	− 3.06	− 1.71
RMSD	5.64	32.03	26.25	4.55	1.77	

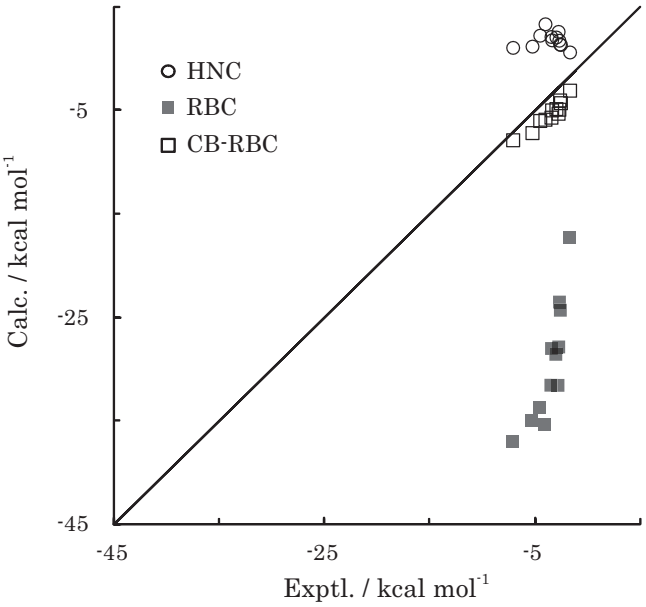

FIG. 5. Comparison between calculated and experimental SFEs. WCA was adopted in the original RBC and the present CB-RBC.

IV. CONCLUSIONS

In the present work, a generalization of RBC is reported to accurately evaluate the solvation free energy based on the integral equation theory for molecular liquids. Utilizing the bonding information in the solvent molecule, an efficient way is proposed to correctly take the repulsive bridge correction into account. SFEs in chloroform and benzene solutions are underestimated by the original RBC.

Aqueous solution (32 solute molecules), chloroform solutions (14 solute molecules), and benzene solutions (12 solute molecules) were examined. In the aqueous solution, SFEs are accurately computed using the original RBC and the present CB-RBC within 4.5 kcal/mol of RMSD from the experiments. In order to improve the agreement, the effect of charge polarization of solute molecule is necessary, which is not dealt with in the present study.

In chloroform and benzene solutions, however, the original RBC severely underestimates the SFEs. On the other hand, the present CB-RBC achieves an excellent agreement with the experimental values (the RMSDs are less than 2 kcal/mol). These results clearly indicate the validity of the present procedure for various solvents.

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